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Assessment of the Prevalence of Abnormal Hysteroscopic Findings in Infertile Women Undergoing ART

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ABSTRACT
Background: The endometrium plays an important role in implantation of good quality embryos in ART. Many studies have proved the negative impact of intra uterine pathologies on reproductive outcome whether spontaneous pregnancy or ART, because uterine anomalies may be associated with many obstetric complications such as miscarriage, preterm birth, premature rupture of membrane, malpresentation, postpartum bleeding and retained placenta. Aim of the work: This study aims to assess the prevalence of abnormal hysteroscopic findings among infertile women undergoing ART at Ain Shams Maternity University Hospital over the period from January 2007 to January 2017. **Patients and Methods:** This descriptive retrospective study was carried out on infertile couples planned for ART who were sent to ECDU for hysteroscopy in Early Cancer Detection Unit (ECDU), Ain Shams University Maternity Hospital. Case reports From January 2007 to January 2017 were reviewed. **Results:** The most prevalent congenital abnormality was endometrial polyp (18.4%) followed by uterine septum (6.9%). **Conclusion:** This study concluded that the most common uterine abnormality was endometrial polyp (18.4%), followed by uterine septum in 6.9% of patients. Also, thick endometrium was very common with a prevalence of 12.9%. Therefore, based on this high prevalence of abnormalities, this study is in agreement with the opinion that all women should be offered hysteroscopy, even if they have normal vaginal ultrasound and hysterosalpingography, because this is supposed to increase the detection rate of minor abnormalities, which theoretically will improve the reproductive outcome. Still, further interventional randomized controlled trials (RCT) are needed to verify the positive impact of routine use of hysteroscopy prior to ART.
Keywords: abnormal hysteroscopy, infertility, ART.

INTRODUCTION

The mean prevalence of Mullerian duct anomalies was estimated to be about 7% in the general population [(1)] and 13.3% in the infertile population [(2)]. The female genital tract is derived from paramesonephric duct (Mullerian) by the lateral fusion of the 2 paired mullerian ducts which unite to form the uterus and upper part of cervix. Septal absorption by apoptosis results in a single cavity [(3)].

Normal development of the female genital tract involves a series of events: mullerian duct elongation, fusion, canalization, and septal resorption, therefore, congenital uterine anomalies result from abnormal formation, fusion or resorption of the mullerian ducts during fetal life [(4)]. Because of the role of the wolffian (mesonephric) ducts in the development of the female reproductive tract and the renal development, the abnormalities originating from the mesonephric maldevelopment are associated with mullerian duct anomalies [(5)].

Renal anomalies are frequently associated with mullerian duct anomalies with a prevalence of (20-30%) such as pelvic kidney, renal agenesis, duplication of the collecting system and ectopic ureters, hypoplasia, malrotation [(6)].

Uterine cavity and its innermost layer; the endometrium play an important role in implantation of the blastocyst [(7)].

Also, many experimental and clinical studies have emphasized the importance of uterus and intrauterine pathology for spontaneous and post-ART fertility [(8)], which makes evaluation of the uterine cavity a basic step in investigation of the infertile women [(9)].

Office hysteroscopy (OH) is increasingly recommended by many studies as a routine procedure in the infertility work up [(10,11,12)] because office hysteroscopy has the advantages of faster ambulation, enhanced cost effectiveness and reduced anesthesiological risks.

Also, correction of most of these abnormalities and restoration of a normal uterine cavity is possible during OH with reported good outcome, similar to that achieved in patients with a normal hysteroscopy [(10,13)].

Despite the great advances in the assisted reproduction technologies, the delivery rate per oocyte retrieval was only 25% for ICSI and 27.41% for IVF [(14)].

There is evidence that performing hysteroscopy before IVF can increase the chance of pregnancy in women who had one or more failed IVF cycles [(15,16)].

This can be explained by its ability to treat uterine abnormalities and therefore restoring the normality of the uterine cavity [(7)].

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In addition to this, many studies have postulated many benefits that extend beyond treatment of intrauterine abnormalities such as:

First, irrigation of the cavity with saline since it mechanically removes harmful anti-adhesive glycoprotein molecules on the endometrial surface involved in endometrial receptivity [i.e. cyclooxygenase-2 (COX-2), mucin-l (MUC-l) and integrin aVb3] [(17)].

Secondly, the hysteroscopic diagnostic act itself may allow easier embryo transfer through studying the course and morphology of the cervical canal [(18)].

Also, many authors have concluded that mechanical manipulation of the endometrium may enhance receptivity by modulating the expression of gene encoding factors required for implantation, as glycodelin *A* laminin alpha-4, integrin alpha-6 and matrix metalloproteinase-l [(19)].

On the other hand, many studies showed that there was no difference in the live birth rate (LBR) and clinical pregnancy rate (CPR) [(20)].

Also, many studies did not recommend hysteroscopy as a routine before ART, claiming that the significance of treating unsuspected intra uterine pathologies are not yet fully proven [(21)].

AIM OF THE WORK

This study aims to assess the prevalence of abnormal hysteroscopic findings among infertile women undergoing ART at Ain Shams Maternity University Hospital over the period from January 2007 to January 2017.

PATIENTS AND METHODS

Study design:

A descriptive retrospective study.

Study site:

Early Cancer Detection Unit (**ECDU)**, Ain Shams University Maternity Hospital.

Study period:

The case reports from January 2007 to January 2017 were reviewed.

Study population:

Infertile couples planned for ART who were sent to ECDU for hysteroscopy.

Exclusion criteria:

- Failure to do complete hysteroscopic examination either due to stenotic cervix, pain, angulation, bleeding or other technical problems.
- Incomplete hysteroscopy reports.

Methods

I-The procedure

1) Instrumentation:

1. Hamou Endomat infusion pump, model 26331020 (Karl Storz, Tuttlingen, Germany) on infusion rate of 300 ml\min, pressure 120 mmHg, suction 0.2.
2. Fibroptic light: Xenon nova, model 20131520 manufactured by (Karl storz, Tuttlingen, Germany).
3. Hysteroscopic equipment (Karl storz, Tuttlingen, Germany) telescope: rigid, 30 Hamou II hysteroscopy, model 26157BT, with a Hopkins 2 lens system. The sheath has a 5 mm outer diameter, with an operative channel for instrument used, model 26163V with 2.9 mm rod lens.
4. Camera: Karl starz –endoscope, telecam DX pal model 20232020 by storz.
5. Monitor: TVCR Goldstar, model NO.KKV-9050, 50\60 HZ, AC 100-27OV to display and videotape the hysteroscopic events.

All hysteroscopy procedures were performed according to the ECDU protocol which compromise the following:

1. Oral consent from the patient.
2. Pre-operative examination
3. Hysteroscopic examination using the hysteroscopic equipment (Karl Storz, Tuttlingen, Germany) telescope was rigid, 30° Hamou II hysteroscope, with a Hopkins II lens system. The sheath has a 5mm outer diameter.

b) Technique (vaginoscopic approach):

The preocedure was performed in an outpatient setting, without anesthesia or dilatation, using the vaginoscopic approach.It is a "no touch"technique that is considered as the standard technique for outpatient hysteroscopy, it reduces the stimulus for pain generated from the cervix and the vagina by the use of speculum and tenaculum.

The vaginoscopic technique involves introducing the hysteroscope into the vagina to distend the vaginal vault with normal saline.

The patient was placed in the lithotomy position. Saline was used for uterine distention connected to the inflow channel on the sheath with intravenous tubing. The introduction of the scope was performed without placing a speculum. The sheath was flushed to remove the air before inserting the hysteroscopy and the sheath into the genital hiatus. The distention fluid was delivered using the endomat infusion at an infusion rate of 100mL/min, pressure 80 mmHg, suction 0.2 psi (pound per square inch).

The tip of the hysteroscope was positioned into the vagina.The scope was driven to the posterior fornix and slowly withdrawn backwards to identify the external cervical os, then the scope

was moved forward to internal os up to cervical canal and the uterine cavity.

Upon access to the uterine cavity, the tubal ostia were identified and the endometrial surface was systematically inspected.The cervical canal was then viewed in its entire length during withdrawal of the hysteroscope.

The procedure was defined as complete (complete examination of the uterine cavity including both tubal ostia) or failed when access into the uterine cavity was not possible.

Normal hysteroscopic appearance is seen in figure (fig.1)

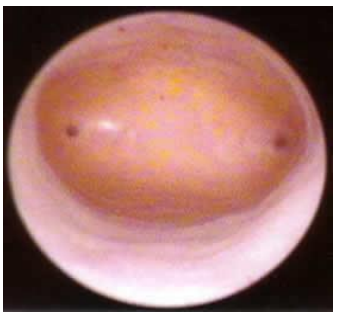

Fig. (1): Normal hysteroscopy.

II- The hysteroscopy report:

After the intervention, a detailed report was completed including the patient informations, diagnostic findings and treatment, with comment on the following finding:

A. The cervix: stenosis, long cervical canal.
B. The uterine cavity: small cavity, double cavity, single uterine horn, thick or atrophic endometrium, endometritis, intra uterine adhesions, endometrial polyps or myoma, uterine septum or fundal depression.
C. Tubal ostia: seen or not seen, peri-osteal fibrosis, reflux of discharge.

III-Reported findings

The following data were reported:

- The total number of reports reviewed.
- Number and percentage of completed reports.
- Number and percentage of incomplete reports.
- Abnormal findings, further classified according to the reported abnormalities.

These data were interpreted as in the following checklist:

Table (1): Data collection form

Case No	**Year**	**Complete procedure**		**Complete reports**		**Cervix**		**Cavity**		**Endometrium**		**mplications of procedure**
		No	**(%)**	**No**	**(%)**							
						Normal		Normal		Normal		Pain
						Polyp		Tubular		Thick		Bleeding
						Discharge		Small		Thin		
						Incontinence		Polyp		Polyp		
						Stenosis		Myoma		Atrophic		
								Adhesions		Endometritis		
								Ostia	Seen			
									Not seen			
								Double				
								Single horn				
								Septum				

IV-Data collection

All hysteroscopy reports in the period from January 2007 till January 2017 were reviewed for the patients who were referred to ECDU, Ain Shams Maternity Hospital.

Collected data was entered into PC and analyzed using version 18 of SPSS (Statistical Package for Social Science).

The reports were reviewed and the failed and incomplete procedures were excluded from the study and data of the complete reports were collected in the checklist for assessment of the prevalence of hysteroscopic abnormalities among women before ART.

Analysis of demographic data including: age, number of parity and duration of infertility was done. **The study was approved by the Ethics Board of Ain Shams University.**

RESULTS

During the period from January 2007 to January 2017, a total of 2725 hysteroscopy reports were reviewed.

Among the 2725 hysteroscopy reports that were reviewed , complete reports were 2652 (97.3%) , only 803 cases were normal , with a prevalence of 30.3%, while 1849 cases had abnormal hysteroscopic findings, with a prevalence of 69.7%.

The reported abnormalities were either vaginal (8 cases representing 0.3%), cervical (581cases representing 21.9%), uterine (819 cases representing 30.9%), endometrial (1251 cases, representing 47.2%) and tubal ostia abnormalities in 428 cases representing 16%.

I-Demographic patient characteristics including age, parity and period of infertility.

The mean age of patients was +/- 32 years old, and the mean period of infertility was +/_ 7.6 years. The great majority of patients had primary infertility with a percentage of 88.1% and only 12% had secondary infertility.

Table (2): Demographic characteristics

		N	Min	Max	Median	Mean	SD
age		2725	18.00	43.00	33.00	32.32	5.40
period of infertility		2725	1.00	34.00	7.00	7.63	4.65
			N		**%**		
Parity	0		2401		88.1		
	1		245		9.0		
	2		75		2.8		
	3		4		0.1		
	Total		2725		100		

Min: minimum, Max: maximum

II- Complete and failed procedures

Complete procedures were 2652 with a rate of 97.3%, and the procedure failed in 73 of cases with a rate of 2.7 %**) (Table 3).**

Procedure failure was attributed to many factors including cervical stenosis in 2% of cases (table 6), tight cervix in 3.5%, severe pain in 2% (table 13) and obliteration of the uterine cavity by intra uterine adhesions that was reported in 139 of cases with a rate of 5.2% (table 10).

Table (3): Number & prevalence of complete and failed procedures

Procedure	N	%
Complete	2652	97.3
Failed	73	2.7
Total	2725	100.0

III- Vaginal abnormalities

Longitudinal vaginal septum was detected in 8 cases, with a prevalence of 0.3%.

IV- Congenital cervical abnormalities

Congenital cervical abnormalities found were tight os, stenosis, patulous os, double cervices (table 4) and abnormalities of cervical canal such as narrow, angulated, short and patulous os (table 7).

Table (4): Congenital cervical abnormalities

Cervix	N	%
Stenosis	54	2.0
tight os	93	3.5
patulous os	19	0.7
Double	8	0.3

Table (5): Cervical canal abnormalities

Canal	N	%
Long	123	4.6
Short	5	0.2
Angulated	17	0.6
Narrow	1	0.04

V- Acquired cervical abnormalities

They included: adhesions, endocervical polyp and myoma, cervical ectopy, chronic cervicitis, nabothian cysts and endometriotic spots. The most common cervical abnormality was found to be long cervical canal.

Table (6): Acquired cervical anomalies:

Cervix	N	%
Polyp	95	3.6
Myoma	2	0.08
Adhesions	43	1.6
fibrotic/chronic cervicitis	23	0.9
Nabothian cyst/cysts	9	0.3
Ectopy	83	3.1
Mosaic	4	0.2
strawberry spots	1	0.04
endometriotic spots	1	0.04

VI - Congenital uterine abnormalities

Normal uterus was reported in 1833 cases (69%). Fig (2).

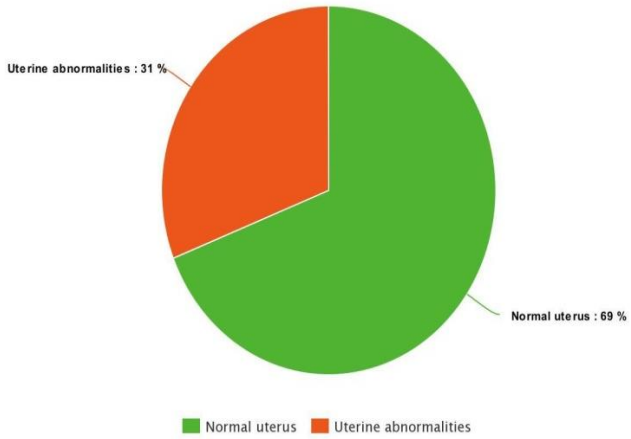

Fig. (2): Pie chart of the prevalence of total uterine abnormalities

The most prevalent congenital abnormality of the uterine cavity was the uterine septum with a rate of 6.8% and the least common abnormality was absent uterus (MRKS) that was reported in one case only (0.04%).

Table (7): Congenital uterine abnormalities:

Uterine cavity	N	%
septum vs bicornuate	184	6.9
arcuate vs subseptate	157	5.9
Didelyphys	11	0.4
Unicornuate	44	1.7
tubular cavity	19	0.7
large size	10	0.4
small size	44	1.7
sagging of uterine wall	28	1.1
absent uterus	1	0.04

VII-Acquired uterine abnormalities

Acquired uterine abnormalities found includes: submucous myoma, intrauterine adhesions, irregular cavity, fistula and mass (table 8).

Table (8): The acquired uterine abnormalities

Uterine cavity	N	%
Submucous myoma	130	4.9
Interstitial myoma	29	1.1
Intrauterine adhesions	139	5.2
Irregular cavity	18	0.7
Fistula	1	0.04
Mass	4	0.15

VIII- Endometrial abnormalities

The most common endometrial abnormality was found to be the endometrial polyp in 487 cases (18.4%), followed by thick endometrium in 344 cases (12.9%).

Table (9): Abnormal endometrial findings

Endometrium	N	%
Normal	1401	52.8
endometrial polyp	369	14
Thick	344	12.9
Polypoid	150	5.7
Thin	248	9.4
Endometritis	22	0.8

IX- Tubal ostia abnormalities

Unilateral tubal block was the most common abnormality in 272 cases with a percentage of 10.2% (table 10).

Table (10): The prevalence of tubal ostia abnormalities:

Ostia	N	%
Normal	2224	83.9
Unilateral block	272	10.2
Bilateral block	156	5.9
Total	2652	100.0

X-Complications of hysteroscopy

Only pain was reported as a complication in 1155 of cases (42.4%) which ranged from mild to moderate to severe (table 11).

Table (11): Hysteroscopy complications:

Pain	N	%
no pain	1570	57.6
Mild	798	29.3
mild to moderate	172	6.3
Moderate	110	4
moderate to severe	20	0.7
Severe	55	2.0
Total	2725	100.0

DISCUSSION

Hysteroscopy was often referred to as the gold standard for diagnosing and treating intra uterine pathologies that affect fertility and the reproductive outcome [(22)].

To date, hysteroscopy is recommended for two main indications: to verify the suspected intra uterine lesion and to assess the cavity after recurrent IVF/ICSI failures [(23)].

Many studies offered evidence that hysteroscopy will result in encouraging outcome in cases of recurrent implantation failures [(24)].

However, its routine use before the first IVF/ICSI trial is still debated and the decision needs further studies given the high cost of ART [(23)].

This study aimed to assess the prevalence of hysteroscopic abnormalities in women undergoing ART.

This study included hysteroscopy reports of 2725 cases, of which 2652 reports were complete, and this population is larger than many previous studies as Fatemi et al. [25] (678 cases), **El mazny**, [18] (152 cases).

In this study, the procedure failed in 73 patients with a percentage of 2.7% which is higher than the prevalence reported by **Fatemi et al.** [25] (1.2%) and lower than the percentage reported by **El mazny** [18] **(**4.6%).

Rate of cervical stenosis was 2% which is close to the percentage reported by **El mazny** [18] (4 cases representing a percentage of 2.8%), but is inconsistent with the percentage reported by Rama ***Raju et al.*** [26] (31.57%).

Overall hysteroscopic abnormalities were found in 1849 patients, which represents a prevalence of 69.7%, and this is much higher than the prevalence reported in other studies such as **El mazny** [18] (48 cases ,33.1%), ***Shawki et al.*** [27] (35 cases, 33.3%); ***Rama et al.*** [26] (37.25%).

Completely normal findings were seen in 803 reports with a prevalence rate of 30.3% which is lower than the prevalence rate reported in other studies such as ***Oliveira et al.*** [10] (54%), **Demirol and Gurgan** [28] (73%), **Rama et al.** [26] (62.75%), ***Fatemi et al***. [25] (87.9%), ***Shawki et al.*** [27] (66.6and this can be explained that this current study took in account all hysteroscopic abnormalities even if minor and of no clinical significance such as arcuate uterus and long cervical canal, the negative impact of which on reproductive outcome cannot be proved.

Another explanation is that many of the previous studies included infertile women with recurrent implantation failures

The overal prevalence of cervical abnormalities in this study is 21.9% (581 cases), which is higher than other studies; ***El mazny*** [18]**,** **(**11 cases, 7.6%).

Regarding cervical abnormalities, the most common abnormality in this study was long cervical canal in 123 reports (4.6%) followed by tight cervical os in 93 (3.4%), and endocervical polyp in 91 of cases (3.4%)which is high in comparison with El mazny, [18] (2.1%), followed by cervical ectopy with a percentage of 3.1% and endocervical adhesions with a percentage of 1.6% and endocervicitis in 0.8% only which is different than the prevalence reported by **El mazny** [18] (2.8%).

This study showed that uterine abnormalities were found in 1306 cases (49.2%), and that is similar to other studies; Oliveira et al. [10] (46%), ***Doldi et al.*** [11] (40%), but is in consistent with **El mazny** [18] **(**16 cases, 11%), **Shawki et al.** [27] **(**9 cases, 8.6%**)**.

In this study, endometrial polyp was the most common uterine abnormality (in 487 cases, 18.4%) which is the same conclusion of many studies as, **Shawki *et al.*** [27] (11 cases, 32.4%), **Rama *et al.*** [26] (32 cases, 33.68%), Oliveira et al. [10] (18%), **Doldi *et al***. [11] (65%,), El mazny, [18] (8 cases, 5.5%).

Our study have shown that the second most common reported abnormal uterine finding was uterine septum in (184 cases, 6.9%) which is lower than the prevalence reported by ***Rama et al***. [26] (8.42%), but higher than that of other studies as ***Fatemi et al.*** [25] (1.9%), El mazny [18] (1case, 0.7%), ***Shawki et al.*** [27] (1case,2.8%).

Arcuate uterus comes in the third place in 157 cases with a rate of 5.9%, followed by intra uterine adhesions in 139 (5.2%) which is the most common abnormality in many studies as ***Fatemi et al.*** [25] ***(2.2%), Rama Raju et al.*** [26] ***(12.63%), El mazny,*** [18] ***(4.1%), Oliveira et al.*** [10] ***(11%), Shawki et al.*** [27] ***(11.4%).***

In this study, submucous myoma was found in 130 cases with 4.9% prevalence which is close to **El mazny** [18] (6 cases, 4.1%), but is lower than the prevalence of Shawki et al. [27] (4 cases, 11.4%) and higher than the prevalence of other studies as ***Fatemi et al***. [25] (6 cases, 1%), ***Rama et al.*** [26] (1 case, 1.05%).

Our results showed that small hypoplastic uterine cavity was found in 44 cases with a percentage of 1.7%, which is close to the prevalence of El mazny, [18] (1.4%).

Our study showed that among the endometrial abnormalities, thick endometrium was the most frequently reported abnormality in 344 cases (12.9%) that is similar to ***Rama et al***. [26] (12 cases, 12.63%) and is more frequently encountered than other studies as **El mazny** [18] (4 cases, 2.8%), ***Shawki et al***. [27] (3 cases, 8.5%).

Thick endometrium is more common in the study performed by ***Doldi et al***. [11] (17%) than this study.

In this study, on the other hand, thin atrophic endometrium was reported in 248 cases (9.3%) which is higher than the prevalence reported by ***Shawki et al***. [27] (2 cases, 5.7%)**.**

In our study, endometrium was polypoid in 150 reports with a prevalence of 5.6%, which is higher than that reported by **El mazny** [18] 4 (2.8%) but is lower than that of ***Shawki et al.*** [27] (7 cases, 20%).

Our study concluded that chronic endometritis were found in 22 reports with a prevalence of 0.8%, which is lower than **El mazny** [18] (2.1%), Shawki et al. [27] (2 cases, 5.7%), ***Oliveira et al***. [10] (13%).

In this study, tubal ostia were visible in 2224 reports (83.9%), there were unilateral block

in 272(10.2%), and bilateral block in 156 (5.9%). In other studies, the prevalence of tubal block is 1.4% **El mazny** [18]

The higher incidence of some hysteroscopic abnormalities in some studies compared to this study can be explained that these studies included infertile patients with recurrent implantation failures [10,26,27].

CONCLUSION

The high incidence of hysteroscopic abnormalities in this study (69.7%) supports the routine use of hysteroscopy in the infertility work up.

Since it increases the detection rate of abnormalities in asymptomatic infertile women, therefore it hypothetically will result in improved reproductive outcome and clinical pregnancy rates after ART.

Also, the ability of hysteroscopy to diagnose and treat intrauterine pathologies in the same setting makes it superior to other diagnostic modalities.

The use of OH in outpatient setting makes it patient friendly with minimal discomfort to the patient and early ambulation after the procedure.

However, interventional (randomized controlled trials) rather than descriptive studies are needed to verify the positive effect of detecting and treating hysteroscopic abnormalities on improving ART outcome.

RECOMMENDATIONS

There is still no sufficient clinical evidence to include hysteroscopy as a routine procedure in all cases seeking fertility.

Therefore, interventional studies are needed to assess:

1) Hysteroscopy versus no hysteroscopy effect on reproductive outcome :

a) Before the first trial of ART.

b) In cases of recurrent implantation failure (RIF).

2) The positive effect of diagnosing and treating subtile hysteroscopic abnormalities on reproductive outcome.

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