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Role of Hysteroscopy in Diagnosis of Uterine Abnormalities in Unexplained Infertility

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Abstract

Infertility is a growing concern of the society. Of couples unable to conceive without any identifiable cause, 30% are defined as having unexplained infertility. Management depends on duration of infertility and age of female partner. Unexplained infertility usually refers to a diagnosis (or lack of diagnosis) made in couples in whom all the standard investigations such as tests of ovulation, tubal patency and semen analysis are normal. Unexplained infertility is a term that has been applied to as many as 30–40% of infertile couples. The potential causes of unexplained infertility have been described as disturbances in endocrinological balance, immunology and genetic and reproductive physiology. Hysteroscopy has become the gold standard for diagnosis of intrauterine abnormalities. Intrauterine lesions such as adhesions, uterine septum polyps or submucous myomas are diagnosed much more precisely by hysteroscopy and are detectable in 10-15% of women seeking subfertility therapy.

Keywords: Hysteroscopy, uterine abnormalities, unexplained infertility.

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1. Introduction

Infertility is a medical condition that can cause psychological, physical, mental, spiritual, and medical detriments to the patient. The unique quality of this medical condition involves affecting both the patient and the patient's partner as a couple [1]. Infertility is a global public health problem that affects around 8 to 12% of couples in reproductive age worldwide. According to the World Health Organization (WHO), infertility is defined as "*a disease of the male or female reproductive system defined by the failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse".* It has a huge impact on the population in cause since the couples can experience depression, anxiety, distress, reduced self-esteem, and a feeling of guilt and blame during the process [2]. Unexplained infertility is diagnosed in the absence of any abnormalities of the female and male reproductive systems after 'standard' investigations [3]. Infertility in couples with apparently normal ovarian function, fallopian tubes, uterus, cervix and pelvis, age ≤40 years and with adequate coital frequency; and apparently normal testicular function, genito-urinary anatomy, and a normal ejaculate [3].

1.1. Causes of infertility

Female infertility affects 12.6% of women worldwide; its aetiology is complex and multifactorial and can be underpinned by uterine pathologies, systemic diseases and age [4].

- ***Female infertility***

The following are considered common causes of infertility in females.

(I) Endocrinal causes

a- Hypothalamic causes

Hypogonadotropic hypogonadism (HH) is caused by deficiencies in hypothalamic endogenous gonadotropin-releasing hormone (GnRH) release or pituitary gonadotropin (Gn) secretion, leading to an imbalance in the hypothalamic-pituitary-gonadal (HPG) axis and diminished ovarian function. HH is classified as WHO type I ovulatory disorder, Due to the long-term deficiency stimulation of Gn, women with HH show symptoms of hypoestrogenism, hypoplasia of uterus, ovulation inefficiency, and amenorrhea [5].

b- Thyroid disorders

The prevalence of thyroid disorders in women aged 20–45 years is high, and that of subfertility is increasing worldwide in part due to improved public awareness and diagnosis. Therefore, female partner in a sub fertile couple carries a high risk of concomitant thyroid disorders. Given the important interplay between thyroid hormone (TH) and its receptor present on reproductive organs, thyroid dysfunction may be directly causative for menstrual disturbances and subfertility. Moreover, thyroid dysfunction may act indirectly by altering secretion of gonadotropin-releasing hormone (GnRH) and other hormones like prolactin

[6]. Thyroid autoimmunity (TAI) is the major cause of (subclinical) hypothyroidism and is more prevalent in women with idiopathic subfertility and polycystic ovarian syndrome (PCOS) than in fertile women. The prevalence of TAI is also higher in women with diminished ovarian reserve (DOR) and premature ovarian insufficiency. Furthermore, serum TSH levels are inversely correlated with the anti-Müllerian hormone, an accurate marker of the ovarian reserve [6].

c- Adrenal disorders

Approximately 10–20% of woman with Addison's disease develop premature ovarian insufficiency (POI), defined by loss of ovarian function before the age of 40 years. High prevalence of Addison's disease and POI is due the presence of cross-reacting autoantibodies to steroid-producing cells (StCA). Interestingly, they observed when StCA titres increased, oligomenorrhoea associated with high gonadotropin levels and subfertility developed, but AMH levels were still detectable albeit significantly lower than those previously found when normal ovulatory menses were still present. Hence, measurement of AMH concentrations may be useful in early clinical phase of POI as finding of decreased but still detectable values may indicate persistence of a residual follicular pool, is particularly relevant for woman wishing to conceive or explore fertility preservation. Primary ovarian insufficiency may precede Addison's disease; however, it is unclear if all women with clinically idiopathic POI should be tested for autoantibodies [7].

d- Prolactin Hormone disorders

Hyperprolactinemia is one of most common causes of infertility in women. Hyper-PRL is associated with short- and long-term consequences including menstrual disorders, decreased quality of life, decreased bone mineral density, and sexual dysfunction. Hyper-PRL affects fertility by impairing gonadotropin-releasing hormone (GnRH) secretion and interfering with ovulation. Common manifestations of Hyper-PRL are anovulation, oligomenorrhea, amenorrhea, and galactorrhea. Morphological changes seen in the follicles in hypothyroidism can be due to production of higher levels of prolactin which may block the secretion and function of gonadotropins [8].

e- Vitamin D disorders

Vitamin D has role in the regulation of sex hormone steroidogenesis, increasing evidence suggest that vitamin D might have regulatory role in polycystic ovary syndrome (PCOS) - associated symptoms including ovulatory dysfunction, insulin resistance and hyperandrogenism**.** Moreover, vitamin D might influence steroidogenesis of both estradiol and progesterone in healthy Women where low levels of 25(OH) D levels might be associated with infertility and high levels might be associated with endometriosis, The most up to date vitamin D studies outside its conventional role of calcium homeostasis in the Middle East so far have covered most of obesity-related diseases including diabetes mellitus, hypothyroidism, and full metabolic syndrome [9].

f- Endocrinal disruptors (ED)

EDs appear to have a role that negatively affects female infertility, examples of well-known EDs for this negative effect are Bisphenol A and its metabolites, phthalates, dioxins, organochlorine, and organophosphate compounds. The reproductive system is the most vulnerable system to EDs actions. They have ability to bind to endocrine receptors and interfere with hormonal signals, representing a threat to the normal function of endocrine system [2].

g- Body Mass Index (BMI)

Although there is little evidence of a specific association between BMI and UI specifically, reproductive outcomes known to be impaired in men and women with low and high BMIs. Standard advice and medical investigation and interventions apply equally to patients with UI as to any other causes of infertility. Patients generally value advice about lifestyle and healthy alternatives to maximize fertility in context of their social and cultural environment [3].

h- Ovarian disorders

Ovulatory disorders make up 25% of the known causes of female infertility. Oligo-ovulation or anovulation results in infertility because no oocyte will be released monthly. In the absence of an oocyte, there is no opportunity for fertilization and pregnancy. To help with treatment and further classification, the World Health Organization subdivided ovulatory disorders into four classes:

1- Hypogonadotropic hypogonadal anovulation:i.e.,hypothalamic amenorrhea

2-Normogonadotropic normoestrogenic anovulation: i.e., polycystic ovarian syndrome (PCOS).

3-Hypergonadotropic hypoestrogenic anovulation: i.e., premature ovarian failure.

4-Hyperprolactinemic anovulation: i.e., pituitary adenoma.

Hypothalamic amenorrhea or functional hypothalamic amenorrhea (FHA) is associated with eating disorders and excessive exercise, which results in a decrease in hypothalamic GnRH secretion.The decreased caloric intake, associated weight loss, or excessive exercise leads to elevated cortisol, which causes a suppression of GnRH. The decreased or absent pulsatility of GnRH results in a decrease in the release of gonadotropins, follicle-stimulating hormone (FSH), and luteinizing hormone (LH) from the anterior pituitary gland. These two deficiencies result in abnormal follicle growth, anovulation, and low estrogen levels. The FSH and LH will have variations ranging from normal to low, but the hormone ratio will resemble a prepubertal female, with FSH higher than LH [1]. The most common type of Normogonadotropic normoestrogenic anovulation is PCOS. PCOS accounts for 80 to 85% of all anovulatory patients and affects 8% of all reproductive-aged females [1]. Polycystic ovary syndrome (PCOS) is a common hormonal disorder which leads to irregular menstrual cycle and anovulation, which affects fertility.

It is the most common cause of anovulation in infertility. Women's fertility can be adversely affected by PCOS, as follows: infrequent ovulation or anovulation, increasing the risk of spontaneous abortion, reducing the quality of oocytes, insulin resistance leading to hyperinsulinemia and increasing the risk of miscarriage, and prolonged intimal hyperplasia, which is harmful for implantation [5]. Endometriosis constitutes one of the numerous medical enigmas resulting in compromised fertility. It is a chronic benign disease characterized by chronic inflammation, principally affecting women of reproductive age. Several studies have suggested that fertilization rate, the number of competent embryos,

blastocyst formation rate, implantation rate and pregnancy rate are impaired in cases of diagnosed endometriosis. Endometriosis detrimentally impairs fertility. Adhesions, chronic inflammation, disturbed folliculogenesis, luteal phase disruption, anti-endometrial antibodies,progesterone resistance and disrupted uterotubal motility constitute some of the proposed mechanisms [10].

(II) Pelvic adhesion

Pelvic adhesions can limit the movement and function of organs, ligaments, muscles, and other anatomical structures. This can distort the pelvic anatomy and restrict blood supply to pelvic tissues, hindering conception. Infertility-associated adhesions may form on uterine walls and ligaments or within the cervix, hindering the progression of sperm to the uterus and Fallopian tubes, as well as potentially increasing uterine spasms, implantation problems, and miscarriage, as well as otherwise hindering conception. Paraovarian adhesions may limit the ability for the fimbria to pick up the oocyte. When they occur at the distal part of the fallopian tube, they restrict the tentacle-like grasping of the ovum by the fimbria, increasing its risk of being wasted in the abdominal cavity. However, if they occur on the inner or outer side of the Fallopian tube, they can lead to partial or total tubal occlusion, decreasing probability of conception, while increasing the risk of ectopic pregnancy [11].

(III) Bilateral tubal obstruction

The fallopian tube is an integral part of sperm attachment and fertilization, and its normal function is necessary for natural conception. Blockage of the fallopian tubes is a common disease and one of the leading causes of infertility. Inflammation is the primary cause of oviduct obstruction, and obstruction of the fallopian tubes due to sexually transmitted infection with Chlamydia trachomatis or Neisseria gonorrhoeae causing salpingitis. Other factors affecting tubal patency are pelvic infections, such as adhesions around the fallopian tube due to abdominal tuberculosis; injury to the fallopian tube due to previous tubal surgeries or sterilization; ischemic nodules; endometriosis; polyps or mucus; tubal spasm; congenitally abnormal tubes. Peritoneal factors such as peritubular adhesions, endometriosis, altered tubal motility, and fimbrial end blockage also affect tubal patency.Infertile women with blocked fallopian tubes and hydrosalpinx account for 30% to 40% of the entire infertile population [12].

(IV) Uterine factor

Uterine factor infertility (UFI) is defined as a complete lack of a uterus (Absolute Uterine Factor Infertility or AUFI) or as a nonfunctional uterus (Non-Absolute Uterine Factor Infertility or NAUFI). The exact prevalence of UFI is currently unknown, there are many causes of UFI, congenital and acquired [13].

- ***Congenital Uterine Abnormalities***

Congenital uterine anomalies result from embryological abnormal organogenesis, fusion or septal absorption of the Müllerian ducts, which present as hypoplasia/agenesis, unicornuate uterus, bicornuate uterus, didelphus uterus, complete septate uterus, partial septate uterus, arcuate uterus, and diethylstilbestrol-related uterus according to American Fertility Society (AFS) classification. Uterine anomalies are often diagnosed during an infertility evaluation because most are asymptomatic. The incidence of uterine anomalies in the infertility population is higher than that in general population [14]. In particular, uterine environment and endometrial health are essential contributors to fertility outcomes. Uterine pathologies include endometriosis, adenomyosis, recurrent implantation failure, uterine septum, endometritis, endometrial micro biome, and endocrine disruptors' effect on endometrial function [15].

(V) Cervical factor

One of the common problems associated with infertility in women is related to uterine cervical diseases. The cervix is an essential part of the sperm passage, so various disorders in the cervix structure and function may be cause of infertility. The most common problems of cervical origin are cervical polyps and stenosis of cervical canal [16].

(VI) Vaginal factors

Although the cause of infertility among patients with bacterial vaginosis (BV) is unclear, several mechanisms have been proposed. One possibility is the association between BV microbiota and subsequent inflammation, which may lead to reduced fertility. BV-related bacteria have been shown to induce immune activation through dendritic cell maturation and to increase levels of proinflammatory cytokines, resulting in mucosal inflammation of the genital tract [17]. Another BV-related mechanism that may contribute to infertility is the effect of sialidase and other mucinases on cervical mucus integrity. In the female reproductive tract, a primary function of cervical mucus is the defense of the upper reproductive tract from microbial invasion. To overcome the mucus barrier, microorganisms may produce a range of hydrolyzing enzymes, including mucinases that are capable of degrading mucins. These enzymes may also work to enhance bacterial adhesion and subsequent colonization in upper reproductive tract by generating attachment sites on the mucosal surfaces and producing nutrition for bacteria from mucin breakdown products, fostering colonization with further propensity for upper reproductive tract disease, including infertility [17].

2. Evaluation of male infertility

The causes of male infertility are complex and encompass a wide range of risk factors including age, body mass index, smoking, alcohol, varicocele, mobile phone usage, and nutritional elements [18]. It is essential to consider that clinically the results of semen examination are used (i) as an important part of the diagnostic process of male factor infertility, (ii) to monitor the effects of medical and surgical interventions aimed to improve male fertility potential. Human semen is very different from other body fluids, it does not exist in the male body. Still, it is formed at ejaculation with the sequential addition of contributions of different origins. This assembling can be affected by physiological, pathological, or external factors (pharmacological or other external factors). Therefore, semen analysis is an essential tool for assessing male fertility potential and understanding the health of the entire male genital tract [19].

2.1. Routine semen analysis

The first edition of the WHO Laboratory Manual on Semen Analysis Processing was published in 1980, and since then, four modified and updated versions have been released

to improve SA standard methods and incorporate new technologies to assess extended and advanced sperm parameters. The new 6th edition of the WHO manual aims to provide not only an update of current methods and thresholds but also an insight in recent developments on semen examination, .One of most notable changes in new 6th edition is change in definition of "abnormal ejaculates", While reference ranges and limits on various sperm parameters have been revised to remove existing dichotomy between "fertile" and "infertile" men and these values should be viewed as continua of normality, borderline or pathological semen parameters. Epidemiological data have repeatedly demonstrated that male fertility can change over years and fertility may vary depending on regions of world [21]. Semen analysis is cornerstone in the evaluation of reproductive hormonal status for men. In cases of abnormal sperm parameters (oligozoospermia and azoospermia), potential hypogonadism is ruled out by reproductive hormone (testosterone and gonadotropins) testing which provide a functional readout of hypothalamic-pituitary-testicular axis.

Thus, the hormonal profile will be helpful in following extended examination to accurately diagnose underlying pathological conditions associated with abnormal semen parameters. However, no evidence was found supporting endocrine testing as a first line of investigation for males with UI and results from a basic semen examination in the reference range according to the WHO criteria [22]. In the human reproductive field, vitamin D receptors and metabolizing enzymes have been primarily found in the prostate, seminal vesicles, epididymis, and germ cells (esp., spermatogonia, and Sertoli cells). Thus, vitamin D could be related to spermatogenesis and maturation of human spermatozoa [18]. It was postulated that vitamin D deficiency may cause poor-quality sperm production. Vitamin D deficiency is a well-recognized, significant public health problem associated with many conditions, including male and female infertility. The role of vitamin D in reproduction and fertility through its receptors in reproductive tissues has been reported [23].

2.2. Theories on possible causes of unexplained infertility

In unexplained infertility, abnormalities are likely to be present but not detected by current methods; so, the cause of unexplained infertility is likely to be heterogeneous with proposed causes (endocrinological, immunological and genetic factors) [24].

(1) Pituitary or follicular dysfunction

Approximately 5% of women with unexplained infertility have elevated levels of Follicle Stimulating Hormone (FSH) in the early follicular phase which reflects diminished ovarian reserve. FSH and Luteinizing Hormone (LH) abnormalities may also reflect a dysfunction in the pituitary-ovarian axis. [25]. Furthermore, serum estradiol levels in the follicular phase and estradiol/progesterone ratio were elevated in women with unexplained infertility, suggesting altered folliculogenesis. In addition, an absent mid-cycle elevation of prolactin hormone is present in infertile women [26]. An impaired luteal phase has been demonstrated in about 30% of women with unexplained infertility. An abnormal follicular LH pulse frequency or decreased follicular FSH level has been postulated to induce an impaired luteal phase, which may be primarily due to a functional imbalance in the hypothalamus [27]. It has been shown that decreased inhibin-B concentrations are associated with increased FSH concentrations, and both may reflect a diminished ovarian reserve, which is sometimes seen in women with unexplained infertility [28].

(2) Gamete dysfunction

Beside hormonal factors, gamete dysfunction may contribute to unexplained infertility; altered folliculogenesis, impaired oocyte maturation, reduced oocyte quality and defects in gamete interaction have all suggested [10]. Total failure of fertilization is reported in 5-30% of the cycles of women with unexplained infertility undergoing conventional IVF, this is more frequent than among other subgroups of infertility. A failure in natural ovum pick-up mechanism by fallopian tube has also been suggested in these women [29].

(3) Altered endometrial function

Another possible explanation for unexplained infertility is altered endometrial function. A subacute inflammation presented as differences in endometrial leukocyte populations have observed between fertile and infertile women [30]. Aberrant patterns of integrin expression e.g. absence of the avb3 subunit in window of implantation despite normal histological maturation of the endometrium have associated with unexplained infertility [31].

(4) Immunological factors

Many types of antibody have suggested as possible causes for unexplained infertility. Anti-ovarian antibodies are frequent (33%) in some reports among women with unexplained infertility, as are elevated anti-spermatozoal and anti-cardiolipin antibodies. The antibody levels have been shown to correlate with uterine artery resistance [32].

(5) Hidden intrauterine infections

Asymptomatic hidden genital tract infections like mycoplasma, ureaplasma, klebsiella, Chlamydia trachomatis and bacterial vaginosis should be screened in women with unexplained infertility who are unable to clearly give a history to explain a source for their tubal adhesions. BV infection reported as a significant association with infertility and its proper treatment had led to pregnancy, emphasizing value of its screening and treatment. It is hypothesized that immunity to infection might be correlated to sperm rejection in women with positive BV, leading to infertility [33].

2.3. Role of hysteroscopy in unexplained infertility

Hysteroscopy has long been considered the gold standard and definitive method for diagnosis and treatment of intrauterine pathology. This procedure provides direct visualization and the immediate treatment of abnormalities to restore normal anatomy as well as the ability to obtain tissue samples for diagnosis. This test can be performed in operating room with general anesthesia or sedation or in office with or without local anesthetic or sedation. Yet, there is important evidence indicating low interrater reliability of diagnostic hysteroscopy, which calls into question the method's status as gold standard [34]. Hysteroscopy was first performed on a patient in 1869 by Pantaleoni, who, using a cystoscope developed by Desormeaux, discovered and treated an endometrial polyp in a 60-year-old patient who presented with postmenopausal bleeding. In the 20th century,

hysteroscopy using distending media developed, first using carbon dioxide in 1925. In-office hysteroscopy introduced into clinical practice in the early 1980s with improvement of distension media options and operative techniques [35].

2.4. Vaginoscopic Approach to Hysteroscopy

Vaginoscopy is a surgical technique involving the insertion of a hysteroscope to visualize the vagina, cervix, uterine cavity, or all of these structures, without the use of a vaginal speculum or cervical tenaculum. Small-diameter rigid or flexible hysteroscopes can be used as vaginoscopic instrumentation. A vaginoscopic technique involves gentle introduction of the hysteroscope into the vagina and use of distending medium, such as normal saline, to expand the vaginal canal. The vaginoscopic approach has been shown to reduce procedural pain substantially compared with traditional hysteroscopy [36].

2.5. Special Considerations for Office Hysteroscopy

Many diagnostic hysteroscopy and operative hysteroscopy procedures are shifted from the operating room to an office-based setting. Patients reported a preference for office-based hysteroscopy as office-based procedures are associated with higher patient satisfaction and faster recovery when compared with hospital-based operative hysteroscopy. Other potential benefits of office hysteroscopy include patient and physician convenience, avoidance of general anesthesia, less patient anxiety related to familiarity with the office setting, cost effectiveness, and more efficient use of the operating room for more complex hysteroscopic cases [37]. Hysteroscope used in this study was Karl Storz (Germany). It is a rigid continuous flow panoramic hysteroscopy 25 cm long, 2.9 mm in diameter, with an outer sheath of 3.2 mm and a 30-degree fibro-optic lens. A metal halide automatic light source from the Circon Acmi G71A/Germany with a 150 W lamp was the used light source. A fibro-optic cable is connected to the light source and to the hysteron scope.

The patient was positioned in dorsal lithotomy position and a vaginal disinfection with povidone-iodine 10% was used. Visualization of cervix first obtained then insertion of the hysteroscope was done. Saline solution was used as distension media insufflated at atmospheric pressure (two 5L bags connected by a urological "Y" outflow and located 1.5 meter above the patient). By rotating the fibre-optic scope, uterine cavity was evaluated, 30 ° lens is rotated to detect any uterine wall abnormality and/or both tubal ostia [38]. In-office diagnostic hysteroscopy represents the gold-standard technique for evaluation and management of intrauterine pathologies that could potentially interact with embryo implantation, reducing chances of achieving a clinical pregnancy. As a matter of fact, intrauterine pathologies are more often discovered in sub-fertile and infertile women [39]. Pathologies identified during hysteroscopy in infertile women include chronic endometritis, endometrial polyps, submucosal myomas, intrauterine adhesions, adenomyosis, thin endometrium, endometrial hyperplasia and/or cancer and uterine malformations such as the uterine septum, T-shaped uterus, arcuate uterus and unicornuate uterus [40].

2.6. *Operative Hysteroscopy*

Obstetrician–gynecologists use operative hysteroscopy to treat intrauterine pathology as endometrial polyps, uterine leiomyomas, uterine septa, retained products of pregnancy, and adhesions. Additional uses of operative hysteroscopy include removal of foreign bodies such as malposition intrauterine devices, tubal cannulation, treatment of isthmoceles, and directed biopsy [37].

2.7. Hysteroscopic Polypectomy and Myomectomy

Hysteroscopic resection of endometrial polyps and submucosal leiomyomas can be performed using either monopolar or bipolar wire loop electrodes. Although the use of a monopolar resectoscope requires an electrolyte-free distending medium (e.g., 1.5% glycine or 3% sorbitol), bipolar resectoscopes can be used with electrolyte-containing distending medium (e.g., normal saline). Another less commonly used hysteroscopic surgical technique is electrosurgical vaporization, which uses a large surface-area vaporization electrode set at higher power density settings (e.g., 120–220 watts) compared with the power density used for conventional wire loop electrodes. Vaporization devices allow for destruction of targeted lesions without creation of tissue fragments, thereby eliminating need for tissue removal; however, this also prohibits histologic evaluation of tissue, which may be necessary in some clinical scenarios [37].

- ***Indications for diagnostic hysteroscopy include***

The most common indications for hysteroscopy are as follows

* Suspicion of the intracavitary lesion.
* Abnormal uterine bleeding.
* Abnormal endometrial thickening.
* Postmenopausal bleeding.
* Infertility.
* Mullerian congenital anomaly.
* Removal of foreign bodies.

Whenever possible, in-office hysteroscopy is preferred. Compared to surgical inpatient hysteroscopy, in-office hysteroscopy offers many potential benefits, including patient and physician convenience, avoidance of general anesthesia, higher patient satisfaction, faster recovery, and cost-effectiveness (ACOG Committee Opinion 800). Factors that challenge outpatient hysteroscopy feasibility include large intrauterine pathology, patient anxiety, lack of appropriate treatment setting and/or personnel, and physician skill and expertise [35].

2.8. Contraindications of Hysteroscopy

The following are absolute and relative contraindications to hysteroscopy

a) Absolute contraindications such as Pelvic inflammatory disease (PID), pregnancy.
b) Relative contraindications such as cervical malignancy, menstruation, known adenocarcinoma of endometrium, cervical stenosis, recent uterine perforation and operator inexperience [35].

2.9. Contraindications

1- Infection

Hysteroscopy in presence of acute pelvic infection can lead to spread of infection. Distension medium flowing through tubes can spread infection to peritoneal cavity. Infection is even more likely when an operative procedure is anticipated & prophylactic antibiotics advised. Hysteroscopy in presence of vaginitis and cervicitis can lead to spread of

infection to endometrial or peritoneal cavity. Only exception is when infection is secondary to a lost IUCD should be removed hysteroscopically under antibiotic cover [41].

2- Pregnancy

Hysteroscopy during pregnancy may be performed to remove a coil. If miscarriage occurs in patients with congenital uterine anomalies, retained products of conception may pose a difficult clinical dilemma. Transvaginal ultrasound scan is able to reliably detect retained products of conception but in difficult cases, hysteroscopic assessment of the uterine cavity can facilitate guided evacuation [42].

3- Cervical cancer

Hysteroscopy in such patients may cause trauma to lymphatics and blood vessels. Malignant cells will also be carried to endometrial cavity. A friable cervical lesion can lead to excessive bleeding during cervical grasping and introduction of hysteroscope. Spread of endometrial cancer is also a concern, but evidence does not confirm this fear [43].

4- Bleeding

Diagnostic hysteroscopy may be performed in the presence of bleeding, but view is likely to be poor. Minimal uterine bleeding may allow adequate visualization of endometrial cavity. Hysteroscopy is best performed in proliferative phase when endometrium is thinnest. If this is difficult to arrange, then preoperative hormonal treatment with progesterone can help to postpone or control bleeding. It is even more difficult to perform operative procedures in presence of bleeding. Preoperative endometrial thinning agents help by decreasing thickness and vascularity of endometrium. This allows good visualization of the endometrial cavity, improves success rates and reduces fluid absorption, particularly when procedure is prolonged. If hysteroscopy is performed during bleeding, continuous-flow uterine distension enables better visualization by removing blood**.** The pressure of the distension medium decreases flow of bleeding as distension pressure reaches the arterial pressure [43].

5- Cervical stenosis

Patients who have a history of cervical surgery or difficult uterine entry in the past are at an increased risk of cervical trauma, perforation and false passage. Prostaglandins inserted 2 hours before hysteroscopy help to soften the cervix, allowing easy dilatation and entry into uterine cavity [41].

Table (I): Normal values of semen analysis according to World Health Organization (WHO) [20].

Parameter	Lower reference limit
Semen volume (mol)	1.5 (1.4-1.7)
Total sperm number (10^6 per ejaculate)	39 (33-46)
Sperm concentration (10^6 per ml)	15 (12-16)
Total	Motility (PR+NP %) 42 (40-43)
Progressive	Motility (PR %) 32 (31-34)
Vitality (Live spermatozoa %)	58 (55-63)
Sperm morphology (Normal forms %)	4 (3-4)
Other consensus threshold values	pH > 7.2
Peroxidase-positive leukocytes (10^6 per ml)	< 1
MAR test (motile spermatozoa with bound particles)	< 50%
Immunobead test (motile spermatozoa with bound bead)	< 50%
Seminal zinc (μmol/ejaculate)	> 2.4
Seminal fructose (μmol/ejaculate)	> 13
Seminal neutral glucosidase (mu/ejaculate)	> 20

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