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Original Research Article

Hysteroscopic evaluation of endometrial cavity in cases of unexplained infertility patients less than 35 years old

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ABSTRACT

Background: The incidence of unexplained infertility about 22-28% of all infertile couples. Several strategies have been implemented to improve the outcome of infertility treatment before shifting to ART. Management of unexplained infertility depends on patients age, ovarian reserve and period of infertility, management starts from simple to more complicated protocols to achieve pregnancy up to assisted reproduction techniques. Hysteroscopy provides diagnostic and therapeutic approach in such group of patients.

Methods: Retrospective analysis of the reproductive outcome in young patients with unexplained infertility was conducted to evaluate such treatment protocol 163 patients included in the study.

Results: Our results showed that around 29.4% of patients had intrauterine abnormalities which varies from endometrial polyps to adhesions and one case found to have cervical stenosis, around 12.17% had endometritis. Patient were left for expectant management for 6 months, 22.7% pregnancy rate following hysteroscopy without any other intervention, patients who had polypectomy got 28% pregnancy rate while patients with apparent normal endometrial cavity got 23.76% pregnancy rate.

Conclusions: Hysteroscopy could be an alternative treatment option in young patients with unexplained infertility because of its diagnostic and therapeutic effect.

Keywords: Hysteroscopy, Endometrium, Infertility

INTRODUCTION

Unexplained infertility defined as inability to achieve pregnancy after unprotected intercourse for one year in absence of justifiable reasons either male factors as sperm parameters or female factors as ovulation problems, tubal factors, uterine factors, and immune factors. The incidence of unexplained infertility about 22-28% of all infertile couples.^{1,2}

Several strategies have been implemented to improve the outcome of infertility treatment before shifting to ART. The treatment of unexplained infertility is empirical and many different protocols have been used, like expectant management, ovulation stimulation with either

clomiphene citrate, aromatase inhibitors, or gonadotrophins, also tubal flushing, intrauterine insemination, and ART were suggested.³ Ideally the treatment protocols start from simple to more invasive and more sophisticated. It is well known that the prognosis for spontaneous pregnancy in such couples is better than in those with diagnosed causes of infertility especially in young patients. Because of the decline in fertility and the increased time to conception that occurs after the age of 35 which may be attributed to decreased ovarian reserve and increased incidence of aneuploidy the roll of expected management and to proceed from simple to more complicated ways of treatment is not applicable.⁴ However, in couples with unexplained infertility the existing treatments such as empirical clomifene and

unstimulated intrauterine insemination are unlikely to offer superior live birth rates compared with expectant management, so the best way is to proceed to gonadotropins stimulated intrauterine insemination for 3 to 6 cycles before shifting to ART especially in patients more than 35 years old or with decreased ovarian reserve.⁵ In patients less than 35 years old the effectiveness of IVF in unexplained infertility remains unproven,⁶ which give a chance of spending more time to try other ways to achieve pregnancy naturally in order to avoid the ART and its possible complications as ovarian hyperstimulation, multiple pregnancy, drug and surgical complications that is increased in such young aged patients, this is beside the cost, time wasting, and psychological burden of ART cycles. From this point of view and in young patients with unexplained infertility and apparently normal infertility workup, laparoscopy and hysteroscopy had been good alternative to ART in those patients. laparoscopy has been suggested as a step to preclude the existence of peri-tubal adhesions and endometriosis in those cases. and it was found that in women without a previous history suggestive of tubal disease and who have a normal HSG, the probability of clinically relevant tubal disease or endometriosis is very low and that laparoscopy does not seem justified or cost effective, and although in minority of cases, laparoscopy might show minimal or mild endometriosis or peri-tubal adhesions, surgery and or medical treatment has not been proven to improve pregnancy rate.⁷ With its invasiveness and the relatively low contribution of diagnostic laparoscopy to the decision-making process of treating patients with a normal HSG, its value in patients with unexplained infertility had been diminished.⁸ Although, hysterosalpingography can be used to evaluate the mechanical tubal function but it provides less information about the uterine cavity (numerous false-positives and false-negatives). And in spite that the pelvic ultrasound used to be helpful for diagnosing interstitial anomalies in the uterus, yet it can miss some of the uterine cavity abnormalities that can affect the implantation and results in inability to conceive. The less invasiveness and the lower cost of hysteroscopy in relation to laparoscopy gave it priority in the group of patients diagnosed with unexplained infertility. Hysteroscopy, allows direct visualization of uterine cavity, endometrial lining, tubal ostia and cervical canal. Beside its diagnostic value, the therapeutic work had been proved to aid the success of treatment modalities of infertility, and this is not attributed to surgical procedure only but to direct visualisation of cavity beside other procedures as cervical dilation in cases of cervical stenosis, scratching effect on the endometrium in case of tissue biopsy which proved its effect in such cases. fluid flow also has effect on tubes that is equal to tubal flushing but under visualisation.^{9,10}

METHODS

Study design

Retrospective cohort study conducted in large private fertility centre in Abu Dhabi, UAE, in period between

September 2013 to the end of December 2015. The study evaluated the outcome of hysteroscopy in patients diagnosed with unexplained infertility. The evaluation included primary and secondary outcomes The primary outcome was including the finding of hysteroscopy and the surgical procedures done. While secondary outcome included the pregnancy rate, miscarriage and live birth rate.

Patients included in our study were infertile patients whether primary or secondary infertility, our patients had been passed through all fertility work up and all revealed normal.

Inclusion criteria

Patients aged 35 years old or less, primary or secondary infertility, had passed through the expectant period for 6 months to 2 years were included in the study.

Exclusion criteria

Patients more than 35 years old, patients with recurrent miscarriages, patients went through ART trials before, patients with low ovarian reserve, patients with a history of genetic disorders in the family, history of chromosomal abnormalities in both couples and patients with very long period of infertility were excluded from the study.

Patients had to be counselled and consented about the outcome, the benefits and possible complications from surgical and anaesthesia side. patients were guided not to have any fertility treatment for the next 6 months.

Presurgical check-up done in all patients included and scheduling to diagnostic hysteroscopy with or without surgical interference in cases that mandates intervention. The procedure done on the first day after her last day of menstruation to ensure absence of pregnancy.

On the day of surgery, patients placed comfortably on the table then had light anaesthesia, patient positioned in the dorsal lithotomy, scrubbed and covered, urinary bladder evacuated, vagina sterilised using diluted povidone iodine solution, Simms speculum inserted in the posterior vaginal wall, cervix was held by forceps, if the patient did not have vaginal delivery before we will proceed with minimal cervical dilation otherwise we proceeded with hysteroscopy directly as the water jet will provide the needed dilation, we used rigid scope of 3-5 mm calibre with ability to use manipulators, scissors, diathermy and other different instruments that helped in case of operative hysteroscopy. The procedure started with visualisation of the cervical canal, gently introducing the scope to visualize the lower uterine part then the fundus and lateral wall inspection, finally inspecting the ostia. if any polyp noticed then polypectomy and biopsy was done, if any adhesion detected lysis to be done. If no problem noticed endometrial scratching and the tissue obtained to be sent for histopathology.

After finishing the procedure, we insured fluid drainage from uterus, secure and ensure haemostasis, patient started on broad spectrum antibiotic for 1 week and simple analgesia to be given if any pain.

Patients were allowed for 6 months at least as expectant period then to evaluate pregnancy rate and outcome. Pregnancy diagnosed by visualisation of intrauterine gestational sac with foetal pole and cardiac activity seen and recorded.

Statistical analysis

All data was on excel sheets, data will be presented as average, means, rate. Data will be displayed in tables.

RESULTS

163 patients were included in the study; 98 (60.1%) patients had primary infertility while patients with secondary infertility were 65 (39.9%) patients. mean age of patients included was 30 ± 26 with a range from 24 to 35 years old, mean body mass index (BMI) was 28 ± 37 with a range from 24 to 31. The mean years of infertility were 4 ± 15 ranging from 1 to 8 years

On hysteroscopy we found that 115 (70.6%) case with no abnormality detected and uterine cavity and endometrial lining appears normal 71 (61.7%) patients with primary infertility and 44 (38.3%) with secondary infertility, 48 (29.4%) patients had abnormalities, 27 (56.3%) of them were with primary infertility and 21 (43.8%) were with secondary infertility.

One case only had cervical stenosis (0.61%) she was a case of primary infertility.

The 39 cases with small endometrial polyps (23.9%) some of the polyps were located very near to the ostia in 27 cases (69.2%), or on the lateral wall near to lower uterine segment in 12 cases (30.8%). All patients had polypectomy. The 13 (33.3%) cases were with secondary infertility and 26 (66.7%) cases only were with primary infertility.

Eight cases founded to have thin adhesions specially near the fundus at lateral wall (20.5%), all of them were with secondary infertility.

Regarding the results of tissue biopsy of the apparently normal cases 101 (87.83%) had normal proliferative endometrium and 14 (12.17%) cases showed endometritis 13 of them were with secondary infertility and one only with primary infertility

After 6 months of expectant protocol: out of the 101 cases with normal cavity 24 (23.76%) patients get pregnant and out of the 39 patients who had polypectomy 11 (28%) got pregnant, out of the 8 patients who had adhesions 1 (12.5%) got pregnant. Patient with cervical stenosis got

pregnant (100%). Patients with endometritis had no pregnancy. total pregnancies were 37 (22.7%) pregnancies in the next 6 months. No twins and no miscarriages detected.

No complication reported regarding the surgical or anaesthesia interventions.

Table 1: Demographic criteria of patients.

Variables	Range or no.	Mean
Age (Years)	24-35	30 ± 26
BMI	24-31	28 ± 37
Years of infertility	1-8	4 ± 15
Primary infertility	98	(60.1%)
Secondary infertility	65	(39.9%)

Table 2: Hysteroscopic finding (primary outcome).

Variables	Total (%)	Primary infertility (%)	Secondary infertility (%)
Normal	115 (70.6)	71 (61.7)	44 (38.3)
Abnormal	48 (29.4)	27 (56.3)	21 (43.7)

Table 3: Types of abnormalities (primary outcome).

Variables	Total (%)	Primary infertility (%)	Secondary infertility (%)
Endometrial polyp	39 (81.25)	26 (66.7)	13 (33.3)
Intrauterine adhesions	8 (16.7)	0	8 (100)
Cervical stenosis	1 (2.1)	1 (100)	0
Chronic endometritis	14 (12.17)	1 (7.1)	13 (92.9)

Table 4: Pregnancy rate (secondary outcome).

Variables	Total (%)	Primary infertility (%)	Secondary infertility (%)
All	37 (22.7)	17 (45.9)	20 (54.1)
Normal cavity	24 (24.76)	11 (45.8)	13 (54.2)
Polypectomy	11 (28.2)	5 (45.5)	6 (54.5)
Cervical stenosis	1 (100)	1	-
Adhesions	1 (12.5)	0	1
Chronic endometritis	0	0	0

DISCUSSION

Management of patients with unexplained infertility depends on the age of patients and ovarian reserve to great extent but to lesser extent the period of infertility could

play role in such situation. Patients more than 35 years old face the problem of decreased ovarian reserve and increased incidence of aneuploidy, those patients when diagnosed with infertility have to start active management without delay to increase their chances of success and obtaining healthy pregnancy that ends with normal livebirths. On the other hand, young patients with good ovarian reserve may opt for less complicated ways of management aiming to have natural pregnancy supported by the fact that they have good prognosis with the expectant management according to different studies. All patients with the diagnosis of unexplained infertility had hysterosalpingography and the results came normal in this category of patients but with the fact that the accuracy of HSG in evaluating the uterine cavity and endometrial lining had mistaken in 30% came the importance of evaluating the uterine cavity by hysteroscopy. In our study we found that abnormality in the uterine cavity were 29,4% in spite of normal hysterosalpingography which is in agreement of study by Benkaddour et al who found uterine cavity abnormalities in 40% of cases and recommended to have hysteroscopy before going for ART.¹¹ In other hand, Niknejadi et al, Ayida et al and La sale et al found that no difference in the diagnostic accuracy between the sono-hystero-graphy and hysteroscopy but with absence of therapeutic effect and immediate intervention of hysteroscopy.¹²⁻¹⁴ A study done by Bozdog et al found that hysteroscopy before IVF increased the pregnancy rate in patients had surgical correction of the abnormality found.¹⁵ In our study we found that the incidence of abnormalities on hysteroscopic evaluation was more in patients with secondary infertility especially the adhesions in this group of patients which might be related to uterine interventions such as curettage or even caesarean or insertion of intrauterine devices, while the presence of intrauterine polyps was found more in patients with primary infertility which might be related to more exposure to ovulation induction, PCOS, and or obesity. The other finding of the apparently normal uterine cavity that can't be diagnosed with HSG was endometritis which were more prevalent in patients with secondary infertility, this is in agreement with study done by Mekled et al who found the prevalence of endometritis in patients with unexplained infertility by about 15% and in our study, it was around 12%.¹⁶

In our study no complications regarding anaesthesia or surgical procedures reported from any patients despite using rigid hysteroscopy, we did not get any complain from patients in the post operative period regarding pain, discomfort, or infection. This is in agreement with different studies done by clinicians in different clinics. Surgical intervention was done on the same sitting and bleeding or pain complication noticed in the post operative period.

Patients with apparently normal cavity had endometrial biopsy that could be considered as scratching so they get the benefit of scratching under vision which could be a

separate procedure to enhance the fertility as per Wadhwa et al 2018.¹⁷

Our patients were entitled for 6 months expectant management without any interference to follow up pregnancy outcome, we got 37 pregnancies that ended all with live births, and no miscarriages and no twins, the pregnancy rate of 22,7% was in agreement with study done by Seyam et al who got pregnancy rate in patients underwent hysteroscopy by (28%) more than control group without hysteroscopy who had pregnancy rate by about 21%.¹⁸ Which may be due to correction of uterine cavity abnormalities or due to the effect of scratching in cases of normal uterine cavity. We noted that the pregnancy rate was more in patients with secondary infertility 20 out of 65 (30.8%) versus cases with primary infertility 17 out of 98 (17.5%) as in primary infertility the embryo quality was never tested in this group of patients which may be contributed to their infertility situation. Pregnancies obtained in patients with apparently normal uterine cavity may be also attributed to the tubal flushing effect of hysteroscopy as tubal flushing considered as one of the empirical ways of treatment in cases of unexplained infertility.^{19,20}

We got 37 pregnancy and 37 live births without the need to pass through the journey of ART with its coast and its physical, psychological burdens and risks.

CONCLUSION

Hysteroscopy could be a good alternative to ART in young patients with unexplained infertility as long as the ovarian reserve allow it. the value of hysteroscopy is not only diagnostic but therapeutic also. The number of the patients included in our study may be a limitation factor that may need a wide scale of patients to be involved.

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