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ROLE OF DIAGNOSTIC HYSTEROSCOPY IN INFERTILE WOMEN WITH NORMAL HYSTEROSALPINGOGRAM

By

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ABSTRACT

Background: The indication for routine hysteroscopy (HSC) in patients undergoing diagnostic hysteroscopy as part of an infertility work up is still a matter of controversy. Although most clinics continue to use hysterosalpingography (HSG) as their routine test to assess the uterine cavity, there is a growing body of literature dealing with the use of HSC as an important instrument to use in the evaluation and treatment of infertile couples.

Objective: To evaluate the role of the diagnostic hysteroscopy in infertile women with normal HSG.

Patients and Methods: This cohort observational study was carried out at Ahmed Maher Teaching Hospital, Egypt, from November 2019 till May 2020, on one hundred women Patients having primary infertility.

Results: The mean age of the studied cases was 29.58 ± 6.75 with range (20-40). The mean period of infertility was 4.89 ± 1.07 with range (3-7), the mean BMI was 28.27 ± 2.13 with range (25-32). There were 10% illiterate, 45% with moderate education and 45% with high education, there were 92% Primigravida and 8% multigravida, and there were 92% with primary type of infertility, and 8% with secondary type of infertility. There were 17% with diabetes, 28% with hypertension and 13% with previous pelvic surgery. Among the studied cases, there were 38 with detected abnormality, i.e. (5%) endometrial polyp, (2%) Cervical Polyp, (6%) cervical stenosis, (3%) chronic endometritis, (3%) hypertrophic endometrium, (2%) atrophic endometrium, (5%) Intrauterine adhesions, (4%) Cornual fibrosis, (2%) cornual inflammation, (4%) Sub mucous myoma and (2%) septum. There was no significant difference between the cases who detected abnormality and who didn't as regard age, period of infertility, BMI, education, parity and type of infertility. There was no significant difference between the cases who detected abnormality and who didn't as regard menstrual history. There was no significant difference between the cases who detected abnormality and who didn't as regard diabetes, hypertension and previous pelvic surgery.

Conclusion: The incidence of uterine pathologies (congenital and acquired) in women with primary or secondary infertility approximated 30%, thus, justifying, the use of diagnostic hysteroscopy in the primary routine investigation of infertile women.

Key words: Diagnostic hysteroscopy, infertility, normal hysterosalpingogram.

INTRODUCTION

Infertility means the inability to conceive following 1 year of unprotectedintercourse in cases where the female is > 35 years of age or following 6 months of unprotected intercourse for women <35 years of age *(Anwar and Anwar, 2016)*.

Hysteroscopy is considered the gold standard for evaluating the uterine cavity, and due to improved endoscopic developments. It can be performed

reliably and safely as an office procedure *(Pundir and El Toukhy, 2010)*.

The presence of uterine pathology may negatively affect the chance of implantation. The prevalence of unsuspected uterine pathology in asymptomatic women with implantation failure has been reported to be as high as 50%. Therefore, one of the common investigations proposed for women undergoing IVF treatment is to evaluate the uterine cavity via hysteroscopy *(Cenksoy et al., 2013)*.

The role of congenital uterine anomalies in infertility remains unclear. However, it has been suggested that uterine anomalies may contribute to infertility, possibly by interfering with normal implantation and placentation *(El-Mazny et al., 2011)*.

HSG is a contrast study of the uterine cavity and fallopian tubes. It is a simple, inexpensive, safe, and rapid diagnostic procedure that, when performed properly, provides valuable information about the uterine cavity and tubal architecture *(Gajbhiye and Gajbhiye, 2017)*.

Hysterography is used predominantly in the evaluation of infertility and recurrent abortion. Also, this procedure can be used in other cases, such as; Chronic pelvic pain, congenital or anatomical uterine abnormalities and abnormal uterine bleeding (AUB) *(Johnstone and Olpin, 2018)*.

HSG must be timed to be done between complete cessation of menstruation and ovulation. This will avoid the risk of disturbing a luteal phase pregnancy. Such timing also avoids radiation exposure to the oocyte that will resume meiosis after the luteinizing hormone surge. Therefore, HSG ideally should be scheduled between day 4 and 7 of the menstrual cycle. This allows time for any residual blood from the menses to clear yet is early enough so that the endometrium has not grown significantly *(Park and Isaacson, 2017)*.

The aim of this study was to evaluate the role of the diagnostic hysteroscopy in infertile women with normal HSG.

PATIENTS AND METHODS

This cohort observational study was carried out on one hundred women having infertility at Ahmed Maher Teaching Hospital, Egypt. Cases were recruited from the outpatient Infertility clinic from December 2019 till May 2020.

Inclusion Criteria:

Patients aged 20-35years, having primary or secondary infertility, women with infertility for more than 1 year, normal hystrosalpingiogram, regular cycle and no male factor.

Exclusion Criteria:

Patient with ages less than 20 years or more than 40 years, contraindications of hysteroscopy like bleeding, suspected or confirmed pregnancy and history suggestive of active infection like history of cervical or vaginal discharge, patients with abnormal HSG and couples with male factor infertility (abnormal semen parameters and/or sexual dysfunctions).

All study patients were subjected to: Full history taking, clinical examination, and blood analysis for a base line hormonal profile- day 2 serum FSH, LH, and prolactin, ultrasonographic examination and hysteroscopic

examination. Rrigid continuous flow diagnostic hysteroscopy was done (Tuttligen, Karl Storz, Germany). It has a 30o panoramic optic which was 4mm in diameter and the diagnostic continuous flow outer sheath was 6.5 mm in diameter. The patient was placed in lithotomy position with the buttocks projecting slightly beyond the table edge.

Statistical analysis was done using Statistical Package for the Social Sciences version 20 (SPSSInc., Chicago, IL, USA). Quantitative variables were described in the form of mean and standard deviation, median and interquartile range (IQR). Qualitative variables were described as number and percent. In order to compare parametric quantitative variables between two groups, Student t test was performed. Qualitative variables were compared using chi-square (X2) test or Fisher's exact test when frequencies were below five. P value < 0.05 was considered significant.

An informed verbal consent from all participants was taken and confidentiality of information was assured.

Permission from the Faculty of Medicine ethical committee was obtained and approval from institutional review board was taken.

RESULTS

The mean age of the studied cases was 29.58 ± 6.75 with range (20-40). The mean period of infertility was 4.89 ± 1.07 with range (3-7). The mean BMI was 28.27 ± 2.13 with range (25-32). There 10 (10%) were illiterate, 45 (45%) with moderate education, and 45 (45%) with high education. There were 92 (92%) primigravida and 8 (8%) multigravida, there were 92 (92%) with primary type of infertility, and 8 (8%) with secondary type of infertility. There were 7 (7%) with diabetes, 8 (8%) with hypertension and 3 (3%) with previous pelvic surgery **(Table 1)**.

Table (1): Distribution of the studied cases according to personal and past history (n=100)

Distribution / Parameters	No.		%	
Age (years)				
Min. – Max.	20.0 –40.0			
Mean ± SD.	29.58 ±6.75			
Median (IQR)	30.0(23.0 –35.50)			
Period of infertility				
Min. – Max.	3.0 –7.0			
Mean ± SD.	4.89 ±1.07			
Median (IQR)	5.0(4.0 –6.0)			
BMI (kg/m^2)				
Min. – Max.	25.0 –32.0			
Mean ± SD.	28.27 ±2.13			
Median (IQR)	28.05(26.25 –29.90)			
Education				
None	10		10.0	
Moderate	45		45.0	
High level	45		45.0	
Parity				
0	92		92.0	
1	8		8.0	
Type of infertility				
Primary	92		92.0	
Secondary	8		8.0	
	No		**Yes**	
	No.	**%**	**No.**	**%**
Diabetes	93	93.0	7	7
Hypertension	92	92.0	8	8.0
Previous pelvic surgery	97	97.0	3	3.0

Among the studied cases, there were 38 (38) with detected abnormality {(5%) endometrial polyp, (5%) cervical Polyp, (3%) cervical stenosis, (5%) chronic endometritis, (3%) hypertrophic endometrium, (5%) atrophic endometrium, (2%) intrauterine adhesions, (2%) cornual fibrosis, (2%) cornual inflammation, (4%) sub mucous myoma and (2%) septum} **(Table 2)**.

Table (2): Distribution of the studied cases according to detected abnormality and hysteroscopic findings (n=100)

Distribution / Detected abnormality	No.	%
No	62	62.0
Yes	38	38.0
Abnormal hysteroscopic findings		
None	62	62.0
Endometrial Polyp	5	5.0
Cervical Polyp	5	5.0
Cervical stenosis	3	3.0
Chronic endometritis	6	6.0
Hypertrophic endometrium	3	3.0
Atrophic endometrium	4	4.0
Intrauterine adhesions	2	2.0
Cornual fibrosis	2	2.0
Cornual inflammation	2	2.0
Sub mucous myoma	4	4.0
Septum	2	2.0

There was no significant difference between the cases who detected abnormality and who didn't as regard age, period of infertility, BMI, education, parity and type of infertility **(Table 3)**.

Table (3): Relation between detected abnormality and personal history (n=100)

Detected abnormality / Parameters	No (n = 62)		Yes (n = 38)		P
	No.	**%**	**No.**	**%**	
Age (years)					
Min. – Max.	20.0 –40.0		20.0 –40.0		0.648
Mean ± SD.	29.82 ±6.60		29.18 ±7.04		
Median (IQR)	30.0(24.0 –35.0)		29.0(23.0 –36.0)		
Period of infertility					
Min. – Max.	3.0 –7.0		3.0 –6.0		0.466
Mean ± SD.	4.95 ±1.11		4.79 ±1.02		
Median (IQR)	5.0(4.0 –6.0)		5.0(4.0 –6.0)		
BMI (kg/m^2)					
Min. – Max.	25.0 –31.80		25.30 –32.0		0.840
Mean ± SD.	28.24 ±2.09		28.33 ±2.23		
Median (IQR)	28.05(26.20 –29.70)		28.15(26.40 –30.40)		
Education					
None	6	9.7	4	10.5	0.679
Middle	30	48.4	15	39.5	
High level	26	41.9	19	50.0	
Parity					
0	57	91.9	35	92.1	^{FE}p= 0.976
1	5	8.1	3	7.9	
Type of infertility					
Primary	57	91.9	35	92.1	^{FE}p= 0.976
Secondary	5	8.1	3	7.9	

There was no significant difference between the cases who detected abnormality as regard diabetes, hypertension and previous pelvic surgery **(Table 4)**.

Table (4): Relation between detected abnormality and past history (n=100)

Detected abnormality / Parameters	No (n=62)		Yes (n = 38)		χ^2	P
	No.	**%**	**No.**	**%**		
Diabetes						
No	52	83.9	31	81.6	0.088	0.767
Yes	10	16.1	7	18.4		
Hypertension						
No	45	72.6	27	71.1	0.027	0.869
Yes	17	27.4	11	28.9		
Previous pelvic surgery						
No	55	88.7	32	84.2	0.422	$^{FE}p=$ 0.516
Yes	7	11.3	6	15.8		

DISCUSSION

The role of hysteroscopy in infertility investigation is to detect possible intrauterine changes that could interfere with implantation or growth or both, of the conceptus *(Cenksoy et al., 2013)*. So, this study was selected to be conducted to evaluate the role of the diagnostic hysteroscopy in infertile women with normal HSG.

The mean age of the studied cases was 29.58 ± 6.75 with range (20-40), the mean period of infertility was 4.89 ± 1.07 with range (3-7), the mean BMI was 28.27 ± 2.13 with range (25-32), there were 10 (10%) was illiterate, 45 (45%) with moderate education and 45 (45%) with high education, there were 92 (92%) Primigravida and 8 (8%) multigravida and there were 92 (92%) with Primary type of infertility and 8 (8%) with Secondary type of infertility.

Our results were supported by study of *Amirian et al. (2019)* as they reported that the mean age of the attending patients and their duration of infertility were 30.9 ± 5.4 and 4.1 ± 5.2 years, respectively. There were 71.8 % of them with primary type of infertility. Furthermore, *Wadhwa et al. (2017)* revealed that a majority of 73.14% had primary infertility and 26.85% had secondary infertility.

The current study showed that among the studied cases, there were 5% detected endometrial polyp, (2%) cervical polyp, (6%) cervical stenosis, (3%) chronic endometritis, (3%) hypertrophic endometrium, (2%) atrophic endometrium, (5%) intrauterine adhesions, (4%) cornual fibrosis, (2%) cornual inflammation, (4%) sub mucous myoma and (2%) septum.

Our results were supported by study of *Muhammad et al. (2016)* as they reported that during hysteroscopic examination, abnormalities were detected in the cervix and uterus in 48 patients (34.3%). More than one abnormality was seen in 8 patients, i.e. 56 abnormalities were recorded, Cervical abnormalities (n = 12) represented 21.4 % of all abnormalities, while uterine abnormalities were 44,

representing 78.6 % all abnormalities. Cervical stenosis was the most frequent hysteroscopic findings, 9 cases was detected. Cervical stenosis and cervical polyp were seen in 21.3 % of cases. The 2 cases with uterine septa had small septum. Intrauterine adhesions were found in 8 patients; 6 with mild adhesions and 2 with moderate adhesions. Cervical stenosis did not hinder passage of the hysteroscope to inspect the uterine cavity in the 9 cases.

Further, *Godinjak and Idrizbegovic (2018)* examined infertile patients using hormonal tests, cervical smear, sonography, Chlamydia antibody, and normal semen analysis. Laparoscopy and hysteroscopy were performed in the follicular phase for all the patients within the age range of 23-42 years whose means of age and infertility duration was 31 and 6.3 years, respectively. Based on the results, hysteroscopy was normal in 75.11%, while it was found abnormal in the remaining 24.89%. Uterine pathologies involved submucosal myomas 11.6%, endometrial polyp cases 7.22%. Asherman syndrome cases in 0.8%, and uterine anomaly cases in 5.27%. 20% of uterine pathologies with short time and low complication (less than 0.01%) were diagnosed simultaneously performing hysteroscopy and laparoscopy.

In the study of *El Huseiny and Soliman (2013)*, normal hysteroscopic findings were reported in 79.63%. The other 20.37% were with abnormal hysteroscopy. The most common reported hysteroscopic abnormality was intrauterine adhesions (IUA) in 31.81% followed by endometrial polyp 26.13%. Pre-hysteroscopic uterine investigations (ultrasound or hysterography) were available. Office hysteroscopy revealed uterine cavity abnormalities in 14.68%. Of those with abnormal pre-hysteroscopic findings, hysteroscopy examinations were normal in 25% of patients.

In another study by *Nigam et al. (2015)*, infertile women with primary infertility received HSG which was found to be abnormal in 78.1% while being normal in 21.9%. Then, laparoscopy and hysteroscopy were conducted in patients with normal HSG. The diagnosed pathologies contained uterine adhesions in 90% and an endometrial polyp in 10%. The false negative percentage was reported 12.69% for the HSG.

In the same vein, *Chauhan et al. (2013)* found that the mean age and duration of infertility of the patients were 30 ± 4 and 4.1 ± 2 years, respectively. The sensitivity, specificity, PPV, and NPV of the hysteroscopy were 50%, 98%, 76.9%, and 88.5%, respectively.

In the study in our hands, there was no significant difference between the cases who detected abnormality and who didn’t as regard age, period of infertility, BMI, education, Parity and Type of infertility. There was no significant difference between the cases who detected abnormality and who didn’t as regard menstrual history. There was no significant difference between the cases who detected abnormality and who didn’t as regard diabetes, hypertension and previous pelvic surgery.

There was no significant difference between the cases who detected abnormality and who didn’t as regard pulse, temp, systolic and diastolic BP.

Our results were supported by study of *Pansky et al. (2016)* as they reported that endometrial polyps were diagnosed in both primary and secondary infertility groups with no statistically significant difference. The true incidence of endometrial polyps in the general population is difficult to determine, because many of them are clinically asymptomatic. No significant difference was found in the rate of intrauterine adhesions comparing the patients with primary versus secondary infertility, in spite of the known relationship between secondary infertility and the existence of adhesions, being mostly the result of uterine curettage for postpartum or post abortion residua.

Furthermore, *Wadhwa et al. (2017)* found that abnormal hysteroscopic findings were detected in 35.44% of women with primary infertility and in 35.71% women with secondary infertility. The difference between two groups was not statistically significant.

In the study of *Amirian et al. (2019)*, the type of infertility made no significant difference in diagnosing uterine pathology in the hysteroscopy.

Hysteroscopy, with the development and miniaturization of equipment, is currently simple, outpatient cost-effective exploration and it is considered the gold standard for diagnosis of intrauterine lesions. However, the benefit of the systematic use of hysteroscopy in the initial assessment of infertility remains unclear and the exploration of the uterine cavity in the initial assessment of infertility should be based on hysterosalpingography or Hyster sonography. Systematic hysteroscopy before IVF is widely accepted practice that is supposed to improve pregnancy rates but still lacks scientific evidence. After repeated implantation failure in IVF cycles, uterine cavity should be reevaluated by hysteroscopy and this practice has been demonstrated to improve pregnancy rates *(Ait et al., 2010)*.

CONCLUSION

Diagnostic hysteroscopy has a similar importance in the evaluation of patients with both primary and secondary infertility.

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دور منظار الرحم التشخيصي في النساء اللاتى يعانين من تأخر الانجاب و ذوات أشعة بالصبغة طبيعية على الرحم والأنابيب

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خلفية البحث: لا تزال الإشارة إلى تنظير الرحم الروتيني (HSC) في المرضى الذين يخضعون لتنظير الرحم التشخيصي كجزء من عملية العقم موضع جدل، على الرغم من أن معظم العيادات تواصل استخدام تصوير الرحم (HSG) كاختبار روتيني لتقييم تجويف الرحم، هناك هي مجموعة متزايدة من الأدبيات التي تتناول استخدام HSC كأداة مهمة لاستخدامها في تقييم وعلاج الأزواج المصابين بالعقم.

الهدف من البحث: تقييم دور تنظير الرحم التشخيصي عند النساء المصابات بالعقم المصابات بـ HSG الطبيعي.

المريضات وطرق البحث: أجريت هذه الدراسة الاستطلاعية في مستشفى أحمد ماهر التعليمي، مصر، من نوفمبر 2019 حتى مايو 2020، على مائة امرأة مصابة بالعقم الأولي تم اختيارهن من الذين يعانون من تأخر الانجاب غير معروف السبب، واللاتى أظهرن نتائج طبيعية فى الفحوصات الطبية. كما أظهرت جميع الحالات نتائج طبيعية باستخدام الأشعة بالصبغة على الرحم وقناتي فالوب مما يشير إلى سلامة الأنابيب وسلامة تجويف الرحم. وحيث يوفر منظار الرحم أداة مباشرة لرؤية وفحص تجويف الرحم.

نتائج البحث: كان متوسط عمر الحالات المدروسة 29.58 ± 6.75 مع المدى (20-40)، وكان متوسط فترة العقم 4.89 ± 1.07 مع المدى (3-7)، وكان متوسط مؤشر كتلة الجسم 28.27 ± 2.13 مع المدى (25- 32)، كان هناك 10٪ أميين، 45٪ لديهم تعليم متوسط و 45٪ تعليم عالٍ، كان هناك 92٪ حوامل للمرة الأولى و 8٪ اللاتى سبق لهن الحمل وكان هناك 92٪ من النوع الأولي من العقم و 8٪ من النوع الثانوي من العقم. كان هناك 17٪ يعانون من مرض السكري، و

28٪ يعانون من ارتفاع ضغط الدم، و 13٪ مع جراحة الحوض السابقة. من بين الحالات التي تم دراستها كان هناك 38 (38) مع وجود شذوذ مكتشف {(5٪) ورم بطانة الرحم، (2٪) سليلة عنق الرحم، (6٪) تضيق عنق الرحم، (3٪) التهاب بطانة الرحم المزمن، (3٪) تضخم بطانة الرحم، ((2٪) بطانة الرحم الضامرة، (5٪) التصاقات داخل الرحم، (4٪) تليف القرنية، (2٪) التهاب القرنية، (4٪) الورم العضلي المخاطي الفرعي و (2٪) الحاجز}. لم يكن هناك فرق كبير بين الحالات التي اكتشفت خلًا والذين لم يتم اعتبارهم من حيث العمر وفترة العقم ومؤشر كتلة الجسم والتعليم والتكافؤ ونوع العقم. لم يكن هناك فرق كبير بين الحالات التي اكتشفت شذوذًا والذين لم يأخذوا تاريخ الحيض في الاعتبار. لم يكن هناك فروق ذات دلالة إحصائية بين الحالات التي اكتشفت خلًا والتي لم تكن تتعلق بمرض السكري وارتفاع ضغط الدم وجراحة الحوض السابقة.

الاستنتاج: نسبة حدوث أمراض الرحم (الخلقية والمكتسبة) لدى النساء المصابات بالعقم الأولي أو الثانوي تقارب 30٪، مما يبرر، في رأينا، استخدام تنظير الرحم التشخيصي في الفحص الروتيني الأولي للنساء المصابات بالعقم.

الكلمات الدالة: منظار الرحم التشخيصي، العقم، الأشعة بالصبغة على الرحم والمبيضين.