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Effect of office hysteroscopy on in-vitro fertilization in a fertility centre in Abuja, Nigeria: A prospective study

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Abstract

Background: Fifteen percent of married couples worldwide experience infertility despite unprotected intercourse and approximately 50% of infertile women has uterine pathologies. The success of in vitro fertilization can be assessed using various measures including pregnancy rate, implantation rate and the most acceptable, live birth rate. Various modalities have been employed to investigate endometrial pathologies responsible for infertility.
Objectives: To determine and compare the incidence, and pathology in infertile women seen on hysteroscopy and TVS, and the effect on IVF success
Methods: This study had 41 participants, 24 had previous Assisted Reproductive Therapy while 17 had not undergone the process. The 41 participants included those that had both TVS and office hysteroscopy. Abnormal findings were recorded and management carried out based on the abnormality detected.
Result: Forty-one infertile women aged 26 to 45 years were included in the study. About fifty-eight percent had history of IVF attempts, while 41.46% had no history of IVF. TVS and hysteroscopic examinations were performed on all the patients. TVS findings indicated 26.83% normal findings and 73.17% abnormal pelvic findings. Hysteroscopic findings showed 90.25% patients had abnormal uterine findings
Conclusion: This study shows that Hysteroscopy is more sensitive and useful in the diagnosis and treatment of infertility than TVS. Diagnostic measures for hysteroscopic detection of uterine lesions revealed a sensitivity of 78.95% (95% CI 62.68- 90.45), 100% specificity and positive predictive value, with a Negative predictive value of 33.33% (95% CI 21.27 – 48.07) and diagnostic accuracy of 80.95% (95% CI 65.88 – 91.40). These are in keeping with other studies.

Introduction

Fifteen percent of married couples worldwide experience infertility despite unprotected intercourse[1] and approximately 50% of infertile women have uterine pathologies.[2-4] In the presence of endometrial pathologies, structural and functional impairments may occur affecting fertility.[5] In Vitro fertilization (IVF) has revolutionized the treatment of infertility, though at a high cost, and there is a need to ensure success to reduce the cost of treatment and improve patient satisfaction. The success of in vitro fertilization can be assessed using various measures including pregnancy rate, implantation rate and the most acceptable, live birth rate. The role of ambulatory diagnostic hysteroscopy (office hysteroscopy) remains controversial as its role in ensuring IVF success is still open to investigation

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and debate.[6] Uterine abnormalities including endometrial polyps, uterine fibroids, endometrial hyperplasia/ hypoplasia, intrauterine adhesions and endometrial cancer, can affect the outcome of IVF. Various modalities have been employed to investigate endometrial pathologies responsible for infertility. These modalities include hysteroscopy, saline infusion sonography, hysterosalpingography, transvaginal ultrasound scan (TVS) and hystero-contrast sonography. The use of office hysteroscopy in the management of infertile women, needs to be further justified in the face of cheaper, less invasive modalities like Transvaginal scan (TVS) and hysterosalpingogram (HSG).

This study aims at determining the incidence of abnormal uterine findings in infertile women, determine the types of pathology seen on hysteroscopy compared to TVS, and to determine the effect such findings have on IVF success.

Methodology

Study setting: The study was conducted at the IVF unit of Nisa Premier Hospital, Jabi, Abuja, Nigeria. Nisa Premier Hospital is one of the foremost private health facility offering Assisted Reproductive Technology and infertility care among other healthcare services. It is located in the Federal Capital Territory, Abuja and conducts over 400 IVF cycles annually. Clients for IVF are all required to have a TVS before the procedure while some have office hysteroscopy performed as well.

Study design and protocol

Study participants: This study was a prospective longitudinal study conducted among all women presenting at the IVF clinic in the 12 month period between November 2020 and October 2021. Clients recruited into the study met the following criteria: age between 18 and 45 years, no history of previously known uterine anomaly and no severe medical or surgical condition as to prevent hysteroscopy or IVF. Those excluded were clients outside the 18 to 45 year age bracket, those with previously known uterine anomalies and those with severe medical or surgical conditions.

An informed consent was obtained from the clients for the study. Each client was assigned a page on the medicplus hospital computer software application, where her detailed history as well as general and systemic examination findings were recorded. Clients included those that had both TVS and office hysteroscopy. Abnormal findings were recorded and further management carried out based on the abnormality detected. Then, ovarian stimulation, IVF and embryo transfer were performed, followed by luteal support. After which a Pregnancy test and sonographic monitoring of the pregnancy were carried out. A 3-dimensional Transvaginal sonography (TVS) was performed in conjunction with an experienced operator, using a GE Voluson P8 Ultrasound machine. The endometrial stripe was assessed in the midline sagittal plane and the point of maximum thickness of the stripe (endometrial thickness) measured on a frozen image at 1.5x magnification. Any focal lesion seen giving an impression of an endometrial anomaly like a polyp, submucous fibroid, intramural fibroid, or suspicions of hyperplasia were noted.

An Office Hysteroscopy was performed with an experienced operator (with a certificate of advanced gynaecological laparoscopy surgery from the National centre for minimal access surgery, institute of medical sciences, Havana, Cuba), in the endoscopic office on an outpatient basis and in the post menstrual phase. The patient emptied her bladder and was placed in lithotomy position. Following proper cleaning and draping, the Meyona (ART/IVF supplies) 2.9mm Betttochi 30º hysteroscope was gently introduced into the vagina. No pharmacological preparations nor local anesthetics was administered before the examination as the technique avoids the need to introduce a speculum nor a tenaculum. The hysteroscope with the distension media (normal saline) was gently introduced through the vagina to the cervical canal, the internal os, and then into the uterine cavity. Upon entering the uterine cavity, a systematic inspection was performed, visualizing the uterine cornu, tubal ostia, uterine fundus, and lateral, anterior and posterior uterine walls.

Hysteroscopic findings were documented on the client's page on the medicplus hospital computer software application. The appearance of the cervical canal and endometrium, and the presence, size, and location of structural anomalies were recorded. In cases with positive findings for intrauterine lesions, surgical management was instituted.

Ovarian hyperstimulation was achieved using the standard short agonist or antagonist protocols or the

long protocol. Subcutaneous Buserelin 0.5ml was the Gonadotropin releasing hormone (GnRH) agonist used. Subcutaneous Cetrotide was the Gonadotropin releasing hormone (GnRH) antagonist used. The gonadotropin used for this study was Menopur (a highly purified human menopausal gonadotropin) and its dose was individualized based on the client's age, baseline day 3 FSH level, antral follicle count and previous response to controlled ovarian hyperstimulation. Human chorionic gonadotropin (HCG) in a dose of 10,000 IU was given as ovulation trigger when at least three follicles attained 18 mm diameter or more in size. Subcutaneous Buserelin 0.5ml was used as trigger for those on antagonist protocol. The Oocytes were retrieved 36 hours after HCG injection under transvaginal ultrasound guidance.

Fertilization of the oocytes and incubation of the embryos were performed by the embryologist using the standard IVF techniques with embryo transfer on day 5 of incubation under ultrasound guidance. This was followed immediately by administration of luteal support according to hospital protocol. The pregnancy test was done 2 weeks after embryo transfer to confirm chemical pregnancy using a serum pregnancy kit while clinical pregnancy was diagnosed three weeks later via abdominal ultrasound for sonographic evidence of intrauterine pregnancy with fetal cardiac activity. The results were recorded.

Statistical analysis: Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 24 (IBM). Diagnostic test was used to find out the diagnostic accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of office hysteroscopy with respect to TVS. Categorical variables were presented in numbers and percentage. A p value of <0.05 was considered statistically significant.

Ethical consideration: This study was approved by the Ethics and Research Committee. The principles of ethics were adhered to – Confidentiality, Justice and Equity, and Beneficence. Clients were not burdened with any extra cost as a result of this study because the procedures were already outlined as part of their management plan.

Results

Table 1: Patients characteristics

Variables	Previous ART	No Previous ART	P value
Number (percentage)	24 (58.53)	17 (41.46)	
Age (Range/mean±SD)	26 -45 (38.95±4.95)	30 -45 (39.11±5.43)	p>0.05
Duration of Infertility(yrs)	1-14 (6.70±4.05)	1-19 (5.00±4.98)	p>0.05
Primary infertility	18 (54.55)	15 (45.45)	
Secondary infertility	6 (75)	2(25)	

ART= Assisted reproduction technique. Values in bracket represent percentages

Table 2: Age distribution

Age Range	Frequency	Mean age	Duration of infertility (Range/mean±SD)
26 – 30	4	28.43±2.14	2 - 4 (3.00±1.15)
31 – 35	4	32.50±1.56	3 -10 (5.75±2.98)
36 – 40	14	38.22±2.29	1-15 (5.21±4.22)
41 – 45	19	42.86±2.19	1-19 (6.94±5.44)
Summary	41	39.20 ± 5.09	1 -19 (5.90±4.60)

Table 3: Transvaginal scan findings

S/No.	Findings	Cases	Previous IVF	No Previous IVI
1.	Intramural myoma	23	14	9
2.	Adenomyosis +intramural myoma	2	1	1
3.	Submucous myoma + intramural myoma	2	1	1
4.	PCOS+ intramural myoma	1	1	0
5.	Ovarian cyst	2	0	2
6.	Normal findings	11	9	2

Table 4: Hysteroscopic findings

S/N	Findings	Cases	Previous IVF	No Previous IVF
1.	Cervical stenosis	4	1	3
2.	Submucous myoma	10	6	4
3.	Cervical incompetence	3	3	0
4.	Uterine adhesion	12	8	4
5.	Atrophic endometrium	1	1	0
6.	Endometrial polyp	2	1	1
7.	Intramural myoma	2	1	1
8.	Uterine septum	2	0	2
9.	Endometrial fluid	1	0	1
10.	Normal findings	4	3	1

Table 5: Intrauterine findings in women with or without previous ART using hysteroscopy and TVS

Variables	TVS	Hysteroscopy
Patients with previous ART and normal finding	9	3
Patients with no previous ART and norma finding	2	1 (p=0.999)
Patients with previous ART and abnormal findings	17	21 (p=0.646)
Patients with no previous ART and abnormal findings	18	17 (p=0.906)
Total normal findings	11	4
Total abnormal findings	32	38 (p<0.05)
Number of patients with normal findings	11	4
Number of patients with abnormal finding	30	37 (p<0.0042)

Table 6: Intervention approaches and outcomes

Intervention	Cases	Outcomes/USS report					
		Previous ART			No previous ART		
		No of case	Positive	Negative	No of case	Positive	Negative
Cervical dilatatio	4	1	0	1	3	0	3
Hysteroscopic myomectomy	7	3	2	2	4	1	3
Open myomector	3	1	0	1	2	1	1
Endometrial scratch	4	4	2	2	0	0	0
Hysteroscopic Polypectomy	2	1	1	0	1	1	0
Adhesiolysis	12	8	5	3	4	1	3
Abdominal cerclage	1	1	1	0	0	0	0
Metroplasty	2	0	0	0	2	2	0
Nil	6	5	3	2	1	1	0
Total	41	24	14(58.33)	11(45.83)	17	7(41.17)	10(58.82) (p<0.0036)

Figures in bracket represent percentages

Table 7: Measurements in detection of intrauterine lesions

Variable	Value	95% CI
Sensitivity	78.95%	62.68-90.45
Specificity	100.0%	39.76-100.00
Positive Predictive value (PPV	100.0%	
Negative Predictive value (NP\	33.33%	21.27-48.07
Diagnostic accuracy	80.95%	65.88-91.40
Positive likelihood ratio	-	
Negative likelihood ratio	0.21	0.11-0.39

In total, 41 infertile women aged 26 to 45 years with mean age 39.20±5.09 years were included in the study. Twenty-four (58.33%) patients (mean age, 38.95±4.95 years) had history of IVF attempts with 6.70±4.05 years as mean duration of infertility, while 17 (41.46%) patients (mean age, 39.11±5.43) with 5.00±4.98 years duration of infertility had no history of IVF (Table 1). There was no statistical difference (p>0.05) in ages and duration of infertility between patients with previous history of IVF attempts and patients without IVF attempts.

Four of them were of the age range 26-30 years and nineteen patients were within the age range of 41-45 years, while 14 patients were between 36-40 years of age.

TVS findings indicated that 11 (26.83%) patients had normal findings, while 30 (73.17%) patients had abnormal pelvic findings which included intramural myoma, adenomyosis, submucous myoma, PCOS, and ovarian cyst. Out of this number, 17 patients with abnormal findings had a history of previous IVF attempts, while 13 patients had no history of previous IVF attempts.

Hysteroscopic findings on the same patients showed that 4(9.75%) patients had normal uterine findings and 37 (90.25%) patients had abnormal uterine findings which included cervical stenosis, submucous myoma, cervical incompetence, uterine adhesion, atrophic endometrium, endometrial polyp, intramural myoma, uterine septum, and endometrial fluid. Among the patients with abnormal findings were 20 patients with history of failed IVF attempts, while 17 patients had no history of IVF attempts. The most common intrauterine abnormality detected via office hysteroscopy was the presence of uterine adhesion 12/41 [29.27%]). Submucuous myomas were diagnosed in 10 patients (24.39%) and cervical stenosis in 4 (9.76%).

In both TVS and hysteroscopy, the total percentage of abnormal intrauterine findings was higher in women with a history of repeated IVF failures in comparison with those with no previous IVF attempts. The results further revealed that the numbers of abnormal intrauterine findings recorded were higher in hysteroscopy than in TVS. In hysteroscopy, 37 patients were detected with 38 abnormal findings, while TVS showed that 30 patients only had 35 abnormal uterine findings. The number of patients with normal intrauterine findings was 11 in TVS and 4 in hysteroscopy respectively. There was a significant statistical difference (p<0.05) in the number of findings (normal/abnormal) and number of patients.

The intervention approaches results showed that adhesiolysis had a higher pregnancy test success rate (5/8) in patients with previous history of IVF and (1/4) in patients without history of IVF attempt.

This was followed by hysteroscopic myomectomy with 2/3 rate in patients with previous IVF attempt and 1/4 in patients without IVF attempt history. The outcomes following various intervention approaches revealed that a positive outcome rate of 14/24(58.33%) confirmed from USS report were recorded in patients with previous history of IVF attempts as against 7/17(41.17%) in patients without history of IVF attempt. Significant statistical difference ($p<0.05$) was also recorded when total outcomes from different intervention approaches in patients with previous history of IVF were compared with those of patients without history of IVF.

Diagnostic measures for hysteroscopic detection of uterine lesions in this study revealed a sensitivity of 78.95% (95% CI 62.68- 90.45), 100% specificity and positive predictive value. Negative predictive value was 33.33% (95% CI 21.27 – 48.07) and diagnostic accuracy was 80.95% (95% CI 65.88 – 91.40).

Discussion

Infertility as a medical problem has many associated societal implications ranging from depression to divorce and even suicidal attempts. Advances in medical sciences through Assisted Reproductive Techniques have been helpful in restoring some families by solving infertility problems thereby bringing happiness and peace to their homes. Despite recent advances in medical fields and in IVF, not all cycles result in pregnancy and fewer still, end in live births.[7] A number of factors are responsible for this, including the failure of the transferred embryo to achieve implantation which depends on several factors such as the quality of the embryo, endometrial receptivity, and uterine integrity.[8] This study was designed to evaluate the beneficial role of hysteroscopy as the preferred gold standard for pre-IVF procedure patient's work-up and whether there is need for it to be carried out on all patients considering the cost and technicality. Hysteroscopy basically assesses the integrity of uterine endometrium and also treats the intrauterine anomalies identified. Contrary to expectations, not all patients even after hysteroscopic treatment give birth, raising some questions bothering on the necessity of hysteroscopy and the need to find alternative IVF approaches to solve infertility problems. There are reports, similar to ours, of substantial increase in pregnancy rate in infertile women after IVF following detection and treatment of intrauterine abnormalities during hysteroscopy,[9,10] while others reported no substantial increase in implantation and live birth rate.[11]

The present study focused on assessing the importance of hysteroscopy as a routine investigation in the management of infertility in women with or without pathologic TVS findings. Though hysteroscopy is recommended by the European Society of Human Reproduction and Embryology for confirmation and treatment of doubtful endometrial disease, it is not employed as a routine examination.[12] Hysteroscopy is a simple and safe procedure with a low incidence of major intraoperative or postoperative complications. It also offers the advantage of making final diagnosis under direct view in cases posing a diagnostic dilemma, coupled with offering treatment during the same session.

The results of this study shows that of the 41 patients registered for this study, TVS detected abnormalities in 30 (73.17%) of them, while 11 (26.83%) were cleared with normal uterine findings. Hysteroscopic findings on the same patients revealed that 37 (90.25%) of the patients have uterine abnormalities, while only 4 (9.75%) were with normal findings. This revealed that significant numbers of abnormalities were left undiagnosed by TVS in a significant number of patients. Sensitivity of hysteroscopy is significantly higher in comparison with TVS (78.95%, CI 62.68-90.45) and enabled a final diagnosis in all cases. In the present study, abnormal findings were higher in patients with a history of repeated IVF failure 21 (51.21%) compared with those with no previous attempts 17 (41.46%), and this was considerable. This trend was observed in both TVS and hysteroscopy. This result is in agreement with those of other clinical studies.[9,13]

The present study further shows that 9 different uterine abnormalities which include; cervical stenosis, submucous myoma, cervical incompetence, uterine adhesion, atrophic endometrium, endometrial polyp, intramural myoma, uterine septum, endometrial fluid were detected by hysteroscopy, while only 5 pelvic

abnormalities; intramural myoma, adenomyosis, submucous myoma, PCOS, and ovarian cyst, were detected by TVS. Two of these were extra uterine pathologies – PCOS and Ovarian cyst. This implies that some abnormalities were missed by TVS confirming a higher sensitivity of hysteroscopy, thereby giving credence to its usefulness in the diagnosis and treatment of cases of infertility. Cases like uterine adhesions, cervical stenosis, cervical incompetence, endometrial polyps among others were not detected by TVS.

The results of intervention outcomes in the present study revealed a positive pregnancy rate of 58.33% in patients with previous history of IVF attempts as against 41.17% in patients without history of IVF attempt (Table 6) (all progressed to clinical pregnancies). Although there are reports of non-statistically significant difference in the outcome of IVF/ICSI after hysteroscopic examination and/or treatment of intrauterine disease in women with or without previous IVF attempts,[8] the results of the present study indicated a significant difference between the two groups. Contrary to the assertion that diagnostic and/or operative hysteroscopy has no additive value on subsequent IVF/ICSI; the result of this study provides strong evidence that hysteroscopic treatment for those with previous IVF attempts, have an effect on the subsequent IVF outcomes. This appears to be an added advantage to those women with previous history of IVF attempts, therefore the possibility of achieving positive outcomes when undergoing subsequent IVF after endometrial disease had been treated in advance via hysteroscopy.

Diagnostic measures for hysteroscopic detection of uterine lesions in this study revealed a sensitivity of 78.95% (95% CI 62.68- 90.45), 100% specificity and positive predictive value, with a Negative predictive value of 33.33% (95% CI 21.27 – 48.07) and diagnostic accuracy of 80.95% (95% CI 65.88 – 91.40). These are in keeping with other studies.[13,14]

This study was not without limitations. First, the relatively limited number of patients included which was due to the duration of the study and the fact that IVF could only be afforded by wealthy couples in Nigeria considering the cost implications. Secondly, the short duration of study also did not afford the opportunity for a follow up study to be done to confirm successful delivery. This was our initial plan so as to correlate the interventions with the successful delivery rate. Thirdly, direct comparison could not be drawn on subsequent IVF outcomes between patient groups with treated and untreated intrauterine disease.

Conclusion

Findings of the present study show increasing incidence of intrauterine disease in women with subfertility especially in women with a history of failed IVF attempts, and also suggests improvement in the IVF outcome rate in women with corrected intrauterine disease. However, due to the limitations faced in this study, it was not possible to justify the physical, emotional, and financial costs to a patient from a failed IVF attempt. Routine Office Hysteroscopy is useful in women having IVF and is superior to TVS in assessing infertile women prior to IVF.

It is therefore recommended that routine Office Hysteroscopy be employed for assessment of patients prior to IVF. It should be performed before the first IVF cycle in all patients including women with normal TVS findings because a significant percentage of them may have undetected uterine conditions that may impair the success of fertility treatment and IVF.

References

1. Sharlip ID, Jarow JP, Belker AM, Lipshultz LI, Sigman M, Thomas AJ, et al. Best practice policies for male infertility. Fertil Steril. 2002;77:873–82.
2. Cumming DC, Taylor PJ. Combined laparoscopy and hysteroscopy in the investigation of the ovulatory female. Fertil Steril 1980;33:475–8.
3. Prevedourakis C, Loutradis D, Kalianidis C, Markis N, Asavan- tinos D. Hysterosalpingography and hysteroscopy in female infertility. Hum Reprod 1994;9:2353–5.
4. Linderman H, Mohr J. CO2 hysteroscopy, diagnosis and treatment. Am J Obstet Gynecol 1976;124:129–33.
5. Alatas C, Aksoy E, Akarsu C. Evaluation of intrauterine abnormalities in infertile patients by sonohysterography. Hum Reprod 1997;12(3):487–90.

6. El-Toukhy T, Sunkara SK, Coomarasamy A, Grace J, Khalaf Y. Outpatient hysteroscopy and subsequent IVF cycle outcome: a systematic review and meta-analysis. Reprod Biomed Online. 2008 May;16(5):712-9. doi: 10.1016/s1472-6483(10)60486-5.
7. Society for Assisted Reproductive Technology/American Society for Reproductive Medicine. Assisted reproductive technology in the United States: 2001 results generated from the American Society for Reproductive Medicine/Society for Assisted Reproductive Technology registry. Fertil Steril. 2007;87:1253–1266.
8. Bakas, P, Hassiakos, D, Grigoriadis, C, Vlahos, N, Liapis, A, Gregoriou, O. Role of hysteroscopy prior to assisted reproduction techniques. Journal of Minimally Invasive Gynecology, 2014;21:(2):234-237.
9. Doldi N, Persico P, Di Sebastiano F, Pathologic findings in hysteroscopy before in vitro fertilization–embryo transfer (IVF-ET). Gynecol Endocrinol. 2005;21:235–237.
10. Karayalc¸in R, Ozyer S, Ozcan S, Office hysteroscopy improves pregnancy rates following IVF. Reprod Biomed Online. 2012;25: 261–266.
11. Yu HT,Wang CJ, Lee CL, Huang HY, Chen CK,Wang HS. The role of diagnostic hysteroscopy before the first in vitro fertilization/intracytoplasmic sperm injection cycle. Arch Gynecol Obstet. 2012;286: 1323–1328.
12. Crosignani PG, Rubin BL. ESHRE Capri Workshop Group. Optimal use of infertility diagnostic test and treatments. Hum Reprod. 2000; 15:723–732.
13. Schiano A, Jourdain O, Papaxanthos A, Hocke C, Horovitz J, Dallay D. The value of hysteroscopy after repeated implantation failures with in vitro fertilization. Contracept Fertil Sex. 1999;27:129–132.
14. Rama RGA, Shashi KG, Krishna KM, Prakash GJ, Madan K. Assessment of uterine cavity by hysteroscopy in assisted reproduction programme and its influence on pregnancy outcome. Arch Gynecol Obstet. 2006 Jun;274(3):160-4. doi: 10.1007/s00404-006-0174-7.