

**Deanship of Graduate Studies
Al-Quds University**



**Risk Factors of Primary Infertility in Gaza: Case
Control Study**

Amal Mohammed Dhair

MPH Thesis

Jerusalem-Palestine

1441-2020

Risk Factors of Primary Infertility in Gaza: Case Control Study

Prepared by:

Amal Mohammed Dhair

M.B., B.CH., in Medicine from Misr University for
Science & Technology

Supervisor: **Professor Doctor Yehia Abed**

MD, MPH, DrPH – Faculty of Public Health

A Thesis Submitted in Partial Fulfillment of Requirements
for the Degree of Master of Public Health
Al-Quds University

1441/2020

Al-Quds University
Deanship of Graduate Studies
School of Public Health



Thesis Approval

Risk Factors of Primary Infertility in Gaza: Case Control Study

Prepared By: Amal Mohammed Dhair

Registration No.: 21711111

Supervisor: Professor Dr. Yehia A. Abed

Master thesis submitted and accepted. Date: / /

The names and signatures of the examining committee members are as follows:

1. Head of committee: Professor Dr. Yehia A. Abed
2. Internal examiner: Dr. Maha Nubani Husseini
3. External examiner: Dr. Abdul-Razak El-Kurd

Signature.....

Signature.....

Signature.....

Three handwritten signatures in blue ink, corresponding to the three members of the examining committee listed on the left.

Jerusalem – Palestine

1441 / 2020

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:

Dr. Amal Mohammed Dhair

Date: / /

Acknowledgement

The willing of Allah is beyond everything and everyone.

I would like to extend my deepest appreciation and gratitude to Professor Dr. Yehia Abed for supervising and guiding me through this work. Dr. Yehia is a dignified, honourable and respectful teacher and person, who provided me, as many others, insight and expertise in my academic and professional life. Dr. Yehia simply taught me to be a researcher.

Special gratitude and respect are conveyed to Dr. Bassam Abu Hamad and Dr. Khitam Abu Hamad for the tremendous support and efforts provided throughout the past couple of years. They demonstrate enthusiastic model as researchers and provided us with insights of how comparative literature, research and academia are engaged with our professional attitude.

I would also like to express my sincere thankfulness to all couples who sacrificed their time and effort in enriching this thesis with their valuable information, also gratitude is extended to the data collectors for their immense efforts and admired talent in the research field.

I am also grateful to all head managers of IVF centers for providing me the opportunity to get access to the required concerned subjects and eventually contribute greatly to the accomplishment of this work.

Last but not least, sincere thanks are conveyed to all experts for sharing their time and knowledge in validating the thesis questionnaire, although any errors which may be detected are my own and should not be related to any of the esteemed persons.

Signature:

Dr. Amal Mohammed Dhair

Date: / /

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 7th 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.

Table of Contents

Dedication.....	
Declaration.....	i
Acknowledgement.....	ii
Abstract.....	iii
Table of Contents	iv
List of Tables.....	vii
List of Figures.....	viii
List of Annexes.....	ix
Acronyms and Abbreviations	x

Chapter One: Introduction..... 1

1.1 Background.....	1
1.2 Problem statement	2
1.3 Justification.....	3
1.4 Study objectives.....	4
1.5 Research questions.....	5
1.6 Context of the study.....	5
1.6.1 Demographic characteristics of Gaza Strip:	5
1.6.2 Health care services:	7
1.6.3 Maternal and reproductive health:	9
1.6.4 Socioeconomic situation:.....	10
1.7 Operational definitions	11
1.7.1 Clinical infertility:	11
1.7.2 Primary infertility:	12
1.7.3 Secondary infertility:	12
1.7.4 Reproductive health:.....	12

Chapter Two: Literature Review..... 13

2.1 Conceptual Framework	13
2.1.1 Socio-Demographic factors:.....	13
2.1.2 Socio-Economic factors:.....	13
2.1.3 Environmental factors:.....	14
2.1.4 Lifestyle:.....	14
2.1.5 Medical causes:.....	14
2.1.5.1 Male factors	14
2.1.5.2 Female factors.....	14
2.2 Literature Review	16
2.2.1 Definition and terminology:	16
2.2.2 Epidemiology of infertility:.....	18
2.2.3 Consanguineous marriage:.....	20
2.2.4 Female medical factors:.....	21
2.2.4.1 Tubal factors	21
2.2.4.2 Ovarian factors.....	23
2.2.4.3 Uterine factors.....	25
2.2.4.4 Hormonal factors	26
2.2.5 Male medical factors:	29
2.2.5.1 Varicocele	29

2.2.5.2 Azoospermia	30
2.2.5.3 Immunological causes.....	31
2.2.6 Environmental conditions:.....	32
2.2.6.1 Pesticides.....	32
2.2.6.2 Stress and war	33
2.2.7 Lifestyle:	34
2.2.7.1 Smoking	34
2.2.7.2 Obesity	35
2.2.7.3 Physical activity	36
Chapter Three: Methodology	37
3.1 Study design.....	37
3.2 Study population	37
3.3 Study setting	38
3.4 Eligibility criteria.....	38
3.4.1 Eligibility criteria of cases:.....	38
3.4.2 Eligibility criteria of control group:.....	38
3.5 Sampling and sampling process.....	39
3.6 Study instruments	42
3.7 Ethical and administrative considerations	44
3.8 Study period.....	44
3.9 Pilot study	44
3.10 Data collection	45
3.11 Scientific rigor	45
3.12 Data entry AND analysis.....	46
3.13 Limitation OF the study.....	47
Chapter Four: Findings and discussion	48
4.1 Demographic situation.....	48
4.1.1 Geographical location:.....	50
4.1.2 Age pattern of infertility:.....	52
4.1.3 Marital age:.....	54
4.1.4 Refugee status and camps:.....	55
4.1.5 Family type before and after marriage:	56
4.1.6 Household size: 57	
4.1.7 Birth order in original family: 57	
4.1.8 Relationship between infertility and various demographic variables:.....	58
4.2 Socioeconomic variabilities.....	59
4.2.1 Education level and household income:	59
4.2.2 Employment:.....	63
4.2.2.1 Work field	64
4.2.2.2 Work shift pattern	66
4.2.2.3 Working hours	67
4.2.3 Consanguinity:.....	68
4.2.4 Relationship between infertility and various socioeconomic variables:	69
4.3 Environmental factors.....	70
4.3.1 Living condition:	70
4.3.2 Agricultural pesticides and herbicides:.....	75
4.3.3 Work environment:.....	76

4.3.4	Gaza as a conflict zone:	78
4.3.4.1	Exposure of female participants.....	79
4.3.4.2	Exposure of male participants.....	80
4.3.4.3	Exposure of couples	81
4.3.5	Relationship between infertility and various environmental predictors:	82
4.4	Medical factors	83
4.4.1	Causes of infertility:	83
4.4.2	Access to health services:	85
4.4.3	Female factors:.....	88
4.4.3.1	Menstrual history	88
4.4.3.2	Medical and gynaecological history	90
4.4.3.3	Family history	96
4.4.3.4	Perceived stress and infertility	97
4.4.4	Male factors:	98
4.4.4.1	Medical exposures	98
4.4.4.2	Family history	101
4.4.5	Relationship between infertility and various medical predictors:	103
4.5	Lifestyle and infertility	104
4.5.1	Smoking and infertility:.....	104
4.5.2	Diet behavior:	108
4.5.3	Physical activity:.....	115
4.5.4	BMI and infertility:.....	119
4.5.5	Relationship between infertility and various lifestyle variables:.....	121
Chapter Five: Conclusion and recommendations		123
5.1	Conclusion	123
5.2	Recommendations.....	128
5.2.1	General recommendations:	128
5.2.2	Recommendations for new areas of research:	130
References.....		131
Annexes.....		159
Arabic Abstract		194

List of Tables

Table (4.1): Distribution of study population by demographic characteristics (N=320) ...	49
Table (4.2): Predictors of primary infertility among demographic variables using binary logistic regression	58
Table (4.3): Distribution of study population in relation to education and household income and expenditure; socioeconomic variables part 1; (N=320).....	60
Table (4.4): Distribution of study population in relation to employment status; socioeconomic variables part 2; (N=320)	64
Table (4.5): Distribution of study population in relation to consanguinity; socioeconomic variables part 3; (N=320)	68
Table (4.6): Predictors of primary infertility among different independent socioeconomic variables using binary logistic regression	69
Table (4.7): Distribution of study population by various living condition variables	71
Table (4.8): Distribution of study population according to agricultural pesticides & herbicides utilization	75
Table (4.9): Distribution of study population in relation to working environment variables	77
Table (4.10): Distribution of study population by war exposure variables - Females	80
Table (4.11): Distribution of study population by war exposure variables – Males	81
Table (4.12): Distribution of study population by war exposure variables – Couples.....	81
Table (4.13): Predictors of primary infertility among different independent environmental variables by using binary logistic regression	82
Table (4.14): Distribution of study population by access to health care	85
Table (4.15): Distribution of study population by menstrual history	89
Table (4.16): Distribution of study population by medical and gynaecological history	91
Table (4.17): Distribution of study population by family history information.....	96
Table (4.18): Distribution of study population according to Perceived Stress Scale results	97
Table (4.19): Distribution of study population by male medical exposures.....	98
Table (4.20): Distribution of study population by family history of certain diseases	101
Table (4.21): Predictors of primary infertility among different independent medical variables by using binary logistic regression	103
Table (4.22): Distribution of study population by various smoking related variables	105
Table (4.23): Distribution of study population by variables related to diet behaviour.....	109
Table (4.24): Analysis of fruits and vegetables servings.....	110
Table (4.25): Distribution of study population by salt intake behaviour.....	114
Table (4.26): Distribution of study population by Physical Activity categorical variables	116
Table (4.27): Distribution of study population by Physical Activity continuous variables	118
Table (4.28): Distribution of study population by Body Mass Index (BMI).....	120
Table (4.29): Predictors of primary infertility among different independent lifestyle variables by using binary logistic regression	121

List of Figures

Figure (2.1): Conceptual Framework for risk factors of primary infertility	15
Figure (3.1): Sampling process	41
Figure (4.1): Demographic distribution of study population per governorate; Cases	50
Figure (4.2): Demographic distribution of study population per geographical area	51
Figure (4.3): Relationship between husband's age and the spousal age gap (cases).....	53
Figure (4.4): Marital age distribution according to governorate – N=320	54
Figure (4.5): Major groups of monthly household expenditure – cases vs controls	62
Figure (4.6): Main source of drinking water before marriage – Female participants.....	74
Figure (4.7): Main source of drinking water before marriage – Male participants.....	74
Figure (4.8): Distribution of female participants by infertility status and war variables ...	79
Figure (4.9): Female causes of primary infertility	84
Figure (4.10): Male causes of primary infertility	85
Figure (4.11): Health insurance ownership – cases vs controls	87
Figure (4.12): Causes of irregular menses – cases vs controls	90
Figure (4.13): Number of NSAID tablets consumed per month – cases vs controls	94
Figure (4.14): Most frequent component of main meal, cases vs controls	112

List of Annexes

Annex (1): Palestine map.....	159
Annex (2): Population in Palestine by governorate and sex - 2017.....	160
Annex (3): Calculation of sample size.....	161
Annex (4): Timeline table.....	162
Annex (5): Questionnaire - English	163
Annex (6): Questionnaire - Arabic	177
Annex (7): List of experts who validated the questionnaire	191
Annex (8): Helsinki Committee Approval.....	192
Annex (9): Report to facilitate a researcher mission - MoH.....	193

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