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Thromboprophylaxis Use among Pregnant Women in Gaza Governorates

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Thromboprophylaxis Use among Pregnant Women in Gaza Governorates

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بسم الله الرّحْمَنِ الرّحِيم

" رَبِّ أَوْزِعْنِي أَنْ أَشْكُرَ نِعْمَتَكَ الَّتِي أَنْعَمْتَ عَلَيَّ وَعَلَى وَالِدَيَّ وَأَنْ أَعْمَلَ صَالِحًا تَرْضَاهُ وَأَصْلِحْ لِي فِي ذُرِّيَّتِي إِنِّي تُبْتُ إِلَيْكَ وَإِنِّي مِنَ الْمُسْلِمِينَ "

صدق الله العظيم

سورة الأحقاف، الآية: ١٥

Dedication

To
My lovely Father

To the greatest man I have in my life, for earing an honest living for us and for supporting and encouraging me to believe in myself.

My lovely Mother

To the biggest heart with the most loving care, who sacrificed a lot for me to become what I am now, my mother.

My Husband

The wonderful person who supported me through each step of the way and for being for me the greatest source of inspiration, my beloved Husband " Imad".

My Daughters and son

To the light of my eyes... my kids "Ahmed, Shada & Sama"

To all those who encouraged, supported, and helped me all the way
I dedicate this research for all of them I would like to convey my deep appreciations to all those who contributed to the completion of this thesis.

Maha Samih Safi

Declaration

I certify that this thesis submitted for the degree of Master, is the result of my own research, except where otherwise acknowledged, and this study (or any part of the same) has not been submitted for a higher degree to any other university or institution.

Signed:

Maha Samih Safi

Date:28/4/2018

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Maha safi

Thromboprophylaxis Use among Pregnant Women in Gaza Governorates

Abstract

Risky pregnancy and bad pregnancy outcomes are increasing in the last years due to accumulated risk factors so the demand of thromboprophylaxis use is increasing to improve pregnancy comes.

Aim: *This study is aimed to determine the main determinants of thromboprophylaxis use identify the possible effects of it on pregnancy outcomes and discuss the different management practices that contribute to the need of thromboprophylaxis among refugee risky pregnant women attended UNRWA health care services in Gaza governorates in order to explore possibilities for improving pregnancy outcomes.*

Method :*An analytical comparative triangulated study has been performed between April 2017 and completed by July 2017, 440 mothers who attending united nations relief and work agency for Palestinian refugees in the near east health centers which divided in two groups (with and without thromboprophylaxis use in last pregnancy), consisted of 220 mothers for each , stratified sampling was used collected through face interviewed questionnaire along with medical records revision and genetic study review . Moreover, in-depth interview with concerned health care providers was done. Statistical analysis was performed using chi-square, odds ratio, (P-value≤0.05). Helsinki and managerial approval were granted and consent form was obtained from participants.*

Findings: *Mothers with thromboprophylaxis use had statically differences (P≤0.05) in maternal age > 30 years (36.6% vs 15.9%) , history of non communicable disease(P=0.000) ,history of surgical operations (p=0.000) , Gravida two and more (P-value=0.000), para two and more (P- value 0.000) ,History of dead children(P-value=0.000), history of SB(P-value=0.000), history of infertility (P-value=0.000), history of early pregnancy loss (P-value=0.000) and history of pregnancy complications (P-value=0.000) , thromboprophylaxis use has a role of improving pregnancy outcomes(78.2% vs 41.9%), majority of cases had high frequency of genetic abnormdities which is abse of thromboprophylaxis use.despite of that majority of cases had access to heparin therby from private sectors with high cost(82.2%).*

Conclusion: *thromboprophylaxis use in pregnancy is a new model in gynecology and obstetrics, there is a significant risk among these women and thromboprophylaxis is improving their pregnancy outcomes compared to women without thromboprophylaxis use. Standardization of diagnosis and harmonization of national guidelines are recommended to improve the use of thromboprophylaxis among pregnant women.*

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List of abbreviations

ACL	Anti Cardiolipin Antibodies
ACOG	American College of Obstetrics and Gynecology
APCR	Anti-protein C Resistance
APH	Anti-Patum Haemorrhage
ACEDI	Angiotensine Converting Enzyem Inhibitor
APL	Antiphospholipid Antibody
CVD	Cardiovascular disease
DMPAD	Depomedroxy Proyesterone Acetate Depot
DVT	Deep Venous Thrombosis
EPCOT	European Prospective Cohort on Thrombophilia
FFHO	Family Field Health Officer
HTN	Hypertension
GG	Gaza Governorates
GDM	Gestational Diabettis Mellitus
SCBU	Special Care Baby Unite
IUFD	Intra-Uterine Fetal Death
IUI	Intra uterine insemination

Chapter 1: Introduction

1.1 Background

Pregnancy and childbirth is an existing event in the women's and family life as to be pregnant is to be vitally alive. At the same time is a big stress of life. Pregnancy process large demands and challenges the women's physiology. Pregnancy is a physiology, not a pathology or diseases, many physiological changes had occurred to an adapt new changes in the pregnant women, This Period of life is a joyful anticipation time but it is carrying many health hazards association that may affect maternal and fetal life.

At the same time is a big stress of life, Pregnancy process large demands and challenges the women's physiology. Different physiological changes occur during the process of pregnancy, which affects all of the woman systems; these include metabolic adaptations and hormonal changes. However, we are interested in those changes that affect the coagulation factors. It is due to a secondary increase in the concentrations of pre-coagulant factor, a reduction of the naturally occurring anticoagulant proteins and increase in fibrinogen that characterized pregnancy with hypercoagulability (Christopher et al, 1998).
Pregnant Women are at an increased risk of both venous and arterial thromboembolism during pregnancy, compared to women who are not pregnant, the risk of arterial thromboembolism (strokes and heart attacks) is increasing 3to 4 folds and the risk of Venous Thromboembolism (VTE) is increasing 4to 5fold,3 folds will increase in the Postpartum, the risk is even higher (James et al, 2005),but the venous thromboembolism and pregnancy complications are rare in healthy pregnant women as natural anticoagulant slow up excessive fibrin formation and finally the fibrin- lytic system gets rid of the formed fibrin Thrombophilia, either acquired or hereditary, may shift the hemostatic balance towards enhanced coagulation thrombophilia can be found in as many as 50% of patients with VTE during pregnancy (Greer, 2003). Thrombophilia can be found up to 40% worldwide in women who had bad pregnancy outcomes (Bogdova Markovo, 2019) Thrombophilia risk factors are also frequent in women with other vascular placental pathologies, such as preeclampsia, intrauterine growth retardation, placental abruption, and late fetal loss (Brenner, 2003). A successful pregnancy is highly dependent on the establishment and maintenance of an adequate placental circulation.It has been postulated that the abnormalities of placental vasculature leading to inadequate feto-maternal

circulation are responsible for some poor pregnancy outcomes, which that is triggered by thrombophilia events, like abortion (either during the first or second trimester), intrauterine fetal death (IUFD), intra uterine growth restriction (IUGR), stillbirth(SB), preeclampsia (PET), abruption placenta (Said, Joanne M. MBBS, 2013) .

The prevalence of thrombophilia among pregnant women worldwide is not known Bates and colleagues (2008) reported that thrombophilia accounts for 8%-15% of whites. Many studies showed that the prevalence of different genetic thrombophilia occurred more frequently with a history of obstetric complications, factor V Leiden, prothrombin and MHFR mutations occur up to (24%,10%,24%) respectively(Australian assessment Report, 2002).

1.2 Research problem

Pregnancy is a unique period in every woman's life, it is a natural goal for every family to get their child, it is characterized by different complicated physiological changes as the woman undergoes many physiological changes, so, pregnancy poses large demands and challenges the woman's physiology, in some women, the adaptation to these changes is insufficient so the pregnancy complication can occur. According to that, one of the most important and the hottest topic among pregnant women is the risk of thrombosis and the use of thromboprophylaxis. Risky pregnancy in Gaza is with many complicated health issues, in the last years the prevalence of risk pregnancy, bad pregnancy outcomes and complications are increasing dramatically, due to socioeconomic deterioration. Thrombophilia and thromboprophylaxis use is a new fashion and a recent Phenomenon among risk pregnancy and the demand for thromboprophylaxis increases in the last years, this study is the first study in Palestine will conduct about thromboprophylaxis use in pregnancy as it will measure the magnitude of the problem among risky pregnant women, It will discuss the differently associated determinants with this phenomena, different pregnancy outcomes and different management practices of thromboprophylaxis use and so will help us to answer the main question, thromboprophylaxis use is a new fashion or a real risk .

1.3 Justification of Study

According to the Center for Disease Control’s National Pregnancy Registry Surveillance System, between 1991 and 1999, pulmonary embolism (PE) was the first cause of maternal

mortality. Pregnancy is a state that conveys 4-5 times the risk of venous thromboembolism (VTE). The prevalence of VTE in pregnancy is 0.8-2.0 per 1,000 pregnancies and accounts for 1.1 deaths per 100,000 pregnancies. Approximately 80% of embolic events in pregnancy are venous (James et al, 2006).

Pregnancy failure is extremely distressing for couples who desire to have children. Pre-eclampsia and HELLP syndrome (hemolysis, elevated liver enzymes, low platelet counts) are leading causes of maternal and perinatal mortality as well as extensive morbidity, which that has an association with thrombophilia in pregnancy. According to American and Society collage, Thrombophilia is associated with 30 % of pregnancy complications.
Palestine is with significant rate of maternal mortality rate which increases from 23,4 per 100000 to 31 per 100000 in the last 5 years , PE is one of the main causes of maternal mortality in Palestine which accounts for 29,4 % of all maternal deaths, 17,6 % of maternal deaths is related hemorrhage, 11,8 % heart diseases,11,8 % PET ,others are unknown (PHIC, MOH, 2015).

In the last years, bad pregnancy outcomes are increasing due to different health hazard and risk changes, Low birth weight accounts of 34% from total infant mortality per 1000livebirths, Neonatal mortality accounts 11.8 per 1000 live births (PHIC, MOH,2014). Spontaneous abortion increases to reach annually 2662 registered cases among refugee pregnant women (UNRWA,2014).On the other hand, risky pregnancy increases in the last 5 years in Gaza Governorates 24.1% risky pregnancy from newly registered pregnant in MOH clinics (PHIC-MOH, 2014), and 15 % high-risk pregnancy and 24.8 % are alert pregnancy from new registered pregnant women in UNRWA Health clinics (UNRWA, 2014).

Many past studies were done on PIH, GDM and its associated relations with bad pregnancy complications and outcomes, thrombophilia is a new Phenomenon among risky pregnancy which plays a significant role in pregnancy complications (Maternal and Fetal complications).

The problem of thromboprophylaixs use in pregnancy is a recent emerging problem and the demand for the uses of different anticoagulants in pregnancy increases dramatically under the role of controlling bad pregnancy outcomes and pregnancy complications, This

study is the first study in Palestine to determine a real picture of the problem, differently associated determinants, different pregnancy outcomes and different management practices.

1.4 Study Objectives

1.4.1 Aim of the study

The main aim of this study is to determine the main determinants either maternal or fetal factors, consequences, management practices that contribute to the need of thromboprophylaixs among refugee risky pregnant women in Gaza Strip, in order to explore possibilities for reducing maternal and fetal complications and controlling phenomena.

1.4.2 Specific objectives

i. To assess the current status of thromboprophylaixs use among risky pregnant women at UNRWA Health Centers in Gaza Governorate
ii. To assess the differences associated determinants of thromboprophylaxis use among risky pregnant women at UNRWA Health Centers in Gaza Governorate.
iii. To identify the maternal and fetal related problems that contribute to thromboprophylaixs use among risky pregnant women.
iv. To assess the management practices of using thromboprophylaixs among pregnant women
v. To propose and suggest recommendations that might help in enhancing proper health care services regarding risky pregnant women and the used thromboprophylaixs in pungency

1.5 Research Questions

i. What is the current status of thromboprophylaixs use among risky pregnant women at UNRWA Health Centers in Gaza Governorate?
ii. What are the epidemiological and statistical features of existing risk factors that enhancing the risk of thromboprophylaixs uses among pregnant women in the study population?
iii. What is the association between maternal age and the use of thromboprophylaxis among risky pregnant women in the study population?

iv. What is the role of family history that contributes to thromboprophylaixs uses among risky pregnant women in the study population?

v. What is the association between maternal history (Past, Current obstetric history, and preexisting medical history) with thromboprophylaixs use among risky pregnant women?

vi. How much inherited and acquired thrombophilia is affecting the use of thromboprophylaixs among risky pregnant women?

vii. How much of thromboprophylaxis use among risky pregnant women is preventing birth outcomes problems?

viii. How much of thromboprophylaixs use among risky pregnant women is preventing maternal complication?

ix. What are the different management practices of thromboprophylaixs use in risky pregnant women among health providers?

x. Is thromboprophylaixs use a fashion or a real risk among risky pregnant women?

1.6 Operational definitions

i. **Thrombophilia:** Is an abnormality of blood coagulation that increases the risk of thrombosis (blood clots in blood vessels) (Heit, 2007).

ii. **Maternal Thrombophilia**: Is a miss balance between the procoagulant physiological changes and thrombosis risk among pregnant ladies (Rosendaal, 2005).

iii. **Inherited Thrombophilia:** It refers to inborn conditions, it can be inherited from one present (Heterozygous), or the same gene for two parents (homozygous), that increase the tendency to develop thrombosis (Rosendaal, 2005).

iv. **Acquired Thrombophilia: It** refers to a group of disorders that an individual is not born with, but may develop throughout his or her life due to another illness or situation. An example of acquired thrombophilia is the development of a lupus anticoagulant or antiphospholipid antibody syndrome (Ruiz-Irastorza et al, 2010)

v. **Fetal Demise**: The National Center for Health Statistics defines fetal death as death prior to the complete expulsion or extraction from its mother of a product of human conception (MacDorman et al, 2012).

vi. **Pregnancy-induced Hypertension**: PIH is defined as hypertension (blood pressure ≥ 140/90mmHg) with or without proteinuria (≥ 300 mg/24 hours (emerging after 20 weeks gestation, but resolving up to 2-6 weeks postpartum (Mageee et al,2008)

vii. **Thrombosis:** Is the formation of a blood clot, inside a blood vessel, impaired the flow of blood through the circulatory system. When a blood vessel is injured, the body uses platelets (thrombocytes) and fibrin to form a blood clot to prevent blood loss (Furie, 2008).

viii. **Thromboembolism:** Is the combination of thrombosis and its main complication, embolism (Furie, 2008).

ix. **Thromboprophylaixs:** Any preventive measure or medication that reduces the likelihood of the formation of blood clots (ACOG, 2010).

1.7 Context of the study

1.7.1 Gaza Governorate demographic characteristics

Gaza is a small piece of land located in the southern west area of Palestine. It is divided into five governorates: North Gaza, Gaza City, Mid Zone, Khanyonis and Rafah (PCBS, 2013). Palestinian population was estimated about 4.8 million mid-year 2016, distributed as (62.2%) in the West Bank and (37.8%) in Gaza Strip, Population Density (Capita/km2) in Gaza Governorate is 5.239 annual growth rate, Mid-Year 2016 is (3.3), an average of household Size, 2015, is -5.7-(PCBS, 2016).That means Gaza is a very crowded area with crowded population, that faces many bad socio-economic due to Israel siege, The percentage of Population Less than 15 Years (42,7%). Unemployment Rate at 15 Years and over, is (41.6 %) which is nearly high in comparison with West bank 18.2%) (PCBS, 2016) .The poverty rate among Palestinian individuals was 25.8 (17.8% in the West Bank, and 38.8% in Gaza Strip). Data revealed that 12.9% of the individuals in the Palestinian Territory was suffering from deep poverty in 2010 according to consumption patterns. (7.8% in the West Bank and 21.1% in Gaza Strip) (PCBS, 2012).

1.7.2 Health Care System and health status

The health services in Palestine, and in Gaza Strip provided by the Palestinian healthcare system which consists of: (1) governmental health care system, (2) NGOs healthcare system (3) UNRWA health care system, (4) private health care system.

Health care is provided through a three-tier system, consisting of primary health care (PHC) clinics, secondary and tertiary healthcare facilities.MOH is the only health authority responsible for supervision, regulation, licensure, and control for all health services is the main healthcare provider in the governorates; it provides PHC, secondary and tertiary services for the whole population. It purchases advanced medical services through

referring patients to the neighboring countries and other private and NGO health care facilities.

UNRWA provides PHC services to the refugee population and purchases secondary and tertiary care services when needed. The NGO sector ranges from missionary hospitals to facilities supported by international organizations, to community health centers. The private for-profit health sector also provides the three levels of care through a wide range of practices.Hospitals are mainly provided by MOH, according to annual reports of MOH (2013). Palestine has 80 hospitals,30 in Gaza governorate, most of them are general and related to MOH with high bed occupancy rate (85%), MOH is with overcrowded hospital beds 1,4 per 1,000 population (MOH, 2013). PHC centers provide accessible and affordable health services for all Palestinians, especially for children and other vulnerable groups MOH is working with other health sectors in providing the primary health services, mainly NGOs organizations

1.7.3 Primary Health Care

PHC is the fundamental care of heath care system and the vertebral column of it, PHC puts all people at the center of health care, Primary Healthcare centers in Palestine 767centers, 604centers in West Bank, 163 centers in Gaza Strip, 61,5% is related to MOH,62 clinics are related to UNRWA Health Centers, 23 clinics are related to NGOs (MOH,2014), PHC ratio per 10000 population is 0,87 population per PHC is 114011, PHC-Centers at Palestine are with highly overcrowded and highly demand from Palestinian population (MOH, 2014)

1.7.4 UNRWA

UNRWA is a United Nations agency established by the General Assembly in 1949 following the first Arab-Israeli War in 1948, which became operational in 1950. It is mandated to provide assistance and protection to a population of over 5 million registered Palestine refugees. Its mission is to help Palestine refugees in Jordan, Lebanon, Syria, West Bank and the Gaza Strip to achieve their full potential in human development, pending a just solution to their plight (UNRWA, 2014). UNRWA has long been providing primary health services in three main programs, is divided into separate clinics within each health center: maternal and child health care (MCH), non-communicable disease (NCD) care, and general outpatient services.

A health reform package was introduced as a part of the Agency-wide organizational development plan, Family Health Team (FHT) is a primary care package focused on providing comprehensive and holistic primary health care for the entire family, emphasizing long-term provider-patient family relationships in late 2011. UNRWA provided a good example of how primary health care reform including the integration of a family practice approach could improve quality of care and patient satisfaction under difficult situations (UNRWA, 2014).

1.7.5 Antenatal Care Coverage at UNRWA

UNRWA encourages pregnant women to receive their first antenatal assessment as early as possible and to have at least four antenatal care visits throughout their pregnancy to promote early detection of risk factors and management of complications. Pregnant women receive a comprehensive initial physical examination and regular follow-up care, including screening for pregnancy-related hypertension, diabetes mellitus, anemia, oral health problems and other risk factors. UNRWA primary health care facilities cared for 88,615 pregnant women which represented a coverage rate of 79.0% of all expected pregnancies among the served refugee population.

Gaza Governorates is with ANC 87.3%, West Bank is with ANC %.(UNRWA, 2014), our focus study will be done at UNRWA clinics among risky pregnant women.

1.7.6 Health issues of Maternal Health in Gaza

Gaza is a small geographical area with many complicated health issues due to, socioeconomic status deterioration. Maternal mortality in Gaza ranges between 20-40 per 100,000 live births, with a most common leading cause is pulmonary embolism 20% (MOH, 2010). The prevalence of pregnancy complicated diseases is increasing among refugee pregnant women in Gaza (UNRWA, 2012), the prevalence of high-risk pregnancy (HRP) increases to 13,9%, the scope of bad pregnancy outcomes among pregnant women increases, there are nearly 3038 reported abortions yearly among registered pregnant women at UNRWA health centers (UNRWA, 2012) ,also Prevalence of late miscarriages and stillbirths are 23.3/1,000 and 7.4/1,000 respectively, and that of premature births 19.6/1,000 (Environ, 2012).

Chapter 2 : Literature Review

2.1 Conceptual framework

The researcher conceptualizes the main framework of the research as it is conceptualized from different literature. This framework joins the different associated variables dependent and independent variables which help to understand the problem of research and its associated dimensions.

2.1.1 Demographic factors

Many Studies showing that demographic factors are as important as physical health variables in affecting of health status outcomes, mainly maternal age as many kinds of the literature confirmed the risk of maternal age for developing thrombotic changes.

2.1.1.1 Maternal age

Many epidemiologic studies have reported advanced maternal age to be associated with increased risk of stillbirth, not explained by age-related risk for pregnancy-related complications such as pre-eclampsia, gestational diabetes, multiple pregnancy or placental abruption, The reported ORs for the risk of IUFD associated with advanced maternal age are in the range 1.3-1.9 for age 35-39 years and 1.7-3.3 for age over 40 years (Froen et al, 2009).Also, Frozen and dear colleagues reported an OR of 5.1 (95% CI 1.3-19.6) for the risk of unexplained intrauterine death among women 35 years and older.

2.1.2 Family history

It is the second factor will be studied as it discusses the risk of a family history of thrombosis and the use for the thromboprophylaixs uses in pregnancy as the researcher will ask about family history of earlier onset of thrombosis (venous, arterial) or any family member with thrombophilia and thromboprophylaixs uses.Sundquis et al (2015) reported that family history of thrombophilia is a risk factor for VTE recurrence in patients who had unprovoked first VTE. Furthermore, the presence of a Family history of venous thromboembolism may be an additional risk factor for VTE recurrence in thrombophilia-positive patients.

2.1.3 Maternal History

This part consist from the following factor

2.1.3.1 Obstetric history

This is the third factor to be studied as the researcher will look for the associated of maternal and fetal problems in past pregnancy histories (PIH, early onset of pre-eclampsia, HEElP syndrome, abruptio-placenta, miscarriages, early and late pregnancy loss, still births, prematurity, perinatal mortality, and IVF.

2.1.3.2 Past Medical History

This is the third factor, to study different associated chronic medical diseases, preexisting medical conditions like HTN, DM, auto-immune diseases, acquired thrombophilia (thrombocytosis, nephrotic syndrome, polycythemia, malignancy, history of venous, arterial thrombosis and DVT).

2.1.4 Inherited thrombophilia

The fourth factor is talking about the association of molecular genetic study and the risk of thrombosis and thrombophilia as the genetic study is diagnostic for hereditary thrombophilia, this genetic study describes factor V, Prothrombin, Protein C, S, antithrombin deficiency, prothrombin, MTHFR, and others.

2.1.5 Acquired Thrombophilia

This fifth factor discusses a number of acquired conditions augment the risk of thrombosis. A prominent example is anti- phospholipid syndrome which is caused by antibodies against constituents of the cell membrane, particularly lupus anticoagulant and anticardiolipin antibodies.

2.1.6 Management Practices

There are different types of anticoagulant medications are used as thromboprophylaxis among risky pregnant women (unfractionated heparin, low molecular weight heparin, low dose aspirin and combinations between two factors), the researcher will look for the type, dose, frequency, continuity, and availability of used medication.

2.1.6.1 Types of different management practices

This item will discuss different medical management practices among health provider, as the researcher will ask about the diagnostic criteria for thromboprophylaxis use, screening about thrombophilia and its adherence to international guidelines .

2.1.7 Pregnancy outcomes

The researcher will discuss the different pregnancy outcomes among the studied population, as it includes fetal outcomes (live birth, fetal demise, full term, preterm delivery, normal weight, low birth weight, SCBU admission, perinatal mortality, associated congenital anomalies) and maternal outcomes (Pregnancy complicated diseases)

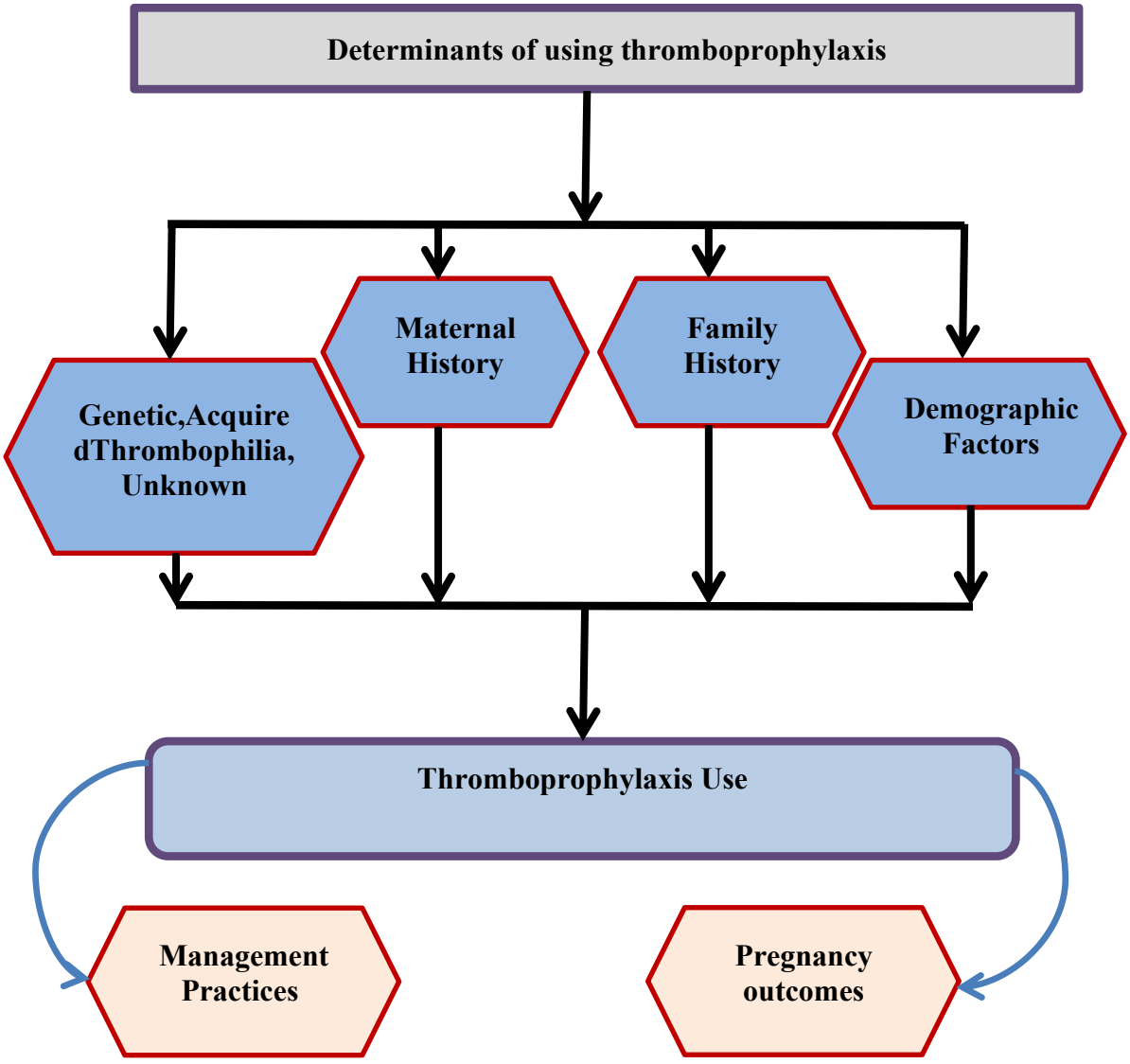


Figure 1.1: Conceptual framework self-developed

2.2 Thrombophilia

Thrombophilia means a predisposition to thrombosis, an increased tendency to have blood clots in veins or arteries. Thrombophilia may be inherited or acquired. Thrombophilia results from perturbations of the normal physiological coagulation cascade. The cascade is a complex, multi-step feedback mechanism with the ultimate of producing thrombin, which in turn cleaves fibrinogen to form a stable fibrin clot. Thrombophilia promotes the formation of thrombosis in individuals by one of two actions (a) facilitating the production of clotting factors in the coagulation cascade or (b) inhibiting anticoagulant function in the coagulation cascade (McLintock et al, 2001; Walker, 2000).

A successful outcome of pregnancy depends on proper placental formation. In the early stage of this process, trophoblastic invasion and fibrin deposition into the wall of the spiral veins play an important part. Pregnancy is an acquired hypercoagulable state and women with a prior tendency to thrombosis may develop clinical symptoms of placental vascular complications such as preeclampsia, intrauterine growth restriction, fetal death for unknown causes, that impact the maternal-fetal morbidity and mortality.

Thrombophilia is associated with an increased risk of pregnancy-related venous thromboembolism (VTE) and may also be linked to placental-mediated pregnancy outcomes, such as fetal loss , Thrombophilia have been recently explored as a cause of placental thrombosis, severe preeclampsia/eclampsia, HELLP syndrome, placental abruption, intrauterine growth restriction, unexplained stillbirth and recurrent miscarriage(Tranquilli, Giannubilo et al, 2004). Thrombophilia can be defined as a predisposition to thrombosis Abnormalities in hemostasis that is associated with clinical thrombophilia include heritable defects, such as mutations in the genes encoding the natural anticoagulants antithrombin, protein C and protein S, or clotting factors prothrombin , factor V, and acquired factors defects, such as antiphospholipid syndrome (Walker, 2003).

A number of studies have examined the association between thrombophilia and complications of pregnancy. The thrombotic disease is a major cause of maternal morbidity and mortality worldwide. Development of thrombosis in pregnancy is multifactorial due to the physiologic changes of pregnancy which induce a relative hypercoagulable state as well as physical changes leading to increased stasis and also the effects of both the inherited and the acquired thrombophilia.

2.2.1 Types of thrombophilia

Inherited thrombophilia includes deficiencies of antithrombin, protein C or protein S, homozygous or heterozygous mutations of factor V (Leiden, G1691A) or prothrombin) G20210A), and homozygosis for the variant of methylenetetrahydrofolate reductase - MTHFR C677T-(Greer, 2000, McLintock et al, 2001; Thomas, 2001; Walker 2000).

2.3 Coagulation Changes of pregnancy

During the course of normal pregnancy, dramatic changes occur in the hemostatic system . Coagulation factors increase physiologically in pregnancy and this is thought to be an evolutionary mechanism to prevent excessive blood loss during childbirth (Lindqvist, Merlo, 2006). Owing to hormonal changes, increased concentrations of procoagulants, decreased numbers of anticoagulant factors and diminished fibrinolysis activity. These changes may be important for reducing intrapartum blood loss, but they determine an increased risk of thromboembolism during pregnancy and puerperium. The changes in the coagulation system in normal pregnancy are consistent with a continuing low-grade process of intravascular coagulation. During pregnancy, the concentrations of coagulation factors VII, VIII, IX, X, XII and von Willebrand factors rise significantly accompanied by a relevant increase in the concentration of plasma fibrinogen.

Thrombin generation markers such as prothrombin F1 and 2 and thrombin-antithrombin (TAT) complexes are also increased (Szecsi, Jorgensen, Klajnbard, 2010). There is also a marked decrease in anticoagulant activity including reduced protein S levels and acquired activated protein C resistance (Sarig, Drori et al, 2011). Fibrin- lytic activity is also reduced with plasminogen activator inhibitor type 1 (PAI).levels increased by five-fold and increases in placental-derived plasminogen activator inhibitor type 2 (PAI-2), particularly during the third trimester (McLean, Bernstein, Brummel, 2012).These changes in the hemostatic system act as a physiological “safety net” for the peripartum period, but can predispose both the mother and fetus to complications during the pregnancy. For the mother, this risk begins from the point of conception well into the postnatal period, with recent data suggesting that the risk extends to at least 12 weeks (Kamel, Navi et al, 2014).

2.4 Thrombophilia affecting natural anticoagulation

This part consist from the following

2.4.1 Factor V Leiden (FV Leiden) mutation

FV is the most common hereditary thrombophilia, which is found in approximately 5% (2–15%) of Western populations. Normally activated protein C inhibits coagulation cascade by splitting activated factor V (Va),(Rees et al, 1995).

This mutation slows down the proteolytic degradation of factor Va by activated protein C (APC), leading to increased generation of thrombin. Resistance to APC has been found in 24–60% of women with pregnancy-associative VTE (Hellgren,2003)

2.4.2 Deficiencies of Antithrombin, protein C, and protein S

Antithrombin deficiency is the most severe thrombophilic condition associated with a 70-90 % lifetime risk of VTE. Antithrombin has its thrombin inhibitory properties, and it can also inactivate coagulation factors Xa, IXa, VIIa, and plasmin so, the lifetime risk of VTE associated with both protein C or S deficiency and both are associated with adverse pregnancy outcome (Girling, Swiet,1998)

2.5 Thrombophilia affecting procoagulants

2.5.1 Prothrombin gene 20210A mutation

Prothrombin is the inactive precursor of thrombin, which is required in order to convert fibrinogen into fibrin, the primary goal of the coagulation cascade is present in 1–2% of the healthy population and it increases the risk of VTE three folds than others (Rosendaal et al, 1998).

2.5.2 High level of factor VIII

The significance of a high level of FVIII is unclear, but it is evident that high levels increase the risk of deep venous thrombosis (Kraaijenhagen et al, 2001).

2.5.3 Hyperhomocysteinemia

Hyperhomocysteinemia is known to cause direct endothelial injury through increased oxidative stress, to induce impairment in the endothelial synthesis of vasodilator substances to increase the expression of procoagulants and increase platelet aggregation Most mild or moderate forms of hyperhomocysteinemia are the result of homozygosis of the methylene tetrahydrofolate reductase (MTHFR) mutations, the prevalence of which

among Europeans is about 11%.Although hyperhomocysteinemia is a risk factor of arteriosclerosis, its role solely in pregnancy complications is not defined (Jaaskelainen et al, 2006)

2.6 Acquired thrombophilia

This item is associated with external events that occur in pregnancy and increase the risk of thrombosis. Acquired thrombophilia is hypercoagulable states secondary to various etiologies. In particular, during pregnancy, the risks are exaggerated due to the underlying physiological changes (Manjiri, Catherine, 2003).

2.6.1 Antiphospholipid syndrome

Antiphospholipid syndrome (aPS) is an autoimmune disorder in which patients have antibodies against phospholipids structures in their blood and at least one clinical manifestation such as adverse pregnancy outcome or thromboembolism (primary aPS).
Literature says that anti phospholipid bodies are found about 1% to 5% of population (Petri, 2000), also Antiphospholipid antibodies can be present in association with some autoimmune conditions (secondary aPS), especially systemic lupus erythematous (SLE) Among such patients aPLs have been found in 30% (Love,2000). The clinical manifestations related to these antibodies include both arterial and venous thrombosis, spontaneous pregnancy losses and others are the same.

Robertson et al (2006) showed significant associations between aPLs and both early and late fetal loss and an increased risk of preeclampsia and lupus anticoagulant Anti phospholipid antibody syndrome is described by its presence of lupus anticoagulant (LAC) and/or anti-cardiolipin antibodies (ACL) with recurrent miscarriage (RM), thrombosis, preeclampsia, IUGR and placental abruption. The most specific clinical features are thrombosis (both venous and arterial thrombosis), RM and fetal loss in the second and third trimester and autoimmune thrombocytopenia (Kupferminc, 2003).

There are many pathological changes occur with placenta vasculature wit APL syndrome, that resulted in placental infarction leading to miscarriage, IUGR, Stillbirth and early sever preeclampsia (Kupferminc, 2003).

Literature says that 10 % to 15% of recurrent miscarriages below 20 weeks with antiphospholipid antibodies (Kupferminc, 2003), also many studies showed the association

between preeclampsia and antiphospholipid antibody syndrome, as there is 16 % estimate of incidence of pre-eclampsia with positive APL, many studies show strong association between early onset of pre-eclampsia and APL (Kupferminc, 2003) .Women with APS are also at a substantial risk for IUGR, which is around 30%. In one study, 24% of mothers delivered of IUGR infants had medium or high positive tests for Anti- cardiolipin antibodies (Kupferminc, 2003).

2.7 Thrombophilia and pregnancy complications

2.7.1 Recurrent fetal loss

The recurrent fetal loss is a common problem of the women in reproductive age group, 1% to 2% with 3 or more losses, and 5% with 2 or more losses (Gottl et al, 2004).
Inherited and/or acquired thrombophilia has been diagnosed in 50% to 65% of women with a history of unexplained RPL and in nearly 20% of women with RPL with age of more than 35 years (Marquard, 2009).

The recurrent Fetal loss has a strong association of inherited and acquired thrombophilia , as there were at least 16 case-control studies have found a high prevalence of VFL in women with the unexplained fetal loss (up to 30%) compared to 1%-10%of control subjects (Kujovich, 2002).

Ohel and colleagues (2000) said that women with thrombophilia have an increased percentage of losses at a later stage of gestations; However, APC resistance with factor V can be associated with pregnancy loss at an earlier stage.

A number of recent meta-analyses have demonstrated an association of factor II with second and third-trimester loss and also first-trimester loss (Hoffman et al, 2002).Some documented studies have reported a statically significant increased frequency of RFL with Prothrombin gene mutation, one of these studies reported a frequency of 9 %in women with recurrent miscarriage, while a frequency of 2% occurred in the control group (Foka et al, 2000).A second study reported a frequency of 6.7 %compared to 8 % in the control group (Pihusch et al, 2001).

In a meta-analysis, protein S deficiency conferred an overall 15 folds increased the risk of recurrent pregnancy and a 7 fold higher risk of late fetal loss (Rey et al, 2003). A meta-

analysis study reported a 3 to 4 folds increased risk of recurrent early pregnancy loss in women with MTHFR mutation (Nelen et al, 2000). There are several studies that have shown the association between hereditary APCR and pregnancy loss. Gradone and colleagues (2007) reported a 31.2% prevalence of factor V Leiden in women with second-trimester fetal losses compared to 4.2 % in matched controls.

A composite study of the association between the known thrombophilia and fetal loss demonstrated that fetal loss occurred among 10 of 48 women with thrombophilia (21%), and among 10 of 60 control women (17%). There was a similar risk of fetal loss in women with the factor V Leiden mutation compared to those without (Vossen et al, 2003).

The NOHA (Nimes Obstetricians and Hematologists) first study, a large case-control study nested in a cohort of nearly32,700women, of whom 18% had pregnancy loss with their first gestation found on multivariate analysis a clear association between unexplained first pregnancy loss between 10 and 39 weeks gestation and heterozygosis for factor V Leiden (OR 3.46; 95%CI, 2.53–4.72) (Lissalde-Lavigne et al, 2005).In addition to that Sarigand colleague(2002) point out that non-factor V Leiden APCR is one of the most common thrombophilic defects associated with recurrent pregnancy loss.

The reported prevalence of acquired activated protein C resistance from studies so far ranges from 9% to 26.8% in women with first, second and third trimester losses. Fifty- one women with recurrent pregnancy loss and acquired APCR was recruited and their factor V gene was intensely analyzed (Dawood et al, 2007) .as Brenner and colleagues (1999) tested women with 3or more first trimester losses, 2 or more second trimester losses or one or more third trimester loss the FV Leiden mutation was more frequent in the fetal loss group compared to controls. Overall, 49% of women with pregnancy loss had a thrombophilia compared to 22% of controls. Other authors studied 1384 women enrolled in the European Prospective Cohort on Thrombophilia (EPCOT), They analyzed the frequencies of miscarriage fetal loss at or before 28 weeks of gestation and stillbirth (fetal loss after 28 weeks of gestation) jointly and separately with cases group.

Kupferminc and colleagues (1999) found a 50% prevalence of Thrombophilia in women with IUFD more than 23 weeks. Another study investigated women with IUFD at 27 weeks' gestation or more In 40 women with unexplained IUFD, the prevalence of inherited

thrombophilia was 42.5% in the study group compared with 15% in controls (Kupferminc, 2002).In addition to that Monari et al (2012), conducted a case-control study showed the presence of thrombophilia defect was significantly more prevalent in mothers with SBs compared to controls. In particular, SB mothers showed an increased risk of carrying Factor II mutation (OR=3.2, 95% CI: 1.3-8.3, p=0.01).

2.7.2 Thrombophilia and Pregnancy-induced hypertension

Pre-eclampsia is an important cause of maternal and fetal morbidity complicating 2-7 % of pregnancies.Pre-eclampsia is one of the leading causes of maternal mortality Preeclampsia and eclampsia cause about 12%of maternal deaths(Tikkanen et al,2009).Numerous studies with different designs have assessed between pre-eclampsia and thrombophilia , many meta-analyses has tried to determine the true association (Helsinki,2011).The first report of an association between early onset and sever pre-eclampsia and APL was described by Branch et al (1989).Later, Dekker et al (1995) reported an association between an inherited thrombophilia mutation and preeclampsia as he reported that 16 % of women had activated protein C resistance .

Recent meta-analysis as Robertson et al (2006) have indicated that pre-eclampsia is significantly associated with factor V Leiden and prothrombin mutations, anticardiolipin,antibodies, MTFHR, homozygosity and hyperhomocysteinemia , where's protein S protein C and anti- thrombin deficiency. Mello et al (2005) showed not only an association between thrombophilia and sever pre eclampsia but also a tendency towards increased risks of maternal complications such early onset of disease less than 28 weeks of gestations.

Van Pamus et al (2000) reported an increase prevalence of activated protein C resistance in 284 women with a history of severing preeclampsia, compared with controls (11.3% vs. 1.5%).

2.7.3 Thrombophilia and IUGR

Intrauterine growth retardation (IUGR) contributes significantly to fetal morbidity and mortality, but its etiology is unknown in most cases. IUGR is a frequent cause of stillbirth, perinatal morbidity, and long-term sequels, but its etiology is unknown in most cases. It has been suggested to be associated with abnormal placental vascular and disturbance of

homeostasis leading to inadequate maternal-fetal circulation. There is a growing view that inherited thrombophilia may predispose to adverse pregnancy outcome.The probable mechanism may be associated with pathological placental vascular leading to inadequate feto-maternal circulation. Some studies showed an association between inherited thrombophilia and complications, such as intrauterine fetal death, preeclampsia and placental abruption but the association between IUGR and thrombophilia is controversial (Hoffman et al, 2012). Mirzaei and Mahajeri (2012) reported in their study case-control study which is conducted at a tertiary center in Iran that 68% of a pregnant lady with IUGR had thrombophilia, 32 %of other ladies don't have thrombophilia.

The association between thrombophilia and IUGR is weaker than in preeclampsia and pregnancy loss. Robertson et al (2006) reported that the only association between thrombophilia and IUGR is anticardiolipin antibodies. On the other hand, Larciprete (2007) described the strong association between genetic thrombophilia and IUGR and percentage of IUGR among cases group reached 12.8 % in contrast to control group no association. Kupfemnic et al (1999) investigated 110 women with sever preeclampsia, IUGR, abruption placenta and IUFD more than 23 weeks, he found that prevalence of thrombophilia with IUGR was 61.4%. Zeev et al (2004) found significantly higher prevalence of thrombophilia (%37) was found in women who delivered small for gestational age stillborn compared with women who delivered normal birth weight stillborn (73% vs.18.4%, $P < 0.0001$).

2.7.4 Thrombophilia and Abruption placenta

Abruption placentae, also called placental abruption, a significant cause of third-trimester bleeding associated with fetal and maternal morbidity and mortality, placental abruption must be considered whenever bleeding is encountered in the second half of pregnancy.

It occurs on average in 0.5%, or 1 in 200 of deliveries(Cunningham et al, 2014).Literature reported a strong associate on between maternal thrombophilia and abruption placenta Giovanni et al (2007) had reported the more prevalent of abruption placenta among cases than control, Kinzler (2009) reported in his case-control study that 63.0% of cases with abruption placenta had at least one diagnosed maternal thrombophilia in comparison with 44% among control .One of the recent studies factor V mutation was found in 20 %of the

women with preeclampsia, placenta abruption, fetal growth retardation, or still birth compared to only 6 %of control women without complication.(Kupfermnic et al, 1999) . Hyperhomocysteinemia was documented in 26 %of women with placenta abruption, in 11%of IUFD, and in 38 %of women delivering babies whose birth weight was below fifths percentile compared with an estimated 2% to 3 % in control population (De Vries et al, 1997)

2.7.5 Thrombophilia and preterm birth

Preterm birth is the most common cause of death among infants worldwide. About 15 million babies are preterm each year (5% to 18% of all deliveries). The chance of survival at less than 23 weeks is close to zero, while at 23 weeks is 15%, 24 weeks 55% and 25 weeks about 80% (Cloherty, 2012) chances of survival without long-term difficulties are lower (Jarjour, 2015).

Kramer and colleagues (2009) had shown in his case-control study association between preterm labor and thrombophilia with adjusted odds ratio (ORs) =1.9.Not all previous studies showed able to replicate the association between thrombophilia and pre-term labor, but Erhardt and collogues (2000) reported an increased risk of mothers with preterm labor and thrombophilia, also, Gopel et al (1999) reported similar risk between thrombophilia and preterm labor.

2.8 Thrombophilia and infertility

A finding of a higher incidence of thrombophilia in women submitted to repeat cycles of in vitro fertilization (IVF) and implantation failure has become increasingly common compared to fertile women. Azem et al (2004) evaluated women were submitted to investigate the following thrombophilic factors: prothrombin gene mutation, MTHFR gene mutation, the presence of factor V Leiden, and antithrombin, protein C and protein S deficiency. A high frequency of thrombophilia was found in the subgroup of women with implantation failure (17.8%) compared to the group of fertile women and the group of women who became pregnant at the first IVF attempt (a frequency of 8.9% in both groups).Grandone et al (2001) also reported similar results in a case-control study involving a smaller sample of women the results of the two above mentioned studies, although indicative of a possible association between thrombophilia and failed implantation, do not positively confirm this association. On the other hand, Martinelli et al (2003) conducted a case-control study with the largest sample size evaluated up to the

present time and found no evidence of a higher frequency of thrombophilia in infertile women.

In 2009, a Turkish group published the findings of a study between thrombophilia and implantation failure was evaluated. This was a case-control study comparing a group of 51 women with implantation failure and a group of 50 fertile women. a finding of at least one thrombophilic factor (62.7%) was more common in the group of women with implantation failure compared to the control group (53.9%). In 2010, Casadei et al, published a case-control study that included a total of 300 women, 100with infertility of no apparent cause and 200 fertile women. The following hereditary factors were investigated: factor V Leiden (G1691A), prothrombin gene mutation (G20210A) and MTHFR enzyme mutation (C677T). This study found no difference in the frequencies of thrombophilic factors between the two populations evaluated (Casadei, 2010). A study was recently published on the prevalence of thrombophilia in a fertile and infertile female population in Brazil. This study found a high frequency of thrombophilia among infertile women (Soligo, 2007). The association between thrombophilia and infertility remains controversial; however ,studies have tended to associate this coagulation disorder with implantation failure.

2.9 Venous thromboembolism and pregnancy

Deep vein thrombosis (DVT) and pulmonary embolism (PE) are major health problems with potentially serious outcomes. Venous thrombo-embolism represents one of the main causes of maternal mortality in the world (2 per 100,000 live births). The overall prevalence of thromboembolic events during pregnancy is approximately 2 per 1000 deliveries, approximately 20% of these events are arterial, and the other 80% are venous. Approximately 80% of venous thromboembolic events during pregnancy are deep vein thrombosis (DVT) and 20% are pulmonary emboli (Jameset al, 2005, James et al, 2006, Heit et al, 2005).

The literature showed the risk of thrombosis and DVT increased by the presence of genetic thrombophilia and acquired thrombophilia. Anderson and Spencer (2003) reported that thrombophilia is one of the major risk factors for thrombosis; the overall prevalence of anticardiolipin antibodies and lupus anticoagulants has been established with cases with DVT.

James (2009) reported that inherited thrombophilia has a big role in thrombo -embolism disorder in pregnancy, as he showed in his case-control study, Factor V homozygous with odds ratio 34.4, Factor V heterozygous with odds ratio 8.32, Prothrombin gene homozygous with odds ratio 26.36, Prothrombin gene heterozygous with odds ratio 6.8 ,protein C deficiency with odds ratio 4.76, protein S deficiency with odds ratio 2.19.

2.10 Thrombo-prophylaxis in pregnancy

The management of thrombosis during pregnancy includes treatment of acute deep vein thrombosis episodes, primary prophylaxis in a symptomatic women, and secondary prophylaxis of recurrences in women with a history of thrombosis.The diagnosis has serious implications not only for the immediate management of the pregnancy but also for the management of future pregnancies.

2.10.1 Thrombo-prophylaxis and pregnancy complications

A recent collaborative study demonstrated the safety of using low-molecular-weight heparin during 486 gestations a success-full outcome was reported in 83 (89%) of 93 gestations in women with a history of recurrent pregnancy loss and in all 28 gestations in women who experienced preeclampsia during a previous pregnancy (Lepercq et al, 2001)
In Carpe et al , (2003) study reported a cohort study undertaken to assess the effect of enoxaparin on subsequent live birth rate in women with 3 or more consecutive pregnancy losses and hereditary thrombophilia, live birth rate was higher in women treated with enoxaparin, 26 (70.2%) of 37 compared with 21 (43.8%) of 48 in untreated patients.

Brenner (2004) demonstrated in his study that Data on antithrombotic prophylaxis for IUGR at index pregnancy and on subsequent gestations are limited. However, in view of the risk for recurrences of other gestational complications including IUGR, prophylaxis can be considered. This case can be managed with LMWH at a prophylactic dose once daily throughout gestation, and for 6 weeks in the postpartum period. This regimen may also be useful for prevention of other vascular complications.

Many Literatures is confirming the management among pregnant ladies with previous VTE, but the problem of managing women with thrombophilia and fetal loss, IUGR, and preeclampsia, Women with a history of VTE with or without thrombophilia are believed to have a higher risk of recurrence in subsequent pregnancies.

Estimates of the rate of recurrent venous thrombosis during pregnancy in women with a history of VTE have varied between zero and 13%, the higher of these estimates has prompted authorities including (the American College of Chest Physicians) to recommend anticoagulant prophylaxis during pregnancy and the postpartum period in women with a history of VTE (Ginsberg, 2001). Also, he confirmed women with recurrent pregnancy loss, including at least one-second trimester miscarriage or a history of intrauterine death or severe or recurrent preeclampsia or growth restriction, should be screened for underlying congenital thrombophilia. In contrast to patients with APLA syndrome with recurrent miscarriage, where a combination of heparin and low-dose aspirin have been shown to be effective in reducing miscarriage rates, we have no data to indicate whether such antithrombotic therapy is beneficial (Ginsberg, 2001),Women with APLAs and neither previous venous thrombosis nor pregnancy losses should probably still be considered to have an increased risk of VTE and should be treated either with careful clinical surveillance for VTE or prophylactic UFH or LMWH. (Ginsberg, 2001).

The treatment of recurrent miscarriage has traditionally been based on evidence, personal bias and the result of uncontrolled trials. The American College of Obstetricians and Gynecologists recommends low-dose aspirin (81mg) orally per day, along with unfractionated heparin (5000 units) subcutaneously, twice daily. This therapy begun when pregnancy is diagnosed is continued until delivery. Although this treatment may improve overall pregnancy success, these women remain at high risk for preterm labor ,prematurely ruptured membranes, fetal-growth restriction, preeclampsia, and placental abruption (ACOG, 2005).

Gris (2004) reported a prospective study for evaluation the effect of low dose low dose aspirin, or LMWH was done in women with one unexplained pregnancy loss, a total of 160 patients with heterozygous factor V Leiden mutation, prothrombin G20210A mutation, or protein S deficiency were given 5 mg folic acid daily before conception, to be continued during pregnancy, and low-dose aspirin 100 mg daily or low-molecular-weight heparin enoxaparin 40 mg was taken from the 8^{th} week. Twenty-three of the 80 patients, treated with low-dose aspirin and 69 of the 80 patients treated with enoxaparin had a healthy live birth odds ratio (OR,15.5, 95 %confidence interval [CI], $P < .0001$).

2.10.2 Thrombo-prophylaxis and venous thromboembolism

Women at risk of venous thromboembolism should ideally have preconception assessment to outline the management plan for their pregnancy. The highest risk for VTE is in the postpartum period but it must be remembered that VTE related deaths occurred in all three trimesters of pregnancy.

Thromboprophylaxis should be instituted from the earliest possible stages of risky pregnancy.Therefore women known to be at risk should be seen and counseled preconceptually (Ireland, Institute of Obstetricians and Gynecologists, 2013).

2.10.3 Primary prophylaxis of thrombosis in asymptomatic women

In asymptomatic women with known protein C deficiency, protein S deficiency, FV Leiden or prothrombin mutation, who have never experienced VTE, recommend either clinical surveillance or prophylactic therapy during the last weeks of pregnancy and 2–6 weeks in the puerperium. (Kupferminc, 2003).

Recently Literature confirmed the need of thromboprophylaxis among pregnant ladies with factor V homozygous and the prothrombin gene mutation to prevent thrombosis (Martinelli et al, 2001).Clinical surveillance is usually reserved for women who are allergic to heparin, refuse to use heparin or LMWH, or who have experienced a previous VTE in association with a transient risk factor (Kupferminc, 2003).

2.10.4 Secondary prophylaxis in women with previous thrombosis:

All patients with a personal or family history of VTE should be considered for antenatal prophylaxis and be screened for a thrombophilia.The two general approaches recommended for pregnant women with previous VTE are active prophylactic therapy with heparin or LMWH and clinical surveillance.Women with thrombophilia and a history of previous VTE should receive thromboprophylaxis during pregnancy and puerperium (Kupferminc, 2003).

Literature show thromboprophylaxis in pregnancy is a controversial and critical issue as the decision of heparin thereby is not easy, it is a very expensive, inconvenient and painful to administer and associated with complications like bleeding and osteoporosis. The researcher will identify the different determinants associated with thromboprophylaxis uses in Gaza among risky pregnant women and the availability of agreement of risk assessment between different health providers, and answer a real question heparin is a new fashion or a real risk.

Chapter 3: Materials and Methodology

3.1 Study Design

The type of this study is an observational, analytic, retrospective, clinic-based comparative design with the triangulated mixed methodology. The present study will enroll a group of risky pregnant women with thromboprophylaxis use and a group of normal pregnant women without use in pregnancy and compared their patterns of previous exposures. The two groups are matched with at least three variables, the site of living (Governorate), the clinic of registration and follow up of antenatal care, the month of delivery.

We select this type of this study because it is inexpensive, short time, it can give complete picture of comparison of determinants, outcomes, and different management practices, also in this study the researcher will use triangulation and mixed methodology because that Triangulation is a powerful technique that facilitates validation of data through cross verification from two or more sources. In particular, it refers to the application and combination of several research methods in the study of the same phenomenon, so the researcher will use qualitative and quantitative methods to validate data and confirm results.

3.2 Study Population

This study consists of two groups:

- **First**, Delivered pregnant women at the last six months of the year (2016), and who were registered and followed up her ANC at UNRWA Health Centers -Gaza governorates-.
- **Second**, Health Providers who are concerned with thromboprophylaxis use among risky pregnant women.

3.3 Sample Population

First, these populations selected randomly from study population as two groups cases group are risky pregnant women and are characterized as alert or high-risk pregnancy according to UNRWA risk scoring program. Each risky case compared with normal pregnant women who were registered, followed up at UNRWA Health Centers and delivered at the same period.

Second. a non-probability purposive sample of three key health providers (health providers who concern with uses among pregnancy).

3.3.1 Study settings

The study carried at UNRWA Primary Health Centers (Gaza Governorates) Nearly, it carried at five Health Centers of UNRWA mainly large clinics (North Gaza, Gaza, Middle Zoon, Khan-Younis, and Rafah).

3.4 Study Period

The study started from April 2016, by conducting the administrative procedures and the ethical approval. The study consumed 12 months It started in April 2016 and completed by July 2017.

- Annex (1) describes the activities of the research and expected duration for each activity.

3.5 Sampling

3.5.1 Sample size

The sample size for this study determined by using the statistical calculator of the EPI_INFO program sample size: The proposed sample size was 430 participants (Annex,2). The researcher increased the actual sample size to 440 participants to compensate any missing or non-respondents. The larger the sample size, the greater representatives and the greater the statistical power.

The researcher studied 220 cases with thromboprophylaxis use and compared it with 220 pregnant women without thromboprophylaxis use, a ratio of one to one.

3.5.2 Sampling Process

Multistage sampling technique used to select 5 UNRWA PHC clinics from the 21 clinics. First, GG areas will be divided into five areas (clusters). In each area, the clinics will be divided into3 groups; Large, Medium, Small, according to refugee population served (Annexes3,4).

The sample of the 440 clients divided among GG areas according to the total number. Also, the sample in each area divided into two groups cases with thromboprophylaxis and comparative normal group without thromboprophylaxis .both groups will be chosen

according to an eligible criteria as all cases of studied phenomena will be taken from the delivered women at the same period of study , comparative normal group will be selected by systemic random selection by selecting the next one (Annex3,4).

A non-probability purposive sample of three key health providers (health providers who concern with thromboprophylaxis uses among pregnancy), they selected. The qualitative component carried out after the quantitative one in order to explore issues that emerge from the quantitative study.

3.6 Eligibility Criteria

Quntatitive Part consisit from the following part :

3.6.1 Inclusion criteria

The participants studied, meet the criteria of the study.

3.6.1.1 Cases with thromboprophylaxis

- Newly delivered women who were categorized as high-risk pregnancy
- Had received thromboprophylaxis during pregnancy.
- Attended antenatal care at UNRWA centers

3.6.1.2 Comparative group without thromboprophylaixs

- Newly delivered women who were classified as normal pregnancy
- Did not received thromboprophylaxis during pregnancy
- Attended antenatal care at UNRWA centers

3.6.2 Exclusion Criteria

Qualitative Part consists from the following part:

3.6.2.1 Cases with thromboprophylaxis

- Delivered risky pregnant women who are not registered at UNRWA Health Centers.
- Delivered risky pregnant women who have not attended UNRWA Health centers in the defined period of study.
- Delivered Risky Pregnant women without Thrombophilia and thromboprophylaxis during her pregnancy.

3.6.2.2 Comparative group without thromboprophylaxis

- Delivered normal Pregnant Women who are not attendant at UNRWA Health centers.
- Delivered normal pregnant women who are not attendant in the defined Health Centers.

3.7 Study instruments

This study utilized three types of instruments; ***the first is an Interviewed*** structured questionnaire for target Clients. The main items for the questionnaire will be:

- Personal and demographic data: Age, address, Years of education, and current occupation.
- Socioeconomic information: such as the type of family, type of house, number of rooms, and monthly income.
- Family History: Thrombophilia, thromboembolic disorders
- Past Medical history: Arterial, venous thrombosis, DVT, chronic diseases, and SLE (systemic Lupus Erythrocytosis).
- Past obstetric history: Gravida, Parity, Age of marriage, infertility, IVF, Abortion, Habitual Abortions, IUFD, Early Fetal Death, still births, perinatal mortality, congenital anomalies, IUGR, LBW, PIH, pre-eclampsia, APH, PPH and Abruption Placenta.
- Current Obstetric History: LMP, GA at registration, BMI at registration, number of ANC visits in her pregnancy, history of medical disorders during pregnancy, indication for pregnancy termination, common disorders associated with or caused by pregnancy.
- Pregnancy outcome
- GA of delivery, Mode of delivery, place of delivery, Live or dead child, Birth Weight at delivery, associated congenital anomalies and H/o of SCBU admission.
- Source of Diagnosis: Hospitals, PHC centers, Private Doctors
- Criteria and investigations of diagnosis: Inherited, A acquired thrombophilia, or others
- The site of Follow up: Primary Health centers, Hospitals or Private.
- Type, availability, and cost of thromboprophylaxis treatment.

The second instrument is an open-ended (semi-structured) questions. these questions will be asked by the researcher within in-depth interviews with 3 key health providers (health

providers concerns of thromboprophylaxis), this sample will be a non-probability purposive sample of five key informants (heath providers concerns of thromboprophylaxis) selected.

The idea of including this sample is to dig deeply and understand in-depth the definite meaning of thromboprophylaxis, risk factors associated, the magnitude of the problem, indications of treatment, consequences of thromboprophylaxis use, harmonization between health providers and recommendations for that. The qualitative component suggests containing these questions:

- What are the magnitude and current status of thromboprophylaxis use among risky pregnant women,?
- What are the different associated risk factors and indicators for thromboprophylaxis uses among risky pregnant women?
- What do you think about the benefits of thromboprophylaxis in pregnancy?
- What do you think about an international guideline for thromboprophylaxis uses in risky pregnancy?
- How can you describe the harmonization between different health providers in understanding this need of thromboprophylaxis among risky pregnancy?

The third instrument is Medical records Review

The researcher selected randomly clients medical records for these who received thromboprophylaxis during their pregnancy as researcher selected the second medical card from 220 cases, as it will be nearly 100 cards.This Review will compare the of adherence thromboprophylaxis management practices with international guidelines, the researcher will construct self-developed abstract sheet that is based on literature review, the domains which will be included with it will be.

- Past Obstetric history
- Past Medical history
- Gestational age of starting thromboprophylaixs treatment
- Continuity of treatment overall pregnancy and 6weeks after delivery
- Diagnostic investigations (Hereditary –Acquired thrombophilia)
- Follow up investigations
- type and dose of treatment
- combinations of thromboprophylaxis

3.8 Data Collection

The researcher and one data collector conducted structured –interviewed questionnaire with target clients and medical records review which is a complementary for the questionnaire. This took place within 6 months with delivered pregnant women at that period, The two data collector are one is a nurse, she is trained to collect data as the researcher.

The second component of the data collection was three in-depth interviews with three key health providers. Semi-structured questions will be designed and questioned for them by the researcher. Notes taken through the interviews and recorded to allow further capturing of information .

3.9 Data entry and analysis

3.9.1 Quantitative Method

The researcher used Statistical Package of Social Science (SPSS) program for data entry and analysis. Data analysis carried out as the following:

- Reviewing the questionnaire.
- Developing an appropriate entry model.
- Coding of the questionnaire.
- Cleaning the data.
- Formulation of frequency table for the study variables.
- Defining and recoding of variables.
- Cross-tabulation of the results .
- Statistical relationship between the risk factors and thrombophilia

These assessed using Chi-Square and Odds ratio with confidence interval 95%. Statistical level of significance used was 0.05.

3.9.2 Qualitative part

Open coding thematic analysis method used to analyze the transcripts of the in-depth interviews. The researcher obtained the main findings from the transcripts of the interviews. Then, categorization of related ideas and comparison and integration between the quantitative and the qualitative findings was done to create rich items for discussion and representation.

3.10 Scientific rigor

3.10.1 Quantitative part (questionnaire)

3.10.1.1 Validity

- The questionnaire tested by experts to assess its relevance, evaluated all the components and the context of the instrument, in order to ensure that it is highly valid and relevance and their comments were taken into consideration. The researcher presented the questionnaire to 8 experts specialized in the field of public health (Appendix 1) in order to take their views and benefits from their long experience on the questions of belonging to the subject of the study, and the accuracy of the wording, the researcher completed the amendments recommended by the arbitrators to delete, add, and amend the questionnaire in its final form consisting of (8) parts as shown in Annex (2).
- . The questionnaire was nicely formatted in order to ensure face validity, this including appealing layout, and logical sequences of questions and clarity of instructions
- A pilot study conducted before the actual data collection to examine clients' responses to the questionnaire and how they understand it.

3.10.1.2 Reliability

The following steps are done to assure instruments reliability

- Training of data collectors on the clients interviewing steps and the way of asking questions. This will assure standardization of questionnaire filling .
- Then, the data entry on the same day of data collection would allow possible interventions.
- Check the data quality or to re-fill the questionnaire when required .
- Re-entry of 5% of the data after finishing data entry will assure correct entry procedure and decrease entry errors.

3 .11 Reliability of questionnaire

Before applying the study tool, the researcher verified the validity and consistency of the questionnaire through the following steps:

3.11.1 Compact Factor

The researcher verified the persistence of the questionnaire by finding the coefficient of agreement between the mobilization of mothers and the data on the medical health records

in the clinic of each mother with the aim of the absence of any ambiguity in the understanding of the questions by the mothers, and it actually measured what was set for measurement, The researcher chose 12 questions, which have an important and direct answers to the study.

The researcher then selected a sample of 100 MHR of chosen clinics in the sample and asked them to fill out the questionnaire. The researcher then obtained answers to the questionnaire of mothers from maternal health records. After monitoring the quantitative estimates of the cases, and the difference between the researcher and the other cases using the Cooper equation, which states:

$$\text{Agreement ratio} = \frac{\text{Number of times of agreement}}{\text{Number of times of agreement + number of times of disagreement}} \times 100$$

It is noted from the previous table that the ratio of the coefficient of agreement ranges between (91.66 - 97.7%) and the total agreement coefficient (95). These ratios are a function of the accuracy of the questionnaire, which reassures the researcher before applying them.

Table (3.1) Ratio of the agreement between the observers

Region	Number of cases	Points of agreement	Points of difference	Total points of agreement and difference	the coefficient of agreement
North of Gaza	٢٠	٢٣٠	١٠	٢٤٠	٩٥,٨٣
Gaza	٢٠	٢٢٥	١٥	٢٤٠	٩٣,٧٥
Central	٢٠	٢٢٠	٢٠	٢٤٠	٩١,٦٦
Khan Younis	٢٠	٢٣٢	٨	٢٤٠	٩٦,٦٦
Rafah	٢٠	٢٣٣	٧	٢٤٠	٩٧,٧٠
total summation	١٠٠	١١٤٠	٦٠	١٢٠٠	٩٥

3.11.2 Qualitative part (in-depth interviews)

The following methods are used assure the trustworthiness of the qualitative part in this study.

- A peer check w did through health experts to revise the in-depth interview.
- Questions to assure that they cover all the required dimensions.
- A member check done to assure accuracy and transparency of the transcripts during the interviews.
- Recording the interviews would enhance the accuracy of the transcripts.
- All the transcripts and recordings will be kept for tracking the information by others at any time (Audit trail).

3.12 Pilot study

A piloting process was conducted before starting the data collection. The piloting process aimed to help in identifying problems in the research design; test the data collection tool for validity and reliability. Also, Piloting allows data collectors training for collecting data and where is the week piont in data collection.

The pilot study was 5% of sample size, as it nearly consists of 20 clients,10 cases, 10 controls with the same eligibility criteria for cases and controls, It was held at Jabalia Health Center as it is a large health center and it contains a large number of risky pregnancies. As a result of piloting some modifications to data collection tools were done. Subjects who have been selected for piloting had been excluded from the study.

3.13 Ethical matters

- An ethical approval will be asked for from Helsinki Committee.
- An Academic approval will be asked for from School of Public Health at Al-Quds University.
- An Admin approval will be asked for from the Director of UNRWA Health Programs in Gaza Governorate.
- Every participant in this study received a complete explanation of the research, purpose, and confidentiality.
- We should guarantee and take approval for every participant health provider is an in-depth interview.

- Every woman of the study population knew that participation in the research is optional and she has the right to refuse.

3.14 Anticipated Limitation of Study

- The study will include a sample from UNRWA clinics and there are other PHC clinics for MOH, NGOs will not be included and private clinics.
- The study will include only clients who are attending UNRWA PHC setting within the study period and it is not including all population which is important for complete reality.
- Case-Control study doesn't give a picture of the prevalence of phenomena, with a risk of recall bias.
- Poor availability of basic systemic studied about studied phenomena.
- Lack of resources and materials needed for the study concern.
- Frequent power shortage.

Chapter 4: Results and Discussion

In this chapter, we draw a framework about how we work in research, how we collect data and describe different statistical, methods used in research. as well as the result and analysis of the work.

4.1 Study Population

The study population consists of delivered pregnant women in the last six months of the year (2016), and who were registered and followed up her ANC at UNRWA Health Centers –Gaza governorates- Cases will be risky pregnant women with thromboprophylaxis, and are characterized as alert or high-risk pregnancy according to UNRWA risk scoring program. Each case (risky with thromboprophylaxis) will be matched with normal pregnancy who is registered, followed up at UNRWA Health Centers and delivered at the same period. Matching criteria include place of living, the month of delivery and the clinic for follow up.

The study carried at UNRWA Primary Health Centers (Gaza Governorates), It carried at five Health Centers of UNRW mainly large clinics (North Gaza, Gaza, Middle Zoon, Khan-Younis, and Rafah).as we found North Gaza had the majority (58 cases) followed by Rafah (52 cases), then Gaza (40 cases), then Khanyounis (38 cases). Finally, the least clinic is Midzoon (32 cases), which is nearly total numbers 220 cases, these cases matched with the same number of another comparative group (control) who do not use thromboprophylaxis during pregnancy.

4.2 Data collection tools

Data collection tools divided into two main parts, as the following

i. Quantitative part
    a. Interviewed Questionnaire
    b. Medical Records Review
    c. Generic Study Review

ii. Qualitative part (In-depth interviews with concerned health providers)

The following Figure describes the explanation of this part

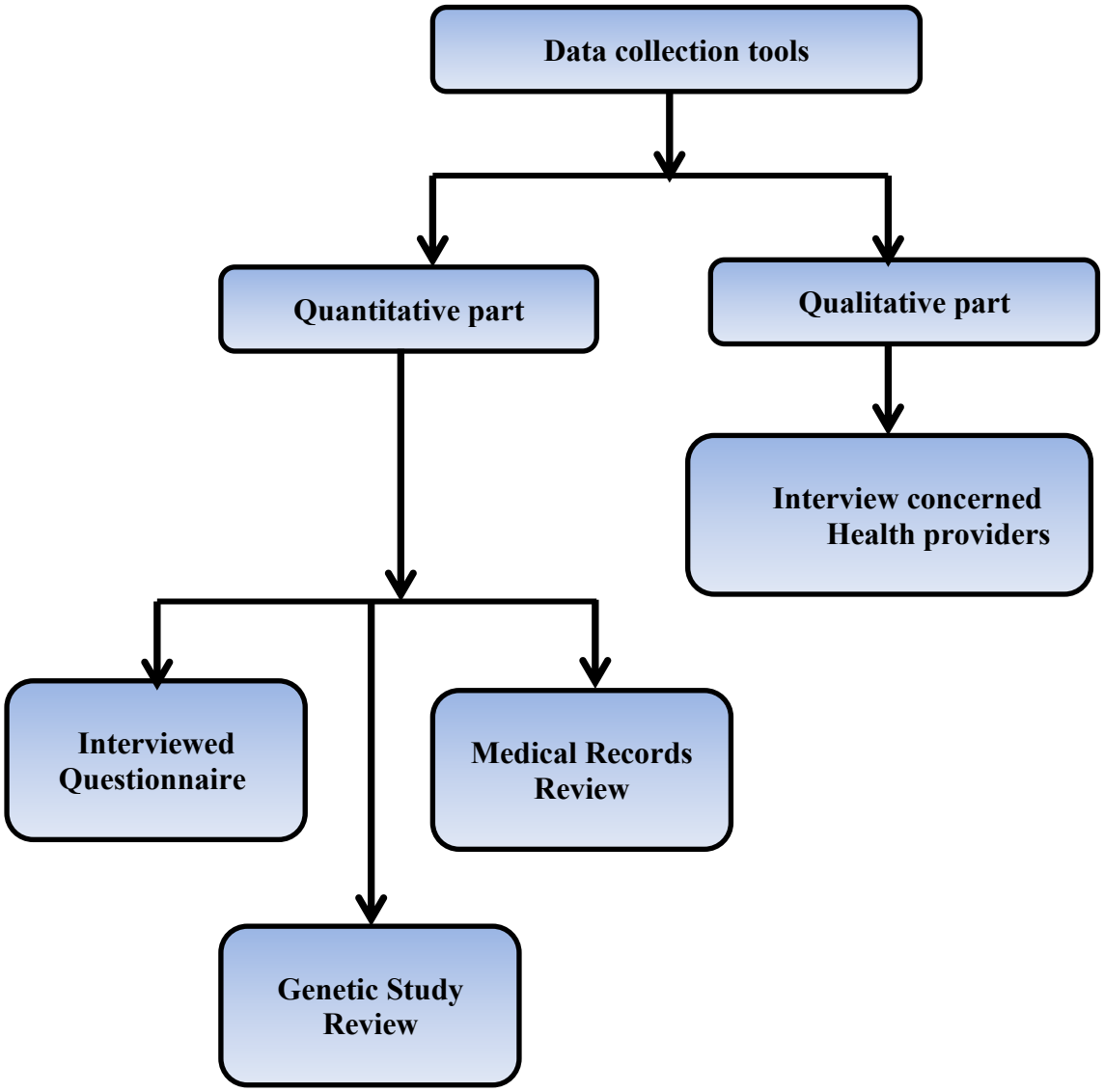


Figure 4.1 : Data collection tools

4.3 Interviewed questionnaire

The study questionnaire designed and prepared to compile information relating to the objectives of the study. An Arabic version of the questionnaire had been used during interviews with participants; the questionnaire had been reviewed by 7 experts who are qualified in many fields related to this study.

The interviewed questionnaire consists of 9 parts, as these main parts compared between both groups and describe the experience of thromboprophylaxis use among cases and different managerial practices.

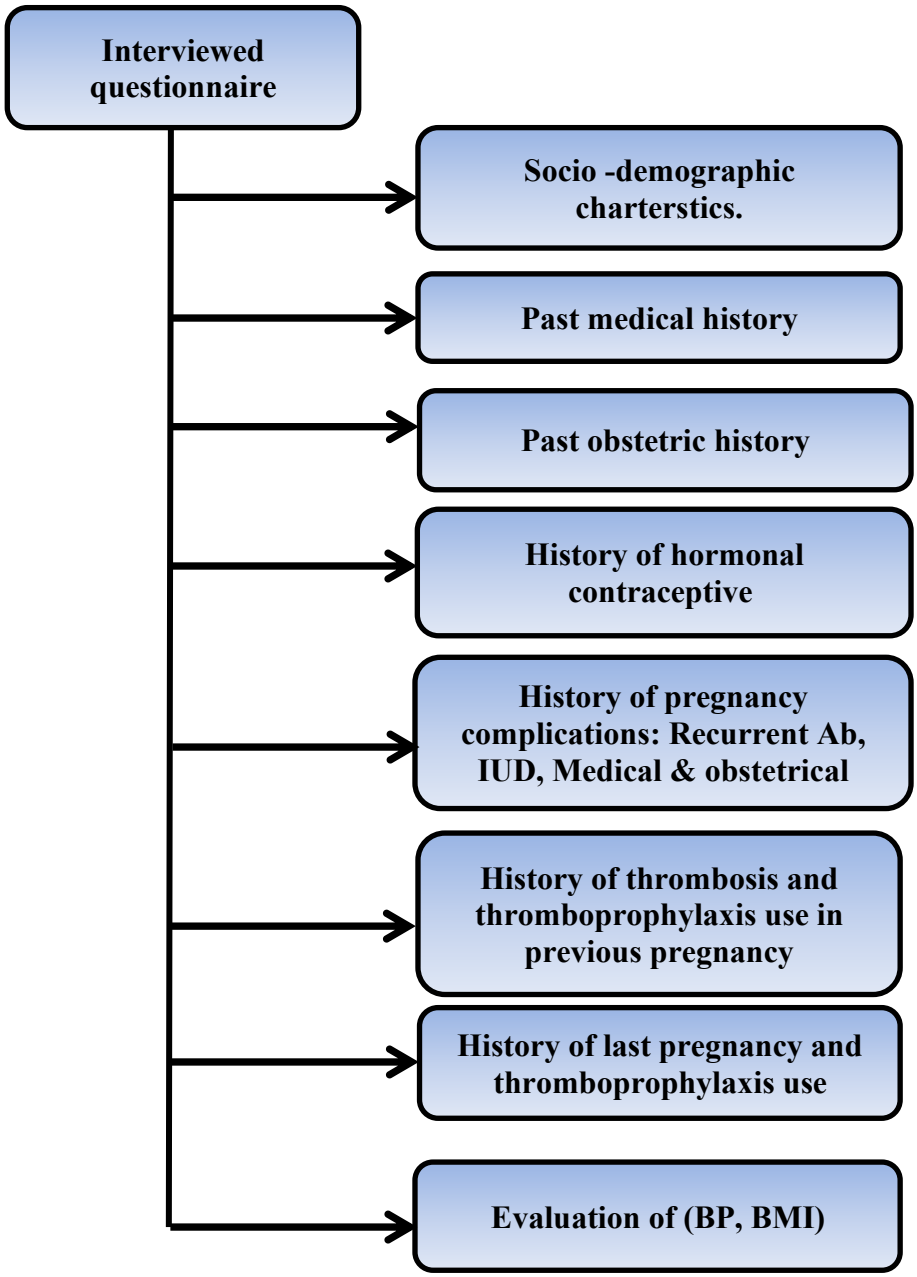


Figure 4.2 : Interviewed questionnaire

4.4 Medical records review

In this section we reviewed 100 files which were randomly selected from cases group, who used thromboprophylaxis during pregnancy, this review is done according to 3 main parts, which include, as described in chapter 4

i. Review of distribution of bad obstetric history
ii. Review of distribution of risk factors
iii. Review of Review of management practices

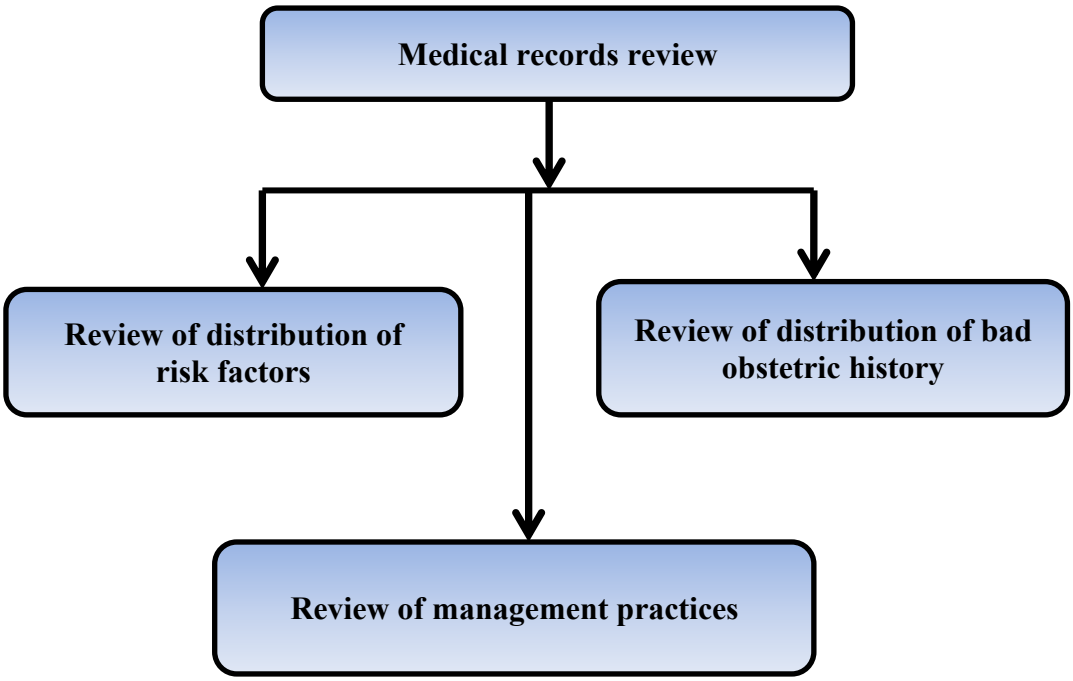


Figure 4.3: Medical records review.

4.5 Genetic molecular study review

According to the questionnaire results, 153 cases did investigation profile, 112 cases did molecular genetic study, we found 96 genetic molecular studies available with studied cases, was reviewed for 6 main genetic studies, 3 main different genetic alleles description

1. Prothrombin G2010A (homozygous, heterozygous, normal)
2. ACE 1/0 (homozygous, heterozygous, normal)
3. PAI - 4G/5G (homozygous, heterozygous, normal)
4. Factor v (homozygous, heterozygous, normal)
5. MTHFR (homozygous, heterozygous, normal)
6. Factor XIII (homozygous, heterozygous, normal)

4.6 Statistical design

The researcher used the Statistical Package for Social Sciences version 23 (SPSS, 2016) for data coding, entry, and analysis. Simple distribution and frequencies of the study variables, the cross tabulation, and normal chi-square had been applied P value had been calculated for the ordinal level measures ($P< 0.05$), variables that are statistically significant by chi-square test had been analyzed using odds ratio and 95% confidence interval.

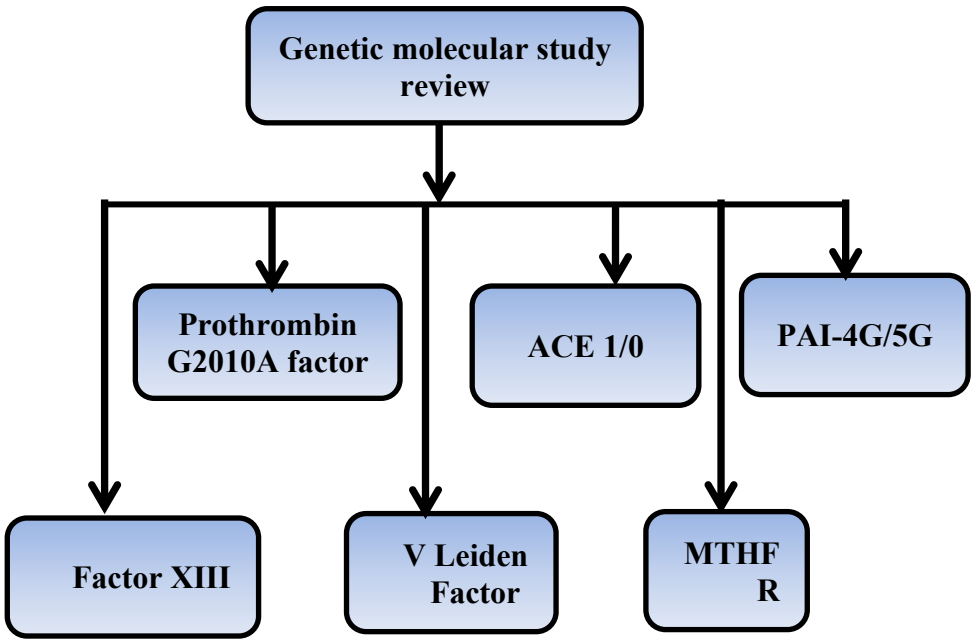


Figure 4.4: **Genetic molecular study reviews**

4.7 Statistical analysis

Chi-square (χ^2) test was used to establish the p-value using SPSS program.

4.7.1 Significance of results

- ✓ When P> 0.05 it is statistically not a significant difference.
- ✓ When P< 0.05 it is the statistically significant difference.
- ✓ When P< 0.01or P< 0.001 it is the highly statistically significant difference.

4.7.1 Significant of odds ratio

Odds ratios are used to compare the relative odds of the occurrence of the outcome of interest (e.g. disease or disorder), given exposure to the variable of interest (e.g. health characteristic, an aspect of medical history). The odds ratio can also be used to determine whether a particular exposure is a risk factor for a particular outcome and to compare the magnitude of various risk factors for that outcome.

- ✓ OR=1 Exposure does not affect odds of outcome
- ✓ OR>1 Exposure associated with higher odds of outcome
- ✓ OR<1 Exposure associated with lower odds of outcome

However, the odds ratio (OR), its standard error and 95% confidence interval are calculated according to (Altman, 1991).

4.8 Interviewed questionnaires

In this chapter, the researcher presents the main results of the study variables that were attained the study objectives, as it includes, this part first quantitative method which is interviewed questionnaire, as explained in previous chapter, the nature of the questionnaire, it consists of main 9 parts, which are related to the main study objectives we use a comparative study design, between both groups, cases in treatment group (220 cases), who use thromboprophylaxis during pregnancy, and control group who did not use thromboprophylaxis, this questionnaire compared the different determinants associated with both groups, it also described the experience of thromboprophylaxis use among treatment group, the results collected from UNRWA health centers as described in chapter 2 and chapter 4, analyzed according to the last version of SPSS by using, chi-square, P-value and odds ratio. The researcher highlights the findings of this study compared with other global and regional studies and tried to interpret the results and its implication.

4.9 Characteristics of the study population

This part explains the Distribution of cases by sociodemographic variables

4.9.1 Distribution of sociodemographic factors of wife

Table 4.1 summarizes the distribution of both treated group and non-treated group regarding sociodemographic factors, it compares the 220 treated women with 220 non treated women. matched by place of residence, clinic of registration and follow up and the month of delivery. In both groups, North Gaza governorate had the largest number of treated women (n=58, 26.4 %) as well as non-treated women, while middle governorate had the smallest number (n=32,14.5%), Rafah, Gaza and Khanyounis Governorates constitute 52, (23.6%), 40, (18.2%) &38, (17.3%), from the total percent of treated women and non-treated women. According to the place of living, the researcher also matches treated women and non-treated women, So women live in cities 42.75 % of treated women and 47.3 5% of non-treated women. Women who live in refugee camps were 54.5%of treated women and 44.1% of non-treated women, while 2.7% of treated women and 8.6% of non-treated women live in villages, as shown most of the women were living in camps and cities as Palestinian refugee demographic distribution (UNRWA, 2016). Regarding to

age groups distribution were divided into four groups, in which 38.6 % of treated clients and 40.9 % non-treated clients were located in the age group 26-30 years which constitute the majority group in the study, the other three groups, less than 20 years old, 20-25 years,

Table 4.1 Demographic characteristics of Wife (N=440)

Variables		Cases		Controls		Total	
		Freq.	%	Freq.	%	Freq.	%
Residency	North Gaza	58	26.4	58	26.4	116	26.4
	Gaza	40	18.2	40	18.2	80	18.2
	Midzoon	32	14.5	32	14.5	64	14.5
	Khanyounis	38	17.3	38	17.3	76	17.3
	Rafah	52	23.6	52	23.6	104	23.6
Place of living	city	94	42.7	104	47.3	198	45.0
	camp	120	54.5	97	44.1	217	49.3
	Village	6	2.7	19	8.6	25	5.7
Age	< 20	21	9.5	12	5.5	33	7.5
	20 – 25	62	28.2	83	37.7	145	33.0
	26 – 30	85	38.6	90	40.9	175	39.8
	> 30	52	23.6	35	15.9	87	19.8
Age at marriage	< 20	130	59.1	107	48.6	237	53.9
	20 – 25	80	36.4	100	45.5	180	40.9
	26 – 30	7	3.2	10	4.5	17	3.9
	> 30	3	1.4	3	1.4	6	1.4
Total Years of education	Primary school	17	7.7	107	48.6	31	7.0
	Preparatory school	53	24.1	100	45.5	56	12.7
	Secondary school	97	44.1	10	4.5	186	42.3
	University / collage	53	24.1	3	1.4	167	38.0
employment	Employed	30	13.6	32	14.5	62	14.1
	Unemployed	190	86.4	188	85.5	378	85.9
It yes, specify employer	Governmental	11	5.0	18	8.2	29	6.6
	Non-Governmental	6	2.7	12	5.5	18	4.1
	Self-employed	13	5.9	2	0,.9	15	3.4

more than 30 years,9.5 % of treated clients and 5.5 % of non –treated clients, 28.2 % of treated clients and 37.7 % of no-treated clients, and 23.6 % of treated clients and 15.9 % of non-treated clients respectively.According to the women age at marriage, were divided into four groups, it is clear from the table that 59.1% of treated women and 48.6% of non-treated women were married at age less than 20 years old. The other three groups 20-25,

26-30, &>30 years, 36.4 %of treated women and 45.5 % of non-treated women, 3.2 % of treated women and 4.5 %of non-treated women respectively, which that constitutes with UNRWA(2015), as percentage of women married by age <18 years at Gaza field 33%, and mean marital age at Gaza 19.2 (UNRWA, 2015). Regarding to the distribution, of women according to educational level, 7.7 % of total treated women, 48.6% of total non-treated women finished primary school, 24.1% of total treated women, 45.5% of non-treated women finished preparatory school, 44.1 % of total treated women, 4.5 %of total non-treated women finished secondary school, while 24.1 % of treated women, 1.4% of non-treated women finished diploma and university level as shown the education level is higher among treated women than non-treated women. Regarding the distribution of women according to their employment status,13.6% of treated women and 14.5% of non-treated women were employed, most of them are governmental employees, 5.9% of treated women, and 8.2 % of non-treated women respectively

4.9.2 Distribution of sociodemographic factors of husband

Table 4.2 summarizes demographic characteristics of husbands, as shown age groups like wife were divided into 4 major groups .it is clear from the table, the majority of the husband were older than 30 years in 53.2% of treated women and 44.1% of non-treated women, respectively. Other age groups, <20 years, 20-25 years, 26-30 years were 0.5% of controls, 13.2% of treated women and 18.2 of non-treated women husbands, 33.2 % of treated women and 37.3 % of non-treated women husbands, respectively. According to husband's age at marriage, as shown in the table, the majority of husband's ages at marriage were between 20-25 age group, 57.7% of treated women and 62.3% of non-treated respectively, other age groups <20 years, 26-30 years,& >30 years 11.4% of treated women and 10 % of untreated women, 26.4% of treated women and 24.5% of non-treated women and 4.5 % of treated cases and 3.2 % of non-treated, respectively.

Regarding the distribution of women husbands to the years of education as shown in table, 19.1% of treated women and 7.3 5% of non-treated women husbands had finished primary school level 14.5% of treated women and 5.9% of non-treated women husbands had finished preparatory school, while 36.4% of treated women and 33.2% of non-treated women husbands had finished secondary school level while 30% of treated women and 53.6% of non-treated women husbands had attained diploma and or a university degree. According to the employment status of husband, it is clear from that table that 68.2% of

treated women husbands and 59.5% of non-treated women husbands were not employed, 31.8% of treated women husbands and 40.5% of non-treated women husbands were employed, the majority of them were governmental employee (32.3% of treated women and 29.5% of non-treated women).

Table 4.2: Demographic characteristics of husbands (N=440)

Variables		Cases		Controls		Total	
		Freq.	%	Freq.	%	Freq.	%
Age	< 20	1	0.5	1	0.5	2	0.5
	20 – 25	29	13.2	40	18.2	69	15.7
	26 – 30	73	33.2	82	37.3	155	35.2
	> 30	117	53.2	97	44.1	214	48.6
Age at marriage	< 20	25	11.4	22	10.0	47	10.7
	20 – 25	127	57.7	137	62.3	264	60.0
	26 – 30	58	26.4	54	24.5	112	25.5
	> 30	10	4.5	7	3.2	17	3.9
Total Years of education	Primary school	42	19.1	16	7.3	58	13.2
	Preparatory school	32		13	5.9	45	10.2
	Secondary school	80	36.4	73	33.2	153	34.8
	University or collage	66	30.0	118	53.6	184	41.8
Employment	employed	70	31.8	89	40.5	158	35.9
	unemployed	150	68.2	131	59.5	282	64.1
If yes, specify type of employer	Governmental	67	30.5	65	29.5	133	30.2
	Non-Governmental	12	5.5	14	6.4	26	5.9
	Self-employed	71	32.3	52	23.6	123	28.0
Consanguineous Marriage	Yes	115	52.3	147	66.8	262	59.5
	No	105	47.7	73	33.2	91	40.5
Specify Consanguinity	First degree	55	25.0	36	16.4	91	20.7
	Second degree	34	15.5	30	13.6	64	14.5
	Far relative	16	7.3	7	3.2	23	5.2

On the other hand, 30.5% of treated women husbands and 23.6% of non-treated women husbands were self-employed, 5.5% of treated women and 6.4% of non-treated women were non-governmental employees. According to the consanguine marriage, as shown by

table (5.2.2), the majority of study population with positive consanguinity, 52.3% of treated women and 66.8% of non-treated women respectively, while 47.7% of treated women and 33.2 % of non-treated women were not, most of the consanguinity degrees, were first degree consanguinity, as shown by table (5.2.2), 25% of treated women and 16.4%of non-treated women with first degree consanguinity.

4.9.3 Economic level

Table 4.3: **Characteristics of economic level of the study population**

Variables		Cases		Controls		Total	
		Freq	%	Freq.	%	Freq.	%
Average family income	less than 1000 NIS.	140	63.6	136	61.8	276	62.7
	1500-2000 NIS.	36	16.4	52	23.6	88	20.0
	more than 2000 NIS.	44	20.0	32	14.5	76	17.3
House	Owned	184	83.6	179	81.4	363	82.5
	Rented	36	16.4	41	18.6	77	17.5
Type of house	Concrete house	154	70.0	169	76.8	323	73.4
	Asbestoses house	58	26.4	45	20.5	103	23.4
	Mud house	8	3.6	6	2.7	14	3.2
Number of rooms	One room	50	22.7	67	30.5	117	26.6
	Two rooms	83	37.7	78	35.5	161	36.6
	Three or more rooms	87	39.5	75	34.1	162	36.8

Table 4.3 summarizes economic level described among study population, by the following variables, average family income, type of house, and number of rooms, Regarding to the average of income, it is clear the majority of them, are less than 1000 NIS, 63.6% of treated women, 61.8% of non-treated women, others 1500 NIS-2000 NIS, &more than 2000 NIS.16.4% of treated women and 23.6% of non-treated women, 20% of treated women and 14.5 %of non-treated women, respectively. Regarding to the type of house, most of them are with owned house ,83.65% of treated women and 81.4%of non-treated women, respectively, most of them had concrete houses, 70 % of treated women and 76.8% of non-treated women but on the other hand, the majority of treated women are 39.5% had three or more, but the majority of non-treated women nearly,37.7% had 2 rooms, 22.7%of treated women and 30.5%of non-treated women have one room,

respectively. All these tables reflected the bad socioeconomic status and the poverty rate among the studied population which is constant with statically of Palestinian refugees.

4.10 Past medical history of the study population

The table 4.4 shows that the majority of non-treated women which is nearly 97.9% did not have chronic non-communicable diseases on the other hand, 87.3% of treated women did not have non-communicable diseases, while 12.7 % of them had non communicable diseases, the calculated chi-square is significant at p-value 0.000, which means that mothers in treated and non-treated conditions are not equal in distribution of chronic non-communicable diseases as odds ratio is (calculated 6.27), that means women who treated with thromboprophylaxis had a risk 6 times than non-treated women of exposure to non-communicable diseases.

Table 4.4: Relationship between past medical history non -communicable diseases and thromboprophylaxis use.

Variables			Cases ((220)		Controls			
			Freq.	%	Freq.	%	Chi	Sig
1	Is there a past history of Non-communicable diseases	Yes	٢٨	12.7	٥	2.3	17.33	.000
		No	١٩٢	87.3	٢١٥	97.7		
Odd ratio = 6.2708 95 % CI =2.3741 to 16.5634								

Table 4.5: Relationship between past medical history- hematological diseases- and thromboprophylaxis use

Variable			Cases (220)	
			Freq.	%
1	Is there a past history of Hematological Diseases?	Yes	76	34.5
		No	144	65.5
1.1	If you choose, yes specify	Congenital thrombophilia	37	48.7
		Acquired thrombophilia	11	14.5
		Thromboembolism disorder	28	36.8
1.2	If you choose i, ii specify	Lab.test done	44	91.7
		Lab. test not done	4	8.3

The table 4.5 part 1 summarizes that 76 cases with 34.5% of total treated women had chronic hematological diseases, while 144 cases with 65.5% of the total treated women did not have hematological diseases, on the other hand, none of the non-treated women had chronic hematological diseases, where calculated value of chi-square is significant at (P-value, 0.000), which is highly statistically significant, that means treated women is with high risk to be exposed to chronic hematological diseases, concerned health providers confirmed "*the use of thromboprophylaxis during pregnancy is a hematological decision, not an obestetriation decision*".

The table 4.5 part 1.1 summarizes 37 cases with 48.7% of the total treated women had congenital thrombophilia, 11 cases with 14.5% of total treated women had acquired thrombophilia and 28 cases (36.8% of cases) had thromboembolism disorders, which is that constant with Hellgren(2003), who confirmed in his study thrombophilia conditions is associated with 70-90%of risk of thrombosis, also that is constant with Robesteron et al (2006), showed significance association between acquired thrombophilia and the risk of thrombosis, also, Kupfeminc (2003), showed strong association between congenital thrombophilia and acquired thrombophilia, and the risk of thrombosis 2-15%&10-15% respectively.

The table 5.4 part 1.2 summarizes lab.test significance among cases with thrombophylxais use, regarding to the cases with thromboprophylaxis use had hematological diseases 44 with 91.7%of the treated women are laboratory-based diagnosis- and 4 with 8.3%of the total cases are not laboratory-based diagnosis, which that is constant with concerned health providers opinions that " *all women with a risk of thrombosis either bad medical history or bad obstetric history should be investigated well to the presence of thrombophilia"*, while other said "*Investigation should not be done in every case, medical history and obstetric history is enough to start thromboprophylaxis during pregnancy*".

Table (4.6 part 1) showed that 26 cases with 11.8% of total treated women cases had positive history of vascular diseases, while 194 cases with 88.2% of total treated women did not have history of vascular diseases, on the other hand only one case with 0.5% of non-treated women had a history of vascular disease, The calculated value of chi-square is highly significant at (P-value- 0.000, odds ratio 29.3), that means cases with

thromboprophylaxis use had a risk of 29.3 times than non-treated women of exposure to vascular diseases.

Regarding to the distribution of vascular diseases types among cases as shown in Table (4.6 part 1.1) , 14 cases with 54% of the total treated women had varicose veins, 3 cases with 12% of the total treated women had thrombophlebitis, 9 cases with 35% of the total treated women had deep venous thrombosis and no any reported cases of vasculitis,these results are constant with literature as James et al (2005), James et al (2006), Heir et al (2005), 80% of venous thromboembolism during pregnancy are deep venous thrombosis, also concerned health providers confirmed this strong association between vascular diseases and thromboprophylaxis one of them said that "*History of one DVT is one of the main indication of starting heparin therapy in pregnancy*", other said "*50% of VTE (venous thromboembolism) link between thromboprophylaxis and pregnancy loss* ".

Table 4.6: Relationship between past medical history -vascular diseases-and thromboprophylaxis use

Variables			Cases (220)	
			Freq.	%
1	Is there a past history of vascular diseases?	Yes	26	11.8
		No	194	88.2
1.1	If you choose, yes specify	Varicose veins	١٤	54
		Thrombophlebitis	3	12
		Deep Venous thrombosis	9	35
		Vascuilitis	٠	0

Table (4.7 part ١) described that 152 cases with 69.1% of total treated women, 62 women with 28.2% of total non-treated women had past history of surgical operations, On the other hand 68 cases with 30.9% of the total treated women, 158 women with 71.8% of the total non-treated women did not have history of surgical operations, calculated chi-square with statistically significant at (P-value 0.001,odds ratio 5.6), that means cases with thromboprophylaxis use had high proportion of positive history of surgical operations

than non-treated groups with a risk 5.6 times more than non-treated group, these results are constant with Gold, M. et al (2012), the risk of thrombosis and thromboprophylaxis need is increasing with positive history of surgical operations as patient with history of surgical operations is with a risk than non-surgical operations. (Odds ratio 21.72, CI 9.44-49.93).

Table 4.7: Relationship between past medical history - surgical operations-and thromboprophylaxis use

Variables			Cases (220)		Controls (220)			
			Freq.	%	Freq.	%	Chi	Sig
١	Is there a past history of surgical operations?	Yes	152	69.1	62	28.2	73.69	.000
		No	68	30.9	158	71.8		
١.1	If yes, specify Number of surgical operations	One	50	33	35	56	86.48	.000
		Two to five	81	53	27	44		
		More than	21	14	0	0		
١.2	Type of surgical operations	Cesarean	117	77	43	69	86.78	00
		Uterine	24	16	4	6		
		.Pelvic surgery	1	1	3	5		
		Abdominal	152	69.1	12	19		
		orthopedic surgery	68	30.9	0	0		

According to the Table (4.7 part ١.1) showed that 50 cases with 33% of treated women and 35 women with 56% of non-treated women had a history of one surgical operation, 81 cases with 53% of total treated women and 27 women with 44% of non-treated women had a history of two to five surgical but on the other hand 21 cases (14%) of the cases had a history of more than five surgical operations, while there was no one had more than 5 operations among non-treated group. the calculated chi-square is highly significant at (P-value 0.000), which showed that cases with thromoprolylaxis use had a proportion with a high number of past surgical operations than the non-treated group which is a strong risk factor.

Table (4.7 part ١.2) describes different surgical operations types distribution among both groups, 117 with 77% of total treated women and 43 with 69% of total non-treated women, had history of caesarean sections, 24 with 16% of treated women had a history of uterine surgery, while 4 with 6% of non-treated women had past history of uterine surgery, one with 1% of treated women, 3 with 5% of non-treated had a history of pelvic surgical operations 9 with 6% of treated and 12 with 19% of non-treated women had a history of abdominal surgery, while there one reported case with 1% of the total treated women with orthopedic surgery which that is not constant with Gold, M. et al (2012) the risk of thrombosis of orthopedic surgery, (with odds ratio 44, CI 42-47), also, and there is no any reported one of the non-treated women for orthopedic surgery, calculated chi-square is calculated and statistically significant at (P-value-0.000), as the proportion of different types of surgical operations is more with treated group rather than non-treated group, mainly with CS section and uterine surgery operations, which that is constant with Gold, M. et al (2012), most of CS surgery with (odds ratio 24, CI 23-26), Gynecology surgery with (odds 16, CI 13-19), Orthopedic surgery with (odds ratio 44, CI 42-47), most of the concerned health providers agreed with these results and one of them said "*When you check MHR, who use thromboprophylaxis use during pregnancy, you will find the most recurrent risk factor for that is CS* ".

Table 4.8: relationship between past medical history–family history-and thromboprophylaxis use

Variables			Cases (220)		Controls(220)			
			Freq.	%	Freq.	%	Chi	Sig
١	**Are there associated family diseases?**	Yes	31	14.09	7	3.2	2.880	0.090
		No	189	85.91	213	96.8		
١.1	**If yes, specify**	Congenital thrombophilia	8	25.8	0	0	-	-
		Acquired thrombophilia	4	12.9	0	0		
		SLE	2	6.5	0	0		
		Inflammatory bowel diseases	15	48.4	2	28.6		
		Rhematologica l diseases	2	6.5	5	71.4		

Odd ratio = 4.99 **95 % CI**= 2.1476 to 11.5986

Table (4.8 part١) describe that 31 cases with 14.09% of the total treated women and 7 women with 3.2 % of the total non-treated woman had family history diseases, while 189 cases with 85.9% of the total treated women and 213 women with 96.85% of the total non-treated women did not have family history diseases. Chi value is calculated and significant at (P-value-0.030, the odds ratio is 4.99), which is statically significant as treated women with Thromboprophylaxis use had more proportion with positive family history diseases than non-treated women,), that means cases with a risk 4.99 times than non-treated women in exposure to the family history diseases.

Table (4.8 part ١.1) describes the distribution of different types of family history diseases among studied groups, 25.8% of total treated women had positive family history of congenital thrombophilia, 12.9 %of total treated women had positive family history of acquired thrombophilia, 6.5%of total treated women had positive family history of SLE diseases, 48.4 % total treated women had positive family history of chronic inflammatory bowel diseases and 6.5 % of total cases with positive family history of rhematological diseases, on the other hand, 71.4% of total non-treated women had positive history of rhematological diseases and 28.6% of total non-treated women had positive family history of inflammatory bowel diseases, and there is no any reported women of positive family history of congenital or acquired thrombophilia and no any related numbers of SLE family history),that means positive family history is with significant value in thromboprophylaxis use , especially positive family history of thrombophilia, which that is constant with kupfemnic (2003), that all patients with a personal or family history of VTE should be considered for antenatal prophylaxis and be screened for thrombophilia, also, that agreed with concerned health providers opinions one of them said that "*family history of thrombophilia and thrombosis is a guide for clinician to look for thrombosis evidence in current pregnancy"* Other said that " *family history of VTE alone, in the absence of a personal history or other risk factors for VTE, does not increase the personal risk of VTE, but is sufficient to warrant antepartum thromboprophylaxis".*

4.11 Past Obstetric history of the study population

Table (4.9 part 1) show the relationship between past obstetric history and thromboprophylaxis use among treated group, where 23cases with 10.5 % of the total treated women and 53 women with 24.1% of the total non-treated women are primigravida, 21cases 55% of the total treated women and 142 women with 64.5% of the

total non-treated women are with Gravida two to Gravida five, 34.5% of treated women and 11.4 % of the non-treated women are gravid 6 or more, chi-square is calculated and is statically significant at (P-value- 0.000), that means the risk of thromboprophylaxis use is high with gravida 2 and more. Also the table shows that 56 cases with 25.5% of the treated women and 73women with 33.2% of the total non-treated women are Para one, 61.8% of treated women and 61.4%total non-treated women are Para two to Para five, while 12.7% of treated women and 5.5% of non-treated women are Para 6 or more respectively . chi-square is calculated and significant at (P-value-.013 as it is clear statically difference between both groups, so the risk of thromboprophylaxis use is high with Para 2 and more, which that is constant with Chan et al (2006), the risk for thrombosis, and the use for thromboprophylaxis is increasing in multipara, as it is more in cases of more than Para 2, also, concerned health providers agreed that one of them said "*Multigravida and Multipara will give a mirror about her obstetric history to be a guide for starting thromboprophylaxis use* "

Table 4.9: Past obstetric history relationship and thromboprophylaxis use

			cases (220)		controls (220)			
			Freq.	%	Freq.	%	Chi	Sig
1	**Gravida (Number of previous pregnancy)**	Primi gravida	٢٣	10.5	53	24.1	39.27	.000
		Gravida two to gravida five	١٢١	55.0	142	64.5		
		Gravida 6 or more	٧٦	34.5	25	11.4		
2	**Parity (number of previous alive complete deliveries)**	Para one	٥٦	25.5	73	33.2	8.644	.013
		Para two to para five	١٣٦	61.8	135	61.4		
		Para 6 or more	٢٨	12.7	12	5.5		
3	**Number of alive children**	Zero	١٦	7.3	6	2.7	5.572	.062
		One to two	٩٦	43.6	110	50.0		
		Three or more	١٠٨	49.1	104	47.3		

On the other hand, 49.1% of the total treated women and 47.3% of the total non-treated women had three and more alive children, 43.6% of total treated women, 50% of the total controls have one to two alive children,7.3% of the total cases did not have a live children,

in the same way,2.7% of the total controls did not have alive children . chi-square is calculated at P-value 0.062 which is statically not significant as there is no difference between both groups.

Regarding to the history of deal children as shown in table (4.10 part 4), 156 cases with 70.9% of the total treated women and 205 women with 93.2% of the total non-treated women did not have a history of dead children while 52 cases with 23.6% of total treated women and 13women with 5.9% of non-treated women had one to two dead children, 12 cases with 5.5% of total treated women and 2 women with 0.9% of total non-treated women had three and more dead children, Chi secure is calculated and is highly statistically significant at (P-value- 0.000), which that means there is a statistical difference between both groups, women with thromboprophylaxis had a significant history of dead

Table 4.10: Relationship between the history of dead children and thromboprop-hylaxis use

Variables			Cases (220)		Controls(220)			
			Freq.	%	Freq.	%	Chi	Sig
1	Number of dead children	Zero	١٥٦	70.9	٢٠٥	93.2	37.19	.000
		One to two	٥٢	23.6	١٣	5.9		
		Three or more	١٢	5.5	٢	0.9		
1.1	Child age at Death	28 GA. weeks - less than one week	٣٥	15.9	٤	1.8	42.60	.000
		One week-less than 28 days	١٣	5.9	٢	0.9		
		29 days to one year	١٥	6.8	٧	3.2		
		More than one year	١	0.5	٢	0.9		
1.2	Causes of death	Unknown	٣٧	16.8	٧	3.2	41.20	.000
		Birth trauma	٠	0.0	٢٠٥	93.2		
		Congenital anomalies	١٧	7.7	١٣	5.9		
		Accidents or injury	١	0.5	٢	0.9		
		others	٩	4.1	٤	1.8		

children, regarding to the age of dead children, 15.9% of treated women and 1.8% of non-treated women had dead children at age less than one week, 5.9% of treated women and

0.9% of non-treated women had dead children at age 29 days to one year, 0.5% of treated women and 0.9%of non-treated women had dead children at age more than one year.
chi-square is calculated and is highly significant at (P-value- 0.000), which is highly statically significant, women who treated women with thromboprophylaxis had history of high proportion of dead children in perinatal and neonatal period (28 weeks gestational age to less than one week, one week to 28 days of infancy period) than non-treated women, that is constant with (Marquard, 2002), who describes there is a strong association, between thromboprophylaxis and thrombophilia to be diagnosed in 50%-65 %of women with history of unexplained recurrent fetal loss, also, Ohel and his colleagues (2000) said that women with thrombophilia have an increased Percentage of losses at later stage of gestations, also, concerned health providers agreed with that, as they said "*Thromboprophylaxis use in pregnancy is improving stillbirth, IUFD, and perinatal mortality"* .

Regarding to the causes of death among dead children, the majority of causes of dead children is unknown cause, 16.8% of total treated women and 3.2% of non-treated women had dead children with unknown causes, 7.7% of treated women, 0.9% of non-treated women had history of dead children due to congenital anomalies, 0.5% of treated women and 0.9% of non-treated women had history of dead children due to accidents or injury causes while 4.1% of treated women and 1.8% of non-treated women had other causes (some of them linked it to the presence of thrombophilia) and there is no any proportion related to birth trauma, chi-square is calculated and significant at(P-value- 0.000), which is highly statically significant as there is a clear statically difference between both groups, as most causes are unknown, it can be related to the presence of thrombophilia, these results are constant with Kupferminc (2002), who confirmed that women with unexplained IUFD nearly 42.5 % of cases in the study group compared with 15 % in controls are at risk of thrombosis, also concerned health providers agreed with that "*Unknown causes of SB, IUFD, and perinatal mortality is related to the presence of unknown thrombophilia and the need of thromboprophylaxis use ".*

Table (4.11 part ١) presents relationship between the Thromboprophylaxis use and past history of infertility, 30.5% of treated women and 3.2% of non-treated women had a history of infertility, chi-square is calculated and is significant at (P-value-0.001,odds

ratio13.3), as there is a significant difference between both groups, treated women had a risk 13.3 times than non-treated women to infertility.

Table 4.11: Relationship between the history of infertility and thromboprophylaxis use

Variables			Case(220)		Control (220)			
			Freq	%	Freq.	%	Chi	Sig
1	history of infertility	Yes	٦٧	30.5	٧	3.2	58.48	.000
		No	١٥٣	69.5	٢١٣	96.8		
1.1	Years of infertility	if yes specify					59.35	.000
		One to two years	١٩	28.4	٤	57.1		
		Three to five	٢٧	40.3	٢	28.6		
		More than five years	٢١	31.3	١	14.3		
1.2	History of associated production technique	Yes	58	86.6	٤	57.1	59.86	.000
		No	9	13.4	3	42.9		
1.2.1	if yes specify	IVF (In vitro fertilization)	28	48.3	3	75	55.04	.000
		IUI (Intra uterine insemination	16	27.6	1	25		
		Ovulation induction	14	24.1	0	0		
If your answer 1 and 2			**44**		**4**			
1.2.2	Number of IVF failure	Non	19	43.1	4	100	38.86	.000
		1-2	21	47.7	0	0		
		More than two	4	9.1	0	0		

- **Odd ratio = 13.3249 95 % CI= 5.9528 to 29.8271**

Regarding to the years of infertility, the majority of treated women, 40.3% of them had a history of infertility three to five years, 31.3% of them had a history of infertility more than 5 years, and 28.4% of total treated women had a history of infertility one to two years, on the other hand, the majority of non-treated women, 57.1% of them had a history of

infertility years (one to two years),28.6% of them had a history of infertility years (three to five years) and 14.3% of them had a history of infertility years more than five years, chi-square is calculated and is significant at (P- value-0.000) as there is clear difference between both groups in infertility years distribution, as treated women had a high proportion of years of infertility, as most of them, had infertility years more than 3 years.

The results are consistent with Azem (2004), high frequency of thrombophilia was found in the subgroups of women with implementation failure (17.8 %), compared to the group of fertile women, also, that confirmed by Turkish study, in 2009, as case-control study comparing 51 women with implementation failure , and group of 50 fertile women, a finding of at least one thrombophilia factor (62.7%)was more common in the group of women with implementation of failure compared to the control group (53.9 %), but these results are not consistent with Marinelli et al (2003) who conducted a case-control study with the largest sample size evaluated up to the present time and found no evidence of a high frequency of thrombophilia in infertile women .

As shown by table (4.11 part ١.2) 86.6% of treated women who had history of infertility had history of associated production technique and 57.1% of non-treated women who had history of infertility had history of associated production technique , odds ratio is calculated (4.8),that means a risk is 4.8 times among treated women than non-treated women to risk of pregnancy induction.

Regarding the types of associated reproduction technique among who suffered from infertility 48.3% of treated women had IVF, 75 % of non-treated women had IVF, while 27.6% of treated women had IUI and 25 % of non-treated women had IUI, on the other hand, 24.1% of treated women had a spontaneous induction. Regarding to the times of success and failure among who suffered from infertility and tried to do pregnancy induction with (IVF- IUI) as shown by table (4.11 part ١.3) 47.7% of treated women had on to two success times, 43.1% of treated women had no history of success, 9.1%of treated women had more than two times of success, While non-treated women had no history of success time of (IVF, IUI), chi-square is calculated at (P-value-0.000), which indicated a high statistically significant difference between both groups as treated women had varying history of success and failure times, the majority of treated women had failure one to two times of (IVF-IUI) as that indicates the use of thromboprophylaxis, on the other hand,

thromboprophylaxis use is improving the infertility induction outcome which that is constant with concerned health providers opinions, as one of them said *that" thromboprophylaxis is indicted at a long time of infertility and in cases with IVF i failure more than twice* ", on the other hand, one of them said "*Thromboprophylaxis use is overestimated in cases with infertility, as many cases had infertility and IVF, and they succeed their pregnancies "*

Table 4.12: Relationship between the history of low birth weight and preterm labor with thromboprophylaxis use

Variables			Case 220)		Control(220)			
			Fre	%	Freq.	%	Chi	Sig
1	Is there a history of low birth weight?(fetal weight <2500gm)	Yes	53	24.1	27	12.3	10.32	.001
		No	167	75.9	193	87.8		
1.1	the weight of the baby	if yes specify					14.50	.001
		less than or equal to 1.5 kg	15	28.3	2	7.4		
		2- > 1.5 -2.5 kg	38	71.7	25	92.6		
1.2	How many times do you have it?	1-once	39	73.6	18	66.7	13.18	.004
		2-twice	8	15.1	8	29.6		
		More than twice	6	11.3	1	3.71		
1.3	Is there a history of preterm labor?	Yes	41	77.4	16	59.3	12.88	.002
		No	12	22.6	11	40.7		
If yes, answer the following			٤١		١٦			
1.3.1	Gestational age at delivery	< 28 weeks	3	7.41	3	18.8	14.47	.002
		28-32 weeks	20	48.8	5	31.3		
		34-36 weeks	18	43.9	8	50		

Odd ratio = 2.2686 **95 % CI**= 1.3655 to 3.7688 For equation ١
Odd ratio = 2.3490 **95 % CI**= 0.8628 to 6.3952 For equation ١.٣

Table (4.12 part ١) presents relationship between history of low birth weight and preterm labor with thromboprophylaxis use during pregnancy, as shown by table 24.1% of treated women and 12.3% of non-treated women had a history of low birth weight babies while 75.9% of treated women and 87.8% of non-treated women did not have a history of low

birth weight babies, chi square is calculated and is significant at (P-value-0.001, odds ratio 2.26) which indicated there is a significant difference between both groups, so treated women with thromboprophylaxis had high 2.26 times of risk of history of low birth weight than non-treated women, regarding to the weight of low birth weight babies among who suffered from a history of low birth weight babies 28.3% of treated women and 7.4% of non-treated women had baby weight less than or equal to 1.5 kg while 71.7% of treated women and 92.6% of non-treated women had baby weight more than 1.5 kg to less than 2.5kg, chi-square is calculated and significant at (P-value-0.001), which is showing a statistical difference between both groups as treated women are with high proportion to have low birth weight, especially below 1.5 kg, which that is consistent with concerned health providers view, both of them said that "Fetal U/S is a guide of detection, abnormal fetal growth ,and to start thromboprophylaxis in pregnancy", also, that is consistent with DeVries JIP.,(1999),that thrombophilia was documented in 38% of women delivering babies whose birth weight was below the fifth percentile, compared with an estimated 2% to 3% in the general control population, also, while on the other hand Kupferminc et al (1999) confirmed that association with thrombophilia and the need for thromboprophylaxis use remains controversial, with conflicting results from different studies, In one recent study, thrombophilia and thromboprophylaxis need was found in 20% of the women with preeclampsia, placental abruption, fetal growth retardation, or stillbirth compared to only 6% of control women without these complications (odds ratio 3.7), regarding to the times of recurrence of history of low birth weight as shown by table (٤،١٢), 73.6% of treated women and 66.7% of non-treated women had once of low birth weight babies, 15.1% of treated women and 29.6% of non-treated women had twice of low birth weight babies, while 11.3%of treated women and 37.1% of non-treated women had more than twice history of low birth weight, chi-square is calculated and significant at (P-value 0.004) which indicated statically difference between both groups, also, the table shows the relationship between low birth weight babies and history of preterm labor, 74.4% of the total treated women who had a history of low birth weight babies with a history of preterm labor, while 22.6% of non-treated women of low birth weight with history of preterm labor, in the other hand 59.3% of non-treated women had a history of low birth weight babies with a history of preterm labor and 40.7% of non-treated women who had a history of low birth weight babies without history of preterm labor, chi-square is calculated and significant at (P-value-0.002, odds ratio2.3), which indicated a statically difference between both groups as cases with thromboproplyxis use had high proportion of

history of low birth weight labor, and preterm with a risk 2.3 times than non-treated women, also as shown by table 48.8% of total treated women with history of preterm labor that occurred at gestational age (28-32 weeks), 43.9% of total treated women with history of preterm labor occurred at gestational age (34-36 weeks) and 7.4% of total treated women with preterm labor occurred at gestational age less than 28 weeks, regarding to non-treated women, the majority of them 50% with history of preterm labor occurred at gestational age 34-36 weeks, 31.3% of non-treated women with history of preterm labor occurred at 28-32 weeks, while 18.8% occurred at less than 28 weeks, Chi square is calculated and significant at (P-value-0.002) which that indicated statically differences as between both groups, that means cases with thromboprophylaxis use had a risk of premature delivery from 28 weeks to 36 weeks.

Table 4.13: Relationship between a history of abortion (Miscarriages) and thromboprophylaxis use

Variables			Case (220)		Control(220)			
			Freq	%	Freq	%	Chi	Sig
7	**Is there a history of miscarriages?**	Yes	171	77.7	35	15.9	168.82	.000
		No	49	22.3	185	84.1		
If yes, answer the following			171		35			
٧.1	**a number of miscarriages?**	One	35	20.5	24	68.6	188.21	.000
		Two	40	23.4	6	17.1		
		More than Two	96	56.1	5	14.3		
٧. ١,١	**If two or// more, were they consecutive?**	Consecutive	109	63.7	15	42.9	171.81	.000
		Non consecutive	62	36.3	20	57.1		
٧,٢	**Pregnancy age at abortion "Gestational age of abortion"**	One Week to 12 week Pregnancy	104	60.8	٢٦	74.2	189.61	.000
		From 13 weeks to 20 weeks Pregnancy	21	12.2	٣	8.57		
		More than 20 weeks Pregnancy	9	5.26	١	2.86		
		Diverse	37	21.6	٥	14.2		

Odd ratio = 18.4461 95 % CI= 11.4024 to 29.8410

Table (4.13) summarizes the relationship between thromboprophylaxis use and history of miscarriage, 77.7% of treated women had a history of miscarriages, while 22.3% of treated women did not have a history of miscarriages, regarding to non-treated women 15.9% of non-treated women had a history of miscarriages, while 84.1% of non-treated women did not have a history of miscarriages, chi-square is calculated and is highly significant at (P-value-0.000,odds ratio18.44), which indicated a significant difference between both groups, as treated women had a risk 18.44) times than non-treated women, that is consistent with Marquard (2009), thrombophilia and the need of thromboprophylaxis has been diagnosed in 50%-60% of patients with history of unexplained recurrent fetal loss, also concerned health providers confirmed that "*if you did not find a cause to unknown fetal loss, you should start thromboprophylaxis to improve outcome ".*

Regarding to the distribution of history of miscarriages numbers which is divided into 3 groups 56.1% of treated women had more than two, 23.4% of the non-treated women had two times and 20.5% of treated women had once abortion, while 68.6% of non-treated women had once, 17.1% of treated women had two and 14.3% of non-treated women had more than two times frequency, chi-square is calculated and significant at (P-value 0.000) which indicated statistically difference between both groups, women with thromboprophylaxis use had a history of risk to habitual miscarriages than non-treated women, which "*That is a clue for many Obstetricians to start thromboprophylaxis in pregnancy to avoid habitual abortions* "as concerned health providers said.

Regarding to the consecutive and nonconsecutive, the table describes that the majority of women with thromboprophylaxis use, 63.7% of treated women had a history of consecutive abortions and 36.3% of treated women had non-consecutive abortion, regarding to non-treated women the majority of them, 57.1% had non- consecutive abortions, while 42.9% of non-treated women had consecutive abortions, chi-square is calculated and highly significant at (P-value-0.000), which indicated statistically difference between both groups, as treated women had high more proportion of consecutive abortions than non-treated women, which that is consistent with concerned health providers opinions "*the need to improve habitual abortions is starting thromboprophylaxis"*, also, that is consistent with foka et al (2000)thrombophilia and the need of thromboprophylaxis use,

reported a frequency of 9 % of in women with recurrent miscarriages, frequency of 2 % occurred in control group .

4.12 History of hormonal contraceptive use

Table 4.14: Relationship between contraceptive pills use and thromboproph-ylaixs use

Variable			Case (220)		Control (220)			
			Freq.	%	Freq.	%	Chi	Sig
1	Is there a history of contraceptive pills use	Yes	47	21.4	41	18.6	.511	.475
		No	173	78.6	179	81.4		
1.1	If yes, specify							
	Type of contraceptive pills	Minipills	18	38.3	21	51.2	4.116	.249
		Combined oral contraceptive pills	26	55.3	20	48.8		
		Injectable hormone(DHPA injection	3	6.4	0	0.0		
1.2	Duration of use	Less than 2 years	41	87.2	29	70.7	6.445	.092
		2 years -5 years	6	12.8	8	19.5		
		More than 5 years	0	0.0	4	9.8		

Odd ratio = 1.1861 95 % CI= 0.7427 to 1.8941

Regarding to the gestational age of miscarriages, 60.8% of treated women and 74.2%of non-treated women had history of pregnancy loss at gestational age from four weeks to 12 weeks (1sttrimester), 12.2% of treated women had a history of pregnancy loss from 13weeks to 20weeks gestational age of pregnancy, 8.57% of total non-treated women had a history of pregnancy loss at gestational age from 13 weeks to 20 weeks, 5.26% of treated women had a history of miscarriages at gestational age more than 20 weeks, 2.86% of non-treated women had a history of pregnancy loss at gestational age more than 20 weeks, calculated chi-square is significant at (P-value-0.000), as cases with high proportion of miscarriages had occurred at first trimester gestational age (9 weeks to 12 weeks pregnancy), that is consistent with Brenner and colleagues(1999), thrombophilia and the

need to thromboprophylaxis is increasing with 3 or more first trimester loss, 2 or more second trimester loss or one or more with third trimester loss. 49% of women with pregnancy loss had a thrombophilia compared to 22 %of controls.

Table (4.14) summarizes relationship between history of hormonal contraceptive use and thromboprophylaxis use as shown, 21.4% of treated women and 18.6% of non-treated women had positive history of Thromboprophylaxis use while 78.6% of treated women and 81.4% of non-treated women didn't have history of hormonal contraceptive use, chi-square is calculated and significant at (P-value-0.475, odds ratio1.1) which is not statistically significant that indicated there are no differences between both groups as both of them with the same history of hormonal contraceptive use, that is not consistent with Yen et al (2013) a strong relation was found between the use of oral contra-captives and the risk of thrombosis and the use of thromboprophylaxis, that also is confirmed in J.AM Study (1979), a perspective study by the Royal College of General Practitioners reported that the risk of developing deep venous thrombosis of the legs in women taking oral contraceptives was 5.66 times higher than women not on medication.

Regarding to the distribution of hormonal Contraceptive use between both groups 38.3% of total treated women used combined oral contraceptive pills and 6.4% of total treated women used injectable hormone (DMPA) injection, while 51.2% of total non-treated women used min-pills, 48.8% of total non-treated women used combined oral contraceptive pills and there are no women of non-treated women used injectable hormone injection, chi-square is calculated to be significant at (P-value 0.2496) that indicated there is no statically difference between both groups, regarding to type of hormonal contraceptive use, 87.2% of total treated women and 70.2% of total non-treated women use hormonal contraceptive less than 2 years, 12.8% of total treated women and 19.5% used hormonal contraceptive method from 2 years to five years, while non-treated women used hormonal contraceptive more than five years and no reported case of treated women used hormonal contraceptive more than 5 years, chi-square is calculated and is significant at (P-value 0.092) which is not statically significant, as there is no difference between in the duration of hormonal contraceptive methods use .

4.13 History of pregnancy complications

In this part we asked about the presence of the previous history of pregnancy complications and compare both groups, also we asked about main pregnancy complications (PIH, GDM, PET, APH, PPH).

Table 4.15: Relationship between the history of pregnancy complications and thromboprophylaxis use

Variables			Cases (220)		Controls 220)			
			Fre	%	Freq.	%	Chi	Sig
1	Is there a history of pregnancy complicated diseases?	Yes	٩٣	42.3	٢٣	10.5	57.36	.0001
		No	١٢٧	57.8	١٩٧	88.2		

Table(4.15) present a comparison between groups in their history of pregnancy complications, as shown by table 42.3 %of total treated women had positive history of pregnancy complicated diseases, while only 10.5 % of total non-treated women had a history of pregnancy complicated diseases, while 57.8 %of total treated women and 88.2 %of total non-treated women did not have a history of pregnancy complicated diseases, chi-square is calculated and significant at (P-value- 0.000, odds ratio 6.2)which indicated highly statically differences between both groups, as treated women had high risk 6 times risk than non-treated women of history of pregnancy complicated diseases, concerned health providers agreed with that "*thromboprophylaxis will improve the circulation of placenta, so will improve pregnancy complications especially preeclampsia and abruption placenta*" .

4.14 History of Thrombosis and thromboprophylaxis use in previous pregnancies.

Table 4.16: Relationship between the history of thrombosis and thromboprophylaxis use

Variables			Cases (220)	
			Freq.	%
1	Is there a history of Thrombosis in pregnancy?	Yes	5	٢,٣
		No	215	97.7

Table (4.16) compares between both groups, in their history of thrombosis during previous pregnancies, as shown cases with thromboprophylaxis use 2.3%total treated women had a history of thrombosis evidence in their pregnancy while 100% of non-treated women did not have a history of thrombosis, chi-square is calculated and significant at (P-value- .000), which is highly statistically significant, treated women with thromboprophylaxis use had a high proportion of thrombosis, which that confirmed by concerned health provider, one of them said that "*Thromboprophylaxis use is really needed when there is a clear thrombosis in previous pregnancies, which is indicated for medically sound basic diagnosis ",*

Rregarding to the distribution of different types of thrombosis, 60%of total treated women who had history of thrombosis are DVT, (1.3% of treated women), 20% of total treated women who had history of thrombosis are pulmonary embolism ,(0.04%of treated women), 20% of total treated women who had history of thrombosis are arterial thrombosis, (0.04%of treated women),, literature confirms thromboembolism represents one of the main causes of maternal mortality with overall prevalence during pregnancy is approximately 2 per 1000 deliveries, approximately 20%, 2005), many literatures is confirming the thromboprophylaxis management among pregnant ladies with previous VTE, estimates of the rate of recurrent venous thrombosis during pregnancy with women positive history of VTE have varied between zero and 13%(American Colleague of Chest Physicians), Ginsberg (2001) agreed with that and recommend thromboprophylaxis during pregnancy and postpartum period is playing an important role in a history VTE.

Table (4.17) describes history of thromboprophylaxis use in previous pregnancies of studied cases (who used thromboprophylaxis in their last pregnancy) .82.8 %of total cases (majority of cases) used thromboprophylaxis in their last previous pregnancies, while 17.3 % of total cases did not use thromboprophylaxis in their previous pregnancies ,That is consistent with concerned health providers view who confirmed "*Thromboprophylaxis use is changing from one pregnancy to another one is due to present pregnancy risk and US findings"* .

Regarding the frequency and the continuity of heparin use in their previous pregnancies, 24.1 %of total cases used heparin therapy in all pregnancies and 58.6 % of total cases did not use heparin therapy in their pregnancies (calculated chi-square 310,3, p-value .0001),

Table 4.17: History of thromboprophylaxis use in previous pregnancies

Variables			Cases (220)	
			Freq.	%
١	Did you take any thromboprophylaxis in previous pregnancies?	Yes	١٨٢	82.8
		No	٣٨	17.3
If your answer yes, specify				
١.1	Was it used in all pregnancies?	Yes	53	24.1
		No	129	58.6
	If No specify			
١.1.1	What was the outcome of that pregnancy?	An abortion	49	38.0
		Alive birth	54	41.9
		Early fetal death	16	12.4
		Congenitally malformed baby	3	2.3
		Intra uterine fetal death.	2	1.6
		IUGR	0	0.0
		Early neonatal mortality	1	0.8
		Low birth weight baby	4	3.1
١.1.2	Is there associated complications of that pregnancy	Yes	22	17.1
		No	107	82.9
	If yes, specify			
١.1.2.1	What was the associated pregnancy complications in the index pregnancy	PIH	15	68.2
		APH	2	9.1
		GDM	3	13.6
		PPH	2	9.1
		both (1,3)	0	0.0
		DVT	0	0.0
١.1.2.2	Was that pregnancy associated with preterm labor	Yes	7	31.8
		No	15	68.2

Regarding to the outcome of pregnancy which heparin therapy was not used, 41.9 %of total cases had alive birth ,38 %of total cases had abortion ,12.4 % of total cases had early fetal death, 2.3% of total cases had congenital malformed baby ,1.6 % of total cases had

intrauterine fetal death , 0.8 %o is of total cases had early neonatal mortalities and 3.1 % of total cases had low birth weight babies while there is no any reported cases of IUGR .

According to pregnancy complications, which heparin therapy was not used, 82.9%of their pregnancies were without complications and 17.1 % of their pregnancies were with complications . Regarding to the types of pregnancy complications in that pregnancies, which heparin was not uses, 68.2 %of total cases complicated by PIH, 13.6 % of total cases complicated by GDM, 9.1%of total cases complicated by PPH , while there are no reported cases complicated with PIH and GDM or reported cases of DVT. Also as shown by the table, 31,5 % of that index pregnancy associated with preterm labor and 68.2 %of total cases not associated with preterm labor in that pregnancy

4.15 History of last pregnancy and thromboprophylaxis use

History of last pregnancy in this part includes many variables we asked about it, some of these variables were compared between both groups (cases and controls), others variables were only related to cases, variables which asked about experiences of thromboprophylaxis use.

4.15.1 Last pregnancy outcomes and thromboprophylaxis use

Table 4.18: last pregnancy outcomes and thromboprophylaxis use.

Variables			Cases (220)		Controls(220)			
			Freq.	%	Freq.	%	Chi	Sig
1	What was the outcome of last pregnancy?	Abortion	٢٤	10.9	٤	1.8	29.43	.000
		Alive baby	١٧٢	78.2	٢٠٨	94.5		
		Premature delivery	٨	3.6	٦	2.7		
		Congenital anomalies	٣	1.4	٠	0.0		
		Early fetal death	٩	4.1	٢	0.9		
		Perinatal mortality	٤	1.8	٠	0.0		
1.1	If your answer “ ii ” the weight of last a live baby	< ٢٥٠٠gm	٢٧	15.7	٢٠	9.6	29.44	.000
		٣٥٠٠-٢٥٠٠gm	١٠٦	51.0	١٣١	63.0		
		٤٥٠٠- ٣٥٠٠ gm	٣٦	17.3	٥٥	26.4		
		>4500 gm	٣	1.4	٢	1.0		

As shown by table (4.18) describe the outcome of last pregnancy, which type of heparin was used, 78.2 %of total cases delivered alive birth,10.9 % of total cases had abortion, 3.6 % of total cases had premature delivery, 1,4 % of total cases had baby with congenital anomalies, 4.1 of total cases had early fetal deaths and1.8 % of total cases had perinatal mortality while 94 .5 % of untreated women had alive baby, 2.7 %of untreated women had premature delivery, 0.9 % of untreated women had early fetal deaths but there are no reported numbers of congenital anomalies and perinatal mortalities chi-square is calculated to significant at (P-value 0.000) which indicates statically differences between both groups as they differ in their last pregnancy outcome, concerned health providers confirmed that by their words "*In the past many clients did not know the cause of their fetal loss, recently thromboprophylaxis use improve really the outcome of many pregnant women ",*Also, in Carpe et al (2003) study confirmed that the live birth rate was higher in women treated with heparin therapy, 26(70.2%) of 37 compared with 21(43.8%) of 48 in untreated patients.

Regarding to the weight of delivered alive baby in both groups, the majority of treated women (who use thromboprophylaxis), and untreated women (who did not use thromboprophylaxis) had normal birth weight (2500gm-3500gm), 51 % and 63 % respectively,15.7 % and 9.6 %of treated and untreated women had low birth weight (less than 2500 gm.) respectively while 17.3% and 26.4%of treated and untreated women had a live baby weight (3500gm-4500gm) respectively, 1.4 % and 1% of treated and untreated women had macrocosmic babies (more than 4500) respectively, chi-square is calculated to be significant at (P-value- 0.000), which indicated significant statistical difference between both groups, as untreated women had high proportion of normal live birth weight than treated women, and cases who used thromboprophylaxis had higher proportion of low birth weight than untreated women as shown by table(5.9.1) thromboprophylaxis use is improving pregnancy outcome especially live birth weight , but some of them still had abnormal birth weight of alive baby mostly low birth weight, "*which that indicated for further investigation, or adjusting the dose of thromboprophylaxis use* " as concerned health providers said.

4.15.2 Thromboprophylaxis used in last pregnancy

In this part the only group who used thromboprophylaxis answered questions as there is no single untreated woman used thromboprophylaxis according to the sampling method which described in chapter(3), The following table shows the experience of thromboprophylaxis use among cases (thromboprophylaxis use)

Table 4.19-A: Thromboprophylaxis used in the last pregnancy (part 1)

Variables			Cases (220)	
			Fre	%
1	Have you used thromboprophylaxis used in the last pregnancy?	yes	220	100
		No	0	0
	If yes, specify			
1.1	What is the type of thromboprophylaxis used in the last pregnancy?	Low dose aspirin alone	٥3	24.1
		Un-Fractioned heparin	٥٠	22.7
		low molecular weight heparin (clexan, fraxiheparin	٤٨	21.8
		Combination of low dose aspirin and heparin therapy	٦٩	31.4
Total number how to answer (ii, iii, iv)			167	
1.1.1	The dose of heparin therapy	5000I.U/U.N heparin/OD/SC	29	17.4
		5000I.U/U.N hepain/BID/SC	83	49.7
		0.3 mg fraxihepain/OD/SC	11	6.6
		Clexan (20,40,60,80) mg/ OD/SC one	37	22.2
		Clexan (20,40,60,80) mg/ OD/SC two	7	4.2
1.1.2	The frequency of heparin therapy	Daily	156	93.4
		Alternative days	11	6.6
		Weekly	0	0.0
		others	0	0.0
1.1.3	Gestational age at starting heparin	First trimester(0-13 weeks)	144	86.2
		Second trimester(14- 26 weeks)	12	7.2
		Third trimester (27- 40 weeks)	11	6.6
1.1.4	Gestational age at stopping heparin	First trimester(0-13 weeks)	11	6.6
		Second trimester(14- 26 weeks)	10	6.0
		Third trimester (27- 40 weeks)	56	33.5
		Directly after delivery	63	37.7
		1 week after delivery	27	16.2

Table 4.19-B: Thromboprophylaxis used in the last pregnancy (part 2)

	Variables		Freq.	%
1.1.5	**Who prescribed that medication for you**	Hospital physicians	38	22.8
		UNRWA physicians	20	12.0
		Private physicians	103	61.7
		others	6	3.6
1.1.6	**How did you access to medication (thromobroph-ylaxis)**	UNRWA clinics	0	0
		Public Hospitals	18	10.8
		Governmental clinics	11	6.6
		Private Pharmacies	134	80.2
		Non-Governmental clinics	4	2.4
1.1.7	**Did you completely comply with regular use of the prescribed medications**	Yes	156	93.4
		No	11	6.6

Table (4.19-A) describe that 31,4% of total cases used combination of both low dose aspirin and heparin thereby, 24.1% of total cases used low dose aspirin only ,22.7% of total cases used un-fractioned heparin and 21.8 %of total cases used low molecular weight heparin (clexan, fraxiheparin), chi-square is calculated to be significant at (P-value 0.000), which is indicated significant statistically differences between different types of used thromboprophylaxis, as majority of cases used combination thereby, and the least proportion is low molecular weight heparin (clexan, fraxiheparin), regarding to concerned health providers, most of them agreed that "*Un-fractioned heparin is the cheapest and the most accessible medication for pregnant women, which that is influenced by socioeconomic status "*, one of them said that "*the trend toward the use of LMWH, because is easy of administration, more effective and did not need to follow up "*

Regarding to heparin prescription, as shown by table (4.19-B), the majority of heparin therapy 61.7 % of total cases prescribed by private physicians, 22.8% prescribed by hospital physicians, 12% prescribed by UNRWA physicians and 3.6% prescribed by others, chi-square is calculated to be significant at (P-value- 0.000), that is consistent with

concerned health providers view "*Thromboprophylaxis is a secondary hospital management, it is not a primary health management, as these cases should be investigated well at hospitals and assessed to heparin therapy* "

Regarding compliance 93.4 % of total cases completely complied with regular use of heparin therapy, while 6.6 % of total cases did not completely comply with regular use of heparin therapy. Chi-square is calculated to be significant at(P-value- 0.000).

Table (4.٢٠) describe the investigation profile to support heparin therapy, 91.6% of total cases performed complete investigation profile, while 8.4% of total cases did not perform complete investigation profile to support heparin therapy, chi-square is calculated to significant at (P-value 0.000).

Regarding to the types of thrombophilia use investigation profile, 84.4 % of total cases performed molecular genetic thrombophilia study, 40.5%of total cases performed coagulation profile, 11.1% of total cases performed anti-phospholipid antibodies and there's no any reported cases performed anti DNA antibodies, "*investigation profile is supporting the need of thromboprophylaxis during pregnancy*"(concerned health providers), on the other hand, both of them said that "*genetic molecular study of thrombophilia is not enough to support thromboprophylaxis, as real genetic study should include 13 genes, while 6 genes were done*", the other said "*Most of the investigations* done *at un-accredited laboratories, so these investigations should be done at accredit able labs*".

Regarding to the total cases of heparin therapy during pregnancy, the majority of cases 66.7% had cost more than 1500NIS, 21.6 % of total cases had cost 5000-1000 NIS,and 20.9 % of total cases had cost 1000 -1500 NIS, calculated chi-square is significant at (P-value-0.000), the cost of heparin therapy is expensive which that is overcome the economic status of treated cases, most of them have access to medication from private pharmacies, from their out pockets.

Table 4.٢٠: Thromboprophylaxis used in the last pregnancy

	Variables		Freq.	%
1.1	Did you perform a complete investigation profile to support the use of heparin therapy during pregnancy?	Yes	153	91.6
		No	14	8.4
If your answer yes specify the following				
1.1.1	Types of used thrombophilia investigation profile	Molecular Genetic thrombophilia study	112	73.2
		Coagulation profile	27	17.6
		Antiphospholipid Antibodies	13	8.5
		Anti DNA antibodies	1	0.7
1.1.2	What was the total cost of heparin therapy?	5000-1000 NIS	33	21.6
		1000-1500 NIS	32	20.9
		More than 1500NIS	102	66.7
1.1.3	Did you suffer any heparin therapy side effects in last pregnancy?	Painful injecting site	52	34.0
		bone ache	86	56.2
		Itching / allergy	20	13.1
		Associated thrombocytopenia	7	4.6
		Ecchymosis patches	1	0.7
		Bleeding	1	0.7
		Others, specify	0	0
1.1.4	Did you have any health complic-ations during last pregnancy?	Yes	54	35.3
		No	113	73.9
1.1.4.1	What are Types of pregnancy complications	PIH	26	17.0
		DVT	9	5.9
		GDM	10	6.5
		APH	2	1.3
		PPH	4	2.6
		Anemia	3	2.0

Table (4.٢٠) shown that, "*UNRWA cannot save this medication at their pharmacies, to be an item in non –inventory drugs list, because a trial was done in 2009, they found there was an overestimation and over diagnosis of heparin thereby prescription* " concerned health provider (FFHO) .

Heparin therapy is very expensive, inconvenient and painful to administer, as shown in table (5.9.2), 56.2% of total cases complained of bone ache, 34% of total cases complained of painful injection site, 13.1 %of total cases complained of itching and allergy, 4.6 % of total cases complained of associated thrombocytopenia, 0.7 % of total cases complained of ecchymosis patches, and 0.7 % of total cases complained of bleeding ,calculated chi-square is significant at (P-value-0.000), which that makes *"heparin prescription is controversial issue, you should weight benefits and risk*" a concerned health providers, (FFHO)

Regarding to the health complications registered in pregnancy who used thromboprophylaxis, 73.9 % of total cases did not have health complications and 35.3 % of total cases had complication, chi-square is calculated to be significant at (P-value- 0.000), regarding to the types of pregnancy-related complications, the majority of cases 17.0 %of total cases complained of PIH, 6.5 % of total cases complained of GDM, 5.9 %of total cases complained of DVT, 2.6 %of total cases complained of PPH, 2 %of total cases complained of anemia and 1.3 % of total cases complained of APH, chi-square to be significant at (P-value 0.000), these results in compare to pregnancy which not treated with thromboprophylaxis, different types of health complications is less(PIH 17% vs. 68.%, GDM 5.9%vs13.6%, APH 1.3%vs 9.1%, PPH 2.6% vs. 9.1%).

Regarding the management practices, as shown in the table (4.21), 96.7 %of total cases had been followed up by a specialist, 12.4 %of total cases were not followed up by a specialist

As showed by the table (4.21), 38.6 % of total cases visited specialist room more than 4 times, 32.0% visited specialist room once only, the remaining of cases 26.1 % visited specialist room from 2 to 4 times during their pregnancy period.

Regarding to times of fetal us during pregnancy period, 35,3 % of total cases did more than 4 times fetal us during pregnancy period, 30.7 % of total cases did 2 -4 times fetal us during pregnancy period, and 30.7% of total cases did once fetal us during pregnancy period .

Table 4.21: Management practices and follow up with cases with thromboprophylaxis use

Variables			Cases (220)	
			Freq.	%
1	Did you follow by a specialist?	Yes	148	96.7
		No	19	12.4
1.1	How many times during pregnancy did you visit a specialist clinic	1 times	49	32.0
		2-4 times	40	26.1
		More than 4	59	38.6
1.2	How many times has a fetal us done for you at the clinic?	one	47	30.7
		2-4 times	47	30.7
		more than 4	54	35.3
1.3	Did you have a follow up at the high-risk department at the hospital?	yes	73	47.7
		No	79	51.6
1.4	Where did you deliver?	Private hospital	39	25.5
		Public hospital	108	70.6
		Private doctor	5	3.3

As shown by table (4.21) 47,7% followed her pregnancies at high-risk department, while 51.6 % of total cases did not follow at high-risk pregnancy department .(P-value-0 .000), when these results were discussed with concerned health providers, they agreed with it, as" *there is no any reported case did not do us during follow up, despite overload, and high waiting time which is being a challenge in front of quality improvement at UNRWA health centers* "

Finally, regarding the delivery place, 70.6 % of total cases delivered at public hospitals, 25.5 % of total cases delivered at private hospitals, while 3.3 % of total cases delivered by a private doctor.

4.16 Evaluation of Blood pressure and obesity indicators among the study population

Table (4.22) describe blood pressure measurements among both groups which there is differences between BP Measurement between them,76.4% of treated women had BP below 130/86, while 90.9 % of untreated women had blood pressure below 130/86, 20.5% of treated women and 17% of untreated women had BP 130-139/86-89, and 3.2 % of treated women and 1.4% of untreated women had BP more or and equal to 140/90 (chi-square 25.42, with P-value-0.000), regarding to that treated women with thromboprophylaxis during pregnancy had a risk of HTN more than untreated , which that is consistent with literature as confirmed a strong relationship between thrombosis and HTN diseases.

Table 4.22: Relationship between blood pressure measurement and thromboprop-hylaxis use

Variables			Cases (220)		Controls(220)			
			Freq.	%	Freq.	%	Chi	Sig
1	Blood Pressure indicators for women	<130/86	١٦٨	76.4	٢٠٠	90.9	25.42	.000
		130-139/86-88	٤٥	20.5	١٧	7.7		
		or > and =140/90	٧	3.2	٣	1.4		

Table (4.23) compare between groups in BMI measurements, the majority of treated women, 35.9 % of them had normal weight (BMI 18.5-24.9), 33.6 % of treated women had overweight (BMI 25-29.9), 13.6 % of treated women had first class obesity (BMI30-34.9), 7.3 % of treated women had second class of obesity (BMI 35-39.9), 7.3 % of treated women had underweight below 18.5 and 2.3 % of treated women had 3rd class of obesity (BMI more than 40), on the other hand the majority of untreated women 50,5 % of them had overweight (BMI 25-29.9), 18.2% of non-treated women had first class obesity (BMI 18.5-24.9), 7.7% of non-treated women had second class obesity (BMI 35-39.9), 5.5 % of non-treated women had under normal weight(BMI below 18.5), and 1.4 % of non-treated women had third class obesity (BMI more than 40).(chi-square 25.13, P-value-0.000), that

means obesity is not a risk among treated women with thromboprophylyxsis use in pregnancy, which that is not consistent with literature which confirmed BMI indicator is one of the main risks to start thromboprophylaxis in pregnancy and to measure risk of thrombosis. (Sultan AA., et al 2013)

Table 4.23: Relationship between BMI (body mass index) measurement and thromboprophylaxis use

Variables			Cases (220)		Controls(220)			
			Freq.	%	Freq.	%	Chi	Sig
1	Obesity indicators for pregnant women	Underweight less than18.5 kg	١٦	7.3	١٢	5.5	25.13	.000
		Natural Weight 18.5-24.9	٧٩	35.9	٣٧	16.8		
		Overweight 25-29.9	٧٤	33.6	١١١	50.5		
		First-class obesity 30-34.9	٣٠	13.6	٤٠	18.2		
		second-class obesity 35-39.9	١٦	7.3	١٧	7.7		
		Third -class obesity More than 40	٥	2.3	٣	1.4		

٤,١٧ Maternal Health Record Review and Genetic Molecular Study Review

This part describes the quantitative results as maternal health records review (MMHR) and molecular genetic study review, MMHRs review includes 100 MR. Files which are selected by random sampling from the whole study cases who received thromboprophylaxis in their pregnancies, they were also selected from all clinics included in the study, we review the most important management practices as high-risk pregnancy, and highlighting the main findings to improve the quality of work, also this part includes another quantitative part which is involving genetic molecular study to evaluate the relationship between thromboprophylaxis use and genetic molecular study.

4.١8 Review of maternal medical health records

This part of the quantitative type of the study, which involves medical maternal health records MMHR, we review nearly 100 files were selected randomly , and we review according to the following domains, distribution of obstetric history, risk factors among cases group(treated women)

Table 4.24: Distribution of risk factors among cases group (thromboprophylaxis use) (100 MRR)

No.	factor	Frequency %	Frequency %
		Yes	No
1	Age>=35	23	77
2	Para>=6	9	91
3	Habitual abortions >=3	23	77
4	Perinatal deaths>=2	3	97
5	Pervious pre-eclampsia	3	97
6	Pervious GDM	3	97
7	History of antepartum hemorrhage	0	100
8	History of post hemorrhage	7	93
9	Pregnancy-induced hypertension	7	92
10	DM with pregnancy	1	99
11	History of CS	38	62
12	Anima below 9	4	96

As shown by previous table (4.24) , the most prevalent risk factors among this group is CS, which accounted 38 % , which that supported thromboprophylaxis therapy and matched high prevalent rate of CS among risk pregnancy, followed by 23 % of cases are more or equal to 35 years old, 23 % of total cases had history of habitual abortions 3 and more which all of these supported thromboprophylaxis use and matched global studies about thrombophilia, and 9% of cases were multipara (P6and more) which had followed by history of PPH and PIH which accounted 7%,7% respectively, while 4% of cases had anemia below 9.3% of cases had previous GDM and previous preeclampsia respectively, and 1% of cases developed DM with pregnancy, these results summarize the most common

risk factors among studied cases(with thromboprophylaxis use), regarding to frequency of occurrence arranged (CS, Age 35 and more, habitual abortion, Multipara, history of PPH and PIH).

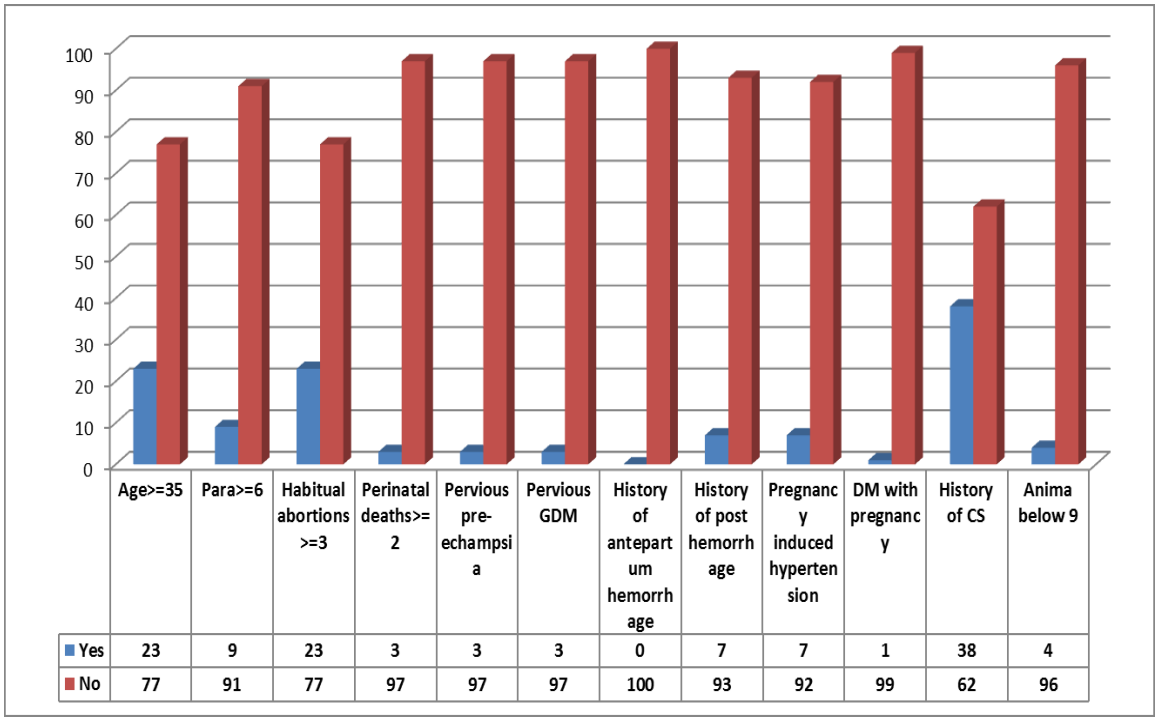


Figure 4.5: Distribution of risk factors among cases group (thromboprophylaxis use). (100 MMRR)

Table 4.25: Frequency of risk factors among cases

	Factor	One risk factor		two risk factor		More than 2 risk factors	
		No.	%	No.	%	No.	%
1	Frequency of risk factors among cases	34	34%	54	54%	12	12%

The table (4.25) summarizes the number of associated risk factors of these cases, the majority of cases had two risk factors (54%), then one risk factor (34%), and followed by

more than two risk factors (12%)of total cases, that means these cases are high-risk pregnancy and they are needing more and special follow up and management.

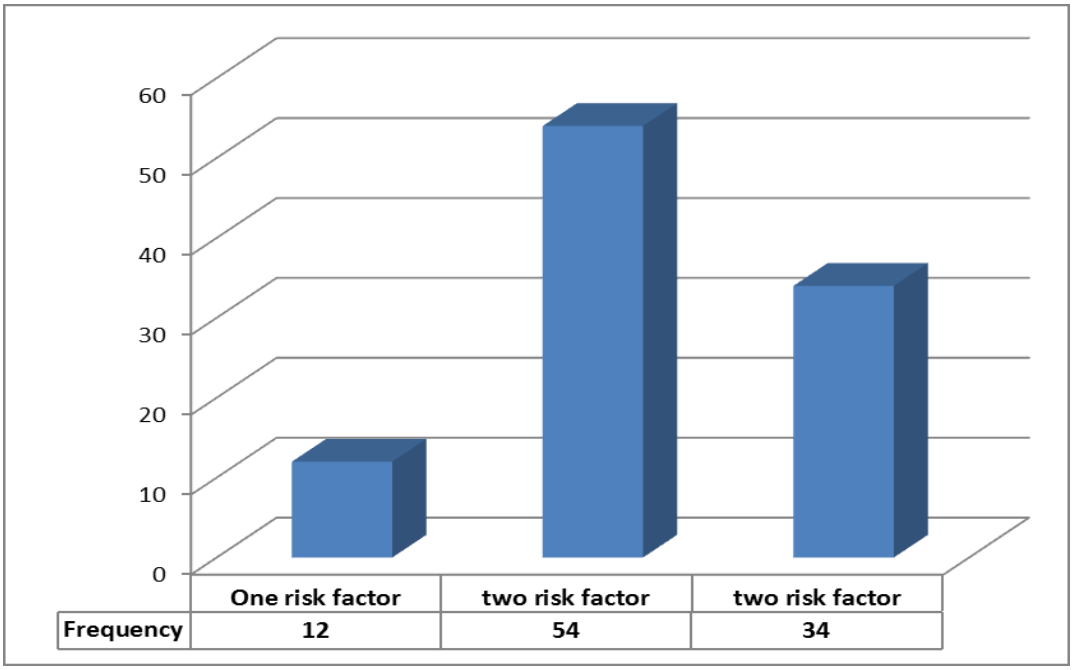
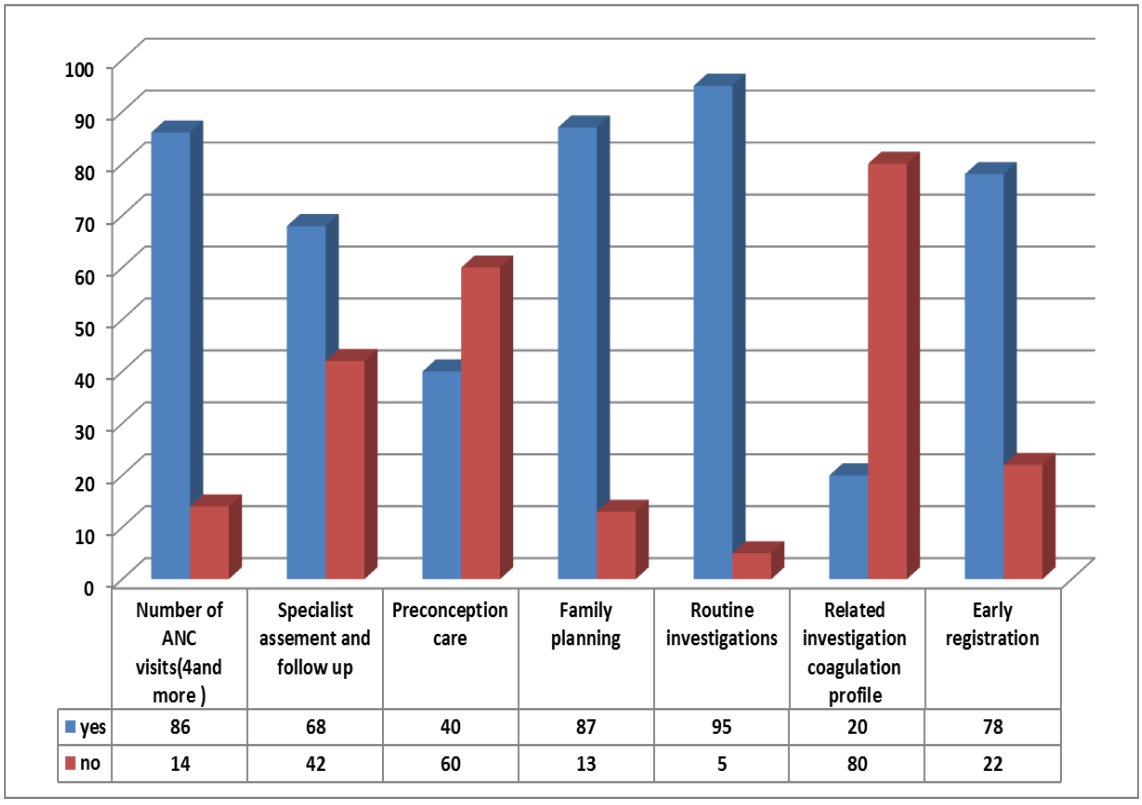


Figure 4.6: **Frequency of risk factors among cases**

Table 4.26: Review of management practices.

No.	Factor	Frequency	Frequency
		Yes	**No**
1	Number of ANC visits(4and more)	86	14
2	Specialist assessment and follow up	68	42
3	Preconception care done	40	60
4	Family planning was done	87	13
5	Routine investigations were done	95	5
6	Thrombophilia related investigation documentation	20	80
7	Early registration	**78**	22

This table (4.26) and figure (4.6|) describes management practices of these risky group, these cases are classified as alert or high-risk pregnancy and reviewed to the eight main items, number of ANC visits, specialist assessment and follow up, preconception care, family planning care, routine investigation done or not, related thrombophilia investigation documented or not and about early registration and these results were discussed with concerned health providers.



	Number of ANC visits(4and more)	Specialist assement and follow up	Preconception care	Family planning	Routine investigations	Related investigation coagulation profile	Early registration
yes	86	68	40	87	95	20	78
no	14	42	60	13	5	80	22

Figure 4.7: Review of management practices.

As shown by previous figure 4.7, regarding to the number of ANC visits, 86% of cases had at least 4 ANC visits, 78 % of cases had early registration in first trimester, 40% of total cases had been registered in PCC program, 87% had family planning attendance, 95% of cases did routine investigations, regarding to investigation regarding thrombophilia documentation, only 20 % of cases had documented related investigation also as shown by table 40% of cases had specialist follow up and assessment, concerned health providers especially FFHO not agreed with some results regarding to early registration (78%vs.22%) "*These results will be more when we consider GA below 16 weeks as defined by UNRWA guidelines*", regarding to the number of ANC visits "*Our goal is to improve that more than 90%, that is explained by women follow up by out clinic specialists* "regarding to specialist follow up and assessment, FFHO said that "*we train our medical officers to get enough*

experiences to work with these cases "other concerned health provider *"The main cause to this weak point, is the lack of medical officers experience of referral at spot time of pregnancy* "regarding to preconception care concerned health provides agreed with that "*this percentage is a great of us, to be nearly 40% of risky groups to be enrolled in PCC program prior to pregnancy, which that is being a challenging in front of us "*, regarding to related investigation documentation (20%vs.80%), "*which that is explained by the electronic medical records, untrained staff members and medical officers, which is a really week pain and is needing for hard efforts to improve"*(concerned health providers).we summarize that with few words, PCC, early registration, and ANC visits more than 4 visits are continuity cycle, and it should be improved to improve the quality of maternal health.

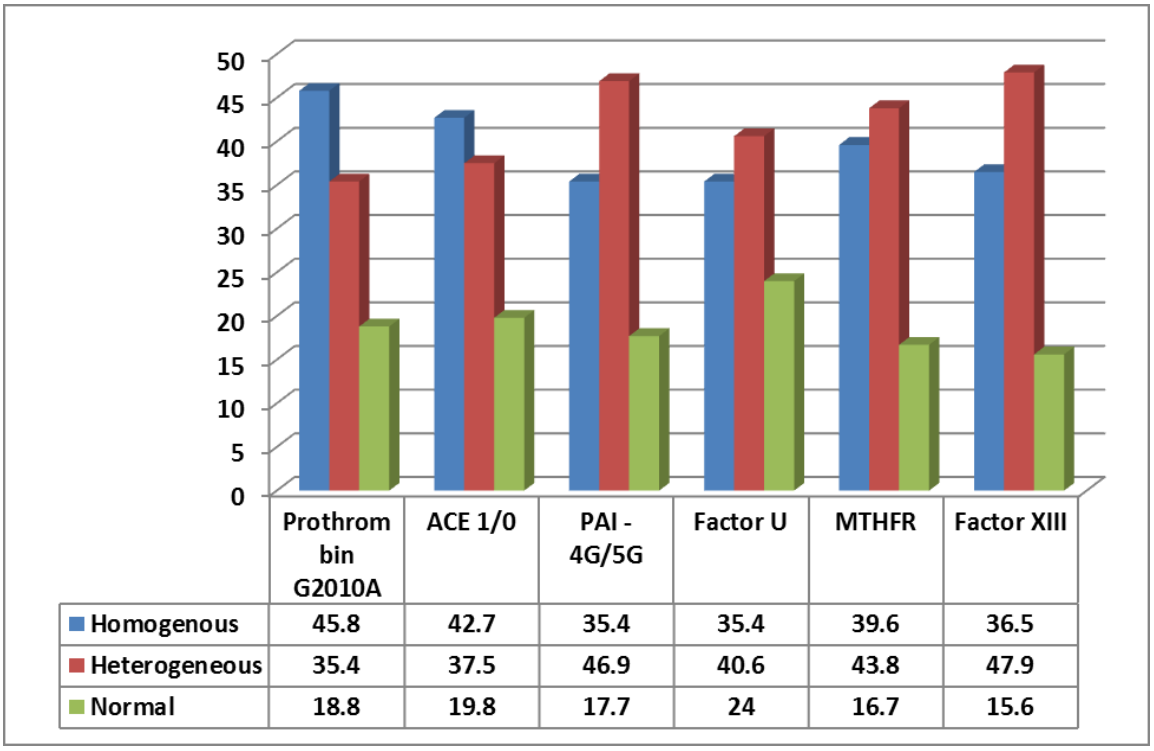
4.19 Genetic Molecular study review

Table 4.27: Genetic Molecular study among cases group who use thromboprophylaixs

No.	Factor	Homogenous		Heterogeneous		Normal		TOTAL
		No.	%	No.	%	No.	%	
1	Prothrombin G2010A	48	45.8	30	35.4	18	18.8	96
2	ACE 1/0	41	42.7	36	37.5	19	19.8	96
3	PAI - 4G/5G	34	35.4	45	46.9	17	17.7	96
4	Factor V	34	35.4	39	40.6	23	24.0	96
5	MTHFR	38	39.6	42	43.8	16	16.7	96
6	Factor XIII	35	36.5	46	47.9	15	15.6	96

Table (4.27) describes the genetic molecular studies among cases who used thromboprophylaxis during pregnancy, each gene has 3 descriptions (homozygous, heterozygous, normal), nearly 154 of cases did genetic profile, 112 of them did genetic molecular study, 96 of them had available investigations, There are six main inherited thrombophilia, factor V Leiden gene mutation (VFL), Prothrombin gene mutation, hyperhomocysteinemia, protein C deficiency, protein S deficiency, and anti-thrombin deficiency, as shown in figure(6.4),factor v, Prothrombin and hyperhomocysteinemia done

in patients who had thromboprophylaxis . Regarding to Prothrombin factor 45.8% is homozygous, 35.4% is heterozygous, and 18.8% of cases is normal, that is constant with literature review the risk of VTE is three folds with Prothrombin factor abnormality (Rosendaal et al, 1998), also with Robesreteron et al (2006) in his met analysis study, pregnancy complicated diseases are associated with Prothrombin abnormalities, but on the other hand literature said that the prevalence of Prothrombin mutation in general population is 2%, and in thromboembolic events patients 6%, regarding to factor v35.4% is homozygous,40.6% is heterozygous, which that is consistent with Carp et al (2003), also Hellegran (2003) confirmed that women who had abnormal factor V genetic study, had a risk of 24%to 26%of thrombosis events in pregnancy, also Gardone and colleagues (2007) reported a 31.2%prevelance of factor V mutation in women with second trimester loss compared to 4.2% in matched controls, concerned health providers confirmed that "*the most common gene is indicated to start heparin thereby is factor v mutation* ", in the other hand literature review showed that 5%of general population had factor v mutation and 25% of patients who had venous thromboembolic events(Carp et al.,2003).



	Prothrombin G2010A	ACE 1/0	PAI - 4G/5G	Factor U	MTHFR	Factor XIII
Homogenous	45.8	42.7	35.4	35.4	39.6	36.5
Heterogeneous	35.4	37.5	46.9	40.6	43.8	47.9
Normal	18.8	19.8	17.7	24	16.7	15.6

Figure 4.8: Genetic Molecular study review

regarding to hyperhomocysteinemia MTHFR 39.6% had homozygous genetic variation, 43.8% had heterozygous genetic variation which that is relevant to literature as Carp et al (2003) said prevalence of MTHFR 3% among population,10% to 25% in patients with thromboembolic events, some of the studies confirmed its role in risk of pregnancy thrombosis as Robesteron et al (2006) described in his meta-analysis study, while Jaakelainen et al (2006) confirmed that there's no role in pregnancy complications. Regarding to factor V111, and ACE factor, high levels are increasing the risk of deep venous thrombosis, but no clear significant in pregnancy complication, as said by (Kraaijenhagen et al, 2001), when these discussed with concerned health providers, as FFHO" *genetic study which was done is incomplete as we need 13 genetic factors to be done to say that cases with positive thrombophilia, most of the genetic study was done at unaccreditable labs, as people usually look for the cheapest one, so this should be considered*" other concerned health provider said "*Genetic study alone is not enough to diagnose thrombophilia and to determine the need of thromboprophylaxis*", another concerned health provider "*if you do genetic study among all population, you will find the same percentages among healthy population who did not take thromboprophylaxis "*

Chapter 5 : Conclusions and Recommendations

5.1 Conclusions

The results of the study are unique in providing detailed documented information on the status of thromboprophylaxis use among pregnant women, by discussed different associated determinants, different management practices, different pregnancy outcomes, and how will thromboprophylaxis improve pregnancy outcomes and pregnancy complications. The aim of the study is to identify associated risk factors of thromboprophylaxis use, consequences, management practices that contribute to thrombophilia and the need of thromboprophylaxis among refugee risky pregnant, in order to explore possibilities for reducing maternal and fetal complications. Study is a comparative study that compares between two groups of women who delivered at last 6 months of 2016, one of them are treated with of thromboprophylaxis and others are non-treated with thromboprophylaxis during their last pregnancy, large five UNRWA health centers were selected for data collection, different associated determinants were discussed through an interviewed questionnaire, as we discuss sociodemographic factors, past medical history, past obstetric history, different associated pregnancy complications history of thrombosis and pregnancy outcome, also we discuss different management practices, different thromboprophylaxis experiences in different pregnancies, and how much the cost and the availability of medications at governmental hospitals and UNRWA health centers at the interviewed questionnaire, also medical record review discuses different associate risk factors and different associated management practices, In-depth interview discuss different related points that support findings of interviewed questionnaire. From the study we conclude that Jabalia UNRWA health center has a high-frequency rate than other clinics most of them are unemployed, had average family income less than 1000NIS, also the majority of them had first-degree relative continuity, accumulation of different risk factors strongly associated and enhancing the use of thromboprophylaxis in pregnancy.

Maternal age was strongly associated with thromboprophylaxis use as most of the cases age is more than 25 years old (62.2%), with early marriage age less than 20 years old(59.1%), and most of them had positive consenguity first degree relative of marriage

(25%). History of non-communicable diseases is strongly associated with the use of thromboprophylaxis use in pregnancy, odds ratio (6.27), mainly DM, HTN, Respiratory diseases and heart diseases respectively.

History of hematological diseases is strongly associated with the risk of thromboprophylaxis use in pregnancy, odds ratio (233.3), as most of them had congenital thrombophilia, history of thromboembolism disorder, and acquired thrombophilia, also history of vascular diseases is strongly associated with thromboprophylaxis use, odds ratio (29.3), mainly varicose veins, deep venous thrombosis and thrombophlebitis respectively, on the other hand, there is a strong relationship between history of surgical operations and thromboprophylaxis use, odds ratio (5.6), mainly CS, abdominal surgery, and orthopedic surgery, women who had positive family history, she had strong indication to thromboprophylaxis (odds ratio4.99), mainly inflammatory bowel diseases, congenital thrombophilia, acquired thrombophilia, SLE and rhematological diseases, respectively.

Regarding to past obstetric history, the risk of thromboprophylaxis use is increasing more in Gravida two and more (89.5%of treated women), Para two and more (74.5%of treated women), also the risk of thromboprophylaxis use is strongly associated with history of dead children, 29.1%of treated women had one and more history of dead children, majority of them 21.8%die after 28 weeks gestational age to less than 28 days after delivery (perinatal mortality).

The risk of thromboprophylaxis use is increasing more in cases of infertility history (odds ratio 13.3), with a high frequency of infertility years more than 3 years (71.6%). Treated women had a risk of a history of pregnancy induction (odds ratio 4.83), 9.1% of treated women had failed IVF more than twice trial.

The risk of thromboprophylaxis use is increasing more in cases with history of low birth weight, less than 2500 gram(odds ratio 2.2), majority of them had fetal weight 1.5-2.5 kg Also thromboprophylaxis use is increasing with history of preterm labor, odds ratio (2.3), majority of them between 28-32 weeks gestational age, also thromboprophylaxis use is increasing more with strong relationship, with positive history of miscarriages(odds ratio 18.4), it is highly indicated with more than twice miscarriages(56.1%), most of them had consecutive miscarriages (63.7%),majority of miscarriages occurred from one week to 12

weeks pregnancy (60.8%), also thromboprophylaxis use is increasing more, also thromboprophylaxis use is increasing more in cases who had positive family history, regarding to history of pregnancy complications, thromboprophylaxis use is increasing more in cases with history of pregnancy complications (odds ratio 57.36), mainly PIH, APH, PPH, PET, and GDM, respectively, also thromboprophylaxis use is strongly associated with history of thrombosis in pregnancy (odds ratio 11.2), mainly deep venous thrombosis, pulmonary embolism and arterial thrombosis respectively.

Research clarifies the role of thromboprophylaxis in pregnancy, majority of cases who use thromboprophylaxis during pregnancy did not complain of pregnancy complications (73.9%vesus 35.3%), on the other hand it describes how pregnancy outcomes improved by thromboprophylaxis use during pregnancy, majority of them had alive baby (78.2%), 10.9% had abortion, 4.1% had early fetal deaths, 3.6% had premature delivery ,1.8% had perinatal mortality and 1.4%had congenital anomalies, in comparison to other pregnancies where thromboprophylaxis is not used 58.6%of cases did not use thromboprophylaxis in all pregnancies, 41.9% had alive birth, 38%of them had abortion ,12.4% had early fetal deaths, 2.3% of them had congenital malformation, 1.6 % of them had intrauterine fetal deaths and 0.8% had early neonatal deaths .

Regarding to fetal weight improvement, most cases (68.4%) who use thromboprophylaxis during pregnancy had normal fetal weight expected fetal weight 2500gm-4500gm, while 15.7% had low birth weight (less than 2500 gm.)and 4.1% of cases had fetal weigh more than 4500 gm. which that confirmed by concerned health providers.

Regarding to different management practices which followed, majority of cases who use thromboprophylaxis used combination therapy between low dose aspirin 100 mg and heparin therapy(69%), most of them started heparin therapy at first trimester of gestational age (86.2%),63% of cases stopped thromboprophylaxis after delivery which that is not consistent with international guidelines which described the use of thromboprophylaxis use in the following 6 weeks after delivery, most of medications prescribed by private physicians, 80.2 % access this medication from out pocket money with high cost which is nearly more than 1500 NIS during pregnancy(66.7%), on the other hand, majority of cases did investigation profile which is supportive to start with heparin therapy 91.5% of them did complete investigation profile , 73.2 % of them had molecular genetic study , 17.6 %

did coagulation profile , 8.5% of them did antiphospholipid syndrome and 0.7% of them did anti DNA antibodies, regarding to genetic thrombophilia abnormalities, cases who use thromboprophylaxis in their pregnancies had abnormalities in the following genes(Prothrombin G2010A homogenous 45.8% heterogeneous 35.4% ACE/0 homogenous 42.7% heterogeneous 37.5%, PAI-4g/5g homogenous 35.4%heterogenous 46.9%, factor V 35.4% homogenous 40.6% heterogenous, MTHFR homogenous 39.6%heterogenous 43.8% and factor X111 36.5 %homogenous and 47.9%hetrogenous which that support the use of thromboprophylaxis during pregnancy, genetic study alone will not be enough to decide to star thromboprophylaxis but it needs both risk factors and supportive investigations.

Most cases of thromboprophylaxis use had accumulated risk factors 54%of them had two risk factors, 34% of them had one risk factor and 12 %had more than two risk factors, these files are high risky ,96.7%had specialist follow up, 38.6% visit specialist room more than 4 visits, 35.3%had fetal us more than 4 times during pregnancy,70.6% of them delivered at public hospitals, which that indicated good follow up by UNRWA health centers for risky pregnancy.

Regarding blood pressure measurement and body mass indexes measurements, cases who use thromboprophylaxis during pregnancy had a risk HTN than women who were not treated by thromboprophylaxis as 20.5 % had pre HTN stage, 3.2% had HTN, in contrast, its association with BMI as women who not treated with thromboprophylaxis is more a risk to Overweight and obesity than non- treated women, which that is not consistent with literature review.

Thromboprophylaxis use among pregnant women had two borders, the first one she presence of real risk, the other border is overuse because of lack harmonization between different health sectors.

٦.2 Recommendations

A high-risk pregnancy is increasing so the risk of thromboprophylaxis demand is increasing and also the research clarifies the role of thromboprophylaxis in improving the pregnancy outcomes, so research recommends

1- Enhancing the availability of clear simple technical guidelines dealing with thromboprophylaxis use in pregnancy in order to control heparin use.
2- Ensuring the access of heparin therapy MO –UNRWA installations with defined instructions in order to control the use of heparin and decrease out of pocket dependence
3- Improve the referral system and feedback between primary and secondary healthcare
4- Expansion of preconception coverage in order to enter pregnancy in optimal health before pregnancy
5- Encouraging teamwork and cooperation between different health sectors in order to improve the quality of health.
6- Encouraging standardization of diagnostic criteria for cases with thromboprophylaxis use in pregnancy.
7- Ensuring the presence of effective management plan of bad pregnancy outcomes in order to early detection of thrombosis risk
8- Ensuring the presence of accreditable labs to do reliable thrombophilia investigations to justify thromboprophylaxis use in pregnancy
9- Improving the comprehensive package of maternal health care services in order to identify the maternal risk factors and improve maternal health
10- Conducting more researchers in different aspects of thromboprophylaxis use, by using hospital-based studies.

٦.3 Area of further research

1- Further analysis to detect confounder and interactions between risk factors of thrombophoplyaxi use among pregnant women
2- Further researchers to detect the significance of genetic factors among thrombophilia and thromboprophylaixs use
3- Further researches on evidence of IVF cases who used thromboprophylaxis
4- Further researches of hospital-based studies of cases who use thromboprophylaxis
5- Other types of researchers to detect the prevalence of thrombophilia, risk factors, and management practices

References

American College of Obstetrician and Gynecologists, (2001). *Management of recurrent pregnancy loss.Clinical management guidelines for Obstetricians – Gynecologists.* Washington, DC(24)

American College of Obstetrician and Gynecologists, (2005).*clinical management guidelines for obstetrician-gynecologists,* (65)

American College of Obstetrician and Gynecologists, (2007) Practice Bulletin No. 77:screening for fetal chromosomal abnormalities,*Obstet Gynecol. Journal* :109(1):217-27

American College of Obstetricians and Gynecologists, (2005).*Antiphospholipid syndrome Practice Bulletin* (No. 68).Retrieved From . https://www.google.ps/#q=+The+american+college+of+obstetricians+and+gynecologists%2C+Practice+Bulletin+Number%2C124%2C+September+2011

Am, J. (1979). A review of the birth control pill and its relationship to thrombophlebitis. *Public med.*,69,6, 376-82.

Anderson,A.,Spencer,F. (2003).Risk Factors for Venous Thromboembolism *Circulation* ,107,9–16. Retrieved from http://circ.ahajournals.org/

Austerlian Assesment Report, (2002) *Antenatal Screening for Hereitable Thrombophilia* ,Retrived from http://www.msac.gov.au

Bates,SM.,Greer,IA.,Pabinger,I.,Sofaer,S.,&Hirsh,J.(2008).Venous. thromboembolism, thrombophilia, antithrombotic therapy, and pregnancy *American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Ed.).Chest.*,133(6):844S-886S

Benjamin,B.(2004).Clinical management of thrombophilia-related placental vascular complications. Review article. Blood .*The American Society of Hematology,*103,4003-4009

Branch,D.W.,Andres,R.,Digre,K.B.,Rote,N.S.,&Scott,J.R.(1989). The association of antiphospholipid antibodies with severe preeclampsia. *Journal Obstetric ,Gynecological* ,73, 541-545.

Brenner,B.(1999).Inherited thrombophilia and pregnancy loss. *Thromb. Haemost*. ,82,634–40

Bogdanova, N., & Markoff, A. (2010*). Hereditary thrombophilic risk factors for recurrent pregnancy loss. Journal of Community Genetics*, 1, 47-53.

Carp,H.,Dolitzky,M.,Inbal,A.(2003).Thromboprophylaxis improves the live birth rate in women with consecutive recurrent miscarriages and hereditary thrombophilia. *Thromb. Haemost.*,1,433-438

Casadei,L.,Puca,F.,Privitera,L.,Zamaro,V.,Emidi,E.(2010). Inherited thrombophilia in infertile women: implication in unexplain infertility. *Fertilility&Sterilility*: 94(2): 755-7

Chang,J.,Elam-Evans,LD.,Berg,CJ.,&et.al.(2003). Pregnancy-related mortality surveill-ance ,United States, 1991-1999. *MMWR Surveillance Summary* :52(2):1-8

Chan,W., Rey,E., Kent,N.,(2014).Venous Thromboembolism and Antithrombotic Therapy in Pregnancy, *SOGC CLINICAL PRACTICE GUIDELINE*, 308.

Christopher,F.,Ciliberto & Gertie F.(1998). Physiological Changes Associated with Pregnancy. *Physiology Issue:*9(2): P.3.Retrived from http://www.nda.ox.ac.uk/wfsa/html

Cloherty,John P.(2012). "Care of the Extremely Low Birth Weight Infant". *Manual of neonatal care* (7th ed.). Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins. p. 146

Coulam,CB.,Jeyendran,RS.,Fishel,LA.,Roussev,RG.(2006). Multiple thrombophilic gene mutations rather than specific gene mutations are risk factors for recurrent miscarriage. *American Journal of Reproductive Immunology*: 55(5):360-368

Dahlback,B.,Carlsson M.,&Svensson,P.J.(1993). Familial thrombophilia due to a previously unrecognized mechanism characterized by poor anticoagulant response to activated protein C: prediction of a cofactor to activated protein C. *Proc. Natl. Acad. Sci. U. S.A.*: 90(3):1004-1008.

Dawood,F.,Farquharson,R.,Quenby,S.,Toh,C.(2003). Acquired activated protein C resistance maybe a risk factor for recurrent fetal loss. *Fertil Steril*,80, 649-650

Ddle,S.,Clark,P.,Lowe,G.D.,Walker,I.D.,Mello,G.,Parretti,E.,Marozio,L.,Pizzi,C., Lojacono,A.,Frusca,T.,Facchinetti,F.,&Benedetto,C.(2005b). Thrombophilia is signify-cantly associated with severe preeclampsia: results of a large-scale, case-controlled study. *Hypertension, American Heart Association ,*46,1270-1274.

Dekker,G.A.,Vries,J.I.,Doelitzsch,P.M.,Huijgens,P.C.,von,Blomberg,B.M., Jakobs,C.,& Van Geijn,H.P.(1995). Underlying disorders associated with severe early-onset preeclampsia . *American Journal Obstetric and Gyncological* ,173,1043-1048.

De Vries JIP., Dekker GA., Huijgens PC., et al. (1997) .Hyperhomocysteinaemia and protein S deficiency in complicated pregnancies- .*Obstet Gynaecol*, 104, 1248–54.

Flenady,V.,Koopmans,L.,Middleton,P.,Froen,JF.,Smith,GC.,Gibbons,K.,Coory,M,Gordon, A.,Ellwood,D.,McIntyre,HD.,Fretts,R,Ezzati,M.(2011) Major risk factors for stillbirth in high-income countries: a systematic review and meta-analysis. *Lancet,*377, 1331-40

Froen,JF.,Gardosi,JO.,Thurmann,A.,Francis,A.,Stray-Pedersen,B. (2004). Restricted fetal growth in sudden intrauterine unexplained death*, ActaObstetGynecol Scand,*83,801-7

Froen,JF.,Pinar,H.,Flenady,V., Bahrin,S., Charles,A.,Chauke,L.,et.al. (2009). Causes of death and associated conditions (Codac): a utilitarian approach to the classification of perinatal deaths. *BMC, Pregnancy Childbirth*:9(22): 286-294.

Furie,B., Furie,BC. (2008). Mechanisms of thrombus formation. *New England Journal of Medicine* :359 (9): 938–949.

Gary,C.,Kenneth,J.Leveno,L.,CatherineY.,Spong,S.,Dashe,B.,HoffmanL.,Brian M., Jeane S. (2014). *Williams obstetrics* (24th edition. ed.)

Ginsberg,J.,Greer,I.,Hirsh,J. (2001). Use of Antithrombotic Agents During Pregnancy. *CHEST*. ,119,122S–131S

Giovanni,L.,Antonio,A.,Danilo,c.,Stefano,G.,Therese,D.,Elisabetta,R.Girling,J., Swiet, M.(1998). Inherited thrombophilia and pregnancy. *Curr. Opin. Obstet. Gynecol*., 10, 135-144.

Gold,m.,Garcia,D.,Wren,sh.et al. (2012). Antithrombotic therapy and prevention of thrombosis. *American colleague of chest physion Evidence –based clinical chest physions, Evidence –based clinical practical guildliunes*. 141, (20),e227s-e277s.

Grandone,E.,Colaizzo,D.,LoBue,A.,Checola,MG.,Cittadini,E.,Margaglione,M.(2001). Inherited thrombophilia and in vitro fertilization implantation failure. . *Fertility and Sterility*: 76 (1): 201-02 .

Greer,I. A.(2000). The challenge of thrombophilia in maternal-fetal medicine. *New England Journal of Medicine*:342 (6): 424-425.

Gris,J.,Mercier,E.,Quere,I.,´Lissald,G.,Nouvellon,E.,Hoffet,M.,Neveu,S.,Tailland,M.,Dauzat,M.,&Mares,P.(2004). Low-molecular-weight heparin versus low-dose aspirin in women with one fetal loss and a constitutional thrombophilic disorder . *The American Society of Hematology* : 103(10):3684-3688.

Greer,I.A.(2003). Inherited thrombophilia and venous thromboembolism. *Best Practice. Res. Clin. Obstet. Gynaecology* . ,17, 413-425

Heit,JA.,Kobbervig,CE.,James,AH.,Petterson,TM.,Bailey,KR.,Melton,LJ.(2005). Trends in the incidence of venous thromboembolism during pregnancy or postpartum: a 30-year population-based study. *Annals Internal Medicine* ,143,397-706.

Heit,JA.(2007). Thrombophilia:common questions on laboratory assessment and management. *Hematology American Society Hematological Education Program* , (1), 127–35

Hellgren,M.(2003). Hemostasis during Normal Pregnancy and Puerperium *Semin. thrombo.Hemost:* 29(4):125-130

Hoffman,E.,Hedlund,E.,Perin,T.,Lyndrup,J.(2012). Is thrombophilia a risk factor for placenta-mediated pregnancy complications. *Arch Gynecol Obstet., 286,585–589(Pubmed)*

Hron G., Eichinger S., Weltermann A., Minar E., Bialonczyk C., Hirschl M. et al,(2006). Family history for venous thromboembolism and the risk for Family history for venous thromboembolism and the risk for recurrence. *Am J Med*;119, 50–3 .

Institute of Obstetricians and Gynecologists, Royal College of Physicians of Ireland and HSE Clinical Care Programme in Obstetrics and Gynaecology and Irish Hematology Society(2013). *Clinical Practice Guideline . Venous Thromboprophylaxis In Pregnan*. Version(1),NO. (20).Retrieved from

https://www.google.ps/#q=Venous++Thromboprophylaxis+in+Pregnancy%2C+Version+1.0%2C+Guideline+No.20

James,AH.,Jamison,MG.,Biswas,MS.,Brancazio,LR.,Swamy,GK.,yers,ER.,(2006). Acute myocardial infarction in pregnancy: A United States Population-Based Studys. *Circulation*,113,1564–1571

Jääskeläinen,E.,Keski-Nisula,L.,Toivonen,S.,Romppanen,E.L.,Helisalmi,S.,Punnonen, K. and Heinonen, S. (2006). MTHFR C677T polymorphism is not, associated with placental abruption or preeclampsia in Finnish women. *Hyper tense Pregnancy,* 25, 73-80.

James,AH.,Bushnell,CD.,Jamison,MG.,Myers,ER.(2005). Incidence and risk factors for stroke in pregnancy and the puerperium. *Journal of Obstetetrical&Gynecological* ,106,50-516

James,AH.,Jamison,MG.,Brancazio,LR.,&Myers,ER.(2006). Venous thromboembolism during pregnancy and the postpartum period.incidence, risk factors, and mortality. *American Journal Obstetric Gynecological* : 194(5):1311-5

James,A.(2009) .Venous Thromboembolism in Pregnancy *Arteriosclerosis, Thrombosis Vascular Biolology Journal* ,29,326-331, Retrived from http://atvb.ahajournals.org

Jarjour,IT.(February,2015). Neurodevelopmental Outcome After Extreme Prematurity: A Review of the Literature. *Pediatric neurology* 52 (2): 143–152

Kamel,H.,Navi,B.B.,Sriram,N.,Hovsepian,D.A.,Devereux, R.B.,Elkind,M.S.(2014). Risk of a thrombotic event after the 6-week postpartum period. *New England Journal of Medicine*, 370, 1307–1315

Kayali F., Najjar R., Aswad F., et al.(2008). Venous thromboembolism in patients hospitalized with nephrotic syndrome. *Am J Med. PubMed*, 121, 26–230.

Keski-Nisula,L.,Toivonen,S.,Romppanen,E.L.,Helisalmi,S.,Punnonen, K.,&Heinonen, S. (2006). MTHFR C677T polymorphism isnot associated with placental abruption or preeclampsia in Finnish women.*Hypertens Pregnancy* :25(2): 73–80

Kinzler,WL.,Prasad,V.,Ananth,CV.(2009). The effect of maternal thrombophilia on placental abruption: Histologic correlates. *Journal Materno- Fetal Neonatal Medicine* :22(3):243-8.(pub med)

Kraaijenhagen,R.A.,Anker,P.S.,Koopman,M.M.,Reitsma,P.H.,Prins,M.H.,vanden Ende,A.and Buller,H.R.(2000). High plasma concentration of factor VIIIc. is a major risk factor for venous thromboembolism. *Thromb. Haemost*., 83, 5-9.

Kupferminc,MJ.,Eldor,A.,Steinman,N.,Many,A.,Bar-Am,A.,Jaffa,A.,Fait,G., Lessing,JB.(1999). Increased frequency of the genetic thrombophilia in women with complications of pregnancy. *Engl J Med*,340,9-13.

Kupferminc,M.(2003). Thrombophilia and pregnancy Review.*Reproductive Biology and Endocrinology*, 1,111 Retrived from **http://www.rbej.com/content/1/1/111**

Lepercq,J.,Conard,J.,Borek-Derlon,A.,*et al*.(2009). Venous thromboembolism during pregnancy: a retrospective of enoxaparin safety in 624 pregnancies. *BJOG*. ,108(11):1134-40.

Letizia,B.,Elio,c.,Domenico,A.(2007). Thrombophilias and Pregnancy Complications :A Case-Control Study. *InternatIonal Journal of BIomedIcal Science*: 3(3) : 74-81.

Levo,A.,Kuismanen,K.,Holopainen,P.,Vahtera,E.,Rasi,V.,Holopainen,P.,Rasi,V.,Krusius,T .,&Partanen,J.(2000). Single founder mutation (W380G) in type II protein C defiency in Finiland. *Thromb. Haemost*., 84, 424-428

Lindqvist,P.,Merlo J.(2006). The natural course of women with recurrent fetal loss. *Journal ThrombHaemost*: 4(4):896-7

MacDorman,MF.,Kirmeyer,S.,Wilson,EC.(2012). Fetal and perinatal mortality, United States. *Natl Vital Stat Rep*.: 60(8):1-22

Magee,L.,Helewa,M.,Moutquin,J.&Dadelszen,P.(2008). Diagnosis, Evaluation and Management of the Hypertensive Disorders of Pregnancy. *Journal of Obstetrics and Gynaecology* :Canada ,30,260-265

Mahmoodi BK., Kate MK., Waanders F., et al.(2008). High absolute risks and predictors of venous and arterial thromboembolic events in patients with nephrotic syndrome, *PubMed Circulation*., 117, 224–230.

Manjiri,K.,Catherine,N.P.,(2003). Acquired thrombophilias and pregnancy.*Review Article, Best Practice & Research Clinical Obstetrics &Gynaecology*: 17(3): 491-507

Many,A.,Elad,R.,Yaron,Y.,Eldor,A.,Lessing,JB.,Kupferminc ,MJ.(2002). Third trimester unexplained intrauterine fetal death is associated with inherited thrombophilia. *ObstetGynecol*, 99,684-687.

Marquard,K.,Westphal,LM.,Milki,AA.,Lathi,RB.(2009). Etiology of recurrent pregnancy loss in women over the age of 35 years. *Fertililty& Sterilility*:91(4): 1215-23.

Martinelli,I.,Legnani,C.,Bucciarelli,P.,Grandone,E.,DeStefano,V.,&Manucci,PM.(2001).Ri sk of pregnancy-related venous thrombosis in carriers of severe inherited thrombophilia. *Thromb .Haemost,* 86,800-803

Martinelli,I.,Taioli,E.,Ragni,G.,Levi-Setti,P.,Passamonti,SM.,Battagliolo,T.,Lodigian, C.,Mannucci,PM.(2003). Embryo implantation after assisted reproductive procedures and maternal thrombophilia . *Haematologica*. : 88(7):789-93

McLean,K.C.,Bernstein,I.M.,Brummel-Ziedins,K.E.(2012).Tissue factor-dependent thrombin generation across pregnancy. *American JournaObstetetric& Gynecology* :207(1): e1–e6

McLintock,C.North,R.A.,&Dekker,G.,(2001). Inherited thrombophilia implications for pregnancy-associated venous thromboembolism and obstetric complications. *Current Problems in Obstetrics, Gynecology and Fertility*:24 (4): 115-149

Ministry of Health,(2010), *Health Status of the Palestinian Population Annual Report* .Ministry of Health: Palestine.

Ministry of Health,(2013), *Health Status of the Palestinian Population AnnualReport.* Ministry of Health:Palestine.

Ministry of Health,(2014), *Health Status of the Palestinian Population Annual Report* .Ministry of Health:Palestine

Ministry of Health,(2015), *Health Status of the Palestinian Population Annual Report* .Ministry of Health:Palestine

Mirzaei,F.,Mahajeri,Z.(2012). Association of hereditary thrombophilia with intrauterine growth restriction. *Iranian Journal Reproductive Medicine*: 11(4): 275–278

Monari,F1.,Alberico,S.,Avagliano,L.,Cetin,I.,Cozzolino,S.,Gargano,G.,Marozio,L,Mecacci ,F.,Neri,I.,Tranquilli,AL.,Venturini,P.,Facchinetti,F.,(2012). Relation between maternal thrombophilia and stillbirth according to causes/associated conditions of death. *Early Human Development*:88(4):251-4.

Morrison,E.R.,Miedzybrodzka,Z.H.,Campbell,D.M.,Haites,N.E.,Wilson,B.J., watson,M .S.,Greaves,M.,&Vickers,M.A.(2002). *Thromb Haemost*.87(5):779-85.

Palestinian Central Bureau of Statistics ,(2008), *Census Semifinal Results in Gaza Strip. Summary for Population and Housing*. Palestinian Central Bureau of Statistic. Ramallah – Palestine

Palestinian Central Bureau of Statistics ,(2009), *Census Semifinal Results in Gaza Strip. Summary for Population and Housing*. Palestinian Central Bureau of Statistic. Ramallah – Palestine.

Palestinian Central Bureau of Statistics ,(2012), *Census Semifinal Results in Gaza Strip. Summary for Population and Housing.* Palestinian Central Bureau of Statistic. Ramallah – Palestine

Petri,M.(2000). Epidemiology of the antiphospholipid antibody syndrome. *J. Autoimmune*:15(2):145-151

Prothrombotic genotypes are not associated with pre-eclampsia and gestational hypertension: results from a large population-based study and systematic review. . *Thromb. Haemost*., 87, 779-785.

Rees,D.C.,Cox,M.,&Clegg,J.B.(1995). World distribution of factor V Leiden .*Lancet*, 346, 1133-1134.

Rey,E.,Kahn,R.,David,M.,Shrier,I.(2003). Thrombophilia disorders and fetal loss: a meta - analysis. *Lancet*,8,361-901

Regitz, V., Blomstrom C., Borghi C., Cifkova R., Ferreira R., Foidart,M.,, et al.(2011).

Guidelines on the management of cardiovascular diseases during pregnancy: The Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). *European Heart Journal*.

Robertson,L.,Wu,O.,Langhorne,P.,Twaddle,S.,Clark,P.,Lowe,G.D.,Walker,I.D,Greaves,M.,Brenkel,I.and Regan,L.,et.al.(2006). Thrombophilia in pregnancy, systematic review. *British Journal of Haematology*:132(2):171-196

Roosendaal,FR.(2005). Venous thrombosis:the role of genes, environment, and behavior. *Hematology American Society Hematological Education Program* ,(1), 1–12

Rosendaal,F.R.,Doggen,C.J.,Zivelin,A.,Arruda,V.R.,Aiach,M.,Siscovick,D.,Hillarp,A.,Watzke,H.H.,Bernardi,F.andCumming,A.M.,et.al.(1998). Geographic distribution of the 20210 G to A prothrombin variant.*ThromboHaemost*., 79, 706-708.

Ruiz-Irastorza,G.,Crowther,M.,Branch,W.,&Khamashta,MA.(2010). Antiphospholipid syndrome. *Lancet*, 376,509-1498

Sarig,G.,Klil-Drori,A.J.,Chap-Marshak,D.,Brenner,B.,Drugan,A.(2011). Activation of coagulation in amniotic fluid during normal human pregnancy. *Thrombosis Research Journal* , 128, 490–495.

Said, Joanne M. MBBS, FRANZCOG, CMFM.(2013). **“ i***nherited Thrombophilia Polymorphisms and Pregnancy Outcomes in Nulliparous Women” Obstetrics & Gynecology: Volume 115 - Issue 1 - p 5-13.*

Snow,V.,Qaseem,A.,Barry,P.,et.al.(2007). The American College of Physicians, American Academy of Family Physicians Panel on Deep Venous Thrombosis/Pulmonary Embolism. . Management of venous thrombo- embolism: a clinical practice guideline from the American College of Physicians and the American Academy of Family Physicians. . *An Internal Medicine* :146(3):204-210

Soligo,A.,Barini,R.,Carvalho,E.,BizzacchiJ,A.(2007). Prevalence Factors of thrombophilia . *Rev. Bras. Ginecol. Obstet.* 2007: 29(5):235-240

Sultan AA., Tata L., West J., Fiaschi L., Fleming K, Nelson-Piercy C., et al.(2013). Risk factors for first venous thromboembolism around *pregnancy.Pubmed Blood*,121, 3953-61.

Sundquist,K.,SundquistJ.,Svensson,PJ.,Zöller,B.,Memon,A.(2015). Role of family history of venous thromboembolism and thrombophilia as predictors of recurrence: a prospective follow-up study. *Thromb Haemost*:13(12):2180-2186

Szecsi,P.,Jorgensen,M.,Klajnbard,A.,Andersen,M.R.,Colov,N.P.,Stender,S.(2010). Haemostatic reference intervals in pregnancy. *Thromb. Haemost*, 103, 718–727

Thomas,R.H.,(2001).Hypercoagulablity syndromes.*Archives of Internal Medicine,* 161,2433-2439.

Thrombo-emolabile variant of-methylenetetrahydrofolate reductase associated with low red-cell folates implications for folate intake recommendation. *Lancet*, 349, 1591-1593.

Tikkanen,M.,Gissler,M.,Metsäranta,M.,Luukkaala,T.,Hiilesmaa,V.,Andersson,S.,Ylikorkala,O.,Paavonen,J.,&Nuutila, M.(2009). Maternal deaths in Finland: focus on placenta abruption. .*Acta ObstetGynecol Scand*,88,1124-7.

Tranquilli,AR.,Giannubilo,SR.,Dell'Uomo,B.,Grandone,E.(2004). Adverse pregnancy outcomes are associated with multiple maternal thrombophilic factors . *European Journal of Obstetrics & Gynecology and Reproductive Biology* :117: 144-147

UNRWA,(2012), *Health Status of the Palestinian Refugee Population Annual Report.* Department of Health

UNRWA,(2014), *Health Status of the Palestinian Refugee Population Annual Report.* Department of Health

Vander.,Molen,EF.,Verbruuggen,B.,Noakova,I.,Eskes,TK.,Mnnens,LA.,Blom,HJ.(2000).Hyperhomocysteinemia and other thrombotic risk factors in women with placental vasculopathy.*Britich Journal Obstetric and Gyncologicl*,107,785-91.

Walker,ID.,(2000). Thrombophilia in pregnancy. *American Journal of Clinical Pathology* :53: 573-580

Weiner,Z.,Fruchter,R.B.,Weiss,A.,Hujirat,Y.,Shalev,E.,Shalev,S.(2004). Thrombophilia and stillbirth: possible connection by intrauterine growth restriction. *an International Journal of Obstetrics and Gynaecology,*111,780-783.

Yen YC., Weng SF., Chen HA., Lin YS.(2013). Risk of retinal vein occlusion in patients with systemic lupus erythematosus. *Br J Ophthalmol.*,97,9, 1192–1196

Annexes

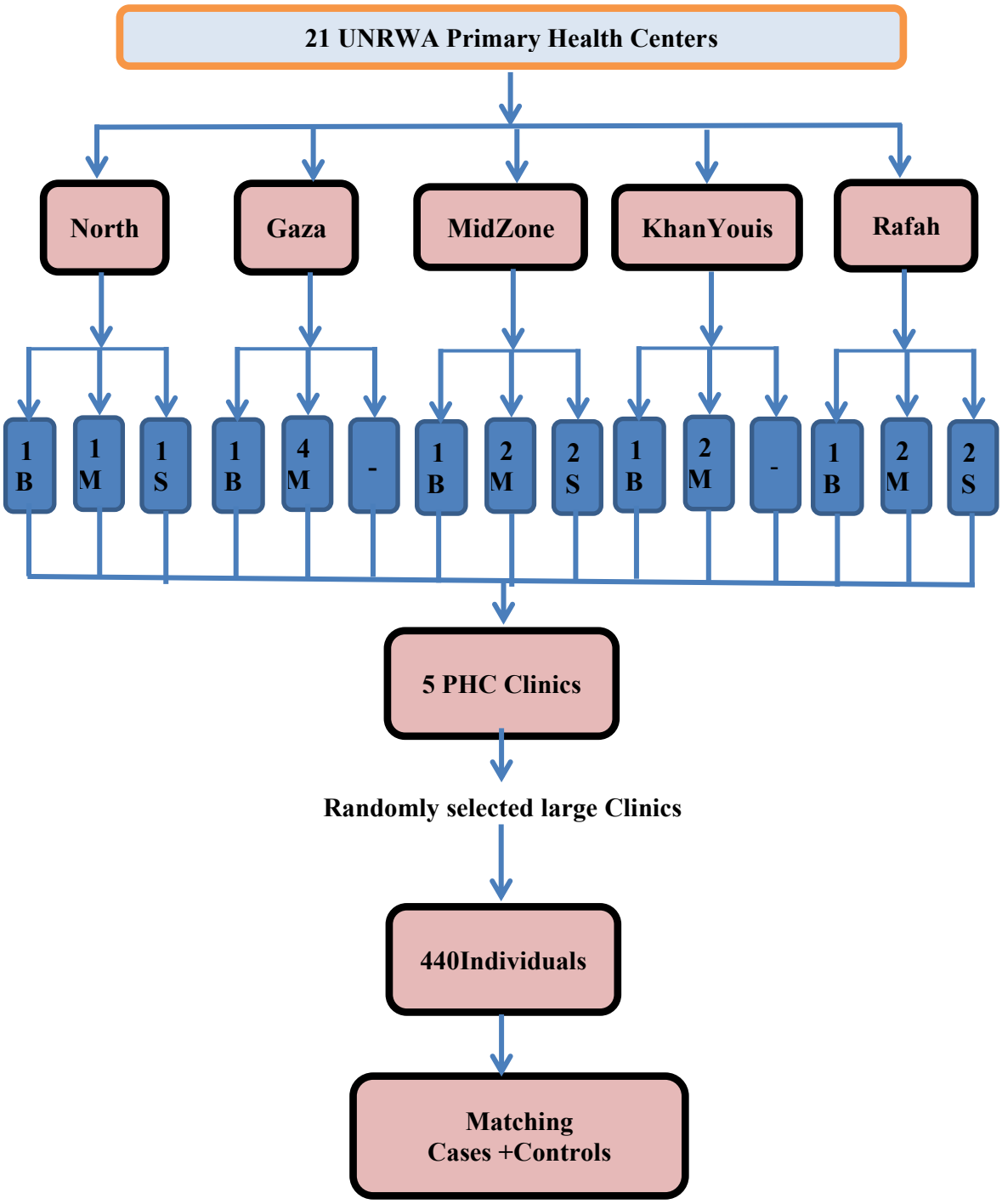
Annex (1) Study activities time table

Activity	Duration	2	3	4	5	6	7	8	9	10	11
Proposal writing	3 month										
Proposal defense And approval	1 month										
Expert committee Check for validity	1 month										
Pilot Study	3 month					3 mo.					
Modifications	2 weeks										
Data Collection	3 months										
Data Entry	3 months										
Data Analysis	2 months										
Research writing	2 months										

Annex (2) Sample size calculation

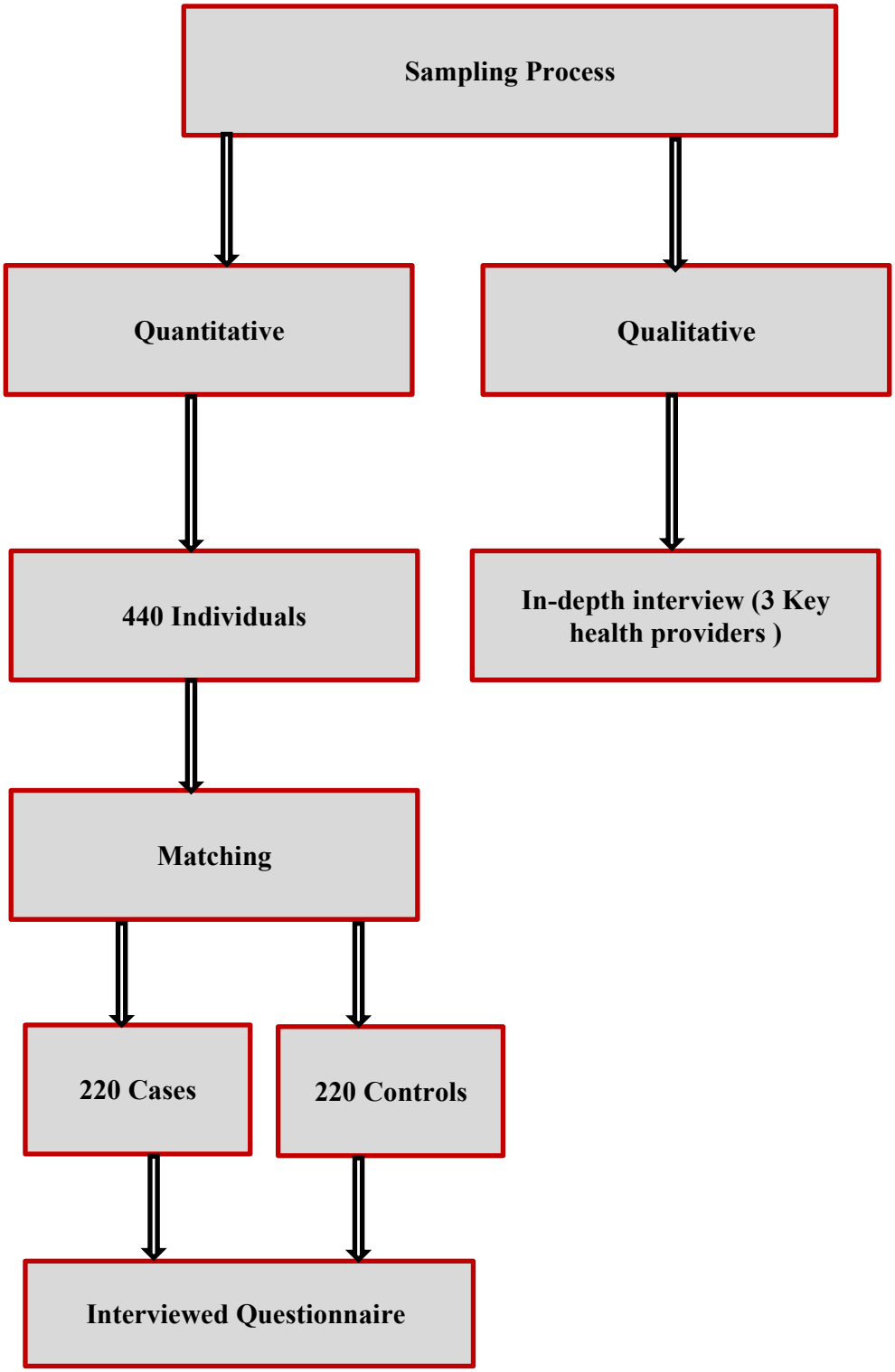
Assumptions:	
Odds ratio	**2**
Exposed controls	**15%**
Alpha risk	**5%**
Power	**80%**
Controls / Case ratio	**1**
Total exposed	**20.5435%**
Estimated sample size:	
Number of cases	**215**
Number of controls	**215**
Total	**430**

Annex (3) Sampling Distribution



B=big , M=middle , S=small

Annex (4) Sampling process



Annex(5) Estimated budget

Item	Unit	Expected USD
Study tools	MP3 recorder	$200
Transportation	Three months-all Gaza Governorates	$1,000
Data collectors	300*$5per questionnaire	$1,500
Training workshop	For data collectors	$200
Data entry and analysis		$1000
Photocopying of research papers	-	$1000
Internet used		$300
	Total	**$5,300**

Annex (6) List of arbitrators

	Name
1-	Dr. Bassam Abu Hamad
2-	Dr. Yehia Abed
3-	Dr. Khitam Abu Hamad
4-	Dr. Zoheir El Khatib
5-	Dr. Reem Lulu
6-	Dr. Jadallaha Ukasha
7-	Dr. Waleed Abu Hatab
8-	Dr. Ashraf YA El-Jedi
9-	Dr. Yousef Aljeesh

Annex (7): The study quantitative instrument - English

Study questionnaire

Dear participant

I am maha safi, collecting data for a research study aboutThromboprophylaxis use among Pregnant Women Gaza Governorates. You have been selected to participate in this study and your participation has no direct or indirect implications on your work.

This questionnaire is part of a study conducted by me as a requirement for a master degree in Public Health at Al Quds University. The findings and conclusions of this study may help in improving our conception. Filling this questionnaire takes about 30 minutes of your valuable time. Confidentiality will be provided and maintained and you don't need to tell your name. Even though I welcomed and appreciate your participation, your participation is optional. This study is self-funded and findings will be used only for the research purpose.

Please answer all questions as much as possible and if there is any ambiguous meaning, don't hesitate to ask for more clarification.

Part # 1 Demographic Characters :

<table>
<tr><th colspan="6">A) Wife</th></tr>
<tr><td>1. Serial number</td><td colspan="5">……..</td></tr>
<tr><td>2. Residency</td><td>North Gaza</td><td>Gaza</td><td>Mid zoom</td><td>Khan Younis</td><td>Rafah</td></tr>
<tr><td>3. Place of living</td><td colspan="2">city</td><td colspan="2">camp</td><td>Village</td></tr>
<tr><td>4. Age
5. Age at marriage</td><td colspan="5">……
……</td></tr>
<tr><td rowspan="3">6. Total Years of schooling</td><td colspan="4">i. Primary school</td><td></td></tr>
<tr><td colspan="4">ii. Secondary school</td><td></td></tr>
<tr><td colspan="4">iii. University or collage</td><td></td></tr>
<tr><td rowspan="2">7. Are you working?</td><td colspan="4">i. No</td><td></td></tr>
<tr><td colspan="4">ii. Yes. If yes specify</td><td></td></tr>
<tr><td rowspan="2"></td><td colspan="4">iii. Housewife</td><td></td></tr>
<tr><td colspan="4">iv. Governmental employee</td><td></td></tr>
</table>

	v. Non-Governmental employee	
	vi. Self-employed	
B) Husband		
1-Age:	……	
2- Age at marriage:	……	
3- Total Years of schooling	i. Primary school	
	ii. Secondary school	
	iii. University or collage	
4- Are you working?	i. No	
	ii. Yes. If yes specify	
	iii. Governmental employee	
	iv. Unemployed	
	v. Non-Governmental employee	
	vi. Self- employed	
5- Consanguineous Marriage	**a)** No	
	b) Yes	
If yes, specify	i. 1-first degree	
	ii. 2-second degree	
	iii. 3- far relative	
C) Economic Level		
1- Average family income	i. less than 1000 NIS.	
	ii. 1500-2000 NIS.	
	iii. more than 2000 NIS.	
2- House	i. Owned	
	ii. Rented	
3-Type of house	i. Concrete house	
	ii. Asbestoses house	
	iii. Mud house	
4-Number of rooms	i. One room	
	ii. Two rooms	
	iii. Three or more rooms	

Part # 2 Past Medical History :

1- Is there a past history of Noncommunicable diseases (Diabetes Mellitus, Hypertension					
a) Yes		**b)** No		**c)** If yes, specify:	
i.	Diabetes Mellitus		ii.	Renal diseases	
iii.	Hypertension		v.	Rheumatic Diseases	
v.	Heart Diseases		vi.	Systemic Lupus Erythroblastosis	
vii.	Respiratory Diseases		ii.	Others: specify	
ix.	Malignancy				
2- Is there a past history of Hematological Diseases?					
a) Yes		**b)** No		**c)** If yes, specify	
i.	Congenital thrombophilia				
ii.	Acquired thrombophilia				
iii.	Thromboembolism disorder				
	➢ If you choose i , ii specify				
i.	Lab-based				
ii.	Not lab based				
3- Is there a past history of vascular diseases?					
a) Yes		**b)** No		c) If you choose, yes specify	
i.	Varicose veins		ii.	Thrombophlebitis	
iii.	Deep Venous thrombosis		iv.	Vaclalitus	
4- Is there a past history of surgical operations					
i. Yes					
ii. No					
➢ **If yes, specify**					
4.1 Number of surgical operations					
i.	One				
ii.	Two to five				
iii.	More than five				
4.2 Type of surgical operations					

i.	Cesarean section				
ii.	Uterine surgery				
iii.	Pelvic surgery				
iv.	Abdominal surgery				
v.	Orthopedic surgery				
5 Are there associated family diseases?					
a) Yes		b) No			
5.1 If yes, specify					
i.	Congenital thrombophilia				
ii.	Acquired thrombophilia				
iii.	SLE				
iv.	Inflammatory bowel diseases				
v.	Rheumatological diseases				
vi.	Inflammatory poly-arthropathy				

Part # 3 Past Obstetric history of the study population

1. Gravida (Number of previous pregnancy)	
I. Primigravida	
II. Gravida two to gravida five	
III. Gravida 6 or more	
2. Parity (number of previous alive complete deliveries)	
I. Para One	
II. Para two to para five	
III. Para 6 or more	
3. Number of alive children	
I. Zero	
II. One to two	
III. Three or more	
4. A number of dead children …….	
I. Zero	
II. One to two	

III. Three or more	
➢ **if you choose the ii or iii, specify for each dead child**	
4.1 Child age at Death	
I. 28 GA. weeks - less than one week	
II. One week-less than 28 days	
III. 29 days to one year	
IV. More than one year	
4.2 Causes of death	
I. Unknown	
II. Birth trauma	
III. Congenital anomalies	
IV. Accidents or injury	
V. others	
5. History of infertility	
a) Yes b) No	
if yes specify	
5.1 Years of infertility	
a) One to two years	
b) Three to five years	
c) More than five years	
5.2 History of pregnancy induction	
a) Yes | b) No |	
5.2.1 If yes, specify	
i. IVF (Invitro fertilization)	
i. IUI (Intra uterine insemination	
i. Sponto ous induction	
5.2.2 If your answer 1 and 2 then answer the following	
i. Time of failure	
a) None	
b) 1-2	
c) More than two	

6. Is there a history of low birth weight?(fetal weight <2500gm) ?							
a) Yes		b) No		c) If yes, answer the following			
6.1 weight of baby							
a) less than or equal to 1.5 kg				b) **2-** > 1.5 -2.5 kg			
6.2 How many times do you have it ?							
a) 1-once		b) 2-twice		c) More than twice			
6.3 Is there a history of pretemlabor?							
a) yes		b) No		If yes specify			
6.3.1 Gestational age at delivery							
i. < 28 weeks		ii. 28-32 weeks		iii. 34-37 weeks			
7. Is there a history of miscarriages?							
a) Yes		**b)** No		If yes, specify the frequency			
7.1 Number of miscarriages							
i. One		**ii.** Two		**iii.** More than Two			
7.1.1 If two or more, were they consecutive?							
i. Consecutive				ii. Nonconsecutive			
7.1.2 Pregnancy age at abortion "Gestational age of abortion "							
One Week to 12-week Pregnancy		From 13 weeks to 20 weeks Pregnancy		More than 20 weeks Pregnancy		Diverse	

Part # 4 History of contraceptive use

1- Is there a history of contraceptive pills use			
a) Yes	b) No	c) If yes, specify	
1.1 Type of contraceptive pills			
i. Minipills			
ii. Combined oral contraceptive pills			
iii. Injectable hormone(DMPA injection)			
1.2 Duration of use			
i. Less than 2 years			
ii. 2 years -5 years			
iii. More than 5 years			

Part # 5 History of Pregnancy Complications

1- Is there a history of pregnancy complicated diseases?					
a) Yes		b) No		c) If yes, specify:	
1.1 Type of pregnancy complications					
i. Pregnancy induced hypertension		ii. Pre- eclampsia			
iii. Gestational diabetes		iv. PIH and GDM			
v. others: specify…					

Part# 6 Thrombo- embolism (TE) &Thromboprophylaix in previous pregnances :

1- Is there a history of TE in pregnancy ?			
a) Yes		b) No	
1.2 If yes, type of TE:			
i. Deep venous TE		ii. Pulmonary Embolism	
iii. Arterial thrombosis (Myocardial infarction, Cerebrovascular accident)		iv. Both (1 and 3)	
2 Did you take any thrombopropylaxis in previous pregnancies?			
a) Yes		b) No c) c) If yes, specify the following	
2.1 Was it used in all pregnancies?			
a) Yes	b) No	c) If No, Answer the following about pregnancy (you do not use heparin therapy)	
2.1.1 What was the outcome of that pregnancy?			
i. An abortion		ii. Alive birth	
iii. Early fetal death		iv. Congenitally malformed baby	
v. Intra uterine fetal death.		vi. IUGR	
vii. Early neonatal mortality		viii. Low birth weight baby	
2.1.2 Is there associated complications of that pregnancy?			
Yes	No	**If yes, specify**	
2.1.2.1 What was the associated pregnancy complications in the index pregnancy?			

i.	PIH		i.	APH	
ii.	GDM		ii.	PPH	
iii.	both (1,2)		iii.	Nothing	
iv.	DVT				
2.1.2.2 Was that pregnancy associated with preterm labor?					
a) Yes			b) No		

Part # 7 Last Pregnancy and thrombopropylaxis

1- What was the outcome of last pregnancy?				
i.	Abortion		ii. Alive baby	
iii.	Premature delivery		iv. Congenital anomalies	
v.	Early fetal death		vi. Perinatal mortality	
1.1 If your answer " ii " the weight of last a live baby				
a)	< ٢٥٠٠gm			
b)	٣٥٠٠-٢٥٠٠gm			
c)	٤٥٠٠- ٣٥٠٠gm			
d)	>4500 gm			
2. Have you used thromboprophylaxis in the last pregnancy?				
a)Yes		b) No		
2.1 What is the type of thromboprophylaxis used in that pregnancy?				
i.	Low dose aspirin alone		**ii.** Un-Fractioned heparin	
iii.	low molecular weight heparin (clexane, fraxiparin)		**iv.** Combination of low dose aspirin and heparin therapy	
If you answer (ii, iii, iv), answer the following				
2.1.1	**The dose of heparin therapy**			
i.	5000I.U/U.N heparin/OD/SC			
ii.	5000I.U/U.N heparin/BID/SC			
iii.	0.3 mg fraxiparin/OD/SC			
iv.	Clexane (20,40,60,80) mg/ OD/SC			
2.1.2	**The frequency of heparin therapy**			

i. Daily	
ii. Alternative days	
iii. Weekly	
iv. others	
2.1.3 Gestational age at starting heparin	
i. First trimester(0-13 weeks)	
ii. Second trimester(14- 26 weeks)	
iii. Third trimester (27- 40 weeks)	
2.1.4 Gestational age at stopping heparin	
i. First trimester(0-13 weeks)	
ii. Second trimester(14- 26 weeks)	
iii. Third trimester (27- 40 weeks)	
iv. Directly after delivery	
v. 1 week after delivery	
2.1.5 Who prescribed that medication for you	
i. Hospital physician	
ii. UNRWA physician	
iii. Private physician	
2.1.6 How did you access to medication (thromobrophylaxis)	
I. UNRWA clinics	
II. Public Hospitals	
III. Governmental clinics	
IV. Private Pharmacies	
V. Non-Governmental clinics	
2.1.7 Did you completely comply with regular use of the prescribed medications?	
i. Yes	
ii. No	
2.1.8 Did you perform a complete investigation profile to support the use of heparin therapy during pregnancy?	
a) Yes | b) No | c) If yes specify:	
2.1.8.1 Types of used thrombophilia investigation profile	
i. Molecular Genetic thrombophilia study	

ii.	Coagulation profile		
iii.	Antiphospholipid Antibodies		
iv.	Anti DNA antibodies		
v.	All of the above		
vi.	None of the above		
2.1.8.2 What was the total cost of heparin therapy?			
i.	5000-1000 NIS		
ii.	1000-1500 NIS		
iii.	More than 1500NIS		
2.1.8.3 Did you suffer any heparin therapy side effects in last pregnancy?			
i.	Painful injecting site		
ii.	bone ache		
iii.	Itching/allergy		
iv.	Associated thrombocytopenia		
v.	Ecchymosis patches		
vi.	Bleeding		
vii.	Others, specify		
2.1.8.4 Did you have any health complications during last pregnancy?			
a) Yes	**b)** No	**c)** if yes, specify	
2.1.8.4.1 What is Types of pregnancy complications			
I.	PIH	II. DVT	
III.	GDM	IV. APH	
V.	BOTH (i and ii)	VI. PPH	
VII.	Anemia		
Management practice and follow up among cases with thromboprophylaxis use			
2.2 Did you follow by specialist?			
I. Yes	**II.** No	**III.** if yes, specify	
2.2.1 How many times during pregnancy did you visit specialist room			
a) 1 times	b) 2-4 times	c) More than 4	
2.2.2 How many times has fetal us done for you at the clinic?			
a)one	b) 2-4 times	C) more than 4	
2.2.3 Did you follow at high-risk department at the hospital ?			

a) yes	b) no	
3 Where did you deliver?		
a) Private hospital	b) Public hospital	c) Private doctor

Part # 8 Evaluation of Blood pressure and obesity indicators among study population

1- Blood Pressure indicators for women		
I. <130/86	**II.** 130-139/86-88	**III.** or > and =140/90

2- Obesity indicators for pregnant women					
Underweight less than18.5 kg	Natural Weight 18.5-24.9	Overweight 25-29.9	First-class obesity 30-34.9	Second class obesity 35-39.9	Third class obesity More than 40

Any notes ……..

With best regards

Annex (8): The study quantitative instrument- Arabic

استخدام موانع التجلط للنساء الحوامل في
محافظات غزة

استطلاع /استبيان

أُعدت بواسطة
الطالبة / مها سميح صافى

تحت اشراف الدكتور
عبد الرزاق الكرد

٢٠١٧/٢٠١٦

عزيزتي .....

تحية طيبة وبعد

يعد الباحث رسالة ماجستير فى الصحة العامة بعنوان " استخدام موانع التجلط للنساء الحوامل في محافظات غزة " ويتضمن المقياس تسع اجزاء مختلفة تتعلق بعدد عوامل متغيرة ويتطلب ذلك قراءة كل القيم بعناية واختيار البديل الذى يتفق مع وجهة نظرك وذلك بوضع علامة(✓) في الخانة التي تتفق مع رأيك

والباحث إذ يشكر لكم تعاونكم الصادق لإنجاز هذا البحث ويؤكد لكم أن ما تدلون به من بيانات تخضع لسرية تامة ولن تستخدم إلا لأغراض البحث العلمي، ولكم وافر التحية.

الجزء الاول : الصفات الشخصية

اولا : الزوجة					
١. . الرقم التسلسلي					
٢. الإقامة	شمال غزة	غزة	الوسطى	خانيونس	رفح
٣. مكان المعيشة	المدينة		المخيم		القرية
٤. العمر **٥. العمر عند الزواج**					
٦. مجموع سنوات الدراسة	**أ.** المدرسة الابتدائية				
	ب. المدرسة الثانوية				
	ت. جامعة أو كلية				
٧. هل تعمل؟	١- نعم	٢- لا	اذا كان نعم. حددي		
	أ. موظفه حكومية				
	ب. موظفه غير حكومية				
	ت. عمل خاص				
تانيا : الزوج					
١. العمر					
٢. العمر عند الزواج					
٣. مجموع سنوات الدراسة	**أ.** خريج المرحلة الابتدائية				
	ب. خريج المرحلة الثانوية				
	ت. خريج جامعة أو كلية				

٤. هل يعمل؟	١- نعم	٢- لا	اذا كان نعم .حددي	
	أ. موظف حكومي			
	ب. موظف غير حكومي			
	ت. عمل خاص			
٥. زواج الأقارب	**أ.** لا	ب. نعم	إذا كانت الإجابة بنعم، حدد	
	a) الدرجه الأولى			
	b) الدرجة الثانية			
	c) قرابة بعيدة			
ثالثا: المستوى الاقتصادي				
١. متوسط دخل الاسرة	**أ.** أقل من ١٠٠٠ شيكل.			
	ب. 1500-٢٠٠٠ شيكل.			
	ت. أكثر من ٢٠٠٠ شيكل.			
٢. منزل	**أ.** ملك خاص			
	ب. مؤجر			
٣. نوع البيت	**أ.** بيت اسمنت			
	ب. بيت اسبست			
	ت. بيت الطين			
٤. عدد الغرف	**أ.** غرفة واحدة			
	ب. غرفتين			
	ت. . ثلاث غرف أو أكثر			

الجزء الثاني : التاريخ الطبي السابق

١. هل تعانى من أمراض الغير المعدية المزمنة (مرض السكري، ارتفاع ضغط الدم، .....)؟			
a. نعم	**b.** لا	إذا كانت الإجابة بنعم، حددي:	
أ. مرض السكري		**ب.** امراض الكلى	
ت. . ارتفاع ضغط الدم		**ث.** الأمراض الروماتيزمية	
ج. أمراض قلبيه		**ح.** الثعلبة الحمراء (الذئبة)	
خ. امراض الجهاز التنفسي		**د.** اورام	

		ذ. اخرى	
٢. هل تعانى من أمراض في الدم			
a. نعم	b. لا	إذا كانت الإجابة بنعم، حدد	
أ. التخثر الوراثي			
ب. التخثر المكتسب			
ت. الجلطات الدموية			
➢ إذا اخترت الأول والثاني تحديد :			
أ. مثبت بالتحاليل الطبية			
ب. غير مثبت بالتحاليل الطبية			
٣. هل تعاني من امراض مزمنة في الأوعية الدموية؟			
a) نعم	b) لا	إذا كانت الإجابة بنعم، حددي	
أ. توسع الأوردة(الدوالي)		**ب.** . التهاب الوريد الخثاري	
ت. جلطة وريدية عميقة		**ث.** التهاب الأوعية الدموية	
٤. هل هناك تاريخ سابق للعمليات الجراحية؟			
a) نعم	b) لا	إذا كانت الإجابة بنعم، حددي:	
١,٤ عدد العمليات الجراحية			
أ. واحد			
ب. مرتين إلى خمس			
ت. أكثر من خمسة			
٢,٤نوع العملية الجراحية			
أ. العملية القيصرية			
ب. جراحة الرحم			
ت. جراحة الحوض			
ث. عملية جراحية في البطن			
ج. جراحة العظام			
٥. هل هناك امراض مرتبطة بالأسرة؟			
a) نعم	b) لا	٥,١ إذا كانت الإجابة بنعم، حددي:	
أ. التخثر الدم الوراثي			
ب. التخثر الدم المكتسب			
ت. مرض الذئبة الحمراء (الذئبة الحمامية الجهازية)			
ث. أمراض الأمعاء الالتهابية			

ج. امراض الروماتزم	
ح. التهاب المفاصل المتعددة	

الجزء الثالث : تاريخ الولادات السابق

٨. . حامل (عدد الحمولات السابقة)	
أ. حمل اولى (بكرية)	
ب. حمل من اثنين إلى خمسة حمولات	
ت. ٦ حمولات او اكثر	
٩. عدد الولادات السابقة	
أ. واحد	
ب. اثنين إلى خمسة	
ت. ستة مرات أو أكثر	
١٠. عدد الأطفال الذين على قيد الحياة	
أ. صفر	
ب. واحد الى اثنين	
ت. ثلاثة أو أكثر	
١١. عدد الأطفال الذين توفوا	
أ. صفر	
ب. واحد الى اثنين	
ت. ثلاثة أو أكثر	
➢ **إذا اخترت الثاني أو الثالث، تحديد لكل طفل ميت**	
١,٤. عمر الطفل عند الموت	
أ. ٢٨ اسبوع حمل – اقل من اسبوع **ب.** أسبوع واحد حتى أقل من ٢٨ يوما	
ت. 29 . يوما إلى سنة واحدة	
ث. أكثر من سنة	
٢,٤ أسباب الوفاة	
أ. غير معروف	

ب. صدمة الولادة		
ت. التشوهات الخلقية		
ث. حوادث أو إصابات		
ج. عوامل اخرى		
١٢. هل تعانى من عقم؟		
a. نعم	**b.** لا	ذا كانت الإجابة بنعم. تحديد:
١,٥ عدد سنوات العقم		
أ. سنة إلى سنتين		
ب. ثلاثة إلى خمس سنوات		
ت. أكثر من خمس سنوات		
٢,٥ هل حاولت لا حداث حمل؟		
a. نعم	b. لا	٥,٢,١ اذا كان نعم . وضحي الطريقة:
أ. التلقيح الاصطناعي (اطفال الانابيب)		
ب. IUI (التلقيح داخل الرحم)		
ت. . الحث الطبي (استخدام المنشطات)		
٥,٢,٢ إذا كان لديك الجواب ا أو ب اجبى على ما يلى:		
١,٢,٥ عدد مرات نجاح الحمل:		
أ. صفر		
ب. ١-٢		
ت. أكثر من اثنين		
١- عدد مرات فشل الحمل		
أ. صفر		
ب. ١-٢		
ت. أكثر من اثنين		
٦. هل لديك مواليد ولدت اقل من الوزن الطبيعي ؟ (وزن الجنين <٢٥٠٠ جرام)		
أ. نعم	**ب.** لا	إذا كان الجواب نعم، الإجابة على ما يلي:
١,٦ وزن الطفل		
أ. أقل من أو يساوي ١,٥ كجم		**ب.** اكبر من ١,٥ -٢,٥ كجم
٢,٦ عدد الحالات		
أ. مرة	**ب.** مرتين	**ت.** ت. اكثر من مرتين
٣,٦ هل حصل ولادة مبكرة؟		

a. نعم	**b.** لا	إذا كان الجواب نعم، الإجابة على ما يلي
١,٣,٦ عمر الحمل عند الولادة		
أ. <٢٨ أسبوعا	**ب.** ٢٨-٣٢ أسابيع	**ت.** ٣٤-٣٦ أسابيع
٧. هل عانيت من اجهاضات سابقة؟		
a. نعم	**b.** لا	إذا كان الجواب نعم، الإجابة على ما يلي
١,٧ عدد مرات الاجهاضات السابقة		
أ. مرة	**ب.** مرتين	**ت.** اكثر من مرتين
١,١,٧ اذا كانت الاجابة ب و ت هل كان الاجهاض		
أ. توالى	**ب.** غير توالى	
٢,١,٧ سن الحمل عند الإجهاض "عمر الحمل للإجهاض"		
أسبوع واحد إلى ١٢ أسبوع الحمل	من ١٣ أسبوعا إلى ٢٠ أسبوعا الحمل	أكثر من ٢٠ أسبوعا الحمل	متنوع

الجزء الرابع: حبوب منع الحمل

٢- هل لديك ماضي طويل من استخدام حبوب منع الحمل؟		
a. نعم	**b.** لا	إذا كانت الإجابة بنعم حددي
a. انواع حبوب منع الحمل		
أ. حبوب أحادية الهرمون		
ب. حبوب تنائيه الهرمون		
ت. هرمون عن طريق الحقن (حقن DMPA)		
٢,١ مدة الاستخدام		
أ. أقل من ٢ سنوات		
ب. ٢ سنة -٥ سنوات		
ت. أكثر من ٥ سنوات		

الجزء الخامس: مضاعفات الحمل السابقة

١. هل عانيتِ من مضاعفات اثناء الحمولات السابقة؟				
a. نعم		**b.** لا		اذا كانت الاجابة. نعم حددي:
١,١ نوع المضاعفات التي حصلت ؟				
أ. ارتفاع ضغط الدم الناجم عن الحمل		**ب.** تسمم الحمل		
ت. سكري الحمل		**ث.** سكر حمل وضغط الحمل معا"		
ج. نزيف ما بعد الولادة		**ح.** النزف ما قبل الولادة (انفصال المشيمة)		
خ. . أخرى (حددي...)				

الجزء السادس : تخثر الدم وموانع التجلط

١. هل عانيت من جلطات دموية في الحمولات السابقة؟					
a. نعم		**b.** لا		**إذا كان الجواب نعم، حددي**	
١,١ نوع الجلطة التي حصلت					
أ. جلطة وريدية عميقة		**ب.** تجلط الدم الشرياني (احتشاء عضلة القلب – الجلطة الدماغية)			
ت. الانسداد الرئوي					
٢. هل استخدمت موانع التجلط في الحمولات السابقة؟					
a. نعم		**b.** لا		إذا كانت الإجابة بنعم، حددي	
b. نوع مانع التجلط					
أ. الأسبرين فقط					
ب. الهبارين					
ت. جرعة منخفضة الوزن من الهيبارين					
ث. الجمع بين الأسبرين والهيبارين					
• **اذا كان الجواب ب ، ت , ث .حددي ما يلى.**					
١,١,٢ عمر الحمل عند بداية مانع التجلط					
أ. الجزء الأول من الحمل (٠-١٣ أسابيع)					

ب. الجزء الثاني من الحمل (١٤- ٢٦ أسبوعا)			
ت. الجزء الثالث (٢٧- ٤٠ أسبوعا)			
٢,١,٢ من الذي وصف لك علاج الهيبارين			
أ. أطباء المستشفى			
ب. أطباء الأونروا			
ت. العيادات الخاصة للأطباء			
٣,١,٢ كم تكلفة العلاج الهيبارين يوميا			
أ. ١٠-٢٠ شيكل			
ب. ٢١-٣٠ شيكل			
ت. ٣١-٤٠ شيكل			
٤,١,٢ هل التزمت باستخدام علاج الهيبارين في الحمل			
أ. نعم	**ب.** لا	**ت.** اذا كان لا اذكري السبب:.....	
٥,١,٢ كيف حصلت على موانع التجلط			
أ. عيادات الأونروا		**ب.** . المستشفيات العامة	
ت. العيادات الحكومية		**ث.** الصيدليات الخاصة	
ج. العيادات غير الحكومية		**ح.** المستشفيات الخاصة	
٦,١,٢ هل تم استخدام موانع التجلط في جميع الحمولات؟			
a. نعم	**b.** لا	**c.** اذا كان لا اجبيى على النقاط التالية: عن الحمل الذى لم تستخدم فيه مانع التجلط	
١,٦,١,٢ : ما هي نتيجة هذا الحمل؟			
أ. الإجهاض		**ب.** الولادة الكاملة	
ت. وفاة الجنين في وقت مبكر(اقل من ٢٨ اسبوع)		**ث.** طفل مشوه خلقيا	
ج. وفاة الجنين داخل الرحم.(٢٨اسبوع واكثر)		**ح.** تأخر النمو داخل الرحم	
خ. جنين متوقى حول الولادة		**د.** طفل اقل من الوزن الطبيعي (٢٥٠٠ جم)	
٢,٦,١,٢ هل حدث مضاعفات في هذا الحمل؟			
a) نعم	b) لا	اذا كانت. نعم حددي:	
١,٢,٦,١,٢ نوع المضاعفات التي حصلت			
أ. ارتفاع ضغط الدم الناجم عن الحمل		**ب.** النزف ما قبل الولادة(انفصال المشيمة)	
ت. سكرى الحمل		**ث.** نزيف ما بعد الولادة	
ج. كل من (3،1)		**ح.** . جلطة وريدية عميقة	
خ. لا شيء			
٢,٢,٦,١,٢ هل صاحب هذا الحمل ولادة مبكرة؟			
أ. نعم		**ب.** لا	

الجزء السابع : الحمل الماضي

١- ماذا كانت نتيجة الحمل الماضي؟				
أ. الإجهاض		**ب.** طفل على قيد الحياة		
ت. ولادة مبكرة		**ث.** التشوهات الخلقية		
ج. وفاة الجنين في وقت مبكر(اقل من ٢٨ اسبوع)		**ح.** وفيات ما حول الولادة		
١,١ إذا كان لديك الجواب "ب" وزن الطفل السابق				
أ. < ٢٥٠٠جم				
ب. ٢٥٠٠-٣٥٠٠ جم				
ت. ٣٥٠٠ -٤٥٠٠ جم				
ث. > ٤٥٠٠ جم				
٢- هل استخدمت موانع التخثر في الحمل الأخير؟				
نعم		لا		
٢,١ما هو نوع مانع التجلط المستخدم في ذلك الحمل؟				
أ. الأسبرين وحده		**ب.** الهيبارين غير المجزأ heparin		
ت. منخفضة الوزن الجزيئي		**ث.** مزيج من الأسبرين و الهيبارين		
إذا أجبت (الثاني، الثالث، الرابع)، الإجابة على ما يلي				
٢,١,١ جرعة علاج الهيبارين				
أ. ٥٠٠٠ وحدة هيبارين مرة واحدة تحت الجلد				
ب. ٥٠٠٠ وحدة هيبارين مرتين تحت الجلد				
ت. ٠,٣ ملجم من مرة واحدة تحت الجلد				
ث. كلكسان(٢٠-٤٠-٦٠-٨٠)ملجم مرة واحدة تحت الجلد				
ج. كلكسان(٢٠-٤٠-٦٠-٨٠) ملجم مرتين تحت الجلد				
٢,١,٢ معدل اخد الهيبارين طول فترة الحمل				
أ. يومي				
ب. ايام متبادلة				
ت. أسبوعي				
ث. اخرى				

٢,١,٣ عمر الحمل عند بدء تناول الهيبارين	
أ. الجزء الأول من الحمل (٠-١٣ أسابيع)	
ب. الجزء الثاني من الحمل (١٤- ٢٦ أسبوعا)	
ت. الجزء الثالث (٢٧- ٤٠ أسبوعا)	
٢,١,٤ عمر الحمل في وقف تناول الهيبارين	
أ. الجزء الأول من الحمل (٠-١٣ أسابيع)	
ب. الجزء الثاني من الحمل (١٤- ٢٦ أسبوعا)	
ت. الجزء الثالث من الحمل (٢٧- ٤٠ أسبوعا)	
ث. مباشرة بعد الولادة	
ج. ١ أسبوع بعد الولادة	
٢,١,٥ من وصف الدواء لك؟	
أ. أطباء المستشفى	
ب. أطباء الأونروا	
ت. العيادات الخاصة للأطباء	
ث. . الآخرين	
٢,١,٦ كيف تمكنت من االحصول إلى الدواء	
a) عيادات الأونروا	
b) لمستشفيات العامة	
c) العيادات الحكومية	
d) الصيدليات الخاصة	
e) العيادات غير الحكومية	

٦,٢ هل التزمت بتعليمات الطبيب في تناول الادوية ؟

أ. نعم	**ب.** لا

a. ما هو السبب الرئيسي لتناول الهيبارين من وجهة نظرك؟ .....

٨,٢ هل قمت بإجراء تحليلات مخبرية لدعم استخدام علاج الهيبارين أثناء الحمل؟

a. نعم	**b.** لا	اذا كانت نعم. فحددي:

١,٨,٢ نوع التحاليل المخبرية

أ. تحاليل التخثر الوراثية(الجينات الوراثية)	
ب. . تحليل عوامل التجلط	
ت. التحاليل الأجسام المضادة	
ث. تحاليل الأجسام مضادة للحمض النووي	
٩,٢ ما هي التكلفة الإجمالية للعلاج الهيبارين خلال فترة الحمل؟	

أ. ٥٠٠٠-١٠٠٠ شيكل			
ب. ١٠٠١-١٥٠٠ شيكل			
ت. أكثر من ١٥٠٠شيكل			
١٠,٢ هل تعاني من أي آثار جانبية اثناء تناول علاج الهيبارين في الحمل الأخير؟			
أ. ألم في منطقة الحقن		**ب.** البقع حمراء (كدمات)	
ت. آلام العظام		**ث.** نزيف	
ج. . حكة / الحساسية		**ح.** أخرى (حددي)	
خ. نقص في الصفائح الدموية			
١١,٢ هل لديك أي مضاعفات صحية أثناء الحمل الأخير؟			
a. نعم	**b.** لا	إذا كانت الإجابة بنعم، حددي.	
١,١١,٢ نوع المضاعفات التي حصلت			
أ. ارتفاع ضغط الدم		**ب.** جلطة وردية عميقة	
ت. سكر الحمل- تسمم الحمل		**ث.** نزيف قبل الولادة (انفصال المشيمة)	
ج. ضغط الحمل وسكر الحمل		**ح.** نزيف قبل الولادة	
١٢,٢ هل كنت تتابعي مع الأخصائي/ الاخصائية فى العيادة ؟			
a. نعم	**b.** لا	اذا كانت الاجابة نعم حدد	
١,١٢,٢ كم مرة خلال فترة الحمل قمت بزيارة غرفة الأخصائي/ الاخصائية؟			
أ. مرة واحدة	**ب.** ٢-٤ مرات	**ت.** أكثر من ٤	
٢,١٢,٢ كم مرة قمت بتصوير الجنين عند الطبيب الأخصائي؟			
أ. واحد	**ب.** ٢-٤ مرات	**ت.** أكثر من ٤	
٣,١٢,٢ هل تابعت في قسم الحمل الخطر في المستشفى؟			
أ. نعم	**ب.** لا		
٤,١٢,٢ مكان الولادة			
أ. مستشفى خاص	**ب.** مستشفى عام	**ت.** الطبيب الخاص	

الجزء التامن : تقييم مؤشرات ضغط الدم والبدانة بين مجتمع الدراسة

١- مؤشرات ضغط الدم للنساء		
I. or > and =140/90	**V.** 130-139/86-88	**IV.** <130/86

٢- مؤشرات السمنة للنساء الحوامل					
الدرجة الثالثة السمنة أكثر من 40	الدرجة الثانية السمنة 35-39.9	السمنة من الدرجة الأولى 30-34.9	وزن زائد 25-29.9	الوزن الطبيعى 18.5-24.9	نقص الوزن أقل من ١٨,٥ كجم

تم بحمد الله

اتقدم بجزيل الشكر لكم

Annex (9): Maternal Health Records Review Checklist

Part (1) Distribution of obstetric history among cases group (thromboprophylaxis use) (100 MRR)

No.	factor	Variable	
		Yes	No
1	Age>=35		
2	Para>=6		
3	Habitual abortions >=3		
4	Perinatal deaths>=2		
5	Pervious pre- eclampsia		
6	Pervious GDM		
7	History of antepartum hemorrhage		
8	History of post hemorrhage		
9	Pregnancy induced hypertension		
10	DM with pregnancy		
11	History of CS		
12	Anima below 9		

Part (2) Distribution of risk factors among cases

No.	Factor	One risk factor	two risk factor	two risk factor
		Number	Number	Number
1	Distribution of risk factors among cases			

Part (3) Review of management practices.

No.	Factor	Frequency	
		Yes	No
1	Type of treatment		
2	Number of ANC visits(4and more)		
3	Specialist assessment and follow up		
4	Preconception care		
5	Family planning		
6	Routine investigations		
7	Related investigation coagulation profile		
8	Early registration		

Annex (10): Genetic Molecular study review

Genetic Molecular study among cases group who use thromboprophylaxis .

No.	Factor	Homogenous		Heterogeneous		Normal		TOTAL
		No.	%	No.	%	No.	%	
1	Prothrombin G2010A							
2	ACE 1/0							
3	PAI - 4G/5G							
4	Factor U							
5	MTHFR							
6	Factor XIII							

Annex (11) In-depth Interview Questions

1- How can you describe the current status of Thromboprophylaxis use among pregnant women in Gaza governorates in the last years?

2- How can you describe the epidemiological statistically features of existing risk factors that enhancing the use of Thromboprophylaxis among pregnant women? Past medical history, past obstetric history, maternal age and family history?

3- How much genetic factors and acquired Thromboprophilia syndrome is affecting the use of Thromboprophylaxis use among pregnant women?

4- What do you think the main basic evidence for starting Thromboprophylaxis use among pregnant women?[Clinical –Investigation – both]

5- How much of Thromboprophylaxis use among risky pregnant women is preventing bad pregnancy outcomes and pregnancy complications?

6- What are the different managerial practices followed by health care providers of thrombophylaxis use in risky pregnant women?

7- How much the distributed different mangment practices is adherent with international guidelines of Thromboprophylaxis among pregnant women? (Is there overuse or misuse)

8- Heparin thereby is highly expensive most of clients buy it from out pocket, how can UNRWA and ministry of health provide this thereby to the clients?

9- Medical records review for these risky pregnant women showed the following?

I. 1٤ % of women had less than 4 A.N.C visits during pregnancy period

II. 42% of women had no specialist assessment and follow up during pregnancy period

III. 60% of women had not enrolled in preconception care program during pregnancy period

IV. ٢٢% of women did not register early in pregnancy follow up

V. ٨٠% of MHR (maternal health records) lost documentation of related Thromboprophillia investigations

VI. ٥% of MHR did not do routine ANC investigation

How can you agree with these results?

10- Describe your recommendations and advices for improving maternal health services in UNRWA clinics?

Annex (12): An official letter of approval

EL-NAJJAR, Kefah

From: maha shaheen [drmahashaheen@hotmail.com]
Sent: 29 December 2016 09:48
To: EL-NAJJAR, Kefah
Subject: Fw: permission

From: DrHamad <ghsrcb@gmail.com>
Sent: Monday, December 26, 2016 3:59 PM
To: 'maha shaheen'
Subject: FW: permission

From: DrHamad [mailto:ghsrcb@gmail.com]
Sent: Monday, December 26, 2016 5:26 PM
To: 'maha shaheen' <drmahashaheen@hotmail.com>
Subject: FW: permission

Mabrook

From: AL-JADBA, Ghada [mailto:G.AL-JADBA@UNRWA.ORG]
Sent: Monday, December 26, 2016 1:30 PM
To: DrHamad <ghsrcb@gmail.com>
Subject: Re: permission

Dear Dr. Bassam,

It is my pleasure to approve it.

My best regards
Ghada

On Dec 26, 2016 12:42 PM, DrHamad <ghsrcb@gmail.com> wrote:

> Dear Dr Ghada
>
> I would highly appreciate your approval to conduct a study titled "**Thromboprophylaxis use among pregnant women in Gaza Governorates**". The study will be conducted by **Dr Maha Safi** (shaheen) from Jabalia Clinic. The study is a mix method, with quantitative and qualitative components. The study will be conducted at Jabalia, Rimal –Al nussirate –Khanyounis --and Rafah clinics. I highly appreciate giving her access to the database about pregnant ladies who have delivered in the last six months of 2016 by their risk scoring (high –alert, and normal). Also, the study includes interviewed questionnaires with women and also, focus Group discussion with the concerned health providers
> Thanks a lot
> Bassam

1

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: 01/08/2016 **Number:** PHRC/HC/151/16

Name: MAHA S. SAFIE **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:

Thromboprophylaxis Use among Pregnant Women in Gaza Governorates

The committee has decided to approve the above mentioned research. Approval number PHRC/HC/151/16 in its meeting on 01/08/2016

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

Signature

Member **Member**

1/8/2016

Chairman

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:-

1/8/16

E-Mail:pal.phrc@gmail.com
Gaza - Palestine غزة - فلسطين
شارع النصر - شرق العيون

استخدام موانع التجلط للنساء الحوامل في محافظات غزة

اعداد: مها سميح صافى

اشراف الدكتور :عبد الرزاق الكرد

ملخص الدراسة :

الحمل والولادة هو حدث قائم في حياة المرأة والحياة الأسرية ولعملية الحمل مطالب كبيرة وتحديات فسيولوجيه ، تحث العديد من التغيرات الفسيولوجية إلى للتكيف مع التغييرات الجديدة في النساء الحوامل، هذه الفترة من الحياة تحمل العديد من المخاطر الصحية التي قد تؤثر على حياة الأم والجنين.

تحدث التغيرات الفسيولوجية المختلفة أثناء عملية الحمل، والتي تؤثر على جميع اجهزة المرأة. تشمل التعديلات الأيضية والتغيرات الهرمونية. و نحن مهتمون في تلك التغييرات التي تؤثر على عوامل التخثر. ويرجع ذلك إلى الزيادة الثانوية في تركيزات عامل ما قبل التخثر، والحد من البروتينات المضادة للتخثر التي تحدث بشكل طبيعي وزيادة في الفيبرينوجين، التي تميز الحمل مع فرط التخثر .

النساء الحوامل في خطر متزايد من كل من الجلطات الدموية الوريدية والشريانية أثناء الحمل، بالمقارنة مع النساء غير الحوامل، خطر الجلطات الدموية الشريانية (السكتات الدماغية والنوبات القلبية) يتزايد ٣ إلى ٤ أضعاف وخطر الجلطات الدموية الوريدية .

امراض التخثر، إما مكتسبة أو وراثية، قد تحول التوازن نحو تعزيز التخثر ما يصل الى ٥٠٪ من المرضى الذين يعانون من التجلط خلال فتره الحمل .امراض التخثر الموروثة والمكتسبة يمكن العثور عليها في أكثر من ٥٠٪ من النساءاللواتي يعانون من فقدان الحمل المتكررة , امراض التخثر هي أيضا متكررة في النساء مع أمراض المشيمة والأوعية الدموية ، مثل تسمم الحمل، وتأخر النمو داخل الرحم، وانقطاع المشيمة، وفقدان الجنين في وقت متأخر .

نجاح الحمل يعتمد اعتمادا كبيرا على نشاط الدورة الدموية فى المشيمة بشكل كافى حيث وجود اى مشاكل فى الاوعية الدموية فى المشيمة يؤدى الى تغدية غير كافية للحمل مما يؤدى الى نتائج حمل سيئة قبل الاجهاض (إما خلال الربع الأول أو الثاني من الحمل)، وموت الجنين داخل الرحم ,تاخر نمو الجنين داخل الرحم , وفاة الجنين داخل الرحم وحول الولادة , انفصال المشيمة . لا يعرف مدى انتشار امراض التخثر بين النساء الحوامل في جميع أنحاء العالم, بعض الدراسات اثبت انها تتراوح من ٨٪ -١٥٪ فى الجنس الابيض وأظهرت العديد من الدراسات أن معدل عوامل التجلط المختلفة تتزايد مع الحالات ذوات نتاج الحمل السئ . الحمل الخطر آخذ في الازدياد في السنوات الأخيرة بسبب تراكم عوامل الخطر المختلفة وزيادة نتائج الحمل السيئة وفى نفس الوقت استخدام موانع التجلط اخد فى الازدياد، لا توجد بيانات متاحة حول المحددات المختلفة من استخدام موانع التجلط وكيفية استخدامه و دوره فى تحسين نتاج الحمل ،فالدراسة تهدف الى تحديد حالة استخدام موانع التجلط بين النساء الحوامل اللواتي تم ولادتهن في السنة الأخيرة من عام ٢٠١٦ وقد تابعت فى المراكز الصحية التابعة للأونروا في محافظات غزة.

مشكلة بحث

الحمل هو فترة فريدة من نوعها في حياة كل امرأة، بل هو هدف طبيعي لكل أسرة للحصول على طفلهم، ويتميز بالتغييرات الفسيولوجية المعقدة المختلفة كما تخضع المرأة للعديد من التغيرات الفسيولوجية، لذلك، الحمل يطرح

مطالب كبيرة وتحديات فسيولوجيا للمرأة ، في بعض النساء، التكيف مع هذه التغييرات غير كافية لذلك يمكن أن تحدث مضاعفات الحمل. وفقا لذلك، واحدة من أهم هذه الموضوع هو خطر تجلط الدم واستخدام موانع التجلط.

الحمل الخطير في غزة هو مع العديد من القضايا الصحية المعقدة، في السنوات الأخيرة انتشار الحمل خطر، نتائج الحمل السيئة والمضاعفات تتزايد بشكل كبير، بسبب التدهور الاجتماعي والاقتصادي.استخدام موانع التجلط ظاهرة حديثة فى الحمل الخطر والطلب على استخدام موانع التجلط يزداد في السنوات الأخيرة، وهذه الدراسة هي الدراسة الأولى في فلسطين ستجري حول استخدام موانع التجلط في الحمل لأنها سوف تقيس حجم المشكلة بين النساء الحوامل المحفوفة بالمخاطر، وسوف نناقش مختلف المحددات المرتبطة بهذه الظاهرة ، كنتائج الحمل المختلفة وكيفية استخدام موانع التجلط وهكذا سوف تساعدنا على الإجابة على السؤال الرئيسي عن استخدام موانع التجلط هو نتيجة الازدياد الحمل الخطر او شائع فى الحمل.

أهداف محددة

١. تقييم الوضع الحالي لاستخدام موانع التجلط بين النساء الحوامل المعرضات للخطر في مراكز الانروا الصحية في محافظات غزة

٢. تقييم مختلف المحددات المرتبطة باستخدام موانع التجلط بين النساء الحوامل المعرضات للخطر في المراكز الصحية التابعة للأونروا في محافظات غزة.

٣. التعرف على مشاكل الولادة والجنين ذات الصلة التي تساهم في استخدام موانع التجلط بين النساء الحوامل المحفوفة بالمخاطر.

٤. تقييم تأثير استخدام موانع التجلط ، لكل من الأمهات ونتائج الولادة

٥. تقييم ممارسات الطبيه فى استخدام موانع التجلط بين النساء الحوامل

٦ - اقتراحات و توصيات يمكن أن تساعد في تعزيز خدمات الرعاية الصحية المناسبة فيما يتعلق بالحوامل المعرضات للخطر

منهجية البحث :

هذه الدراسة هى دراسة وصفية وتحليلة لدراسة محددات استخدام موانع التجلط للسيدات الحوامل فى قطاع غزة وما هى الممارسات الطبية لاستخدام هذه الموانع فى الحمل وكيفية تاثير هذه الموانع على نتائج الحمل وقد اجريت هذه الدراسة فى المراكز الصحية التابعة للوكالة الغوث UNRWA , حيث تم اختيار خمس عيادات كبرى (جباليا – غزة النصيرات –خان يونس –رفح) بشكل عشوائى . وقد اجريت هذه الدراسة على مجموعتين فى السيدات الحوامل التى ولدت خلال الستة الاشهر الاخيرة فى عام ٢٠١٦ م . نتقسم جميع البيانات الى جزئين كمى ونوعى , فالكمى عبارة عن استبيان يشمل مجموعتين ,فالمجموعة الاولى , ٢٢٠سيدات مصنفات حمل خطر وفقا لتصنيف النظام الصحى فى الوكالة , وكانت على موانع التجلط خلال فتره الحمل , والمجموعة الثانية ٢٢٠ سيدات مصنفات حمل طبيعى وفقا لتصنيف النظام الصحى فى الوكالة ولم تستخدم موانع التجلط خلال فتره الحمل وقد تم مقارنة جميع الحمولات والمؤثرات التى قد تؤثر فى استخدام موانع التجلط (العوامل الاجتماعية والاقتصادية – التاريخ الطبى السابق – التاريخ الجراحى السابق –التاريخ الولادة السابق) كما أنه تم مراجعة ١٠٠ ملف تابع لرعاية الامومة والاطفال , من تلك السيدات التى استخدمت موانع التجلط خلال فتره الحمل – وفقا لعوامل عديدة . اما الجزء النوعى هو عباره عن

مقابلات تم اجراءهامع اخصائين نساء وولادة تابع عملهم للمراكز الصحية UNRWA , ولقد تم دعم ما حصلنا عليها فى الجزء النوعى مع ما تم حصوله فى الجزء الكمى مما ادى الى قوة النتائج ودعمها الاحصائى

الاستنتاجات والتوصيات:

نتائج الدراسة فريدة من نوعها في تقديم معلومات مفصلة موثقة عن حالة استخدام موانع التجلط بين النساء الحوامل، من خلال مناقشة مختلف المحددات المرتبطة، والممارسات الطبية المختلفة، نتائج الحمل المختلفة، وكيفيه استخدام موانع التجلط على تحسين نتائج الحمل ومضاعفات الحمل ، والهدف الرئيسي من هذه الدراسة هو تحديد عوامل الخطر الرئيسية إما عوامل الأم أو الجنين، والعواقب، والممارسات الطبية التي تساهم في استخدام موانع التجلط لدى الحوامل المخفوفة بالمخاصر، من أجل اكشاف إمكانيات للحد من مضاعفات الأم والجنين. الدراسة هي دراسة مقارنة تقارن بين مجموعتين من النساء اللواتي ولادتهن فى الاشهر الستة الأخيرة من عام ٢٠١٦، وتم التعامل مع مجموعة استخدمت موانع التجلط واخرى لم يستخدم موانع التجلط اثناء حملهن الاخير وتم اختيار خمسة مراكز صحية تابعة للأونروا من أجل البيانات وتم مناقشة مجموعة من المحددات المرتبطة بها من خلال استبيان ، حيث نناقشنا العوامل الاجتماعية الديموغرافية والتاريخ الطبي الماضي وتاريخ الولادة السابق ومضاعفات الحمل المرتبطة بها وتاريخ تخثر الدم وحصيلة الحمل، كما نناقشت الممارسات الطبيه المختلفة، ، ومقدار تكلفة وتوافر الأدوية في المستشفيات الحكومية والمراكز الصحية التابعة للأونروا , كما تم مراجعة السجلات الطبية لهولاء السيدات , وفى مقابلة مع اخصائين تم مناقشة العوامل التى تدعم نتائج الاستبيان , استخلصنا من الدراسة ان مركز جباليا الصحي التابع للأونروا يتمتع بمعدل مرتفع عن العيادات الأخرى وفى عدد الحالات التى تستخدم موانع التجلط ومعظمهم من العاطلين عن العمل، وكان متوسط دخل الأسرة أقل من ١٠٠٠ شيكل، كما أن غالبيتهم كانوا يتمتعون لدرجة اولى من القرابة بقوة المرتبطة وتعزيز استخدام موانع التجلط في الحمل.

كان ان عمر الأم يرتبط ارتباطا وثيقا باستخدام موانع التجلط كما أن معظم الحالات العمرية أكثر من ٢٥ سنة (٦٢,٢٪)، مع سن الزواج المبكر أقل من ٢٠ سنة (٥٩,١٪)، وكان معظم درحة قرابة لمعظمهم مني الدرجة الأولى بنسبة (٢٥٪).

يرتبط تاريخ الأمراض غير المعدية ارتباطا وثيقا باستخدام موانع التجلط حيث ان السيدات التى استخدمت الموانع لديها تاريخ من الامراض الغير معدية يفوت السيدات فى المجموعى الاخرى ٦ مرات , واهم هذه الامراض السكر – الضغط- امراض الجهاز التنفسى وامراض القلب .

كما اثبت الدراسة وجود علاقة قوية بين استخدام موانع التجلط وامراض الاوعية الدموية وبقدر ٢٩ مرة عن الحالات الطبيعية والتى تشمل امراض توسع الاوعية الدموية , التخثر الوريدى العميق , والتعاب الوريد الخثارى على التوالى .كما اثبتت الدراسة وجود علاقة قوية بين استخدام موانع التجلط وتاريخ العمليات الجراحية السابقة بقدر ٥ مرات واهمها القيصرية و عمليات البطن وعمليات العظام.

كما اوضحت الرسالة وجود علاقة قوية ما بين وجود د تاريخ اسري واستخدام موانع التجلط بقدر ٤ مرات – ٥ مرات في الحالات المرضية عن الحالات العادية واهم هده الا مراض التهابات الامعاء المزمنة وأمراض التخثر الوراثية و امراض التخثر المكتسبة و الثعلبة الحمراء وامراض الروماتزم الرحم والاطفال المتوفيين.

فيما يتعلق بتاريخ الحمولات السابقة فقد اوضحت الدراسة عدة نتائج منها : استخدام موانع التجلط يزدهد مع الحالات التي لديها اطفال متوفين خاصة حالات الاطفال المتوفين داخل الرحم و الاطفال المتوفيين حول الولادة بنسبة ٢١,٨٪

كما أثبتت الدراسة ان استخدام موانع التجلط يزداد مع الحالات التي عانت من عقم خاصة فترة العقم التي تجاوزت اكثر من عامين ودللك بقدر ١٣ مرة ومع محاولات زراعة طفل الانابيب الفاشلة بقدر ٤ مرات عن الحالات الطبيعية.
كما ان استخدام موانع التجلط يزداد مع الحالات التي تعاني من ولادات اطفال اقل من ٢٥٠٠ جم بقدر ٢ مرة عن الحالات العادية , كما انه يزداد استخدامه مع حالات الولاد ة المبكرة بقدر ٢ مرة عن الحالات الطبيعية.
اثبتت الدراسة ان استخدام موانع التجلط في الحمل يزداد مع وجود تاريخ مسبق من الاجهاضات خاصة الاجهاضات المتكررة أكثر من مرتين بنسبة ٦٣,٧٪ من الحالات المرضية وخاصة الربع الاول من الحمل بنسبة ٦٠,٨٪.
كما ان الدراسة اثبتت ان استخدام موانع التجلط اثناء الحمل يزداد في حالة وجود تاريخ طبي من التجلط ودلك بقدر ١١ مرة ويفوق الحالات الطبيعية.

كما اوضحت الدراسة ان استخدام موانع التجلط فالحمل قد حسن من صحة الأمهات في الحمل وصحة نتاج الحمل ٧٣,٩٪ من الحالات لم تعاني من مشاكل صحية متعلقة بالحمل ٧٨,٢٪ من الحالات انجبت اطفالا اصحاء كاملين النمو ٦٨,٤٪ من الاطفال دو اوزان طبيعية ما بين٢٥٠٠-٤٥٠٠.
كما اوضحت الدراسة ان معظم الحالات علا علاجات مزيجه من الاسبرين و الهبارين ٦٩٪و معظم الحالات تبدا العلاج من بداية الحمل ٨٦ % والمعظم ٦٣٪ ينهي العلاج مع نهاية الحمل وهدا يتناقض مع القوا نبين المحكمة لاستخدام موانع التجلط. كما ان الغالبية العظما من الحالات تحصل علا موانع التجلط من الصيدليات الخاصة بأثمان غالية ويوصف من قبل القطاع الخاص و لسبب فقدان التنسيق بين قطاعات الصحة المختلفة. كم ان الدراسة اوضحت ان السيدات اللواتي استخدمن موانع التجلط لديهن نسب مرتفعة من عوامل التجلط الوراثية (Prothrombin-ACE-FactorV-MTHFR and factor X111)
حيث وجود ذلك دعم استخدام موانع التجلط .بالرغم من ان معظم الحلات التي يتم تشخيصها من القطاع الخاص انها تحظى برعاية خاصة من قبل الاخصائيين داخل المراكز الصحية UNRWA مع الاحتفاظ ببعض المؤشرات الصحية التي يستوجب العمل علا تحسينها مثل الالتحاق فى برنامج رعاية ما قبل الحمل , التسجيل المبكر فى الحمل وعدد الزيارات التى يجب ان تفوق ٤ زيارات خلال الحمل , وبالتالى قد اوضحت الرسالة ان استخدام موانع التجلط , يفسر نتيجة زيادة نسبة الحمل الخطر مع وجود زيادة فى الاستخدام لعدم وجود تنسيق واضح بين قطاعات الصحة المختلفة وبروتوكلات واضحة لحكم الصرف.

التوصيات :

١. توحيد البروتوكلات التى تحكم استخدام موانع التجلط ما بين قطاعات الصحة المختلفة.
٢. تحفيز وجود مناغمة بين الرعاية الاولية والرعاية الثانوية لتحسين خدمات الامومة والطفل.
٣. تشجيع برامج رعاية ما قبل الحمل لتحسين نتاج الحمل والولادة .
٤. المراقبة والتعليم المستمر لتحسين الخدمات الصحية المقدمة للامهات المراجعات .
٥. تحفيز البحث العلمى وخاصة action researchللحصول على معلومات كافية فى استخدام موانع التجلط فى الحمل .