INTRODUCTION

Infertility is a common problem. Approximately one sixth of marriages are involuntarily childless. In recent years, there has been an increase in publicity about infertility and reproductive medicine technologies, which has gone some way to reduce the stigma of infertility and the reluctance of couples to seek advice ***(Balen and Jacobs, 2003).*** Infertility is defined as an inability to conceive within twelve months of having regular unprotected intercourse ***(Norwitz and Schorge, 2001).***

Infertility said to be primary if the couple have no previous pregnancy and secondary if there has been at least one pregnancy irrespective of its outcome (miscarriage, ectopic pregnancy, and preterm or term delivery). The male partner is solely responsible in 35% of infertility causes while the female partner is responsible for 50% (Ovarian factor 20 % tubal and peritoneal factors 20% and uterine factor 10%) and 15 % of unexplained infertility. The common causes of infertility are evaluated by performing in order: semen analysis documentation of ovulation, post-coital test, evaluation of tubal patency (HSG, hystero-salpingo contrast sonography, laparoscopy with tubal lavage) ***(Godwin, 2001).***

Infertility investigation has changed over the past twenty years in the assessment of infertile women. The

most frequently used procedures have been hysterosalpigography (HSG) and laparoscopy ***(Kupesic et al., 2000).***

Recently, several authors reported the use of ultrasound contrast media in the assessment of infertile women during transvaginal ultrasound, and have emphasized the place of three-dimensional hystero-salpingo contrast sonography in the imaging of infertile women. The benefits of three-hystero-salpingo contrast sonography compared to hysterosalpingo-graphy (HSG) include: reproducible and reliable assessment of tubal patency, better assessment of uterine cavity, enables visualization of ovarian morphology and soft tissue abnormalities such as fibroids (fibroids are not seen on HSG unless they are calcified or the uterine cavity is distorted and the cause will not usually be apparent) or congenital anomalies of the uterus; feasible, minimal invasiveness and relatively few contraindications; of exposure to X-ray, allergic reactions and general anesthesia; the possibility of being performed as an outpatient procedure; the fact that it is well tolerated, rapid and shows tubal patency to patient in real time; and appears to have an 80-90% concordance with laparoscopy and dye insufflations ***(Balen and Jacobs, 2003).***

AIM OF THE WORK

The aim of the study is to compare three-dimensional hystero-sonosalpingography versus hystero-salpingography (HSG) in the assessment of the women with secondary infertility.

SECONDARY INFERTILITY

Secondary infertility is defined as failure to conceive after two year of previous conception although regular unprotected intercourse.

Oxford and Copenhagen revealed that at least a quarter of all couples experience unexpected delay in achieving their desired family size, although only half may seek treatment ***(Balen and Jacobs, 2003).***

The overall incidence of infertility has remained relatively unchanged over the past 3 decades. However, the evaluation and treatment of infertility have changed dramatically during that time ***(Kupesic et al., 2000).***

The incidence of infertility among women aged 15-44 years has increased slightly over the past 30 years, reaching 10-20% in 1999 ***(Ventura et al., 2003).***

Infertility investigation has changed over the past twenty years in the assessment of infertile women. The most frequently used procedures have been X-ray hysterosalpingography (X.HSG) and laparoscopy ***(Kupesic et al., 2000).***

Causes and evaluation of infertility

The causes of infertility include ovulatory dysfunction (15%), tubal and peritoneal pathology (30-40%), and male factors (30-40%); uterine pathology is

generally uncommon, and the rest is largely unexplained ***(Carby and Trew, 2004).***

The prevalence of each cause varies with age. Ovulatory dysfunction is more in younger than older couples, tubal and peritoneal factors have a similar prevalence, and male factors and unexplained infertility are somewhat more common diagnoses in older couples ***(Miller et al., 1999).***

Physical examination should consider: in the female:

1. Body shape and stature.
2. Calculation of the body mass index (BMI = ratio between weight in kilograms and height in square meters).
3. Evaluation of secondary sexual characteristics (hair distribution, breast development, spontaneous and manually induced galactorrhea, inspection of external genitalia).
4. Abnormalities such as fibromyomata, ovarian cysts, or fixed retroversion of the uterus can be diagnosed with a bimanual examination of the uterus associated with the palpation of the fornices. The vagina and the cervix must be examined, and any discharge should be further investigated for infection.
5. The cardiovascular, respiratory, and gastrointestinal systems must be carefully examined before pregnancy is planned ***(Forti and Krausz, 1998).***

Table (1): Interpreting results of investigations of females partners

Test	Result	Interpretation
Progesterone	<300 nmol/I	**Anovulation:** Check cycle length and timing in mid luteal phase; complete other endocrine tests; scan for polycystic ovaries; advise on weight gain or loss; may need ovulation induction; clomifene should not be started without tubal patency test.
FSH	> 10 IU/I	**Reduced ovarian reserve:** May respond poorly to ovulation induction; may need egg donation
LH	> 10 IU/I	**May be polycystic ovaries:** ultrasonography to confirm
Testosterone	>2.5 nmol/I	**May be polycystic ovaries:** ultrasonography to confirm
	> 5 nmol/l	**Congenital adrenal hyperplasia:** check 17-OHP and DHEAS
Prolactin	>1000 IU/I	**May be pituitary adenoma:** Repeat prolactin to confirm raised concentration; exclude hypothyroidism; arrange magnetic resonance image or computed tomograms; if confirmed hyperprolactinaemia start dopamine agonist
Rubella	Non-immune	Offer immunization and one month contraception
HSG or HyCoSy	Abnormal	**May be tubal factor:** Arrange laparoscopy and dye test to evaluate further; may be intrauterine abnormality – for example, fibroid or adhesions; evaluate further by hysteroscopy
Laparoscopy and dye	Blocked tubes	**Tubal factor confirmed:** Possibly suitable for transcervical cannulation, surgery or in vitro fertilization (also depends on semen quality)

(Cahill and Wardle, 2002)

Infertility after CS

Focusing on CS as a probable cause of infertility in ovulatory patients with no male factor as documented by semen analysis, it was declared by ***Hememenki et al. (1996)*** that thought the underlying mechanism is unclear tubal adhesions and intrauterine adhesions play an important role, HSG, laparoscopy and hysteroscopy may give an idea about tubal and uterine factors.

The relevant female history for infertility after CS should focus on uterine and tubal factors including, pelvic/ abdominal surgery, pelvic infections/ sexually transmitted diseases. ***(McClure and Thompson, 1997).***

TUBAL FACTOR INFERTILITY

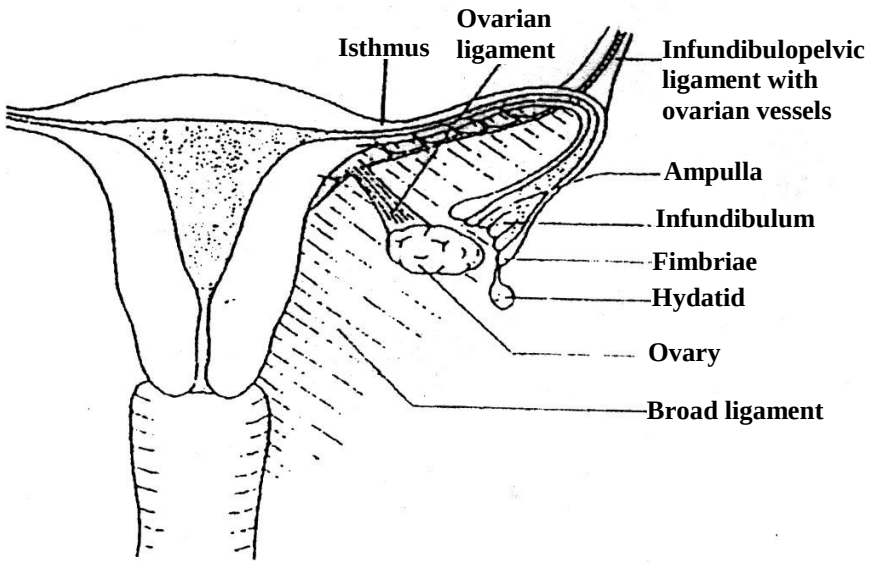

Figure (1): Anatomy of the female internal genitalia ***(Khalaf, 2003).***

Tubal and peritoneal factors account for 30-40% of cases of female infertility ***(Hornstein and Schust, 1996).***

Partial or complete bilateral tubal obstruction can caused by previous salpingitis: most commonly, this is postabortal, puerperal, gonococcal, chlamydial or tuberculous in nature ***(Jeffcoate, 2001).***

A history of pelvic inflammatory disease, septic abortion, ruptured appendix, tubal surgery, or ectopic pregnancy suggest possibility of tubal damage ***(Khalaf, 2003).***

A- Pelvic inflammatory disease (PID)

Is defined as: acute clinical syndrome associated with ascending spread of micro-organisms (unrelated to pregnancy or surgery) from the vagina or cervix to the upper genital or reproductive tract. PID can involve infection of the endometrium (endometritis), the oviduct (salpingitis), the ovary (oopheritis), the uterine wall (myometritis), or portion of the parietal peritoneum (peritonitis) ***(Beck, 1993 and Kurjak et al., 2000b)***.

PID is mostly ascending and polymicrobial. Rarely the infection is hematogenus or spread directly from other abdominal organ ***(Kurjak et al., 2000b).***

Among the sexually transmitted organisms Neisseria gonorrhoea and Chlamydia trachomatis are most commonly identified. While Gonorrhea still plays an important role in PID infection and tubal disease, it has been surpassed by Chlamydia. Infections by Chlamydia trachomatis are now the most common causes of infection related tubal pathology. In addition a history of tuberclosis can be associated with a diagnosis of tubal damage ***(Beck, 1993; Forti and Krausz, 1998; Kurjak et al., 2000b).***

Chlamydia trachomatis has currently emerged as the most common sexually transmitted pathogen. Chlamydial infection produces less severe symptoms than other sexually transmitted diseases. These deceptively mild

symptoms allow the infection to go unnoticed with minimal patient awareness until secondary or tertiary symptoms develop. The sequelae of undetected and thus untreated infections like acute salpingitis and pelvic inflammatory disease lead not only to significant morbidity but far more importantly to infertility ***(Abida Malik et al., 2006)***.

There is no doubt that Chlamydia is responsible for a significant amount of salpingitis but it is not possible to determine how much. There is discordance between identification of Chlamydia positive cultures and the titre of immunoglobulin gamma M; this titre does not correlate with the severity of salpingitis found at the time of laparoscopy ***(Margara and Trew, 1997).***

Infertility results after acute PID in 6% to 60% of cases, depending on the severity and the number of episodes of infection. The incidence of tubal infertility has been reported to be 12%, 23% and 54% after one, two, and three episodes of PID respectively. For tubal damage which has on identifiable risk factors for tubal disease, most of these women are presumed to have subclinical Chlamyida infection ***(Hornestien and Schust, 1996 and Beck, 1993).***

B- Surgery:

Pelvic or tubal surgery is associated usually with post operative tubal damage or obstruction. Operative procedures that are used to correct anatomic disorders often

produce adhesions ***(Hornestein and Schust, 1996and Helsa and Rock, 1997).***

C- Endometriosis:

Is the presence of endometrial gland and stroma at ectopic sites (outside the uterus). It is most frequently found on the peritoneum and ovaries ***(Hooghe and Hill, 1996).***

The endoemtriotic lesions vary in size from very small black or red dots (typically on the uterosacral ligaments and peritoneum of the recto-vaginal pouch) to a large cystic mass filled dark rather viscous (Chocolate) material in the ovaries. If there is hemorrhage from the endometriotic tissue or a cystic lesion ruptures into the peritoneal cavity, a reactive peritonitis follows with a fibrotic reaction around the lesion ***(Steve, 1997).***

The prevalence of endometriosis within the infertile population is between 20% - 40%. The relationship between endometriosis and infertility is complex and poorly understood. Advanced form of the disease can understandably cause infertility by mechanical interference with ovulation, ovum pickup, tubo-ovarian adhesions, severe pelvic adhesion and distorted tubal anatomy. Where fallopian tubes are normal and there are no adhesions around ovaries, the exact mechanism by which

endometriosis impairs fertility, if at all, remains speculative ***(Odukoya and Cook, 1996).***

Common pattern of adhesion development include:

- Immobilization of the ovary against the posterior leaf of the broad ligament or pelvic wall fixation of the distal oviduct to the ovary and broad ligament.
- Envelopment of the ovarian cortex by vascular adhesion.
- Scaring of the fembria ovarica and encapsulation of the distal end of the fallopian tube.
- Obliteration of the posterior cul-de-sac.

(Helsa and Rock, 1997)

UTERINE FACTOR INFERTILITY

The uterus supports the journey of spermatozoa from the cervix to the fallopian tube and performs the following roles:

- Retention of the zygote after arrival from the fallopian tube for several days before implantation.
- Provision of a suitable environment for implantation.
- Protection of the embryo/ fetus from the external environment

(Coney, 1993)

The uterus resembles a flattened pear in shape. The uterus consists of two major but unequal parts: an upper triangular portion, the body, or corpus; and a lower, cylindrical, or fusiform portion, the cervix, which projects into the vagina. The isthmus is that portion of the uterus between the internal cervical os and the endometrial cavity. It is of special obstetrical significance because it forms the lower uterine segment during pregnancy. The oviducts, or fallopian tubes, emerge from the cornua of the uterus at the junction of the superior and lateral margins. The convex upper segment between the points of insertion of the fallopian tubes is called the fundus. The round ligaments insert below the tubes on the anterior side. They are covered by a fold of peritoneum that extends to the pelvic

sidewall. These folds are called the broad ligaments, however, they do not constitute the anatomical definition of a ligament. The prepubertal uterus varies in length from 2.5to 3.5 cm ***(Coney, 1993).***

<u>Uterine factor infertility may be caused by:</u>

1. Abnormalities of the mullerian ducts.
2. Defective endometrium
3. Polyps and tumors.
4. Intrauterine synechia
5. Adenomyosis

1. Abnormalities of the mullerian ducts

Mullerian duct anomalies are uncommon. Patients with mullerian duct anomalies are known to have a higher incidence of infertility. Congenital anomalies of Mullerian system are estimated to occur in approximately 0.1% to 1.5% of females in the general population. However, the true prevalence is unknown because the anomalies are usually discovered in patients presenting with infertility. Full term pregnancies have occurred in patients with forms of bicornuate, septate, or didelphys uteri; therefore, true prevalence may be slightly higher than currently estimated ***(Raga et al., 1996).***

Two paired Mullerian ducts ultimately develop into the structures of the female reproductive tract. The

structures include the Fallopian tubes, uterus, cervix and the upper two thirds of the vagina ***(Raga et al., 1996).***

Mullerian duct anomalies are categorized most commonly into 7 classes according to the American Fertility society (AFS).

Classification scheme (1988) as follows:

Class I (hypoplasia/ agenesis): This class includes entities such as uterine/cervical agenesis or hypoplasia. The most common form is the Mayer-Rokitansky-Kuster-Hauser syndrome, which is combined agenesis of the uterus, cervix, and upper portion of the vagina. Patients have no reproductive potential aside from medical intervention in the form of in vitro fertilization of harvested ova and implantation in a host uterus occur in 15-40% and also sometimes skeletal abnormalities.

Class II (unicornuate uterus): A uni-cornuate uterus is the result of complete, or almost complete, arrest of development of one Mullerian duct if the arrest is incomplete, as in 90% of patients, a rudimentary horn with or without functioning endometrium is present. If the rudimentary horn is obstructed, it may come to surgical attention when presenting as an enlarging pelvic mass. If the contra lateral healthy horn is almost fully developed, a full term pregnancy is believed to be possible.