DIAGNOSTIC HYSTEROSCOPY AS A PRIMARY TOOL IN BASIC INFERTILITY WORKUP.

Nabil Mohammed Eloraby, Mohammed Anwar Elnory, Amr Ali Sharaf Eldeen, Safaa Mohammed Mansour.

Abstract

Objective:- To assess the value of diagnostic hysteroscopy in basic workup of infertility.

Patients and Methods: - This is across sectional study including 100 infertile patients referred to the outpatient clinic in Banha university hospital between January 2015 and September 2015. Their ages range from (18-40) years, They were recruited based on their complaint from infertility either primary or secondary. Patients underwent a diagnostic hysteroscopy.

Results: - Abnormal hysteroscopic findings were observed in 36 % of infertile cases. Uterine polyps were the most common hysteroscopic abnormalities reported in 12%. Intrauterine adhesions 8%, submucus myoma 6%, congenital uterine malformations 6%, chronic endometritis 4%. Postoperative symptoms (nausea – mild lower abdominal pain) were recorded in 32% of patients that resolved by antiemetic and analgesic. All patients discharged from hospital after 6 hours. No cases postoperative pelvic infection was recorded.

Conclusion: - Routine diagnostic hysteroscopy should be part of an infertility workup in primary and secondary infertility.

Introduction:-

Infertility is defined as one year of unprotected intercourse without conception (1). About one of seven couples in developed countries and one of ten couples in developing countries experience infertility (2). It is defined as secondary if a previous conception had occurred regardless of the outcome (3). Infertility evaluation is typically initiated after 1 year of trying to conceive, but in couples with advanced female age (>35 years), most practitioners start diagnostic evaluation after an inability to conceive for 6 months. The Practice Committee of the American Society for Reproductive Medicine (ASRM) has published guidelines for a standard infertility evaluation. It includes a semen analysis, assessment of ovulation, hysterosalpingogram, and, if indicated, tests for ovarian reserve and laparoscopy (4). The incidence of unexplained infertility in the 1950s was greater than 20%, whereas literature preview, since 1980, have showed an incidence of 10% to 15%. Although the prevalence has been stable during the past 50 years, different potential factors may contribute to unexplained infertility, including age of partners, infertility duration, coital frequency, and professional status. The delay in conception may represent a chance delay or may be the result of an abnormality in the reproductive process (1). The main causes of infertility include male factor, decreased ovarian reserve, (ovulatory factor), tubal factor, uterine factors, systemic conditions, cervical factor, immunologic factor, and unexplained factors (5). Uterine abnormalities that have been implicated in infertility include endometrial polyps, submucus fibroids, intrauterine adhesions, mullerian anomalies, previous exposure to diethylstilbestrol (DES) (5). Assessment of the endometrium is an important step in the management of women with diagnosed infertility (6). Hysteroscopic examination is probably superior to hysterosalpungraphy in evaluating the endometrial cavity. Office hysteroscopy has been proven to have superior sensitivity and specificity in evaluating the endometrial cavity (7). Diagnostic hysteroscopy provides information, which is not obtained by blind endometrial
sampling such as the detection of endometrial polyps or submucous liomyomas\(^7\). Hysteroscopy is performed for evaluation or treatment of different pathologies of the endometrial cavity, tubal ostia, or endocervical canal for diagnostic alone or for diagnostic and treatment in the same operative time\(^8\). A review published on Up To Date in 2011 summarized the indications of diagnostic and operative hysteroscopy as follows: abnormal premenopausal or postmenopausal uterine bleeding, endometrial polyps, sub mucosal, and some intramural, fibroids, intrauterine adhesions, Müllerian anomalies (eg, uterine septum), retained intrauterine devices or other foreign bodies, retained products of conception, desire for sterilization, endocervical Polyps\(^9\). Hysteroscopy is a relatively safe procedure. However, as with any type of surgery, complications are possible. Hysteroscopy complications occur in less than 1 percent of cases and can include: risks associated with anesthesia, heavy bleeding, infection, injury to the cervix, uterus, bowel or bladder, intrauterine scarring and reaction to the substance used to expand the uterus\(^10\). Contraindications to hysteroscopy are: viable intrauterine pregnancy, active pelvic infection (including genital herpes infection) and known cervical or uterine cancer\(^11\). The aim of this study is to assess the value of diagnostic hysteroscopy as a primary tool in infertility workup.

**Patient and methods:**

This cross sectional study included 100 infertile women who had undergone hysteroscopy as part of infertility workup in the infertility clinic, Benha University Hospital between January 2015 and September 2015. Patients were informed about study characteristics, and those agreeing to participate, an informed consent was obtained. The study was approved by the hospital's ethical committee. Women with at least one year of infertility, Patients > 40 years of age, were excluded. All participant were subjected to a complete infertility evaluation that included complete history taking, examination, hormonal assay semen analysis, ultrasound and hysterosalpingography.

**Hysteroscopic procedure:**
The hysteroscopy was performed in early proliferative phase. Preparing the cervix for dilation was achieved with 200 micrograms of misoprostol, (Cytotec, Pfizer), orally or vaginally the evening prior to the procedure antibiotic prophylaxis was administered. Appropriate antibiotics include a cephalosporin or doxycycline. Diagnostic hysteroscopy was performed using a rigid 5.5-mm continuous flow hysteroscopy based on a 2.9 mm 30 degree lens system (Karl Storz, Tattling, Germany). Xenon cold light fountain 482 (KARL STORES GERMANY) will be used with 100 watt xenon lamp connected to a fiber optic light cable. 0.9 percent saline solution was used as distension media insufflated at atmospheric pressure (two bags connected by a urological “Y” outflow and located 1.5 meter above the patient). By doing a flow of 150-200 ml/min with a resulting intrauterine pressure of around 40 mmHg, were obtained which created no problems. An accurate assessment of the calculated deficit was be made. This was done by measuring the volume infused and subtracting the volume recovered giving the presumed volume absorbed by the patient. If the deficit exceeds 2000 ml then the procedure should be abandoned unless it is nearly complete. A reflex camera Olympus that has a focal length varies from f70 to f140 together with KARL STORES special zoom lens was used.

**Statistical analysis:**
1. Data were reported as mean ± SD or number and percentage.
2. P < 0.05 was considered significant.

**Results**

**Table I:** Patients characteristics (n=100)

| Variable | Value |
|----------|-------|
| Age mean ± SD years (range) | 29.13 ± 5.72 (19-40) |
| Duration of infertility mean ± SD years (range) | 4.05 ± 3.15 (1-15) |
| Infertility: | |
| Primary No. (%) | 54 (54%) |
| Secondary No. (%) | 46 (46%) |
| Indications for hysteroscopy No. (%): | |
| As part of infertility workup | 84 (84%) |
| Before IVF treatment | 10 (10%) |
| After ≥1 failed IVF cycles | 6 (6%) |
This table shows that mean patients age was 29.13 ± 5.72 years and the mean infertility duration was 4.05 ± 3.15 years.

46% percent of patients complain of secondary infertility and 54% of patients complain of primary infertility. Hysteroscopy was performed as part of infertility workup. Before IVF treatment and after ≥ 1 failed IVF cycles in 84%, 10% and 6% respectively.

Fig 1:- Indication for hysteroscopy

Table II:- Hysteroscopic findings in infertile women (n=100)

| Hysteroscopic findings                  | Number of cases (%) |
|----------------------------------------|---------------------|
| Normal hysteroscopic findings          | 64 (64%)            |
| Abnormal hysteroscopic findings        | 36 (36%)            |
| Uterine polyps                         |                     |
| Endometrial polyps                     | 11 (11%)            |
| Cervical polyps                        | 1 (1%)              |
| Submucus myoma                         | 6 (6%)              |
| Chronic endometritis                   | 4 (4%)              |
| Intrauterine synechia                  | 8 (8%)              |
| Congenital uterine malformations       |                     |
| Intrauterine septum                    | 2 (2%)              |
| Bicornuat uterus                       | 1 (1%)              |
| Unicornuat uterus                      | 1 (1%)              |
| Arcuate uterus                         | 2 (2%)              |

This table shows that abnormal hysteroscopic findings were observed in 36% of infertile cases. Uterine polyp were the most common hysteroscopic abnormalities reported in 12%, Intrauterine synechia 8%, submucus myoma 6%, congenital uterine malformations were found in 6% and chronic endometritis in 4(4%).

Table III:- Duration of hysteroscopy.

| Procedure              | Range(min) | Mean ±SD(min) |
|------------------------|------------|---------------|
| Hysteroscopic          | 3-12       | 5.77±2.77     |

The mean time taken by surgeon for diagnostic hysteroscopic was 5.77 ± 2.77 min

Table IV:- Operative and post Operative complications.

| Variables              | No (%)     |
|------------------------|------------|
| Bleeding from cervical tear | 4 (4%)    |
| Nausea & lower abdominal pain | 32 (32%)  |

This table shows that slight bleeding from cervical tear was recorded in 4% of cases which controlled by cervical compression with tampon.

Postoperative symptoms (nausea – mild lower abdominal pain) were recorded in 32% of patients that resolved by antiemetic and analgesic (non steroidal anti inflammatory). All patients discharged from hospital after 6 hours. No cases postoperative pelvic infection was recorded.
Table (V): Hysteroscopic findings in infertile women (n=100) in primary and secondary infertility.

| Hysteroscopic findings                      | 1ry infertility | 2ry infertility | Z test | P value |
|---------------------------------------------|-----------------|-----------------|--------|---------|
| Normal hysteroscopic findings               | 36(66.7)        | 28(60.9)        | 1.01   | 0.16    |
| Abnormal hysteroscopic findings             |                 |                 |        |         |
| Uterin polyps                               |                 |                 |        |         |
| Endometrial polyps                          | 6 (11.1)        | 5 (10.9)        | 0.303  | 0.38    |
| Cervical polyps                             | 0(0.0)          | 1(2.2)          | -      | -       |
| Submucus myoma                              | 3(5.6)          | 3(6.5)          | 0.0    | 0.5     |
| Chronic endometritis                        | 2(3.7)          | 2(4.3)          | 0.0    | 0.5     |
| Intrauterine synchia                        | 5(9.3)          | 3(6.5)          | 0.73   | 0.23    |
| Congenital uterine malformations            |                 |                 |        |         |
| Intrauterin septum                          |                 |                 |        |         |
| Bicornuat uterus                            | 1(1.9)          | 1(2.2)          | 0.0    | 0.5     |
| Unicornuat uterus                           | 1(1.9)          | 0(0.0)          | -      | -       |
| Arcuate uterus                              | 1(1.9)          | 0(0.0)          | -      | -       |
| Intrauterine septum                         | 1(1.9)          | 1(2.2)          | 0.0    | 0.5     |

Fig 2:- Abnormal hysteroscopic findings in primary and secondary infertility in 100 infertile patients.

Fig 3:- Abnormal hysteroscopic finding in 36 infertile patients.

\------ Discussion:------

Uterine factors are responsible for 2-3% of infertility cases and intrauterine lesions more common in infertile women (40-50%)\(^{(12)}\). IVF is an expensive treatment results in a successful outcome in only a third of treatment cycles\(^{(13)}\). It has been suggested that unsuspected intrauterine abnormalities may negatively affect the uterine environment and the likelihood of achieving an ongoing pregnancy \(^{(14)}\). This study included 100 infertile patients who had hysteroscopy for different indications, 36 patients (36%) were found to have abnormal hysteroscopic findings despite normal HSG and TV/US, hormonal profile, semen analysis. The types and frequencies of the
detected uterine abnormalities were as follows: uterine polyps showed the highest prevalence 12(12%), followed by intrauterine synechiae 8(8%), then equal prevalence for submucous myomas and congenital uterine malformation 6 (6%) each, then chronic endometritis 4 (4%). In this study, uterine poly were diagnosed in 12% of Patients. Up to 25% of women with unexplained infertility have endometrial polyps on hysteroscopy (13). However, their effect on endometrial receptivity and fertility is unclear. Hypotheses include mechanical obstruction hindering ostium function and affecting sperm migration (15). In this study, intrauterine synechia were diagnosed in 8% of patients. Incidence of Asherman’s syndrome is between 19 and 23.6 % of women who undergo diagnosis for repeated miscarriage or infertility(16). Infertility may be caused by adhesions occluding the tubal ostia, uterine cavity, or the cervix, thereby interfering with the migration of sperm or implantation of embryo(17). In this study, submucous myomas were diagnosed in 6% of patients. The incidence of fibroids ranges from 5.4 to 77% in premenopausal women, with a fibroid being only detected abnormality in 1–2.4% of infertile women (18). Fibroids may impede sperm or egg transport through displacement of the cervix or obstruction of the fallopian tubes and pouch Douglas. Implantation may be affected by deformity of the cavity but increased contractility of the myometrium and a chronic inflammatory response by the endometrium to underlying fibroids may also be important. Many studies look at a single mechanism but it is most probably a combination of factors that contributes to any associated fertility difficulties (19). In this study uterine malformations were observed in 6 % of infertile cases. The role of uterine malformations as a cause of infertility is still debatable. The prevalence of major uterine anomalies is estimated to be 5% in general fertile population, 3% in infertile patient, and 5 – 10% in recurrent miscarriage (20). The septate uterus is one of the most common structural uterine anomaly. The septum may have a role in implantation failure or early pregnancy development. There are several ideas about the underlying mechanism of the implantation failure or pregnancy loss. These include diminished size of the uterine cavity, maturation defects of the endometrium covering the septum with a reduced number of glandular ostia, altered maturation of the cilia, altered proportions between muscular and fibro elastic connective tissue, or an abnormal vascularization in the histologic examination of uterine septa (21). In a study comparing the value of each of office hysteroscopy and TV/US in the assessment of the uterine cavity prior to IVF found that TVS in comparison with hysteroscopy has 84.5% sensitivity, 98.7% specificity and 98% positive predictive value and 89.2% negative predictive value. Transvaginal ultrasound may not diagnose submucosal fibroids in the presence of multiple fibroids, a large polyp from hyperplasic endometrium and, or differentiate between an arcuate and septate uterus (22). HSG alone is recommended by the World health Organization (WHO) in management of infertile women (23); as it gives information on tubal patency or blockage (23), in their study which evaluated the role of each of office hysteroscopy, hysteosalpingiogram and saline infusion hysterosgraphy in assess the uterine cavity, found that office hysteroscopy should be used only in patients with abnormal hysterosalpingiogram. However, the results of this study in concordance with other similar studies and studies comparing the role of each HSG, office hysteroscopy and transvaginal ultrasound, agree on the lack of specificity and sensitivity of both hysterosalpingiogram and transvaginal ultrasound compared to office hysteroscopy in assessment of the uterine cavity. Hence, the need to do office hysteroscopy as a routine investigation in infertile females especially prior to IVF. In this study the mean time taken by surgeon for diagnostic hysterectomy was 5.77 ± 2.77 min. In this study slight bleeding from cervical tear was recorded in 4 % of cases which controlled by cervical compression with tampon. Postoperative symptoms (nausea – mild lower abdominal pain) were recorded in (32%) of patients that resolved by antiemetic and analgesic (non-steroidal anti-inflammatory) all patients discharged from hospital after 6 hours no cases of postoperative pelvic infection was recorded. While debating the need for routine diagnostic hysteroscopy in the evaluation of infertile women one must keep in mind that this procedure today is no longer a complicated (inpatient general anesthesia one) but rather a simple, fast, outpatient procedure, requiring short training with high success rate (24). Diagnostic hysteroscopy allows complete, accurate identification of intrauterine abnormalities that might negatively affected endometrial receptivity and implantation. The information delivered from hysteroscopy helps the physician to institute appropriate therapy and improve conception rate over shorter intervals.

**Conclusion:**
Thirty six percent women, undergoing infertility evaluation, had abnormal uterine findings on hysteroscopy. According to frequency of occurrence they were uterine polyps, intrauterine synechia, sub mucous myomas, uterine malformation and chronic endometritis. Hysteroscopy is a safe, fast test for the accurate diagnosis of intrauterine abnormalities in infertile women.
References:
1. Speroff L, Fritz and Marc A (2011): Clinical gynaecologic endocrinology and infertility. Eighth edition. Lippincott Williams & Wilkins. Philadelphia New York.; (27):1137-90.
2. Duckitt K (2002): Infertility and sub fertility Clinical Evidence; 7:1679-704.
3. Valentine AA et al., (2003): Tubal damage in infertile women: prediction using Chlamydia serology. Hum Reprod.; 18:1841-7.
4. The Practice Committee of the American Society for Reproductive Medicine (2006): Effectiveness and treatment for unexplained infertility. Fertil Steril; 86(suppl. 5):S111-S114.
5. Burney R, Schust D and Yao M (2007): Infertility, Jonathan S B,(editor), Berek & Novak's Gynecology , Lippincott Williams &Wilkins.ch 30.
6. Balic D, Balic A (2011): Office hysteroscopy, transvaginal ultrasound and endometrial histology: a comparison in infertile patients. ActaMedica Academica; 40(1):34-38.
7. Barati M, Zargar M, Masihi S et al., (2009): Office Hysteroscopy in Infertility. International Journal of Fertility and Sterility. 2009. (3) ,17-20.
8. Koekas M, Mergui JL, Yazbeck C, et al., (2010): Office hysteroscopy for infertility: a series of 557 consecutive cases. Obstet GynecolInt:168096.
9. Bradley LD (2010): Overview of hysteroscopy, Up To Date Last literature review version; 18:3.
10. American Society for Reproductive Medicine.(2013): Laparoscopy and Hysteroscopy: A Guide for Patients.; (25) :32.
11. Price TM and Harris JB(2001): Fulminate hepatic failure due to herpes simplex after hysteroscopy. Obstet Gynecol; 98:954.
12. Ait Benkaddour Y, Gervaise A and Fernandez H (2010): [Which is the method of choice for evaluating uterine cavity in infertility workup?]. J Gynecol Obstet Biol Reprod (Paris) ;39(8):606–13.
13. Bouwmans CA, Lintsen BM, Eijkemans MJ et al., (2008): A detailed cost analysis of in vitro fertilization and intracytoplasmic sperm injection treatment. Fertil. Sterile; 89, 331–341
14. Taylor E and Gomel V (2008): The uterus and fertility. Fertil Steril; 89(1): 1–16.
15. Shokeir TA, Shalan HM and El Shafei MM (2004): Significance of endometrial polyps detected hysteroscopically in eumenorrheic infertile women. J Obstet Gynaecol Res; 30:84–9.
16. Dendrinos S, Grigorou O, Sakkas EG et al., (2008): Hysteroscopy in the evaluation of habitual abortions. Eur J Contracept Reprod Health Care ;13(2):198-200.
17. Yu D, Wong YM, Cheong Y et al.,(2008): Asherman syndrome one century later. Fertil Steril, 89:759–79.
18. Lethaby A and Vollenhoven B (2002): Fibroids. Clin. Evid.,8, 1666-78.
19. Rackow BW and Taylor HS (2010): Submucosal uterine leiomyomas have a global effect on molecular determinants of endometrial receptivity. Fertile. Steril,93, 2027-34.
20. Paul C Lin (2004): Reproductive outcome in women with uterine anomalies, article at medscape.com 13(1):33-9.
21. Pabuccu R and Gomel V (2004): Reproductive outcome after hysteroscopic metroplasty in women with septate uterus and otherwise unexplained infertility. Fertil Steril ; 81(6): 1675–8.
22. Pundir J and El Toukhy T (2010): Uterine cavity assessment prior to IVF. Women Health (Lond Engl) ; 6: 841-8.
23. Brown SE, Cuddington CC, Schnorr J et al., (2000): Evaluation of outpatient hysteroscopy, saline infusion hysterosonography, and hysterosalpingography in infertile women: a prospective, randomized study. Fertil Steril;74(5):1029–34.
24. Oliveira FG, Abdelmassih VG, Diamond MP et al., (2003): Uterine cavity findings and hysteroscopic interventions in patients undergoing in vitro fertilization-embryo transfer who repeatedly cannot conceive. Fertil Steril, 80(6):1371-75.