























Sudan University of Sciences and Technology

College of Graduate Studies

Assessment of Causes of Miscarriage in the Early Pregnancy Using Ultrasonography

تقويم أسباب اجهاض الحمل المبكر باستخدام الموجات فوق الصوتية

A thesis Submitted for Partial Fulfilment for the Requirement of
Master Degree in Diagnostic Medical Ultrasound

By:

Madina Ahmed Ali Suliman

Supervisor:

Dr. Ahmed Mostafa Abukonna

October 2015

DEDICATION

I dedicate my research work to my family and many friends. A special feeling of gratitude to my loving parents, for their words of encouragement. My children have never left my side and are very special.

.....

I also dedicate this research to my husband who has

.....

Supported me throughout the process. I will always appreciate all they have done, helping me to master the leader dots.

.....

I dedicate this work and give special thanks to my best friend I tidal for helping me.

ACKNOWLEDGEMENT

I wish to thank my committee members who were more than generous with their expertise and precious time. A special thanks to Dr. Ahmed Abukonna, my committee chairman for his countless hours of reflecting, reading, encouraging, and most of all patience throughout the entire process. My thanks extend to Dr. Mohammed Omer for agreeing to serve on my committee.

I would like to acknowledge and thank my college for allowing me to conduct my research and providing any assistance requested. Special thanks go to the members of staff development and human resources department for their continued support.

Finally I would like to thank the group of this patch for encouraging and pushing to do our best to complete the master.

ABSTRACT

Miscarriage is defined as the spontaneous loss of a pregnancy during the first 24 weeks of gestation. Early miscarriage' is defined as pregnancy loss during the first trimester of pregnancy (less than 12 weeks of gestation) and occurs in up to one in five pregnancies. Late miscarriage occurs during the second trimester (12–24 weeks of gestation) and is less common.

The aim of this study was to identify the causes of miscarriage as well as to correlate ultrasound findings to the main causes and clinical presentation of maternal.

The study conducted at Zayed city Hospital in U.A.E, 75 patients were enrolled in the study. All patients were scanned with ultrasound using transabdominal and transvaginal probe (3.5 - 7.7 Hz). Clinical data as well as ultrasound findings were collected and analysed.

The study revealed that the causes of miscarriage were unexplained in 64% of study sample. Infection was also contributed with 15%; furthermore vitamin D deficiency and high risk pregnancy represent the same percentage (6%). Less common cause was gestational diabetes.

Further research can be conducted using well controlled and large sample size to identify more causes. In addition new policies including public education to raise awareness and screening programmes for appropriate causes associated with adverse pregnancy outcomes could result in a decrease in the number of miscarriages.

المخلص

الاجهاض هو فقدان الفجائي للحمل أثناء الأربع وعشرون الأسبوع الأولي من الحمل و يعرف أيضا بفقدان الحمل في فترة الحمل الاولي (اقل من 12 اسبوع) ويحدث في ما يصل إلي واحد في خمسة حالات حمل.

كان الهدف من هذه الدراسة التعرف علي اسباب الاجهاض وكذلك مقارنة نتائج الموجات فوق الصوتية مع الاسباب الرئيسية والسريية للاجهاض

أجريت الدراسة بمستشفى مدينة زايد في الإمارات العربية المتحدة ،تم تسجيل 75 مريض في الدراسة. شملت كل المرضى الذين تم مسحهم بالموجات فوق الصوتية فوق جدارالبطن وعبرالمهبل. تم جمع البيانات السريية وكذلك نتائج الموجات فوق الصوتية وتحليلها

كشفت الدراسة أن أسباب الإجهاض غيرالمبررة تمثل 64% من عينة الدراسة. وقد مثلت العدوي أيضا نسبة 15%. علاوة على ذلك فان نقص فيتامين D والحمل الحرج تمثل نفس النسبة (6%). وقد كان أقل سبب للاجهاض هو سكري الحمل.

يمكن إجراء المزيد من الأبحاث باستخدام عينات مضبوطة وكبيرة الحجم لتحديد المزيد من الأسباب. فبالسياسات الجديدة بما في ذلك التعليم العام لرفع برامج التوعية والكشف عن الأسباب المرتبطة بالاجهاض يمكن تقليل نسبة حدوث الاجهاض المبكر.

LIST OF TABLES

Serial	Topic	Page No
4.1	Age distribution	24
4.2	Blood Groping	25
4.3	Causes of Miscarriage	25
4.4	Ultrasound Findings	26

List of Figures

No	Figure representation	Page No
2.1	Arterial blood supply to the pelvis.	26
2.2	Nerve supply to the pelvis	26
2.3	Pelvic descent of the ovary	27
2.4	The pelvic ligaments in the postnatal female	28
2.5	Differentiation of the paramesonephric (Müllerian ducts	29
2.6	IUFD no blood flow	33

List of Abbreviations

RPL	Recurrent pregnancy loss
PCOS	Poly cystic ovarian syndrome
LPD	Luteal phase defect
TSH	Thyroid stimulating hormone
APS	Antiphospholipid antibody syndrome
HSG	Hysterosalpingography
MTHFR	Tetrahydrofolatereductase
SPSS	Statistical Package for the Social Sciences
LDA	Low-dose aspirin
GS	Gestational sac
IUFD	Intra uterine fetal demise
RPL	Recurrent pregnancy loss

Table of contents

Serial	Topic	Page No
i	Dedication	i
ii	Acknowledgement	ii
iii	Abstract	iii
iv	List of Tables	iv
v	List of Figures	v
vi	List of Abbreviations	vi
vii	Table of contents	vii
Chapter One		
1.1	Introduction	1
1.2	Problem of the study	11
1.3	Objectives	11
Chapter Two		
2.1	Anatomy	13
2.2	Embryology of the Female Genitourinary Tract	16
2.3	Pathology of female pelvis	18
2.4	Ultrasound Machine	20
2.5	Previous study	21
Chapter Three		
3.1	Material	22
3.2	Methods and Techniques:	22
Chapter Four		
4.1	Results	24
Chapter Five		
5.1	Discussion	28
5.2	Conclusion	30
5.3	Recommendation	31

Chapter One

Chapter One

1. Introduction

1.1 Preface

Miscarriage is the loss of fetus before the 20th week of pregnancy. The medical term for a miscarriage is spontaneous abortion, but the condition is not an abortion in the common definition of that term.

Miscarriage is one of the most common yet under-studied adverse pregnancy outcomes. In the majority of cases the effects of a miscarriage on women's health are not serious and may be unreported. However in the most serious cases symptoms can include pain, bleeding and a risk of haemorrhage. Feelings of loss and grief are also common and the psychology and mental health of those affected can suffer (Engelhard et al., 2001).

Miscarriage can be classified as threatened, inevitable, incomplete, missed, or recurrent. Threatened miscarriage presents as vaginal bleeding/spotting with or without cervical dilatation. It will become inevitable when gross rupture of fetal membranes occurs along with severe vaginal bleeding and cervical dilatation; imminent fetal loss is almost certain in these cases. Incomplete miscarriage refers to the internal cervical os remaining open and allows for passage of blood, but the products of conception could remain entirely or partially in utero extrude . Missed miscarriage is used to describe dead fetus and placenta that remained for days or weeks in the uterus with a closed cervical os and/or without any symptoms of abortion (Bajekal N et.al. 200)

Recurrent miscarriage is generally defined as spontaneous abortions repeated consecutively over three or more times. At present, there exist a small number of accepted aetiologies for RPL these include parental chromosomal abnormalities, untreated hypothyroidism, uncontrolled diabetes mellitus, certain uterine anatomic abnormalities, and antiphospholipid antibody syndrome (APS). Other probable or possible aetiologies include additional endocrine disorders, heritable

and/or acquired thrombophilias, immunologic abnormalities, infections, and environmental factors (Abo-Shehadeh MN et.al. 2011)

Appropriate evaluation of RPL should include parental karyotyping. Genetic counselling is indicated in all cases of RPL associated with parental chromosomal abnormalities. Depending on the particular diagnosis, directed therapy may include in vitro fertilization with preimplantation genetic diagnosis. The use of donor gametes may be suggested in cases involving genetic anomalies that always result in embryonic aneuploidy (i.e., Robertsonian translocations involving homologous chromosomes).

1.2 Anatomic Aetiologies:

Anatomic abnormalities account for 10% to 15% of cases of RPL and are generally thought to cause miscarriage by interrupting the vasculature of the endometrium, prompting abnormal and inadequate placentation. Thus, those abnormalities that might interrupt the vascular supply of the endometrium are thought to be potential causes of RPL. These include congenital uterine anomalies, intrauterine adhesions, and uterine fibroids or polyps. Although more readily associated with second trimester losses or preterm labor, congenital uterine anomalies also play a part in RPL. The uterine septum is the congenital uterine anomaly most closely linked to RPL, with as much as a 76% risk of spontaneous pregnancy loss among affected patients.⁴ Other Müllerian anomalies, including unicornuate, didelphic, and bicornuate uteri have been associated with smaller increases in the risk for RPL.^{4,5} The role of the arcuate uterus in causing RPL is unclear. The presence of intrauterine adhesions, sometimes associated with Asherman syndrome, may significantly impact placentation and result in early pregnancy loss. Intramural fibroids larger than 5 cm, as well as submucosal fibroids of any size, can cause RPL.⁶ although congenital anomalies caused by prenatal exposure to diethylstilbestrol are clearly linked to RPL; this is becoming less clinically relevant as most affected patients move beyond their reproductive years.

Diagnostic evaluation for uterine anatomic anomalies should include office hysteroscopy or hysterosalpingography (HSG). Hysteroscopic resection of intrauterine adhesions and intrauterine septa are indicated if these abnormalities are identified. Patients undergoing successful hysteroscopic septum resection seem to enjoy near normal pregnancy outcomes, with term delivery rates of approximately 75% and live birth rates approximating 85%.⁷ Myomectomy should be considered in cases of submucosal fibroids or any type fibroids larger than 5 cm. Resection has been shown to significantly improve live birth rates from 57% to 93%.⁶ Myomectomy can be performed via open laparotomy, laparoscopy, or hysteroscopy.

1.3 Endocrine Aetiologies

Luteal phase defect (LPD), polycystic ovarian syndrome (PCOS), diabetes mellitus, thyroid disease, and hyperprolactinemia are among the endocrinologic disorders implicated in approximately 17% to 20% of RPL.^{2,8}

Traditionally, LPD has been proposed to result from inadequate production of progesterone by the corpus luteum and endometrial maturation insufficient for proper placentation. It is diagnosed when there is a persistent lag of longer than 2 days in the histologic development of the endometrium compared with the day of the menstrual cycle. Today, the true role of LPD in RPL is controversial and endometrial biopsies for LPD diagnosis are rarely indicated. Some studies have noted abnormal elevations in luteinizing hormone or in androgens (both features associated with PCOS) among patients experiencing RPL, suggesting that these abnormalities may result in premature aging of the oocyte and/or dyssynchronous maturation of the endometrium.^{9,10} This hypothesis is not without question. Studies have found evidence of PCOS in at least 40% of women with RPL (Garland SM, Ni' et al 2002).¹¹ Insulin resistance and the resultant hyperinsulinemia that is often present in cases of PCOS (as well as type II diabetes mellitus) may also play a role in RPL, as evidenced by the decreased rate of spontaneous pregnancy loss when patients undergo therapy

with the insulinsensitizing drug, metformin.¹² Poorly controlled type 1 diabetes mellitus is also associated with an increased risk of spontaneous abortion.¹³ Although untreated hypothyroidism is clearly associated with spontaneous miscarriage and RPL,¹⁴ the connection between antithyroid antibodies and RPL in euthyroid patients is currently under great debate.^{15,16} There are data to suggest that euthyroid women with antithyroid antibodies, especially those undergoing fertility therapy, are likely to become clinically hypothyroid very soon after the onset of pregnancy.¹⁷ Because pregnancy outcomes in these women may improve with early (possibly prenatal) thyroid hormone replacement,¹⁸ similar approaches are presently being studied among women with RPL.(Carr AC, et al1999) Evaluation of endocrine disorders should include measurement of the thyroid-stimulating hormone (TSH) level. Other testing that might be indicated based on the patient's presentation include insulin resistance testing, ovarian reserve testing, serum prolactin in the presence of irregular menses, antithyroid antibody testing, and, very rarely, luteal phase endometrial biopsies. Therapy with insulin-sensitizing agents for the treatment of RPL that occurs in the presence of PCOS has recently gained popularity.

1.4 Infectious Aetiologies

Certain infections, including *Listeria monocytogenes*, *Toxoplasma gondii*, rubella, herpes simplex virus (HSV), measles, cytomegalovirus, and coxsackieviruses, are known or suspected to play a role in sporadic spontaneous pregnancy loss. However, the role of infectious agents in recurrent loss is less clear, with a proposed incidence of 0.5%² to 5%.⁸ The proposed mechanisms for infectious causes of pregnancy loss include: (1) direct infection of the uterus, fetus, or placenta, (2) placental insufficiency, (3) chronic endometritis or endocervicitis, (4) amnionitis, or (5) infected intrauterine device. Because most of these are isolated events, it appears that there is a limited role for infections as a causative factor in RPL.

Evaluation and therapy should be tailored to individual cases. If a patient with RPL has a condition that leaves her immunocompromised or a history suggestive of sexually transmitted diseases, evaluation for chronic infections may be warranted. There is no evidence that routine infectious evaluation is appropriate or productive.

1.5 Immunologic Aetiologies

Because a fetus is not genetically identical to its mother, it is reasonable to infer that there are immunologic events that must occur to allow the mother to carry the fetus throughout gestation without rejection. In fact, there have been at least 10 such mechanisms proposed.²⁰ It therefore follows that there may be abnormalities within these immunologic mechanisms that could lead to both sporadic and recurrent pregnancy loss. Despite the intense interest in this potential etiology for RPL, there is no consensus on appropriate diagnostic workup or therapy. Therapies such as paternal leukocyte immunization, intravenous immune globulin, third-party donor cell immunization, and trophoblast membrane infusions have been shown to provide no significant improvement in live birth rates, and are only available for use in approved studies.

One specific autoimmune disorder, APS, requires particular attention as it has been clearly linked with many poor obstetric outcomes, including RPL. The discussion of APS could also appear within the context of thrombophilias, given that it is the most frequently acquired risk factor for thrombophilia, with a prevalence of 3% to 5% in the general population. APS is characterized by the presence of at least 1 clinical and 1 laboratory criterion²²:

- Clinical

- 1 or more confirmed episodes of vascular thrombosis (venous, arterial, or small vessel)
 - Pregnancy complications including either 3 or more consecutive pregnancy losses at less than 10 weeks of gestation, 1 or more

fatal deaths at greater than 10 weeks of gestation, or at least 1 preterm birth (< 34 weeks) due to severe preeclampsia or placental insufficiency

Laboratory (repeated at least 2 times, more than 12 weeks apart)

Positive plasma levels of the anticardiolipin antibodies (IgG or IgM) at medium to high levels

Positive plasma levels of the lupus anticoagulant

The mechanisms by which APS results in RPL are incompletely understood. A complete evaluation for RPL should include testing for anticardiolipin antibodies and lupus anticoagulant. Once diagnosed, treatment recommendations include low-dose aspirin (LDA, 81–100 mg/d) plus prophylactic low-molecular-weight heparin in otherwise healthy women (ie, absence of a systemic autoimmune disease such as systemic lupus erythematosus, or a history of thrombosis). LDA should be started before conception or with a positive pregnancy test. Heparin should be started with a positive pregnancy test.²² Heparin is a large complex of molecules that do not cross the placenta and, as such, is regarded as safe during pregnancy.

1.6 Thrombotic Aetiologies

Both inherited and combined inherited/acquired thrombophilias are common, with more than 15% of the white population carrying an inherited thrombophilic mutation.²³ The most common of these are the factor V Leiden mutation, mutation in the promoter region of the prothrombin gene, and mutations in the gene encoding methylene tetrahydrofolatereductase (MTHFR). These common mutations are associated with mild thrombotic risks, and it remains controversial whether homozygous MTHFR mutations are associated with vascular disease at all.²⁴ In contrast, more severe thrombophilic deficiencies, such as those of antithrombin and protein S, are much less common in the general population.

The potential association between RPL and heritable thrombophilias is based on the theory that impaired placental development and function secondary to venous and/or arterial thrombosis could lead to miscarriage. Based on studies that have shown maternal blood to begin flowing within the intervillous spaces of the placenta at approximately 10 weeks of gestation, the link between thrombophilias and pregnancy losses at greater than 10 weeks of gestation is more widely accepted than a link to those that occur prior to 10 weeks of gestation. However, evidence that the transfer of nutrition from the maternal blood to the fetal tissues depends on uterine blood flow, and thus may be affected by thrombotic events occurring there, suggests a role for thrombophilias in pregnancy losses regardless of gestational age. The heritable thrombophilias most often linked to RPL include hyperhomocysteinemia resulting from MTHFR mutations, activated protein C resistance associated with factor V Leiden mutations, protein C and protein S deficiencies, prothrombin promoter mutations, and antithrombin mutations. Acquired thrombophilias associated with RPL include hyperhomocysteinemia and activated protein C resistance. Although definite causative links between these heritable and acquired conditions have yet to be solidified, the best available data suggest testing for factor V Leiden mutation, protein S levels, prothrombin promoter mutations, homocysteine levels, and global activated protein C resistance, at least in white women.

Appropriate therapy for heritable or acquired thrombophilias should be initiated once the disorder is diagnosed. Therapy is disorder specific and includes (1) supplemental folic acid for those patients with hyperhomocysteinemia, (2) prophylactic anticoagulation in cases of isolated defects with no personal or family history of thrombotic complications, and (3) therapeutic anticoagulation in cases of combined thrombophilic defects. Homocysteine levels should be retested after initial treatment, and prophylactic anticoagulation considered when hyperhomocysteinemia is refractory to dietary intervention.

1.7 Environmental Aetiologies

Because of its propensity to result in feelings of responsibility and guilt, patients are often particularly concerned about the possibility that environmental exposures may have caused their pregnancy losses. Links between sporadic and/or RPL and occupational and environmental exposures to organic solvents, medications, ionizing radiation, and toxins have been suggested, although the studies performed are difficult to draw strong conclusions from because they tend to be retrospective and confounded by alternative or additional environmental exposures.^{3,8}

Three particular exposures-smoking, alcohol, and caffeine-have gained particular attention, and merit special consideration given their widespread use and modifiable nature. Although maternal alcoholism (or frequent consumption of intoxicating amounts of alcohol) is consistently associated with higher rates of spontaneous pregnancy loss, a connection with more moderate ingestion remains tenuous.³⁰ Studies linking moderate alcohol intake with pregnancy loss have shown an increase in risk when more than 3 drinks per week are consumed during the first trimester (odds ratio [OR] 2.3)³¹ or more than 5 drinks per week are consumed throughout pregnancy (OR 4.8).³² It seems logical that cigarette smoking could increase the risk of spontaneous abortion based on the ingestion of nicotine, a strong vasoconstrictor that is known to reduce uterine and placental blood flow. However, the link between smoking and pregnancy loss remains controversial, as some, but not all, studies have found an association.^{32–34} Although still not undisputed,³⁵ there appears some evidence that caffeine, even in amounts as low as 3 to 5 cups of coffee per day, may increase the risk of spontaneous pregnancy loss with a dose-dependent response.^{32,36,37} The association of caffeine, alcohol, and nicotine intake with recurrent pregnancy loss is even weaker than their associations with sporadic loss.

1.8 Unexplained Aetiologies

Directed interventions for patients with RPL are outlined in Table 2. However, when all known and potential causes for RPL are accounted for, almost half of patients will remain without a definitive diagnosis. The optimal management of these patients is often as unclear as the etiology of their RPL. Progesterone has been shown to be beneficial in decreasing the miscarriage rate among women who have experienced at least 3 losses. LDA has also been investigated as a potential therapy for unexplained RPL. Its use prior to and during pregnancy has only been proven to increase live birth rates among those women with previous miscarriages beyond 13 weeks of gestation. In fact, the most effective therapy for patients with unexplained RPL is often the most simple: antenatal counseling and psychological support. These measures have been shown to have subsequent pregnancy success rates of 86% when compared with success rates of 33% in women provided with no additional antenatal care. Therapeutic Interventions for Recurrent Pregnancy Loss Based on Etiologic Prognosis

Although the diagnosis of RPL can be quite devastating, it can be helpful for the physician and patient to keep in mind the relatively high likelihood that the next pregnancy will be successful. A particular individual's prognosis will depend on both the underlying cause for pregnancy losses and the number of prior losses. Correction of endocrine disorders, APA, and anatomic anomalies enjoy the highest success rates, approximately 60% to 90%. Patients with a cytogenetic basis for loss experience a wide range of success (20%–80%) that depends on the type of abnormality present.^{42,43} Overall, the prognosis for RPL is encouraging. Even with the diagnosis of RPL and as many as to prior losses, a patient is more likely to carry her next pregnancy to term than to have another loss.

Main Points

- Spontaneous pregnancy loss is common, with approximately 15% of all clinically recognized pregnancies resulting in miscarriage.
- When recurrent pregnancy loss (RPL) is defined as 3 consecutive pregnancy losses prior to 20 weeks from the last menstrual period, 1% to 2% of women will be affected.
- Because the risk of subsequent miscarriages is similar among women that have had 2 versus 3 miscarriages, and the probability of finding a treatable etiology is similar among the 2 groups, most experts agree that there is a role for evaluation after 2 losses.
- Accepted etiologies for RPL include parental chromosomal abnormalities, untreated hypothyroidism, uncontrolled diabetes mellitus, certain uterine anatomic abnormalities, and the antiphospholipid antibody syndrome (APS). Other probable or possible etiologies include additional endocrine disorders, heritable and/or acquired thrombophilias, immunologic abnormalities, and environmental causes. After evaluation for these causes, more than 33% of all cases will remain unexplained.
- Diagnostic evaluation should include maternal and paternal karyotypes, assessment of the uterine anatomy, and evaluation for thyroid dysfunction, APS, and selected thrombophilias. In some women, evaluation for insulin resistance, ovarian reserve, antithyroid antibodies, and prolactin disorders may be indicated.
- Therapy should be directed toward any treatable etiology, and may include in vitro fertilization with preimplantation genetic diagnosis, use of donor gametes, and surgical correction of anatomic abnormalities, correction of endocrine disorders, and anticoagulation or folic acid supplementation.

- In cases of unexplained RPL, progesterone has been shown to be beneficial in decreasing the miscarriage rate in women who had experienced at least 3 losses. Low-dose aspirin benefits those with a history of losses at more than 13 weeks of gestation.
- Antenatal counseling and psychological support should be offered to all couples experiencing RPL, as these measures have been shown to increase pregnancy success rates.
- Prognosis will depend on the underlying cause for pregnancy loss and the number of prior losses. Patients and physicians can be encouraged by the overall good prognosis, as even after 4 consecutive losses a patient has a greater than 60% to 65% chance of carrying her next pregnancy to term.

1.9 Problem of the study:

The researcher notice that the number of patient with miscarriage is increased in the last few years ago in Zayed City Hospital –UAE .

1.10 Objectives:-

1.10.1 General objective

To study the causes of miscarriage in early pregnancy.

1.10.2 Specific objectives:

- To determine the causes of miscarriage.
- To correlate the cause of miscarriage to age.
- To identify the correlation between weight and miscarriage.

Chapter Two

Chapter Two

2. Literature review and theoretical background

2.1 Literature review

Numerous studies were reviewed prior to selection for inclusion in this integrated review of literature. Seven studies related to the nursing management of miscarriage were included for clarification of the topic. All studies examined the experience of women having miscarriages occurring within the first trimester of pregnancy.

Although miscarriage is considered the most common adverse pregnancy outcome, worldwide figures are not available. In 2012–2013 there were 729 674 live births recorded in England and Wales (Office for National Statistics, 2012). Loss of one in five pregnancies suggests that this figure is accompanied by 200 000 miscarriages. Statistics from England and Wales for 2012/13 report that 39 800 miscarriages resulted in a hospital stay (Office for National Statistics, 2012).

In an Australian prospective cohort including 14 247 women aged 18–23 years, the rate of miscarriage varied from 11.3 to 86.5 per 100 live births amongst different groups; overall, miscarriage occurred in 25% of the women in the study when the women were 31–36 years old (Hure et al., 2012).

The causes of miscarriage are often unknown. However, in 50% of early miscarriages the fetus exhibits chromosomal aberrations such as a structural alteration or abnormal chromosomal numbers (Eiben et al., 1990; Suzumori and Sugiura-Ogasawara, 2010).

Several other factors have been associated with increased risk of miscarriage. The age of both parents has a significant role as the risk of an adverse pregnancy outcome is increased if the parents are 35 years old or older and it is 50% higher if the mother is 42 years of age (Andersen et al., 2000). In addition, factors such

as ethnic origin, psychological state of the mother, very low or very high pre-pregnancy BMI, feelings of stress, use of non-steroidal antiinflammatory drugs, smoking and alcohol consumption have also been associated with significantly higher rates of miscarriage (Coste et al., 1991). Moreover, it has been reported that women whose first pregnancy resulted in miscarriage are at a higher risk of the second pregnancy resulting in miscarriage compared with women who had a live birth (Kashani et al., 2006). Finally, a number of infections have been linked to miscarriage (Benedetto et al., 2004) and to other adverse outcomes, such as stillbirth (Goldenberg and Thompson, 2003) and preterm delivery (Garland et al., 2002). Specifically, 15% of early miscarriages and 66% of late miscarriages have been attributed to infections (Baud et al., 2008). In a recent study, 78% of 101 tissue samples from miscarriage were infected with bacteria (chorioamnionitis), whereas all the control samples from medically induced abortions were uninfected (Allanson et al., 2010).

2.2 Theoretical background

2.2.1 Anatomy

The female pelvis is morphologically different (different in form) from a male's but most of the differences are not apparent until puberty. The pelvic bones are larger and broader as they have evolved to create a larger space for childbirth.

The most noticeable differences are the width of the pubic outlet, the circular hole in the middle of the pelvic bones, and the width of the pubic arch, or the space under the base of the pelvis.

The bones of the pelvis are the hip bones, sacrum, and coccyx. Each hip bone contains three bones — the ilium, ischium, and pubis — that fuse together as we grow older. The sacrum, five fused vertebral bones, joins the pelvis between the crests of the ilium. Below the sacrum is the coccyx, or tailbone, a section of

fused bone that is the end of the vertebral column. The pelvis forms the base of the spine as well as the socket of the hip joint.

The hip joint is a ball-and-socket joint created by the femur and a part of the pelvis called the acetabulum. This joint and its ability to rotate in many angles is one of many pieces of anatomy that allows humans to walk.

The external female genitals include the vaginal opening, clitoris, urethra, labia minora, and labia majora. Collectively, these parts are called the vulva.

The vaginal opening is also home to the urethra, the tube through which the body expels urine. It is an extension of the ureters, or tubes that deliver urine from the bladder. The bladder is situated below the uterus.

The uterus is a pear-shaped, hollow organ where a fetus would develop prior to being born. Eggs, the female reproductive cells, are produced in the ovaries. A tube leads from each ovary to the uterus. These tubes are called the oviducts, or fallopian tubes.

The pelvic region also holds several digestive organs. These include the large intestine and small intestine. Both are vital to digesting food and expelling solid waste. The large intestine ends in the rear of the pelvis at the anus, a sphincter muscle that controls the disposal of solid waste.

The intestines are supported by a series of muscles known as the pelvic floor. These muscles also help the anus function and help push a baby through the vaginal opening during childbirth.

2.2.2 Blood and nerve supply:

The internal iliac (hypogastric) artery supplies most of the blood to the pelvis. It arises from the common iliac artery in front of the sacro-iliac joint. Although the internal iliac artery is often described as ending in anterior and posterior

divisions, its various branches arise in a variable manner. They may be divided into parietal and visceral branches.

2.2.3 Nerves

The pelvis is innervated chiefly by the sacral and coccygeal spinal nerves and by the pelvic part of the autonomic nervous system.

Figure 2.1 arterial blood supply to the pelvis.

Figure 2.2 nerve supply to the pelvis

2.2.4 Embryology of the Female Genitourinary Tract

In females the genital organs comprise of gonads, reproductive ducts and external genitalia. Gonadal differentiation occurs before the end of the embryonic period. Both the reproductive ducts and external genitalia differentiate before the end of the first trimester.

Development of the female genital tract continues in utero. The gonads descend in utero in girls.

Maturation of the genital tract is continuous during childhood through to puberty. As the cortical cords develop the primitive germ cells are incorporated in the mesenchyme of the ovaries. Gonadal differentiation takes place in the second month of fetal life. The primitive germ cells differentiate under the influence of placental gonadotropins.

The germ cells migrating to the genital ridge undergo successive mitotic divisions whilst in contact with the coelomic epithelium differentiating into several million oogonia. By 4–5 fetal months, the primitive follicles

organise within the fetal ovarian cortex. By 5–6 months gestation the ovaries contain 6–7 million primordial follicles. At this time, the primordial follicles are enveloped by a layer of epithelial cells, and are referred to as primary oocytes. The fate of an oocyte is determined once meiosis begins and no further mitotic division is possible thereafter. The vast majority of oocytes eventually degenerate over time.

Figure 2.3 Pelvic descent of the ovary

Figure 2.4 the pelvic ligaments in the postnatal female

Figure 2.5 Differentiation of the paramesonephric (Müllerian ducts)

2.2.5 Pathology of female

1. Vulvovaginitis is an inflammation of the vulva and vagina. It may be caused by irritating substances such as laundry soap, bubble baths. Symptoms include redness and itching in these areas and sometimes vaginal discharge. It can also be caused by an overgrowth of candida, a fungus normally present in the vagina.
2. Nonmenstrual vaginal bleeding is most commonly due to the presence of a foreign body in the vagina. It may also be due to urethral prolapse, a condition in which the mucous membranes of the urethra protrude into the vagina and forms a tiny, donut shaped mass of tissue that bleeds easily. It can also be due to a straddle injury or vaginal trauma from sexual abuse.

3. Ectopic Pregnancy occurs when a fertilized egg or zygote doesn't travel into the uterus, but instead grows rapidly in the fallopian tube.
4. Ovarian tumors, although rare, can occur. Women with ovarian tumors may have abdominal pain and masses that can be felt in the abdomen. Surgery may be needed to remove the tumor.
5. Ovarian cysts are noncancerous sacs filled with fluid or semi-solid material. Although they are common and generally harmless, they can become a problem if they grow very large. Large cysts may push on surrounding organs, causing abdominal pain. In most cases, cysts will pass or disappear on their own. If the cysts are painful and occur frequently, a doctor may prescribe birth control pills to alter their growth and occurrences. Surgery is also an option if they need to be removed.
6. Polycystic ovary syndrome is a hormone disorder in which too many hormones are produced by the ovaries. This condition causes the ovaries to become enlarged and develop many fluid filled sacs or cysts. It often first appears during the teen years. Depending on the type and the severity of the condition, it may be treated with drugs to regulate hormone balance and menstruation.
7. Trichomonas vaginalis inflammatory condition of the vagina usually a bacterial infection also called vaginosis.
8. Dysmenorrhea is painful periods.
9. Menorrhagia is when a woman has very heavy periods with excess bleeding.
10. Oligomenorrhea is when a woman misses or has infrequent periods, even though she has been menstruating for a while and is not pregnant.
11. Amenorrhea is when a girl has not started her period by the time she is 16 years old or 3 years after puberty has started, has not developed signs of

puberty by 14, or has had normal periods but has stopped menstruating for some reasons other than pregnancy.

12. Toxic shock syndrome is caused by toxins released into the body during a type of bacterial infection that is more likely to develop if a tampon is left in too long. It can produce high fever, diarrhea, vomiting, and shock.

13. Candidiasis symptoms of yeast infections include itching, burning and discharge. Yeast organisms are always present in all people, but are usually prevented from "overgrowth" (uncontrolled multiplication resulting in symptoms) by naturally occurring microorganisms

2.2.6 The ultrasound wave properties

Ultrasound relies on high frequency sounds to image the body and diagnose patients. Ultrasounds are therefore longitudinal waves which cause particles to oscillate back and forth and produce a series of compressions and rarefactions.

The amplitude is the distance a particle moves back or forth.

Compressions are areas of the wave where particles are close together and there is high pressure.

2.2.7 Production of sound waves

Ultrasound waves are produced when an electrical signal is applied to a piezoelectric crystal, it is produced by a piezoelectric crystal that has a dipole regions of positive and negative charges, when the piezoelectric crystal is stimulated electrically, the crystal expands along its short axis.

If the polarity of the electric signal changed is reversed, the crystal will contract.

When the crystal regains its original size and shape, it emits ultrasound waves.

Conversely if the ultrasound waves hits the piezoelectric crystal, it will produce the same shape deformity and after stability it will produce an electrical signal.

2.2.8 Frequencies used in ultrasound diagnosis

Ultrasound uses high frequency sounds that are higher than the human ear can hear. ie. 20 000 Hz. Ultrasound can't detect objects that are smaller than its wavelength and therefore higher frequencies of ultrasound produce better resolution. On the other hand, higher frequencies of ultrasound have short wavelengths and are absorbed easily and therefore are not as penetrating. For this reason high frequencies are used for scanning areas of the body close to the surface and low frequencies are used for areas that are deeper down in the body.

2.2.9 Ultrasound transducers

Transducers convert electrical energy into mechanical energy to produce ultrasound and vice versa.

The part of the transducer which does this work is a piezo electric crystal. It can be synthetic or natural. They have an inherent property of vibrating when an electric current is applied and thus produce ultrasonic waves and conversely produce electric impulse when vibrated thus helping the acquisition of data for the formation of image. This effect is called "Piezoelectric effect".

2.2.10 Doppler Basics

Doppler imaging can determine the presence and the direction of blood flow. The movement of the blood cells toward the transducer compresses the soundwaves and creates shorter wavelengths and higher frequencies than those emitted by the transducer and called a positive shift or red shift.

The movement of the blood cells away from the transducer expands the sound waves and creates a longer wavelengths and lower frequencies than those emitted by the transducer which is called a negative shift or Blue shift.

Figure 2.8 IUFD no blood flow

Chapter Three

Chapter Three

3. Materials and Method

3.1 Materials:

3.1.1 Machine used

The study conducted at Zayed City Hospital using GE ultrasound machine with nice probes ranges from 3.5 to 7.5 Hz

3.1.2 Sample size:

A sample of sufficient size is essential to describe the variable under study. Sample size in this study was 75 subjects.

3.2 Method:

3.2.1 Data collection

A data collection sheet has been designed to meet the purpose of the study, it has been filled by three mentioned observers then all sheets will be analyzed using SPSS software.

3.2.2 Technique used:

In pelvic ultrasound the uterus should be scanned clearly to check intra uterine gestational sac, Care should be taken to confirm the fetal heart beat.

Most pelvic ultrasounds are performed using both the transabdominal and transvaginal approaches; Transabdominal ultrasound involves scanning through your lower abdomen. Transabdominal ultrasound usually provides an overview of the pelvis rather than detailed images. The transabdominal assessment is particularly helpful for the examination of large pelvic masses extending into the abdomen, which are not always well viewed with transvaginal ultrasound.

A small amount of ultrasound gel is put on the skin of the lower abdomen, with the ultrasound probe then scanning through this gel. The gel helps improve contact between the probe and your skin.

Transvaginal ultrasound is an internal ultrasound. It involves scanning with the ultrasound probe lying in the vagina. Transvaginal ultrasound usually produces better and clearer images of the female pelvic organs, because the ultrasound probe lies closer to these structures.

The transvaginal ultrasound probe is thin, about 2cm diameter. The probe is covered with a disposable protective sheath. A small amount of ultrasound gel is placed on the end of this probe. The probe is then gently inserted a short distance into the vagina. All transvaginal probes have been cleaned and sterilised according to recommended protocols.

Figure 3.1 longitudinal view of uterus TAS

Figure 3.2 longitudinal view of uterus

Chapter Four

Chapter four

4. Results

The following tables and diagrams illustrate the demographic data, age, causes of miscarriage, blood groups and ultrasound findings results:

Table 4 -1 descriptive statistic for age, Height and weight

	N	Range	Minimum	Maximum	Mean	Std. Deviation
Age	75	29	18	47	32.81	7.109
Height	75	70	108	178	159.08	8.446
Weight	75	119.5	46.5	166.0	77.955	22.5136

Figure 4-1 age distribution

Figure 4-2 Blood Groping

Figure 4-3 Causes of Miscarriage

Figure 4-4 Ultrasound Findings

Table 4-2 ultrasound findings for gestational sac

Gestational Sacs	Frequencies	Percentages
EmptyGS	37	%49.4
NonEmptyGS	38	%50.6
Total	75	%100.0

Table 4-3ultrasound finding for Product of Conception:

R.P.C.	Frequencies	Percentages
Retained	12	%15.6
Non retained	63	%84.4
Total	75	%100.0

Table 4-4 5ultrasound findings of Fetal Cardiac Activity:

N.F.C.A.	Frequencies	Percentages
Negative	25	%32.5
None	52	%67.5
Total	77	%100.0

Chapter Five

Chapter 5

Discussion, conclusion and recommendations

5.1 Discussion:

Spontaneous pregnancy loss can be physically and emotionally taxing for couples, especially when faced with recurrent loss that's one of the reasons this research has been carried out to spot more light on this universal challenge. Seventy five pregnant women of different ages were enrolled in this study.

The age distribution showed that the majority of age was 33years old and more, which put the maternal at risk factor of miscarriage as suggested by previous studies. The age of both parents has a significant role as the risk of an adverse pregnancy outcome is increased if the parents are 35 years old or older, and it is 50% higher if the mother is 42 years of age (Moonachie et al., 2007). In addition, factors such as ethnic origin, psychological state of the mother, very low or very high pre-pregnancy BMI have also been associated with significantly higher rates of miscarriage (Moonachie et al., 2007). This also clearly seen in the result of this study, as the majority of women were over weighted.

The result of the study revealed that the majority of cases were unexplained, where infection was the second cause of miscarriage, vitamin D deficiency, high risk and gestational diabetes were few numbers. This result in line with previous studies which stated that the causes of miscarriage are often unknown (Giakoumelou et.al., 2015). Furthermore in a recent study, 78% of 101 tissue samples from miscarriage were infected with bacteria, whereas all the control samples from medically induced abortions were uninfected (Alanson et al., 2010). It is well established that pregnancy is a balance between tolerance and rejection, as the maternal immune system is re-programmed to tolerate the allergenic (paternal) fetal antigens (Thellin and Heinen, 2003). An active infection could destabilize this balance resulting in rejection, especially if it

leads to a serious illness of the mother. Evidently, further research is required to understand the causes of pregnancy failure considering other causes such as previous miscarriage, feelings of stress, use of non-steroidal anti inflammatory drugs, smoking and alcohol consumption.

5.2 **Conclusion:**

The research studied different cases of miscarriage from week (3) to (24) pregnant women ages varied between 18 and 47 and was conducted in Madinat Zayed Hospital (MZH) in United Arabs Emirates (Western Region).

All procedures done by using ultrasonography instrument with transducer type (3.5 Hz), both transabdominal scan and transvaginal scan were carried out.

Ultrasound is necessary throughout pregnancy period especially in first trimester because it can help in identifying different causes of miscarriage.

5.3 **Recommendations:**

- Doubling the efforts in medical domain in general and obstetrics and gynaecology in particular for avoiding and reduction of infants and children mortality.
- Frequent ultrasound check throughout the pregnancy period and in first trimester specifically is recommended.

References

- Abo-Shehada MN, Abu-Halaweh M. Seroprevalence of Brucella species among women with miscarriage in Jordan. *East Mediterr Health J* 2011; 17:871–874.
- Allanson B, Jennings B, Jacques A, Charles AK, Keil AD, Dickinson JE. Infection and fetal loss in the mid-second trimester of pregnancy. *Aust N Z J Obstet Gynaecol* 2010; 50:221–225.
- Anderson A, Bijlmer H, Fournier P-E, Graves S, Hartzell J, Kersh GJ, Limonard G, Marrie TJ, Massung RF, McQuiston JH et al. Diagnosis and management of Q fever—United States, 2013: recommendations from CDC and the Q Fever Working Group. *MMWR Recomm Rep* 2013; 62:1–30.
- Baud D, Goy G, Jatton K, Osterheld M-C, Blumer S, Borel N, Vial Y, Hohlfield P, Pospischil A, Greub G. Role of Chlamydia trachomatis in miscarriage. *Emerg Infect Dis* 2011; 17:1630–1635.
- Bajekal N, Li TC. Fibroids, infertility and pregnancy wastage. *Hum Reprod Update*. 2000; 6:614–620.
- Benedetto C, Tibaldi C, Marozio L, Marini S, Masuelli G, Pelissetto S, Sozzani P, Latino MA. Cervicovaginal infections during pregnancy: epidemiological and microbiological aspects. *J Matern Fetal Neonatal Med* 2004; 16 Suppl 2:9 – 12.
- Clifford K, Rai R, Regan L. Future pregnancy outcome in unexplained recurrent first trimester miscarriage. *Hum Reprod*. 1997; 12:387–389.
- Coste J, Job-Spira N, Fernandez H. Risk factors for spontaneous abortion: a case-control study in France. *Hum Reprod* 1991; 6:1332–1337.
- Eiben B, Bartels I, Baˆhr-Porsch S, Borgmann S, Gatz G, Gellert G, Goebel R, Hammans W, Hentemann M, Osmers R. Cytogenetic analysis of 750

spontaneous abortions with the direct-preparation method of chorionic villi and its implications for studying genetic causes of pregnancy wastage. *Am J Hum Genet* 1990; 47:656–663.

Engelhard IM, van den Hout MA, Arntz A. Posttraumatic stress disorder after pregnancy loss. *Gen Hosp Psychiatry* 2001; 23:62–66.

Fox-Lee L, Schust DJ. Recurrent pregnancy loss. In: Berek JS, editor. *Berek and Novak's Gynecology*. Philadelphia: Lippincott Williams & Wilkins; 2007. pp. 1277–1322.

Garland SM, Ní Chuileanna'ín F, Satzke C, Robins-Browne R. Mechanisms, organisms and markers of infection in pregnancy. *J Reprod Immunol* 2002; 57:169–183.

Giakoumelou, Sevi, Nick Wheelhouse, Kate Cuschieri, Gary Entrican, Sarah EM Howie, and Andrew W. Horne. "The role of infection in miscarriage." *Human reproduction updates* (2015): dmv041.

Glueck CJ, Wang P, Goldenberg N, Sieve-Smith L. Pregnancy outcomes among women with polycystic ovary syndrome treated with metformin. *Hum Reprod*. 2002;17:2858–2864.

Goldenberg RL, Thompson C. The infectious origins of stillbirth. *Am J ObstetGynecol* 2003; 189:861–873.

Haas DM, Ramsey PS. Progestogen for preventing miscarriage. *Cochrane Database Syst Rev*. 2008;2 CD003511.

Hure AJ, Powers JR, Mishra GD, Herbert DL, Byles JE, Loxton D. Miscarriage, preterm delivery, and stillbirth: large variations in rates within a cohort of Australian women. *PLoS One* 2012; 7:e37109.

Kashanian M, Akbarian AR, Baradaran H, Shabandoust SH. Pregnancy outcome following a previous spontaneous abortion (miscarriage). *GynecolObstet Invest* 2006; 61:167 –170

Kutteh WH, Yetman DL, Carr AC, et al. Increased prevalence of antithyroid antibodies identified in women with recurrent pregnancy loss but not in women undergoing assisted reproduction. *FertilSteril*. 1999;71:843–848.

Lane DA, Grant PJ. Role of hemostatic gene polymorphisms in venous and arterial thrombotic disease. *Blood*. 2000;95:1517–1532. [PubMed]

Macklon NS, Geraedts JPM, Fauser BCJM. Conception to ongoing pregnancy: the “black box” of early pregnancy loss. *Hum Reprod Update*. 2002;8:333–343.

Maconochie N, Doyle P, Prior S, Simmons R. Risk factors for first trimester miscarriage—results from a UK-population-based case-control study. *BJOG* 2007; 114:170 –186.

Management of Recurrent Early Pregnancy Loss. Washington, DC: The American College of Obstetricians and Gynaecologists; 2001. The American College of Obstetricians and Gynaecologists. (ACOG Practice Bulletin No. 24).

Office for National Statistics. Live births England and Wales 2012. 2012. Available at: [http:// www.ons.gov.uk/ons/rel/vsob1/birth-summary-tables-england-and-wales/2012/stb-births-in-england-and-wales-2012.html](http://www.ons.gov.uk/ons/rel/vsob1/birth-summary-tables-england-and-wales/2012/stb-births-in-england-and-wales-2012.html)

(15 February 2015, date last accessed).

Porter TF, LaCoursiere Y, Scott JR. Immunotherapy for recurrent miscarriage. *Cochrane Database Syst Rev*. 2006;2 CD000112.

Rai R, Backos M, Baxter N, et al. Recurrent miscarriage—an aspirin a day? *Hum Reprod*. 2000; 15:2220–2223.

Rai R, Backos M, Rushworth F, Regan L. Polycystic ovaries and recurrent miscarriage—a reappraisal. *Hum Reprod*. 2000; 15:612–615.

Rushworth FH, Backos M, Rai R, et al. Prospective pregnancy outcome in untreated recurrent miscarries with thyroid autoantibodies. *Hum Reprod*. 2000; 15:1637–1639

Suzumori N, Sugiura-Ogasawara M. Genetic factors as a cause of miscarriage. *Curr Med Chem* 2010; 17:3431–3437

Stephenson MD, Sierra S. Reproductive outcomes in recurrent pregnancy loss associated with a parental carrier of a structural chromosome rearrangement. *Hum Reprod*. 2006; 21:1076–1082.

Stray-Pedersen B, Stray-Pedersen S. Etiologic factors and subsequent reproductive performance in 195 couples with a prior history of habitual abortion. *Am J Obstet Gynecol*. 1984; 148:140–146.

Sugiura-Ogasawara M, Ozaki Y, Suzumori N, Suzumori K. Poor prognosis of recurrent aborters with either maternal or paternal reciprocal translocations. *FertilSteril*. 2004;81:367–373.

Thellin O, Heinen E. Pregnancy and the immune system: between tolerance and rejection. *Toxicology* 2003; 185:179–184.

Vaquero E, Lazzarin N, De Carolis H, et al. Mild thyroid abnormalities and recurrent spontaneous abortion: diagnostic and therapeutical approach. *Am J ReprodImmunol*. 2000;43:204–208.

Watson H, Kiddy DS, Hamilton-Fairley D, et al. Hypersecretion of luteinizing hormone and ovarian steroids in women with recurrent early miscarriages. *Hum Reprod*. 1993;8:829–833.

Windham GC, Von Behren J, Fenster L, et al. Moderate maternal alcohol consumption and risk of spontaneous abortion. *Epidemiology*.1997; 8:509–514.

Prefix