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Risk Factors of Primary Infertility in Gaza: Case Control Study

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Risk Factors of Primary Infertility in Gaza: Case Control Study

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Dedication

This thesis is proudly dedicated to

My respectful father, my nurturing mother and

My dearest sisters and brothers.

Thanks for all the love, prayers and your endless faith in me.

If it wasn't for you, it wouldn't have been ……

I would also like to dedicate this work to my inspiring supervisor

Professor Dr. Yehia Abed …. You are and will always be

the light that shines our path…

Declaration

I certify that this thesis submitted to the degree of master is the result of my own research, except where otherwise acknowledged, and that this thesis or any of its parts has not been submitted for higher degree to any other university or institution.

Signature:

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Date: / /

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Signature:

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Abstract

Introduction & main objective:

Many couples around the world are struggling the gloomy feeling of childlessness. Besides the lack of parenthood potentials, they may suffer from relative social and societal exclusion. This brings the importance of identifying main risk factors associated with primary infertility in Gaza Strip and ultimately searching for steps that would enhance management plans or even prevent the occurrence of such condition for the sake of improving couples' health and their quality of life.

Methodology:

This study is an observational analytic case control study, comprised 320 total sample population. Cases (160) were selected based on being married, sexually active, non- contracepting women aged (19-49) with no previous pregnancies, while controls (160) were fertile women matched with residency of cases. Data was collected using an interviewed questionnaire through two trained data collectors and it was analyzed using various descriptive and inferential methods; central tendency, crosstabulation and chi square, independent t-test, correlation and binary logistic regression.

Results:

The distribution of study population was 20.6% North Gaza, 34.4% Gaza, 12.5% Middle area, 20% Khan-Younis and 12.5% Rafah. Results showed that females' marital age beyond 29 years held a prominent risk for infertility (OR:8.3,95%CI,2.8-24.3), while 10yrs age difference between couples was 2 times risky ($p=0.02$). Living in extended families after marriage, being refugee and men born as the 7^{th} or more sibling also projected the same risk (OR:1.9,1.6,2.3 respectively). Also, the type of females' work field, pattern of work shifts and stress perception held significant association. Moreover, females and males who used to drink from rooming tankers before marriage ($p<0.001$ for both) and couples using septic porous sewer tanks ($p=0.02$) had the same risk. Other environmental factors were lack of practicing safety measures while using pesticides, the frequency of using them, heavy physical labour in females and exposure to excessive heat, noise, dust, or gases in males (OR:11.9,3.6,3.6,1.6 respectively). Also, infertile husbands who used to live in a partially demolished house or deal with after-war remnants or had their nearby source of drinking water been bombed, were significantly more than their counterparts ($p=0.03,0.006,0.033$ respectively).

Age of menarche below 14 (OR:1.8) and menstrual irregularities (OR:5.7) were among the risk factors detected. Additionally, infertile females suffering from Poly cystic Ovaries (PCOs), Oligomenorrhea, Hyperprolactinemia, Hirsutism or uterine fibroids were at more risk (OR:9.4,9.3,4.6,9.6 respectively). The more the duration of untreated PCOs, the more the likelihood of infertility ($p<0.001$), while using oral combined contraceptives seemed to have protective effect, although continuous use of non-steroidal anti-inflammatory drugs held significant association (OR:0.3,7.9). The main medical exposures among men were the presence of varicocele ($p<0.001$) and the frequency of genitourinary infection more than 5 times in 2 years duration ($p=0.001$). Family history of infertility in both males and females, subfertility and varicocele among males also had positive association.

Lifestyle variables showed that the duration and frequency of tobacco smoking among men and passive smoking among females are risky ($p=0.007$). Fertile couples seemed to consume more vegetables and fruits in terms of servings/day ($p=0.004$ females, $p=0.01$ males) and frequency/week ($p=0.001$ both). Also, having sugar, chips, fries, soda and canned juice regularly and spending longer periods of time sedentarily per day ($t=3.79$, $p<0.001$) had significant association.

Conclusion and recommendations:

This study succeeded to identify part of the risk factors associated with infertility in Gaza Strip including those related to demographic, socio-economic, environmental, medical factors and different lifestyle variables. Accordingly, it is concluded that more efforts are needed to improve water and sanitation quality control, develop occupational health, enhance infertility diagnosis and management and its inclusion in reproductive health care agenda and enhancing various lifestyle practices of population in Gaza Strip.

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Acronyms and Abbreviations

ART	Assistive Reproductive Technology
BMI	Body Mass Index
CDC	Centers of Disease Control and Prevention
COC	Combined Oral Contraceptives
DHS	Demographic and Health Survey
FSH	Follicular Stimulating Hormone
GDP	Gross Domestic Product
GnRH	Gonadotropin Releasing Hormone
GS	Gaza Strip
ICMART	International Committee for Monitoring Assisted Reproductive Technology
ICPD	International conference on Population and Development
IPAQ	International Physical Activity Questionnaire
IVF	In Vitro Fertilization
LH	Luteinizing Hormone
MBS	Metabolic Syndrome
MCH	Maternal and Child Health
MoH	Ministry of Health
NGOs	Non-Governmental Organizations
NSAID	Non-Steroidal Anti-Inflammatory Drugs
PCBS	Palestinian Central Bureau of Statistics
PCC	Preconception Care
PCOs	Polycystic Ovary Syndrome
PCR	Polymerase Chain Reaction
PID	Pelvic Inflammatory Disease
PHC	Primary Health Care
PSS	Perceived Stress Scale
UNFPA	United Nations Funds for Population Activities
UNRWA	United Nations Relief and Works Agency for Palestine Refugees in the near east
WB	West Bank
WHO	World Health Organization

Chapter One
Introduction

1.1 Background

Reproductive and maternal health is a health issue that has a global priority and is listed in the development agenda of almost all nations (UN, 2016). In 1994, the United Nation conducted an International Conference on Population and Development (ICPD) inviting envoys from 179 countries with variety of perspectives on reproductive health, gender equality and sustainable development (UNFPA, 2014). Since then, a global assent was adopted on putting individual free choice, including one's right to build a family, as one of the main components of nation's development and prosperity, as its wide range benefits had been widely recognized. After 20 years, the United Nations Funds for Population Activities (UNFPA) extended the implementation of key principles of ICPD and published a report that convoys with contemporary demographic, cultural and social transition and transformation (UNFPA, 2014). This finally lead to defining reproductive health as a "state of complete physical, mental and social well-being (not merely the absence of disease and infirmity) in all matters relating to the reproductive system and its functions and processes" (IAWG, 2018).

Conception is considered a complex biological and physiological process that is usually associated with interrelated, and at the same time, multidimensional factors. However, failure to conceive is considered one of the most distressful reproductive health conditions that is common globally, but with higher rates in the developing countries. Despite the fact that both men and women have equal opportunity to be the cause of being infertile, in Eastern Mediterranean countries all the blame and responsibility is commonly encountered on the females (Abushahla, 2013). It is well noted that about one third of the cases are linked to paternal medical causes, while female causes are accounted for the other third of the cases. Around 15-20% of the problem has idiopathic etiologies (Ashour, 2014). On the other hand, the World Health Organization (WHO) recognizes infertility as a public health problem in terms of physical and mental health for both partners although it is not recognized till couples determine to endure a child. It differs than other public health problems. The problem does not float on the surface till deciding to build a family. Accordingly, the WHO defined clinical primary infertility as a condition that refers to

"inability to conceive despite cohabitation and exposure to risk of pregnancy for a period of 12 months or more in a sexually active non-contracepting, and non-lactating women 15 to 49 year old" (Parvez, Sugunan, & Saha, 2016). While secondary infertility is considered when there is "a failure to conceive following a previous pregnancy" (Rutstein & Shah, 2004).

Reproductive health is a well-known area in which tremendous global and national efforts are excreted. Infertility in particular could affect demographic and social determinants of a nation through various aspects. Providing that it is attributed to many factors and occur in different rates across different regions, many studies suggested that multiple environmental, social and demographic factors play an important role in aggravating its incidence. However, many factors including lifestyle and nutrition, epidemic infection, sexually transmitted diseases and prolonged exposure to stress and pollutants could be problematic mainly in developing countries (Mascarenhas, Flaxman, Boerma, Vanderpoel, & Stevens, 2012).

1.2 Problem statement

Failure to conceive and having a child is a misfortune for any united couples. This mainly manifests clearly in developing countries, where religious, interpersonal and social prospects are highly appreciated. In Mediterranean countries, childless couples may be excluded socially and exempted from many family functions and events. Moreover, relationship between couples themselves could be risked in the context of blaming and dishonoring (Rutstein & Shah, 2004). In Palestine the condition is much similar to other Mediterranean countries where most of the blame and responsibility is held upon the females. Eventually, this suffering may lead to further social, psychological and economic implications which in turn adversely affect fertility status, as if being trapped in a vicious circle (Abushahla, 2013).

The condition in Palestine is not clear as there is insufficient updated statistical data about the prevalence of infertility. Although the Palestinian Central Bureau of Statistics (PCBS) reported decline in fertility rate during 2011-2013 to 4.1 births compared to about 5.9 births in 1999, there are barely documented reports or published scientific and demographic research papers highlighting associated medical and sociodemographic risk factors attributing to infertility (PCBS, 2014). The latest survey that included data about rate of infertility in Palestine was conducted in 2010 through the Palestine Family Survey.

The survey concluded that the rate of infertility among Palestinian women in the reproductive age was 8.4% and the rate of primary infertility among the same age group was 4.8% (4.5% in the West Bank and 5.2% in GS) (PCBS, 2011). Neither the current situation is clear, nor the risk factors associated with such condition is ever comprehensively studied. So, being an important public health area to be scrutinized and for the information gap in this specific subject, it is worth to study associated risk factors and socio-demographic determinants contributing to primary infertility in Palestine.

1.3 Justification

Infertility is a global public health problem that has been gaining the focus of attention of many governments and researchers. According to WHO, there is one from every four couples in the developing countries suffering from infertility (WHO, 2014[a]). In spite of the fact that infertility is more common in developing countries, its incidence differs from one region to the other. Regardless to its cause, it affects different cultures and various communities, accompanied with numerous causes and factors that are usually overlapping. This is more apparent in the Middle East region, where the heterogenic combination of cultural and social determinants is prevailing, as well as the willingness of societies to be directed towards modernizing their lifestyle, but with keeping the risks and hazards of such transition accompanying their life pattern (Serour, 2008). Although there are known risk factors that are associated with infertility, the context of each country plays an important role in determining the main causes associated with such public health issue. These factors could be smoking, obesity, lack of exercise, and other lifestyle variables, which are confirmed to have detrimental effect on fertility status (Abusief, Rossi, & Missmer, 2016). Accordingly, this study will try to highlight this area through identifying the prevailing risk factors present in Palestine and will determine their existence and association with primary infertility among Palestinian couples.

Along with determining healthy life style patterns, people have the right to receive a well-integrated reproductive health care and should live in a balanced and healthy environment where risks are explored and eventually controlled and with no associated consequences and implications. Although we know more about the effect of social, environmental and demographical factors on certain diseases, we do not have enough knowledge about the implications of these variables on infertility. Accordingly, the results of this study could be passed to all relevant health care providers, mainly the first line managers and health practitioners, to enrich their knowledge regarding the risky groups and the possible ways to

early detect and properly manage such condition. Additionally, policy makers shall be invited to propose a constructive dialogue in order to develop suitable preventive measures and intervention programmes and also to prepare for a health messages to be disseminated and conveyed to all concerned local community members through well-developed health education programmes and campaigns. As this study will be the first to be done in Palestine, through which it will explore the main risk factors of primary infertility among married couples, it could be used for further in-depth research in the future.

1.4 Study objectives

General objective

To identify main risk factors associated with primary infertility among married couples in Gaza Governorates. This study is trying to propose recommendations to health care providers, health managers and policy makers to identify risky groups and risk factors associated with primary infertility as well as helping in implementing prevention methods and intervention programmes that may alleviate the burden of this public health problem and substantially improve the overall quality of Palestinian couples' life.

Specific objectives

1- To identify main medical causes of primary infertility among couples seeking treatment at fertilization centers in Gaza Governorates.

2- To verify differences within various socio-demographic and socio-economic characteristics variables in reference to infertility.

3- To explore the impact of existing or pre-existing environmental conditions, as agricultural pesticides, various living conditions and war related exposures, and assess their relation to fertility status.

4- To examine the relationship between different lifestyle practices, as smoking, diet and physical activity, with the fertility status of couples.

5- To determine the effect of different daily physical activities patterns on infertility.

6- To propose recommendations that might participate in developing prevention and control methods and intervention programmes directed towards main risk factors of primary infertility among Palestinian citizens.

1.5 Research questions

1- What are the main medical causes of infertility among couples visiting In Vitro Fertilization (IVF) centers seeking advice and management?
2- What is the relationship between certain chronic diseases and infertility?
3- How much would gynecological problems affect the fertility condition among couples?
4- Is the consumption of certain medications related to the infertility status of couples?
5- What are the social determinants prevailing among infertile couples?
6- To what extent dose the consanguineous marriage affect fertility?
7- Dose the economic status of the couples as well as their original families affect their fertility status?
8- Will early or late marriage have a significant impact on the fertility status of couples?
9- Is there an association between geographical residency and primary infertility?
10- Is there an association between education level of couples and primary infertility?
11- Have drinking water sources and type of sanitation any relationship with infertility?
12- Is there an association between various patterns of physical activities practiced regularly and fertility status of couples?
13- What is the impact of certain dietary habits on the fertility status of couples?
14- Will tobacco smoking, whether cigarettes or water pipe smoking, have a significant impact on the fertility status of couples?
15- Dose work environment as well as work attributes be associated with primary infertility?
16- Will existing or pre-existing environmental conditions, like stress, war and exposure to pesticides affect fertility?

1.6 Context of the study

1.6.1 Demographic characteristics of Gaza Strip:

About 1.9 million Palestinians are locked in a narrow geographical piece of land since for around 12 years. This piece of land, which is known as Gaza Strip (GS), is located at the west southern edge of Palestine along the Mediterranean Sea just northeast to the Sinai Peninsula. It is formed of five governorates, North Gaza, Gaza, Dair Al-Balah, Khan-Yunis and Rafah, from north to south respectively **(Annex 1)**. Although GS forms a total

land area of 365 square kilometers, it is considered as being one of the most densely populated areas in the globe where, according to the PCBS, for each one square kilometer area, there are about 5324 individual Palestinians living (PCBS, 2018[d]). Even nationally there is remarkable difference between West Bank's (WB) and GS's population density which is well apparent and represented in many indicators. According to the latest national census, average housing density (average number of persons in one room) in GS is more than that in WB by about 23 percent. The highest results were recorded in Rafah governorate where the average housing density is 1.7. The results also revealed that households living in housing units with three persons or more per room is 2.5 times more in GS than in the WB (PCBS, 2018[d]). This is more obvious among the eight refugees' camps distributed along the five governorates where almost 600,000 registered refugees, representing about 32% of the total population living in GS, accommodate these camps (UNRWA, 2018).

GS's total land area is relatively small comparative to the WB. Nevertheless, almost 40% of the total population live in GS (PCBS, 2018[b]). The overcrowded living situation and the challenging sociocultural and economic circumstances that GS has been going through, did not hinder the efforts of female population to grow and develop in many perspectives. Looking at the demographic distribution of males and females (1,008,632 males and 981,338 females), we can recognize that females in Palestine society forms almost half the population **(Annex 2)**. Nationally, there are 103.5 males for every 100 females where the ratio is almost the same in both WB (1.039) and GS (1.028). Providing that, and since the past ten years, illiteracy rates among women have declined to reach 5% while men achieved only 1.7% rate, although the engagement of female in the secondary stage of education (91%) is higher than male enrollment (71%) (PCBS, 2018[c]). However, the participation of women in labour force (21%) is still low and the unemployment rate (51%) still shows high figures. It is also realized that 64% of women above the age of 18 are married, while almost quarter never married (PCBS, 2019[a]).

The relative increase in women education and employment, although still less than recommended, is one of the main causes of decrease in fertility rate that Palestine is witnessing overtime. In the context of GS, population under the age of 15 represent almost 39 percent of the total population while the working age group aged 15-64 forms almost half the total. During the past ten years the population under the age of 15 decreased significantly comparing to the increase in the working age group that increased

remarkably. Accordingly, it is concluded that there is ongoing decrease in fertility rate which resulted in decrease in the group of young persons in relation to the working age group (PCBS, 2018[d]).

1.6.2 Health care services:

The health care system in Palestine is considered a complex system being served through four providers, Ministry of Health (MoH), United Nations Relief and Works Agency for Palestine Refugees in the Near East (UNRWA), non-governmental organizations (often as a gap fillers) and private for-profit service providers. The MoH is the main provider and is responsible of all health services provided through its governmental institutions and by all other aforementioned providers. MoH provides primary, secondary and tertiary health services and also purchases unavailable tertiary services from other local facilities or from outside GS through referral abroad system (MoH, 2017). In order to maintain a systematic monitoring and evaluation system that guarantee adequate sustainability and promote development of the health system in Palestine, MoH continuously measures its performance through various health indicators. These health indicators are measured on regular intervals in order to provide sufficient information on the overall performance of health sector including effectiveness, efficiency, appropriateness and impact of services provided (Irene & Peter, 2013). According to the latest records, life expectancy among Palestinian population is 73.8 which is higher among females (75.4) than males (72.3), with population natural increase rate of 2.7%. Crude birth rate in Palestine per 1000 population is 29, in which GS reported 31.1 comparing to 27.6 per 1000 population in WB (PCBS, 2018[d]).

Twelve years is the duration through which the health sector is being drained and exhausted due the Israeli blockade imposed on GS. Since the unilateral Israeli's drop-out and the dismantling of its military facilities in GS and after HAMAS won the majority in the Palestinian Legislative Council election followed by their forced control over all military and governmental institution in 2006, Occupation Israeli Forces imposed a tight restriction and full control on the movement of people and goods from and to GS (Piper, 2017). Moreover, repeated hostilities during the past nine years also caused a disastrous humanitarian crisis that has been inflating by time putting the region on the edge of explosion. Regarding all the fore mentioned adversities, health services was, among all, the

most affected and the most damaged. It has been imposed with additional remarkable strains, including lacking adequate physical infrastructure and staff development opportunities on the already compromised sector (WHO, 2016[b]). This in turn affected the health component of people's quality of life and constrained the need of people to receive effective and fully comprehensive health services. Among the health condition that may cause long term consequences and that has been neglected due to limited access to health services is Sexually Transmitted Diseases, mainly chlamydial infection. Moreover, the premature postoperative discharge is also associated with high rates of postoperative adhesions and complications. These are examples, along with other examples, that result from deteriorated health system and causes long term effect as primary infertility and many other chronic health issues.

Since March 2018 and in the context of Great March of Return demonstrations, the health system, which is already overloaded and weak, have faced another challenge. The operation of all essential health care services has been functioning in a low performance manner due to the continuous electricity crisis that faces GS since about 12 years of blockade and siege. To compensate, hospitals have been using rationalizing techniques through delaying the process of sterilization, cleaning, and some diagnostic services. The problem rises more when there are lifesaving interventions and is associated with episodes of electricity supply interruption and further threatening the health of the population, which is already at risk. Till the time of preparing this proposal, the Health Cluster of WHO reported 277 people killed and 31,214 injured in the Great March of Return demonstrations. If the situation continued on the same rhythm, it is projected to have about 40,000 people, during 2019, who will be in need for multiple health care services including trauma care, extensive surgeries and rehabilitation services. Lack of capacity in hospitals and difficulties facing interventions due to electricity and fuel shortage in addition to the massive influx of traumatic injuries that exceed the hospitals' capacities caused most elective surgeries to be postponed, which is accompanied with early hospital discharge with more possibilities of postoperative complications (WHO, 2019). Adding to that, the enormous psychological impact on at least 52,098 people, half of which (26,049) are children in need of Mental Health and Psychosocial Support services. Women and girls were also targeted, forming two killed and about 1,800 injured. From all women injured, 68% were affected by the gas thrown through the Israeli forces and 10% were shot by live fire (OCHA, 2018[a]). The implications of such violence accompanied with lack of medical

and psychological support may not be apparent till several years. Exposure to stress, chemicals and noncomprehensive medical and surgical interventions all are considered associated factors to long term medical and pathological consequences including the fertility status of exposed population.

1.6.3 Maternal and reproductive health:

In 1994, the MoH first took the responsibility of health system in Palestine and, among other important health system components, adopted the implementation of primary health care (PHC) principles. Since then, the MoH has been providing tremendous efforts to establish and develop PHC services in Palestine to meet people's need and to provide optimal health services. To provide such services, the MoH owns and operates 743 PHC centers distributed throughout Palestine (160 in GS), from which 62.7% are governmental and 37.3% provide PHC services through UNRWA, Non-Governmental Organizations (NGOs) and military medical services. Provision of services through these health centers differs and comprise variety of levels depending on the size and area of population served. Accordingly, health centers are classified into four levels in which each should include for the least, preventive health services for the mother and child (MoH, 2017). However, PHC clinics play an important role in providing significant services related to maternal and reproductive health to the Palestinian population. One of the most important programmes included to Maternal and Child Health (MCH) care as a part of protection and promotion of mothers' and children's health is the preconception care (PCC). The programme was introduced in 2009 in all UNRWA clinics as a domestic violence screening programme, then in 2011 it was fully integrated within the PHC system in order to detect and manage any health deviation before initiation of pregnancy. PCC also plays an important role in early detection of causes of primary infertility through comprehensive medical examination of women attending PHC clinics, such as hypothyroidism, hirsutism, Polycystic Ovary Syndrome (PCOs) and Sexually Transmitted Diseases (UNRWA, 2017).

The right to health is a worldwide demand and requires countries to sustain particular investment in maternal and reproductive health. It is not only considered a crucial part of general health and a central feature of human development, but also have social and economic imperatives on human energy and individuals' creativity which are, in turn, considered the driving forces for development. Reproductive health must not be confined

to lists of problems and diseases and implementing programs. Reproductive health should go beyond that and to be understood in the context of fulfilling the opportunity of having the desired child. This further contributes enormously to the social and psychological stability of the society and so, to further safe and healthy reproduction condition, as if it is a vicious circle. The demand for such services is also controlled by several factors including fulfilling people's expectations. In GS context, there is recognizable difference in demand for health services between MoH PHC centers and UNRWA clinics. This is due to the critical conditions the governmental health services is going through and that is well apparent in the form of frequent stock rupture of medical stores, lack of motivation of staff due to chronic underpayment, deterioration of physical infrastructure of health facilities and lake of staff development opportunities. In 2017, the antenatal care coverage among Palestinian population in MoH PHC clinics was 43.6%, while the percentage of coverage among registered refugees attending UNRWA clinics in GS and WB reached about 89%. In the same context, average number of antenatal visits was 4.5 and 6 respectively (MoH, 2017).

People suffering from infertility in GS usually attend in-vitro specialized centers seeking medical advice in addition to private clinics of specialized physicians. In GS, the total licensed fertility centers are nine including one hospital for Dr. Tharwat El Helow. All centers perform assisted reproductive techniques and provide variety of maternal health services regarding other gynecological and obstetric health issues. Although eight centers are located in Gaza Governorate and only one in Rafah, people attending centers come from all five governorates to seek medical advice and treatment.

1.6.4 Socioeconomic situation:

The Socioeconomic situation in Palestine, mainly in GS, has been going to a downward slope for years. The ongoing restriction and siege imposed by Israeli Forces on the strip and the impact of three rounds of hostilities which the region have witnessed, all contributed to stifling Gaza's economy and reduced any chance for future development. According to World Bank statistics, the Gross Domestic Product (GDP) growth rate has been waving up and down from 2004 till 2012, with lowest growth rate of -8.6% and the highest of 20.9%. Currently, the Gaza's per capita GDP in the first quarter of 2018 decreased 9% than 2017 (Worldbank, 2018).The instability and unpredictability of the

economic situation, which is due to periodic hostilities, unplanned pooling of external aids and unstable political context, all exhausted the internal indicators for a nation to develop (UNDP, 2015).

The main results of Labour Force Survey revealed that there is national wide gap between females and males in the labour force participation rate. Seven out of ten male participate in the labour force compared to 2 out of ten females. Moreover, the unemployment rate among Palestinians is 30.8% in which in GS the rate exceeded 51 percent with even high figures for women (78%), which is the highest rate ever recorded (PCBS, 2019[a]). Furthermore, in GS there are around 22,000 employees recruited by Hamas authorities who receive almost 40% of their basic salaries on irregular intervals since ages (OCHA, 2018[b]), while only 30% of youth aged 15-29 were active in the labour market (PCBS, 2018[e]).

Poverty is considered one of the main social determinants of health. Even in the most developed countries, people who are less well-off have less life expectancy than rich people and the poorest people have the worst health around the globe. Poor socioeconomic status affect health in many perspectives but not people down the social ladder are those who are only affected but also social position and gradient among people have tremendous negative health effects (Brunner & Marmot, 2003). Poor people are those who live on less than 4.6 US dollars per day, the minimum to cover essential household needs, while deep poverty is referred to people who live on less than 3.6 US dollars per day. Household Expenditure and Consumption Survey revealed that poverty rate in the GS increased to be 53% in 2017 comparing to the rate of 38.8% in 2011 (PCBS, 2018[a]). About two third of them are considered as living in deep poverty with the minimum to cover only shelter, cloths and food needs (OCHA, 2018[b]). This means that one from every two in GS are poor with rates that would have reached 60% and the deep poverty up to about 40% if the social assistance and transfers are not included.

1.7 Operational definitions

1.7.1 Clinical infertility:

"It is a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse" (Zegers-Hochschild et al., 2009).

1.7.2 Primary infertility:

"When a woman is unable to ever bear a child, either due to the inability to become pregnant or the inability to carry a pregnancy to a live birth she would be classified as having primary infertility. Thus, women whose pregnancy spontaneously miscarries, or whose pregnancy results in a still born child, without ever having had a live birth would present with primarily infertility" (WHO, 2016[a]).

1.7.3 Secondary infertility:

"The inability to conceive or inability to bear a child and carry a pregnancy to a live birth following a previous pregnancy or previous ability to do so" (WHO, 2016[a]).

1.7.4 Reproductive health:

"A state of complete physical, mental and social well-being (not merely the absence of disease and infirmity) in all matters relating to the reproductive system and its functions and processes" (IAWG, 2018).

Chapter Two
Literature Review

2.1 Conceptual framework

The conceptual framework is a diagram that explains the content of the study. It could be illustrated in the form of a diagram or narratively. The main goal is to show the different variables that had been recognized during the literature review process in a self-explanatory way and describing simply the relations between different concepts, assumptions or domains (Miles & Huberman, 1994).

In this study, the researcher studied the risk factors attributed to primary infertility in Gaza governorates in a case control design. As shown in **Figure (2.1)**, the researcher demonstrates the dependent variable as primary infertility and the independent variable as the risk factors causing infertility which is divided into five main domains, Socio-demographic, Socio-economic, Environmental factors, Lifestyle and Medical causes.

2.1.1 Socio-Demographic factors:

This domain describes the social and demographic characteristics of united couples. The social characteristics are those related to the rank of each participant in the original family, birth order and size and type of households. On the other hand, the demographic variables included the age of participants, marital age of females, age gap between couples and place and type of residency of couples before and after marriage.

2.1.2 Socio-Economic factors:

Socioeconomic factors used in this study describe all sources of monthly income of couples and monthly income in the original family as literature review revealed that economic status of couples before and after marriage can affect fertility health in different perspectives (Logan, Gu, Li, Xiao, & Anazodo, 2019; Wang & Geng, 2019; Currie & Schwandt, 2014). The factors also describe, education level and work characteristics along with consanguineous marriage attained among the surveyed population.

2.1.3 Environmental factors:

Several studies revealed that environmental factors can adversely affect fertility (Oliva, Spira, & Multigner, 2001). Among the environmental factors that may affect infertility are the exposure to pesticides, exposure to war residuals or remnants, the water and sanitation condition and tenure and type of the household settings. Simply through health education, many of these environmental factors could be avoided, prevented and even managed.

2.1.4 Lifestyle:

In this section, the researcher is interested in exploring the effect of smoking and bad dietary habits on the fertility health of couples. A special concern is provided to the effect of different types of physical activities on infertility. The study included an international instrument that examine the daily physical activities assumed by both populations and eventually classify each into low, moderate and high categories based on the metabolic rate exerted through different activities **(Annex 5)**. Then, the results of each are subsequently related with the fertility condition of the selected sample.

2.1.5 Medical causes:

Medical causes related to infertility are numerous and could be related to either women or men (Ashour, 2014). Sometimes pathological conditions may exist in both but in some circumstances, causes cannot be determined which is called idiopathic causes. Idiopathic is a term used when causes could not be ruled out to the given condition (Nieschlag, 2011).

2.1.5.1 Male factors

About one third of the cases are linked to paternal medical causes while female causes are accounted for the other third of the cases (Ashour, 2014). Male factors could be related to varicoceles, semen abnormalities (including ductal obstruction) or immunological causes. These causes could be classified to pre-testicular causes, testicular and post-testicular causes.

2.1.5.2 Female factors

Female factors included in this study are divided into ovarian factors that comprise polycystic ovaries, tubal factors including obstruction and infection, uterine factors including fibroids and endometriosis and endocrinal factors along with stress related infertility (Cunningham et al., 2001).

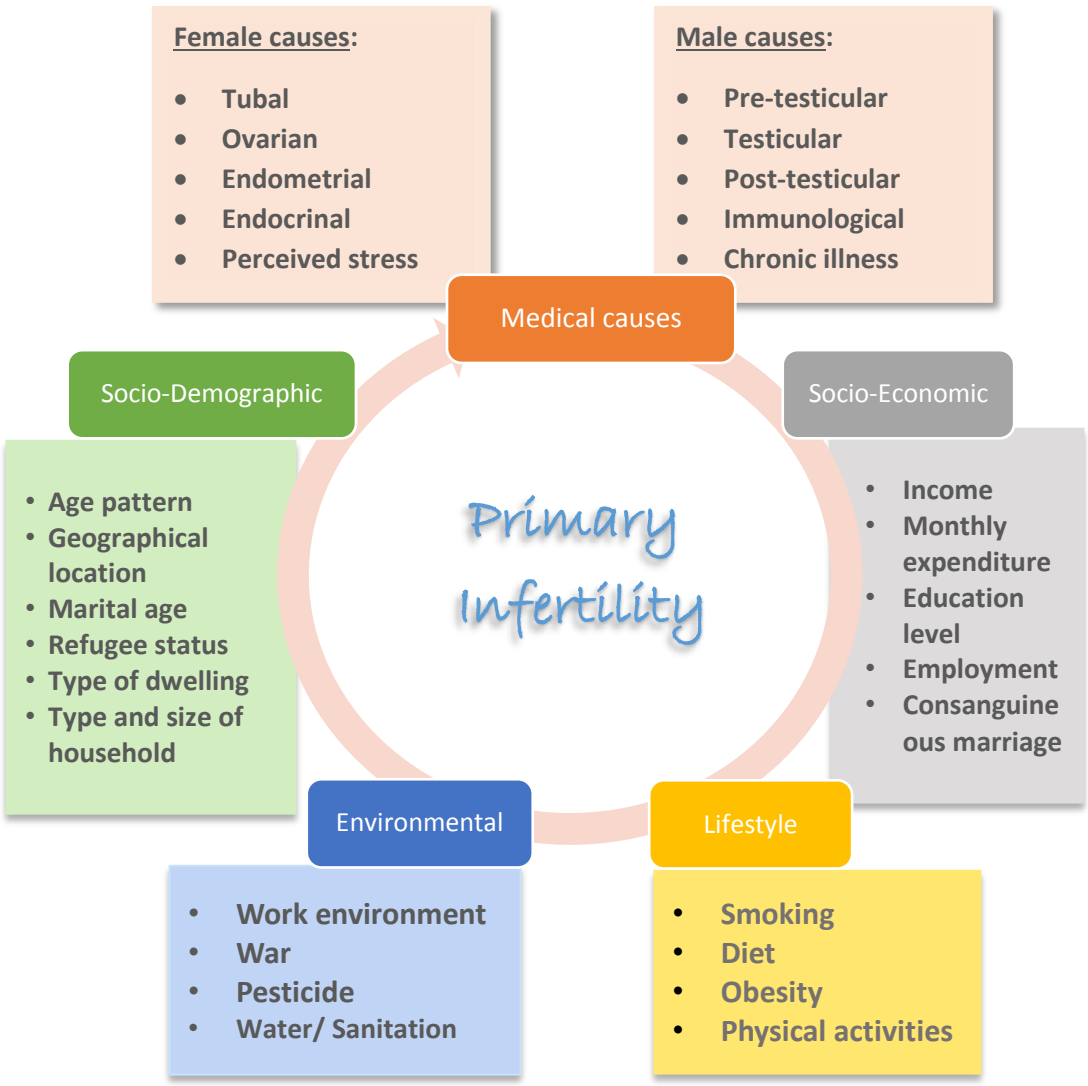


Figure (2.1): Conceptual Framework for risk factors of primary infertility

2.2 Literature review

2.2.1 Definition and terminology:

According to WHO, there are 60 to 80 million couples suffering from infertility and represent 8-12% of total couples worldwide (Parvez, Sugunan, & Saha, 2016). The lack of universal standardized definition of infertility and agreed upon monitoring process caused unharmonized data to be used for regional and global prevalence estimation. The 60-80 prevalence value, that is often quoted, has been used in accordance with 2 years interval of infertility and represented only those who attended medical care. This proportion represents only half the suffering population and even less in developing countries where seeking medical advice is governed by various economic, psychological and religious considerations (Van, 2012).

Pregnancy or sometimes called conception is a natural condition through which a fetus develops and grows to form a live birth. While, fertility is a term that is usually used to show the quantity of off spring rather than the physiological ability to reproduce, "the inability of a sexually active, non-contracepting couple to achieve pregnancy within one year" is known as infertility (WHO, 2016[a]). This definition is the clinical term which is used by the WHO since 2009 when the International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the WHO worked on developing a glossary that comprise all definitions to be used in Assistive Reproductive Technology (ART) and its related research (Vanderpoel et al., 2009). These definitions are made to be disseminated and used internationally in order to harmonize the process of data collection and so promoting comparability and benchmarking of studies and procedures among different areas in the globe. The National Institution of Health defines infertility as "the failure to conceive after regular unprotected sexual intercourse after two years in the absence of a known reproductive pathology". Epidemiologists define infertility for the purpose of monitoring and surveillance as all "women of reproductive age (15–49 years) at risk of becoming pregnant (not pregnant, sexually active, not using contraception and not lactating) who report trying unsuccessfully for a pregnancy for two years or more". On the other hand, Demographic and Health survey (DHS) reports used in comparative measures define infertility as an "inability of those of reproductive age (15-49 years) to become or remain pregnant within five years of exposure to pregnancy". A one year period exposure is often used in clinical studies while demographic studies usually rely on five years period

interval (Rutstein & Shah, 2004). Being an area rich in information and data to be analyzed and studied, infertility caught the attention of many researchers since many years ago. Accordingly, the WHO planned and convened an international meeting to discuss various aspects of ART. The results were first published in 2006 by the ICMART and comprising comprehensive glossary for all definitions related to this field. A complementary meeting was held in 2008 along with the Low-Cost IVF Foundation and the International Federation of Fertility Societies in order to update and disseminate the content of terminology output and eventually for having the most use and benefit of global work (Vanderpoel et al., 2009).

Many research studies are interested in discovering the variances among population-based approaches exploring prevalence of infertility and its impact on comparative procedures and generalizability. A meta-analysis for observational studies that was published in 2011 showed that most studies lack consistency in the process of defining infertility and so the generalizability of the research findings was quite controversial. The study aimed to collect and analyze only observational population-based reports, surveys and studies that are related to infertility and other reproductive health problems published in the last quarter of the 20th century and through 2010. Out of 29,657 studies found through electronic search, only 70 studies were analyzed for illegibility which include using appropriate representative sampling process, high response rate and adequate measurement tool. The final agreed decision was made to put 39 studies under quality assessment. Upon full text review and assessment, the study found that demographic definition was used in 11 studies through which data was collected from censuses and DHS. All eleven studies used cross sectional techniques and was performed in the USA, China, Australia and in African and Sub-Saharan region. Another four studies used the epidemiological definition to calculate the prevalence of infertility and these studies were performed in England, Denmark, China and Scotland. From the 39 analyzed studies, five applied 24 months interval of inability to conceive as an indicator to calculate infertility while only four used one-year infertility to calculate the prevalence. The heterogenicity was revealed not just in the duration of failure to achieve pregnancy but also it appeared in women age group and in the denominator used to calculate infertility (Gurunath, Pandian, Anderson, & Bhattacharya, 2011).

Another study published in 2005 and performed on 15 located areas in Tanzania. The study was developed as a cross sectional approach and included 2,203 women in their reproductive age with 99.5% response rate. The researcher examined six different

definitions of infertility through a detailed questionnaire in order to explore the effect of different terminology on the estimation of infertility in a designed population and also to identify which definition is more relevant to be used. Results implied that although "Unprotected intercourse for at least 2 years" measured infertility in a significantly higher values (12.1%, 95% CI, 9.4-14.8) than "Tried to conceive for at least 2 years" (6.9%, 95% CI, 5.2-8.6) the former did include women who do not desire having a child but at the same time are not using contraceptive methods (Larsen, 2005).

2.2.2 Epidemiology of infertility:

Demographic characteristics of a population could be affected by increase in the incidence of both fertility and infertility. Although high rate of infertility may affect the population growth, but by time the rise in rate may enhance developing means and technologies that assess conception and in turn may pamper efforts to control rapid increase in fertility rate (Rutstein & Shah, 2004).

Twenty five percent of couples in developing countries suffer from infertility (WHO, 2014[a]). It is essential to estimate prevalence of infertility in a nation so that to avoid social, psychological and demographic implications and also to intensify efforts towards prevention and treatment (Thoma et al., 2013). Although infertility represents a significant public health problem, there are many regions, mainly in low and middle-income countries, that have limited data regarding this topic (Polis et al., 2017). According to a systematic analysis study that identified and analyzed 277 DHS in one hundred and ninety countries, only 6 countries in the middle east possessed surveys that were implemented through a "Pan Arab Project for Family Health" during the period from 2002 till 2004 and only 10 countries that engaged in child development surveys during 1990-1997. The study also revealed that slight undetectable change in prevalence of primary and secondary infertility was detected since 1990 till 2010. The study estimated the prevalence based on the five years interval of failure to conceive with specific concerns regarding live birth outcome, contraception and confidence interval were considered. Among all surveys gathered and analyzed, the region that recorded the most data availability was the Sub-Saharan Africa region, while only 53 percent of countries had available national data and only 36 percent had two or more infertility and reproductive health surveys. The authors declared that prevalence trends of primary infertility did not much change during the 20

years study period. Primary infertility prevalence in 1990 was 2.0 percent comparing to 1.9 percent in 2010 although the number of infertile couples increased remarkably to reach up to 19.2 million couples globally in 2010. The slight change was attributed to the change in the desire to obtain a child and the global orientation of independency and individualism along with increased population growth. The study also recognized pattern of infertility among different regions that showed North Africa and Middle East countries as having much higher prevalence than other countries, while Middle Income countries in Latin America showed the lowest results of prevalence during 2010. It also showed that primary infertility is higher among young aged women, with the peak was recognized among women aged 20 to 24 [2.7% (2.4%-3.0%)]. On the other hand, secondary infertility among women aged 20-24 was 2.6% (2.3%-3.0%) that increased dramatically among women aged 40-44 which was 27.1% (24.7%-29.9%). Speaking of absolute numbers, globally in 2010, 48.5 million couples suffered from infertility, from which 19.2 million couples had primary infertility while secondary infertility was detected among 29.3 million (Mascarenhas et al., 2012). However, what is noted from this study is that the prevalence of infertility is lower than that in other regional studies because of using five years interval of inability to have the desired child.

It is well known that infertility is an important public health problem. It affects 10-15% of couples worldwide if we considered the duration of inability to conceive to be 12 months (Evers, 2002). The prevalence rate in the developed countries varies from 3.5% to 16.7 %, while in less developed countries the least prevalence estimated was 6.9% and the highest was 9.3% (Boivin, Bunting, Collins, & Nygren, 2007). In the united states, 6.7% of married women are unable to conceive after one year of trying so (Centers for disease control and prevention [CDC], 2016). Moreover, the WHO estimated an incidence of about 20% in the Eastern Mediterranean countries (Abushahla, 2013). As the 12-month prevalence rate have completely different figures, a paper was prepared using 25 population surveys and studies in which 172,413 women were sampled for the prevalence of infertility. Three studies showed that 9.2% of Gambia population suffer from infertility while Shanghai constitute 9.3% of the condition among women aged 20-44. The average is much close to that in the developed countries where the paper showed a prevalence of about 9% for 12-month delay among women aged 20-44. The author concluded that there is similarity in the prevalence of infertility between developed and less developed countries, but the mechanism behind the prevalence differs by region (Boivin et al., 2007).

In Africa most cases usually report infection, while in more developed countries female age-related infertility is more common (Lunenfeld & Van Steirteghem, 2004).

A study which was performed in Canada, estimating the prevalence of infertility among Canadian people using 12 months duration in 2009-2010, revealed that 11.5% of couples reported "no pregnancy, did not use any form of birth control, reported having sexual intercourse during the previous 12 months and tried at some point to become pregnant with their current partner". The study also suggests that over time, the prevalence of infertility in Canada is increasing and estimation the prevalence help informing the programme initiatives to reduce social, economic and health burdens of the condition (Bushnik, Cook, Yuzpe, Tough, & Collins, 2012).

The case in Palestine differs. During the Family survey held in 2010, the PCBS announced a national prevalence of primary infertility of 4.8 in which it is 4.5 in the WB and 5.2 in GS (PCBS, 2011). However, the PCBS (2014) reported that, the total fertility rate has decreased to reach 4.1 in 2011/2013 comparing to 5.9 in 1999. Also, in this regard there is decline in the proportion of children aged 0-14 by 3.6% during the past ten years while the working age group 15-64 increased by 3.7% (PCBS, 2018[d]).

2.2.3 Consanguineous marriage:

Consanguineous marriage has been known since ancient people. According to research studies, worldwide prevalence of consanguinity is 20% (Modell, 2002). Most of this practice is known to be controlled by social, cultural and religious concepts adopted mainly by Arab countries. Consanguinity differs among these countries as well as in the same country. The phenomenon appears more in rural area than in urban regions (Wahab & Ahmad, 1996). Reviewing a study concerned with the effect of relative marriage among Arabs revealed that Sudan reported the highest rate (49.5) among Arab countries while Morocco showed the least figure **(**10). Egypt was among the highest countries to report consanguineous marriage of 47.2. The condition in Palestine and Jordon is converged where Palestine showed 34.2 and Jordon revealed 39 rates (Tadmouri et al., 2009). In another study, published almost at the same period, showed higher figures in the context of Palestine. The study interviewed 16,197 women and showed that prevalence of relative marriage among Palestinian women is 45% (Assaf & Khawaja, 2009). In the former study, the authors declared that there are many factors that contribute to the existence of relative

marriage among Arabs. Among these factors, which is well apparent in Palestine, is the persistent willing to keep the family structure and property intact within family members (Tadmouri et al., 2009).

Consanguineous marriage has been known to affect reproductive health among couples. A study conducted in Lebanon and examining 220 fertile and infertile cases revealed that azoospermia and severe oligospermia appeared to be of higher rates among first degree relatives' parents than people with non-relative parents. Also, the study showed that infertility is 2.58 times more among consanguineous married men than control cases. And when separating the cases with azoospermia and severe oligospermia from the total infertile men, the consanguinity was amplified. The results showed that 50% of them have either a first or a second degree consanguinity marraige and 40% reported at least one relative suffering from a diagnosed infertility cause but not idiopathic cause (Inhorn, Kobeissi, Nassar, Lakkis, & Fakih, 2009).

2.2.4 Female medical factors:

2.2.4.1 Tubal factors

The fallopian tubes are part of the female genital system in which the ovum is fertilized by the male sperm to form a zygote. The zygote, while still in the fallopian tubes, undergo several rounds of division and cleavages until it forms a mulberry-like ball of cells called the morula. This process takes about 3 days after which the morula proceeds in its journey towards the uterus for the formation of a complete viable fetus (Cunningham et al., 2001). These three days are essential component of the process of pregnancy. Adhesions or damage in these tubes usually prevent the sperm from reaching the ovum and eventually prevent pregnancy. Many causes can provoke this condition. Among these causes, abdominal or pelvic surgeries that may complicate to intra-abdominal adhesions and in-turn close the tubes. Also, pelvic inflammatory diseases that can be caused by chlamydial, gonorrheal or any other sexually transmitted diseases may contribute significantly to impairing the function of the fallopian tubes among women (Mayoclinic, 2018).

Salpingitis is a condition that is characterized by the presence of inflammatory reaction affecting the tubes that connect the ovaries with the uterus. These tubes are called the fallopian tubes (Putten, Engel, & Well, 2008). The condition is most commonly caused by

gonorrheal or chlamydial infection (Moodley, Wilkinson, Connolly, Moodley, & Sturm, 2002). However, many researchers linked chlamydial infection of the fallopian tubes with the development of infertility and subfertility among women during their reproductive age period. A case control study examining the evidence of chlamydial infection in women with tubal cause of infertility revealed that about two third of the cases were identified to have the specific immunoglobulin G antibodies in their blood while only about third of the fertile controls (35%) are seropositive. Women suffering from infertility due to causes other than tubal conditions showed seropositivity in about 55% of total (Sharma, Sethi, Daftari, & Malhotrs, 2003). Another study was conducted in Nigeria showed nearly the same results. 188 women were selected for a case control study. 94 cases were confirmed radiologically to have tubal origin infertility and another 94 women representing control group were already pregnant. The study confirmed that 61.7% of the cases group showed seropositive results while control group presented with 34% prevalence rate. Interestingly, the study also determined that women with seropositive chlamydial trichomonas infection were three times more likely to be infertile than seronegative women (Ojule, Ibe, & Theophilus, 2015). A recent cohort study was also conducted in Netherlands where 5,704 women participated to understand the relationship between chlamydial infection, pelvic inflammatory diseases and infertility. The women included in the study were invited previously to perform screening for chlamydia six to seven years before the study was conducted. Then the incidence of infertility among PCR positive and negative screened women was explored. The incidence rate of infertility was 1.3 per 1000 person-year (0.8-2.1) among seropositive women, while incident rate among seronegative women was 0.2 per 1000 person-year (0.1-0.4) during the study (Hoenderboom et al., 2019).

Tubal pathology accounts for almost third of the causes attributed to primary and secondary infertility among females worldwide (Briceag et al., 2015). On the basis of contemporary revolution of IVF, the fallopian tube role in being the site of fertilization has been much ignored (Sacks & Trew, 2004). In this context, a group of researchers studied 104 full text articles and 4 textbooks dealing with etiology, diagnosis and management of tubal infertility in order to raise awareness regarding this subject. Subsequently, they concluded that age is an important factor contributing to tubal infertility where women aged 35-39 are twice more likely to suffer from tubal infertility (OR=2.2, 95% CI, 1.7-2.7) in relation to women less than 30 years age. Also, special concerns were raised regarding relaying on polymerase chain reaction (PCR) testing rather than histopathological and

microscopic examination of acid-fast bacilli to enable earlier diagnosis of genital tuberculosis. Adding to that, the use of intrauterine device and having vaginal infection within twenty days of insertion is highly associated with tubal secondary infertility (Briceag et al., 2015).

The condition in Palestine is not much different. One of the most common etiological risk factors for infertility among women during their reproductive age in GS is fallopian tube problems. Women with fallopian tube pathology are 13 times (OR=13.63, 95% CI, 1.43-129.91, *P*=0.023) more likely to suffer from infertility or subfertility than those with normal findings (Sirdah, Abushahla, Ghalayeni, & Aburamadan, 2013). Two studies examining the prevalence of Chlamydial infection showed different results. The first concluded that 164 women out of 1207 examined (13.6%) provided positive cultures (Houso, Farraj, Ramlawi, & Essawi, 2011). Another descriptive analytic cross sectional study conducted in GS revealed only 5.8% prevalence rate of Chlamydial infection (Maqadma, 2014).

2.2.4.2 Ovarian factors

The ovaries are two oval shaped organs located at either side of the uterus just beneath the fimbriated end of each fallopian tube. It produces graafian follicles in which one of them dominate and in turn releases an ovum to reach the fallopian tube in a process called ovulation. Any disturbances in the function of ovaries may result in high possibility for infertility.

One of the most common pathological disorders of female ovaries is PCOs (McGowan, 2011). The global prevalence of PCOs constitutes variety in values. The reason was attributed to many factors including limitation in cases presentation due to different ethnic considerations and unavailability of standardized definitions. While the National Institution of Health considered 6% as a global prevalence, the Rotterdam and Androgen Excess Society declared the prevalence to be 10% (Bozdag, Mumusoglu, Zengin, Karabulut, & Yildiz, 2016). PCOs is an endocrine and reproductive disorder which is characterized by the presence of cysts in the ovaries and inducing hormonal imbalance. It is considered the primary cause of increased level of androgens among women and the main cause of either oligo/amenorrhea during presenting to seek medical treatment (Azziz et al., 2004). However, many women may present with infertility accompanied with no significant

clinical symptoms and consider themselves to have normal menstrual cycle. In a study of 257 volunteers who did not complain from neither hirsutism (clinical symptoms of increased level of androgens hormone in blood) nor any menstrual cycle abnormalities or infertility were examined by ultrasound scanning for PCOs. 18% of the participant were noticed to have irregular cycles. Although 116 women representing 73% of the participant were found to have normal ovaries, 23% had been determined to have PCOs. From the 36 PCOs cases, 76% were found to have irregular menstrual cycles and about 7% were diagnosed to have hirsutism (Polson, Wadsworth, Adams, & Franks, 1988). Moreover, it has been noticed recently that clinical presentation differs according to the geographical region and ethnicity. A cross sectional study examined the type of clinical presentation, a woman with PCOs would approach with, among European, Maori and Pacific Island women revealed that European women were the least to present with infertility (46% versus 68% $P<0.05$) while 43% of women who were from both the Maori and European were more likely to present with hirsutism (Williamson, Gunn, Johnson, & Milsom, 2001).

One of the most common causes of infertility among young females is PCOs. According to many research studies, PCOs was accounted for more than two third of all anovulatory cases presented with infertility (Brassard, AinMelk, & Baillargeon, 2008). However, obesity is highly linked with PCOs which eventually causes infertility in many cases. While ovulatory problems and iatrogenic causes accounted for 50% of all infertility cases, most of these causes were related to obesity (Talmor & Dunphy, 2015). A study was conducted on 207 women with known PCOS and where classified into groups according to their body mass index (BMI). The study showed that the higher the BMI of the woman the more probability of having oligomenorrhea and amenorrhea. In addition, the response rate among normal BMI index women to ovulation induction was much higher (79% $p<0.001$) than those with obese category (15.3% $p<0.001$) and also comparing to women with grossly obese classification (11.8% $p<0.001$). The author concluded that "The pregnancy rate and outcome was also adversely affected by obesity" (Al-Azemi, Omu, & Omu, 2004). Another study conducted retrospectively in Taiwan explored the differences between obese and nonobese women with PCOs in terms of clinical and biochemical variables. The researchers found that nonobese women with PCOs were 2.5 (95% CI) times less likely to develop PCOs than obese women and that obese women with PCOs have higher incidence to develop both androgenic manifestation and menstrual abnormalities (Liou et al., 2009).

Upon literature review, there are no scientific papers or clinical data demonstrating the prevalence of PCOs in GS. Nevertheless, some researchers studied the link between PCOs and characteristics of metabolic syndrome (MBS) (abdominal obesity, glucose intolerance, hypertension, dyslipidemia and cardiovascular disease) in GS. In one study, two hundred and eight women were selected in a case control study, 104 were known to have PCOs as cases while the same sample size for controls were selected to be free from PCOs, hirsutism and have no menstrual abnormalities. The researcher found that MBS was found in 31.7% of women with PCOs compared to 3.8% among the control group. These results were based on the criteria of the European Group for the Study of Insulin Resistance. The age variable shows positive correlation with MBS among PCOs cases. The prevalence of MBS among women with PCOs aged less than 20 was 37.9% that increased among women aged 21-29 to reach up to 48.8% and also another elevation was noted among women aged above 30 to be 76.8% (Mousa, 2009). Moreover, a case control study was performed with the participation of 284 women to identify the etiological risk factors of subfertility among Palestinian women in GS. The participants were subjected to a variety of tools to evaluate their socio-demographic and medical variables in a consistent manner. Eventually, it was noticed that the percentage of women with PCOs were statistically significant higher in the infertile group than the control group and women with PCOS are 10 times more likely to be infertile or sub-infertile than women not suffering from PCOs (OR=10.29, 95% CI, 1.88-56.10, P=0.007). The author recommended comprehensive evaluation of women should be adopted as a strategic approach (Sirdah et al., 2013).

2.2.4.3 Uterine factors

Usually infertility is accompanied with functional abnormalities in the endometrium of the uterus (Dallenbach-Hellweg, 1984). Many anatomical and pathological disorders of the uterus may contribute significantly to the inability to conceive when desired. Inability to conceive which is due of uterine origin could be caused by either acquired or congenital conditions related to the uterus (Taylor & Gomel, 2008). Acquired causes could be uterine polyps and fibromas, endometrial hyperplasia, intrauterine adhesions and adenomyosis. On the other hand, congenital conditions associated with infertility are classified according to the American Fertility Society Classification into uterine hypoplasia and agenesis, unicornuate uterus, uterus didelphys, bicornuate uterus, septate uterus, arcuate uterus and

diethylstilbestrol-related anomalies. It is worth to mention here that about three percent women suffering from infertility have associated congenital anomalies in the uterus that causes the sterility (Irani, Ahmadi, & Javam, 2017). On the contrary, other studies showed higher percentage. A study was published in 2008 and demonstrated the prevalence of uterine congenital anomalies causing infertility to be the same as the overall prevalence among the general population 6.7% (95% CI, 6.0-7.4) (Saravelos, Cocksedge, & Li, 2008). Controversially, another study which used meta-analysis systemic review approach and examined 94 observational studies to identify the prevalence of uterine congenital anomalies among high risk population (89,861 women) revealed that the prevalence is 8% (95% CI, 5.3-12) among the infertile group (Chan et al., 2011).

A literature review was conducted to assess infertility in relation to different uterine. Accordingly, the researcher found an association between septate uterus and infertility, but this relation was mainly confined to performing metroplasty. Furthermore, reduction in the rate of spontaneous abortion from 91% to 17% after hysteroscopic metroplasty is demonstrated in several case series studies. Moreover, the average pregnancy rate among women who were previously diagnosed as infertile and had metroplasty was 47% while half the women who performed laparoscopic or hysteroscopic myomectomy became pregnant. According to Sanders (2006), there is little known about the link between intrauterine adhesions and infertility or pregnancy loss and also lesser were published regarding the relation between polyps in the uterus and sterility. The author provided that only one study revealed that after hysteroscopic polypectomy, 78% of women became pregnant.

2.2.4.4 Hormonal factors

The reproductive system is prone to be affected by many internal and external influences. Although both male and female systems are vulnerable to such factors but the female's tend to be more sensitive (Chang & Auchus, 2018). The functioning mechanism of the female reproductive system is completely regulated with certain body hormones. These hormones are:

1- Gonadotropin releasing hormone (GnRH): A hormone that is secreted from the hypothalamus as a response to higher central impulses and stimulates the release of FSH and LH hormones from the anterior pituitary gland.

2- Follicular stimulating hormone (FSH): A hormone that is released from the anterior pituitary gland through which it stimulates the ovaries to produce and mature follicles.
3- Luteinizing hormone (LH): A hormone that is also produced from the anterior pituitary gland and stimulates both the secretion of estrogen and progesterone from the ovaries. It also plays an important role in the process of rupture and release of the ovum from the mature graafian follicle and subsequently the formation and development of corpus luteum.
4- Estrogen is produced mainly from the ovaries in nonpregnant women and from the placenta in pregnant ladies. It is essential for ovum maturation till the surge is reached then the release of the ovum (ovulation) occurs.
5- Progesterone suppresses the release of estrogen after surge and helps in preparing the endometrium to receive the fertilized ovum.

Diseases that affect the hormonal cycle of ovulation are various. Some of these disorders are Cushing disease and syndrome, hypo and hyperthyroidism, hyperprolactinemia and PCOs. Most of these diseases can cause impaired pregnancy outcome, subfertility or even primary infertility. Some affects the ovulation cycle directly and others have an indirect impact on the whole or part of the process.

Hypothyroidism is a disorder characterized by subnormal level of thyroid hormones released from the thyroid gland. These hormones are responsible of almost all metabolic function of the cells in the body. The decrease in the serum level of these hormones, will directly stimulate the release of thyrotropin releasing hormone from the hypothalamus which in turn will stimulate the release of thyroid stimulating hormone from the pituitary gland. The thyroid stimulating hormone release is accompanied with the release of prolactin hormone, a hormone that suppress the process of ovulation when released in certain amounts. Eventually, any condition associated with malfunctioning in the thyroid gland will indirectly affect ovulation. A new Harvard Medical School study found that even mild low levels of thyroid hormones may affect fertility among some females. More than 25% of females with unexplained infertility who participate in the study show thyroid hormone results to be in the lower edge of the normal reference (Pouneh, 2017). Another study support the same results and found that subclinical hypothyroidism could be associated with impaired function of ovulation and subsequently affect pregnancy outcome (Trokoudes, Skordis, & Picolos, 2006). However, a study that estimated the prevalence of

hypothyroidism among infertile women revealed that about quarter of the infertile cases were diagnosed to have hypothyroidism of which more than two third of the cases got pregnant within six weeks to one year of treatment. More interestingly, women who had both hypothyroidism and hyperprolactinemia had their prolactin level returned to normal upon treating the deficiency of thyroid hormones (Verma, Sood, Juneja, & Kaur, 2012). On the contrary, some researchers doubted the practice of some Obstetricians and Gynecologist in requesting thyroid hormones and prolactin serum level for infertile normally menstruating cases as a routine procedure. The study revealed that prospective collection of these tests to all attending females for infertility management showed only 21 out of 846 females (2.48%) had abnormal thyroid hormone results while high prolactin serum levels was found in only 1.77% of cases (Olivar et al., 2003). The condition in GS is quite different. Sirdah et al. (2013) found that 13 out of 169 infertile females (7.7%) had abnormal thyroid hormone profile while 47% of cases suffered from associated sex hormones abnormalities.

Hyperprolactinemia is a condition where there is raised levels of prolactin hormone in blood. It is caused by disturbances in either the hypothalamus or the pituitary gland. The condition can also occur in accompanying with other pathological diseases. The prolactin hormone, till a certain limit, can prevent the secretion of GnRH responsible of initiating and ongoing process of ovulation. Some research studies showed that hyperprolactinemia occurs in 30-40% of infertile women (Thirunavakkarasu et al., 2013). A recent hospital based cross-sectional study involving 300 infertile women (79.6% primary infertility, 20.4% secondary infertility) showed that the prevalence of hyperprolactinemia among infertile women is 24.67% (Nallusamy & Gracelyn, 2016). On the contrary, a cross sectional study involving 1,163 infertile women (73% primary infertility, 27% secondary infertility) was performed during 2010/2011 revealed that 15.7% only of the participants had hyperprolactinemia, 88% of which were diagnosed to have true idiopathic hyperprolactinemia (Thirunavakkarasu et al., 2013). Another study had nearly the same results. The researcher examined 200 infertile women (65% primary infertility, 35% secondary infertility) for their serum prolactin and found that 23 women had hyperprolactinemia (Agrawal, Samal, Hariharan, & Agrawal, 2014). It is worth to mention that both studies recommended that serum prolactin test should be part of routine investigations performed to couples attending infertility clinics seeking advice.

2.2.5 Male medical factors:

2.2.5.1 Varicocele

Varicocele is a medical condition that is characterized by dilatation in the pampiniform plexus of veins located in the scrotum of the male genital system. The varicocele could attain different sizes classifying the condition into three types. The first is large varicocele that could be diagnosed by simple inspection, the second is moderate varicocele that is diagnosed simply by palpation and the third is small that cannot be diagnosed unless the patient bend forward in a maneuver called Valsalva maneuver. According to the American Urological Association, varicocele occurs in about 15% of adult males and attributes to 40% of causes related to primary infertility among men (Sharlip et al., 2001). Although varicocele affects mostly the left side, it occurs bilaterally in 50% of cases (Alsaikhan, Alrabeeah, Delouya, & Zini, 2016). The left sided commonality occurs because the left spermatic vein drains in a right angle connection with the left renal vein while the right spermatic drains directly into the inferior vena cava (Wallace & Amaya, 2011).

There are no established mechanisms that explain how varicocele affects the morphology, count and function of sperms and semen, but theories were placed and not proven. Some of these theories proposed the effect of heat injury, oxygen deprivation, toxins unresolved by impaired venous return and pressure imposed on the testicles. A meta-analysis study exploring the effect of oxidative stress in varicocele patient showed that reactive oxygen species concentration is much higher (mean difference 0.73, 95% CI, 0.40-1.06, $P<0.0001$) among patients with varicocele than in the control group, but the researcher recommended further confirmation (Agarwal, Prabakaran, & Allamaneni, 2006). Another interesting study demonstrated that varicocele is more likely to be inherited among male siblings in the family. The study results showed that the prevalence of varicocele among first degree relatives is about 55% with 67% prevalence among sons of affected fathers (Zelkovic & Kogan, 2010). Some studies found that scrotal temperature is not different among both people with varicocele and people without, although the semen quality differs significantly between the two cases and controls groups (Lund & Nielsen, 1996). In the same context, other studies found that elevation of scrotal temperature contribute much to the impairment of sperms function and morphology in varicocele patients (Shiraishi, Takihara, & Matsuyama, 2010).

In Palestine, the situation is controversial. A study conducted in GS revealed that among the risk factors associated with male infertility, varicocele contributes to about 10.1%, of which only 16% showed seminal problems (Abushahla, 2013). Another study performed in the WB showed that there are eight main causes of infertility among men in Palestine, of which varicocele is considered the second main cause comprising 32.4% of all causes. The study also found that 70% of the cases had left sided varicocele while bilateral affection was among 28.5% of cases, which is concomitant with the national prevalence (Al-Haija, 2011).

2.2.5.2 Azoospermia

Azoospermia is the absence of sperms in the seminal fluid. According to the American Society for Reproductive Medicine, this condition accounts for 1% of all men and for 10%-15% of infertile individuals (Oates, 2012). In order to comprehend the cause of any defect in the production, morphology and functionality of the sperms the hormonal regulatory system should be clear. The hypothalamic pituitary axis regulates the excretion of LH and FSH through the regulatory effect of GnRH. The LH stimulates Leydig cells of the testes to release testosterone and FSH maintains a continuous process of spermatogenesis through the Sertoli cells (Friedman & Dull, 2012). Any disorder in the release of GnRH will eventually affect the spermatogenesis process as well as the production of sperms. Azoospermia could be caused through three mechanisms:

1- Pretesticular which is a condition by which the pathway is interrupted before the testicles and demonstrated mainly through decrease in the production of sex hormones and subsequently no sperms are produced. These disorders could arise from either congenital anomaly (Kallmann syndrome) or acquired condition (Post radiation or chemotherapy applied to the brain affecting the hypothalamus or pituitary gland).
2- Testicular where the defect is in the testis structure and function.
3- Post-testicular, and sometimes called obstructive causes, where it could be due to epididymal, vas deferens or ejaculatory duct obstruction, each of which could be either acquired or congenital defect. This type occurs less frequently than the other two types and occur in 15%-20% of all azoospermia cases (Dohle, 2016).

It is essential to diagnose the cause of azoospermia carefully in order to reach out possible curative plans, if possible. Men with azoospermia and with normal semen volume, considering that there is neither vasal agenesis nor testicular atrophy, would have abnormalities in spermatogenesis or obstruction in either the epididymis or the vas deferens. In case of suspecting spermatogenesis, hormonal essay would be helpful. If the semen volume is low, the most probable diagnosis would be ejaculatory disorder (Gudeloglu & Parekattil, 2013).

Azoospermia occur in 1% of the total male population but comprise 10%-15% of infertility causes related to men. A study performed between March 2011 and October 2016 in three Turkey clinics showed that from 9733 men involved in the study, 850 (5.9%) were suffering from azoospermia. From total participants, 32% were determined to be infertile from which 18.3% were diagnosed with azoospermia (Karabulut et al., 2018). Similarly, a study conducted in WB showed that azoospermia occurred in 20.3% of the total infertile male cases. In this study, the researcher evaluated 1392 medical records for infertile couples visiting Razan center in Ramallah and Nablus. Although most research studies revealed that about third of the infertility causes is related to men, the prevalence among male participants in this study was much higher (52%). The author attributed the high results to the challenging occupational environment in which the region is experiencing (Al-Haija, 2011). Two years later, Abushahla (2013) concluded that the main cause of infertility among men in GS was seminal problems (51.8%), of which azoospermia has the highest value (22.9%) of all causes detected.

2.2.5.3 Immunological causes

Infertility due to immunological cause is a condition which is characterized by the presence of anti-sperm immunological reaction that interferes with the fertility mechanism at different stages (Dondero, Gandini, Lombardo, & Lenzi, 2011). Many experiments suggested that anti-sperm antibodies, including immunoglobulins (IgG, IgA and/or IgM), are produced against different parts of the spermatozoa disturbing any of its vital functions of fertilization. Usually the antibodies are polyclonal and are directed to more than one antigen resulting in interfering with the process of fertilization at different levels. The infertility outcome of the immunological reaction could be through disturbing spermatogenesis leading to oligospermia or azoospermia or by affecting the mobility of the

sperm and thus preventing its ascent through the female cervical mucus. The mechanism may also be accompanied with disorders in the sperms capacitation or even blocking of the sperm-ovum interaction (Sheynkin, 2018).

Immunological causes of infertility cannot be neglected. A study involved 860 men, 750 were infertile and 110 had normal fertility history, were examined for semen analysis and serum latex binding test. 13% of the infertile group showed positive immunological reaction to IgG and 6.2% had 40% binding capacity (Sinisi et al., 1993). On the contrary, another study was done on 766 semen samples revealed that the prevalence of immunological infertility was about 4.5% (Hinting, Soebadi, & Santoso, 2009).

2.2.6 Environmental conditions:

Contemporary life eased the daily life of people, but inevitably, negative impact is being witnessed over time. People are exposed to various types of pollutants in their everyday lives and are exposed to variety stressors related to the pace of modern life. Among these factors, the researcher is keen to review literature for increasing knowledge about pesticides, stress and war residuals with infertility.

2.2.6.1 Pesticides

Pesticides are used in many ways and are present in many sources, but the main source through which people are largely exposed, mainly organophosphorus, is through diet (Lu, Barr, Pearson, & Waller, 2008). A recent US study published in 2018, suggested that women exposed to food with certain levels of pesticides residues are more likely to have adverse fertility outcomes. The study was held from 2007 through 2016 involving monitoring of 325 reproductive aged women in a prospective cohort design. Selected women had diet assessment and had 541 cycles of assisted reproductive technology during which each step of the ovulation cycle was scrutinized and analyzed in relation to demographic, dietary and medical history variables. The results demonstrated that women consuming high pesticides residue diet are 18 times less likely to have pregnancy and are also 26 times less likely to have live births than those with low intake. The study found no relation between consumption of low residue containing diet and assisted reproductive technology outcome (Chiu et al., 2018).

Another study was conducted to determine the effect of herbicides and fungicides on women's fertility status. The retrospective case control study, which involved 644 women (322 cases and 322 controls), examined various occupational, health and lifestyle exposure variables. Eventually, it was found that two years history of exposure to herbicides or fungicides were more common among infertile women (OR=27, 95% CI, 1.9-380), (OR=3.3,95% CI, 0.8-13). The researcher recommended further studies regarding pesticide biomonitoring (Greenlee, Arbuckle, & Chyou, 2003).

Men as women are affected by continuous exposure to pesticides in a way that compromise their fertility status. A recent case control study, conducted in GS, examining 192 men for the impact of exposure to pesticides on testicular function found that testosterone levels among exposed farmers were significantly lower than those who were not exposed and mainly among men aged between 31 to 45 years with the least was recorded in Rafah with mean testosterone level of 4.3ng/dl (SD ± 1.2, $P<0.05$) and -20.8% difference between cases and controls (Al-shanti & Mohamed, 2017).

2.2.6.2 Stress and war

Is it stress that causes infertility or is it infertility that causes stress? A question that have too long confused researchers. Researchers used to estimate stress among infertile couples through self-reported measures. The accuracy of these measures is considered the main challenge in most studies. It is possible that women may conceal symptoms of distress and anger in order to appear in a healthier status, or they may have hopefulness feelings during the initiation of treatment, which is the place where the cases are found and assessed (Rooney & Domar, 2018). Some studies pointed that it is not possible to link stress to infertility. A recent Danish study, published in 2016, utilized a self-reported psychological stress measure. The cross-sectional study estimated the quality of semen and serum reproductive hormones of 1,215 men and the association of the results with the stress measures. Subsequently the researchers found that there is a dose-response relationship between the "intermediate and high stress level" expressed by participants and the quality of semen examined, but also revealed that there is no significant association between self-reported stress and serum hormones (Nordkap et al., 2016). However, in 2008, a study was conducted on 545 infertile couples and found that almost third of the cases are suffering from psychiatric disorder, most of which were major depression with more rates among

females (10.9%) compared to male cases (5.1%) (Volgsten et al., 2008). Almost similarly, Chen et al. (2004) found that 40% has psychiatric disorders but with most common cause was generalized anxiety disorder. However, little is definite about the impact of stress on infertility (Nordkap et al., 2016).

Exposure to war may have various reproductive related risk factors, including injuries, stress and exposure to toxins, that is believed to affect fertility conditions (Kobeissi et al., 2008). In a retrospective study, males with and without infertility problems were examined between 1985 and 1989, Lebanese civil war period, for semen analysis and compared to another corresponding group during the post war period from 1991 to 1995. The study provided that sperm concentration significantly declined during the war period while percentage of morphological disturbances increased after the war finished (Abu-Musa, Nassar, Hannoun, & Usta, 2007). Another clinic-based, case control study, examined 120 infertile men and 100 fertile control group for fertility status, revealed that individuals who lived through the Lebanese civil war are more likely to have infertility than others (Kobeissi et al., 2008). Subsequent research had supported these findings. A retrospective cohort analysis of 42,818 questionnaire respondents (53% Britain Gulf veterans, 42% non-Gulf veterans) showed that infertility was higher among Gulf veterans (Primary; [OR=1.41, 95% CI, 1.05-1.89] Secondary; [OR=1.5, 95% CI, 1.18-1.89]) than among non-Gulf veterans (Maconochie, Doyle, & Carson, 2004).

2.2.7 Lifestyle:

2.2.7.1 Smoking

Smoking is the cause of 6 leading causes of death globally. Undeniably, it causes more than 7 million deaths and kills approximately 174,000 women each year (CDC, 2008). A meta-analysis published in 2004 identified that smoking women are more prone to infertility than non-smoking women. Data involved 10,928 smoking women and 19,179 unexposed women revealed that the odds ratio of infertility in cigarette smoking women is 1.6 (95% CI, 1.34-1.91) compared to non-smokers. The case control studies showed odds ratio as 2.27 (95% CI, 1.28-4.02) while data from cohort studies pointed to a 1.42 (95% CI, 1.27-1.58) odds ratio. The narrow range of confidence interval denoted the high accuracy of estimation and that the results are most likely not by chance (ASRM, 2004). Another cross-sectional study was conducted among Iranian women and demonstrated that primary infertility was independently related to active smoking women (OR: 1.47; 95% CI, 1.38-3.53).

Although, prevalence of smoking among men decreased 10% from 1980 till 2012, the total number of smokers increased to be 967 million in 2012 (Ng et al., 2014). According to the WHO, smoking men aged 15 and above represent 35% (WHO, 2016[c]). A recent meta-analysis study, published in 2019, concluded that there is no effect of tobacco on the hormonal imbalance among smoking infertile men. However, the study analyzed data of 10,823 infertile participants included in 16 studies and found that both oligospermia (RR: 1.29, 95% CI, 1.05-1.59, *P*=0.02) and morphological abnormalities in spermatozoa (MD: 2.4, 95% CI, 0.99-3.89, *P*=0.001) are significantly higher among smokers than nonsmokers (Bundhun et al., 2019).

2.2.7.2 Obesity

One of the most leading causes of preventable morbidity and mortality is obesity. The WHO defines overweight and obesity as "abnormal or excessive accumulation of fat that presents risk to health" (WHO, 2014[b]). Although obesity is preventable, more than 1.9 billion people aged 18 years and above are recorded to be overweight in 2016, of which 13% are obese (WHO, 2018[b]). For the reason of being a major public health problem for many developed countries and for its known detrimental effect on both the individual and the national level, obesity has been occupying a large area in research and mainly studies related to infertility. The adverse effect of obesity appears during the early stages of reproductive age and continues to cause impaired conception outcome and ending up with multiple consequences like post abortion infection, tubal and pelvic pathology, stress and many other factors that hinder fertility (Pasquali, Patton & Gambineri, 2007).

Obesity have several morbidity effects. In particular among females, obesity interfere with the hypothalamic pituitary ovarian hormonal axis and causes menstrual disturbances and infertility. Additionally, it may interact with ovulation and endometrial implantation (Silvestris, Pergola, Rosania, & Loverro, 2018). A study examining the relationship between IVF success rate and BMI revealed that decreasing body weight has significant beneficial effect on the results of assisted reproductive techniques (Dağ & Dilbaz, 2015). Another study confirmed that 62.7% of infertile women who had treatment for obesity, underwent successful pregnancy with live birth outcome (Musella et al., 2011). Upon all what have been mentioned, some research studies also provided the effect of early onset of obesity on the fertility status of both males and females (Pasquali et al., 2007).

2.2.7.3 Physical activity

Physical activity is any body movement a person performs either during his daily life or with preplanned schedule. According to WHO (2018[c]), physical inactivity contributes to the risk factors of leading causes of death globally, including risk factors for diabetes, cancer and cardiovascular diseases. It is important not to confuse between physical activity and exercise. Exercise is the planned part of physical activity that is intended to improve one's fitness and health. It is a repetitive and structured muscle movement approach (WHO, 2017). Although there is evidence that suggested that increasing physical exercise may lead to anovulation, there are some studies provided that structured physical training may improve menstrual abnormalities and subsequently fertility status (Palomba et al., 2008). A recent systematic review was conducted and published in 2017 revealed that excessively intensive exercisers are more prone to infertility than others, but literature review in the same study showed that half to one-hour vigorous exercise daily decreases the risk of infertility due to anovulation. During the same review, studies provided that PCOs women who were subjected to a structured training had their menstruation improved and significant increase in fertility status. The authors also concluded that there is a gap in the literature in identifying the effect of exercise on normal weight anovulatory women and also the presence of only short period intervention with limited results (Hakimi & Cameron, 2017).

Chapter Three
Methodology

3.1 Study design

This study is an observational analytic case control study. The use of observational method in this study is believed to provide the desired results as the study acquires multiple exposures to be observed that might be related to a single outcome under investigation. The analytic property assesses in determining the causal relationship between infertility and different variables included in this study. The researcher specifically selected this design in order to observe retrospectively two groups of people (infertility as cases and fertile couple as controls), one with the outcome of interest (primary infertility) and the other one is free from such condition but with the same study base of the first group, and define the causal relationship between different exposures (risk factors) and primary infertility. Exploring differences between cases and controls helps in identifying possible predictors of the outcome. At this stage, no intervention shall be made by the researcher.

3.2 Study population

The study is composed of two populations, cases and controls. The population of the cases was estimated based on the Palestinian Family Survey conducted in 2010, which was the latest study to be performed in this respect, that revealed the prevalence of infertility among married women in Palestine as 8.4% and the rate of primary infertility as 4.8%, from which 4.5% is in WB and 5.2 in GS (PCBS, 2011). Given that, the total female population in the reproductive age in GS is 452,175, then the projected number of married women with primary infertility is 15,048, which is the study population, when considering the total married females as 64% of the total population (PCBS, 2019[a]).

The study population of the controls are all women matching the eligibility criteria attending Governmental PHC clinics seeking MCH care services.

3.3 Study setting

The study was conducted in two settings in Gaza governorates. Five fertilization centers were selected to seek out cases, while controls were observed from the Governmental PHC clinics.

3.4 Eligibility criteria

3.4.1 Eligibility criteria of cases:

Inclusion criteria

1- Married, sexually active women in the reproductive age period (19-49) at the time of diagnosis who are confirmed to be suffering from inability to conceive for 12 months or more.
2- Married women with no previous pregnancies.
3- Married women not using contraceptive methods.
4- Married women attended fertilization centers for medical management during the period from January 2016 till December 2018.

Exclusion criteria

1- All women attending fertilization centers for the reason of failure to conceive after having previous delivery or deliveries (Subfertility).
2- All women attending fertilization centers for clinical problems other than failure to conceive.

3.4.2 Eligibility criteria of control group:

Inclusion criteria

1- Married women in the reproductive age period (19-49) not known to have clinical infertility during their life time.
2- Women with at least two previous deliveries without assisted reproductive history.
3- All women attending Governmental PHC clinics for family planning services.
4- Women living in a place within the same Governorate from which the case belong to.

Exclusive criteria

1- Attendants for other MCH departments.
2- Women living outside the governorate and came for health consultation.

3.5 Sampling and sampling process

Sample size

The total population with primary infertility in GS was estimated by the researcher according to the prevalence established and stated by PCBS which is 15,048. Being a case control study, it was more appropriate to use a confidence level of 95% (how precise I want my estimate to be) and a power of 80% (the probability of finding an association when an association actually exists). With these three findings, the researcher used epi-info 7 sample size statistical calculator as shown in **Annex (3)** and considered the followings:

- Two-sided confidence level (95%) as we tested two independent groups.
- Power of the study of 80%.
- Ratio of cases to control is 1.
- Percentage of exposed controls is 50% as there is limited information about the exposure risk among the control group.
- Odds ratio assumed as 2
- The selected sample size for cases was 148 and 148 for controls.

In order to compensate missing or non-responding cases, the researcher increased the number of cases to 160 and accordingly increased the controls to 160 to have a total of 320 sample size for the study.

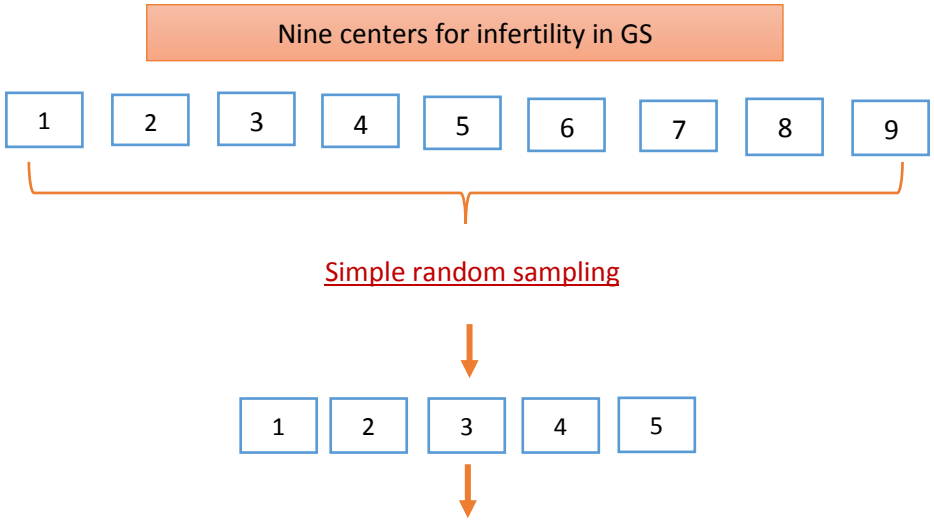
Sampling process

Multistage sampling technique was used to select the calculated sample of cases. The population frame selected for the study was demonstrated from the lists of patients registered for treatment in the fertility centers in Gaza governorates. The first stage of sampling process was based on the selection of five fertility centers through simple random technique. Then, in each center the patients registered from January 2016 till December 2018 were classified into clusters according to their residency per governorate (list of patients per governorate). Finally, a 4^{th} patient was chosen from each sub cluster (North

Gaza, Gaza, Middle Area, Khan Younis and Rafah). Since the breakdown of total female population in reproductive age in GS according to governorates is 88,042 in North Gaza, 155,385 in Gaza, 66,858 in Middle Area, 86,260 in Khan Younis and 55,630 in Rafah that represent 19%, 34%, 15%, 20% and 12% respectively, the number of patients extracted systematically from each cluster were governed by this distribution as illustrated in **Figure (3.1)**.

The researcher sought controls from Governmental PHC clinics. Controls have been attending PHC clinic desiring MCH care services and matching the illegibility criteria mentioned before. Then the researcher identified and selected those who were congruent with the residency of the corresponding cases (Governorate). The five Governmental PHC centers selected for controls identification were:

1- Jabalia Health center
2- Rimal Health Center
3- Nuseirat Health Center
4- Khan Younis Health Center
5- Rafah Health Center



Number of cases / cluster /centers	North Gaza	Gaza	Middle area	Khan Younis	Rafah	Total
Center 1	6	11	5	6	4	32
Center 2	6	11	5	6	4	32
Center 3	6	11	5	6	4	32
Center 4	6	11	5	6	4	32
Center 5	6	11	5	6	4	32
Total	30	55	25	30	20	**160**

Systematic stratified sampling

Governorate	Percentage of female distribution	Distribution of cases	Number of cases / cluster / centers
North Gaza	19%	30	6 x 5
Gaza	34%	55	11 x 5
Middle area	15%	25	5 x 5
Khan Younis	20%	30	6 x 5
Rafah	12%	20	4 x 5
Total	100%	160	**160**

Figure (3.1): Sampling process

3.6 Study instruments

Two instruments were used in the study. The first was self-constructed questionnaire and the second measured the stress conceptual domain among participants and its association with infertility. The self-constructed part is face to face interviewed questionnaire that was developed after reviewing the literature for infertility and other maternal health issues. As shown in **Annex (5)** the questionnaire comprises all domains illustrated in the conceptual framework and was formulized in a way to be capable of gathering data and fully describing each domain. It was constructed to compulsory achieve the objectives of the study and at the same time to be feasible and well comprehended by respondents. The interviewed questionnaire constitutes the following conceptual domains:

1- Sociodemographic variables
2- Socioeconomic variables
3- Environmental variables
4- Lifestyle and obesity
5- Medical and maternal history

The dietary behaviour section of the questionnaire was adopted from the WHO STEP wise questionnaire, but with slight modification so that it adapts the study environment. Also, the last section of the questionnaire is based on part of WHO International Physical Activity Questionnaire (IPAQ), through which it explores the pattern of physical activity as a life style factor that individuals involves in during their daily pace.

IPAQ collects information and data about three levels of physical activity; walking, moderately intense and vigorously intense physical activity; in addition to the period an individual spends sedentarily. Each activity was described clearly to each participant along with the administration of show cards that contain pictures about all possible and relevant types of physical activities that could be practiced by the population in our study context. Examples for moderate intensity activities were provided like, cycling, jogging, drawing water, gardening, walking with load on head and many other examples that accelerate the breathe quite more than normal, while vigorous intensity physical activities are those that make the breathe much harder than normal like, sawing hardwood, digging, shoveling sand, grinding with pestle …etc. Information collected for each type comprise the frequency of doing such activity in the last week and duration in minutes spent in one of these days. Responses were collected from both females and males in separate forms and

data was analyzed according to the recommended guidelines developed and provided by the WHO.

IPAQ also, produces two forms of outputs, one is categorical (low activity level, moderate activity level or high activity level) and the other is continuous variable (MET minutes a week). MET is a ratio between work metabolic rate, which is the energy expended during carrying out physical work, to a standard resting metabolic rate, which is the energy expended by the body during rest period. So MET is considered a multiple of an individual estimated resting energy expenditure. To get a continuous variable from this particular variable, each category of physical activity shall be multiplied by an average MET value calculated through the Ainsworth et al. Compendium (2000) of physical activity, where the following values were used for analysis:

- **Walking MET-minutes/week** = 3.3 × walking minutes × walking days.
- **Moderate MET-minutes/week** = 4.0 × moderate-intensity activity minutes × moderate days.
- **Vigorous MET-minutes/week** = 8.0 × vigorous-intensity activity minutes × vigorous days.

Total physical activity MET-minutes/week = Walking + Moderate + Vigorous MET-minutes/week scores

The second instrument used, was the Perceived Stress Scale (PSS) by Sheldon Cohen **(Annex 5)**. A recent study revealed that, preconception stress increases the risk of infertility (Zaidouni et al., 2018). Accordingly, and after scrutinizing the literature, the researcher acknowledged the importance of exploring the effect of perceived stress on the fertility status of couples and as demonstrated in **Annex (5)**, the scale is formed of 14 questions involving enquiries about major events and their relation to stress in a five-scale set of answers.

After formalizing the instrument, it was reviewed by ten experts and further modification was performed upon their comments, although any errors are my own and should not be related to these esteemed persons. As a final step, a cognitive qualitative testing of the questionnaire was accomplished through iterative pilot work on members from the selected sample, after which the questions' format were optimized and the instrument was explored for its effectiveness and whether it fully achieved the purpose of the study.

3.7 Ethical and administrative considerations

In order to launch this study, an academic approval from the School of Public Health at Al-Quds University was obtained after submitting the study proposal to the research committee for discussion. Subsequently, an ethical approval was obtained from the ethical committee in GS (Helsinki Committee) **(Annex 8)**. In the perspective of commitment to research ethics, the researcher was committed to provide an informed consent along with each questionnaire and guaranteed that each participant was fully aware and fully apprehend each section of the attached consent form, with their clear right to withdraw participation at any time **(Annex 5)**. The consent explained the aim of the study along with clarifying to respondents that their participation is voluntary and their confidentiality will be assured. The respondents were full acquainted with the content of the form and the researcher or the data collectors did not proceed till the former accepted participation willingly. Additionally, an administrative approval was acquired from the director of MoH **(Annex 9)**, as well as the specialists running the IVF centers for the purpose of having access to the institutions' database.

3.8 Study period

The period exhausted for all stages of the study to be conducted was 9 months. It extended from March 2019 till November 2019. Detailed timeline is shown in **Annex (4)**.

3.9 Pilot study

A pilot study is a small study that is conducted in the field in order to examine the study design, the appropriateness of the research instrument and to identify problem areas and deficiencies in the instrument content and structure so that to be amended before data collection process. In this context, a pilot study was conducted using 10% of the projected sample, which included 32 participants. While conducting the study, it showed to help identifying the feasibility of the collection techniques and assessed the researcher and the data collectors to get familiar with the procedure. During the early stages of the pilot, the data collectors faced some problems in guiding and proposing the questions, but then the process was much easier after interviewing the third and fourth subject. Some modifications were performed on the questions' format to suit the local language and invalid inquiries were excluded. Additionally, the pilot study provided a preliminary scope about the way data would be processed and analyzed and whether it fulfills the study objectives or not.

3.10 Data collection

The data was collected by the researcher and well-trained data collectors of medical background. The data collectors have experience and affinity with data collection procedure and with the study population as well. They were provided with sufficient background knowledge about the study and were trained on the research instrument to guarantee standardization, minimize inter-observer variation and eventually assure reliability of the study. A comprehensive training was delivered including the content of the instrument, the way questions are provided, the type of terms and digits used in recording, the technique to compare responses with medical reports or drug prescriptions and the use of show cards and adjuvant tips attached or included in the questionnaire to facilitate accuracy of responses. The researcher performed series of double check on the collected data and joined the data collectors frequently in the field to inspect data as it is recorded and to verify the accuracy of collection process.

3.11 Scientific rigor

Validity

The instrument of the research was reviewed by 10 experts. The experts were epidemiologists, gynecologists, researchers, statisticians and experts working in the field **(Annex 7)**. They were requested to perform content validity to estimate how much the items in each domain are able to measure what intended to be measured and to ensure the instument relevancy. All comments and recommendations were considered for instrument modification, although any errors are of my own and not to be related to these esteemed persons. Additionally, a pilot study was performed, before the data collection process, to detect appropriateness of the instrument and to ensure that the questions were clear enough for respondents to answer. Also, the data collectors were selected upon having high experience and affinity to the procedure and were trained well on the process. A pilot study was performed to examine the study design, the appropriateness of the research instrument and to identify defects and deficiencies in the instrument’s content and structure so that to be amended before data collection process. Finally, medical records related to certain medical conditions and drugs were checked to ensure validity of the provided information.

Reliability

The researcher performed the following steps to ensure reliability:

1- The data collectors were trained on interviewing skills and on how to ask every question in order to standardize and harmonize the process of data collection.
2- The data entry was done only by the researcher and was performed on daily basis to allow reviewing quality of data and any invalid feedback was re-filled.
3- Upon entry of the whole data, re-filling of 5% of the collected data was performed to ensure proper data entry.

3.12 Data entry and analysis

The data entry was performed by the researcher on daily basis. The quality of the data was verified and any invalid questionnaires were refilled by phone calls paid to the related subjects. Upon completing the process, 5% of the data was re-filled to ensure correct entry procedure with minimum errors as much as possible. Before analysis, the data was coded, where required, and was cleaned for any errors or unlogic values. Then, the researcher used SPSS version 22 for data analysis through:

- Descriptive analysis in the form of measures for central tendency, as for marital age, duration of infertility, average monthly income …etc., and measures of variability as for standard deviation and variances.
- Analyzing relationship between categorical variables among cases and control through using cross tabulation method in chi square analysis.
- Exploring relationship between continuous variable, e.g. Marital age and BMI, among cases and control using correlation tests.
- Using independent t-test when examining the relationship between a dependent continuous variable, e.g. years of infertility, with two categorical variables, e.g. employment status, residency, or using ANOVA test when three or more independent categorical variables are intended to be analyzed.
- Predicting risk factors associated with infertility using binary logistic regression analysis.

3.13 Limitation of the study

- Being a retrospective study, recall biases were particularly expected especially when investigating events that occurred in the past. The researcher attempted to minimize this type of bias by verifying information given with a reliable third party or with other trustworthy sources, e.g. medical records.
- Also, response bias was expected specially regarding responses to stress exposure as many people try to appear mentally healthier through masking their actual symptoms. This is one of the challenges that faced the researcher and the data collectors which was avoided by using a high-quality questionnaire and through ensuring that the interviewers are well trained.
- The population of the cases represents only infertile couples who are/used to attend IVF centers seeking medical treatment. People suffering from primary infertility who did not seek medical advice were not included.
- Scarcity of statistical data regarding primary infertility in GS. All recent health reports published by the main health provider (MoH) contain data and indicators related to the WB only, while no data is available that supports prevalence and distribution in GS.
- The research was unable to perform comparative analysis in certain areas of the findings and results due to the scarcity of research in this field conducted in Palestine.
- Tubal factors of infertility were not possible to be measured or scrutinized in this study. All cases were selected from IVF centers and specialists in these centers prefer to provide IVF module once couples were confirmed as infertile with irreversible or idiopathic causes before excluding tubal factors to avoid their exposure to invasive techniques twice, one for exploring tubal causes and the other for fertilization.

Chapter Four

Findings and Discussion

This chapter provides an overview of the findings concluded from this study. The findings were reached after collecting data, through an interviewed questionnaire **(Annex 5)**, from 160 infertile women attending IVF centers (cases) and from another matched 160 fertile women visiting governmental PHC clinics (controls) for receiving MCH services. Data about husbands were collected from both cases and controls. Then, comparative description and inferential statistics were used to outline the main risk factors believed to have causal relationship with primary infertility.

First, in this chapter, the study population is described in terms of their demographic distribution in which the results have also been included among the main risk factors causing infertility. Then, socioeconomic, environmental and medical variables are explored. Lifestyle differences between fertile and infertile groups are outlined including dietary habits, smoking, physical activity and exposure to stress. For results to be conceptually grounded, whenever applicable, comparative analysis has been used.

4.1 Demographic situation

The first section in this chapter is discussing, in-depth, the demographic situation of the surveyed population and its relation to primary infertility in the context of GS. Several variables were selected to describe the overall demographic variability between the two groups, which will eventually explore possible association that would shed light on potential risk factors. As illustrated in **Table (4.1)**, various demographic variables are analyzed including the geographic location of couples in terms of locality or camps, age of both the female and male participants, marital age of women, refugee status of couples, family type before and after marriage along with household size before and after marriage and birth order of the wife and the husband in the family of origin. The variables are classified into subthemes and each subtheme is accompanied by detailed analyses and discussion.

Table (4.1): Distribution of study population by demographic characteristics (N=320)

Demographic profile		Cases		Controls		Total (%)	χ^2	P-value
		No	%	No	%			
Age (Years)	< 30	87	54.4	71	44.4	158 (49.4)	3.201	0.074
	≥ 30	73	45.6	89	55.6	162 (50.6)		
	Mean	29.80		30.49		30.15	t= 1.125	0.261
	SD	6.178		4.761		5.518		
Husband's age	< 30	47	29.4	27	16.9	74 (23.1)	7.031	*0.008
	≥ 30	113	70.6	133	83.1	246 (76.9)		
	Mean	35.68		34.89		35.28	t= 0.821	0.413
	SD	10.265		6.295		8.511		
Age difference between couples	≤ 10	136	85.0	149	93.1	285 (89.1)	5.422	*0.020
	> 10	24	15.0	11	6.9	35 (10.9)		
Marital age	< 18	23	14.4	27	16.9	50 (15.6)	20.001	**<0.001
	18-28	109	68.1	129	80.6	238 (74.4)		
	≥ 29	28	17.5	4	2.5	32 (10.0)		
	Mean	22.79		20.61		21.70	t= 3.892	**<0.001
	SD	6.187		3.418		5.108		
Geographical area - Camps	Inside camps	50	31.2	52	32.5	102 (31.9)	0.058	0.810
	Outside camps	110	68.8	108	67.5	218 (68.1)		
# Geographical area - Location	Downtown	105	52.5	122	60.1	227 (56.3)	4.381	*0.036
	Agricultural	27	13.5	26	12.8	53 (13.1)	0.023	0.880
	Near borders	57	28.5	35	17.2	92 (22.8)	7.384	*0.007
	Coastal	11	5.5	20	9.9	31 (7.7)	2.893	0.089
Refugee status	Refugee	112	70.0	94	58.8	206 (64.4)	4.415	*0.036
	Nonrefugee	48	30.0	66	41.3	114 (35.6)		
Family type	Nuclear family	107	66.9	127	79.4	234 (73.1)	6.361	*0.012
	Extended family	53	33.1	33	20.6	86 (26.9)		
Family type before marriage	Nuclear family	133	83.1	125	78.1	258 (80.6)	1.128	0.258
	Extended family	27	16.9	35	21.9	62 (19.4)		
Husband's family type pre- marriage	Nuclear family	120	75.0	132	82.5	252 (78.7)	2.689	0.101
	Extended family	40	25.0	28	17.5	68 (21.3)		
Household size	< 3	100	62.5	5	3.1	105 (32.8)	128.509	**<0.001
	3-10	57	35.6	142	88.8	199 (62.2)		
	> 10	3	1.9	13	8.1	16 (5.0)		
Household size before marriage	≤ 6	11	6.9	21	13.1	32 (10)	3.970	0.137
	7-10	95	59.4	83	51.9	178 (55.6)		
	> 10	54	33.7	56	35.0	110 (34.4)		
	Mean	9.87		9.69		9.78	t= 0.622	0.535
	SD	2.560		2.655		2.605		
Household size of husband's family before marriage	≤ 6	31	19.4	20	12.5	51 (15.9)	4.433	0.109
	7-10	79	49.4	75	46.9	154 (48.1)		
	> 10	50	31.2	65	40.6	115 (35.9)		
	Mean	9.26		9.94		9.60	t= 1.983	*0.048
	SD	3.042		3.105		3.087		
Birth order in original family	1^{st} - 3^{rd} sibling	76	47.5	78	48.7	154 (48.1)	0.064	0.969
	4^{th} – 6^{th}	54	33.7	52	32.5	106 (33.1)		
	≥ 7^{th}	30	18.8	30	18.8	60 (18.8)		
Birth order of husband in original family	1^{st} - 3^{rd} sibling	97	60.6	96	60.0	193 (60.3)	6.058	*0.048
	4^{th} – 6^{th}	40	25.0	53	33.1	93 (29.1)		
	≥ 7^{th}	23	14.4	11	6.9	34 (10.6)		

* Significant at $p < 0.05$, **Highly significant at $p < 0.001$

Some subjects were specified in more than one location e.g.: Living in agricultural area and near border

4.1.1 Geographical location:

The population selected for this study are 320 participants in total and are divided into two groups, one with the intended medical condition to be studies (160 cases) and another known to be free from such condition (160 controls). To guarantee randomization, selection of cases across GS was based on the breakdown of total female population in reproductive age per governorate according to the results obtained from the 2017 Palestinian Census (PCBS, 2018[d]). As shown in **Figure (4.1)**, 33 cases were selected from North Gaza, 55 cases from Gaza, 20 cases from Middle area, 32 cases from Khan Younis and 20 cases from Rafah, which represent 20.6%, 34.4%, 12.5%, 20% and 12.5% of the study population respectively. This distribution is almost congruent with the Palestinian population distribution of females in reproductive age by governorate which is illustrated in the last Palestinian Census and that represent 19% in North Gaza, 34% in Gaza, 15% in Middle area, 20% in Khan Younis and 12% in Rafah. The cases were matched with a control group of fertile females according to their residency status per governorate and were approached within governmental PHC clinics in each governorate. Controls distribution per governorate are 33 from North Gaza, 55 from Gaza, 20 from Middle area, 32 from Khan Younis and another 20 from Rafah.

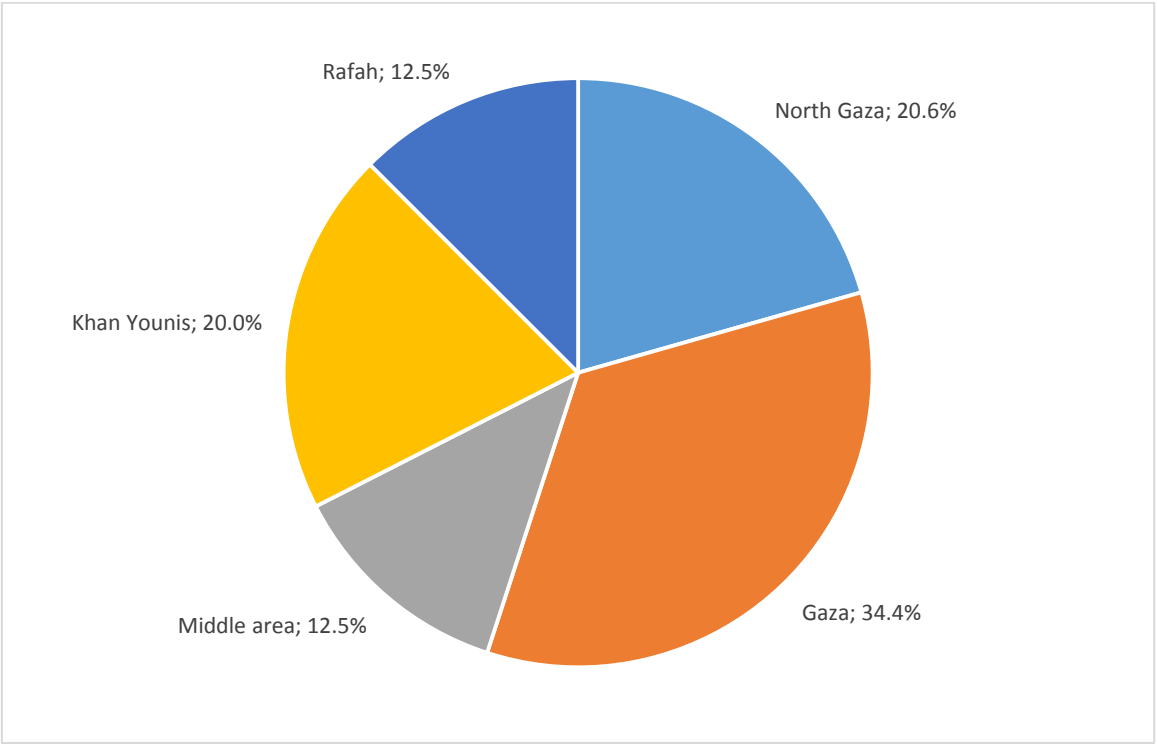


Figure (4.1): Demographic distribution of study population per governorate; Cases

To study main geographical risk factors, the study population was assessed for their location in different areas and how spatial variation in distribution can be related to the condition under investigation. As shown in **Figure (4.2)**, 105 cases are living downtown, 27 in agricultural areas, 57 near borders and 11 are living along the Mediterranean Sea coast, comparing to 122, 26, 35 and 20 controls respectively. The main variation is among people who live near borders; **(Table 4.1)** as they appear to be 1.97 times more likely to have primary infertility than those living in other areas apart from northern, southern or eastern borders, OR = 1.97 (95% CI, 1.20-3.24, p = 0.007). Most of the citizens living near borders are usually at risk of exposure to military attacks from the Israeli soldiers like, tear gases and bombardments. Poverty, education status and limited access to health care could be other causes that need more analysis, some of which are discussed later on in this study. On the other hand, of all 56% of surveyed population who live downtown, about 42% were cases compared to 58% controls with no significant difference between the two groups. Also, almost the same frequency of cases and control are detected to be living in agricultural areas, while 5.5% and 9.9% of each group respectively reported being living at the Mediterranean Sea coast.

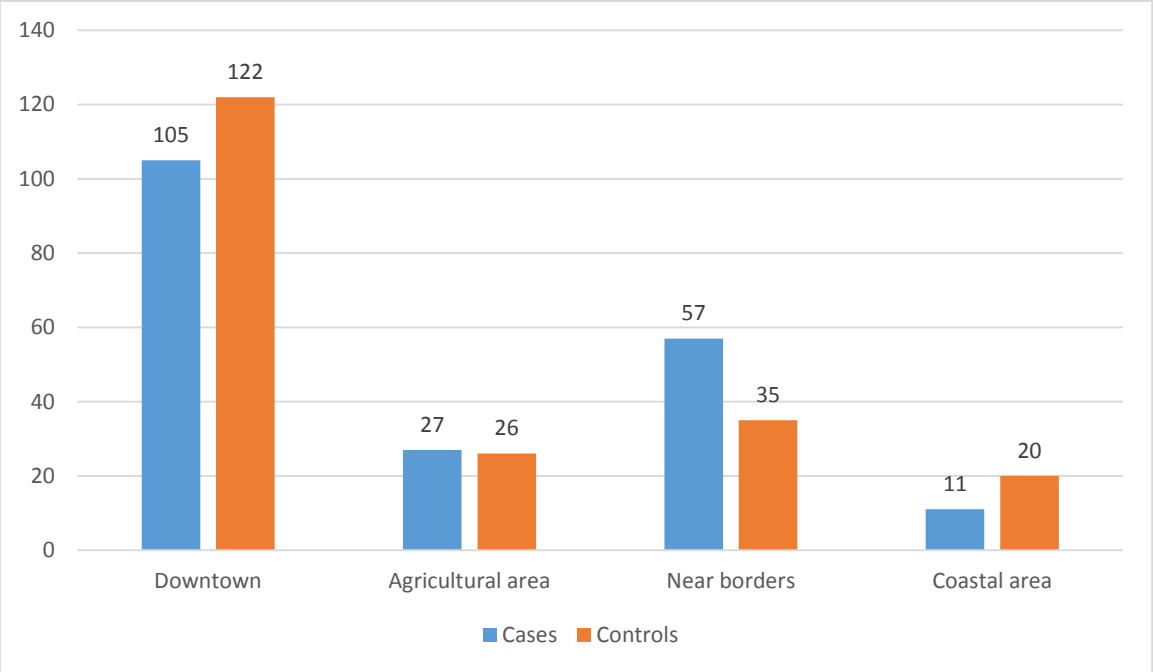


Figure (4.2): Demographic distribution of study population per geographical area

4.1.2 Age pattern of infertility:

Of all 320 participants, the age of female respondents in the two categories; below and above 30 years age; shown in **Table (4.1)** are almost equal, providing a distribution of 49.4% and 50.6% respectively. Performing more analysis revealed differences among and between the two groups, where 87 female cases, representing 54.4% of the total cases, reported to be younger than 30 years age compared to 71 females forming 44.4% of the total participants in the control group. Females above or equal 30 years age are 73 (45.6%) for cases and 89 (55.6%) for controls. Although the difference between the two groups is apparent, the association did not reach a statistically significant level, χ^2 (1, N = 320) = 3.20, p = 0.074. Searching in the literature revealed that, many studies have suggested the probability of female age as a risk factor associated with primary infertility. A cross-sectional study in Scotland that comprised 7172 women, confirmed that there the female age is significantly related to the cause of infertility. Women beyond the age of 35 were two times more likely of having tubal factor infertility than women below 30 years age, OR = 2.2 (95% CI, 1.7-2.7), and also the odds of being idiopathically infertility increased by 80% at the age of 35 and beyond compared to women less than 30, OR = 1.8 (95% CI, 1.4-2.2) (Maheshwari, Hamilton, & Bhattacharya, 2008). Another recent study was performed with the participation of 206 females known to have infertility revealed that tubal factor among females increases by the increase of women's age, $p < 0.001$ (Kafeel, 2012). On the contrary, a prospective cohort study conducted in seven European centers, including a sample of 782 couples, concluded that the chance of becoming pregnant decreases by age but the overall rate of sterility is not affected (Dunson, Baird, & Colombo, 2004)

Correspondingly, the picture for the respondents' husband age is completely different. Among all responses, most of the husbands are noticed to be beyond the age of thirty (76.9%, range 22-73). This may indicate that the marital age of women is much lower than that of men. However, the husbands in the group of cases are much younger than thirty (29.4%) than those in the control group (16.9%) and the way around where 70.6 % of cases are above or equal thirty years age comparing to 83.1% of controls. While the mean age of husbands in the group of cases (35.68 ± 10.26) and that of the controls (34.89 ± 6.29) shows no difference, the association between the two groups reached a statistically significant level, χ^2 (1, N = 320) = 7.03, p = 0.008. Findings are quite similar to a cross-sectional study that was conducted in 2011 in WB. The study found that the mean age of

723 men suffering from primary infertility was 32.7 ± 6.76 with a range from 20 to 77 (Al-Haija, 2011).

Another interesting observation noticed in this section is the age gap between couples. The mean of age difference between couples in cases (5.88, range -6 to 31) is less than that of the controls (4.40, range -1 to 15). The difference here reached statistically significant level, $t = 2.53$, $p = 0.01$. In addition, the age gap among couples in the cases group increase by the increase in husband's age as illustrated in **Figure (4.3)** ($r = 0.82$, $p < 0.001$), giving a strong positive correlation between the husband's age and the spousal age difference. An explanation that could be applied in this situation, is the presence of polygynous marriage among infertile couples which occurs usually when conceiving is delayed upon the first marriage. The percentage of polygynous marriage among all married women age 15-49 years in GS is 6 % (PCBS, 2014). However, literature had supported the relationship between age gap among couples and infertility in only one study. A cross sectional study that was published in 2016 indicated that, the age gap between couples is significantly related to sexual dysfunction (OR = 1.43, 95% CI, 1.21-1.82, $p = 0.004$) (Tokmak et al., 2016). But relating spouse age difference to fertility rate, some researchers in Bangladesh observed that fertility rate decreases with the increase in the age gap between couples after analyzing 117,000 birth registers in 132 villages (Stoeckel & Chowdhury, 1984).

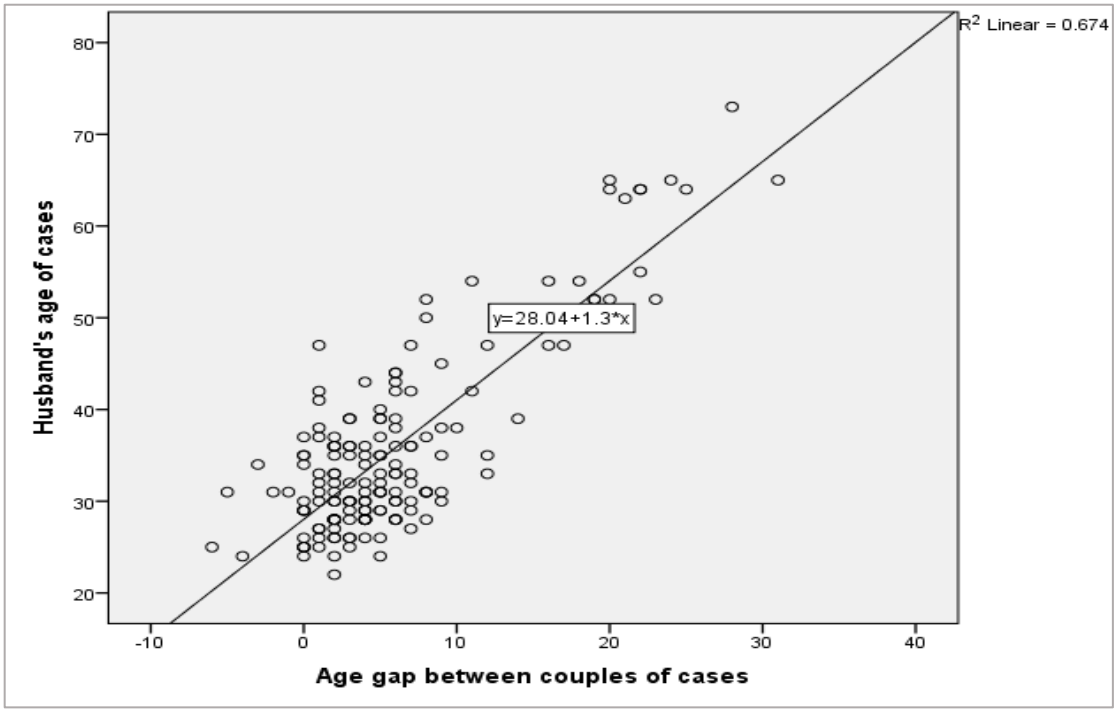


Figure (4.3): Relationship between husband's age and the spousal age gap (cases)

4.1.3 Marital age:

Overtime, Gaza has witnessed marked decline in the rate of early marriage among females. According to PCBS, the percentage of early marriage (less than 18 years age) among 20-24 years age married women has decreased from 31.7% in 1997 to reach 13.8% in 2017 (PCBS, 2019[a]). In this study **(Table 4.1)**, 15.6% of all participants reported a marital age of less than 18 years age; 23 representing 14.4% of total female cases compared to 27 forming 16.9% of those of the control group. Of all surveyed population, Gaza and North Gaza have the major proportion of early marriage, 48% and 22% respectively, while early marriage is found in only 10% of the participants for each of Rafah, Khan Younis and Middle area **(Figure 4.4)**. Contradicting to global trends, early marriage in Palestine is more common in urban than in rural areas. PCBS findings at the end of 2016 reported that, the highest rate of early marriage was in Gaza (42.1%) and the lowest was in Dier Al-Balah (7.1%) (PCBS, 2019[a]). In the same context, Sirdah et al. (2013) found that subfertility is more common in urban areas than rural localities, $p < 0.001$. This could be related to the financial and physical insecurity among families with multiple daughters, especially after the exposure to three consecutive hostilities, which can explain why some families favour early marriage. Moreover, the preservative traditional customs prevailing in GS along with lack of clear legal framework that determines the legal age of marriage for boys and girls, are among the main causes behind early marriage in our context.

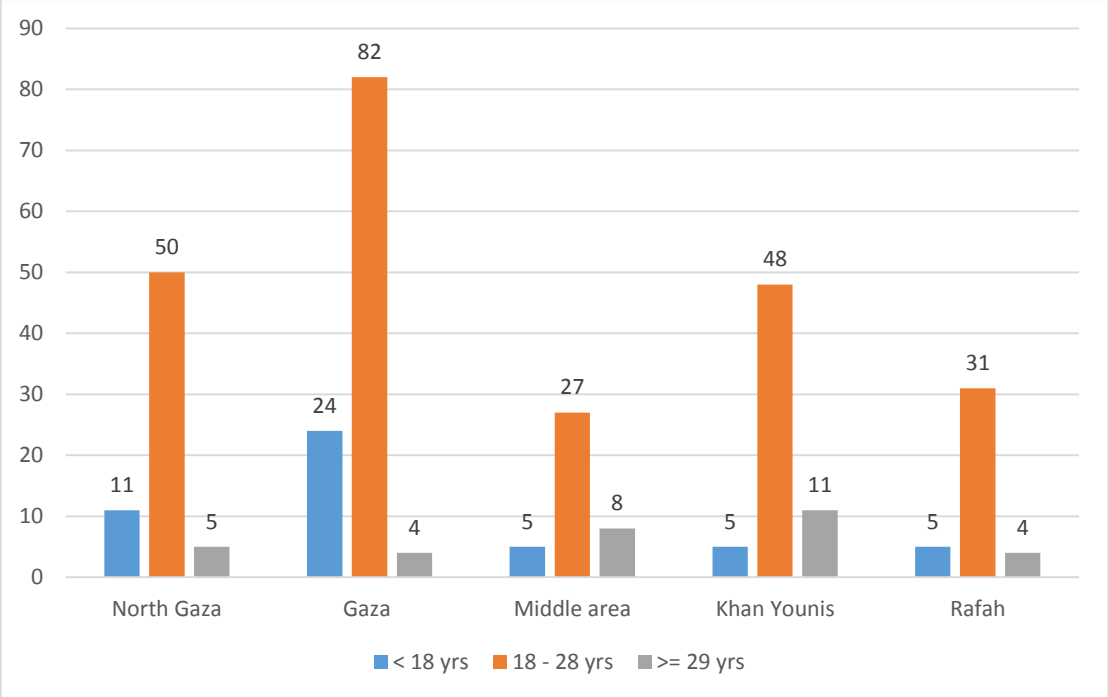


Figure (4.4): Marital age distribution according to governorate – N=320

Large proportion of the surveyed population reported a marital age between 18- and 28-years age; 109 (68.1%) cases and 129 (80.6%) controls. The marked difference appears in marital age beyond or equal the age of 29, where 28 (17.5%) cases compared to only 4 (2.5%) controls were married after their 29th birth date. A two-way contingency table was conducted to explore the relationship between marital age in three levels (< 18, 18-28 and ≥ 29) and fertility status demonstrated in cases and controls. The results showed significant association, χ^2 (2, N = 320) = 20.001, p < 0.001. Here, the association is considered strong, Cramer's V = 0.25, p < 0.001, in which using adjusted residuals revealed that people married beyond or equal the age of 29 years make most of the contribution to such association. The presence of this association might be due to what was revealed by many studies, as mentioned later, that tubal factors are the main causes of infertility among women older than 35 years age. Tubal causes of infertility usually occur as a result of gonorrheal or chlamydial infection (Moodley et al., 2002). Taking all that into consideration, along with the conservative nature of Arab societies, oblige young females to be restricted from receiving early health education and management to genitourinary issues before marriage. Accordingly, targeting adolescents and young females to be among awareness and reproductive health education campaigns shall be extremely helpful.

4.1.4 Refugee status and camps:

Palestine, and in particular GS, has a unique demographic context. The population who are living in a small geographical area are divided in to two groups; refugees and non-refugees; and are affected with different social determinants that may affect their health through different perspectives. According to PCBS (2019^{b}), refugees constitute about 64% of total population in GS. Out of all refugees in GS, 41.8% live in camps where the minimum life requirements are limited (UNRWA, 2019). In this study **(Table 4.1)**, 64.4% of the surveyed population are refugees, while 35.6% constitute the non-refugee group. From all 206 refugees, 82 (39.8%) live inside camps and almost more than half of them (54.4%) are infertile. Although living inside or outside camps did not make difference on the outcome, χ^2(1, N = 320), 0.058, p = 0.81, but being a refugee increases the risk of infertility by 64%, (95% CI, 1.03 – 2.60, p = 0.036). But at the same time, we must also consider that, reporting living outside camps as a current event, does not exclude spending childhood and adolescence period in camps.

4.1.5 Family type before and after marriage:

Among the queries that have been included in the study questionnaire, the participants were asked to provide information about their current family type and which family type they used to live with before marriage (**Table 4.1)**. The respondents were asked to describe their families as either nuclear or extended family. A nuclear family is composed of both parents and their siblings, while extended families refer to grandfathers, grandmothers, uncles, aunts and cousins in addition to the members of the nuclear family.

As a matter of fact, the Palestinian National Census for 2017 declared that 85.7% of total population in GS live in nuclear families, while people living in extended families represent 14.1% (PCBS, 2018[d]). Notably, responses of cases regarding their family type before marriage (83.1% nuclear, 16.9% extended) revealed to be very near to what has been announced in the national census, which is quite different from those of the fertile women (78.1% nuclear, 21.9% extended). However, the relationship between the two groups did reach statistically significant level, $p = 0.258$. The family type of husbands before marriage also did not make an effect on the infertility outcome ($p = 0.101$), where 75% of the cases' husbands lived in nuclear families and 25% lived in extended ones comparing to 82.5% and 17.5% of the control group respectively.

But what has been noticed remarkably is that, after marriage the fertile women's family type did not change (79.4% nuclear, 20.6% extended) than before marriage, while almost double the cases (66.9% nuclear, 33.1% extended) had shifted to be living with extended families after marriage, giving a risk of living with an extended family and being infertile 1.9 times more likely than when living independently, (95% CI, 1.15 – 3.16, $p = 0.012$). The increasing proportion by time, largely reflects the difficult economic conditions of families. Also, rising unemployment might have forced married couples to be unable to live independently. Moreover, the mean marital duration for the surveyed cases is about 7 years, which is the time period after which the region has been exposed to multiple hostilities, where a lot of families have been internally displaced and eventually might be sharing the same house. Upon reviewing literature, no studies were noticed to explore the family structure and how it influences fertility rate and pattern in various societies and settings. Accordingly, such area is worth further in-depth investigation to analyze more the future consequences of such phenomena.

4.1.6 Household size:

Another basic demographic characteristic that reflects the family structure and its effect on its members' health is the family size. Confirming to what previously mentioned about the relatively high percentage of extended families among infertile couples, 60 cases (37.5%) reported a household size after marriage of more than three, indicating that more than third of the surveyed couples known to have primary infertility actually live in extended families **(Table 4.1)**. On the other hand, and of all 160 cases, only 11 (6.9%) reported household size before marriage of less than seven, 95 (59.4%) reported a range from seven to ten and 54 (33.7%) used to live in a house with more than ten inhabitants. The control group showed almost the same distribution of 21 (13.1%), 83 (51.9%) and 56 (35%) respectively. The relationship between the two groups did not reach a statistically significant level, p = 0.137.

Responses related to husband's household size before marriage did not differ much from that of the females' responses in the study, which extended from low of 15.9%, with less than 7 members per family, to high of 48.1% with range of 7 to 10 members.

4.1.7 Birth order in original family:

Some studies indicated the effect of birth order during childhood and its effect on the fertility status of an individual (Morosow & Kolk, 2019). As shown in **Table (4.1)**, the 320 female participants showed almost the same frequency of birth order in both cases and controls. Birth order of 1st to 3rd constitutes 76 cases and 78 controls. Being the 4th, 5th or 6th in the family rank were among 54 and 52 respectively and 30 were born as the 7th or more sibling in the family of origin in both groups. There is no association detected between the two groups, p = 0.969. On the contrary, male participants presented higher differences. Among all husbands, 97 of the cases group and 97 of the control group were born as the 1st to the 3rd sibling and 40 compared to 53 respectively were born as the 4th, 5th or 6th sibling. The main difference is among the third category, where 23 (14.4%) of the cases group were the 7th or more sibling, while controls were only 11 (6.9%), OR= 2.77 (95% CI, 1.21-6.34, p = 0.048). From the 23 husbands born as the 7th or more sibling, the cause of infertility was related to male factor among 74% of them. This could be explained and related to childhood exposure to poverty, under-education and child labour, which are usually accompanied by large family sizes mainly in a context like GS.

4.1.8 Relationship between infertility and various demographic variables:

Several demographic risk factors were identified in the above section as having a statistically significant association with primary infertility. Marital age of participant ladies, age of husbands, refugee status of couples, family type after marriage and birth order of the husband are among these risk factors that might interact and affect each other. Hence, the covariance among these variables and the possible confounding effect will be resolved by using logistic regression analysis. The following **Table (4.2)** demonstrates the regression model's results followed by a brief analysis about the main findings.

Table (4.2): Predictors of primary infertility among demographic variables using binary logistic regression

Demographic variables	***β***	***S.E.***	**Wald χ^2**	***p-value***	***Odds Ratios (95% CI)***
Women's marital age (continuous)	0.112	0.029	15.353	**<0.001	1.12 (1.06-1.18)
Husband's age (continuous)	-0.017	0.016	1.081	0.298	0.98 (0.95-1.02)
Refugee status of couples (Refugee = reference)	0.460	0.247	3.459	0.063	1.58 (0.98-2.57)
Family type after marriage (Extended = reference)	0.757	0.270	7.893	*0.005	2.13 (1.26-3.62)
Birth order of husband (continuous)	0.091	0.047	3.714	0.054	1.10 (0.10-1.20)
Constant	-2.641	0.701	14.202	**<0.001	0.071

β=beta coefficient, S.E.=standard error, χ^2=chi square, CI=confidence interval, Model coefficient chi^2=31.39, p<0.001, Nagelkerke r^2=0.125, Membership for cases, *significant=p<0.05, **highly significant=p<0.001

The age at which females get married shows to affect the outcome remarkably. As shown above, the increase in female's marital age increases the odds of being primary infertile by 12%. Providing that, the tubal factor is among the most common causes of infertility in females and that it is usually attributed to recurrent chlamydial infection at young age (CDC, 2018), this would highlight the importance of providing comprehensive reproductive health services at early life stages that involve adolescents and young adults. Moreover, couples living in extended families after marriage are twice more likely to be infertile than those who live independently. Living in extended families may indicate that, couples have limited free will to practice socially and economically pattern of life, which in turn has the possibility of being physiologically and psychological disabled in the larger society.

4.2 Socioeconomic variabilities

Social and economic status usually refer to a person's position in the community. Different levels may have notable psychological and physical consequences on both the individual and the society as a whole (Wang & Geng, 2019). Proceeding from this conclusion, various socioeconomic variables have been explored in this study to measure individual's or family's economic and social position in terms of education, employment, housing unit and income. The variables selected are analyzed and examined against their relationship to primary infertility and also several self-explanatory graphs are used for further clarification when applicable.

4.2.1 Education level and household income:

Socioeconomic disparities in health have been long attracting the attention of researchers and policy makers (Adler & Newman, 2002). As a major component, education is a socioeconomic element that determines a person's professional attainment and future prosperity. Linking education to income and eventually to health will be always among the main concerns that public health professionals strive to achieve. Undoubtedly, Palestine is ranked among the countries with the highest literacy rate in the world. In 2017, PCBS reported an illiteracy rate of 3.3% of total Palestinian population aged 15 years and older (PCBS, 2018[c]). In this study and from all surveyed population **(Table 4.3)**, zero subjects reported to be unable to read and write although PCBS announced an illiteracy rate of 0.6% among people aged 15-29 and a rate of 1.3% among 30-40 years age population. Additionally, female participants of the cases group showed that 7 (4.4%) of them had preparatory or less as education, 59 (36.8%) managed to finish high school and 94 (58.8%) had a university degree or more. The control group had almost the same figures of (10) (6.3%), 62 (38.7%) and 88 (55%) respectively. The relationship between the two groups did not show statistically significant association.

Table (4.3): Distribution of study population in relation to education and household income and expenditure; socioeconomic variables part 1; (N=320)

Socioeconomic variables (Part 1)		**Cases**		**Controls**		**Total (%)**	χ^2	**P-value**
		No	**%**	**No**	**%**			
Years of schooling (Female)	Preparatory or less	7	4.4	10	6.3	17 (5.3)	0.802	0.670
	High school	59	36.8	62	38.7	121 (37.8)		
	University or PG	94	58.8	88	55.0	182 (56.9)		
Years of schooling (Male)	Preparatory or less	22	13.8	28	17.5	50 (15.6)	2.552	0.279
	High school	55	34.3	63	39.4	118 (36.9)		
	University or PG	83	51.9	69	43.1	152 (47.5)		
Average monthly income (NIS)	≤ 1500	127	79.4	118	73.8	249 (77.8)	8.690	*0.013
	1500-2500	16	10.0	33	20.6	45 (14.1)		
	> 2500	17	10.6	9	5.6	26 (8.1)		
	Mean	1209.69		1211.56		1210.63	t=0.017	0.986
	SD	916.76		1006.98		961.42		
Average monthly spending on food items (NIS)	< 300	42	26.3	39	24.4	81 (25.3)	1.200	0.549
	300-500	74	46.2	68	42.5	142 (44.4)		
	≥ 500	44	27.5	53	33.1	97 (30.3)		
	Mean	483.75		499.69		491.72	t=0.414	0.679
	SD	367.96		318.43		343.64		
Average monthly spending on non-food items (NIS)	< 300	90	56.3	75	46.9	165 (51.6)	2.946	0.229
	300-500	44	27.5	51	31.9	95 (29.7)		
	≥ 500	26	16.2	34	21.2	60 (18.7)		
	Mean	346.06		395.63		372.27	t=1.180	0.239
	SD	357.12		348.24		200.00		
Major group of household expenditure	Food & Drink	73	45.6	124	77.5	197 (61.6)	71.206	**<0.001
	Medical care	66	41.3	5	3.1	71 (22.2)		
	Loans & Depts	10	6.3	23	14.4	33 (10.3)		
	Rent/Utilities	11	6.9	8	5.0	19 (5.9)		

* Significant at $p < 0.05$, **Highly significant at $p < 0.001$

Comparatively **(Table 4.3)**, women in this study have higher educational attainment than men in both groups. Comparing to what mentioned previously, males with preparatory or less years of schooling form 13.8% of all cases and 17.5% of those in the control group, while 34.3% and 39.4% respectively have completed high school only and did not achieve a university degree. The only difference noticed, is among men who have succeeded to obtain a university degree or more, where the proportion is more among cases (51.9%) than controls (43.1%). But this should be considered with caution, because the group of cases was selected only from the population who have attended IVF centers, while

ignoring those who did not afford such treatment. Conclusively, the relationship between the two groups also did not reach a statistically significant level. Upon reviewing literature, several researches were found trying to explore the relationship between education and infertility. A cross sectional survey that was held in Maryland USA found that, tubal causes of infertility were highly associated with low educated and low-income earners of African American and Hispanic women compared to Caucasian ones (p<0.01) (Jain, 2006). Another study compared the risk of female sexual dysfunction with their owns' and their husband's educational level. Assessment of 604 infertile women from twelve IVF centers in Iran revealed an increased risk among this category of females than those with higher education level (Pakpour, Yekaninejad, Zeidi, & Burri, 2012).

Out of all 320 couples, more than three quarters (76.6%) gain less than 1500 New Israeli Shekel (NIS) on monthly basis. The proportion of cases (79.4%) earning less than 1500 NIS is quite more than controls (73.8%), while 10% of cases compared to 20.6% controls earn between 1500 and 2500 NIS per month. Additionally, couples who have more than 2500 NIS as an average monthly income are reported to be more among cases (10.6%) than controls (5.6%). Conclusively, there is a statistically significant association between the groups, $\chi^2(2, N = 320)$, 8.690, $p = 0.013$, explaining that people with more skills, knowledge and eventually professional attainment usually gain better opportunity to have access to information and resources.

In the same context **(Table 4.3)**, performing further analysis revealed that men in the group of cases have lower chance to be employed in relation to their education degree, $r_s = 0.425$, $p < 0.001$, than men in the control group, $r_s = 0.514$, $p < 0.001$. On the other hand, the employment of infertile women shows negligible correlation with their level of education, $r_s = 0.264$, $p = 0.001$, comparing to those of the control group, $r_s = 0.335$, $p < 0.001$. This might indicate that loosing chance in employment after exerting effort in gaining an academic degree could be indirectly related to the fertility status of an individual. However, these results are confirmed by what has been stated through PCBS (2019[a]) that there is still a gap between women participation rate in labour force (21%) and men (72%). A study in Michigan revealed a contradictory result, where age was the only factor affecting infertility and women's education and income did not appear to affect her chance to get pregnant (Rapaport, 2019). Although, another study performed in china, exploring the cultural, society and needs for reproductive health counselling, confirmed that prevalence of infertility is higher among the least educated and those with low income (Logan, Gu, Li, Xiao, & Anazodo, 2019).

The largest proportion of the surveyed population spend 300-500 NIS monthly on food items. 26.3% of infertile couples spend less than 300 NIS per month, while 46.2% spend from 300-500 NIS. Less than third of total cases (27.5%) spend more than 500 NIS per month on groceries. Couples of the control group shows the same range of 24.4%, 42.5% and 33.1% respectively. Correspondingly, people tend to spend less on non-food items. Nearly half of the infertile couples spend less than 300 NIS on non-food items, while 27.5% spend 300-500 NIS and only 16.2% pay more than 500 NIS monthly. Fertile couples show a quite similar range of 51.6%, 29.7% and 18.7% respectively. The association of both variables did not reach a statistically significant level.

Interestingly, medical care is noticed to be the second major group of monthly household expenditures among infertile couples (41.3%), while loan and depts occupied the second major group among controls (14.4%) **(Figure 4.5)**. This might indicate an additional burden of medical expenses that would contribute more to the psychological, social and cultural constrains any infertile couples would face. As a matter of fact, it is worth to mention that the manifestation of medical care among responses shall be considered as a result rather than being a cause. Rents and utilities form the smallest contribution in the major expenses for both cases (6.9%) and controls (5%) with little difference between the two groups. The major group of household expenditure variable among cases and control reached a statistically significant level, $\chi^2(3, N = 320), 71.20, p < 0.001$.

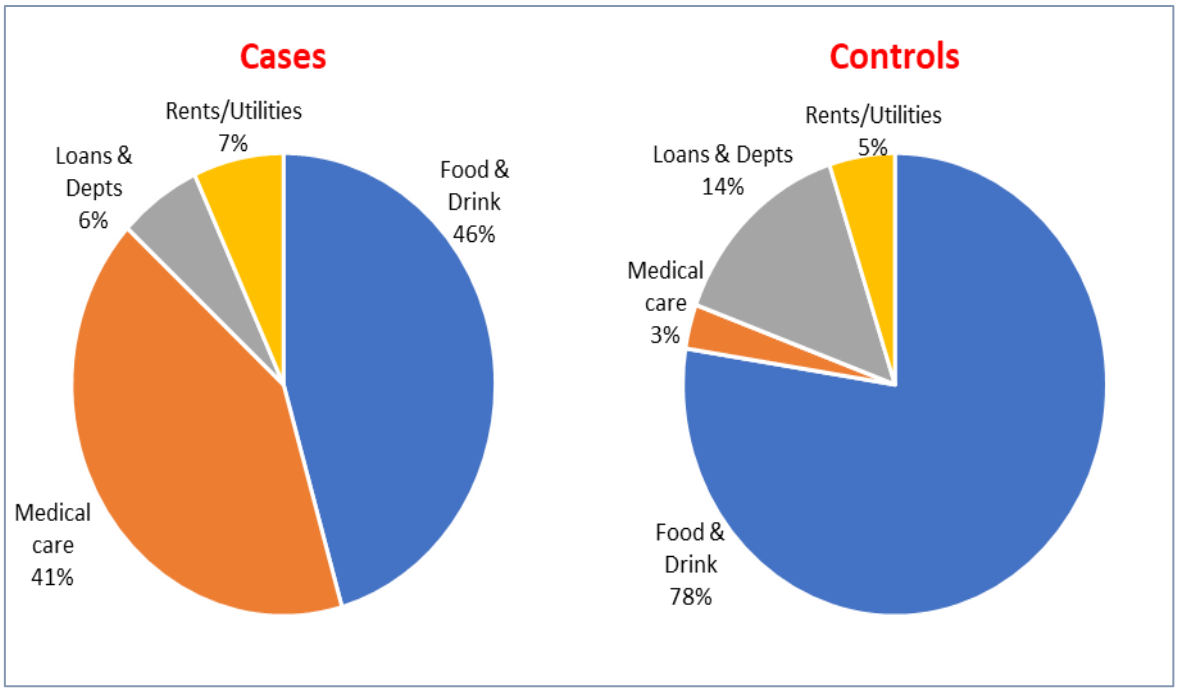


Figure (4.5): Major groups of monthly household expenditure – cases vs controls

4.2.2 Employment:

The second socioeconomic variable explored in this study is the employment status of the surveyed population **(Table 4.4)**. Results show that, more than two third of female respondents (83.1%) are unemployed. Specifically, more female cases are unemployed than controls, where 23 (14.4%) cases practice a daily job comparing to 31 (19.4%) females in the control group, while 137 (85.6%) and 129 (80.6%) respectively do not have jobs. Although the difference between the two groups is quite apparent, but the difference did not reach a statistically significant level. Confirming to what has been reached, a study that was held in Iran on 370 infertile women revealed that, there is no significant association between employment and depression and reasons of infertility (Ramezanzadeh et al., 2004). Moreover, a study found that infertility is neither associated with employment nor with income, but a significant relationship was confirmed with the education level in a 580 female surveyed population (McQuillan, Greil, White, & Jacob, 2003). However, other cohort study that was performed using 140 million birth records in the United States reached controversy results. To examine the long term effect of unemployment on fertility, researchers followed women who remained childless till the age of 40 and found that 14.2 conceptions / 1000 women were lost for every one percentage increase in unemployment (Currie & Schwandt, 2014). The controversy results that has been reached may provide an opportunity for further scrutinizing this area.

Husbands of the surveyed population have more chance in professional life than their wives. Two third of the cases' husbands (75%) hold a daily job compared to the husbands of the controls (66.8%) **(Table 4.4**). This might be because, the cases were selected from the people who can afford treatment in IVF centers, while ignoring those who cannot. However, the relationship here is not statistically significant.

Health and occupation are rather a complicated issue depending on one's perspective about what is significant to be explored. The association could be as simple as being employed or unemployed since who are employed seem to have better health than unemployed ones (Ross & Mirowsky, 1995), if the psychological aspect is taken in to consideration. Otherwise, other perspectives, such as the type, duration and rhythm of the job, would be appropriate to be scrutinized more through the causal effects against health. In this study **(Table 4.4)**, some aspects have been investigated, including the field in which the respondents work, pattern of job shifts and time spent during working. These variables are examined in relation to infertility and findings has been reached as illustrated below:

Table (4.4): Distribution of study population in relation to employment status; socioeconomic variables part 2; (N=320)

Socioeconomic variables (Part 2)		Cases		Controls		Total (%)	X^2	P-value
		No	%	No	%			
Employment (Female)	Yes	23	14.4	31	19.4	54 (16.9)	1.426	0.232
	No	137	85.6	129	80.6	266 (83.1)		
Employment (Male)	Yes	120	75.0	110	68.8	230 (71.9)	1.546	0.214
	No	40	25.0	50	31.3	90 (28.1)		
Work field (Female)	Professionals	19	82.6	15	48.4	34 (63.0)	Fisher exact	*0.012
	Technicians & Associate professionals	4	17.4	16	51.6	20 (37.0)		
Work field (Male)	Professionals	36	30.0	34	30.9	70 (30.4)	0.068	0.966
	Technicians & Associate professionals	45	37.5	42	38.2	87 (37.8)		
	Elementary occupations & craft workers	39	32.5	34	30.9	73 (31.7)		
Work shift (Female)	Night & rotation	8	34.8	3	9.7	11 (20.4)	Fisher exact	*0.039
	Morning	15	65.2	28	90.3	43 (79.6)		
Work shift (Male)	Night	13	10.8	15	13.6	28 (12.2)	0.473	0.790
	Rotation	49	40.8	42	38.2	91 (39.6)		
	Morning	58	48.3	53	48.2	111 (48.3)		
Working hours /week (Female)	< 36	3	13.0	10	32.3	13 (24.1)	Fisher exact	0.122
	≥ 36	20	87.0	21	67.7	41 (75.9)		
	Mean	36.5		36.0		36.2	t=0.315	0.754
	SD	6.93		5.95		6.33		
Working hours / week (Male)	< 36	22	18.3	22	20.0	44 (19.1)	0.103	0.748
	≥ 36	98	81.7	88	80.0	186 (80.9)		
	Mean	43.3		45.1		44.2	t=0.896	0.371
	SD	14.28		16.06		15.15		

* Significant at $p < 0.05$

4.2.2.1 Work field

Data collected regarding the participants' field of work has been classified into three categories; professionals, technicians & associate professionals and elementary occupations. The categories were adopted from the international standard classification of occupations formalized and published by the international labour organization (ILO, 2008). Not all categories are used in this study, but only the ones that matched the results which the surveyed population have submitted. Some examples of professionals' category are, medical doctors, dentists, pharmacists, physiotherapists, nutritionists, engineers, teachers, lawyers, judges, finance professionals, journalists and information and technology professionals. Technicians and associate professionals include engineering science technicians, medical and pharmaceutical technicians, and associate professionals of other

fields. Some, but not all, of the elementary occupations and craft workers include cleaners, clerks, agricultural labourers, food preparation assistants, builders and painters. Notably, 82.6% of the employed female cases are engaged in professional type of work and 17.4% work as technicians and associate professionals, while the distribution among controls is nearly the half; 48.4% and 51.6%; for each category respectively, giving a statistically significant association between the two groups, OR = 5.07 (95% CI, 1.40-18.37, p = 0.012). This could be because, women practicing professional careers are often required to be engaged in longer duration of education. This might expose them to a higher marital age rate which is eventually could be one of the causal effects of infertility. It is worth to mention that marital age in this study is one of the causal factors reached to affect the ability to conceive among females **(Table 4.2)**. Another explanation could be related to stress accompanied with high demanding jobs during lifetime that may affect fertility among women overtime (Noorbala, Ramezanzadeh, Abedinia, & Naghizadeh, 2009). In 2006, a group of researchers studied the impact of psychological stress of women's occupation on their fertility status. They followed 75 working infertile women through their treatment journey in infertility centers in a prospective cohort study and substantially found that women with perceived higher workload and high demanding jobs are less likely to get pregnant, RR = 0.6 (95% CI, 0.42-0.96). Additionally, women with actual high workload were less likely to have a complete pregnancy, RR = 0.3 (95% CI, 0.11-0.96) (Barzilai-Pesach, Sheiner, Sheiner, Potashnik, & Shoham-Vardi, 2006). Another study that was published in 2010 revealed contradictory results. Examining 728 women in rural areas of Shropshire in England revealed that, there is no association between occupation and infertility (Buckett & Bentick, 2010).

Husbands in this study show different results **(Table 4.4)**. The distribution of all 230 working husbands is almost equal among all three occupational categories, where 30% of cases' husbands work as professionals, 37.5% work as technicians and associate professionals and 32.5% have elementary occupations as their daily job. Respectively, the husbands of the control group are distributed according to their jobs as 30.9%, 38.2% and 30.9%. There is no association between the two groups, p = 0.966. Literature review revealed that many researchers found controversially conclusions. One study was investigating the potential association between working conditions and type of occupation on male infertility with the participation of 202 men attending fertility centers in the Occupied Palestinian Territory and showed that, male infertility had significant association

with those who work in constructive fields, p = 0.044, as they were exposed to more physical exertion at work, OR = 3.35 (95% CI, 1.44-7.80), and were exposed to more noise, OR = 3.84 (95% CI, 1.63-9.14) (Sheiner, Sheiner, Carel, Potashnik, & Shoham-Vardi, 2002). Another study that was conducted in 2003, confirmed that men who are exposed to certain chemical while practicing their daily jobs may suffer from infertility on the long term (Claman, 2004). A third study that was performed on 1695 male participants revealed that, the average sperm count was higher in the administrative and professional group of working men while those working in agriculture and transport provided the lowest concentration (Henderson, Rennie, & Baker, 1986).

4.2.2.2 Work shift pattern

Among all 54 working women, 65.2% of female cases work in morning shifts and 34% work through night or rotation shifts, compared to 90.3% and 9.7% of the control group respectively, giving a significant association, OR = 4.98 (95% CI, 1.15-21.60, p = 0.039). Night and rotation shift and how they would affect fertility in women have long been a subject of debate among researchers. Shift workers may experience an increased rate in menstrual abnormalities (Stocker, Macklon, Cheong, & Bewley, 2014). Also, the continuous and intermittent alteration in females circadian rhythm might affect the reproductive hormones and eventually the quality of the produced ovum (Gaskins, Rich-Edwards, et al., 2015). A European multicenter study measured the effect of work shift on infertility through analyzing several studies conducted on infertile couples in Europe. The analysis showed that, no association has been identified between working in shifts and the presence of menstrual abnormalities, but an association with infertility existed that needs further biological investigation (Bisanti, Olsen, Basso, Thonneau, & Karmaus, 1996). Another study conducted recently in 2015 was examining the effect of type of work, work shift as well as their leisure time physical activities. Researchers investigated 313 women for the ovarian reserve, FSH level and ovarian response in a prospective cohort study from 2004 till 2015. Among the results they found is that women who works in night and rotation shifts are 2.3 lesser mature ovum than those working in a straight morning pattern, p < 0.001, while no association has been detected with the FSH level (Mínguez-Alarcón et al., 2017). Most of the studies explored were observational studies that could be subjected

to several confounders with different controversial conclusions that offer good potential for further in-depth investigations.

Husbands in this study seem to be not affected by work shifts. Nearly half of the working husbands in the surveyed population work through morning shifts; 48.3% of cases' husbands versus 48.2% of controls' husbands. The other half work at night or in rotation shifts either full duty or through on-call pattern, where 10.8% of working husbands of the cases work at night and 40.8% work in rotation shifts comparing to 13.6% and 38.2% of the working husbands respectively. Although, there is no association between work shifts and infertility in this study, many studies concluded that male urological health could be affected. A recent meta-analysis study found that, shift workers are more subjected to poor semen parameters and impaired fertility (Deng, Kohn, Lipshultz, & Pastuszak, 2018), while other study scrutinized deeply the substantial differences and revealed that infertile shift workers are highly susceptible to low sperm density, low total motile sperm count and low FSH and LH serum level, (p = 0.012, 0.019, 0.026 respectively) (Kohn & Pastuszak, 2017).

4.2.2.3 Working hours

Working hours is one of the subdomains explored in this study to evaluate more the working conditions that might be associated with infertility in Palestine context. The frequency of working more than 36 hours per week among female participants is more in female cases (87%) than controls (67.7%) and working less than 36 hours a week is less among cases (13%) than controls (32.3%). In spite of the apparent difference, the relationship did not reach a statistically significant level. However, working hours of husbands are quite more similar in both groups, as nearly 80% in both the cases' and the controls' husbands work more than 36 hours per week. Upon reviewing literature, it was noticed that there is limited information in this regard. Only one study that was found in this regards and was considered as bad news for working women in Hong Kong who are known as nurturers for long working hours. A US prospective cohort study among 1739 women concluded that, women working more than 40 hours a week are more subjected to 20% more longer duration to get pregnant when desiring so, than those working between 21-40 hours per week (Gaskins, Rich-Edwards, et al., 2015).

4.2.3 Consanguinity:

Consanguineous marriage is culturally acceptable and fairly common among Arab nations. It forms about 20% to 50% of all marriages (Bittles, 2012). In Palestine, the percentage of first cousin marriage among ever married women aged 15-29 is 30.2% (PCBS, 2019[a]), while in this study (**Table 4.5)**, 31.5% of all 320 couples have practiced a first cousin consanguineous marriage, where 20.6% of cases' couples are double first-cousin married and 20.6% are first-cousin, compared to 21.1% and 8.8% of the controls' couples respectively.

Table (4.5): Distribution of study population in relation to consanguinity; socioeconomic variables part 3; (N=320)

Socioeconomic variables (Part 3)		**Cases**		**Controls**		**Total (%)**	χ^2	**P-value**
		No	**%**	**No**	**%**			
Consanguinity of couples	Double 1st cousin	33	20.6	34	21.2	67 (20.9)	1.188	0.552
	1st cousin	20	12.5	14	8.8	34 (10.6)		
	Not relatives	107	66.9	112	70.0	219 (68.4)		
Consanguinity of parents (Female)	Double 1st cousin	42	26.3	36	22.5	78 (24.4)	0.999	0.607
	1st cousin	21	13.1	26	16.3	47 (14.7)		
	Not relatives	97	60.6	98	61.2	195 (60.9)		
Consanguinity of parents (Male)	Double 1st cousin	56	35.0	51	31.9	107 (33.4)	3.543	0.170
	1st cousin	14	8.8	25	15.6	39 (12.2)		
	Not relatives	90	56.3	84	52.5	174 (54.4)		

Although several studies declared the significant association between consanguineous marriage and infertility, the relationship in this study did not reach a significant level. This could be due to the presence of multiple marriages among infertile couples which is known to lower the percentage of first-cousin marriage (Sirdah, 2014). As the data was collected from the current married couples, attending either the IVF centers as cases or the PHC clinics as controls, no questions in the used instrument were intended to identify multiple or previous marriage among these couples. Reviewing literature showed that many studies concluded this relationship. A case control study that was held in Lebanon, reached a significant relationship between consanguineous marriage and male factor infertility, OR = 2.58, where infertile male patients with azoospermia and severe oligospermia had 50% consanguineous marriage (Inhorn et al., 2009). Another study that was conducted in Iran

and examined 5200 married couples for etiological risk factors of infertility found that, consanguineous marriage was among the main factors that have significant effect on the fertility status of couples (Aflatoonian, Seyedhassani, & Tabibnejad, 2009).

In the same respect, parents of the female participants showed higher proportion of consanguineous marriage than the current generation. Of all 160 female cases, 26.3% of their parents were engaged in a double first-cousin marriage while only 13.1 were married as first-cousin. The control group had 22.5% of their parents married as double first cousin and 16.3% as first cousin. A greater proportion is noticed among parents of the surveyed population's husbands, where almost third of their parents were married as double first cousin; 35% for parents of cases' husbands and 32% for those of controls. When only 8.8% of husbands' parents of the cases group are first cousin married, there is 15.6% of those of controls are first-cousin. In both conditions the relationship did not reach a significant level of association.

4.2.4 Relationship between infertility and various socioeconomic variables:

The following table demonstrates binary logistic regression of all statistically significant socioeconomic variables, where it is worthy to note that the model has a high predictive capacity of 70%:

Table (4.6): Predictors of primary infertility among different independent socioeconomic variables using binary logistic regression

Socioeconomic variables	***β***	***S.E.***	**Wald χ^2**	***p-value***	***OR (95% CI)***
Average monthly income (≤1500 NIS=reference)			1.423	0.491	
1500-2500 NIS	-0.378	0.805	0.221	0.639	0.69 (0.14-3.32)
>2500 NIS	-0.925	0.780	1.405	0.236	0.40 (0.07-1.83)
Work field of wives (professional=reference)	1.818	0.749	5.889	*0.015	6.16 (1.42-26.75)
Work shift of wives (Night & rotation=reference)	1.821	0.874	4.338	*0.037	6.18 (1.11-34.26)
Constant	-1.441	0.829	3.018	0.082	0.24

β=beta coefficient, S.E.=standard error, χ^2=chi square, CI=confidence interval, Model coefficient chi^2=14.39, p<0.001, Nagelkerke r^2=0.314, Membership for cases, *significant=p<0.05,

Apparently, the odds of working as professionals is six times more likely among infertile women than fertile ones. As mentioned before, educational attainment and academic achievements gained by females, in order to be categorized as professionals in their field of work, need longer years of education which is often associated with higher marital age than average. Moreover, professionals are more exposed to stress and could be more prone to sedentary long working hours. Additionally, what seems to be concluded in this study is the effect of work shifts on females' fertility status. As described in **Table (4.6**), the odds of practicing night or rotation shifts in a women's career is six times higher in infertile women than among women with normal fertility status. Several researchers have discussed the circadian rhythm and the consequences of its long-term alteration that may encounter the normal secretion of reproductive hormones (Gaskins, Rich-Edwards, et al., 2015). To be more precise, this result should be taken with much caution, as the study did not take into consideration the duration in which the females have been engaged in this type of job, the pattern of rotation, the number of rotation cycles per week and month, the number of hours a night or an evening shift include and other factors that would add more substantial evidence to this area. So, further in-depth exploration is foreseen.

4.3 Environmental factors

People are often surrounded or persistently exposed to several agents present in the space that surrounds them and that affects them directly or in an indirect way. Specifically, the reproductive system of humans is known to be highly sensitive to different environmental factors (Spira & Multigner, 1998). These factors could be due to certain occupations practiced by individuals on regular basis or could simply be attributed to general living conditions, which usually have spatial patterns and differ geographically across and within countries (Woolf & Aron, 2013). Accordingly, this study explores various environmental variables couples might have been exposed to during their life course, which have negative implications on their fertility status. Among these variables that are mentioned below, housing conditions, the source from which people supply their drinking water and various physical and chemical exposures.

4.3.1 Living condition:

Of the inquiries that were included in this study, the surveyed population were asked to specify the type of dwelling they used to live in before marriage along with the one they are occupying currently after marriage **(Annex 5)**. Reponses revealed that most of the

surveyed population (98.1%) used to live before marriage in a separate house or apartment, where there is quite no difference between cases (97.5%) and controls (98.8%), while a small proportion used to live in an independent room or caravan; 2.5% cases and 1.3% controls (**Table 4.7)**. However, results showed 6% increase in the proportion of females who moved to live in an independent room or caravan after marriage, with more frequency among cases (15%) than controls (10.6%). Nevertheless, the relationship did not reach a statistically significant level. Actually, living in unsatisfactory conditions may expose couples to variety of genital tract infections which is strongly related to tubal factor infertility or could be associated with immune sperm rejection (Mania-Pramanik, Kerkar, Sonawane, Mehta, & Salvi, 2012).

Table (4.7): Distribution of study population by various living condition variables

Living condition variables		**Cases**		**Controls**		**Total (%)**	χ^2	**P-value**
		No	**%**	**No**	**%**			
Type of dwelling "Before marriage"	Independent house, apartment	156	97.5	158	98.8	314 (98.1)	Fisher exact	0.685
	Room or Caravan	4	2.5	2	1.3	6 (1.9)		
Type of dwelling "After marriage"	Independent house, apartment	136	85.0	143	89.4	279 (87.2)	1.371	0.242
	Room or Caravan	24	15.0	17	10.6	41 (12.8)		
Tenure of housing unit	Owned	119	74.4	137	85.6	256 (80.0)	6.701	*0.035
	Rent	23	14.4	11	6.9	34 (10.6)		
	Without payment	18	11.3	12	7.5	30 (9.4)		
Toilet facility	Piped sewer system	136	85.0	149	93.1	285 (89.1)	5.422	*0.020
	Septic porous tank	24	15.0	11	6.9	35 (10.9)		
Source of drinking water "Before marriage" Wife	Municipal water/Wells	27	16.9	53	33.1	80 (25.0)	22.807	**<0.001
	Rooming tankers	128	80.0	89	55.6	217 (67.8)		
	Filter/Mineral water	5	3.1	18	11.3	23 (7.2)		
Source of drinking water "Before marriage" Husband	Municipal water/Wells	27	16.9	49	30.6	76 (23.8)	15.367	**<0.001
	Rooming tankers	129	80.6	98	61.3	227 (70.9)		
	Filter/Mineral water	4	2.5	13	8.1	17 (5.3)		
Source of drinking water "After marriage"	Municipal water/Wells	16	10.0	9	5.6	25 (7.8)	5.496	0.064
	Rooming tankers	137	85.6	135	84.4	272 (85.0)		
	Filter/Mineral water	7	4.4	16	10.0	23 (7.2)		

* Significant at $p < 0.05$, **Highly significant at $p < 0.001$

Housing tenure is usually concomitant with the social determinants of health (Gibson et al., 2011), which is also related to environmental factors that surrounds public and possess certain influence on health (Bonnefoy, 2007). When most of the surveyed couples (80%) declared self-owning the house they are currently living in, there is apparent difference

between infertile (74.4%) and fertile (85.6%) couples. On the other hand, infertile couples who use the housing unit without any payment represent 11.3%, while fertile ones form only 7.5%. The main contributor to the statistically significant relationship between the two groups is those who are living in housing units and pay for rents on monthly or annual basis, where 14.4% of the infertile couples is compared to 6.9% of the fertile group, OR = 2.41 (95% CI, 1.13-2.14, p = 0.02). It is worth to mention that, the total results of the surveyed population are congruent to what has been published through the PCBS (2018[d]), where about 80% of the total households in GS own their house, 6.5% pay rents and 10.1% live in housing units without payment. However, housing tenure and its relation to health has been generously explored by researchers, but literature review did succeed to find any studies that linked this variable particularly to infertility status of individuals. Accordingly, this area is foreseen as an appropriate potential for further in-depth investigation.

Safe sanitation system is known to have remarkable effect on combating pathogens that are related to infertility (WHO, 2018[a]). In this study, information about the type of sanitation system used by participants' households is collected to explore its relation to infertility. Consequently, analysis revealed that 136 (85%) infertile couples have their household unit connected to a piped sewer system, compared to 149 (93.1%) fertile ones. The remaining 24 couples, representing 15% of the total cases, have their household unit's sewer system connected to a septic porous tank compared to 11 (6.9%) respectively, providing a twice more likely risk for being infertile, OR = 2.39 (95% CI, 1.13-5.06, p = 0.02). The significant association between the two groups might be due to the possibility of exposure to various genital tract infections associated with inappropriate sanitation and hygiene among people using unsafe toilet services. Several researchers confirmed this explanation. One study investigated the sociodemographic correlation of Indian population with infertility and used the water and sanitation facilities utilized by the population as one of the proxy indicators for wealth index showed that, women categorized within the poor wealth quantile had 57% higher risk of primary infertility than those within the rich wealth quantile (Sarkar & Gupta, 2016). Another study was performed to evaluate the relationship between maternal and perinatal health with sanitation and hygiene through a systematic review approach. The study revealed that poor outcomes is combined with inappropriate sanitary facilities (Campbell, Benova, Gon, Afsana, & Cumming, 2015).

One of the essential components of public health is the human right to access clean and safe water (FIGO, 2019). Upon studying this particular area, people living in GS seemed to

depend on five main sources of drinking water; municipal source, protected and unprotected wells, rooming tankers, mineral water and home installed filters. The most prevailing source used by almost 85% of infertile couples and that of fertile couples after marriage, is the rooming tankers. Although twice more cases (10%) than controls (5.6%) use municipal water or wells and nearly half cases (4.4%) compared to control couples (10%) drink mineral or filtered water, the difference between the two groups did not reach a statistically significant level. The situation before marriage is completely different **(Figure 4.6)**. More than two third of the female participants in the cases group (80%) declared depending on rooming tankers as a source of drinking water before marriage, compared to only about half those of the control group (55.6%), while less cases used municipal/wells water (16.9%) or filter/mineral water (3.1%) than control couples (33.1%, 11.3% respectively). Almost the same distribution is noticed among men in the surveyed population **(Figure 4.7)**. Having the home installed filter or mineral water as a reference, the use of rooming tankers as a main source of drinking water is five times more likely among infertile females than fertile ones (95% CI, 1.85-14.46) and four times more likely among infertile males than those who practice a normal reproductive life (95% CI, 1.35-13.53). These findings would provide an opportunity for further serious public health measures to be negotiated and formalized by policy makers and environmental specialist for water supply quality assessment and control. In the same context, Iranian researchers examined the relationship between the fluoride level in drinking water and infertility without known causative factor and found that, females living in areas with low level fluoride containing water are more fertile with less prevalence of abortion and infertility with unknown cause (Yousefi, Mohammadi, Yaseri, & Mahvi, 2017). Another study was concerned with the presence of endocrine disruptors in drinking water and its effect mainly on men. Endocrine disruptors are environmental chemical factors that have the ability to disrupt the normal function of reproductive hormones in males; testosterone; and so, interferes with the androgenic effect of the hormone. Estrogen-like chemicals is among the main disruptors which recently has been manufactured and used more frequently either as a contraceptive method or as a hormonal replacement therapy. Researchers were concerned that, inappropriate disposal of such chemicals has caused leakage to ground water and eventually utilized as a domestic or a drinking source (Di Nisio & Foresta, 2019).

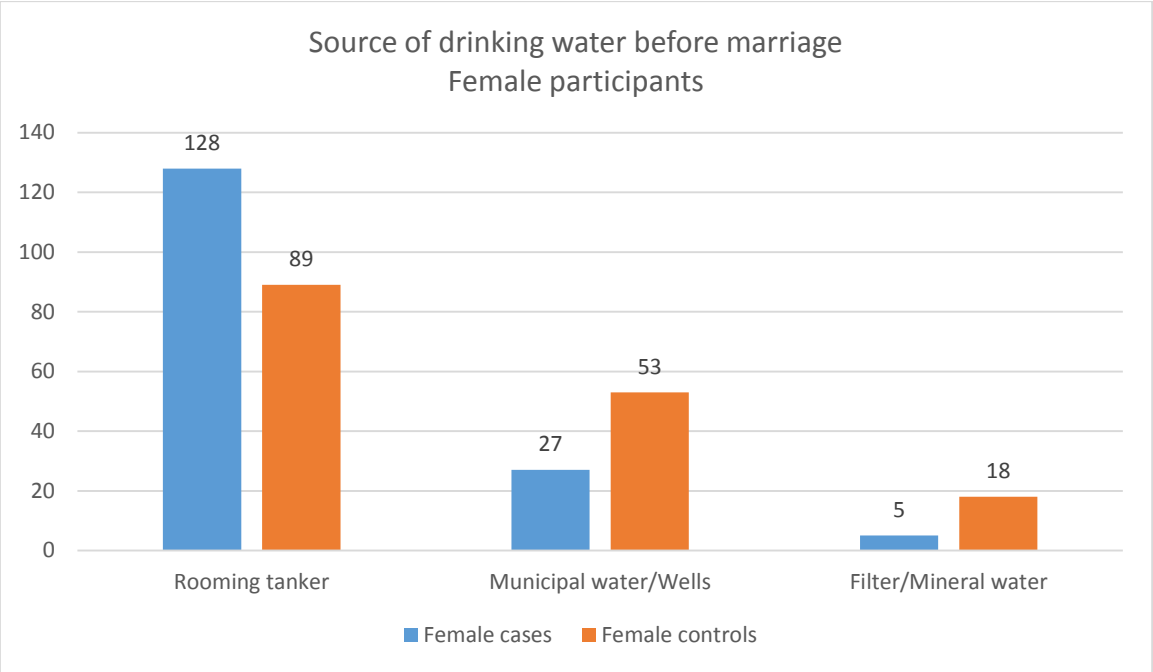


Figure (4.6): Main source of drinking water before marriage – Female participants

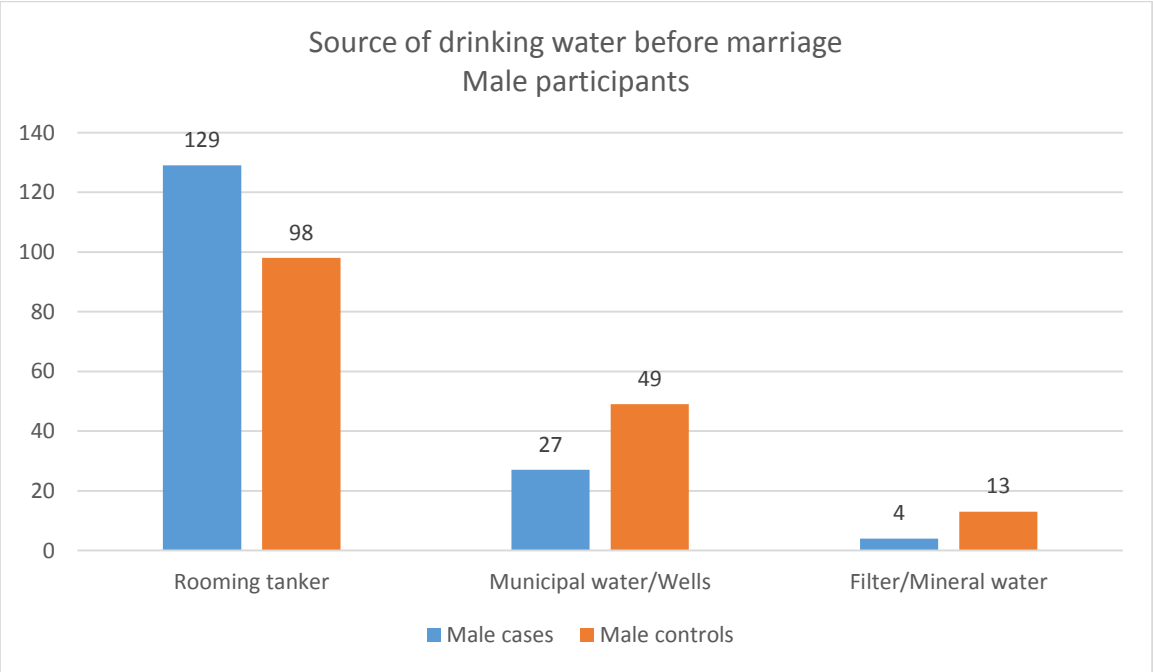


Figure (4.7): Main source of drinking water before marriage – Male participants

4.3.2 Agricultural pesticides and herbicides:

Among all responses, a total of 51 participants declared mixing and applying agricultural pesticides and herbicides (APH), from which more cases (17.5%) than controls (14.4%) were noticed. Participants were asked whether they use APH as farmers, dealers, distributors or simply because they own a farm, but all responses were either a farmer or a farm owner. As shown in **Table (4.8)**, cases who worked as farmer are equal to those of the controls; 9 of each; while those who own a farm and taking care of it personally were 19 (67.9%) cases and 14 (60.9%) controls.

Table (4.8): Distribution of study population according to agricultural pesticides & herbicides utilization

Agricultural pesticides & herbicides (APH) variables		Cases		Controls		Total (%)	χ^2	P-value
		No	%	No	%			
Dealing with APH	Yes	28	17.5	23	14.4	51 (15.9)	0.583	0.445
	No	132	82.5	137	85.6	269 (84.1)		
Using APH as	Farmer	9	32.1	9	39.1	18 (35.3)	0.270	0.603
	Farm owner	19	67.9	14	60.9	33 (64.7)		
Frequency of using APH	Weekly	14	50.0	5	21.7	19 (37.3)	4.314	*0.038
	Monthly or more	14	50.0	18	78.3	32 (62.7)		
Duration of using	≤ 5 y	11	39.3	7	30.4	18 (35.3)	0.433	0.510
	> 5 y	17	60.7	16	69.6	33 (64.7)		
Practicing safety measures	Yes	2	7.1	11	47.8	13 (25.5)	11.004	**<0.001
	No	26	92.9	12	52.2	38 (74.5)		

* Significant at $p < 0.05$, **Highly significant at $p < 0.001$

Although the variability appearing in dealing with APH and in the reason behind using it between the fertile and infertile women did not reach a statistically significant level, the effect of mixing and applying APH on the fertility status of participants showed to be apparent when inquiring about the frequency of using such chemicals. The results show that, half of the infertile women exposed to APH deal with it on weekly basis compared to only 21.7% of those of the control group, while those who are dealing with APH on monthly basis or more are 50% and 78.3% respectively, OR = 3.6 (95% CI, 1.04-12.40, p = 0.03). The more frequent exposure to these chemicals has been repeatedly related to the disruption of the reproductive hormonal cycle at all stages; starting from hormonal synthesis, release and storage till hormonal transport, recognition and binding to receptors; ending up with ovulatory or tubal cause of infertility (Bretveld, Thomas, Scheepers, Zielhuis, & Roeleveld, 2006). However, the relationship between different pesticides and infertility has been widely investigated and researched. A study that was conducted in the US revealed that women working in agricultural occupations have increased risk of infertility, OR = 7.0 (95% CI, 2.3-20.8) than other occupations (Hanke & Jurewicz, 2004).

Another study that investigated four years retrospectively the relationship between pesticides exposure and infertility concluded that, 2 years exposure is more common among infertile women, OR = 27 (95% CI, 1.9-380) (Greenlee, Arbuckle, & Chyou, 2003). Along with many other studies that have congruent results, this may raise the urgency of planning for prevention and control measures. It is suggested there is a need for providing adequate health education and training to agricultural workers and dealers on the recommended safety measures. In this respect, this study revealed that only 2 (7.1%) cases of those dealing with APH use protective and safety measures compared to 11 (47.8%) of the control group, while 26 (92.9%) and 12 (52.2%) respectively do not apply these practices, OR = 11.9 (95% CI, 2.28-62.34, $p < 0.001$).

4.3.3 Work environment:

Occupational related infertility has long been a virtual concern to many environmental health specialists. In spite of having many studies conducted in this respect, it is almost impossible to define the total proportion of the population with infertility caused by occupational factors (Baranski, 1993). In this observational study, both the female and male participants were inquired for different occupational exposures, hoping to contribute towards the advancement of occupational health knowledge and public health research **(Table 4.9).**

All working participants were asked whether their job requires heavy physical labour or not. Although more male participants (63.1%) practice heavy physical work in their job than females (31.7%), but the female cases (45.2%) are found to be more exposed than those of the controls (18.8%), when the men have nearly equal distribution in both groups; 65.6% and 60.6% respectively **(Table 4.9)**. Conclusively, heavy physical labour in females' job is statistically significant with infertility. A study that has been widely published in 2017, reported that highly demanding jobs which include high physical requirements and lifting heavy objects are associated with decrease in the ovarian reserve, demonstrated in lesser total oocytes, lesser mature oocytes and lesser antral follicles, in relation to women who reported no lifting of heavy objects in their daily work (Mínguez-Alarcón et al., 2017). Other researchers applied a cohort study on 1739 women to examine the duration needed to get pregnant among nurse field workers. The study revealed that women desiring pregnancy had longer duration of attempting when their work requires moving or lifting more than 25 pounds objects for more than fifteen times a day (Gaskins, Rich-Edwards, et al., 2015).

Table (4.9): Distribution of study population in relation to working environment variables

Working environment variables		Cases		Controls		Total (%)	χ^2	P-value
		No	%	No	%			
Heavy physical labour Wife	Yes	14	45.2	6	18.8	20 (31.7)	5.039	*0.024
	No	17	54.8	26	81.3	43 (68.3)		
Heavy physical labour Husband	Yes	105	65.6	97	60.6	202 (63.1)	0.859	0.354
	No	55	34.4	63	39.4	118 (36.9)		
Noise, dust, gases, chemicals, polluted air Wife	Yes	6	19.4	4	12.5	10 (15.9)	Fisher exact	0.509
	No	25	80.6	28	87.5	53 (84.1)		
Noise, dust, gases, chemicals, polluted air Husband	Yes	84	52.5	65	40.6	149 (46.6)	4.534	*0.033
	No	76	47.5	95	59.4	171 (53.4)		
Work stress (time pressure, concentration) Wife	Yes	18	58.4	20	62.5	38 (60.3)	0.129	0.719
	No	13	41.9	12	37.5	25 (39.7)		
Work stress (time pressure, concentration) Husband	Yes	82	68.9	82	74.5	164 (71.6)	0.894	0.344
	No	37	31.1	28	25.5	65 (28.4)		
Overtime, long working hours Wife	Yes	4	12.9	3	9.4	7 (11.1)	Fisher exact	0.708
	No	27	87.1	29	90.6	56 (88.9)		
Overtime, long working hours Husband	Yes	53	44.5	39	35.5	92 (40.2)	1.962	0.161
	No	66	55.5	71	64.5	137 (59.8)		
Overheat (e.g. Ovens, Solarium houses) Husband	Yes	30	18.8	17	10.6	47 (14.7)	4.215	*0.040
	No	130	91.3	143	89.4	273 (85.3)		

* Significant at $p < 0.05$

Of all 63 working ladies, 6 (19.4%) cases are exposed to noise, dust, gases, chemical or polluted air during performing their daily job compared to 4 (12.5%) controls. On the other hand, more men are exposed to these agents than women, where 84 (52.5%) husbands of the cases group experience such exposure in their working environment compared to 65 (40.6%) of the control group. In spite of the apparent difference between women in both groups and men also, the association did not reach a significant level in both. Moreover, work stress including time pressure and high concentration is explored as an occupational risk factor against infertility. Notably, more females in the control group (62.5%) experience work stress than female cases (58.4%) which is also reported among their husbands where more husbands in the control group are exposed to work stress than those of the cases, 74.5% and 68.9% respectively. However, upon reviewing literature different results were reached. In 2002, a group of researchers studied the effect of occupational stress and exposure to different chemical and their relation to sperm parameters. In the study, male infertility was significantly associated with job burnout ($p < 0.001$), noise (OR = 3.84, 95% CI, 1.63-9.14), welding (OR = 4.40, 95% CI, 1.11-1.76) and constructive jobs with dust ($p = 0.044$) (Sheiner et al., 2002). Another study examined the association between occupational stress among females and the infertility treatment outcome in a

prospective cohort study following 75 working infertile females. The study found that women who are exposed to stress during their daily job have less successful infertility treatment than those who perceive their job positively (Barzilai-Pesach et al., 2006).

Responses collected regarding long working hours and/or overtime showed that, 12.9% of female cases compared to 9.4% of the controls perceived their career as having such exposure. On the other hand, more men perceived having long working hours, with a proportion of 44.5% and 35.5% respectively. The association was neither significant among the female participants nor among their husbands.

The exposure to overheat among men was specifically presented as a sole variable after personal observation and experience in the field of reproductive health. As indicated in **Table (4.9)**, the proportion of men from the cases group who have been exposed to overheat through working in closed manual bakeries, preparing falafel in public restaurants or working in solarium houses were 30 (18.8%) compared to 17 (10.6%) of those in the control group. Having a statistically significant association between the two groups, may raise the possibility of having testicular affection due to continuous exposure to high temperature resulting in infertility (Jung & Schill, 2000). Many research studies confirmed that exposure to elevated temperature would alter the normal pattern, morphology or amount of sperms with direct testicular affection. In France, a case control study compared 60 military couples who attended the fertility centers to treat absence of conception for more than 12 months with 165 fertile couples. The study concluded that heat exposure was 4.5 (1.9-10.6) more likely among infertile men than the fertile control group, where the occupations that entailed heat exposure were bakers, welders, submariners and metallurgy workers (de la Calle et al., 2001). Another study also in France examined the duration needed to achieve a pregnancy in different occupations among men. Drivers sitting more than 3 hours a day had an average of 14.4 months to attain successful conception and occupations that entails heat exposure like bakers and welders had an average of 11.8 months duration to obtain a pregnancy (Thonneau, Ducot, Bujan, Mieusset, & Spira, 1997).

4.3.4 Gaza as a conflict zone:

GS has been exposed to several military escalations during the past 10 years. Since then, people living in GS have manifested a lot of direct and indirect health hazards. Reproductive related risk factors, including injuries, stress and exposure to toxins are believed to affect fertility status in different aspects (Kobeissi et al., 2008). Accordingly, this study explores different risk factors that might have been experienced by the

population and could be related to infertility. Variables demonstrated hereunder are shown in three sections; one for females and one for males, that is congruent with the time they experienced the war either individually or after marriage and the third is for them after marriage as couples.

4.3.4.1 Exposure of female participants

Results show that, most of those affected by the war either directly or indirectly, continued to live in the same household setting **(Table 4.10)**. Almost the same proportion of cases (22.5%) and controls (23.1%) had their house been totally or partially demolished, also nearly the same proportion experienced living in a partially demolished house, 24.4% and 21.3% respectively. On the other hand, about half of the infertile ladies (51.3%) reported their neighbours' house been demolished, the same as for the fertile females (51.9%). Again, most of them continued living in the same household setting, 48.8% and 47.5% respectively, while their neighbours' house been demolished. The relationships in all variables did not approach a statistically significant level. This could be because women are usually protected during emergency situations from any hazardous activities. This is proved by exploring if this proportion of cases endures the cause of infertility or not as shown in **Figure (4.8)**.

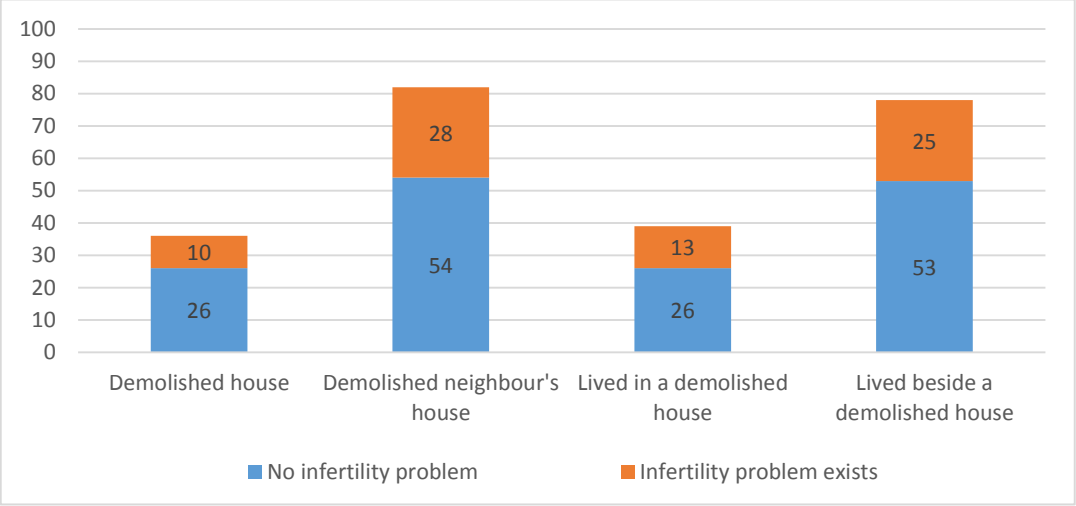


Figure (4.8): Distribution of female participants by infertility status and war variables

The situation is also the same regarding working in a renewed place after being demolished during the escalation period or dealing with after war remnants, where 3.8% of female participants of the cases group declared working in a renewed place compared to 4.4% of those of the control group and 3.8%, 0.6% respectively had experienced dealing with after war remnants.

Table (4.10): Distribution of study population by war exposure variables - Females

War exposure variables – Females		Cases		Controls		Total (%)	χ^2	P-value
		No	%	No	%			
House has been totally or partially demolished	Yes	36	22.5	37	23.1	73 (22.8)	0.018	0.894
	No	124	77.5	123	76.9	247 (77.2)		
Neighbours' house has been demolished	Yes	82	51.3	83	51.9	165 (51.6)	0.013	0.911
	No	78	48.8	77	48.1	155 (48.4)		
Lived in a partially demolished house	Yes	39	24.4	34	21.3	73 (22.8)	0.444	0.505
	No	121	75.6	126	78.8	247 (77.2)		
Lived beside a demolished house	Yes	78	48.8	76	47.5	154 (48.1)	0.050	0.823
	No	82	51.3	84	52.5	166 (51.9)		
Work in a renewed place	Yes	6	3.8	7	4.4	13 (4.1)	0.080	0.777
	No	154	96.3	153	95.6	307 (95.9)		
Dealing with "after war remnants"	Yes	6	3.8	1	0.6	7 (2.2)	Fisher exact	0.121
	No	154	96.3	159	99.4	313 (97.8)		

4.3.4.2 Exposure of male participants

Of total 320 male responses, 22.8% had their house either totally or partially demolished **Table (4.11)**. The proportion between husbands of the cases (25%) and those of the controls (20.6%) did not vary much. The situation is similar when asking about neighbors' demolished house, where almost half of each group confirmed the incidence. The reason behind having a nonsignificant relationship in both cases could be because survivours might have been distanced from the scene and were not exposed to the incident. Accordingly, participants were asked if they lived in or beside a partially or completely demolished house. 30% of the cases' husbands declared living in a partially demolished house compared to 19.5% of the controls', OR = 1.77 (955 CI, 1.05-2.97, p = 0.03), while living beside a demolished house is nearly the same between cases (45.6%) and controls (46.9%). The frequency of husbands working in places that have been exposed to bombardments and then reconstructed is 13 among cases and 10 among controls giving a total of 7.2% of the total surveyed population with nonsignificant difference between the two groups. On the other hand, dealing with after-war remnants shows high significant difference, where 15 (9.4%) of husbands in the cases group have declared holding, lifting, dusting or even disassembling an after-war remnant, OR = 5.41 (95% CI, 1.48-29.63, p = 0.006), compared to 3 (1.9%) of the control group. Although, relationships showed significant association within several variables, results should be taken with caution, as these are observational conclusions that could be affected with accompanying confounders. Providing that many studies examined the effect of war on semen parameters in male (Abu-Musa, Kobeissi, Hannoun, & Inhorn, 2008), these results may offer potential opportunity for additional experimental investigations.

Table (4.11): Distribution of study population by war exposure variables – Males

War exposure variables – Males		Cases		Controls		Total (%)	χ^2	P-value
		No	%	No	%			
House has been totally or partially demolished	Yes	40	25.0	33	20.6	73 (22.8)	0.870	0.351
	No	120	75.0	127	79.4	247 (77.2)		
Neighbors' house has been demolished	Yes	79	49.4	80	50.0	159 (49.7)	0.013	0.911
	No	81	50.6	80	50.0	161 (50.3)		
Lived in a partially demolished house	Yes	48	30.0	31	19.5	79 (24.8)	4.722	*0.030
	No	112	70.0	128	80.5	240 (75.2)		
Lived beside a demolished house	Yes	73	45.6	75	46.9	148 (46.3)	0.050	0.823
	No	87	54.4	85	53.1	172 (53.8)		
Work in a renewed place	Yes	13	8.1	10	6.3	23 (7.2)	0.422	0.516
	No	147	91.9	150	93.8	297 (92.8)		
Dealing with "after war remnants"	Yes	15	9.4	3	1.9	18 (5.6)	Fisher exact	*0.006
	No	145	90.6	157	98.1	302 (94.4)		

* Significant at $p < 0.05$

4.3.4.3 Exposure of couples

Continued to what has been explored in this section, couples were requested to report some information about they have experienced during the period of their marriage to help identifying any long-term effect in this regard **(Table 4.12)**.

Table (4.12): Distribution of study population by war exposure variables – Couples

War exposure variables – Couples		Cases		Controls		Total (%)	χ^2	P-value
		No	%	No	%			
Living in a renewed house	Yes	43	26.9	31	19.4	74 (23.1)	2.531	0.112
	No	117	73.1	129	80.6	246 (76.9)		
Source of drinking water exposed to bombardments	Yes	14	8.8	5	3.1	19 (5.9)	4.532	*0.033
	No	146	91.3	155	96.9	301 (94.1)		
Bombardments 50-100m around the house	Yes	83	51.9	79	49.4	162 (50.6)	0.200	0.655
	No	77	48.1	81	50.6	158 (49.4)		

* Significant at $p < 0.05$

Among the inquiries that were included to explore further analysis of exposure, couples were requested to report if they are currently living in a house that was reconstructed after being partially or completely demolished **(Table 4.12)**. More cases (26.9%) than controls (19.4%) responded positively, while 73.1% and 80.6% respectively did not experience the given exposure. In spite of the apparent difference between the two groups, the relationship did not reach a significant level. Moreover, nearly equal proportions of couples in the cases group (51.9%) and the control group (49.4%) suffered witnessing at least one bombardment hitting the nearby land area (50-100m) that surrounds their residential

setting, providing an additional nonsignificant relationship. On the contrary, when inquiring if these bombardments had ever struck a source of drinking water, 14 cases compared only to 5 control couples responded positively, $p = 0.03$.

4.3.5 Relationship between infertility and various environmental predictors:

The following **Table (4.13)** demonstrates a model of binary logistic regression for different environmental variables with a predictive capacity of 62.8%. The environmental variables shown below were discussed previously as having a relationship with infertility that approached a statistically significant level. Among all, the most significant risk factor is the females' source of drinking water before marriage, where women who used rooming tankers for drinking water are more than two times more likely to have infertility in relation to their counterparts. No previous studies supported this particular finding in GS and so, provides a potential opportunity for environmental health researchers to scrutinize this area. Moreover, couples using a septic porous sanitary system have double the chance to develop infertility in relation to those who are connected to the public piped sewer system. Poor perinatal and antenatal outcome has been approved to be related to inappropriate sanitary system (Campbell et al., 2015). Most of the couples in this study with household setting not connected to the public sewer pipes were noticed to be living in marginalized areas. These areas are recommended to be targeted for health education campaigns and national efforts to be directed toward providing them with the basic human rights; safe water and sanitation.

Table (4.13): Predictors of primary infertility among different independent environmental variables by using binary logistic regression

Environmental Variables	***β***	***S.E.***	**Wald χ^2**	***p-value***	***OR (95% CI)***
Tenure of housing unit Owned or without payment=Reference	0.892	0.404	4.879	*0.027	2.44 (1.11-5.38)
Sanitary system used by couples Public sewer system=Reference	0.968	0.430	5.066	*0.024	2.63 (1.13-6.11)
Source of drinking water before marriage – wife Municipal water=Reference			19.490	**<0.001	
Rooming tankers	1.010	0.283	12.702	**<0.001	2.75 (1.58-4.78)
Filter/Mineral water	-0.668	0.578	1.332	0.248	0.513 (0.17-1.59)
Nearby drinking water source or its surroundings bombed No=Reference	1.041	0.562	3.427	0.064	2.83 (0.94-8.53)
Dealing with after war remnants husband No=Reference	1.381	0.672	4.221	*0.040	3.98 (1.07-14.85)
Constant	-0.963	0.255	14.284	**<0.001	0.382

β=beta coefficient, S.E.=standard error, χ^2=chi square, CI=confidence interval, Model coefficient chi^2=44.58, p<0.001, Nagelkerke r^2=0.173, Membership for cases, *significant=p<0.05, **highly significant=p<0.01

The odds of living in housing units and paying for rent on monthly or annual basis is also two times more likely among infertile couples than fertile ones. Furthermore, dealing with after war remnants among husbands of infertile couples is nearly four time more than that of the fertile ones. The extent of contamination with remnants and other explosive hazards in GS from the previous three hostilities need to be re-estimated within a risk assessment approach. The UN Mine Action Service (UNMAS) had applied protection measure shortly after 2014 hostilities which included detection and safe disposal of any hazards along with a series of training and education sessions for workers and communities mainly adolescents and care providers (OCHA, 2016). In the light of what has been mentioned and living in a politically unstable region, this may urge to have preparedness emergency plans and emergency drills to avoid any unexpected long-term health hazard like infertility.

4.4 Medical factors

4.4.1 Causes of infertility:

Data from this study were obtained from cases that had already been diagnosed with primary infertility and are seeking medical advice in fertility centers. Of all 160 couples, infertility was identified in women alone in 33 (20.6%) couples, in men alone in 49 (30.6%) couples and causes of infertility found in both couples were 46 (28.8%). Infertility of unknown cause (idiopathic) was pertained to 32 (20%) couples. These results are nearly congruent to what has been concluded through a retrospective research that was held in Ashdod and Holon. Researchers found that factors identified in the husband alone was in 29.2%, in the wife alone was in 30.6%, in both was 18.5% and 20.7% was the rate of unexplained infertility (Farhi & Ben-Haroush, 2011).

About three quarter (72%) of the causes related to women were ovulatory disorders, including 47.6% PCOs, 14% were hormonal and immunological and 11% were uterine related causes **(Figure 4.9)**. Cases with tubal obstruction are not identified because it is believed that instead of exposing females to invasive diagnostic and curative procedures applied in tubal obstruction conditions, they are enrolled to less invasive highly successful IVF process once other causes are ruled out (Briceag et al., 2015).

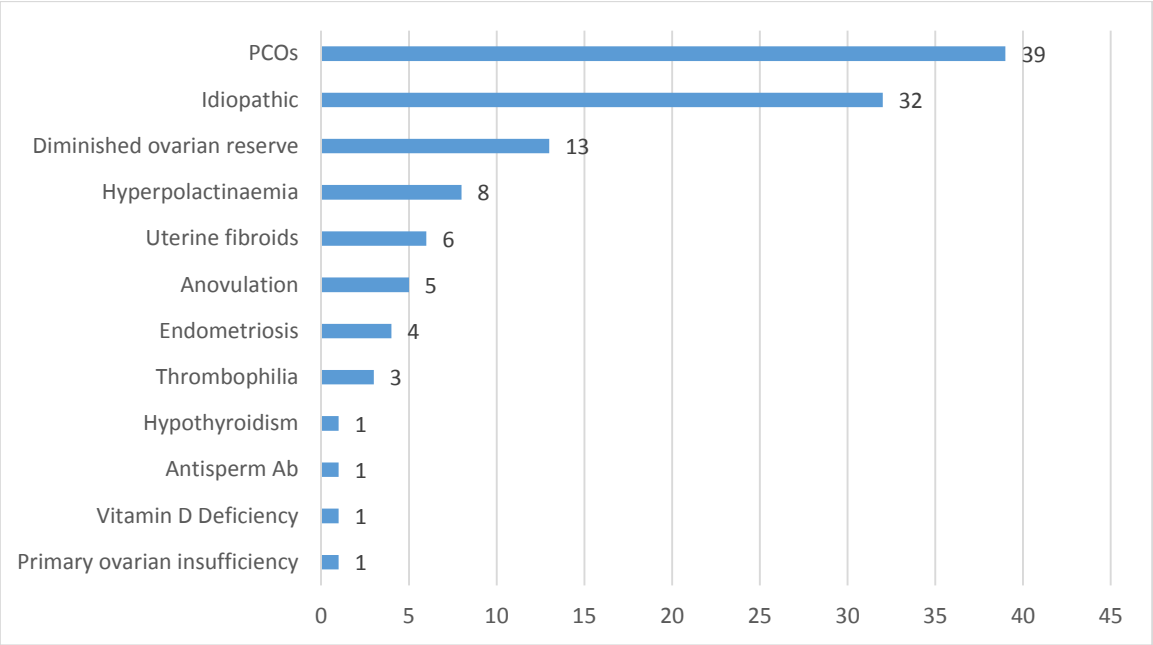


Figure (4.9): Female causes of primary infertility

Almost 80% of all causes related to male infertility are found to be attributed to suboptimal sperm parameters **(Figure 4.9)**. Oligospermia has the major contribution, where 72.5% of all husbands with abnormal sperm parameters suffer from low sperm count, 11% reported complete absence of sperms (Azoospermia), 7% have high semen viscosity, 4.4% have low sperm motility (Asthenospermia) and 2.2% for dead sperms (Necrospermia) and high levels of leucocytes in semen (Pyospermia) in each. Additionally, 15 (13%) men suffer from varicocele, 6 (5.3%) from obstructive factors and 3 (1.7%) reported immunological infertility. Decline in semen quality has been the concern of many researchers since late 20th century (Kumar & Singh, 2015). A meta-analysis was performed in 2000 on 101 research studies published from 1934 till 1996 and concluded that, sperm count has been falling in a trend pattern throughout years (Swan, Elkin, & Fenster, 2000). Another study that explored trends in semen quality between 1996 and 2007 in Tunisia reported that, sperm count decreased over the 12 years study period among men who were engaged in an infertile relationship. They suggested genital infectious disease as the main potential cause (Feki et al., 2009).

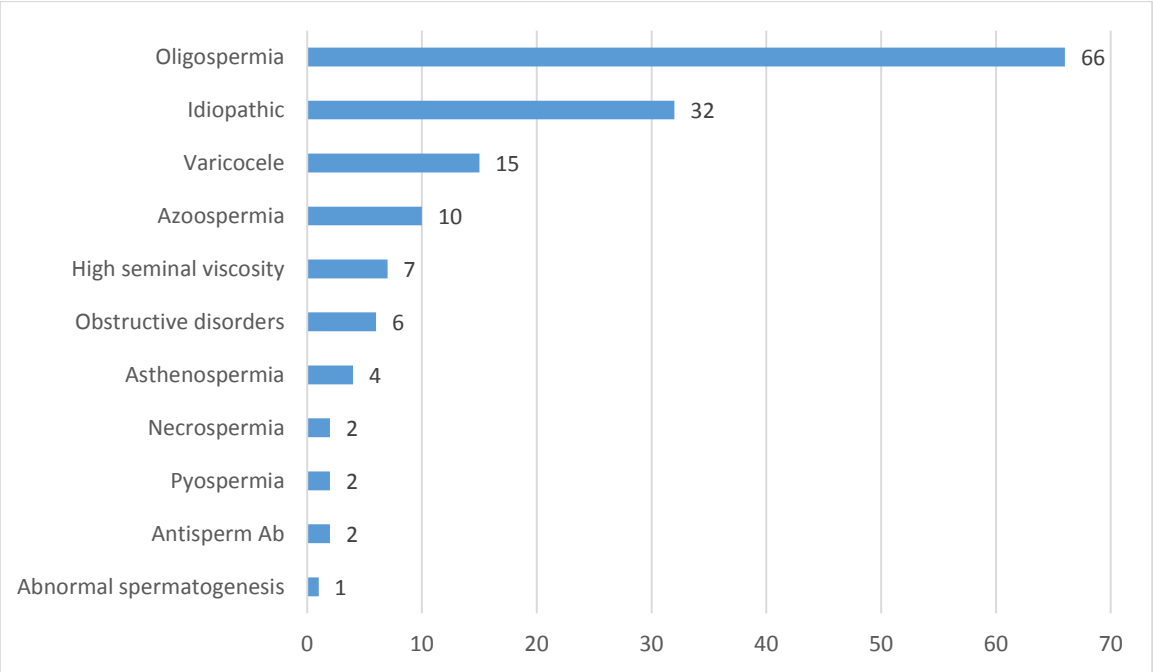


Figure (4.10): Male causes of primary infertility

4.4.2 Access to health services:

Various risk factors of infertility are known to be preventable (Crawford, Smith, Kuwabara, & Grigorescu, 2017). Study research confirmed the importance of combating the spread of sexually transmitted diseases, smoking, obesity and many other public and reproductive health problems that would be associated directly or indirectly to infertility among population (CDC, 2014). Hence, barriers to adequate and effective access to health care are essentially regarded and are addressed in this study in the form of geographical barriers, insurance coverage, service barriers and sociocultural factors.

Table (4.14): Distribution of study population by access to health care

Health care access variables		Cases		Controls		Total (%)	χ^2	P-value
		No	%	No	%			
Health insurance ownership	No	26	16.3	7	4.4	33 (10.3)	12.197	**<0.001
	Yes	134	83.8	153	95.6	287 (89.7)		
Type of health insurance	Public	119	88.1	149	97.4	268 (93.1)	Fisher exact	*0.002
	Private	16	11.9	4	2.6	20 (6.9)		
Living near a health facility	No	38	23.8	22	13.8	60 (18.8)	5.251	*0.022
	Yes	122	76.3	138	86.3	260 (81.3)		
Easy access to any health facility	No	16	10.0	12	7.5	28 (8.8)	0.626	0.429
	Yes	144	90.0	148	92.5	292 (91.2)		
Easy access to medical drugs	No	72	45.0	70	43.8	142 (44.4)	0.051	0.822
	Yes	88	55.0	90	56.2	178 (55.6)		
Seeking medical advice for Genitourinary infection	No	7	7.3	9	7.9	16 (7.6)	0.027	0.870
	Yes	89	92.7	105	92.1	194 (92.4)		

* Significant at $p < 0.05$, **Highly significant at $p < 0.001$

Of all 320 couples **(Table 4.14)**, 89.7% are health insured in which the figure is less than what has been published by PCBS (95%) through the latest national census (PCBS, 2018[d]). The regarded decline could be due to the ongoing deterioration in the economic status and increasing rate of poverty mainly among unemployed individuals and persons with chronic deducted salaries. Apparently, the proportion of infertile couples with health insurance (83.8%) are less than the control couples (93.1%). Moreover, less infertile couples have governmental insurance (88.1%) than fertile ones (97.4%) **(Figure 4.11)**. Having the lack of health insurance possession significantly associated with infertility, OR = 4.24 (95% CI, 1.78-10.08, $p < 0.001$), this provides raising a question of what role would the health care system play in combating infertility in a nation during the premarital age period. What national preventive programmes would reproductive health professionals and policy makers formulate and develop in order to enhance surveillance, research and services provided during childhood and adolescence period (Macaluso et al., 2010).

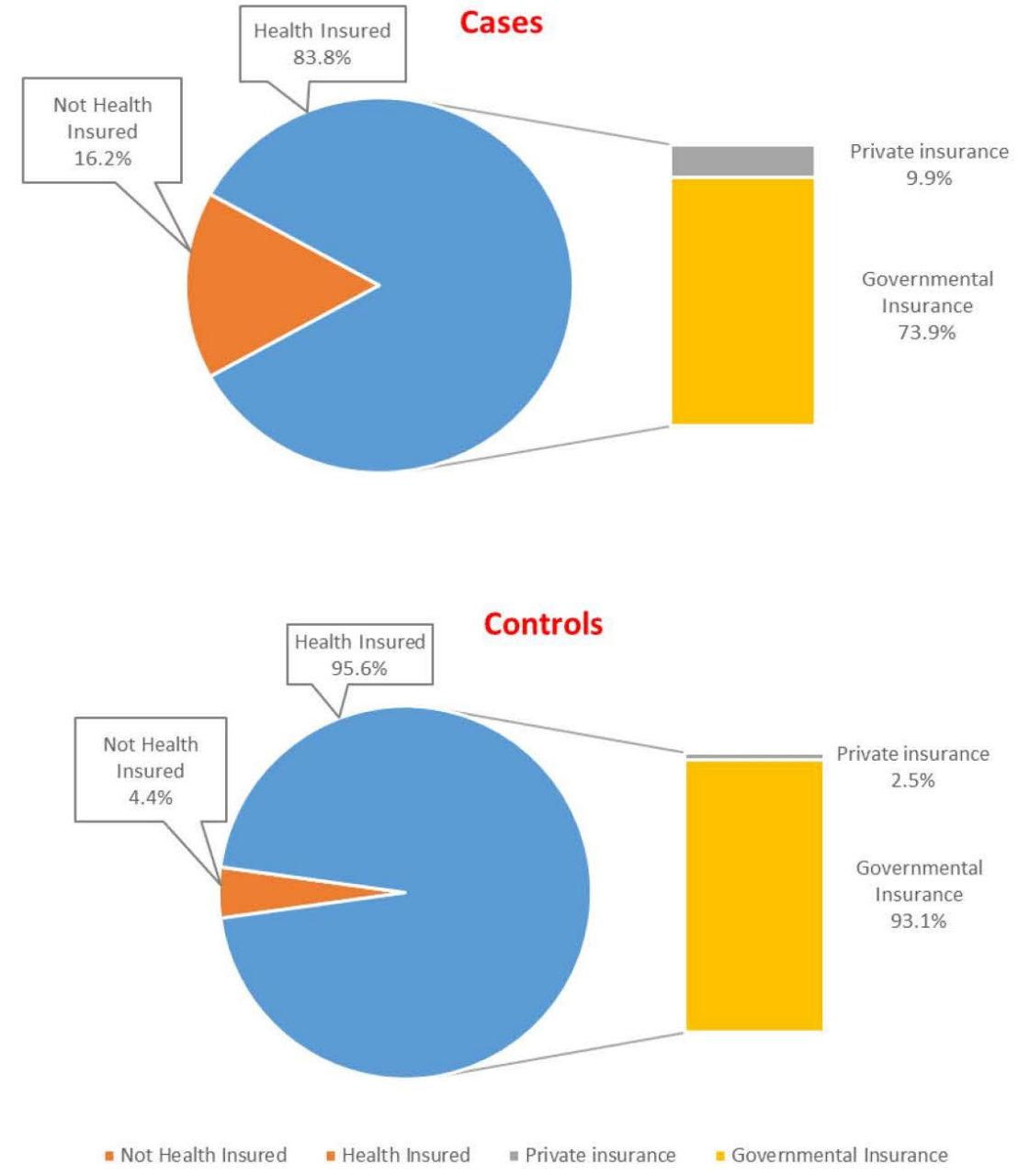


Figure (4.11): Health insurance ownership – cases vs controls

In the same context, the study revealed that people living far away from a health facility have 95% increase in the odds of having infertility than those living near a health facility, (95% CI, 1.10-3.49, p = 0.022). Again, this explains the importance of adequate accessibility to comprehensive and effective reproductive health services. Although easy access to any health facility among cases (90%) and among controls (91.2%) are almost the same and the access to drugs among infertile couples (55%) and control couples (56.2%) are quite equal, further scrutinizing of the financial, social and infrastructural accessibility along with the quality and efficiency of related services in this area is needed. A study that was published recently confirmed that, lack of research regarding male infertility in health services resulted in further barriers in early detection, prevention and control. The authors recommended to improve patient's knowledge through health education and enhance political will for change (Leung, Henry, & Mehta, 2018).

As seen in **Table (4.14)**, the proportion of women with normal fertility seeking medical advice upon suffering from genitourinary infection (92.1%) is almost equal to the infertile ladies (92.7%). Only 16 women from all surveyed population denied having medical care for such condition. But the causes behind not approaching health care is quite interesting where 3 women could not afford reaching the health facility, 5 could not afford buying the prescribed medicine, 2 do not trust health care providers and 6 ladies prefer traditional medicine. Again, this would shed the light on empowering reproductive health education among adolescents and young aged population for both genders and encouraging the political will to provide comprehensive reproductive health at the national level.

4.4.3 Female factors:

4.4.3.1 Menstrual history

Menstrual cycle is a gross indicator that represents maturation of the reproductive functioning system of females during a specific period of their lives. Delayed age of menarche or irregular menstruation is supposed to signal a disturbed reproductive mechanism and accordingly have been investigated by almost all infertility medical and public health researchers. Trying to explore this area, several variables are selected to describe the menstrual pattern of female participants and how it could be related to infertility.

Results revealed that **(Table 4.15)**, more infertile women (54.4%) started menarche at age below 14 years than women with normal fertility status (40%), in which the difference approached significant association. Some researchers demonstrated that early age of menarche (below 13) is significantly associated with diminished ovarian reserve in infertile women (Weghofer, Kim, Barad, & Gleicher, 2013). In the same respect, other researchers linked early menarche with increased risk of pelvic inflammatory disease and spontaneous abortion (Helm, Münster, & Schmidt, 1996). On the contrary, Chen et al. (2015) and Guldbrandsen et al. (2014) both concluded that the risk of infertility increases by the increase in the age of menarche among ladies.

Table (4.15): Distribution of study population by menstrual history

Menstrual history variables		**Cases**		**Controls**		**Total (%)**	χ^2	**P-value**
		No	**%**	**No**	**%**			
Age of Menarche	< 14	87	54.4	64	40.0	151 (47.2)	6.633	*0.010
	≥ 14	73	45.6	96	60.0	169 (52.8)		
	Mean	13.42		13.73		13.58	t=2.121	*0.035
	SD	1.35		1.29		1.32		
Regular menstrual cycle	No	33	20.6	7	4.4	40 (12.5)	19.314	**<0.001
	Yes	127	79.4	153	95.6	280 (87.5)		
Average menstrual cycle "days"	> 35	30	18.8	5	3.1	35 (10.9)	24.205	**<0.001
	20-35	127	79.4	143	89.4	270 (84.4)		
	< 20	3	1.9	12	7.5	15 (4.7)		
Duration of menstrual flow days	> 8	2	1.3	4	2.5	6 (1.9)	Fisher exact	0.685
	2-8	158	98.8	156	97.5	314 (98.1)		
	Mean	5.46		5.68		5.57	t=1.411	0.159
	SD	1.27		1.41		1.35		
Menstrual pattern	Poly/menorrhagia	8	5.0	17	10.6	25 (7.8)	26.412	**<0.001
	Oligo/Amenorrhea	32	20.0	4	2.5	36 (11.3)		
	Normal	120	75.0	139	86.9	259 (80.9)		

* Significant at $p < 0.05$, **Highly significant at $p < 0.001$

Of all females, 12.5% have irregular menstrual cycle, 33 (20.6%) infertile women and 7 (4.4%) fertile ones, forming a significant relationship with infertility. Additionally, having average days of menstrual cycle more than 35 is five times more among infertile women than fertile ones, (95% CI, 2.43-13.27, $p < 0.001$), providing that the reference group is women with average menstrual cycle of 20-35 days. Study that confirmed these results was held in 2014 in Finland using a prospective cohort design targeting 4567 women born in 1986. Researches collected information at the age of 16 and 26 and concluded that menstrual irregularity at age of 16 is significantly associated with infertility at age of 26 (West et al., 2014). However, the frequency of abnormal duration of menstrual flow is almost neglectable in both groups, where only 2 cases and 4 controls experience more than 8 days flow. No participants reported less than 2 days. Moreover, only 5% of all infertile women suffer either from progressive increase in quantity or duration of flow

(Polymenorrhea) or from increased frequency of periods (Menorrhagia) compared to 10.6% of the fertile group, while 20% and 2.5% respectively suffer from progressive decrease in frequency (Oligomenorrhea) or complete absence of menses (Amenorrhea), OR = 9.27 (95% CI, 3.18-26.95, $p < 0.001$). Conclusively, these evidences would demonstrate the importance of early detection of menstrual irregularities and early proper management which is only possible through health education and adequate access to effective reproductive health services.

Causes related to menstrual irregularities varies between cases and controls. Out of 33 infertile women suffering from irregular menses, 32 (97%) of them approached medical advice and reached a known diagnosis. Correspondingly, only 4 (57%) fertile ladies from total 7 were interested in knowing the causes behind such disturbances **(Figure 4.12)**. The possible explanation of such discrepancy is that women are not seeking medical advice for emerging reproductive health problem unless it interferes with her social life. Again, these results highlight the importance of having reproductive health available and reachable to all, in addition to empowering women with the required potentials for self-willing to improve health.

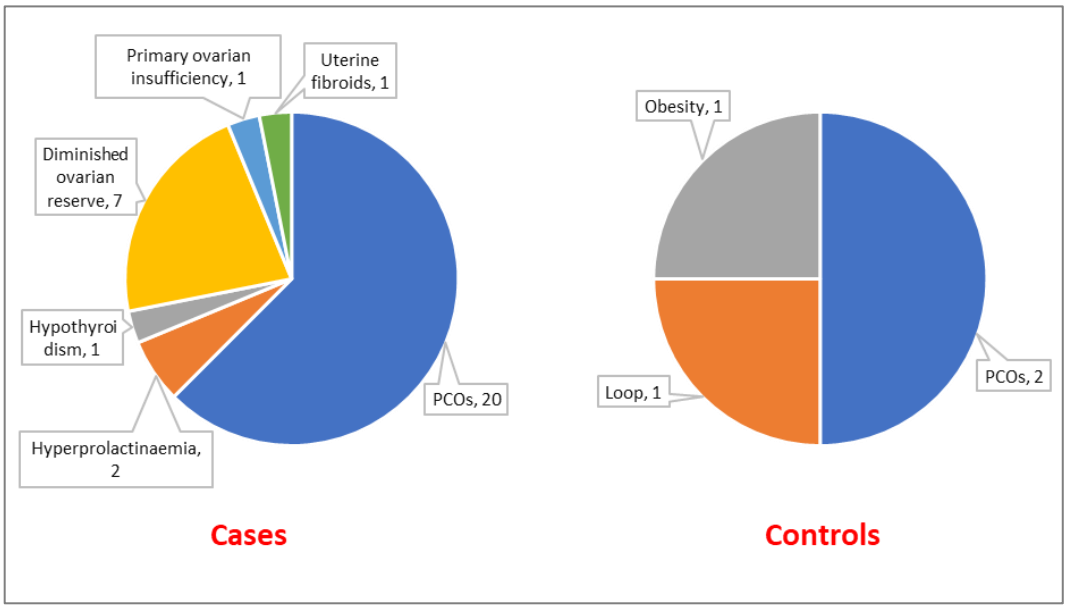


Figure (4.12): Causes of irregular menses – cases vs controls

4.4.3.2 Medical and gynaecological history

Information related to the surveyed population's medical and gynaecological history are demonstrated in this section to provide further clarity about possible risk factors associated with primary infertility. As shown in **Table (4.16)**, history of chronic illness, surgical history, drug intake and gynaecological history are included and discussed in details.

Table (4.16): Distribution of study population by medical and gynaecological history

Medical and gynaecological variables:		Cases		Controls		Total (%)	χ^2	P-value
		No	%	No	%			
Past or current history of hyperprolactinemia	Yes	13	8.1	3	1.9	16 (5.0)	Fisher exact	*0.018
	No	147	91.9	157	98.1	304 (95.0)		
Past or current history of PCOs	Yes	43	26.9	6	3.8	49 (15.3)	32.990	**<0.001
	No	117	73.1	154	96.3	271 (84.7)		
Duration of PCOs	Mean	3.79		1.50		3.51	t=1.976	**<0.001
	SD	2.81		0.55		2.74		
Using combined oral contraceptive pills	Yes	44	27.5	59	36.9	103 (32.2)	3.221	0.073
	No	116	72.5	101	63.1	217 (67.8)		
Duration of COC use	≥ 6m	15	34.1	35	59.3	50 (48.5)	6.423	*0.011
	< 6m	29	65.9	24	40.7	53 (51.5)		
Previous history of major surgery	Yes	49	30.6	42	26.3	91 (28.4)	0.752	0.386
	No	111	69.4	118	73.8	229 (71.6)		
History of PID	Yes	8	5.0	5	3.1	13 (4.1)	0.722	0.396
	No	152	95.0	155	96.9	307 (95.9)		
Intake of NSAID	Continuous	12	18.2	1	1.9	13 (10.9)	Fisher exact	*0.005
	Intermittent	54	81.8	52	98.1	106 (89.1)		
Duration of continuous intake of NSAID	> 2 years	56	84.8	47	88.7	103 (88.7)	0.371	0.543
	≤ 2 years	10	15.2	6	11.3	16 (13.4)		
NSAID tablets/month	Mean	8.06		5.25		6.81	t=2.226	*0.029
History of genitourinary infection	Yes	97	60.6	114	71.3	211 (65.9)	4.021	*0.045
	No	63	39.4	46	28.8	109 (34.1)		
Frequency of genitourinary infection during the past 2 years	> 3 times	34	35.1	30	26.3	64 (30.3)	1.893	0.169
	≤ 3 times	63	64.9	84	73.7	147 (69.7)		
Hypothyroidism as a chronic illness	Yes	3	1.9	3	1.9	6 (1.9)	Fisher exact	1.000
	No	157	98.1	157	98.1	314 (98.1)		
History of uterine fibroids	Yes	12	7.5	1	0.6	13 (4.1)	Fisher exact	*0.003
	No	148	92.5	159	99.4	307 (95.9)		
Types of uterine fibroids	Intramural	4	33.3	0	0	4 (30.8)		
	Pedunculated	1	8.3	0	0	1 (7.7)		
	Submucosal	6	50.0	0	0	6 (46.2)		
	Subserosa	1	8.3	1	100	2 (15.4)		
Hypertension as a chronic disease	Yes	3	1.9	8	5.0	11 (3.4)	Fisher exact	0.218
	No	157	98.1	152	95.0	309 (96.6)		
Duration since HTN diagnosis	> 2 years	2	66.7	3	37.5	5 (45.5)	Fisher exact	0.545
	≤ 2 years	1	33.3	5	62.5	6 (54.5)		
Intake of low dose aspirin	Yes	25	15.6	15	9.4	40 (12.5)	2.857	0.091
	No	135	84.4	145	90.6	280 (87.5)		
Duration of low dose aspirin intake	≥ 6 months	10	40.0	7	46.7	17 (42.5)	0.171	0.680
	< 6 months	15	60.0	8	53.5	23 (57.5)		
Suffered or suffering from hirsutism	Yes	12	7.5	3	1.9	15 (4.7)	Fisher exact	*0.031
	No	148	92.5	157	98.1	305 (95.6)		

NSAID=Non-Steroidal Anti-inflammatory Drugs, PCOs=Polycystic Ovary Syndrome
PID=Pelvic Inflammatory Disease, * Significant at $p < 0.05$, **Highly significant at $p < 0.001$

Participants were requested to provide information related to experiencing any past or current chronic illnesses where medical reports were reviewed when possible. Increased serum level of prolactin hormone (Hyperprolactinemia) was found to be existing or had existed in 5% of all participant with much greater percentage among infertile women (8.1%) than fertile ones (1.9%). Some research studies concluded that hyperprolactinemia prevalence among women with infertility ranges from 15 to 20% (Thirunavakkarasu et al., 2013; Kredentser, Hoskins, & Scott, 1981), while others reached a 9-17% prevalence rate (Biller et al., 1999). The low percentage revealed in this study could be because serum prolactin is not routinely requested for all women with reproductive problems. High serum level of prolactin can be caused by prolactin-secreting pituitary tumours which are 90% microadenomas (Shibli-Rahhal & Schlechte, 2011), and occur symptomatically in 10 per 100,000 to 50 per 100,000 of the general population (Melmed et al., 2011). Other causes could be related to certain medications, thyroid, renal or hepatic diseases.

PCOs is one of the most common hormonal related disorders that prevails in reproductive aged females by 6 to 16% in middle eastern region (Ding et al., 2017). From all surveyed population, 15.3% reported to have PCOs either currently or as a past experience problem. Higher rate is concluded among infertile women (26.9%) than women with normal reproductive function (3.8%), with a highly statistically significant association reached. A study that was conducted in GS showed that 17.8% of cases attending Al Basma Fertility Center suffering from subfertility in 2010 had been diagnosed with PCOs (Sirdah, et al., 2013). The lack of adequate information regarding this particular area and having more than forth of the studied infertile population suffering from PCOs, propose the need for more exploration for possible existing risk factors that might have contributed to the increasing rate. Moreover, hyperprolactinemia has long been linked to patients suffering from PCOs, although no clinical evidence was established (Bracero & Zacur, 2001). In this study, about half of participants (43.8%) who suffer from high serum prolactin were diagnosed to have PCOs, while 56.3% of them were presented with PCOs alone. This may suggest the necessity of evaluating the serum level of prolactin for every woman with definitive diagnosis of PCOs.

Although, 49 participants reported having PCOs, suffering from hirsutism appeared to be only among 15 cases. Not all those who were diagnosed with hirsutism had a history of PCOs, providing that some cases were diagnosed as idiopathic hirsutism. Twelve (7.5%) were reported to be among the infertile group compared to only 3 (1.9%) from their

counterparts. The significant association and the provision that not all cases are linked to PCOs, offer the indication for including management of hirsutism as a risk factor that hinders fertility.

Current evidence on resuming fertility after using Combined Oral Contraceptive pills (COC) has been inconclusive (Kent, 2009). All responses collected entitling the use of COC, either for birth control or as a part of plan of management for certain reproductive disorders, showed that 32.2% of all participants had used COC during a certain period of their life, with more proportion of fertile women (36.9%) than infertile ones (27.5). Nevertheless, the association did not reach a significant level. Some researchers assumed that fertility is delayed upon the use of COC in which only fifth of the users achieved pregnancy after the first cycle of pills caseation (Kent, 2009). Additionally, a systematic review analysis revealed that 83.1% of discontinuers resumed pregnancy within 12 months with no association with the duration of COC use (Girum & Wasie, 2018). On the contrary, the duration of COC use in this study seems to have a protective effect, OR = 0.36 (95% CI, 0.16-0.80, p = 0.01) where 35 (59.3%) fertile women used COC for more than 6 months compared to 15 (34.1%) infertile ladies, while 24 (40.7%) and 29 (65.9%) respectively used the pills for less than 6 months.

More than a quarter of the population surveyed underwent major surgery during a given period of their life at least once. Of all infertile women, 49 (30.6%) reported experiencing a major surgery compared to 42 (26.3%) of those of the fertile group. Moreover, more cases (5%) than controls (3.1%) reported a previous history of Pelvic Inflammatory Disease (PID), where the relationship did not reach a significant level. Acute lower abdominal pain in women at their reproductive age usually form a challenge for health care providers to diagnose. Misdiagnosis to other conditions, like acute urinary tract infection, may be the most possible cause through which the patient is treated with antibiotics and the condition resolve without accurate diagnosis (Wølner-Hanssen, 1997).

Non-steroidal anti-inflammatory drugs (NSAID) are known as anti-prostaglandins. They act mainly on inhibiting the cyclooxygenase-2 enzyme, which plays an important role in the synthesis of prostaglandins, which in turn is an essential component of the process of ovulation, implantation and placentation (Mendonça, Khamashta, Nelson- Piercy, Hunt, & Hughes, 2000). Twelve infertile women has been discovered to practice continuous ingestion of Ibuprofen; more than 15 tablets per month, compared to only one woman in

the corresponding group, while 54 and 52 respectively consume the medicine in an intermittent pattern. On the other hand, nearly the same proportion of infertile women (84.8%) reported using the medicine for more than 2 years as their counterparts (88.7%). As demonstrate in **Figure (4.13)**, the number of tablets consumed per month among cases and controls show apparent discrepancy. When the rhythm of NSAID ingestion is significantly associated to infertility, the duration of intake seems to have no effect. This could explain the reversable effect of the drug which has been evidently proved through several research studies (Skomsvoll et al., 2005).

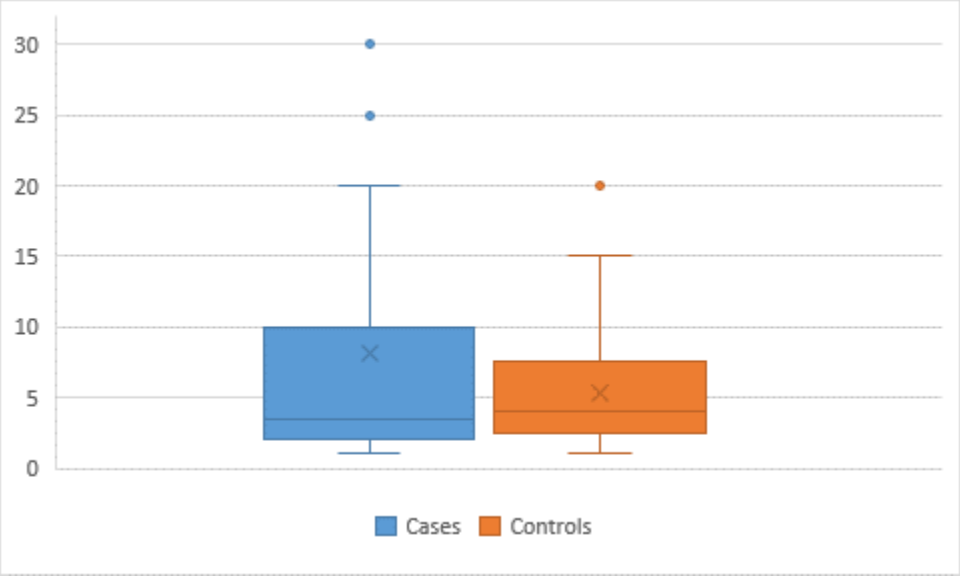


Figure (4.13): Number of NSAID tablets consumed per month – cases vs controls

Responses regarding history of genitourinary infection showed notable results. Women of the infertile couples (60.6%) revealed to be less exposed to genitourinary infection than those of the fertile couples (71.3%) with a relationship reaching a protective significant level. Nevertheless, the frequency of infection among exposed group; more than 3 times during the past two years; is more in infertile women (35.1%) than in fertile ones (26.3%), but still the association did not approach a significant level. On the contrary, several research studies confirmed the relationship between genitourinary infection and infertility. A case control study conducted in India revealed that, 28.1% of infertile women were infected with Chlamydia Trachomatis compared to 3.3% of the fertile women (Malik, Jain, Hakim, Shukla, & Rizvi, 2006). Another study conducted in Nigeria concluded that, women with seropositive chlamydial trichomonas infection were three times more likely to be infertile than seronegative women (Ojule, Ibe, & Theophilus, 2015).

Hypothyroidism is one of the chronic illnesses that explored in this study. Only six cases (1.9%) were diagnosed to have hypothyroidism of all total participants; 3 infertile women and 3 fertile women. A study that was held in south of Hebron revealed that the prevalence of hypothyroidism among surveyed population was 5.2%. Likely wise, the exposure to chronic hypertension did not differ much, where only 3 (1.9%) cases reported suffering from chronic HTN compared to 8 (5%) of the corresponding group. The duration during which hypertension has been first diagnosed also did not affect the results. Two cases were diagnosed since more than 2 years and one case since less than 2 years, while 3 and 5 respectively were noticed from the control group. Women in the cases group were aged 30, 34 and 36 with a marital duration of 6, 11 and 18 years respectively, without the ability to conceive. Provided information may offer a hint that the hypertension in the cases group could be an effect rather than a cause. In the same respect, the use of low dose aspirin was investigated among the two groups. Participants showed a percentage of 12.5% of whom are consuming low dose aspirin on daily basis. Although marked difference appeared between infertile women (15.6%) and fertile ones (9.4) the association did not reach a significant level. More infertile women consume low dose aspirin than fertile ones contemplating with the evidence that low dose aspirin consumption increases the rate of pregnancy among couples attending fertility centers for IVF therapy (Wang et al., 2017). The duration of low dose aspirin also showed that, 40% of infertile women are consuming the medicine for more than 6 months compared to 46.7% of the fertile ladies. The lower proportion detected among infertile women was because some of the infertile couples included in the study were actually at the first stages of fertility therapy. Upon reviewing literature, controversial evidences were concluded in this regard. In 2003, a randomized controlled trial revealed that low dose aspirin has no significant role in either improving the blood flow to the ovaries and uterus nor in modifying ovarian functions (Lok, Yip, Cheung, Yin Leung, & Haines, 2004). But in 2007, a meta-analysis review revealed that clinical pregnancy rate increase by the daily administration of low dose aspirin (Ruopp, Collins, Whitcomb, & Schisterman, 2008). Accordingly, this issue is still open for more arguments and debate to be scrutinized more.

Uterine fibroids has long been linked to fertility impairment (Lisiecki, Paszkowski, & Woźniak, 2017) which is well apparent in this study. The total number of participants discovered to have uterine fibroids are 13 (4.1%) females, 12 (7.5%) are infertile and only one lady (0.6%) with normal fertility status. 38.5% of the cases under went hysteroscopic

myomectomy, 23% were left to shrink alone without intervention, 23% had laparoscopic myomectomy and 7.7% forms abdominal myomectomy and medical treatment for each. Similarly, a case control study that was held in GS examining etiological risk factors of infertility among females attending IVF centers revealed that 7.1% of infertile females were diagnosed with uterine fibroids (Sirdah et al., 2013).

4.4.3.3 Family history

As it is discussed in many studies, family history taking is an essential component in the course of exploring possible risk factors and causality behind infertility in couples (Vance & Zouves, 2005). Hereunder is a brief discussion about the relationship between various family history diseases and infertility.

Table (4.17): Distribution of study population by family history information

Family history variables – Female		Cases		Controls		Total (%)	χ^2	P-value
		No	%	No	%			
Family history of infertility	Yes	24	15.0	12	7.5	36 (11.3)	4.507	*0.034
	No	136	85.0	148	92.5	284 (88.8)		
Degree of relatives having infertility	1st degree	11	45.8	4	33.3	15 (41.7)	Fisher exact	0.330
	2nd degree	13	54.2	8	66.7	21 (58.3)		
Family history of subfertility	Yes	17	10.6	20	12.5	37 (11.6)	0.275	0.600
	No	143	89.4	140	87.5	283 (88.4)		
Family history of hypothyroidism	Yes	10	6.3	11	6.9	21 (6.6)	0.051	0.821
	No	150	93.8	149	93.1	299 (93.4)		
Family history of PCOs	Yes	18	11.3	12	7.5	30 (9.4)	1.324	0.250
	No	142	88.8	148	92.5	290 (90.6)		

* Significant at $p < 0.05$

Responses to positive infertility family history **(Table 4.17)** formed 11.3% of the total surveyed population. The proportion of infertile women with positive family history (15%) is significantly higher than those of the fertile group (7.5%). Nevertheless, the condition did not approach significant level when linking it to the degree of relativeness. Positive family history for infertility in infertile women was 45.8% related to first degree relatives and 54.2% was related to second degree, while the percentage was 33.3% and 66.7% respectively among the fertile group. Correspondingly, the frequency of positive family history for subfertility is more among fertile women (12.5%) than the infertile ones (10.6%). This could be because people who already have children, usually do not declare about having difficulty is resuming pregnancy and eventually are not known by their relatives to be sub-fertile. On the contrary, a case control study that was held in GS

revealed that subfertility family history is significantly higher among infertile group of women (Sirdah et al., 2013).

Positive responses regarding family history of hypothyroidism among infertile and fertile women are almost the same. The frequency of positive hypothyroidism family history is 6.3% for infertile females and 6.9% for fertile females. On the other hand, family history of PCOs is much higher among infertile women (11.3%) than women with normal fertility status (7.5%), but the relationship did not approach significant level.

4.4.3.4 Perceived stress and infertility

To measure the level of how stress is appraised among participants, a PSS that was originally developed by Sheldon Cohen and his colleagues (Cohen, Kamark, & Mermelstein, 1983) has been adopted and applied. The tool consists of 14 items with a scale of answers that range from 0 (Never) till 4 (Very Often). Having seven positive questions (4, 5, 6, 7, 9, 11 &13), the scores are summed for each subject after reversing the results of the seven positive items so that 0=4, 1=3, 2=2, 3=1, 4=0.

Table (4.18): Distribution of study population according to Perceived Stress Scale results

Perceived Stress Scale	**Cases**		**Controls**		**Total (%)**	χ^2	**P-value**
	No	**%**	**No**	**%**			
High perceived stress Scores 27-56	111	69.4	94	58.8	205 (64.1)	3.923	*0.048
Moderate perceived stress Scores 0-26	49	30.6	66	41.3	115 (35.9)		
Mean	28.89		27.43		28.16	t=2.46	*0.014
SD	4.98		5.58		5.33		

* Significant at $p < 0.05$

Of all 320 participating females **(Table 4.18**), the score results showed a mean of 28.16 with a range from 13 to 43 and a statistically significant difference between the average score results of cases (28.89) and that of the controls (27.43), $p = 0.014$. Infertile women who perceived stress moderately were 49 (30.6%) compared to 66 (41.3%) fertile women, while 111 (69.4%) and 94 (58.8%) females respectively scored high levels, OR = 1.59 (95% CI, 1.004-2.521). The high perception and appraisal of stress among infertile women could have been concluded from various social and psychological implications encountered by time. However, some authors believe that stress is a concomitant risk factor to infertility and subsequently raising perplexity of which comes first; stress or infertility (Rooney & Domar, 2018). In Morocco, researchers studied infertility stress

through cross sectional approach applied on 120 couples who visited a fertility center seeking treatment for infertility. The researchers used the same tool and concluded that stress perceived among infertile group is significantly associated with the duration and the type if infertility (Zaidouni et al., 2018). On the contrary, another study that was applied through a prospective cohort approach with the participation of 485 women concluded that perceived stress and stress accompanied with infertility has no effect on pregnancy outcome for women desiring IVF treatment (Cesta et al., 2018).

4.4.4 Male factors:

4.4.4.1 Medical exposures

Male infertility are accounted to various medical conditions or could be related to certain agents or genetic abnormalities (Punab et al., 2017). Reviewing literature showed controversial results regarding certain medical exposures, thus the main concern is to explore more in this area for the purpose of further contribution.

Table (4.19): Distribution of study population by male medical exposures

Medical exposures variables - Male		Cases		Controls		Total (%)	χ^2	P-value
		No	%	No	%			
Chronic medical illness	Yes	18	11.3	11	6.9	29 (9.1)	1.858	0.173
	No	142	88.8	149	93.1	291 (90.9)		
Undescended testis	Yes	4	2.5	1	0.6	5 (1.6)	1.829	0.176
	No	156	97.5	159	99.4	315 (98.4)		
Varicocele	Yes	77	48.1	20	12.5	97 (30.3)	48.064	**<0.001
	No	83	51.9	140	87.5	223 (69.7)		
Type of varicocele	Bilateral	42	54.5	12	60.0	54 (55.7)	0.191	0.662
	Unilateral	35	45.5	8	40.0	43 (44.3)		
Nonspecific urethritis	Yes	14	8.8	9	5.6	23 (7.2)	1.171	0.279
	No	146	91.3	151	94.4	297 (92.8)		
Mumps	Yes	2	1.3	1	0.6	3 (0.9)	0.336	1.000
	No	158	99.8	159	99.4	317 (99.1)		
Genitourinary infection	Yes	60	37.5	56	35.0	116 (36.3)	0.216	0.642
	No	100	62.5	104	65.0	204 (63.8)		
Frequency of genitourinary infection in past 2 years	≥ 5 times	17	28.3	3	5.4	20 (17.2)	Fisher exact	*0.001
	< 5 times	43	71.7	53	94.6	96 (82.8)		
Pelvic surgeries	Yes	66	41.3	19	11.9	85 (26.6)	35.388	**<0.001
	No	94	58.8	141	88.1	235 (73.4)		

* Significant at $p < 0.05$, **Highly significant at $p < 0.001$

Men in the infertile group presented with chronic illness (11.3%) are more than those in the fertile group (6.9%) **(Table 4.19)**. Diabetes mellitus is the most prevalent chronic disease noticed among participant, where 7 infertile men compared to 4 of the corresponding group reported suffering from diabetes. Bronchial asthma is reported in 2 fertile and 2 infertile

men, epilepsy is in one for each group, lung fibrosis is also one in each group and only one case reported suffering from hypertension and one from Familial Mediterranean Fever in the infertile group. Although the apparent discrepancy between the two groups, the relationship did not reach a significant level.

Proportion of male participants with undescended testis forms 2.5% in the infertile group and 0.6% in the fertile one. The problem of undescended testis has long been linked to infertility and subfertility. About one to four percent of all full term newborns usually suffer from this condition (Goel, Rawat, Wakhlu, & Kureel, 2015). The low percent reported in this study might be due to recall bias or because repair of undescended testis often occurs in early stages of life and grown up men happened to be ignorant to this particular information. This might offer the need for a unified well-structured reporting criterion to be included in the primary and secondary health care reporting system for the purpose of adequate surveillance and research and subsequently to be able to provide optimal prevention and control care regarding this issue.

Of all male participants **(Table 4.19)**, 30.3% suffered or still suffering from varicocele which is either bilateral or unilateral. Almost half of the males in the infertile group reported having varicocele while only 12.5% of those of the control group complained the same. The association between the two groups is highly significant giving more than six times risk of infertility, OR = 6.49 (95% CI, 3.702-11.39, $p < 0.001$). The study also included inquiries about the type of varicocele, whether it is bilateral or unilateral. Results shows that unilateral or bilateral varicocele do not affect the outcome. Infertile men reported 54.5% having bilateral varicocele and 45.5 reported unilateral affection, while 60% and 40% respectively were reported among their counterparts. Most studies referred to varicocele as presenting in 40% of all infertile men (Agarwal, Prabakaran, & Allamaneni, 2006). For so long, a debate has grown on whether varicocele prevents men from fathering and whether varicocelectomy improves the chance of pregnancy in healthy women (Kroese, de Lange, Collins, & Evers, 2012). Recently quite more evidence suggested that there is remarkable chance for fathering upon varicocele repair. A randomized control trial was conducted in 2009 revealed that varicocelectomy not only increases the chance of pregnancy but also improve sperm quality among affected infertile men (Abdel-Meguid, Al-Sayyad, Tayib, & Farsi, 2011). A more recent review study concluded that repair of varicocele may reduce seminal oxidative stress and eventually improve seminal (Ficarra, Crestani, Novara, & Mirone, 2012).

The wide debate about whether infection of the genital and/or the urinary tract have a particular role in infertility or not, inquiries about non-specific urethritis and genitourinary tract infection has been applied. Exposure to nonspecific urethritis represents 7.2% of the total surveyed population which is congruent with the evidence based predicted percentage (Schuppe et al., 2017). The proportion of infertile men with the condition (8.8%) is greater than that of the control group (5.6%), but in spite of that, the association is not significant. This could be because many nonspecific urethritis conditions are asymptomatic and exist without being diagnosed (Horner, 2005). Genitourinary infection did not differ between men in the cases and in the control group. 60 men out of 160 in the cases group reported experiencing genitourinary tract infection during the past two years at least once, and also 56 out of 160 of those in the control group. The main concern was to explore the frequency of infection during a pertained period of time. The proportion of infertile men (28.3%) who suffered from infection for more than 5 times during the past two years were much more than the fertile men (5.4%), providing a highly significant association. This would be rather due to the developing of orchitis or epididymitis upon repeated exposure to infectious agents. One of the most exceptional randomized control trails that was conducted with the participation of 120 men with impaired sperm quality and genitourinary infection had shown that, there is dramatic effect when antibiotic therapy has been used, where sperm quality improved and about 28% of the couples succeeded pregnancy (Wall & Jayasena, 2018).

Inquiries about mumps as a childhood illness revealed that only two (1.3%) infertile men and one (0.6%) male participant with normal fertility status had suffered from mumps during their life time. Palestine has been exposed to several attacks of mumps outbreaks since 2003 (MoH, 2012). The results presented are against the reports published nationally which could be because mumps infection usually occur during a period of persons' life during which they cannot recall. The importance of studying mumps as a risk factor for infertility among men has been explored frequently in research, and recommendation not to neglect asymptomatic inflammation in the testis to develop to chronic orchitis (Schuppe et al., 2008). Therapeutic guidelines for complicated cases are not available and highly recommended.

Responses regarding history of pelvic surgery revealed 26.6% of all participants being exposed to a pelvic surgery during a certain period of their life. Infertile men with previous pelvic surgery (41.3%) appear to be way more than fertile men (11.9%). The highest

proportion of surgeries was varicocele repair which is reported from 62 infertile men and 17 fertile men. Undescended testis repair is reported once through an infertile participant along with 2 inguinal hernial repair and one fertile man declared having a Great March of Return injury in the pelvis that needed surgical intervention. The association is highly significant.

4.4.4.2 Family history

Again, and as mentioned before, family history is explicitly important in revealing underlying risk factors particularly in infertility subject. In this distinct regard, various diseases possibly known to be related to infertility were explored as presented hereunder:

Table (4.20): Distribution of study population by family history of certain diseases

Family history variables – Male		Cases		Controls		Total (%)	χ^2	P-value
		No	%	No	%			
Family history of infertility	Yes	36	22.5	19	11.9	55 (17.2)	6.345	*0.012
	No	124	77.5	141	88.1	265 (82.8)		
Degree of relatives having infertility	1st degree	23	63.9	11	57.9	34 (61.8)	0.189	0.663
	2nd degree	13	36.1	8	42.1	21 (38.2)		
Family history of subfertility	Yes	27	16.9	9	5.6	36 (11.3)	10.141	*0.001
	No	133	83.1	151	94.4	284 (88.8)		
Family history of hypothyroidism	Yes	8	5.0	6	3.8	14 (4.4)	0.299	0.585
	No	152	95.0	154	96.3	306 (95.6)		
Family history of varicocele	Yes	18	11.3	8	5.0	26 (8.1)	4.186	*0.041
	No	142	88.8	152	95.0	294 (91.9)		
Family history of undescended testis	Yes	1	0.6	2	1.3	3 (0.9)	Fisher exact	1.000
	No	159	99.4	158	98.8	317 (99.1)		

* Significant at $p < 0.05$

More family history for infertility **(Table 4.20)** is reported among infertile men (22.5%) than fertile ones (11.9%), which appears to be more than what has been reported by their wives, 15% and 7.5% respectively. Nevertheless, both have shown a significant association with infertility. Infertile men reported 1st degree positive family history with a proportion of 63.9%, which is quite similar to what has been reached in the fertile group (57.9%), offering an conclusion that no matter the degree of relatedness, family history provides more than 2 times risk among the infertile group, OR = 2.154 (95% CI, 1.18-3.95, p = 0.012). One of the most research subjects that has been perpetually explored is the association of azoospermia and its genetic pertinence. It is worth to mention here that, 66 (44.9%) azoospermia cause of infertility is reported from all diagnosis collected from 160 infertile couples. A recent study claimed that mutation of 17 genes in the Y male

chromosome that cause infertility is actually found in human genes (Miyamoto et al., 2017).

Family history of subfertility is positive in 16.9% and 5.6% of the infertile men and fertile men respectively. The significant association here could be related to other potential causes than genetic factors. More conceivable causes could be related to shared environmental factors that may have long term effect like that which have mentioned before regarding occupational exposure and sources of drinking water. This assumption may offer an area for further investigation and research which is unfortunately not applicable in this study.

Of all 320 participants, 18 (11.3%) of the infertile men compared to 8 (5%) fertile ones declared having a positive family history of varicocele. Although the association is significant between the two groups, but what is noticed is that there is increasing trend of varicocele among men (30.3%) in the studied generation in relation to their families (8.1%), in spite of most studies revealed that the prevalence of varicocele increases by age (Alsaikhan et al., 2016).

As mentioned previously in different aspects of this study, hypothyroidism shown to be not related to infertility in both the females and males. Only 8 (5%), compared to 6 (3.8%) infertile and fertile men respectively, have reported hypothyroidism occurring in one or more of their family members. The association here is not significant. Contradictory to these results, most research findings found that hypothyroidism affects the erectile function, sperm quantity, sperm morphology and also sperm motility in infertile men (Ranjender, Monica, Walter, & Agarwal, 2011). Other studies confirmed the effect of hypothyroidism on sperm morphology and claimed that further research is needed for revealing its effect on sperm motility (Krassas, Papadopoulou, Tziomalos, Zeginiadou, & Pontikides, 2008)

Undescended testis is among the least reported cases. Only three participants reported having a positive family history in this regard. From my experience as a health care provider in the primary health care field, the percentage of undescended testis could be way much greater than what has been reached in this study. This might again, offer an opportunity for scaling an adequate reporting system in primary health care and hospital neonatology hospital department for the purpose of proper surveillance, research and control, as several studies revealed the link between undescended testis and the chance of adulthood infertility or even malignant development (Cortes, Thorup, & Visfeldt, 2001).

4.4.5 Relationship between infertility and various medical predictors:

Binary logistic regression is performed to predict the relationship between infertility and different medical independent variables related to both the females and males participating in this study. Selected medical variables have been chosen from already tested statistically significant ones and that formulate the best fit model as shown in **Table (4.21)**.

Table (4.21): Predictors of primary infertility among different independent medical variables by using binary logistic regression

Medical Variables	*β*	*S.E.*	Wald χ^2	*p-value*	*OR (95% CI)*
Living near a health facility Yes=Reference	0.550	0.353	2.424	0.119	1.73 (0.87-3.47)
Age of menarche ≥14=Reference	0.684	0.272	6.325	*0.012	1.98 (1.16-3.38)
Menstrual regularity Yes=Reference	1.118	0.519	4.644	*0.031	3.06 (1.11-8.45)
Suffered or suffering from PCOs No=Reference	1.729	0.519	11.100	*0.001	5.63 (2.04-15.58)
Perceived stress 1-26=Reference	0.308	0.283	1.181	0.277	1.36 (0.78-2.37)
History of varicocele No=Reference	1.554	0.554	7.864	*0.005	4.73 (1.60-14.02)
History of pelvic surgery No=Reference	0.295	0.584	0.254	0.614	1.34 (0.43-1.22)
Family history of infertility – Female No=Reference	0.695	0.444	2.452	0.117	2.00 (0.84-4.78)
Family history of infertility – Male No=Reference	0.279	0.384	0.527	0.468	1.32 (0.62-2.81)
Family history of subfertility – Male No=Reference	0.861	0.475	3.282	0.070	2.36 (0.93-6.00)
Family history of varicocele – Male No=Reference	-0.265	0.545	0.236	0.627	0.77 (0.26-2.23)
Constant	-1.649	0.299	30.490	**<0.001	0.19

β=beta coefficient, S.E.=standard error, χ^2=chi square, CI=confidence interval, Model coefficient chi^2=105.23, p<0.001, Nagelkerke r^2=0.374, Membership for cases, *significant=p<0.05, **highly significant=p<0.001

It is clear that PCOs is one of the most variables expected to be related to infertility in this study. The odds of suffering from PCOs are five times more likely among infertile ladies than fertile ones. As mentioned before, no sufficient information and research regarding this subject have been conducted in Palestine. Studying the prevalence and possible

correlated risk factors would provide opportunity for setting nationally suitable measures to control such phenomenon. Additionally, women who had experienced their first menarche before the age of 14 were more likely to suffer from primary infertility. Early menarche (below 14 years age) increased the odds of primary infertility by 98%. Although research studies had controversy results, but most of what has been reviewed concluded that early menarche was significantly associated with diminished ovarian reserve and with increased risk of pelvic inflammatory disease and spontaneous abortion (Weghofer et al., 2013). Moreover, the odds of irregular menses are three times more likely among infertile women than women with normal fertility status. In this respect, health education, preconception care and other components of early reproductive care would be essential and may offers remarkable contribution to managing causes of menstrual irregularities at early stages.

Only one male medical variable appeared to be significant in the illustrated model **(Table 4.21)**. Suffering from varicocele seems to be more likely among infertile men than men with normal reproductive status. It increases the odds by 4.73 times. As mentioned before, the results reached are congruent with many studies, but there is still opposing arguments on whether managing varicocele improve fertility status or other confounders affect the outcome. This area shall be an interesting aspect of male infertility to be deeply investigated.

4.5 Lifestyle and infertility

4.5.1 Smoking and infertility:

The main four components of lifestyle that are included in this study are, smoking status, nutrition, physical activities and BMI. Smoking status is explored in the form of being active, former or passive tobacco smoker, the type of tobacco used whether it is cigarettes or waterpipe, the number of cigarettes or waterpipe consumed per day and the time during which the participant has been practicing this habit **(Table 4.22)**.

The latest records presented cigarette smoking prevalence in Palestine was published in 2018 and revealed that 39.7% of men in Palestine smoke cigarettes (Abdulrahim & Jawad, 2018). Of all 320 male responses obtained in this study, 40.3% of men are known to be active cigarette smokers. It is obvious from the results that the proportion of infertile men who are active cigarette smokers (38.1%) are less than those of the control group (42.5%).

Correspondingly, who quit smoking from the infertile group (36.5%) are more than formers from the control group (27.5%), where the difference did not approach a significant level. The results show that infertile men are quitting smoking more than those who have a normal fertility status, which could be related to the medical recommendation provided to them during their repeated visits to fertility centers or because they might have autonomously quitted any bad habits that they think would adversely affect their fertility status. On the other hand, only one woman reported being active smoker and this woman is among the infertile group. However, there would be under-estimation in the numbers of smoking females, because living in a restrictive and very conservative landscape as Arab countries and specifically in GS, prevent females from disclosing such information for the fear of societal rejection.

Table (4.22): Distribution of study population by various smoking related variables

Variables related to smoking habits		**Cases**		**Controls**		**Total (%)**	χ^2	**P-value**
		No	**%**	**No**	**%**			
Current cigarette smokers - Husband	Yes	61	38.1	68	42.5	129 (40.3)	0.636	0.425
	No	99	61.9	92	57.5	191 (59.7)		
Former cigarette smokers - Husband	Yes	59	36.9	44	27.5	103 (32.2)	3.221	0.073
	No	101	63.1	116	72.5	217 (67.8)		
# cigarettes consumed/d – Husband	> 5	51	83.6	43	63.2	94 (72.9)	6.749	*0.009
	≤ 5	10	16.4	25	36.8	35 (27.1)		
Duration of smoking by years - Husband	> 2	52	85.2	48	70.6	100 (77.5)	3.964	*0.046
	≤ 2	9	14.8	20	29.4	29 (22.5)		
Current waterpipe smokers - Wife	Yes	3	1.9	1	0.6	4 (1.3)	Fisher exact	0.623
	No	157	98.1	159	99.4	316 (98.8)		
Current waterpipe smokers - Husband	Yes	38	23.8	35	21.9	73 (22.8)	0.160	0.689
	No	122	76.3	125	78.1	247 (77.2)		
Using waterpipe/day – Husband	> Once/day	19	50.0	6	17.6	25 (34.7)	8.287	*0.004
	Once/day	19	50.0	28	82.4	47 (65.3)		
Duration of waterpipe use by years - Husband	> 5	16	42.1	16	47.1	32 (44.4)	0.178	0.673
	≤ 5	22	57.9	18	52.9	40 (55.6)		
Passive smoking - Wife	Yes	84	52.5	60	37.5	144 (45.0)	7.273	*0.007
	No	79	47.5	100	62.5	176 (55.0)		

* Significant at $p < 0.05$

Cigarette smoker is defined here as anyone who smokes at least one cigarette on daily basis. As shown in **Table (4.22)**, being a smoker has no significant effect on infertility, but the number of cigarettes consumed per day and the period during which the participant has been practicing this habit show different results. From all 61 infertile men who are active smokers, 51 (83.6%) consume more than 5 cigarettes per day compared to only 44 (27.5%)

smokers in the fertile group. Additionally, the proportion of infertile men who have been smoking for more than two years are 85.2% compared to 70.6% of the total smokers in the fertile group. The relationship in both variables approached a significant level, indicating the effect of both the number of cigarettes and the duration of smoking on fertility status. Literature supported the results in many occasions. A cross sectional analysis that was performed in Denmark found that, there is a dose-response relationship between smoking cigarettes and quality of semen analysis (Ramlau-Hansen et al., 2007). In the same respect, some authors reached different results, where a meta-analysis showed that there is a relationship between smoking and impaired sperm quality with no clear dose-response effect found (Vine, Margolin, Morrison, & Hulka, 1994). Although, authors reported controversary results, but what has been established is that men with impaired fertility and who quitted smoking were found to be gaining significant benefits in relation to their semen quality (Mostafa, 2010).

Waterpipe smoking is another type of tobacco smoking that has recently gained a lot of popularity mainly in the middle eastern countries (Naeem, 2011). Accordingly, we were interested in this study to explore the relationship between using waterpipe as a tobacco smoking and infertility, given that it gained a lot of popularity in Palestine mainly among university students (Tucktuck, Ghandour, & Abu-Rmeileh, 2017). So, results showed that the proportion of men using waterpipe smoking (22.8%) is less than those smoking cigarettes (40.3%). Infertile men (23.8%) and fertile men (21.9%) are found to have nearly the same frequency, in which the relationship did not reach a significant level of association. Female waterpipe smokers were found only in 2 cases and one control. However, the results were against to what has been reviewed in literature. Research revealed that both cigarettes and waterpipe smoking have toxic effect on reproductive functions, but the instant consequences of waterpipe smoking is way much more. A cross sectional study that was performed in Egypt found that, there a toxic effect of waterpipe smoking on almost all semen parameters, including spermatogenesis and spermatozoa function (Fawzy, Kamal, & Abdulla, 2011). In spite of the growing interest in this field, research seems to be scarce and limited and rarely reached the extent to explore all areas.

According to a meta-analysis research, the use of waterpipe smoking on daily basis is equivalent to 10 cigarettes smoked per day (Neergaard, Singh, Job, & Montgomery, 2007). In this study, half of the infertile men who reported practicing waterpipe smoking, consume it more than once daily, compared to only 6 (17.6%) of the waterpipe smokers in the fertile group, providing a significant relationship, $p = 0.004$. The duration upon which smokers have been practicing this habit revealed to be not significant between the two groups, where 42.1% of the infertile smokers claimed that they have been smoking for more than five years compared to 47.1% of those of the opposite group. Information related to the mode of use during the proposed period of consumption; whether intermittent or continuous; and practicing both cigarettes and waterpipe tobacco smoking at the same time is needed to be explored for further in-depth clarification.

Inquiries about passive smoking among females revealed that more than half of the women in the infertile group are exposed to such phenomenon, compared to only 37.5% of those of their counterparts, providing a significant increase in the odds of infertile females who are exposed to secondhand smoke, OR = 1.84 (95% CI, 1.18-2.88, $p = 0.007$). Confirming to the attained results, a retrospective study showed that unsuccessful IVF session were significantly detected to be higher among females exposed to secondhand smokers than unexposed women, OR = 1.52 (95% CI, 1.20-1.92) (Benedict et al., 2011). Similarly, a new study that was performed using 88,732 postmenopausal women reported that secondhand smoking women are 18% more likely to experience failure of conceiving than those who are tobacco free (Hyland et al., 2016). Living in a landscape that do not prohibit public smoking and identifying the scarcity of research in this field, may offer the opportunity to perform more related research studies in order to communicate evidence-based information to policy makers and to encourage formulation of tobacco control public health measures.

4.5.2 Diet behavior:

To keep up with the contemporary pace, many people have recently changed their diet to follow the meat/sugar western food custom (Nazni, 2014). Not so much is known about the effect of such shift on the fertility status of the population and little, if any, research have been conducted in this setting. In this section, dietary components, habits and behaviours are discussed against infertility along with referring to relevant literature when applicable. Some of the inquires applied below **Table (4.23)**, are adopted from Stepwise WHO questionnaire (WHO, 2012), both the core and expanded section of diet and behavioural measurements, in addition to other self-instructed inquiries to suit the site and purpose of the study.

Participants were asked about the number of days in which they usually eat fruits in a typical week. The typical week demonstrates the week when the diet is not affected by cultural, religious or other events. Recalling information revealed that 41.2% of infertile women eat fruits only in less than three days a week, compared to 48.8% of the fertile women while 39.4% and 48.8% respectively represent the male responses. However, participants were asked also to provide information about the number of fruit servings consumed in one of these days. According to WHO criteria, one typical fruit serving represents one medium sized piece or half a cup of chopped, cooked, juiced or canned fruit that is equivalent to 80 grams weight. The participants were aided with show cards "image assisted responses" to help provision of requested information.

Table (4.23): Distribution of study population by variables related to diet behaviour

Diet behavioural variables:		Cases		Controls		Total (%)	χ^2	P-value
		No	%	No	%			
Female participants								
Eating fruits in a typical week	< 3 d/w	66	41.2	78	48.8	144 (45.0)	1.818	0.178
	≥ 3 d/w	94	58.8	82	51.2	176 (55.0)		
Number of fruit servings/day	< 2	87	54.4	78	48.8	165 (51.6)	1.013	0.314
	≥ 2	73	44.6	82	51.2	155 (48.4)		
	Mean	1.54		1.62		1.58	t=0.844	0.399
	Median	1		2		1		
Eating vegetable in a typical week	< 4 d/w	30	18.8	11	6.9	41 (12.8)	10.099	*0.001
	≥ 4 d/w	130	81.2	149	93.1	279 (87.2)		
Number of vegetable servings/day	≤ 2	108	67.5	72	45.0	180 (56.2)	16.457	**<0.001
	> 2	52	32.5	88	55.0	140 (43.8)		
	Mean	2.23		2.61		2.42	t=3.631	**<0.001
	Median	2		3		2		
Number of meals per day	Only one/d	13	8.1	6	3.8	19 (5.9)	2.742	0.098
	Two or more	147	91.9	154	96.2	301 (94.1)		
Having breakfast regularly	No	45	28.1	36	22.5	81 (25.3)	1.339	0.247
	Yes	115	71.9	124	77.5	239 (74.7)		
Having as a snack most frequently	Sugar/chips/Fries	37	23.1	22	13.8	59 (18.4)	4.676	*0.031
	Fruits/Nuts/Dairy	123	76.9	138	86.2	261 (81.6)		
Having as a drink most frequently	Soda/Canned	46	28.8	24	15.0	70 (21.9)	9.609	*0.022
	Tea/Coffee	63	39.4	72	45.0	135 (42.2)		
	Natural Juice	14	8.8	22	13.8	36 (11.3)		
	Water	37	23.1	42	26.2	79 (24.7)		
Oil often used for cooking or processing	Vegetable	139	86.9	123	76.9	262 (81.9)	5.391	*0.020
	Olive	21	13.1	37	23.1	58 (18.1)		
Male participants								
Eating fruits in a typical week	< 3 d/w	63	39.4	78	48.8	141 (44.1)	2.853	0.091
	≥ 3 d/w	97	60.6	82	51.2	179 (55.9)		
Number of fruit servings/day	< 2	78	52.3	68	45.9	146 (49.2)	1.218	0.270
	≥ 2	71	47.7	80	54.1	151 (50.8)		
	Mean	1.63		1.71		1.67	t=0.602	0.547
	Median	1		1.5		1		
Eating vegetable in a typical week	< 4 d/w	31	19.4	11	6.9	42 (13.1)	10.963	*0.001
	≥ 4 d/w	129	80.6	149	93.1	278 (86.9)		
Number of vegetable servings/day	≤ 2	104	63.1	65	40.6	166 (51.9)	16.223	**<0.001
	> 2	59	36.9	95	59.4	154 (48.1)		
	Mean	2.27		2.68		2.47	t=0.964	**<0.001
	Median	2		3		2		
Number of meals per day	Only one/d	10	6.3	6	3.8	16 (5.0)	1.053	0.305
	Two or more	150	93.8	154	96.3	304 (95.0)		
Having breakfast regularly	No	42	26.3	34	21.3	76 (23.8)	1.104	0.293
	Yes	118	73.8	126	78.8	244 (76.3)		

* Significant at $p < 0.05$, **Highly significant at $p < 0.001$

Of all female participants, 54.4% of infertile females reporting consuming less than 2 fruit servings in a typical day, compared to 48.8% of the fertile group. Similarly, more infertile men (52.3%) declared eating less than 2 fruit servings in a typical day, compared to 45.9% of the control group. Although, there is apparent difference among both female and male participants, but the relationship did not approach a significant level. More than half of the total participants appeared to be consuming less than the recommended amount of fruits. This could be related more to the unprecedented deterioration of socioeconomic status of GS population rather than individual free choice of food selection.

Regarding vegetable consumption, more infertile females (18.8%) consume vegetables for less than 4 days in a typical week than fertile women (6.9%), providing a significant association. This could be because, as mentioned before, people are becoming more involved in the western pattern of food customs that rely on fast fried vegetable free type of food. Moreover, husbands show almost the same frequency, where 19.4% compared to 6.9% respectively consume vegetables in less than 4 days a week. Additionally, even more infertile women (67.5%) and men (63.1%) consume less than three servings of vegetable a day, than those with normal fertility status; 45% and 40.6% respectively. The relationship in both groups in highly statistically significant. This can provide a prominent massage how healthy food is remarkably essential for our growth and prosperity.

According to WHO recommendation, a person have to consume at least 400 grams of fruits and vegetables per one day. Since each serving is estimated as an equivalent of 80 grams, one should eat at least 5 servings of fruits and vegetables a day.

Table (4.24): Analysis of fruits and vegetables servings

WHO STEP wise diet variables		**Cases**		**Controls**		χ^2	**P-value**
		No	**%**	**No**	**%**		
Female-Total servings/d	< 5 servings	123	76.9	99	61.9	8.472	*0.004
5 servings = 400 grams	≥ 5 servings	37	23.1	61	38.1		
Mean		3.77		4.23		t=2.71	*0.007
SD		1.38		1.62			
Male-Total servings/d	< 5 servings	116	72.5	94	58.8	6.705	*0.010
5 servings = 400 grams	≥ 5 servings	44	27.5	66	41.3		
Mean		3.90		4.38		t=2.60	*0.010
SD		1.60		1.71			

* Significant at $p < 0.05$

Analysis of collected data showed that **(Table 4.24)**, the proportion of infertile females who consume less than the recommended quantity (76.9%) are statistically significantly less than women in the fertile group (61.9%). Similarly, the infertile men (72.5%)

consuming less than 5 servings of total fruits and vegetables a day are less than their counterparts (58.8%). The high frequency noted in the results may offer the need for more public health efforts to raise public awareness, nutrition education and change in food environment, with paying particular attention to children and youth.

Literature demonstrated the importance of balanced nutritional diet in both restoring fertility and ensuring adequately successful conceiving process (Nazni, 2014). A prospective cohort approach was conducted in USA of which 17,544 women, in the reproductive age with no history of infertility, were followed for eight years. At the end of the study, researchers concluded that increasing consumption of vegetables rather than meet, decreasing sugar intake, eating diet rich in vitamins and using monosaturated fat rather than highly saturated one decrease the risk of ovulatory disorders among otherwise medically free females (Chavarro, Rich-Edwards, Rosner, & Willett, 2007).

Participants were asked to provide information about the number of meals consumed per day and whether they attend regular breakfast or not. Responses from 320 females and 320 males as couples revealed that, only 13 (8.1%) infertile females declared eating one meal per day on most days compared to 6 (3.8%) fertile ladies. Correspondingly, their husbands reported quite similar responses of 6.3% and 3.8% respectively. Similarly, having breakfast regularly revealed non-significant relationship, where 28.1% of infertile women and 26.3% of infertile men claimed missing the early morning meal comparing to 22.5% and 21.3% of fertile women and men respectively.

Female participants were also investigated for their dietary components that are most frequently consumed in their main meal. As shown in **Figure (4.14)**, more infertile females consume red meat (16.3%) and white chicken (62.5%) than fertile females (11.9% and 56.9% respectively), while fertile females eat more seafood (10.6%) as a most frequent component of the main dish than ladies with conceiving problems (15%). Almost the same percentage is reported regarding using farm raised chicken in both groups (3.8%, 3.1%) although it is the least consumed among others. Conclusively, all components did not show statistically significant relationship in spite of the apparent difference between the illustrated items. Additionally, using vegetable oil for cooking is noticed to be higher among infertile couples (86.9%) than fertile ones (76.9%), showing a statistically significant association. Upon searching literature, only two studies were found to have investigated different diet patterns in relation to infertility. One study concluded that

women with dietary component, where vegetables prevail animal proteins and the use of monosaturated fat is more than the trans-fat, couples have a better chance for pregnancy than those whose meals are dominated with meat and highly saturated fatty acids (Chavarro et al., 2007). Another study concluded that couples following Mediterranean food style have better chance for successful IVF sessions than couples relaying on fast food western pattern (Vujkovic et al., 2010).

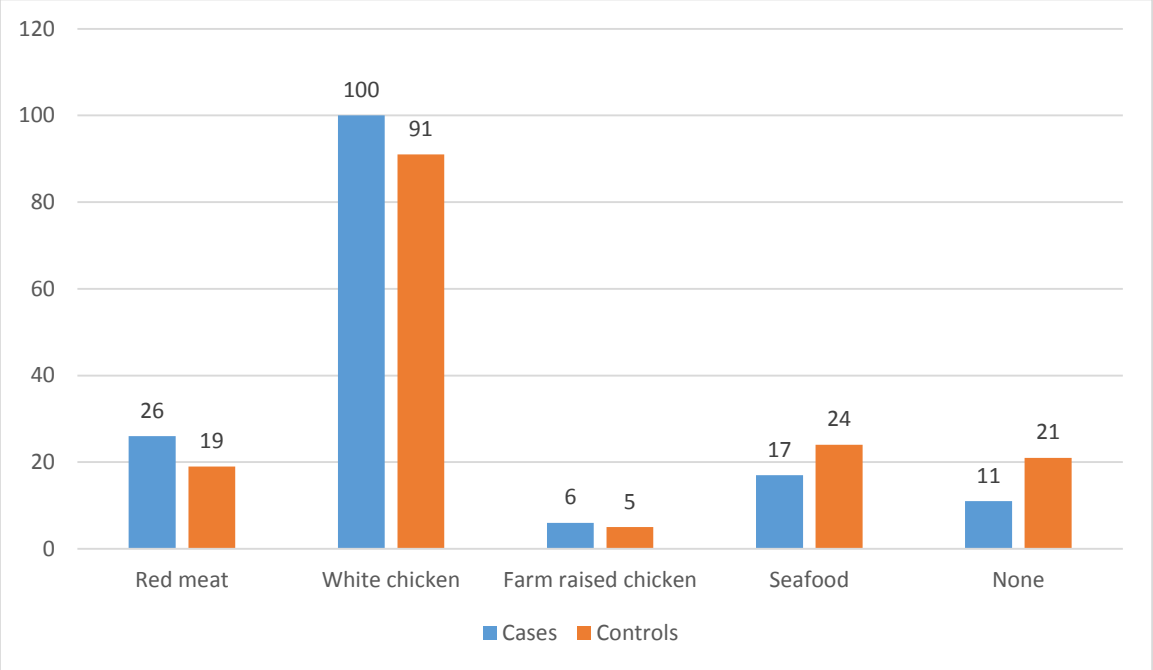


Figure (4.14): Most frequent component of main meal, cases vs controls

Inquiries about the most frequently used diet items in snacks and drinks by female participants were introduced in the study instrument. Upon analyzing responses, sugary food, chips and fries were found to be used as snacks more among infertile women (23.1%) than fertile ones (13.8%). Although, the relationship reached a significant level, what seems to be fortunate is that, 81.6% of the total surveyed population consume healthy food like fruits, nuts and dairy products as snacks, even though not reaching the recommended amount. On the other hand, analysis revealed that women who use soda and canned juice products as a regular drink are more than twice likely to have infertility than those who drink water regularly OR = 2.16 (95% CI, 1.12-4.22, p = 0.021). Moreover, the proportion of infertile females (39.4%), who reported tea and coffee as a regular drink, are less than their counterparts (45%), and those who reported drinking natural juice (8.8%) are also less than the ones in the control group (13.8%). In both cases, the relationship did

not approach a significant level. Additionally, one quarter of the surveyed population reported that water is their favorite drink, which demonstrate 23.1% of the infertile group and 26.2% of the fertile ones and which was used as a reference in the analysis. These results are supported by several studies recognized from literature review. A prospective study following 3,628 women, revealed that soda drinking; any type and from 1 to 3 servings per day; lower the fertility status among women desiring pregnancy with no apparent infertility problem (Hatch et al., 2012). Also, many studies found no relation between caffeine consumption and reduced fertility (Gaskins & Chavarro, 2018). Nevertheless, further studies would be essential if the amount of recommended daily consumption of both tea and coffee are explored.

One of the dietary behaviours addressed in this study is the way and amount of salt used and consumed by participants. Upon analysis **(Table 4.25)**, results provided that women who reported adding salt or salty sauce to the food right before eating or during the meal and eating processed food high in salt in a frequent manner, are more in the infertile group (50.6%) than the fertile ones (46.9%). Also, 82 (51.3%) infertile men compared to 76 (47.5%) men in the control group claimed a similar attitude. In this study, the processed food high in salt is referred to the packaged salty snacks as nuts and salty biscuits, canned salty food like noodles and pickles, salty pastries, pizza and salty cheese. However, in spite of the difference between the two groups, the relationship did not reach a significant level.

Additionally, while inquiring about how participant perceive themselves as salt consumers, more infertile women (26.9%) and men (27.5%) think that they eat too much salt and salty sauce than women (6.3%) and men (5.6%) in the control group. On the other hand, 67.5% of infertile women and 67.5% of infertile men perceive themselves as consuming the right amount of salt, compared to 85.6% and 84.4% respectively.

The close approximation of frequencies among females and males in the same group is noticeably apparent. This could be because that over time, most couples learn to share the same food custom and dietary behaviours that might become by time quite similar. Bearing in mind that, females are the ones who are responsible of preparing and processing food in any household setting in most Arab societies, so efforts for providing females with adequate dietary education and the embodying of nutritional health into preconception care protocols may result in remarkably efficient and effective outcomes. In the same respect, women were asked about how often they season food with salt or add salty sauce during

preparing food. 132 (82.5%) infertile women provided "Frequently" as an answer, compared to 134 (83.1%) fertile women, and 28 (17.5%) compared to 26 (16.3%) respectively declared as "Rarely or Never".

Table (4.25): Distribution of study population by salt intake behaviour

Bahaviour of salt intake variables:	**Cases**		**Controls**		**Total (%)**	**OR (95%CI)**	**P-value**
	No	**%**	**No**	**%**			
Female participants							
- Adding salt or salty sauce to the food right before eating or during the meal: **- Eating processed food high in salt:**							
Frequently	81	50.6	75	46.9	156 (48.4)	0.450	0.502
Rarely or Never	79	49.4	85	53.1	164 (51.3)		
- How much salt or salty sauce do you think you consume?							
Too much	43	26.9	10	6.3	53 (16.6)	24.707	**<0.001
Just the right amount	108	67.5	137	85.6	245 (76.6)		
Too little	9	5.6	13	8.1	22 (6.9)		
- Salt, salt seasoning or salty sauce is added in cooking or preparing foods in household:							
Frequently	132	82.5	134	83.8	266 (83.1)	0.089	0.765
Rarely or Never	28	17.5	26	16.3	54 (16.9)		
Male participants							
- Adding salt or salty sauce to the food right before you eating or during the meal: **- Eating processed food high in salt:**							
Frequently	82	51.3	76	47.5	158 (49.4)	0.450	0.502
Rarely or Never	78	48.8	84	52.5	162 (50.6)		
How much salt or salty sauce do you think you consume?							
Too much	44	27.5	9	5.6	53 (16.6)	28.780	**<0.001
Just the right amount	108	67.5	135	84.4	243 (75.9)		
Too little	8	5.0	16	10.0	24 (7.5)		

**Highly significant at $p < 0.001$

The overall conclusion, is that salt intake is not associated with infertility although more infertile participants were noticed having higher degree of consumption. Afterall, literature review revealed results against what has been attained through this study. A recent study concluded that sodium chloride may alter the body lipoproteins causing elevation in the levels of serum lipids and spermatogenic defect (Lee & Cho, 2016), and others showed that extremes of salt intake; whether very high or very low intake; may harm spermatogenesis (Iranloye, Morakinyo, Oludare, Ekeh, & Esume, 2013). Correspondingly, little is known about the effect of salt intake in various forms and amounts on the reproductive health of females, offering a possibility for further research in this particular area.

4.5.3 Physical activity:

Physical activity is the repetitive muscular movement that result in a measurable degree of energy expenditure (WHO, 2017). Relationship between physical activity and fertility has long been subjected to controversy debate (Rich-Edwards et al., 2002). In a complex context like GS, it appears to be appropriate to measure the possible relationship between various types, frequencies, duration and intensities of physical activities adopted by couples and their fertility status. Inquiring about physical activity is presented in the study instrument through an interviewed administered questionnaire acquired from the short form of IPAQ created and published by the WHO **(Annex 5)**. IPAQ collects information and data about three levels of physical activity; walking, moderately intense and vigorously intense physical activity; in addition to the period an individual spends sedentarily. Each activity was described clearly to each participant along with the administration of show cards that contain pictures about all possible and relevant types of physical activities that could be practiced by the population in our study context. Examples for moderate intensity activities were provided like, cycling, jogging, drawing water, gardening, walking with load on head and many other examples that accelerate the breathe quite more than normal, while vigorous intensity physical activities are those that make the breathe much harder than normal like, sawing hardwood, digging, shoveling sand, grinding with pestle …etc. Information collected for each type comprise the frequency of doing such activity in the last week and duration in minutes spent in one of these days. Responses were collected from both females and males in separate forms and data was analyzed according to the recommended guidelines developed and provided by the WHO.

To estimate the amount of energy expended and to compute the weight of each type of activity by its energy requirements, multiples of resting metabolic rate was calculated for the three categories (Ainsworth et al., 2000). Then, the concluded scores are proposed to predefined criteria that classify the population in to three levels; low active, moderately active and highly active; according to the WHO scoring guidelines for short form IPAQ as shown in **Table (4.26)**:

Table (4.26): Distribution of study population by Physical Activity categorical variables

Physical Activity categorical variables:		Cases		Controls		Total (%)	OR 95% CI	P-value
		No	%	No	%			
Female participants								
Categorical Scores	Low	53	33.1	31	20.1	84 (26.7)	2.47 (1.27-4.78)	*0.006
	Moderate	80	50.0	84	54.5	164 (52.2)	1.37 (0.77-2.45)	0.279
	High	27	16.9	39	25.3	66 (21.0)	# Ref	
Sedentary time min/day	Mean	274.6		225.3		250.4	t=3.788	**<0.001
	SD	126.5		102.7		117.9		
Male participants								
Categorical Scores	Low	34	21.5	27	16.9	61 (19.2)	1.32 (0.71-2.46)	0.374
	Moderate	66	41.8	72	45.0	138 (43.4)	0.96 (0.59-1.57)	0.884
	High	58	36.7	61	38.1	119 (37.4)	# Ref	
Sedentary time min/day	Mean	248.9		269.9		227.4	t=1.006	0.316
	SD	141.7		124.9		133.6		

* Significant at $p < 0.05$, **Highly significant at $p < 0.001$

As described in **Table (4.26)**, more than quarter the surveyed females are categorized as low active, while nearly half are moderately active and 21% are high active women. The proportion of high active infertile females (16.9%) are less than the fertile ones (25.3%), and the distribution of moderate active among cases (50%) and controls (54.5%) is almost the same. Additionally, results revealed that low activity is more than two times likely among infertile women. This is also apparent in the time spent sedentarily, in which infertile women spends more time sitting (Mean=274.6, ±1.26.5 minutes per day) than fertile women (Mean =225.3, ±102.7 minutes per day). Sedentarily time is calculated in minutes per day and it includes the time spent sitting at home, work, during a class or doing a course, visiting friend, reading or watching television. It has been evidenced that aerobic exercise offers a remarkable effect on follicular phase of ovulation and enhance the development of graafian follicles among women suffering from PCOs (Costa, de Sá, de Medeiros, Soares, & Azevedo, 2013) , while sedentary life may expose females to increase risk of having PCOs (Moran et al., 2013). This may explain the significant association between low active lifestyle and infertility revealed in this context, as almost 34% of infertility causes noticed are attributed to PCOs with a mean duration of 3.8 years since discovery. A study that supported these findings examined prospectively females with ovulatory infertility against 26,125 fertile females and found that sedentary lifestyle and overweight is more likely among ovulatory infertile women, while relative risk of ovulatory infertility decreases with increase in vigorous activity (Rich-Edwards et al., 2002). It was always believed that the regularity of the female's reproductive axis is

negatively proportionated with highly intense physical activity (Ellison, 1990). Others thought that women practicing vigorous activity less than one hour a day will not be at risk (Green, Daling, Weiss, Liff, & Koepsell, 1986), while those who consume inadequate energy producing diet along with exercising intensely are more prone to infertility (Derbyshire, 2007). In the same regard, a study revealed that no significant association between the three types of self-reported physical activity and infertility (Esmaeilzadeh, Delavar, Basirat, & Shafi, 2013). All proposed arguments may offer the need for a unified weighting and scoring technique, to ensure comparability among countries in order to be able to speculate public health measures, given that lifestyle is one of the most preventable and cost-effective health measures that have high impact on the long term.

Physical activity examined among male participants, showed no significant effect on their fertility status. Of all participating men, 37.4% are practicing high active lifestyle, of which 36.7% are infertile compared to 38.1%. Moderately active pattern is found among 41.8% and 45% of men respectively. Regarding low active males, the proportion of infertile men (21.5%) were much more than fertile ones (16.9%), but the relationship did not reach a significant level. The deteriorated socioeconomic status and lack of jobs opportunity along with the chronic state of payment without work, all contribute to the high level of low active lifestyle among male participants. Recently, it was found that prolonged confinement to watching television and practicing low active pattern of life is not beneficial to semen quality in males (Gaskins, Mendiola, et al., 2015).

Literature supported these finding in several settings. Examining semen parameters of males with various lifestyle patterns revealed that, there is no differences between moderately to vigorously active men in terms of sperm motility, count and concentration (Mínguez-Alarcón, Chavarro, Mendiola, Gaskins, & Torres-Cantero, 2014). Another study found that semen quality is not associated with regular physical activity except for bicycling (Wise, Cramer, Hornstein, Ashby, & Missmer, 2011), which could be associated with other specific physical factors. On the other hand, some researchers found that reducing time spent on watching television was associated with improvement in semen parameters (Gaskins, Mendiola, et al., 2015).

IPAQ produces two forms of outputs, one is categorical (low activity level, moderate activity level or high activity level) and the other is continuous variable (MET minutes a week). MET is a ratio between work metabolic rate, which is the energy expended during

carrying out physical work, to a standard resting metabolic rate, which is the energy expended by the body during rest period. As shown in **Table (4.27)**, the median of energy expended on walking was higher among infertile females (396) than fertile ones (264), although 15% of each group showed a MET-min/w more than 396 and 420 respectively providing a statistically significant association using Mann-Whitney U test. Energy expended on moderate-intense physical activity did not differ much between both groups of females. On the other hand, fertile females seemed to practice more vigorous activity, where the median energy expended in this respect was zero among infertile females compared to 240 MET-min/w for those who enjoy normal fertility status, $p = 0.003$. A retrospective study that was performed in Iran while using the same short form of IPAQ concluded that, there was significant relationship between infertile and fertile females regarding intensity of walking, moderate, vigorous or even total physical activity (Esmaeilzadeh et al., 2013). Correspondingly, a metanalysis study that was performed and published recently showed that physical activity pattern did not affect the rate of miscarriage, but physical activity before IVF cycles was associated with increase rate of clinical pregnancy and live births (Rao, Zeng, & Tang, 2018).

Table (4.27): Distribution of study population by Physical Activity continuous variables

Physical Activity continuous variables:	**Cases**		**Controls**		**P-value**
	Median	**IQR**	**Median**	**IQR**	
Female participants					
Walking MET-min/w	396	396	264	420	*0.002
Moderate MET-min/w	510	830	360	1200	0.425
Vigorous MET-min/w	0	480	240	720	*0.003
Total MET-min/w	1314	1159	1229	1791	0.905
Male participants					
Walking MET-min/w	396	528	396	594	0.890
Moderate MET-min/w	480	2040	480	1440	0.140
Vigorous MET-min/w	40	720	480	960	0.077
Total MET-min/w	1872	2815	2118	2047	0.681

IQR = Interquartile range * Significant at $p < 0.05$

As shown in **Table (4.27)**, the median of energy expended on walking was higher among infertile females (396) than fertile ones (264), although 15% of each group showed a MET-min/w more than 396 and 420 respectively providing a statistically significant association using Mann-Whitney U test. Energy expended on moderate-intense physical activity did not differ much between both groups of females. On the other hand, fertile females seemed to practice more vigorous activity, where the median energy expended in this respect was zero among infertile females compared to 240 MET-min/w for those who enjoy normal

fertility status, $p = 0.003$. A retrospective study that was performed in Iran while using the same short form of IPAQ concluded that, there was significant relationship between infertile and fertile females regarding intensity of walking, moderate, vigorous or even total physical activity (Esmaeilzadeh et al., 2013). Correspondingly, a metanalysis study that was performed and published recently showed that physical activity pattern did not affect the rate of miscarriage, but physical activity before IVF cycles was associated with increase rate of clinical pregnancy and live births (Rao, Zeng, & Tang, 2018).

Male participants showed almost the same amount of energy expended on walking in both groups, where the median MET-min/w for each group was 396. The situation was detected to be almost the same when examining the moderate-intensity physical activity, 480 MET-min/w for each, but with higher rate among infertile men than fertile ones. The association here did not reach a significant level. Additionally, the median vigorous-MET-min/w was way less among infertile men (40) than fertile ones (480) and 15% of each group excreted more than 720 and 960 MET-min/w on vigorous activities respectively. It is concluded that patterns, duration and intensity is not associated with primary infertility among males which was confirmed several times in the literature (Mínguez-Alarcón et al., 2014; Wise et al., 2011; Gaskins, Mendiola, et al., 2015).

4.5.4 BMI and infertility:

BMI is considered an index for adults' nutritional status. It is known as the weight of a person in kilograms divided by square the height in meters. According to the WHO, BMI is used as a symbol for categorizing body fat distribution in a person into standard classification; underweight (<18.5), normal (18.5-24.9), overweight (25-29.9) and obese (≥ 30) (WHO, 2009). Referring to a study research that was performed in Palestine, the prevalence of obesity and overweight range from 57% to 67.5% in urban and rural areas (El Kishawi, Soo, Abed, & Muda, 2014). Acknowledging such high figures, it seemed essential to shed the light on the possibility of a relationship between impaired BMI and primary infertility. Accordingly, BMI is calculated for all female and male participants to explore if any association exits, where the following table illustrate the results **(Table 4.28)**.

Table (4.28): Distribution of study population by Body Mass Index (BMI)

Fat distribution variables:		Cases		Controls		Total (%)	χ^2	P-value
		No	%	No	%			
Female participants								
BMI	Obese	30	18.8	36	22.5	66 (20.6)	1.535	0.674
	Overweight	63	39.4	61	38.1	124 (38.8)		
	Normal	65	40.6	59	36.9	124 (38.8)		
	Underweight	2	1.3	4	2.5	6 (1.9)		
	Mean	26.27		26.77		26.52	t=0.924	0.353
	SD	4.94		4.73		4.83		
Weight	Mean	69.52		70.39		69.96	t=0.606	0.545
	SD	13.17		12.63		12.89		
Childhood obesity	Yes	11	6.9	9	5.6	20 (6.3)	0.213	0.644
	No	149	93.1	151	94.4	300 (93.8)		
Male participants								
BMI	Obese	42	26.3	33	20.6	75 (23.4)	2.366	0.500
	Overweight	70	43.8	83	51.9	153 (47.8)		
	Normal	46	28.8	42	26.3	88 (27.5)		
	Underweight	2	1.3	2	1.3	4 (1.3)		
	Mean	27.59		27.33		27.46	t=0.524	0.601
	SD	4.70		4.17		4.44		
Weight	Mean	82.99		80.28		81.63	t=1.802	0.073
	SD	14.29		12.65		13.54		
Childhood obesity	Yes	28	17.5	18	11.3	46 (14.4)	2.539	0.111
	No	132	82.5	142	88.8	274 (85.6)		

Of all infertile female participant, 18.8% are obese, 39.4% are overweight, 40.6% are normal and only 1.3% are underweight, while the fertile group form 22.5%, 38.1%. 36.9% and 1.9% respectively. Association is not accomplished between the two groups **(Table 4.28)**. By scrutinizing male fat distribution and its relation to infertility status, obesity among men with primary infertility (26.3%) is more than that of the fertile group (20.6%), but the relationship did not approach a significant level. Overweight is less among infertile men; 43.8% and 51.9% respectively; while those with BMI between 18.5 and 24.9 showed a more proportion among infertile men (28.8%) than fertile men (26.3%). Two cases are found to be underweight in each group. However, to search for more potential associations, childhood obesity was inquired and only 11 (6.9%) infertile women comparing to 9 (5.6%) fertile ladies reported obesity, while 28 (17.5%) comparing to 18 (11.3%) men respectively reported being obese during their childhood period. The difference is way apparent among male participants than it appeared among females, but the relationship in both conditions is not significant. Seeking more information in this respect showed that these results are against what have been published by other researchers. Some authors found that overweight and obesity interferes with normal ovulation in females. They also found that loosing excess weight improved success rate of

assisted reproductive techniques (Dağ & Dilbaz, 2015). Others researchers claimed that obesity is accompanied with poor life style habits and with accumulation of environmental toxins which may contribute to altered semen parameters in men (Hammoud, Gibson, Peterson, Meikle, & Carrell, 2008).

4.5.5 Relationship between infertility and various lifestyle variables:

As discussed in the previous section, different lifestyle variables appeared to be highly correlated with infertility. The variables that are shown to be useful in predicting the outcome are selected to form the best fit model as described in **Table (4.29)**.

Table (4.29): Predictors of primary infertility among different independent lifestyle variables by using binary logistic regression

Medical Variables	*β*	*S.E.*	Wald χ^2	*p-value*	*OR (95% CI)*
Passive smoking - wife Reference=No	0.555	0.243	5.218	*0.022	1.74 (1.08-2.81)
Eating vegetables days/w - wife Reference ≥4d/w	1.098	0.389	7.951	*0.005	3.00 (1.40-6.43)
Number of vegetable servings - wife Reference >2 servings	0.752	0.245	9.385	*0.002	2.12 (1.31-3.43)
Oil used in cooking - couples Reference=olive oil	0.503	0.332	2.299	0.129	1.65 (0.86-3.17)
Snack consumed regularly – wife Reference=Fruits/nuts/dairy	0.615	0.318	3.729	0.053	1.85 (0.99-3.45)
Drinks consumed regularly – wife Reference=water			6.224	0.101	
Soda/Canned sugary drinks	0.822	0.358	5.284	*0.022	2.28 (1.13-4.59)
Tea/Coffee	0.164	0.301	0.297	0.586	1.18 (0.65-5.12)
Natural juice	0.043	0.448	0.009	0.924	1.04 (0.43-2.51)
Constant	-1.582	0.421	14.122	**<0.001	0.206

β=beta coefficient, S.E.=standard error, χ^2=chi square, CI=confidence interval, Model coefficient chi^2=44.239, p<0.001, Nagelkerke r^2=0.172, Membership for cases, *significant=p<0.05, **highly significant=p<0.001

It became obvious how smoking affects health, but what has not been thoroughly investigated is the impact of living in a tobacco poisoned environment on an individual's fertility status. Studying this particular area showed that, the odds of being passive smoker is 74% higher among infertile females than women with normal fertility. Again, these results may alarm public health experts to the persistent need for the right of living in a tobacco-free environment. Among other lifestyle variables is the amount and frequency of vegetables consumption. Females who eat vegetables for three or less days per week are

three times more likely of infertility risk. Additionally, those who take less than two servings a day are more than twice as likely to be infertile. At the same time, the odds of eating chips, fries and sweets as regular snacks are 84% more among infertile women, while drinking soda and canned preserved sugary beverages expose females to twice folds the risk. Reasoning from these results, and base on the univocal supported literature, policy makers and health professionals may need to change their perspectives and strategies towards food labeling and advertising, nutrition education, school food supply and other policies that would raise public health awareness and self-health control.

Chapter Five

Conclusion and recommendations

5.1 Conclusion

Many couples around the world are struggling the gloomy feeling of childlessness. Besides the lack of parenthood potentials, they may suffer from relative social and societal exclusion in various ways. This brings the importance of identifying possible risk factors associated with primary infertility and ultimately searching for steps that would prevent the occurrence of such condition for the sake of improving couples' health and their quality of life. For risk factors to be explored and identified, the study examined different aspects hypothesized to be related to primary infertility in GS, including demographic, socioeconomic, medical, environmental factors and various lifestyle variables.

Being the first study to be conducted in this landscape, it will be recognized that several dimensions have been explored in the respect of the intended purpose. The first domain examined was the demographic characteristic of the population. Among the explored features of the population is the marital age of females. Results showed that, the more the female age of marriage, the greater is the risk for infertility. When, age difference between couples beyond 10 years, also projected the same risk. Infertility was apparent among couples living near borders who may have been exposed to a phenomenal environmental field, but further research would be appropriate in this regard. Also, living in an extended family after marriage and being refugee expose couples to the same risk, but it did not appear to differ whether living inside or outside camps. Moreover, living in a crowded house before marriage seemed to have no effect on being infertile for both women and men, but men born at the end of a long line of offspring appeared to be at more risk. Birth order more than 6^{th} among siblings may denote old maternal age at pregnancy, and this would explain the increasing risk among higher birth order rank.

The effect of variant socioeconomic prospects against infertility has been investigated thoroughly. Infertility appeared to be neither linked to whether women or men are well educated or simply illiterate, nor to the pattern of household spending on food and non-food items. Nevertheless, deficiency in some diet components, mainly vegetables, revealed to carry a high risk of infertility. This provides that, no matter how much a household spends on food, the quality of food consumed has a greater effect on the outcome. On the

other hand, being employed or unemployed men or women was not related to the risk of infertility, but the type of work field and the shift pattern seemed to have great risk particularly on females. The study proved that women working as professionals and who are experiencing either straight night or rotation shifts during their daily job embed more risk than others, regardless how much hours they work during the week. The reason behind such relation could be due to the neuroendocrinal changes women may experience in relation to either disturbed circadian rhythm or stress accompanied with their career attributes. In the same respect, stress was studied as a subdomain of medical factors which showed that high perceived stress among females expose them to greater risk of infertility. On the contrary, features of men's career showed that there is no link between the shift pattern and working hours of their profession and their fertility status. However, men exposed to noise, dust, gases, chemicals and/or polluted air during practicing their daily job evidenced to be of more risk for primary infertility. Moreover, those who are exposed to overheat through working in closed manual bakeries, preparing falafel in public restaurants or working in solarium houses were more prone to infertility than men working in other circumstances. This may raise the possibility of having testicular affection due to continuous exposure to high temperature resulting in impaired fertility.

Consanguineous marriage as a social factor has been proved to be strongly linked to the occurrence of primary infertility. On the contrary, in this study the results revealed that there is no relationship between consanguineous marriage of either the couple's parents or the couples themselves and the risk of being infertile. Although, the difference between cases and controls was apparent in the situation of both couples' and females' parents, the association did not reach a significant level. Family history of infertility showed clear risk for both men and women, but respective subfertility was among men only. Hypothyroidism and PCOs family history were unrelated to both. Men with positive family history of varicocele carried risk of infertility, in which a remarkable percentage of infertile men reported suffering from this condition. Searching for risk factors associated with varicoceles, in the researcher's point of view, would contribute much to the field of prevention and management of infertility among men.

Many environmental factors have manifested to be linked to the conceiving ability of couples. Those who are living in a household setting connected to a sewer system other than the public one, were more prone to primary infertility. This may raise the importance of reproductive health education and self-hygiene promotion among adolescents and young

adults and to be included in the primary health care protocols in combating infectious diseases. It is obvious that the connection between inappropriate sewer system in one hand and the link between chronic genitourinary tract infection and infertility on the other hand, comprise most of the association in such situations. Additionally, females who used to use rooming tankers as a source of drinking water before marriage, have more risk to infertility than those who drink municipal, filtered or mineral water. In the same respect, males showed the same risk. The relationship is not apparent regarding the type of water used after marriage. Moreover, the type of dwelling where couples are living or used to live in before marriage also did not appear to be related to infertility, but couples who pay rents for accommodation had significant risk than those who live in an owned house or even without pay.

Using APH in GS is usually linked to farmers, traders and distributors. Neither dealing with APH as one of the mentioned categories, nor the duration during which an individual uses this type of chemicals, has shown to be associated with primary infertility. But what seemed to trigger the risk of infertility was the way people practice safety measures while dealing with these chemicals and the frequency with which they use them.

Other work-related environmental factors have shown that, lifting heavy objects and exercising heavy physical labour were significantly associated with primary infertility for females but not for males. Conversely, men who were exposed to noise, dust, gases, chemicals and/or polluted air were more at risk, while females were not. Time pressure and concentration at work showed no relation to infertility among both. The same results appeared for those who practiced long working hours and overtime. As mentioned before, men who were exposed to high temperature in their work place are at more risk of infertility.

GS, as a conflict zone, has been exposed to several hostilities during the past 10 years. Couples were examined for potential hazardous exposures during and after the aforementioned period against their fertility status. The demolishing of their home or their neighbours' totally or partially, was not related to infertility among both men and women. But living in a partially demolished house appeared to have great risk on men but not on women. Also, dealing with afterwar remnant was clearly associated with infertility among men. The association is not apparent among women. Moreover, working in a place that has been affected during the hostilities and was renovated carried no potential risk on both

females and males. Interestingly, couples who had their source of drinking water exposed to bombardments were of high risk to be infertile.

Living far away from a health care facility, having private health insurance rather than public one or even being deprived of any form of health insurance appeared to expose couples to higher risk of infertility. Nevertheless, most people declared having easy access to health care, with limited access to medicine, but mostly willing to seek medical advice upon suffering from genitourinary infection. The willingness and readiness to control over one's own health appeared to be high among people, so that may encourage health care providers to take advantage of this attitude and ultimately provide appropriate health messages to people regarding reproductive health. Preconception care is one of the most essential components of maternal and reproductive health, which may involve detection and management of causes related to irregular menstrual cycles among females that appeared in this study to be significantly associated with infertility. Age of first menstrual cycle less than 14 years also, seemed to have potential risk of infertility. Simultaneously, oligomenorrhea held the same risk. Searching for the most common cause of infertility, PCOs which is usually linked with oligomenorrhea and amenorrhea, prevailed the most among females. Moreover, the more the duration in which a woman is suffering from PCOs showed to have increasing risk of being infertile. In the same regard, women with present or past history of hyperprolactinemia or hirsutism are more prone to primary infertility than other ladies. History of PID, hypothyroidism or previous history of any major surgery seemed to be unrelated, while uterine fibroids had an embedded significant association. Other chronic diseases were not related to infertility, particularly essential hypertension. On the other hand, using combined oral contraceptives for more than six months appeared to have a protective effect but, intake of NSAID in a continuous manner had provided potential risk, although consuming low dose aspirin had neither protective effect nor a potential risk among females.

Non-communicable diseases among men, like Diabetes mellitus, hypertension or bronchial asthma, were not related to their fertility status. However, results revealed that suffering from varicocele was highly associated with infertility, although being unilateral or bilateral did not differ much. Undescended testis provided no relationship, but recall bias is suspected because repair of undescended testis often occurs in the early stages of life and grown-up men happened to be ignorant to this particular information. Quite high frequency of genitourinary tract infection revealed to be associated with infertility, but nonspecific

urethritis and mumps did not carry any risk. It is also worthy to mention that, the most common cause of primary infertility among men detected to be oligospermia.

Smoking tobacco is among the different lifestyle variables that were examined in this study. Although being a cigarette smoker or a nonsmoker was not related to infertility among men, the number of cigarettes smoked per day and the duration during which males spent smoking held major risk. Similarly, smoking waterpipe more than once daily was significantly associated with infertility, but the relationship was not visible regarding the duration of use. Women suffering from second-hand smoking carried a great risk.

It is very obvious from the results, that diet component is very essential for the reproductive capability of an individual. Couples eating vegetables more frequently and who consume the recommended daily requirements, appeared to have more patent fertility status, but having a lot of sugary food, chips and fries showed to provide tremendous risk. Moreover, using vegetable or sunflower oil rather than olive oil in cooking or preserving food, provide a great risk to infertility. Females used to drink soda and canned juices containing preservative ingredients, were more prone to the risk than females drinking tea, coffee, natural juice or water as a favourable drink. In the same respect, some couples prefer to have only just one meal a day because of the attributes of their jobs, and others persist to keep the healthy tradition of having three full serving meals a day. Scrutinizing this area revealed that, regardless of the number of meals consumed per day, it did not affect the fertility status of couples. Additionally, couples missing the breakfast meal regularly had no risk to develop infertility. Regarding salt consumption, the relationship is not significant, although the difference in the study was apparent. Nevertheless, infertile couples declared positive perception regarding consuming salt and processed food high in salt in more frequent manner than normal.

Conducting IPAQ short form questionnaire of WHO revealed that, females attaining high and moderate activity lifestyle were not considered to be related to infertility, while low active women and those who adopt long sedentary time are more prone to the risk. On the other hand, all physical activity patterns of men did not any relationship with infertility, including low, moderate and high active males. Also, the sedentary time between fertile and infertile men did not differ much. Comparatively, BMI for males and females were explored and showed that neither obesity nor overweight are related to infertility. The relationship in men was not clear. There is apparent difference but the association did not

approach a significant level. History of childhood obesity showed nearly the same results for both couples. Similarly, being underweight in both females and males did not make difference in relation to infertility.

5.2 Recommendations

5.2.1 General recommendations:

Sociodemographic:

- The need for greater efforts towards raising the awareness of the population about early marriage and its consequences for the future health of couples, in particular their fertility status. Ensure the right of children to live their childhood before they immerse themselves in the lives of adults.

Socioeconomic:

- Since poverty and impaired living conditions of many couples were found related to their fertility capacity, policy makers may need to consider finding approaches to improve the population economic status and to design strategies that contributes effectively to offer at least the basic humanitarian needs of a population.

Environmental:

- Occupational health should be regarded more intensively in terms of implementation, monitoring and evaluation. Policy makers may need to formalize ever updated, occupation specified, guidelines and protocols.
- The importance of providing safe drinking water supply to households with comprehensive risk assessment and risk management approach, and to formulate an inspection and quality control unit to ensure distribution of non-contaminated potable water that is in line with the international safety standards. It is also essential to increase awareness of households about practicing safety measures which could be linked to hygiene health education programmes,
- The Palestinian Water Authority may need to expand the public sewerage network to include all populated areas, especially the marginalized, and may consider enhancing existing infrastructure to be part of national infection control strategies.
- Agricultural pesticides and herbicides safety practicing programmes are prerequisite for every farmer, trader and distributer along with comprehensive intervention measures to control health hazards associated with pesticides risky exposure.

- Provision of health education and raising community awareness about the health consequences of excessive exposure to heat mainly among men working in closed manual bakeries, preparing falafel in public restaurants or working in solarium houses.

Medical:

- The willingness and readiness of people to control over their own health appeared to overwhelming, so this may encourage health care providers to make use of this attitude and ultimately provide appropriate health messages to people regarding reproductive health.
- Health care provider should be fully acquainted with updated knowledge about early diagnosis of PCOs, genitourinary tract infection and varicocele. Developing guiding tools and protocols for providers and conducting training workshops on prevention techniques and proper options for intervention and referral at the level of both primary and secondary health care.
- Infertility services may need to be included in the national strategies and policies of maternal and child health and reproductive health.
- Standardizing the definition of infertility adopted in social science and epidemiological research conducting in Palestine to reach out for accurate prevalence and to ensure comparability and understand the need for access to infertility diagnosis and treatment services.
- The role of Mental health and psychosocial support may need to be enforced and to be a complementary section in infertility management protocols in primary health and IVF fertility centers. The outcome of application of psychotherapy in ART has been proven to be very promising and plays an essential role in increasing the successful rate of conceiving and pregnancy outcome.

Lifestyle:

- Public programmes may be needed to be launched about the hazards of smoking on fertility status of the population, mainly the effect of secondhand smoking on women. There should be national efforts to provide a tobacco free environment especially in public areas through increasing cigarettes taxes and prohibition of public smoking.
- The need to formulize nutritional health programmes including nutritional health education in primary care health facilities, food standards in schools and street and fast food quality control.

5.2.2 Recommendations for new areas of research:

- Health professionals and researchers should pursue more insight methodologies in exploring occupational risk factors related to infertility.
- Palestinian water authority may need to work jointly with MoH to investigate the potential health hazards of drinking water supplies, particularly that is related to infertility.
- Unsafe sanitation as a potential source of infection related infertility.
- Heavy physical labour among females may affect their fertility status.
- Efficiency of varicocele treatment to reduce chances of infertility
- Epidemiology and risk factors for Polycystic Ovary Syndrome
- Prevalence and risk factors of oligospermia among infertile men in Palestine.
- The link between hyperprolactinemia, hirsutism, Polycystic Ovary Syndrome and infertility in the Gaza Strip.
- Molecular pathophysiology of NSAIDs and its effect on the females' reproductive viability.

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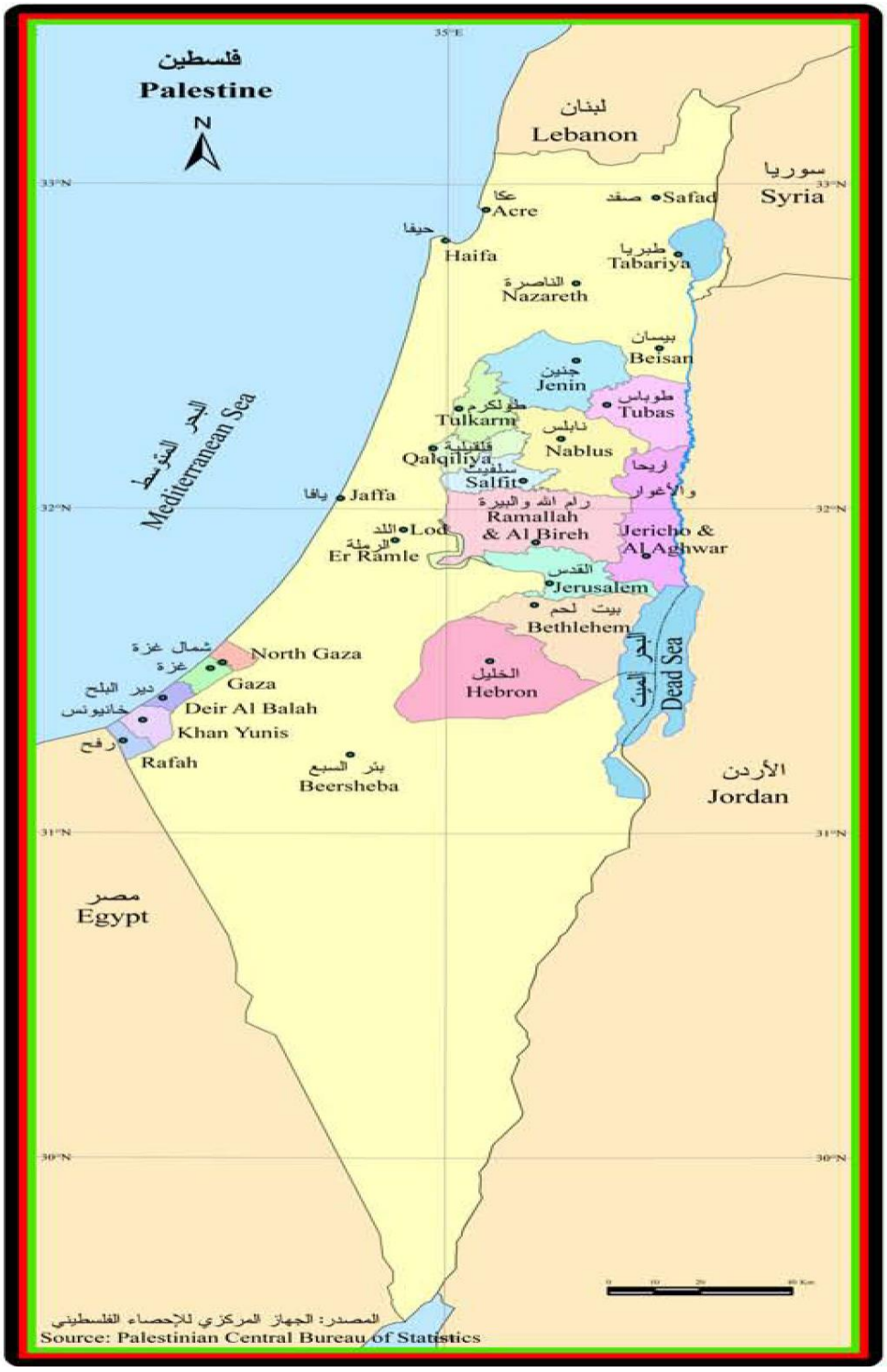
Annexes

Annex (1): Palestine map



Annex (2): Population in Palestine by governorate and sex - 2017

Governorate	نسبة الجنس	متوسط حجم الأسرة	الأسر Households		Population* Females	إناث	Males	ذكور	Both Sexes	السكان* كلا الجنسين	المحافظة
	Sex Ratio	Average Household Size	النسبة Percentage	العدد Number	النسبة Percentage	العدد Number	النسبة Percentage	العدد Number	النسبة Percentage	العدد Number	
Palestine	103.6	5.1	100	929,221	100	2,348,052	100	2,433,196	100	4,781,248	فلسطين
West Bank	104.2	4.8	64.0	594,511	60.1	1,411,664	60.4	1,470,293	60.3	2,881,957	الضفة الغربية
Jenin	103.6	4.7	7.0	65,495	6.6	154,635	6.6	160,231	6.6	314,866	جنين
Tubas & Northern Valleys	104.7	4.8	1.3	12,411	1.3	29,758	1.3	31,169	1.3	60,927	طوباس والأغوار الشمالية
Tulkarm	103.6	4.7	4.2	39,360	3.9	91,743	3.9	95,017	3.9	186,760	طولكرم
Nablus	102.8	4.7	8.9	82,235	8.2	191,460	8.1	196,861	8.1	388,321	نابلس
Qalqiliya	105.1	4.8	2.4	22,507	2.3	54,814	2.4	57,586	2.4	112,400	قلقيلية
Salfit	104.1	4.7	1.7	15,677	1.6	36,967	1.6	38,477	1.6	75,444	سلفيت
Ramallah & Al-Bireh	102.2	4.6	7.6	70,188	6.9	162,664	6.8	166,197	6.9	328,861	رام الله والبيرة
Jericho & Al Aghwar	100.8	4.8	1.1	10,234	1.1	24,901	1.0	25,101	1.0	50,002	أريحا والأغوار
Jerusalem	107.7	4.4	10.2	95,234	8.9	209,844	9.3	225,909	9.1	435,753	القدس
Bethlehem	103.9	4.7	4.9	45,556	4.5	106,630	4.6	110,770	4.5	217,400	بيت لحم
Hebron	104.2	5.2	14.6	135,614	14.8	348,248	14.9	362,975	14.9	711,223	الخليل
Gaza Strip	102.8	5.6	36.0	334,710	39.9	936,388	39.6	962,903	39.7	1,899,291	قطاع غزة
North Gaza	103.6	5.7	6.9	64,012	7.7	181,215	7.7	187,763	7.7	368,978	شمال غزة
Gaza	103.5	5.7	12.2	113,238	13.7	320,612	13.6	331,985	13.6	652,597	غزة
Dier al Balah	101.1	5.5	5.3	49,202	5.8	135,860	5.6	137,340	5.7	273,200	دير البلح
Khan Yunis	102.9	5.5	7.2	66,510	7.8	182,674	7.7	187,964	7.8	370,638	خانيونس
Rafah	101.6	5.6	4.5	41,748	4.9	116,027	4.8	117,851	4.9	233,878	رفح

* Includes population counted in Palestine, and also includes the uncounted population estimates according to post enumeration survey.

* يشمل السكان الذين تم عدهم فعلاً في فلسطين، وتقديرات عدد السكان الذين لم يتم عدهم على ضوء نتائج الدراسة البعدية.

Annex (3): Calculation of sample size

Unmatched Case-Control Study (Comparison of ILL and NOT ILL)

Two-sided confidence level:	95%
Power:	80 %
Ratio of controls to cases:	1
Percent of controls exposed:	50 %
Odds ratio:	2
Percent of cases with exposure:	66.7 %

	Kelsey	Fleiss	Fleiss w/ CC
Cases	138	137	148
Controls	138	137	148
Total	276	274	296

Annex (4): Timeline table

Activities	**March**	**April**	**May**	**June**	**July**	**Aug**	**Sep**	**Oct**	**Nov**	**Dec**
Writing proposal										
Defense and approval										
Expert validation of instrument										
Pilot study										
Data collection										
Data entry										
Data analysis										
Writing thesis & defense										

Annex (5): Questionnaire - English

Risk Factors of Primary Infertility in Gaza: Case Control Study

Dear Respondent,

I am Dr. Amal Dhair, a student enrolled in Master of public Health at Al Quds University and conducting a study examining risk factors of primary infertility in Gaza Governorates. Primary infertility is an important public health issue that we know less about in Palestine and so, this study may hopefully contribute to exploring main risk factors which could be used for applying prevention and control measures in the future.

I am delighted to inform you that you have been selected, through a random procedure, to engage in this study along with other 319 participants. The study, that would take about one year to be accomplished, will be tackling information about the social, economic, demographic and medical characteristics of both infertile and fertile couples. The information will be gathered through a questionnaire that will take about 25 minutes of your time to be completed. There is no identified risk from providing such information. On the contrary, let me inform you that your participation will be of much benefits to the study, but it is completely voluntary from you side. If you choose to participate, you shall know that all efforts to protect your identity and keep the information you provide confidential will be taken.

Finally, please notice that further clarification shall be provided instantly and do not hesitate to use contact information illustrated hereunder.

Yours sincerely,
Dr. Amal
0595920302

Name: …… Serial Number: ……

Date.: …… Contact information: ……

□ **Case**	□ **Control**
Demographic variables:	
1. Age: …… (Please, record this information from official document if possible)	2. Age of husband: …… (Please, record this information from official document if possible)
3. Marital age: …….	
4. Duration of marriage (in years): ……	
5. Consanguinity of couples: □ 1st degree (1st cousin) □ 2nd degree (2nd cousin) □ No	
6. Consanguinity of the parents: □ 1st degree □ 2nd degree □ No	
7. Consanguinity of the husband's parents: □ 1st degree □ 2nd degree □ No	
8. Refugee status:	□ Registered refugee □ Non-registered refugee □ Non-refugee
9. Residency:	□ North Gaza □ Gaza □ Middle area □ Khan Younis □ Rafah
10. Name of city or village: …… ……	
11. Residency in relation to camps: □ Inside camp □ Outside camp	
12. Site of residency: (You can mark multiple answers)	□ Coastal □ Downtown □ Industrial area □ Agricultural area □ Eastern border □ Northern border □ Southern border □ Beside a factory □ Beside a landfill
13. What type of dwelling unit are you living in? Caravan\Barracks: Separate established building, usually comprised of one or more rooms. The main construction material of the ceiling and the external walls is made of zinc, tinplate or reinforced fiber	□ Villa □ House □ Apartment □ Independent Room □ Tent □ Marginal\Caravan\Barracks
14. What type of dwelling unit you used to live in before marriage?	□ Villa □ House □ Apartment □ Independent Room □ Tent □ Marginal\Caravan\Barracks
15. What is your living status? □ Homeowner □ Renter □ Without payment but not homeowner	
16. What is the family type you are living with? □ Nuclear Family □ Extended Family	

17. What is the family type you used to live with before marriage?	*You:* □ Nuclear Family □ Extended Family	*Your Husband:* □ Nuclear Family □ Extended Family
18. Rank in the original family: …… (Please, in numbers 1, 2, 3…...etc.)		
19. Rank in the original family for the husband: …… (In numbers, please)		
20. Household size: □ less than 3 □ 3-5 □ 6-10 □ More than 10		
21. Household size of original family: ……...		
22. Household size of original family for the husband: ……...		
23. Main source of drinking water after marriage:	□ Municipal water □ Protected well □ Unprotected well □ Rooming tankers □ Public taps □ Mineral water	
24. Main source of drinking water before marriage:	*You:* □ Municipal water □ Protected well □ Unprotected well □ Rooming tankers □ Public taps □ Mineral water	*Your husband:* □ Municipal water □ Protected well □ Unprotected well □ Rooming tankers □ Public taps □ Mineral water
25. Type of toilet facility: □ Flush to piped sewer system □ Flush to septic porous tank □ Flush to septic tight tank □ Flash to open drain		
Socio-economic variables:		
26. Years of schooling completed:	*You:* □ Illiterate □ Primary □ Preparatory □ Secondary □ Higher education	*Your husband:* □ Illiterate □ Primary □ Preparatory □ Secondary □ Higher education

27. Employment status and working field: (Please, if the answer is Housewife or unemployed, move to Q32)	*You:*	*Your husband:*
	□ Housewife □ Employed in public sector □ Employed in private sector □ Employed in NGOs □ Freelancer □ Self-employed	□ Unemployed □ Employed in public sector □ Employed in private sector □ Employed in NGOs □ Freelancer □ Self-employed
28. In which field do you work?	*You:*	*Your husband:*
	□ Computer and Technology □ Teaching □ Social services □ Agriculture □ Engineering □ Hairdresser □ Pharmacist □ Physiotherapist □ Body fitness trainer □ Others (Please, specify): …….	□ Computer and Technology □ Teaching □ Social services □ Agriculture □ Engineering □ Hairdresser □ Pharmacist □ Physiotherapist □ Body fitness trainer □ Others (Please, specify): …….
29. In which shift do you work?	*You:*	*Your husband:*
	□ Morning shifts □ Evening shifts □ Night shifts □ Rotation Shifts □ Split shifts □ on-call shifts	□ Morning shifts □ Evening shifts □ Night shifts □ Rotation Shifts □ Split shifts □ on-call shifts
30. Average working hours per week: (in hours please)	*You:* ……..	*Your Husband*: …….
31. Is your job characterized by?	*You:*	*Your husband:*
	□ Heavy physical labor □ Noise, dust, gases, chemicals, vapors, polluted air □ Work stress (time pressure, concentration) □ Overtime, long working hours	□ Heavy physical labor □ Noise, dust, gases, chemicals, vapors, polluted air □ Work stress (time pressure, concentration) □ Overtime, long working hours

32. Average amount of household monthly income from all sources: ……
(In NIS please)

33. Do you think it is enough regarding your daily expenses?
□ Yes □ No

34. Average monthly expenditure on food items: ……. (In NIS please)

35. Average monthly expenditure on non-food items: ……... (In NIS please)

36. What is the major group of expenditure do you exercise as a household?
(Only one answer please)

□ Food and Soft Drinks
□ Tobacco
□ Clothing and outfits
□ Housing
□ Furniture
□ Medical care
□ Transportation
□ Mobiles bills
□ Education expenses
□ Loans/Depts

37. Do you have health insurance?
□ Yes □ No, go to Q39

38. If yes, what type of health insurance?
□ Public □ Private

39. Do you live near a health facility?
□ Yes □ No

40. Do you have easy access to any health facility?
□ Yes □ No

41. Do you have easy access to drug treatment?
□ Yes □ No

Female Medical Variables:

42. Age of onset of 1st menstrual period: ……. years old

43. Do you have regular menstrual period?
□ Yes □ No
(If Yes please, go to Q46)

44. If no, did you seek medical advice?
□ Yes □ No

45. If yes, what is the diagnosis? ……
(Please, fill unknown in case no diagnosis reached)
(Please, confirm information with medical reports, if any)

46. What is the interval of your menstrual cycle?
□ Less than 20days □ 20-25 □ 26-30
□ 31-35 □ More than 35days
(Please, skip this Q if menses is irregular)

47. What is the duration of menstrual flow?.....
(Please, average days in last 12 months)

48. Did you have any change in the menstrual pattern?
□ Progressive increased periods due to increase in quantity or duration of flow.
□ Increased frequency of periods.
□ Progressive decrease in frequency of periods (Less than 5times/year).
□ Complete cessation of menstruation.
□ No change

49. Have you ever used combined oral contraceptives?

□ Yes □ No, go to Q52

50. For how long? ……..

(In years and months please)

51. For what reason did you use contraceptive methods?

□ Medical treatment □ Birth control

52. Have you ever suffered from Pelvic Inflammatory Disease? (Please, confirm with medical reports)

□ Yes □ No,

53. Did you suffer from any Genito-urinary infections?

□ Yes □ No, go to Q57

54. If yes, during the past two years, how many times did you suffer from Genito-urinary infection? ……..

(In numbers please)

55. Did you seek medical advice?

□ Yes □ No

56. If no, why you didn't? (Multiple choices could be used)	□ I can't afford reaching the health facility □ I can't afford buying the prescribed medicine □ I don't trust doctors □ I prefer traditional treatment □ Others/ please, specify …….

57. Please, specify the cause of infertility diagnosed by a specialist:

(Please, skip this Q for control group)

(Please, confirm with medical reports)

□ Male factor: Specify: ……...

□ Female factor: Specify: …….

58. Did you suffer or still suffering from one or more of the followings?

□ Diabetes ……. □ Epilepsy ……

□ Hypertension ……. □ Ulcerative colitis …….

□ Congenital heart disease □ Psoriasis ……

□ Bronchial asthma ……. □ Vitiligo ……

□ Hypothyroidism ……. □ SLE …….

□ Congenital anomalies in uterus □ PCOs ……

□ Hirsutism ……... □ Cushing syndrome ……

□ Hyperprolactinemia …… □ Rheumatic disease ……

□ Cancer: ……. □ Mumps

□ Others: …….

(Please, confirm information with medical reports)

(Please, insert duration of illness in yrs in front of selected item/s except cancer, mumps & Cong. Heart & Uterus)

59. If you have any of the previous disease, file number please: ……

60. Have you been through any general surgery during your lifetime? □ Yes □ No	61. If yes, specify the reason or kind of surgery, please: 1…… 2……

62. Please, specify the following in terms of drug intake:

Drug	Continuous/intermittent	Average consumption/month (Tab/Month)	Duration (Please record m or y for months or years)
Ibuprofen			
Diclofenac			
Indomethacin			
Aspirin			
Celecoxib			
Naproxen			
Piroxicam			
Methotrexate			
Chemotherapy			
Clozapine			
Risperidone			
Olanzapine			
Spironolactone			

63. Have you ever suffered from uterine fibroids?

□ Yes, please specify ……. □ No

64. If yes, please select the plan of management you received:

□ No intervention, left till shrink alone □ Hysteroscopic myomectomy

□ Medical treatment □ Laparoscopic myomectomy

□ Interventional radiology □ Abdominal myomectomy

65. Does anyone in your family has a history of:

- Infertility Yes No Relationship: ……
- Subfertility Yes No Relationship: ……
- Hypothyroidism Yes No Relationship: ……
- PCOs Yes No Relationship: ……
- Endometriosis Yes No Relationship: ……
- Premature ovarian failure Yes No Relationship: ……
- Hyperprolactinemia Yes No Relationship: ……

Husband Medical Variables:

66. Do you have any chronic medical problems?

□ Yes □ No

67. If yes, please specify:

Type of illness …… Duration of illness …….

(Please, confirm information with medical reports if possible)

68. Are you or have you ever experienced any of the followings?

□ Undescended testis

□ Testicular trauma

□ Varicocele, if yes ……. □ Bilateral…… □ Unilateral

□ Nonspecific urethritis

□ Mumps

69. Did you suffer from any Genito-urinary infections?

□ Yes □ No

70. If yes, during the past two years, how many times did you suffer from Genito-urinary infection? ……..

(In numbers please)

71. Did you use to or currently been exposed to any of the followings?

- □ Heavy physical labor
- □ Noise, dust, gases, vapors, polluted air
- □ Agricultural pesticides
- □ Overheat (e.g. Ovens, solarium houses)

72. Do you have history of pelvic surgery?

□ Yes/Specify please ……... □ No

73. Do you or have you ever been taking any medicine frequently?

□ Yes □ No

74. If yes, please specify:

Name:	Duration of intake:
……	……..
……	……..
……	……

75. Does anyone in your family has a history of:

- Infertility □ Yes □ No Relationship: ……
- Subfertility □ Yes □ No Relationship: ……
- Hypothyroidism □ Yes □ No Relationship: ……
- Varicocele □ Yes □ No Relationship: ……
- Undescended testes □ Yes □ No Relationship: ……

Environmental variables:

A. War effect:

Question:	*You*	*Your Husband*
76. Have you witnessed one or more of the last three wars that has been held against GS?	□ Yes □ No	□ Yes □ No
77. If yes, how many wars have you witnessed?	……	……..
78. Has your house been totally or partially demolished?	□ Yes □ No	□ Yes □ No
79. Has one of your neighbors' houses been totally or partially demolished?	□ Yes □ No	□ Yes □ No
80. Did you live in a partially demolished house?	□ Yes □ No	□ Yes □ No
81. Did you ever live beside a house that has been partially or completely demolished?	□ Yes □ No	□ Yes □ No
82. Currently, do you live in a place that has been renewed after complete or partial demolishing?	□ Yes □ No	
83. Do you work in a place that has been renewed after complete or partial demolishing?	□ Yes □ No	□ Yes □ No
84. In the place that you are living, are there any sites (10-50m) that has been exposed to bombardments?	□ Yes □ No	

85. If your source of drinking water is a nearby well, has the site of the well or its surroundings been exposed to bombardments?	□ Yes □ No	
86. Did you work at the field during the war period?		
• Rescuer	□ Yes □ No	□ Yes □ No
• Field health staff	□ Yes □ No	□ Yes □ No
• Field volunteer	□ Yes □ No	□ Yes □ No
• Searcher	□ Yes □ No	□ Yes □ No
• Evacuator	□ Yes □ No	□ Yes □ No
• Field Journalist	□ Yes □ No	□ Yes □ No
• Others/ please, specify	……	……
87. Did you ever deal with "after war remnants"?	□ Yes □ No	□ Yes □ No

B. Agricultural pesticides and herbicides effect:

88. Do you deal with pesticides and/or herbicides?
□ Yes □ No, (Please, go to Lifestyle section)

89. You use pesticides and/or herbicides as:
□ Farmer □ Farm Owner □ Dealer □ Distributer

90. How often do you deal with pesticides and/or herbicides?
□ Daily □ Weekly □ Monthly □ Rarely

91. For how long have you been using pesticides and/or herbicides regularly: …… (y/m, please)

92. Do you practice safety and protective measures when dealing with pesticides, like protective clothes, gloves and eye shields?
□ Yes □ No

Lifestyle:

A. Diet:

93. Weight: (In Kg, please)	You: ……		
	Your Husband: ……		
94. Height: (In centimeter, please)	You: ……		
	Your Husband: ……		
95. Did you suffer from obesity when you were child?	You:	□ Yes	□ No
	Your Husband:	□ Yes	□ No
96. Are you allergic to any food item/s? (If no, please go to Q98)	You:	□ Yes	□ No
	Your Husband:	□ Yes	□ No
97. If yes, please specify:	You: ……...		
	Your Husband: …….		

98. In a typical week, on how many days do you eat fruit?		You:	Your Husband:
(Ask the participant to think of any fruit on the showcard. A typical week means a "normal" week when the diet is not affected by cultural, religious, or other events. Ask the participant not to report an average over a period)	Number of days:	……	……..

99. How many servings of fruits do you eat on one of those days? (Ask the participant to think of one day he/she can recall easily. Refer to the showcard for serving sizes.)	Number of servings:	You: ……	Your Husband: ……..
100. In a typical week, on how many days do you eat vegetables? (Ask the participant to think of any vegetable on the showcard. A typical week means a "normal" week when the diet is not affected cultural, religious, or other events. Ask the participant not to report an average over a period)	Number of days:	You: ……	Your Husband: ……..
101.How many servings of vegetables do you eat on one of those days? (Ask the participant to think of one day he/she can recall easily. Refer to the showcard for serving sizes.)	Number of servings:	You: ……	Your Husband: ……..
102. How often do you add salt or salty sauce to your food right before you eat it or as you are eating it? (Read out all options and use showcard please)	You: □ Always □ Often □ Sometimes □ Rarely □ Never	Your husband: □ Always □ Often □ Sometimes □ Rarely □ Never	
103. How often is salt, salt seasoning or salty sauce added in cooking or preparing foods in your household? (Read out all options and select the appropriate response please)	You: □ Always □ Often □ Sometimes □ Rarely □ Never		
104. How often do you eat processed food high in salt? By processed food high in salt, I mean foods that have been altered from their natural state, such as packaged salty snacks, canned salty food including pickles and preserves, salty food prepared at a fast food restaurant, cheese and processed meat. (Please, read out all options. Use showcards that shows processed food high in salt, please)	You: □ Always □ Often □ Sometimes □ Rarely □ Never	Your husband: □ Always □ Often □ Sometimes □ Rarely □ Never	
105. How much salt or salty sauce do you think you consume? (Read out all options and select the appropriate response)	You: □ Far too much □ Too much □ Just the right amount □ Too little □ Far too little	Your husband: □ Far too much □ Too much □ Just the right amount □ Too little □ Far too little	

106. How many meals do you eat frequently per day?	You: ……	
	Your Husband: ……	
107. Do you have breakfast regularly?	You: □ Yes	□ No
	Your Husband: □ Yes	□ No
108. What do you eat for main dish most frequently? (One answer, please)	□ Meat □ White chicken □ Farm raised chicken	□ Turkey □ Seafood □ None
109. What do you eat for main dish most frequently? (One or two answers, please)	□ Vegetables □ Beans □ Pasta	□ Diary Food □ Rice □ Bread
110. What do you eat for snacks most frequently? (One answer, please)	□ Fruits □ Nuts □ Dairy Products	□ Sweets and Sugary Food □ Chips & fries
111. What do have as a drink most frequently? (One answer, please)	□ Soda drinks □ Natural Juice □ Canned Juice □ Juice from concentrate	□ Tea □ Coffee □ Herbal drinks □ Water □ None
112. What kind of oil do you often use in your food either for cooking or processing?	□ Olive oil	□ Vegetable oil
B. Smoking:		
113. Do you smoke tobacco?	You: □ Yes	□ No
	Your Husband: □ Yes	□ No
114. Have you ever smoked tobacco? (If "No" please, go to Q117)	You: □ Yes	□ No
	Your Husband: □ Yes	□ No
115. How many cigarettes do you or used to smoke per day?	You: ……	
	Your Husband: ……	
116. For how long did you or have you been smoking?	You: ……	
	Your Husband: ……	
117. Do you smoke Water Pipe?	You: □ Yes	□ No
	Your Husband: □ Yes	□ No
118. Have you ever smoked Water Pipe? (If "No" please, go to Q121)	You: □ Yes	□ No
	Your Husband: □ Yes	□ No
119. How many times do you or used to smoke Water Pipe per day?	You: ……	
	Your Husband: ……	
120. For how long did you or have you been smoking Water Pipe?	You: ……	
	Your Husband: ……	
121. Does any other household smoke? □ Yes □ No		

Short Physical activity questionnaire:

Female participant

I am going to ask you about the time you spend doing different types of physical activity in a typical week.

The first question: is about the time you spent sitting during the last 7 days include time spent at work, at home, while doing course, work, and during leisure time. This may include time spent sitting at a desk, visiting friend, reading or setting or lying down to watch television (Sedentarily)

During the last 7 days, how much time did you spend sitting during a day?	*Hours:* …….	*Minute:* …….	*Don't know* ☐	*P1*

The second question: is about the time you spent walking in the last 7 days this include at work and at home, walking to travel from place to place and any other walking that you might do solely for recreation sport, exercise or leisure

During the last 7 days on how many days did you walk for at least 10 minutes at a time?	*Days:* …….	*No days* ☐	*Don't know* ☐	*P2*
How much time did you usually spend walking on one of those days?	Hours: …….	Minute: …….	Don't know ☐	P3

The third question: during the last days, on how many days did you do moderate physical activity like gardening, cleaning, bicycling at regular pace, swimming or other fitness activities (do not include walking).

Think only about those *Physical activities that you did for at least 10 minutes.*	*Days:* …….	*No days* ☐	*Don't know* ☐	*P4*
How much time did you usually spend doing moderate activities on one of those days?	Hours: …….	Minute: …….	Don't know ☐	P5

The fourth question: during the last 7 days on how many days did you do vigorous physical activity like heavy lifting heavier garden or construction work, aerobic jogging, running or fast bicycling

Think only about those *Physical activities that you did for at least 10 minutes at a time.*	*Days:* …….	*No days* ☐	*Don't know* ☐	*P6*
How much time did you usually spend doing vigorous physical activities on one of those days?	Hours: …….	Minute: …….	Don't know ☐	P7

Short Physical activity questionnaire:

Male participant

I am going to ask you about the time you spend doing different types of physical activity in a typical week.

The first question: is about the time you spent sitting during the last 7 days include time spent at work, at home, while doing course, work, and during leisure time. This may include time spent sitting at a desk, visiting friend, reading or setting or lying down to watch television (Sedentarily)

During the last 7 days, how much time did you spend sitting during a day?	*Hours:* …….	*Minute:* …….	*Don't know* ☐	*P1*

The second question: is about the time you spent walking in the last 7 days this include at work and at home, walking to travel from place to place and any other walking that you might do solely for recreation sport, exercise or leisure

During the last 7 days on how many days did you walk for at least 10 minutes at a time?	*Days:* …….	*No days* ☐	*Don't know* ☐	*P2*
How much time did you usually spend walking on one of those days?	Hours: …….	Minute: …….	Don't know ☐	P3

The third question: during the last days, on how many days did you do moderate physical activity like gardening, cleaning, bicycling at regular pace, swimming or other fitness activities (do not include walking).

Think only about those *Physical activities that you did for at least 10 minutes.*	*Days:* …….	*No days* ☐	*Don't know* ☐	*P4*
How much time did you usually spend doing moderate activities on one of those days?	Hours: …….	Minute: …….	Don't know ☐	P5

The fourth question: during the last 7 days on how many days did you do vigorous physical activity like heavy lifting heavier garden or construction work, aerobic jogging, running or fast bicycling

Think only about those *Physical activities that you did for at least 10 minutes at a time.*	*Days:* …….	*No days* ☐	*Don't know* ☐	*P6*
How much time did you usually spend doing vigorous physical activities on one of those days?	Hours: …….	Minute: …….	Don't know ☐	P7

Perceived Stress Scale:

	Never 0	Almost never 1	Sometimes 2	Fairly often 3	Very often 4
1. In the last month, how often have you been upset because of something that happened unexpectedly?	☐	☐	☐	☐	☐
2. In the last month, how often have you felt that you were unable to control the important things in your life?	☐	☐	☐	☐	☐
3. In the last month, how often have you felt nervous and "stressed"?	☐	☐	☐	☐	☐
4. In the last month, how often have you dealt successfully with day to day problems and annoyances?	☐	☐	☐	☐	☐
5. In the last month, how often have you felt that you were effectively coping with important changed that were occurring in your life?	☐	☐	☐	☐	☐
6. In the last month, how often have you felt confident about your ability to handle your personal problems?	☐	☐	☐	☐	☐
7. In the last month, how often have you felt that things were going your way?	☐	☐	☐	☐	☐
8. In the last month, how often have you found that you could not cope with all things that you had to do?	☐	☐	☐	☐	☐
9. In the last month, how often have you been able to control irritations in your life?	☐	☐	☐	☐	☐
10. In the last month, how often have you felt that you were on top of things	☐	☐	☐	☐	☐
11. In the last month, how often have you been angered because of things that happened that were outside of your control?	☐	☐	☐	☐	☐
12. In the last month, how often have you found yourself thinking about things that you have to accomplish?	☐	☐	☐	☐	☐
13. In the last month, how often have you been able to control the way you spent your time?	☐	☐	☐	☐	☐
14. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?	☐	☐	☐	☐	☐

Annex (6): Questionnaire - Arabic

جامعة القدس

Al-Quds University

عوامل خطر العقم الأولي في قطاع غزة

عزيزي/تي المشارك/ة:

أنا الدكتورة أمل ضهير طالبة ماجستير في قسم الصحة العامة بجامعة القدس. كمتطلب جامعي للحصول على درجة الماجستير أقوم حالياً بإجراء دراسة تفحص عوامل خطر العقم الأولي في محافظات غزة. العقم هو قضية مهمة تتعلق بالصحة العامة لا نعرف عنها الكثير في فلسطين ، ولذا نأمل أن تساهم هذه الدراسة في إكتشاف عوامل الخطر الرئيسية التي يمكن استخدامها لتطبيق تدابير الوقاية والسيطرة في المستقبل.

يسعدني أن أبلغكم أنه تم اختياركم ، من خلال إجراء عشوائي ، للمشاركة في هذه الدراسة باللإضافة الى 319 مشتركين آخرين. ستتناول الدراسة ، التي ستستغرق حوالي عام واحد ، معلومات عن الخصائص الاجتماعية والاقتصادية والديمغرافية والطبية لكل من الأزواج المصابين بالعقم والأزواج ذوي الخصوبة. سيتم جمع المعلومات من خلال استبيان سيستغرق استكماله حوالي 25 دقيقة. لا يوجد خطر محدد من تقديم هذه المعلومات. على العكس من ذلك، اسمحوا لي أن أبلغكم أن مشاركتك ستكون ذات فائدة كبيرة للدراسة ، ولكنها طوعية تمامًا من جانبك. إذا اخترت المشاركة ، يجب أن تعلم أن كل التدابير اللازمة لحماية هويتك والحفاظ على سرية المعلومات التي سوف تقدمها سيتم اتخاذها.

أخيرًا ، يرجى ملاحظة أنه في حال احتجت لمزيد من الإيضاحات و المعلومات المتعلقة بطبيعة الدراسة أو النتائج النهائية لا تتردد في استخدام معلومات التواصل الموضحة أدناه.

د. أمل ضهير

0595920302

الاسم: ..... الرقم التسلسلي: .....

التاريخ: ..... معلومات للتواصل:.....

☐ Case	☐ Control
متغيرات ديموغرافية:	
1. العمر: ..... (الرجاء تسجيل هذه المعلومات من وثائق رسمية)	2. عمر الزوج: ..... (الرجاء تسجيل هذه المعلومات من وثائق رسمية)
3. العمر عند الزواج:	
4. مدة الزواج (بالسنوات):	
5. هل أنت و زوجك أقارب: ☐ أقارب درجة أولى ☐ أقارب درجة ثانية ☐ لا	
6. هل الوالدين أقارب؟ ☐ أقارب درجة أولى ☐ أقارب درجة ثانية ☐ لا	
7. هل والدين الزوج أقارب؟ ☐ أقارب درجة أولى ☐ أقارب درجة ثانية ☐ لا	
8. حالة اللجوء: ☐ لاجئ مسجل ☐ لاجئ غير مسجل ☐ غير لاجئ	
9. مكان السكن: ☐ شمال غزة ☐ غزة ☐ المنطقة الوسطى ☐ خانيونس ☐ رفح	10. اسم المدينة او القرية : ....
11. مكان السكن بالنسبة للمخيمات: ☐ داخل المخيمات ☐ خارج المخيات	
12. موقع السكن: (إحتمال أكثر من إجابة واحدة) ☐ الساحل ☐ وسط المدينة ☐ منطقة الصناعية ☐ منطقة زراعية ☐ الحدود الشرقية ☐ الحدود الشمالية ☐ الحدود الجنوبية ☐ بجوار مصنع ☐ بجوار مكب نفايات	
13. ما نوع الوحدة السكنية الذي تعيش فيه حاليا؟ براكيه/ كرفان/ بركس: هو مبنى قائم بذاته مؤقت وغير تقليدي للسكن، ويتكون من غرفة واحدة أو اكثر وتكون المادة الغالبة للجدران الخارجية والسطح من الزنك (الصاج) أو التنك أو الاسبست، أو البلاستيك المقوى (فيبر كلاس) أو الخشب	☐ فيلا ☐ منزل ☐ شقة ☐ غرفة مستقلة ☐ خيمة ☐ الهوامش/ منزل متنقل/ باراكس
14. ما نوع الوحدة السكنية قبل الزواج ؟	☐ فيلا ☐ منزل ☐ شقة ☐ غرفة مستقلة ☐ خيمة ☐ براكيه/ كرفان/ بركس

15. ما هي طبيعة حيازة المسكن الذي تعيش فيه حاليا ؟

□ ملك □ إيجار □ بدون مقابل ولكن ليس ملك

16. ما هي طبيعة العائلة التي تعيش معها حاليا ؟

□ عائلة نووية □ عائلة ممتدة

17. ما هي طبيعة العائلة التي كنت تعيش معها قبل الزواج؟	*الزوجة:*	*الزوج:*
	□ عائلة نووية □ عائلة ممتددة	□ عائلة نووية □ عائلة ممتددة

18. الترتيب في العائلة قبل الزواج: .....

(الرجاء الإجابة بالأرقام 1 ،2، 3 ... إلخ)

19. ترتيب الزوج في عائلته:.....

(بالأرقام رجاء)

20. عدد سكان البيت حالياً:

□ أقل من 3 □ 3-5 □ 6-10 □ أكثر من 10

21. عدد سكان بيت الزوجة قبل الزواج: .....

22. عدد سكان بيت الزوج قبل الزواج: .....

23. مصدر مياه الشرب بعد الزواج:	□ مياه بلدية □ بئر محمي □ بئر غير محمي □ بائعين متجولين للمياه □ صنابير عامة □ مياه معدنية

24. مصدر مياه الشرب قبل الزواج:	*الزوجة:*	*الزوج:*
	□ مياه بلدية □ بئر محمي □ بئر غير محمي □ بائعين متجولين للمياه □ صنابير عامة □ مياه معدنية	□ مياه بلدية □ بئر محمي □ بئر غير محمي □ بائعين متجولين للمياه □ صنابير عامة □ مياه معدنية

25. نوع الصرف الصحي:

□ صرف بواسطة شبكة رئيسية □ صرف بواسطة حفرة امتصاصية

□ صرف بواسطة حفرة صماء □ صرف بواسطة مصرف مفتوح

متغيرات إجتماعية و إقتصادية:

26. درجة التعليم :	*الزوجة:*	*الزوج:*
	□ غير متعلم □ ابتدائي □ إعدادي □ ثانوي □ جامعة □ تعليم عالي	□ غير متعلم □ ابتدائي □ إعدادي □ ثانوي □ جامعة □ تعليم عالي

27. الوظيفة أو مجال العمل:	*الزوجة:*	*الزوج:*
	□ ربة منزل □ موظفة في القطاع العام □ موظفة في القطاع الخاص □ موظفة في المؤسسات الغير حكومية □ عمل بالقطعة □ العمل للحساب الخاص	□ عاطل عن العمل □ موظف في القطاع العام □ موظف في القطاع الخاص □ موظف في المؤسسات الغير حكومية □ عمل بالقطعة □ العمل للحساب الخاص

28. ما طبيعة عملك؟	*الزوجة:*	*الزوج:*
	☐ الكمبيوتر و تكنولوجيا المعلومات ☐ التعليم ☐ الخدمات الاجتماعية ☐ الزراعة ☐ الهندسة ☐ مصفف شعر ☐ الصيدلة ☐ العلاج الطبيعي ☐ مدرب لياقة بدنية ☐ أخرى (الرجاء حدد):	☐ الكمبيوتر و تكنولوجيا المعلومات ☐ التعليم ☐ الخدمات الاجتماعية ☐ الزراعة ☐ الهندسة ☐ مصفف شعر ☐ الصيدلة ☐ العلاج الطبيعي ☐ مدرب لياقة بدنية ☐ أخرى (الرجاء حدد): .....
29. توقيت العمل؟	*الزوجة:*	*الزوج:*
	☐ فترة صباحية ☐ فترة مسائية ☐ قترة ليلية ☐ نظام مناوبات ☐ ساعات مجزءة ☐ على الطلب	☐ فترة صباحية ☐ فترة مسائية ☐ قترة ليلية ☐ نظام مناوبات ☐ ساعات مجزءة ☐ على الطلب
30. معدل ساعات العمل بالأسبوع (بالساعة رجاءً):	*الزوجة:*	*الزوج:* .....
31. هل لدى وظيفتك إحدى المواصفات الآتية؟	*الزوجة:*	*الزوج:*
	☐ مجهود بدني شاق ☐ ضوضاء، غبار، غازات، كيماويات، ابخرة، هواء ملوث ☐ ضغط العمل (ضغط الوقيت، التركيز) ☐ عمل عدد ساعات إضافية، عمل ساعات طويلة	☐ مجهود بدني شاق ☐ ضوضاء، غبار، غازات، كيماويات، ابخرة، هواء ملوث ☐ ضغط العمل (ضغط الوقيت، التركيز) ☐ عمل عدد ساعات إضافية، عمل ساعات طويلة
32. متوسط مقدار دخل الأسرة الشهري من جميع المصادر: ..... (بالشيقل رجاءً)		
33. هل تظنين أن الدخل الشهري كاف بالنسبة للنفقات اليومية؟ ☐ نعم ☐ لا		
34. متوسط الإنفاق الشهري على المواد الغذائية: ..... (بالشيقل رجاءً)		
35. متوسط الإنفاق الشهري على المواد غير الغذائية: ..... (بالشيقل رجاءً)		
36. ما هي المجموعة الرئيسية من النفقات التي تمارسونها كأسرة؟ (إجابة واحدة فقط من فضلك)	☐ الطعام والمشروبات ☐ الدخان ☐ الملابس ☐ اعمار السكن ☐ الأثاث ☐ الرعاية الصحية ☐ التنقل والمواصلات ☐ فواتير الهواتف ☐ مصاريف التعليم ☐ القروض	

37. هل لديك تأمين صحي؟
□ نعم □ لا اذهب ل سؤال 39

38. إذا لديك تأمين، ما نوعه؟
□ حكومي □ خاص

39. هل تعيش بالقرب من أي منشأة صحية؟
□ نعم □ لا

40. هل تستطيع الوصول إلى أي منشأة صحية بسهولة؟
□ نعم □ لا

41. هل تستطيع الحصول على الدواء بسهولة ؟
□ نعم □ لا

متغيرات طبية للزوجات:

42. سن بداية الدورة الشهرية الأولى: ..... بالسنوات

43. هل الدورة الشهرية منتظمة ؟
□ نعم (نعم ، اذهب لسؤال 46) □ لا

44. إذا أجبت ب لا ، هل حصلت على مساعدة طبية ؟
□ نعم □ لا

45. إذا أجبت بنعم ، ماذا كان التشخيص ؟ .....
(الرجاء الإجابة ب "غير معروف " إذا لم تتوصل لتشخيص)
(يرجى تأكيد المعلومات بواسطة التقارير الطبية ، إن وجدت)

46. ما هو متوسط الأيام للدورة الشهرية ؟
□ أقل من 20 يوم □ 21-25 □ 26-30
□ 31-35 □ أكثر من 35 يوم
(الرجاء تخطي هذا السؤال إذا الدورة الشهرية غير منتظمة)

47. ما هي مدة تدفق الدورة؟ .....
(من فضلك ، متوسط المدة في الإثنى عشر شهر الماضية)

48. هل كان لديك أي تغيير في نمط الدورة الشهرية؟

□ زيادة تدريجية بسبب الزيادة في كمية أو مدة التدفق.
□ زيادة في عدد مرات الدورة.
□ نقصان تدريجي في عدد مرات الدورة الشهرية (أقل من خمس مرات في السنة).
□ انقطاع تام للدورة الشهرية.
□ لا تغير.

49. هل سبق لك استخدام حبوب منع الحمل الثنائية؟
□ نعم □ لا (إذهب للسؤال 52)

50. ما هي مدة استعمالها ؟ .....
(بالشهور أو بالسنوات من فضلك)

51. لأي سبب كنت تستخدم وسائل منع الحمل؟
□ كوسيلة علاج □ لتنظيم الأسرة

52. هل حدث أن عانيت من مرض التهاب الحوض؟ Pelvic inflammatory disease
□ نعم □ لا (الرجاء التحديد بالتقارير الطبية إذا أمكن)

53. هل عانيت من أي التهابات في الجهاز البولي التناسلي؟
□ نعم لا؛ (إذهب للسؤال 57)

54. إذا نعم ، خلال السنتين الفائتتين ، كام عدد مرات الإصابة بالتهاب القنوات البولية التناسلية؟ .....
.....

55. هل حصلت على مساعدة طبية ؟
□ نعم □ لا

56. إذا "لا " لماذا لم تحصل على مساعدة طبية ؟ (يمكنك الإجابة بأكثر من سبب)	☐ لم أستطيع تحمل تكاليف الوصول إلى المنشأة الصحية ☐ لم أستطيع شراء الدواء الموصوف ☐ لم أثق بالطبيب ☐ أنا أفضل الطب العربي ☐ أسباب أخرى \ الرجاء التحديد: .....

57. من فضلك ، حدد سبب العقم الذي تم تشخيصه بواسطة أخصائي:
(من فضلك ، تخطي هذا السؤال ل controls)
(يرجى تأكيد التشخيص بواسطة التقارير الطبية)

☐ من الزوج: ☐ من الزوجة:
حدد: ..... حدد:.....
....

58. هل عانيت او مازلت تعاني من واحدة أو أكثر من الأمراض الأتية؟

☐ السكر	☐ صرع	
☐ ضغط الدم	☐ التهاب القولون التقرحي	Ulcerative colitis, Chron's
☐ أمراض القلب الوراثية	☐ صدفية	Psoriasis
☐ الربو الشعبي	☐ بهاق	Vitiligo
☐ كسل الغدة الدرقية	☐ ذئبة الحمراء	Systemic Lupus Erythromatosis
☐ تشوه خلقي في الرحم	☐ متلازمة المبيض متعدد الأكياس	PCOs
☐ نمو الشعر المفرط	☐ متلازمة كوشنغ	Cushing disease
☐ فرط إفراز هرمون الحليب	☐ مرض الروماتيزم	
☐ سرطان ب:	☐ أبو داج	
☐ أمراض أخرى :.....		

(الرجاء التأكيد بتقارير طبية) (الرجاء كتابة مدة إكتشاف المرض أمام الإجابة المختارة ماعدا أبو داج و العيوب الخلقية في القلب والرحم)

59. إذا لديك أي من الأمراض السابقة . ما هو رقم الملف :.....

60. هل خضعت لأي عمليات جراحية خلال حياتك ؟ ☐ نعم ☐ لا	61. إذا أجبت ب "نعم " ، الرجاء توضيح السبب ونوع العميلة : 1..... 2..... 3.....

62. يرجى تحديد ما يلي فيما يتعلق بتناول الأدوية العقارية:

العقار	استخدام دائم / متقطع	متوسط الاستهلاك (حبة/الشهر)	المدة **(الرجاء كتابة أشهر أو سنوات بجوار المدة الزمنية لاستخدام العلاج)**
Ibuprofen			
Diclofenac			
Indomethacin			
Aspirin			
Celecoxib			
Naproxen			
Piroxicam			
Methotrexate			
Chemotherapy			
Clozapine			
Risperidone			
Olanzapine			
Spironolactone			

63. هل عانيت يوما من الأورام الليفية الحميدة في الرحم؟ (Uterine fibroids)
☐ نعم (الرجاء توضيح نوعها): ..... ☐ لا

64. إذا أجبت بنعم ، الرجاء تضيح خطة العلاج التي خضعت لها:

□ لا تدخل طبي ، تركت حتى تقلصت □ استئصال الورم بعملية جراحية Abdominal myomectomy

□ علاج بالأدوية □ استئصال الورم بمنظار رحمي Hysteroscopic myomectomy

□ علاج بالإشعاع □ استئصال الورم بمنظار بطني Laparoscopic myomectomy

65. هل يوجد تاريخ عائلي للأمراض التالية؟

- عقم نعم لا علاقتك بالمصاب :.....Infertility
- ضعف خضوبة نعم لا علاقتك بالمصاب :.....Subfertility
- كسل الغدة الدرقية نعم لا علاقتك بالمصاب :.....Hypothyroidism
- تكيسات المبيض نعم لا علاقتك بالمصاب :.....PCOs
- انتباذ بطانة الرحم نعم لا علاقتك بالمصاب :.....Endometriosis
- فشل المبيض مبكر نعم لا علاقتك بالمصاب :.....Premature ovarian failure
- فرط بروﻻكتين الدم نعم لا علاقتك بالمصاب :..... Hyperprolactinemia

متغيرات طبية للأزواج:

66. هل لديك أي أمراض مزمنة ؟

□ نعم □ لا

67. إذا كانت الإجابة نعم، الرجاء تحديد:

□ اسم المرض: ..... (بالإنجليزي رجاءً) □ منذ متى: ..... (بالسنوات/أشهر)

....

....

68. هل كنت أو مازلت تعاني من أي من الأمراض التالية؟

□ الخصية المعلقة (Undescended testis)

□ صدمة علي الخصية (Testicular trauma)

□ دوالي الخصية ..... □ في الجهتين □ في جهة واحدة (Varicocele)

□ التهاب مجرى البول (Nonspecific urethritis)

□ النكاف (Mumps)

69. هل عانيت من أي التهابات في الجهاز البولي التناسلي؟

□ نعم □ لا

70. إذا نعم ، خلال السنتين الفائتتين ، كام عدد مرات الإصابة بالتهاب القنوات البولية التناسلية؟ .....

71. هل تعرضت من قبل أو حاليا لأي من التالي ؟

□ مجهود بدني شاق

□ ضجيج ، غبار ، غازات ، أبخرة ،هواء ملوث

□ مبيدات حشرية زراعية

□ درجات حرارة عالية جدا (أفران، حمامات شمسية زراعية)

72. هل تعرضت لعمليات جراحية بالحوض ؟

□ نعم / الرجاء التحديد:..... □ لا

73. هل تتناول أدوية بشكل مستمر ؟

□ نعم □ لا

74. إذا كانت الإجابة نعم، الرجاء تحديد:

□ اسم الدواء: (بالإنجليزي رجاءً) □ مدة تناول الدواء: (بالسنوات/أشهر)

....

....

75. هل يوجد أحد من أفراد العائلة مصاب ب :

- العقم نعم لا علاقتك بالمصاب :.....
- ضعف الخضوبة نعم لا علاقتك بالمصاب :.....
- كسل الغدة الدرقية نعم لا علاقتك بالمصاب :.....
- دوالي الخصية نعم لا علاقتك بالمصاب :.....
- الخصية المعلقة نعم لا علاقتك بالمصاب :.....

المتغيرات البيئية

1- تأثير الحروب :

السؤال:	*الزوجة*	*الزوج*
76. هل شهدت واحد أو أكثر من أخر ثلاث حروب تمت على قطاع غزة؟	☐ نعم ☐ لا	☐ نعم ☐ لا
77. إذا أجبت ب" نعم " كم عدد الحروب التي شهدتها ؟	.....	.....
78. هل تعرض منزلك للهدم الكلي أو الجزئي ؟	☐ نعم ☐ لا	☐ نعم ☐ لا
79. هل تعرض منزل أحد جبرانك للهدم كليا أو جزئيا ؟	☐ نعم ☐ لا	☐ نعم ☐ لا
80. هل كنت تعيش بمنزل تعرض للهدم الجزئي ؟	☐ نعم ☐ لا	☐ نعم ☐ لا
81. هل كنت تعيش بالقرب من منزل تعرض للهدم كليا أو جزئيا ؟	☐ نعم ☐ لا	☐ نعم ☐ لا
82. حاليا هل تعيش بمكان تم إصلاحه أو إعادة بناءه بعد القصف؟	☐ نعم ☐ لا	
83. هل تعمل بمكان تم إصلاحه أو إعادة بناءه بعد القصف ؟	☐ نعم ☐ لا	☐ نعم ☐ لا
84. مكان سكنك الحالي ، هل يوجد أي مكان (10-50m) قد تعرض للقصف بالصواريخ؟	☐ نعم ☐ لا	
85. إذا كان مصدر مياه الشرب بئر قريب ، هل تعرض البئر أو الأماكن المجاورة للبئر للقصف بالصواريخ ؟	☐ نعم ☐ لا	
86. هل عملت بالميادين التالية بأوقات الحروب ؟ • منقذ • ضمن طاقم الصحة الميداني • متطوع ميداني • باحث • مخلي و منقذ • صحفي ميداني مجالات أخرى / الرجاء التحديد:	☐ نعم ☐ لا ☐ نعم ☐ لا ☐ نعم ☐ لا ☐ نعم ☐ لا ☐ نعم ☐ لا ☐ نعم ☐ لا	☐ نعم ☐ لا ☐ نعم ☐ لا ☐ نعم ☐ لا ☐ نعم ☐ لا ☐ نعم ☐ لا ☐ نعم ☐ لا .....
87. هل تعرضت أو استعملت يوما أي من مخلفات " بقايا ما بعد الحرب " ؟	☐ نعم ☐ لا	☐ نعم ☐ لا

2- .تأثير المبيدرات الحشرية و الأدوية الزراعية:

88. هل تتعامل مع المبيدات الحشرية و الأدوية الزراعية؟

☐ نعم ☐ لا (الرجاء التوجه لقسم نمط المعيشة)

89. انت تستخدم المبيدات الحشرية و الأدوية بصفتك :

☐ مزارع ☐ مالك مزرعة ☐ تاجر ☐ موزع

90. كم مرة تتعامل مع المبيدات الحشرية و الأدوية الزراعية :
□ يوميا □ أسبوعيا □ شهريا □ نادراً

91. منذ متى وأنت تتعامل مع المبيدات الحشرية و الأدوية الزراعية (بالسنوات \ الأشهر رجاءً):
.....

92. هل تمارس تدابير السلامة والوقاية عندما تتعامل مع المبيدات الحشرية و الأدوية الزراعية، كملابس واقية ، قفازات ، ودرع للعيون ؟
□ نعم □ لا

نمط المعيشة:

1. الغذاء

93. **الوزن رجاءً:** (بالكيلوغرام)	الزوجة :.....	
	الزوج :	
94. **الطول رجاءً:** (بالسنتيمتر)	الزوجة :.....	
	الزوج :	
95. هل عانيت من السمنة بعمر الطفولة ؟	الزوجة: □ نعم □ لا	
	الزوج : □ نعم □ لا	
96. هل لديك حساسية لنوع محدد من الأطعمة؟	الزوجة: □ نعم □ لا	
	الزوج : □ نعم □ لا	
97. إذا يوجد حساسية، الرجاء تحديد المسبب:	الزوجة :.....	
	الزوج :	

98. في أسبوع نموذجي ، ما هو عدد الأيام التي تتناول فيها الفاكهة؟ (الأسبوع اللنموذجي هو أسبوعًا "عاديًا" عندما لا يتأثر النظام الغذائي بأحداث ثقافية أو دينية أو أحداث أخرى. اطلب من المشارك عدم الإبلاغ عن متوسط فترة زمنية)	عدد الأيام:	*الزوجة:*	*الزوج:* .....
99. كم عدد حصص الفاكهة التي تتناولها في أحد تلك الأيام؟ (اطلب من المشارك أن يفكر في يوم واحد يمكن تذكره بسهولة. ارجع إلى بطاقة العرض للتعرف على أحجام الحصص)	عدد الحصص:	*الزوجة:*	*الزوج:* .....
100. في أسبوع نموذجي ، ما هو عدد الأيام التي تتناول فيها الخضراوات؟	عدد الأيام:	*الزوجة:*	*الزوج:* .....
101. كم عدد حصص الخضراوات التي تتناولها في أحد تلك الأيام؟	عدد الحصص:	*الزوجة:*	*الزوج:* .....

102. كم مرة تضيف الملح أو الصلصة المالحة إلى طعامك مباشرة قبل تناوله أو أثناء تناوله؟	*الزوجة:*	*الزوج:*
	□ دائماً	□ دائماً
	□ غالباً	□ غالباً
	□ أحياناً	□ أحياناً
	□ نادراً	□ نادراً
	□ أبداً	□ أبداً

103. كم مرة يتم إضافة الملح أو توابل الملح أو الصلصة المالحة في الطهي أو إعداد الأطعمة في منزلك؟	*الزوجة:*	
	□ دائماً	□ نادراً
	□ غالباً	□ أبداً
	□ أحياناً	

104. كم عدد المرات التي تتناول فيها طعاماً معالجاً يحتوي على نسبة ملح كبيرة؟ (أطعمة مالحة معلبة بما في ذلك المخللات والمحفوظات ، أطعمة مالحة محضرة في مطعم للوجبات السريعة ، جبن واللحوم المصنعة)	*الزوجة:* ☐ دائماً ☐ غالباً ☐ أحياناً ☐ نادراً ☐ أبداً	*الزوج:* ☐ دائماً ☐ غالباً ☐ أحياناً ☐ نادراً ☐ أبداً
105. ما مقدار الملح التي تعتقد أنك تستهلكه؟	*الزوجة:* ☐ كثيراً جداً ☐ كثيراً ☐ الكمية المناسبة ☐ قليل ☐ قليل جدا	*الزوج:* ☐ كثيراً جداً ☐ كثيراً ☐ الكمية المناسبة ☐ قليل ☐ قليل جدا
106. كم عدد وجبات الطعام التي تتناولها عادة في اليوم المثالي ؟	الزوجة :..... الزوج :	
107. هل تتناول الإفطار عادة ؟	الزوجة: ☐ نعم ☐ لا الزوج : ☐ نعم ☐ لا	
108. ما الذي تتناوله كطبق أساسي عادة ؟ (أجب إجابة واحدة فقط رجاءً)	☐ لحوم ☐ الدجاج الأبيض ☐ الدجاج المزارع	☐ الديك الرومي ☐ الأسماك ☐ لاشيء من السابق
109. ما الذي تتناوله كطبق أساسي عادة ؟ (أجب إجابتين رجاءً)	☐ خضروات ☐ بقوليات ☐ معكرونة	☐ منتجات الألبان ☐ الأرز ☐ الخبز
110. ما الذي تتناوله كوجبات خفيفة عادة ؟ (أجب إجابة واحدة فقط رجاءً)	☐ فواكه ☐ مكسرات ☐ منتجات الألبان	☐ الحلويات ☐ الشبس و الإندومي
111.ما الذي تتناوله من المشروبات عادة ؟ (أجب إجابة واحدة فقط رجاءً)	☐ المشروبات الغازية ☐ العصائر الطبيعية ☐ العصائر المعلبة ☐ العصائر المركزة	☐ الشاي ☐ القهوة ☐ الأعشاب الطبيعية ☐ المياه ☐ لاشيء من السابق
112. ما نوع الزيت الذي تستخدمه عادة لطهي الطعام و تحضيره؟	☐ زيت زيتون	☐ زيت نباتي ☐ السمن
2. التدخين :		
113. هل تدخن السجائر ؟	الزوجة: ☐ نعم ☐ لا الزوج : ☐ نعم ☐ لا	
114. هل سبق لك التدخين ؟ (اذا الإجابة "لا"، إذهب للسؤال 117)	الزوجة: ☐ نعم ☐ لا الزوج : ☐ نعم ☐ لا	
115. كم عدد السجائر التي تقوم بتدخنها يوميا ؟	الزوجة :..... الزوج :.....	
116. منذ متي تقوم بتدخين السجائر ؟	الزوجة :..... الزوج :.....	

117. هل تدخن الشيشة ؟	الزوجة: □ نعم □ لا الزوج : □ نعم □ لا	
118. هل سبق لك بتدخين الشيشة سابقا ؟ (اذا الإجابة "لا"، إذهب للسؤال 121)	الزوجة : □ نعم □ لا الزوج : □ نعم □ لا	
119. كم عدد المرات التي تدخن بها أو أعتدت بها تدخين الشيشة يوميا ؟	الزوجة :..... الزوج :.....	
120. منذ متى تقوم بتدخين الشيشة ؟	الزوجة :..... الزوج :.....	
121. هل يوجد أحد آخر من أفراد العائلة يدخن ؟ □ نعم □ لا		

إستبيان النشاط البدني القصير:

Female participant

سوف أقوم بالسؤال عن الوقت الذي تقضيه في القيام بأنواع مختلفة من النشاط البدني في أسبوع نموذجي.

السؤال الأول: هو الوقت الذي قضيته في الجلوس خلال آخر 7 أيام ، ويشمل الوقت الذي قضيته في العمل ، في المنزل ، أثناء القيام بدورة ، وأثناء وقت الفراغ. قد يشمل ذلك الوقت الذي تقضيه في الجلوس على مكتب ، زيارة صديق ، القراءة أو الجلوس أو الاستلقاء لمشاهدة التلفزيون.

خلال آخر 7 أيام ، كم من الوقت قضيته جالسًا خلال اليوم؟	*ساعات: .....*	*دقائق: .....*	*لا أعلم*	*P1*

السؤال الثاني: هو الوقت الذي قضيته في المشي في آخر 7 أيام ، ويشمل ذلك في العمل والمنزل ، والمشي للتوجه من مكان إلى مكان وأي نوع اخر من المشي الذي قد تفعله فقط لممارسة الرياضة أو الترفيه.

خلال آخر 7 أيام كم عدد الأيام التي سرت فيها لمدة 10 دقائق على الأقل في المرة الواحدة؟	*أيام: .....*	*ولا يوم*	*لا أعلم*	*P2*
كم من الوقت قضيت عادة في المشي في أحد تلك الأيام؟	*ساعات: .....*	*دقائق: .....*	*لا أعلم*	***P3***

السؤال الثالث: خلال الأيام الأخيرة ، كم عدد الأيام التي مارست فيها نشاطًا بدنيًا معتدلًا مثل البستنة أو التنظيف أو ركوب الدراجات الهوائية بوتيرة منتظمة أو السباحة أو غيرها من أنشطة اللياقة البدنية (لا تشمل المشي).

<u>فكر فقط في الاتي.</u> *الأنشطة البدنية التي قمت بها لمدة 10 دقائق على الأقل.*	*أيام: .....*	*ولا يوم*	*لا أعلم*	*P4*
كم من الوقت تقضيه عادة في القيام بأنشطة معتدلة في أحد تلك الأيام؟	*ساعات: .....*	*دقائق: .....*	*لا أعلم*	***P5***

السؤال الرابع: خلال آخر 7 أيام ، كم عدد الأيام التي مارست فيها نشاطًا بدنيًا قويًا ، مثل: أعمال البناء الثقيلة أو رفع الأحمال الثقيلة أو الركض أو ركوب الدراجات الهوائية السريعة

<u>فكر فقط في الاتي.</u> *الأنشطة البدنية التي قمت بها لمدة 10 دقائق على الأقل.*	*أيام: .....*	*ولا يوم*	*لا أعلم*	*P6*
ما مقدار الوقت الذي تقضيه عادة في ممارسة الأنشطة البدنية القوية في أحد تلك الأيام؟	*ساعات: .....*	*دقائق: .....*	*لا أعلم*	***P7***

Male participant

إستبيان النشاط البدني القصير:

سوف أقوم بالسؤال عن الوقت الذي تقضيه في القيام بأنواع مختلفة من النشاط البدني في أسبوع نموذجي.

السؤال الأول: هو الوقت الذي قضيته في الجلوس خلال آخر 7 أيام ، ويشمل الوقت الذي قضيته في العمل ، في المنزل ، أثناء القيام بدورة ، وأثناء وقت الفراغ. قد يشمل ذلك الوقت الذي تقضيه في الجلوس على مكتب ، زيارة صديق ، القراءة أو الجلوس أو الاستلقاء لمشاهدة التلفزيون.

خلال آخر 7 أيام ، كم من الوقت قضيته جالسًا خلال اليوم؟	*ساعات: .....*	*دقائق: .....*	*لا أعلم*	*P1*

السؤال الثاني: هو الوقت الذي قضيته في المشي في آخر 7 أيام ، ويشمل ذلك في العمل والمنزل ، والمشي للتوجه من مكان إلى مكان وأي نوع اخر من المشي الذي قد تفعله فقط لممارسة الرياضة أو الترفيه.

خلال آخر 7 أيام كم عدد الأيام التي سرت فيها لمدة 10 دقائق على الأقل في المرة الواحدة؟	*أيام: .....*	*ولا يوم*	*لا أعلم*	*P2*
كم من الوقت قضيت عادة في المشي في أحد تلك الأيام؟	ساعات:	دقائق:	لا أعلم	P3

السؤال الثالث: خلال الأيام الأخيرة ، كم عدد الأيام التي مارست فيها نشاطًا بدنيًا معتدلًا مثل البستنة أو التنظيف أو ركوب الدراجات الهوائية بوتيرة منتظمة أو السباحة أو غيرها من أنشطة اللياقة البدنية (لا تشمل المشي).

<u>فكر فقط في الاتي.</u> *الأنشطة البدنية التي قمت بها لمدة 10 دقائق على الأقل.*	*أيام: .....*	*ولا يوم*	*لا أعلم*	*P4*
كم من الوقت تقضيه عادة في القيام بأنشطة معتدلة في أحد تلك الأيام؟	ساعات:	دقائق:	لا أعلم	P5

السؤال الرابع: خلال آخر 7 أيام ، كم عدد الأيام التي مارست فيها نشاطًا بدنيًا قويًا ، مثل: أعمال البناء الثقيلة أو رفع الأحمال الثقيلة أو الركض أو ركوب الدراجات الهوائية السريعة

<u>فكر فقط في الاتي.</u> *الأنشطة البدنية التي قمت بها لمدة 10 دقائق على الأقل.*	*أيام: .....*	*ولا يوم*	*لا أعلم*	*P6*
ما مقدار الوقت الذي تقضيه عادة في ممارسة الأنشطة البدنية القوية في أحد تلك الأيام؟	ساعات:	دقائق:	لا أعلم	P7

مقياس الإجهاد المدرك:

	أبدا	على الاغلب لا	بعض الأحيان	في كثير من الأحيان	غالبا
1. في الشهر الماضي ، كم مرة شعرت بالضيق بسبب شيء حدث بشكل غير متوقع؟	☐	☐	☐	☐	☐
2. في الشهر الماضي ، كم مرة شعرت أنك غير قادر على التحكم في الأشياء المهمة في حياتك؟	☐	☐	☐	☐	☐
3. في الشهر الماضي ، كم مرة شعرت بالتوتر و "الإجهاد"؟	☐	☐	☐	☐	☐
4. في الشهر الماضي ، كم عدد المرات التي تعاملت فيها بنجاح مع المشاكل اليومية والإزعاجات؟	☐	☐	☐	☐	☐
5. في الشهر الماضي ، كم عدد المرات التي شعرت فيها أنك تعاملت بفعالية مع التغييرات المهمة التي حدثت في حياتك؟	☐	☐	☐	☐	☐
6. في الشهر الماضي ، كم مرة شعرت بالثقة حول قدرتك على التعامل مع مشاكلك الشخصية؟	☐	☐	☐	☐	☐
7. في الشهر الماضي ، كم مرة شعرت أن الأمور تسير في طريقك؟	☐	☐	☐	☐	☐
8. في الشهر الماضي ، كم مرة وجدت أنك لا تستطيع التعامل مع كل الأشياء التي كان عليك القيام بها؟	☐	☐	☐	☐	☐
9. في الشهر الماضي ، كم مرة تمكنت من التحكم في التوتر في حياتك؟	☐	☐	☐	☐	☐
10. في الشهر الماضي ، كم مرة شعرت أنك تتصدر الأمور؟	☐	☐	☐	☐	☐
11. في الشهر الماضي ، كم مرة كنت غاضبًا بسبب الأشياء التي حدثت والتي كانت خارجة عن إرادتك؟	☐	☐	☐	☐	☐
12. في الشهر الماضي ، كم مرة وجدت نفسك تفكر في الأشياء التي يجب عليك إنجازها؟	☐	☐	☐	☐	☐
13. في الشهر الماضي ، كم مرة تمكنت من التحكم في الطريقة التي قضيت بها وقتك؟	☐	☐	☐	☐	☐
14. في الشهر الماضي ، كم عدد المرات التي شعرت فيها أن الصعوبات تتراكم لدرجة أنك لا تستطيع التغلب عليها؟	☐	☐	☐	☐	☐

Annex (7): List of experts who validated the questionnaire

1	Professor Dr. Yehia Abed	Al-Quds University
2	Dr. Bassam Abu Hamad	Al-Quds University
3	Dr. Khitam Abu Hamad	Al-Quds University
4	Dr. Abd Razeq Kurd	Emirates Helal Hospital
5	Dr. Walid Abu Hatab	Naser Hospital
6	Dr. Tharwat Y. Alhelou	Alhelou International Hospital
7	Dr. Jadallah Ukasha	UNRWA
8	Dr. Ahmad El Shaer	Islamic University
9	Dr. Arifa Al-Namri	Islamic University
10	Dr. Ashraf Al-Jidi	Islamic University

Annex (8): Helsinki Committee Approval

المجلس الفلسطيني للبحث الصحي

Palestinian Health Research Council

تعزيز النظام الصحي الفلسطيني من خلال مأسسة استخدام المعلومات البحثية في صنع القرار

Developing the Palestinian health system through institutionalizing the use of information in decision making

Helsinki Committee

For Ethical Approval

Date: 2019/04/09

Number: PHRC/HC/548/19

Name: Amal M. H. Dhair

الاسم:

We would like to inform you that the committee had discussed the proposal of your study about:

نفيدكم علماً بأن اللجنة قد ناقشت مقترح دراستكم حول:

Risk Factors of Primary Infertility in Gaza: Case Control Study

The committee has decided to approve the above mentioned research. Approval number PHRC/HC/548/19 in its meeting on 2019/04/09

و قد قررت الموافقة على البحث المذكور عاليه بالرقم والتاريخ المذكوران عاليه

Signature

Member

Dr. Yehia Abed

Member

Chairman

Dr. Assad Yousef 2019

Genral Conditions:-

1. Valid for 2 years from the date of approval.
2. It is necessary to notify the committee of any change in the approved study protocol.
3. The committee appreciates receiving a copy of your final research when completed.

Specific Conditions:-

9/4/2019

E-Mail:pal.phrc@gmail.com

Gaza - Palestine غزة - فلسطين

شارع النصر - مفترق العيون

Annex (9): Report to facilitate a researcher mission - MoH

State of Palestine
Ministry of health

دولة فلسطين
وزارة الصحة

التاريخ:01/07/2019
رقم المراسلة 336195

السيد : رامي عيد سليمان العبادله المحترم

مدير عام بالوزارة /الإدارة العامة لتنمية القوى البشرية ـ /وزارة الصحة

السلام عليكم ,,,

الموضوع/ تسهيل مهمة الباحث// د. أمل ضهير

التفاصيل //
بخصوص الموضوع أعلاه، يرجي تسهيل مهمة الباحث/ د. أمل محمد ضهير
ـ الطبيبة في وكالة الغوث مركز صحي رفح ـ الملتحق ببرنامج ماجستير الصحة العامة – مسار الإدارة الصحية – جامعة القدس أبوديس في إجراء بحث بعنوان:ـ
"Risk Factors of Primary Infertility in Gaza: Case Control Study"
حيث الباحثة بحاجة لتعبئة استبانة واخذ قياسات الطول والوزن من عدد من النساء المتزوجات والغير منجبات للأطفال من المترددات على مراكز الاخصاب في قطاع غزة وعينه ضابطة من النساء المترددات على عيادات النساء للحصول على وسائل منع الحمل في مراكز الرعاية الأولية المستوى الخامس.
نأمل توجيهاتكم لذوي الاختصاص بضرورة الحصول على الموافقة المستنيرة من النساء اللاتي هن على استعداد للمشاركة في الدراسة ومن ثم تمكين الباحثة من التواصل معهن ، بما لا يتعارض مع مصلحة العمل وضمن أخلاقيات البحث العلمي، ودون تحمل الوزارة أي أعباء أو مسئولية.
وتفضلوا بقبول التحية والتقدير،،
ملاحظة / تسهيل المهمة الخاص بالدراسة أعلاه صالح لمدة 6 شهر من تاريخه.

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Arabic Abstract

العنوان: عوامل خطر العقم الأولي في قطاع غزة

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الملخص:

كثير من الأزواج في جميع أنحاء العالم يكافحون الشعور القاتم بعدم الإنجاب. إلى جانب الافتقار إلى إمكانات الأبوة، فقد يعانون من الاستبعاد الاجتماعي والمجتمعي بطرق نسبية ومختلفة. من هنا تكمن أهمية تحديد عوامل الخطر الرئيسية المرتبطة بالعقم الأولي في قطاع غزة والبحث عن الخطوات التي من شأنها تعزيز خطط الإدارة أو حتى منع حدوث مثل هذه الحالة من أجل تحسين صحة الأزواج ونوعية حياتهم.

هذه الدراسة عبارة عن دراسة مراقبة تحليلية، تضم 320 عينة سكانية. تم اختيار الحالات (160) على أساس كونها متزوجة وغير قادرة على الحمل والإنجاب لمد سنة واحدة على الأقل، دون استخدام وسائل منع الحمل و من النساء اللواتي تتراوح أعمارهم بين 19 و 49 سنة، في حين أن الضوابط (160) كانت من النساء اللواتي سبق لهن الحمل والإنجاب و اللاتي تتطابق مكان إقامتهن مع مكان سكن الحالات. تم جمع البيانات باستخدام استبيان من خلال جامعي البيانات المدربين تدريباً جيداً وتم تحليله باستخدام طرق وصفية واستنتاجية و لوجستية مختلفة.

لضمان التوزيع الطبيعي قدر الإمكان، تم تحديد عدد الحالات المرجو إدراجها في الدراسة بما يتناسب مع انتشار العقم الأولي في كل محافظة (20.6٪ شمال غزة، 34.4٪ غزة، 12.5٪ وسط ، 20٪ خان يونس و 12.5٪ رفح). وبالتالي، أظهرت النتائج أن عمر الزواج الذي يتجاوز 29 عامًا لدى السيدات كان يحمل خطرًا بارزًا للإصابة بالعقم الأولي (*OR:8.3, 95%CI, 2.8-24.3*)، في حين كان فارق السن أكثر من 10 سنوات بين الأزواج محفوفًا بالمخاطر مرتين (*p=0.02*) بالمقارنة بالأزواج ذوي فارق السن أقل من 10 سنوات. أضف الى ذالك، أن العيش في أسر ممتدة بعد الزواج بالإضافة لكونهم لاجئين يعرض الأزواج لخطر العقم، وكذالك الرجال المولودون كالإبن السابع أو أكثر يتوقعون نفس الخطر (*OR:1.9,1.6,2.3*،على التوالي). كما أن نوع مجال عمل الإناث، وتوقيت فترات العمل، بالإضافة لكيفية إدراكهن للإجهاد والضغط المصاحب للعمل، يمثلان خطراً كبيراً على حالة الخصوبة لديهن. علاوة على ذلك، أظهرت النتائج أن الإناث والذكور الذين اعتادوا الشرب من مياه مصدرها البائعين المتجولين قبل الزواج (*p<0.001* لكليهما) والأزواج الذين يستخدمون الحفرالمسامية كنظام صرف صحي (*p=0.02*) أكثر عرضة لخطر العقم. ومن العوامل البيئية الأخرى التي يبدو أن لها صلة كبيرة بالعقم عدم ممارسة تدابير السلامة أثناء استخدام مبيدات الآفات الزراعية، وتكرار استخدامها، والعمل البدني الثقيل عند الإناث والتعرض للحرارة المفرطة أو الضوضاء أو الغبار أو الغازات عند الذكور (*OR:11.9, 3.6, 3.6, 1.6*على التوالي). في الوقت نفسه، كان الأزواج الذين يعانون من العقم والذين اعتادوا العيش في منزل مُهدم جزئيًا أو أولئك الذين اعتادوا على التعامل مع بقايا ما بعد الحرب أو حتى أولئك الذين تعرضوا لمياه الشرب القريبة للقصف، أكثر بكثير من نظرائهم (*p=0.03,0.006,0.033*على التوالي).

كان عمر سن الطمث أقل من 14 عامًا لدى السيدات (OR:1.8) وإختلالات الدورة الشهرية (OR:5.7) من بين عوامل الخطر المرتبطة بالعقم، على الرغم من أن الحصول على المشورة الطبية للالتهابات البولية و التناسلية كان مرتفعًا نسبيًا (92.4٪). ومع ذلك، فإن الأزواج الذين يعانون من العقم والذين لم يلتحقوا بأي نظام تأمين طبي هم أكثر من الأزواج الخصيبين ($p<0.001$). بالإضافة إلى ذلك، كانت النساء المصابات بالعقم اللاتي يعانين من متلازمة تكيسات المبايض، قلة الطمث، فرط بروﻻكتين الدم، نمو الشعر المفرط أو الأورام الليفية الرحمية أكثر عرضة للإصابة بالعقم من غيرهن ($OR:9.4,9.3,4.6,9.6$على التوالي). فكلما زادت مدة متلازمة تكيسات المبايض من غير علاج، كلما كان احتمال الإصابة بالعقم أكبر. علاوة على ذلك، يبدو أن استخدام موانع الحمل المركبة له تأثير وقائي، في حين أن الاستخدام المستمر لمضادات الالتهاب غير الستيروئيدية كان له علاقة كبيرة مع العقم ($OR:0.3,7.9$)، حيث أن متوسط الأستهلاك الشهري كان أعلى لدي الإناث المصابات بالعقم من نظرائهم (8.06 مقابل 5.25 على التوالي). أضف إلى ذالك، تعرض الرجال لأمراض معينة، كدوالي الخصية ($p<0.001$) والإصابة المتكررة بالإلتهابات البولية و التناسلية أكثر من خمس مرات في مدة سنتين على الأقل ($p=0.001$)، أظهرت وجود صلة كبيرة بينها وبين الإصابة بالعقم. أيضاً كان التاريخ العائلي للعقم في كل من الذكور والإناث، والعقم والدوالي الخصية بين الذكور يوضح وجود علاقة إيجابية مع وجود لعقم بين الأزواج.

أظهرت متغيرات نمط الحياة أن مدة تدخين التبغ و عدد المرات التي يقوم بها الرجال بالتدخين خلال اليوم الواحد، إما الشيشة أو السجائر، تشكل خطراً كبيراً على حالة الخصوبة لديهم، وأن الإناث المعرضات للتدخين السلبي يحملن نفس الخطر ($p=0.007$). من ناحية أخرى، يبدو أن الأزواج الخصبين يستهلكون المزيد من الخضار والفواكه أكثر من نظائرهم المصابين بالعقم، من حيث الحصص / اليوم ($p=0.004$ للإناث، $p=0.001$ للذكور) وعدد المرات/ الأسبوع ($p=0.001$ لكليهما). كما أن تناول السكر والبطاطا المقلية والصودا والعصائر المعلبة كوجبات خفيفة أومشروبات بطريقة منتظمة يعرض الإناث لخطر أكبر. وتكمن نفس الخطورة لدى الأزواج المعتادين على قضاء فترات طويلة بالجلوس بشكل يومي ($t=3.79, p<0.001$).

نجحت هذه الدراسة في تحديد جزء من عوامل الخطر المرتبطة بالعقم الأولي في قطاع غزة بما في ذلك تلك المتعلقة بالعوامل الديموغرافية والاجتماعية والاقتصادية والبيئية والطبية ومتغيرات نمط الحياة المختلفة. بناءً على ذلك، تم استنتاج أن هناك حاجة إلى بذل المزيد من الجهود لتحسين نوعية المياه والصرف الصحي، وتطوير الصحة المهنية، وتشجيع وتعزيز تشخيص العقم وإدارته في جدول أعمال الرعاية الصحية الإنجابية وتعزيز مختلف ممارسات نمط الحياة بين سكان قطاع غزة.