CHARACTERISTIC, ACCURACY AND OUTCOME OF HYSTEROSALPINGOGRAM IN HOSPITAL UNIVERSITI SAINS MALAYSIA

by

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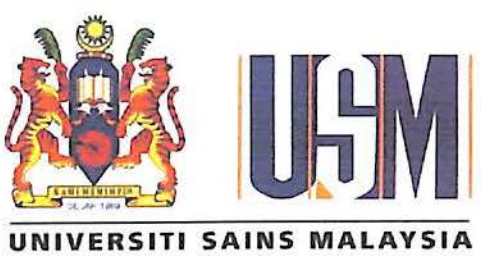
Dissertation Submitted in Partial Fulfillment Of The Requirements For The Degree Of Master Of Medicine (RADIOLOGY)



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Specially dedicated to:

My beloved and supportive husband, **Mohd. Amram bin Awang** for providing his never ending love, support and the tolerance to allow me to pursue my master programme without reservation.

&

My enchanting little angels **Qaisara Safiyyah** and **Qaisara Syauqina**. Both of you are very special to me, my whole life.

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My lovely parents, **Syed Yasin bin Haji Hitam** and **Serimas binti Abdul Manaf** for providing love, support and encouragement for me to complete the master programme.

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ABBREVIATIONS

FSH	Follicular stimulating hormone
HSG	Hysterosalpingogram
HUSM	Hospital Universiti Sains Malaysia
HyCoSy	Hysterosalpingo-contrast sonography
LH	Luteinizing hormone
PACS	Picture Archiving and Communication System
RIS	Radiology Information System
WHO	World Health Organization

ABSTRAK

Tajuk:

Ciri, ketepatan dan hasil pemeriksaan histerosalpingogram di HUSM.

Pengenalan:

Ketidaksuburan dialami oleh satu daripada tujuh pasangan di Malaysia. Lebih berabad berlalu, kadar ketidaksuburan di negara ini telah meningkat di antara 10 - 15 %. Walaupun demikian, kesedaran masyarakat tentang cara pengubatan yang ada masih kurang. Ramai yang tidak mengetahui bahawa ketidaksuburan merupakan penyakit sistem reproduktif yang kebanyakannya boleh diubati. Faktor saluran fallopian menyumbang 15 -30% kes ketidaksuburan dalam kebanyakan wanita di negara-negara membangun dengan kadar penyakit radang pelvis yang tinggi. Histerosalpingogram merupakan ujian diagnostik yang penting untuk menganalisis penyakit rongga rahim dan keutuhan saluran fallopian dalam penyiasatan ketidaksuburan dalam kalangan wanita. Banyak penyelidikan telah dilakukan untuk mengetahui tentang ketepatan histerosalpingogram berbanding laparoskopik yang dianggap sebagai tanda aras. Penyelidikan yang terkini menunjukkan keputusan kedua-dua modality adalah dalam kadar yang sejajar/selaras.

Objektif:

Untuk mengenalpasti ciri, ketepatan dan hasil pemeriksaan histerosalpingogram di HUSM.

Metodologi:

Kajian ini merupakan kajian secara retrospektif untuk selama 6 tahun bermula dari Januari 2003 hingga Disember 2008. Sebanyak 197 pesakit yang memenuhi kriteria dikaji. Senarai pesakit yang layak diperolehi daripada sistem PACS dan rekod pesakit dianalisis. Data yang diperlukan direkodkan dalam helaian pengumpulan data. Laporan histerosalpingogram diambil daripada sistem RIS.

Keputusan:

Seramai 197 orang pesakit diambil untuk kajian ini. Daripada 197 pesakit, 171 (86.8%) orang adalah Melayu, 16 (8.1%) orang pesakit Cina, 5 (2.5%) orang adalah Siam, 1 (0.5%) pesakit India dan 4 (2%) orang adalah daripada bangsa-bangsa lain. Purata jangka masa ketidaksuburan adalah 5.21 tahun dan purata umur adalah 32.38 tahun. Lebih daripada separuh pesakit dalam kajian ini mengalami ketidaksuburan "primary" (56.3%). Penyakit yang paling kerap ditemui ialah penyumbatan saluran fallopian sama ada berlaku penyumbatan pada sebelah ataupun kedua-dua belah saluran tersebut (17.8% dan 3.6%).

Ketepatan HSG bergantung kepada sensitiviti, spesifisiti, "positive predictive value" dan "negative predictive value". Dalam kajian ini, HSG didapati mempunyai spesifisiti yang sangat tinggi (100%) dan sensitiviti yang sederhana (58.3%) untuk mengesan keutuhan saluran fallopian. Ia mempunyai sensitiviti yang rendah (15.38%) untuk mengesan penyakit radang pelvis. Sejumlah 12.7% daripada pesakit mengandung dalam tempoh 6 bulan selepas menjalani pemeriksaan HSG dan mempunyai keputusan HSG yang normal dengan 2.35 kali lebih peluang berbanding pesakit yang mempunyai keputusan HSG yang abnormal.

Kesimpulan:

Dalam kajian ini, kami membuat kesimpulan bahawa prestasi diagnostik pemeriksaan histerosalpingografi untuk mendiagnosa penyakit radang pelvis adalah rendah. Oleh sebab HSG mempunyai sensitiviti yang rendah, kegunaannya untuk mengesan keutuhan saluran fallopian adalah terhad tetapi ia mempunyai spesifisiti yang tinggi menjadikan ia ujian yang berguna untuk mengesahkan penyumbatan saluran fallopian. Ia sepatutnya ditempatkan sebagai ujian saringan yang awal untuk mengesan keutuhan saluran fallopian. HSG mempunyai nilai prognostik yang rendah dan keputusan pemeriksaannya tidak begitu menyumbang pada jangkaan kehamilan akan berlaku.

ABSTRACT

Title:

Characteristic, accuracy and outcome of hysterosalpingogram in HUSM.

Introduction:

In Malaysia, infertility affects one out of seven couples. And over the decades, infertility rates in the country have been increasing between 10 and 15 per cent. Despite this figure, awareness of this and the treatments available are still lacking. Many are not aware that infertility is a disease of the reproductive system which in the majority of cases can be treated. Tubal factor accounts for 15 – 30% of infertility in all women in developing countries with high rates of pelvic inflammatory disease. Hysterosalpingogram is an important diagnostic test in the evaluation of intrauterine abnormalities and tubal patency in the infertility workup of female patients. Many studies had been done to assess the accuracy of hysterosalpingogram as compared to laparoscopy as the gold standard. The recent study showed good concordance rate of the findings investigated by both modalities.

Objectives:

To identify the characteristics, accuracy and outcome of hysterosalpingography in HUSM.

Methodology:

This was a cross-sectional study on retrospective data over a period of 6 years starting from January 2003 till December 2008. A total of 197 patients that fulfilled the inclusion criteria were studied. List of eligible patients were obtained from PACS and the patient's medical records were reviewed and data needed were entered in the data collection sheet. Reports of HSG were taken from PACS and Radiology Information System (RIS).

Results:

A total of 197 patients were included in this study. Out of 197 patients, 171 (86.8%) were Malays, 16 (8.1%) were Chinese, 5 (2.5%) were Siamese, 1 (0.5%) was Indian and 4 (2%) were other races. The mean duration of infertility was 5.21 years and mean age was 32.38 years. More than half of the patients in our study had primary infertility (56.3%). The commonest pathology detected at HSG was tubal occlusion either one-sided or two-sided occlusion (17.8% and 3.6% respectively). The diagnostic accuracy of HSG was based on sensitivity, specificity, positive predictive value and negative predictive value.

In our study, HSG is shown to have very high specificity (100%) and moderate sensitivity (58.3%) in detecting tubal patency and has low sensitivity (15.38%) in the detecting pelvic pathology. A total of 12.7% of our patients were pregnant within 6 months following normal HSG examination with 2.35 higher chances as compared to those with abnormal HSG.

Conclusion:

In this study, we conclude that the diagnostic performance of hysterosalpingography in the diagnosis of pelvic pathology is poor. HSG has a limited use for detecting tubal patency because of its low sensitivity; however its high specificity makes it a useful test for ruling in tubal obstruction. It should be placed as first line screening investigation of tubal patency. HSG has low prognostic value and the findings at HSG do not contribute much in predicting the occurrence of pregnancy.

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CHAPTER 1

INTRODUCTION

1 INTRODUCTION

The World Health Organization (WHO) reported in 2002 that infertility affects about 80 million people worldwide, and estimated that 1 in 10 couples experiences infertility. The incidence of infertility is approximately 10 – 15% and seems to be on the rise. According to WHO, global infertility rate is about 15% while the Malaysian figure is between 10 to 15% (Ishak and Norain, 2008). In Malaysia infertility affects one out of seven couples and over the decade's infertility rates in the country has been increasing to between 10 and 15%. Life style factors e.g. diet, obesity, substance abuse, increased exposure to environmental toxins and stress influences the reproductive process negatively (Asifa Ghazi *et al.*, 2007).

An increased in public awareness about infertility and its treatment options, more and more couples are expected to seek treatment for this condition. Tubal factors are believed to be responsible for 35 – 50% of infertility, evaluation of tubal dysfunction is thus important in the investigation of female infertility (El-Yazied, 2007). Lash MM et al., have demonstrated that a women with secondary infertility have a higher likelihood of fallopian tube obstruction on HSG when compared with those with primary infertility. He recommended that routine evaluation of tubal patency should be done in patients with secondary infertility (Akinola R. A. *et al.*, 2009).

Hysterosalpingography (HSG) is a method used for screening purposes in the routine infertility evaluation. It was used in many centers as a preliminary investigation tool. It is helpful in evaluating anatomy of uterine cavity and patency of fallopian tube. A properly performed HSG will give an idea of the morphology of uterine cavity, lumen of fallopian tubes and finally tubal patency by visualizing peritoneal spillage of the contrast material.

Despite the development of other diagnostic tools such as, Magnetic Resonance Imaging, hysteroscopy and laparoscopy, HSG remains the main examination for the fallopian tubes in developing countries (Belen Ubeda *et al.*, 2001). With the recent advances in reproductive medicine, HSG has become a relatively quick and non-invasive examination to evaluate the fallopian tubes and uterine cavity. The radiation risk from a typical HSG are also low (Eng C W *et al.*, 2007). The ovaries are said to be exposed to 500 to 1000mRads of radiation during HSG (Gokhan Goynumer *et al.*, 2008).

This study was conducted to identify the characteristics, accuracy and outcome of hysterosalpingogram in HUSM.

CHAPTER 2

LITERATURE REVIEW

2 LITERATURE REVIEW

2.1 General Overview

Infertility is a complex disorder with significant medical, psychosocial and economic aspects. Both the prevalence of infertility and the number of patients seeking treatment of this disorder are increasing. In today's modern society, conceiving a child has become somewhat of a challenge for many couples (S. Indramalar and Za, 2006). According to Medically Assisted Conception (MAC) unit Universiti Kebangsaan Malaysia, at least 1 in 6 couples will experience some degree of infertility. There are an estimated 400,000 couples between the ages of 20 to 40 who suffered from infertility in Malaysia (UKMMC Departments, 19 May 2009). It is usually a devastating life event as most couples plan for a family upon marriage. Infertility is considered a stigma and a major public health problem in Africa which can cause great family problems, instability and suicidal tendencies (EO, 1987).
Infertility affects both men and women. WHO had done a comprehensive study of infertility involving 5,800 infertile couples seeking help at 33 medical centers in 22 developed and developing countries; found that men were either the sole cause or a contributing factor to infertility in more than half of couples.

Overall the studies found that female causes accounted for between 25 to 37% of infertility worldwide (with larger proportions in sub-Saharan Africa and Southeast Asia), male causes accounted for between 8 to 22%, and both male and female causes accounted for between 21 to 38% (Sherris, 1997). The most common identifiable female factors is tubal abnormalities which account for approximately 35

- 40% of cases (Ludovico Muzii *et al.*, 1996). Since tubal factors are believed to be a responsible cause for majority of the female infertility, evaluation of tubal dysfunction is of obvious importance in the infertility investigation (Marc J. N. C. Kierse and Vandevellen, 1973).

HSG is one of the most commonly used techniques for the initial evaluation of infertility. It is primarily used for the evaluation of fallopian tubes, it's a reliable procedure, quick and easy to perform, safe and cost effective as compared to other modalities (Saima Naqi *et al.*, 2008). HSG is especially useful for assessment of tubal causes of infertility as well as developmental defects of the uterus (Joanna Konarzewska *et al.*, 2009).

There is a wide variation in defining infertility in terms of duration. It is best defined as inability to conceive after one year of unprotected regular intercourse. In general, it was estimated that 84% of all women would conceive after a year of intercourse and the figure rises cumulatively to 92% after 2 years and 93% after 3 years (S L Yu and Yap, 2003).

Infertility can be divided into two types, primary and secondary infertility. Primary infertility is difficulty conceiving for a couple who have not had a baby before or when there is an absence of a preceding pregnancy. Secondary infertility is defined as inability to become pregnant again when the same partners have had a baby before or also can be defined as when there was a preceding pregnancy, irrespective of the outcomes (Asifa Ghazi *et al.*, 2007).

Both partners in relationship contribute to potential fertility and both may be sub fertile (MS and MD, 2006). The most common etiological factor for infertility is anovulatory cycle which was documented in about 45% of the women. Unexplained infertility contributes about 20%, male and tubal factors about 10% each. Other causes are due to endometriosis, fibroid, mixed factors and hyperprolactinemia (N.Hazlina NH *et al.*, 2005). Standard investigations for infertile couples include laboratory assessment of normal ovulation and luteal phase, evaluation of tubal patency and semen analysis (El-Yazied, 2007).

Tubal factors are believed to be responsible for 35 – 50% of infertility, evaluation of tubal dysfunction is thus important in the investigation of female infertility (El-Yazied, 2007). After proper and detailed history, physical examination, semen analysis and investigation of ovulation, assessment of tubal patency is the next step in the standard examination of infertile couple.

Due to the noninvasive nature and cheap, HSG is widely used as a first-line approach to assess the patency of the fallopian tubes in routine fertility workup (D.A.M. Perquin *et al.*, 2006).

HSG is a radiographic examination of endocervical canals, uterine cavity and fallopian tubes with the use of a radiographic contrast medium. It involves catheterization of the cervix to yield a watertight seal and injection of contrast material under pressure in order to follow its path by obtaining radiographic images of the process (Lousine Boyadzhyan *et al.*, 1995).

HSG is used in many infertility centers as a preliminary investigation tool (Egle Tvarijonaviciene and Nadisauskiene, 2008). It is helpful in evaluating anatomy of uterine cavity and patency of fallopian tube.

HSG is noninvasive, readily detects abnormal tubes and it can be therapeutic (Denise E. Duff *et al.*, 1983). The therapeutic effect of HSG has been reported in several studies. In the study done by Rasmussen et al., (1991) rates of term pregnancy were approximately 30% with oil-soluble contrast media and 10% with the water-soluble contrast media diatrizoate meglumine.

However, Spring et al., (2000) found that there were no significant difference in the proportions of pregnancies resulting in live birth after the use of oil-soluble contrast media, water-soluble contrast media or both.

Some authors have reported an increase in conception after HSG with both water-soluble and oil-based contrast media. The reported conception rate with water-soluble contrast media ranges from 13% to 40% (Denise E. Duff *et al.*, 1983). Pregnancy rate within 6 months after performing HSG was 26% (D.A.M. Perquin *et al.*, 2006).

In the other study in California, the overall rate of pregnancy within 12 months after HSG was 30.6% (David B. Spring *et al.*, 2000). 30 to 50% of patients with a normal HSG conceived within a period of 6 months (Mahmoud F. El-Minawi *et al.*, 1978). HSG should be the routine diagnostic procedure to commence the investigation of infertility.

Patients with a normal HSG should be managed conservatively for 6 months, and then if conception does not occur, the patient should be scheduled for laparoscopy. There is no urgency to perform a laparoscopy when there is a normal HSG.

The mechanisms for the therapeutic effect of HSG were not known and they were matters of speculation. Some possibilities include a mechanical cleaning of the fallopian tubes and uterine cavity, a stimulatory effect on the ciliary activity of the tubal epithelium, establishment of a more favorable environment for the ascent and penetration of the spermatozoa, direct stimulation of the activity and/or longevity of the spermatozoa, a favorable effect on the cervical mucosa, a bacteriostatic effect on the mucous membranes of the uterus and fallopian tubes, and a fibrinolytic effect of the iodine in reducing edema of the tubal wall (Finn Rasmussen *et al.*, 1991).

There are few other indications for HSG which includes recurrent spontaneous abortions, postoperative evaluation following tubal ligation or reversal of tubal ligation and preoperative evaluation prior to myomectomy (William L. Simpson *et al.*, 2006).

2.2 Causes of infertility

2.2.1 Etiology of female infertility

The most common etiology of female infertility is ovulation disorders. Second is the tubal factor followed by endometriosis, other factors and uterine/cervical factor.

Ovulation disorders are the major causes of infertility in female. These can be caused whether by the defects of regulation of reproductive hormones by hypothalamus and pituitary gland or ovary problem. A few problems that are categorized in ovulation disorders such as abnormal follicle stimulating hormone (FSH) and luteinizing hormone (LH) secretion, polycystic ovary syndrome (PCOS), luteal defect and premature ovarian failure (Chan, 2010).

2.2.2 Pathophysiology of female infertility

FSH and LH play an important role in stimulating the follicle. Therefore, if abnormality occurs in the secretion of these two essential hormones, ovulation process might be affected.

Polycystic ovary syndrome (PCOS) is the problem which some of the eggs develop into cyst. This cyst is build up inside the ovary and may enlarge. This formation of cyst could be due to high production of androgen inside female body. Therefore, women with this problem would have irregular menstrual cycle.

Luteal defect occur because of the production of progesterone is low. Progesterone is essential to prepare uterine lining for fertilization and implantation of zygote. Therefore, fertilization cannot occur when this problem occurs.

Premature ovarian failure is also one of the ovulation disorders. It is caused by autoimmune response at which the immune system attacks the ovarian tissues, resulting in loss of ovum and decrease of estrogen production.

Other factors that contribute to female infertility are age, stress level, poor diet intake, sexually transmitted disease, drugs, smoking and genetic (Chan, 2010).

2.2.3 Etiology of male infertility

There are many factors contributes to male infertility such as impaired sperm production, impaired sperm delivery, lifestyle and environmental exposure. Impaired sperm production is affected by many causes such as varicocele, undescended testis, testosterone deficiency, chromosome defect, infections and hormonal disorders.

Impaired sperm delivery can be caused by blockage of epididymis or vas deferens, retrograde ejaculation, no semen, hypospadias, anti-sperm antibodies and cystic fibrosis. Lifestyle also can contribute into male infertility such as alcohol, drug, tobacco smoking, emotional stress, age, malnutrition and obesity.

Environmental factors also can affect male infertility such as pesticides and other chemical agents, overheating the testicles, exposure to radiation or X-ray and cancer and its treatment (Chan, 2010).

2.2.4 Pathophysiology of male infertility

Varicocele is a dilated vein of the scrotum that may reduce normal cooling effects of testicles. This results in reduction of sperm count and motility.

Second condition is undescended testis. It s a condition at which the one or both of the testis did not descend from the abdomen to the scrotum during fetal development. Sperm production might be impaired by this condition because the testicles are exposed to higher internal body temperature inside the scrotum.

Testosterone deficiency also can contribute to impaired sperm production. Infertility can also caused by abnormality affecting the glands in the brain that produce

hormones that control the testicles (the hypothalamus or pituitary glands). Sperm delivery can be impaired by blockage of epididymis or vas deferens. Therefore, sperms cannot be transport from testis out to penis.

The absent of semen can affect sperm delivery as sperm cannot be transport from penis to vagina because semen brings along the sperm to the vagina (Chan, 2010).

2.3 Anatomy of the female reproductive system

The female reproductive system consists of the external and internal genitalia. The internal genitalia comprise the ovaries, fallopian tubes, uterus and vagina whereas the external genitalia include the mons pubis, labia minora and majora, clitoris, introitus and perineal body.

HSG is a study of the internal genitalia, predominantly used in the evaluation of the fallopian tubes. Thus, in this study, only the internal genitalia structures will be discussed.

2.3.1 The vagina

The vagina is a muscular tube, approximately 8 cm long, which extends up and back from the vulva to surround the cervix of the uterus. It has anterior and posterior walls which are normally in opposition. Superiorly, the cervix divides the vagina into a shallow anterior and deep posterior and lateral fornices (Paul Butler *et al.*, 1999).

2.3.2 The uterus

The uterus is a pear-shaped muscular organ lying between the rectum and bladder. The non-pregnant uterus is 8 cm long, 5 cm across and 3 cm thick. It has a fundus, body and cervix. The cavity of uterus is triangular in coronal section, but is a mere cleft in the sagittal plane.

The cervix constitutes the most inferior aspect of the uterus and extends into the vagina. The isthmus is the uterine portion immediately above the cervix.

The majority of the uterus is composed of the body, or corpus. The uppermost aspect of the uterus is the fundus, which can be concaved, flattened, or slightly convex. The fallopian tubes connect to the fundus at the cornua, or lateral extremes of the base of the triangular cavity (William L. Simpson *et al.*, 2006). Normally the long axis of the uterus lies horizontally in the sagittal plane, forming an angle of ninety degrees with the vagina. The fundus is flexed anteriorly in relation to the cervix in a position which is referred to as anteverted and anteflexed (Paul Butler *et al.*, 1999).

2.3.3 The uterine tubes

The fallopian tubes serve as the passageway for the ovum to travel from the ovary to the uterus. Each fallopian tube is about 10 cm long and course along the superior aspect of the broad ligament, extending out from the uterine cornua (William L. Simpson *et al.*, 2006).

They are divided into four parts:

(a) The infundibulum, the funnel-shaped lateral part which extends beyond the broad ligament and overhangs the ovary with its finger-like fimbriae, one of which is attached to the ovary

(b) The ampulla, a wide, dilated tortuous outer part

(c) The isthmus is a long and narrow structure just lateral to the uterus

(d) The interstitial part, which pierces the uterine wall (Paul Butler *et al.*, 1999).

2.3.4 The ovaries

Ovary is a paired organ which is almond-shaped, lies in the ovarian fossae, situated in the lateral pelvic sidewalls between the obliterated umbilical artery anteriorly and the internal iliac artery and ureter posteriorly. Their size and appearance varies with age. Normal adult dimensions are approximately 3 x 1.5 x 2 cm with a weight of 2 – 8 g (Paul Butler *et al.*, 1999).

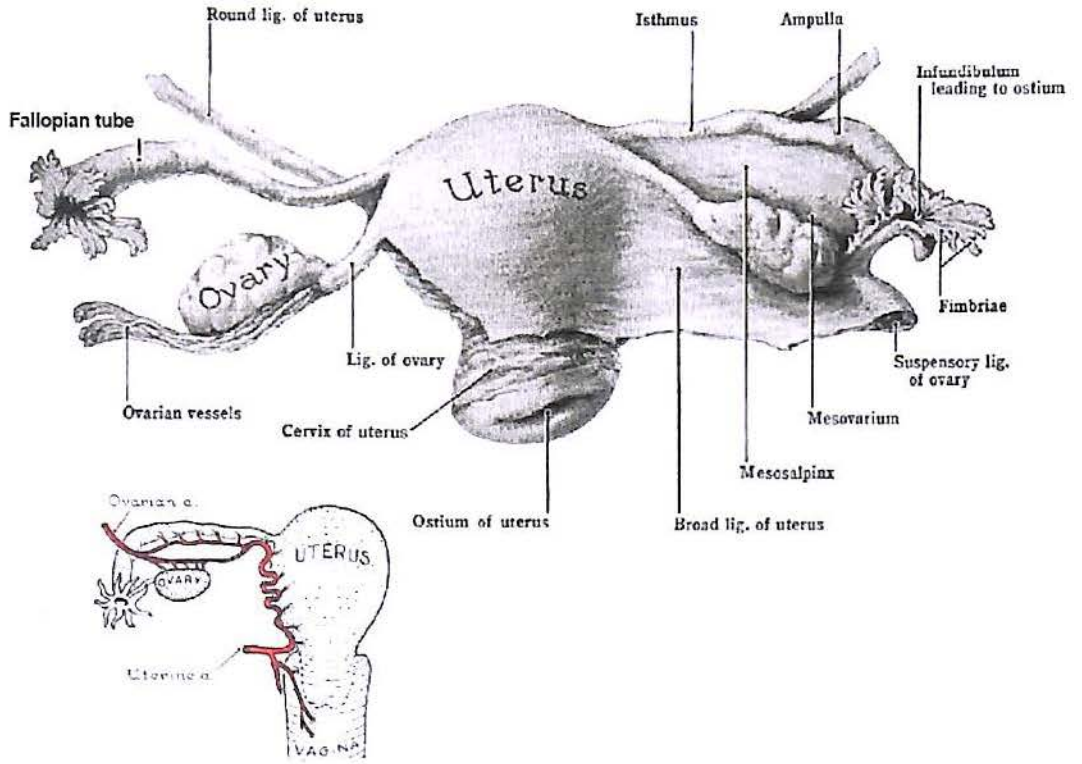

Figure 2-1: Anatomy of female genital tract.

Adapted from Functional anatomy of female genital system

2.4 Menstrual cycle

The menstrual cycle is a cycle of physiological changes that occurs in the fertile females. It may be divided into three phases which are the menstruation, the follicular phase and the luteal phase. The length of each phase varies from women to women and cycle to cycle. The average menstrual cycle is 28 days. The menstrual cycle is regulated by the complex interaction of hormones: luteinizing hormone (LH), follicle-stimulating hormone (FSH), and the female sex hormones estrogen and progesterone.

The menstrual cycle begins with menstrual bleeding (menstruation), which marks the first day of the follicular phase. Bleeding occurs after estrogen and progesterone levels decrease at the end of the previous cycle. This decrease causes the top layers of thickened lining of the uterus (endometrium) to be shed. About this time, the FSH level increases slightly, stimulating the development of several ovarian follicles. Each follicle contains an egg. Later, as the FSH level decreases, only one follicle continues to develop. This follicle produces estrogen.

The ovulatory phase begins with a surge in LH and FSH levels. LH stimulates egg release (ovulation), which usually occurs 16 to 32 hours after the surge begins. The estrogen level peaks during the surge, and the progesterone level starts to increase.

During the luteal phase, LH and FSH levels decrease. The ruptured follicle closes after releasing the egg and forms a corpus luteum, which produces progesterone. During most of this phase, the estrogen level is high. Progesterone and estrogen

causes the endometrium (uterine lining) changes to prepare for potential implantation of an embryo to establish a pregnancy. If implantation does not occur within approximately two weeks, the corpus luteum will involutes, causing sharp drops in levels of both progesterone and estrogen. This causes the uterus to shed its lining and a new menstrual cycle begins (Peter L. Rosenblatt, July, 2007).

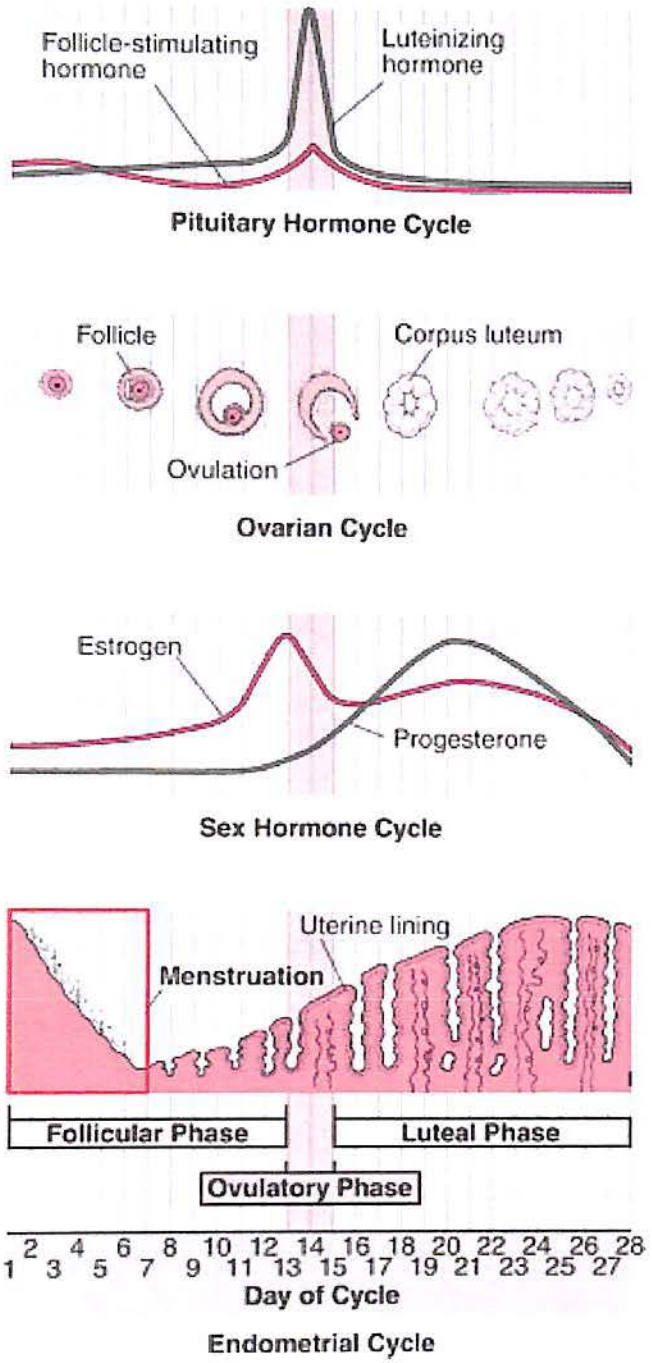

Figure 2-2: Changes during the menstrual cycle.

Adapted from Menstrual Cycle: Biology of the Female Reproductive System: Merck Manual Home Edition

2.5 Normal Pregnancy (Stages of Development)

2.5.1 Fertilization

There are many stages involved in the development of normal pregnancy which includes fertilization, development of blastocyst, development of the embryo and development of the fetus and placenta. For the purpose our study, only fertilization process will be discussed. During each normal menstrual cycle, one egg (ovum) is usually released from one of the ovaries, about 14 days before the next menstrual period. The ovum is swept into the funnel-shaped end of one of the fallopian tubes.

At ovulation, the mucus in the cervix becomes more fluid and more elastic, allowing sperm to enter the uterus rapidly. Within 5 minutes, sperm may move from the vagina, through the cervix into the uterus, and to the funnel-shaped end of a fallopian tube (which is the usual site of fertilization). The cells lining the fallopian tube facilitate fertilization process.

Upon encountering the ovum, the acrosome of the sperm produces enzymes which allow it to burrow through the outer jelly coat of the egg. The sperm plasma then fuses with the egg's plasma membrane, the sperm head disconnects from its flagellum (Encyclopedia, 2009).

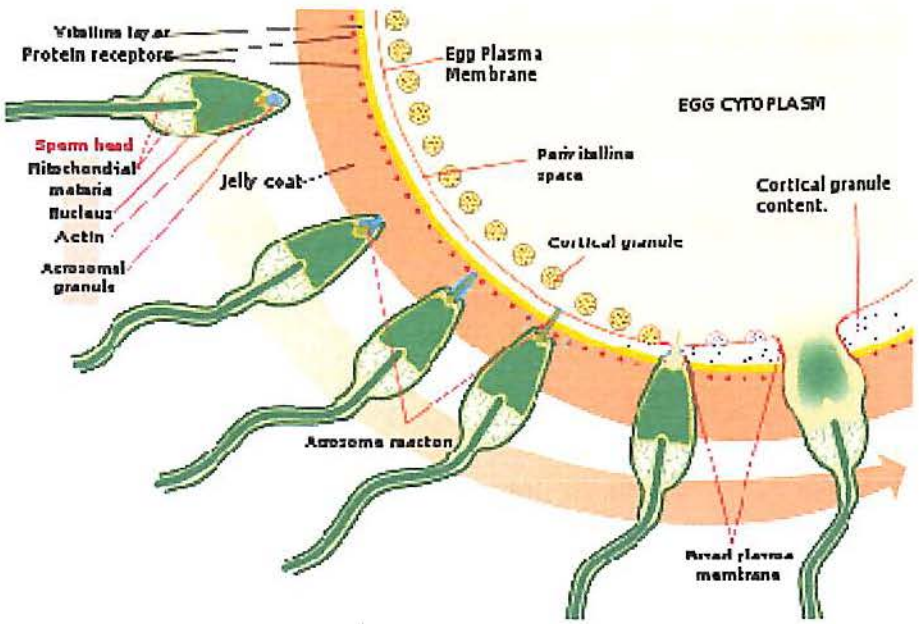

Figure 2-3: The acrosome reaction.

Adapted from Human fertilization – Wikipedia, the free encyclopedia

2.5.1.1 Corona radiata

The ovum and the sperm bind through the corona radiata, a layer of follicle cells on the outside of the secondary oocyte. Fertilization occurs when the nuclei of a sperm and an ovum fuse. The successful fusions of gametes form a new organism.

2.5.1.2 Acrosome reaction

The acrosome reaction must occur to mobilise enzymes within the head of the spermatozoon to degrade the zona pellucida.

2.5.1.3 Zona pellucida

After binding to the corona pellucida the sperm reaches the zona pellucida, which is an extra-cellular matrix of glycoprotein. A special complementary molecule on the surface of the sperm head binds to a ZP2 glycoprotein in the zona pellucida. This binding triggers the acrosome to burst; releasing enzymes that help the sperm get through the zona pellucida.

Some sperm cells consume their acrosome prematurely on the surface of the egg cell, facilitating the penetration by other sperm cells. As a population, sperm cells have on average 50% genome similarity so the premature acrosomal reactions aid fertilization by a member of the same cohort. It may be regarded as a mechanism of kin selection.

Recent studies have shown that the egg is not passive during this process.

2.5.1.4 Cortical reaction

Once the sperm cells find their way past the zona pellucida, the cortical reaction occurs: cortical granules inside the secondary oocyte fuse with the plasma membrane

of the cell, causing enzymes inside these granules to be expelled by exocytosis to the zona pellucida. This in turn causes the glyco-proteins in the zona pellucida to cross-link with each other, making the whole matrix hard and impermeable to sperm. This prevents fertilization of an ovum by more than one sperm (Encyclopedia, 2009).

Tiny hair like cilia lining the fallopian tube propels the fertilized ovum (zygote) through the tube toward the uterus. The cells of the zygote divide repeatedly as it moves down the fallopian tube. The zygote enters the uterus in 3 to 5 days. In the uterus, the cells continue to divide, becoming a hollow ball of cells called a blastocyst. If fertilization does not occur, the ovum degenerates and passes through the uterus with the next menstrual period.

If more than one ovum is released and fertilized, the pregnancy involves more than one fetus, usually two (twins). These twins are fraternal. Identical twins result when one fertilized ovum separates into two embryos after it has begun to divide (Brown, 2007).

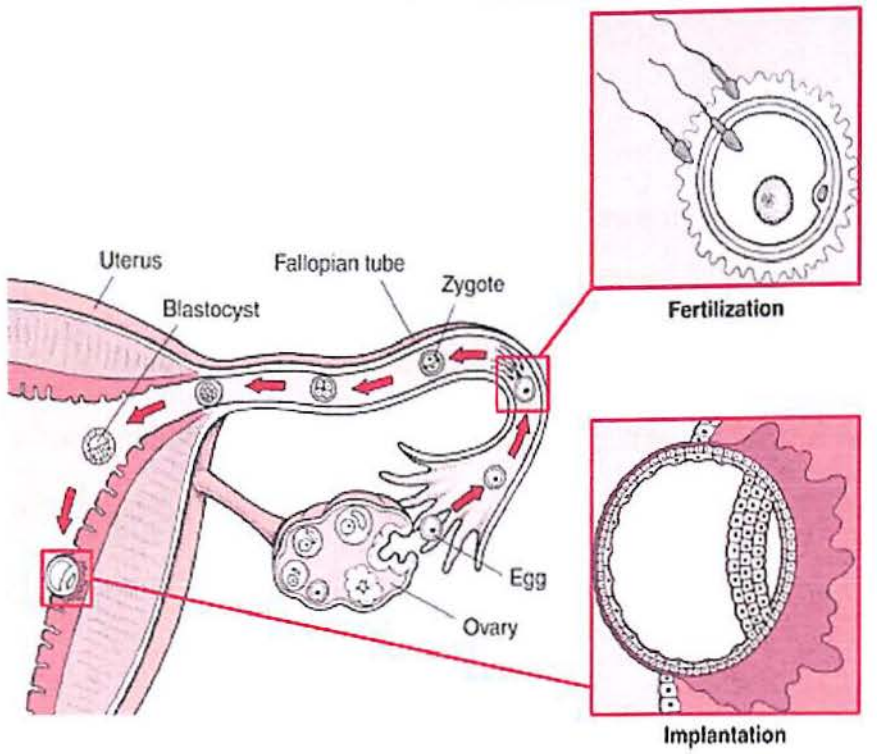

Figure 2-4: Development of ovum to embryo

Adapted from Stages of Development: Normal Pregnancy: Merck Manual Home Edition

2.6 Hysterosalpingography

2.6.1 Technique

HSG was carried out during the proliferative phase i.e. between day four and ten of the menstrual cycle and when menstrual flow had ceased (Eng C W *et al.*, 2007). The endometrium is thin during proliferative phase, it can facilitates image interpretation and should ensure that there is no pregnancy. The patient was advised to abstain from sexual intercourse from the time menstrual bleeding ends until the day of the procedure, to avoid a potential pregnancy (William L. Simpson *et al.*, 2006).

The patient was placed in supine position on the fluoroscopy table in the lithotomy position. The perineum was cleaned with Hibitane solution and draped with sterile towels (William L. Simpson *et al.*, 2006). A sterile Sim's speculum was inserted into the vagina and the cervix was localized and cleaned, the anterior lip of cervix was held with tenaculum. Before the cannula or catheter was inserted through the cervical canal, the contrast material should first be passed through the instrument so as to expel the air and minimize or eliminate the air bubbles. Leech-Wilkinson cannula or 8F Foley's catheter was positioned in the cervical canal. The tenaculum and Sim's speculum were then pulled out from the vagina and a preliminary radiograph of the pelvis was obtained with the instrument in place before contrast material was instilled.

Low osmolar contrast material was injected slowly under intermittent fluoroscopic screening. The first image was obtained during early filling of the uterus and was

used to evaluate for any filling defect or contour abnormality because small filling defect were best seen at this stage.

The second image was obtained with the uterus fully distended as the shape of uterus is best evaluated at this stage. The third image was obtained to demonstrate and evaluate the fallopian tubes and the fourth image should exhibit free intraperitoneal spillage of contrast material. Oblique views were needed for better appreciation of the axis and the configuration of the uterine cavity. A normal HSG depicts a smooth triangular outline with opacification of both fallopian tubes and free spillage of contrast into the peritoneum (Eng C W *et al.*, 2007).

2.6.2 Complications of HSG

Some complications can occur following HSG, the two most common complications are bleeding and infection. The patient should be made aware that she might experience light spotting or per vagina bleeding after the procedure which is usually last for less than 24 hours. The procedure should be done in sterile condition and use sterile instruments to minimize the risk of infection.

2.6.3 Technical artifacts

2.6.3.1 Air bubbles

Air bubbles are often introduced into the uterine cavity during HSG. When there are multiple air bubbles, they are easily recognized. However, a single air bubble can be mistaken for other uterine pathologies, such as polyp, blood clots, endometrial

hyperplasia, or a submucosal fibroid. Air bubble is seen as a well-defined round filling defect which can usually be recognized by its mobility, lack of persistence and move to a non-dependent part of the uterus when patient turns (Eng C W *et al.*, 2007).

2.6.3.2 Contrast intravasation

Contrast intravasation can occur via venous or lymphatic routes. It can take place in up to 6% of patients undergoing HSG (Lousine Boyadzhyan *et al.*, 1995). It is most commonly occurs due to excessive pressure during the injection of contrast material. Endometrial scarring, fibrosis and ulcerations can promote entry of the contrast material into myometrial vessels. Precautions should be given to patients with uterine adhesions, tubal disease and/or obstruction, history of recent uterine operations, uterine malformations, history of uterine tuberculosis, and submucous tumors.

It is seen radiographically as multiple thin lines, forming a reticular pattern and should not be mistaken for opacification of the fallopian tubes. Sometimes the ovarian veins may be opacified.