

Detection of Uterine Abnormalities Using three-Dimensional Vaginal Ultrasound in Infertile Women Undergoing Assisted Reproductive Techniques

Huda Ali Hussaini, Asmaa Kadhim Gatea¹, Suhaila F. Al-Shaikh¹

Department of Surgery, College of Medicine, Al Nahrain University, Baghdad, ¹Department of Obstetrics & Gynecology, College of Medicine, University of Babylon, Hillah, Iraq

Abstract

Background: Uterine shape and cavity abnormalities form a common cause of subfertility, for which thorough assessment is considered as a core part in infertility evaluation. A variety of modalities (invasive and none invasive) such as hysterosalpingography, transvaginal sonography, diagnostic hysteroscopy, two-dimensional hysterosonography, and three-dimensional hysterosonography can be used for the diagnosis of uterine abnormalities. **Objectives:** To address the detection rate of uterine and endometrial abnormalities in infertile women undergoing assisted reproductive techniques (ART) using three-dimensional vaginal ultrasonography. **Materials and Methods:** A cross-sectional observational study that involved 211 subfertile women who were arranged to undergo ART for different causes of infertility. After taking their verbal consent for participation in this study, all women examined by 2D vaginal U/S for initial assessment of their pelvic anatomy then followed by three-dimensional U/S with or without saline infusion for further assessment of the uterine and endometrial cavity morphology. Women with ultrasound detected endometrial abnormalities further underwent hysteroscopic assessment, histopathological specimens were taken and were treated as recommended by their gynecologist. **Results:** Twenty-two percent of the studied group discovered to have uterine and/or endometrial abnormalities including endometrial polyps and uterine myomas are the most commonly detected abnormalities while congenital uterine malformation detected in 3.8% of the total patients using three-dimensional ultrasonography. **Conclusion:** Uterine and endometrial abnormalities are common in subfertile patients, the prevalence of uterine and endometrial abnormalities (endometrial polyps or irregularities, uterine myomas including submucous one) was 22%, whereas congenitally maldeveloped uteri were detected in 3.8% of women undergoing ART (using 3D U/S) which may have a negative impact on ART outcome.

Keywords: 3D-U/S, congenital uterine anomalies; endometrial polyp, infertility, SIS 3D U/S, uterine abnormalities

INTRODUCTION

Uterine and endometrial abnormalities can be one of the etiologies of infertility by interfering with implantation so assessment of uterine abnormalities is a core part in infertility evaluation.^[1]

Evaluation of infertility is multimodal in nature, and imaging plays an integral role in assessing anatomic abnormalities, tubal occlusion, and even ovarian reserve.^[2]

Ultrasound is preferred as the initial imaging modality for assessing possible causes of female infertility because of its low cost and convenience, providing a basic assessment of ovarian morphology, uterine structure, and detection

of such pathology as uterine fibroids and Müllerian anomalies.^[3]

Ultrasound can also be coupled with color Doppler and 3D/4D scans. It is non-invasive, radiation-free; relatively less time consuming and easily repeatable; moreover, it can

Address for correspondence: Dr. Suhaila F. Al-Shaikh,
Department of Obstetrics & Gynecology, College of Medicine,
University of Babylon, P. O. Box: 473, Hillah, Iraq.
E-mail: drsuhaila_alshaikh@uobabylon.edu.iq

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be used as part of interventional techniques in treatment of some cases of female infertility.^[4]

Three-dimensional transvaginal sonography (TVS) represents a new technique of imaging. It has the ability to register all three imaging plane simultaneously as well as to visualize surfaces three dimensionally. Three-dimensional TVS enables visualization of the uterus in the coronal plane,^[3] which is rarely seen on conventional scans.^[5]

The simultaneous display of three perpendicular planes offers a more comprehensive overview of the examined area and provides access to planes unobtainable by conventional two-dimensional examinations. Surface rendering of the intra-cavitary pathological findings enables visualization of their surface areas and provides valuable information about their topographical orientation.^[6]

This approach enables more accurate examination of the endometrial and subendometrial lesions as well as the assessment of the uterine anatomy in congenital uterine anomalies.^[7]

Whereas TVS as an initial investigation is unable to differentiate intrauterine pathology with complete certainty, 3-dimensional hysterosonography (3-DHS) as a noninvasive procedure may be recommended as a proper alternative for diagnostic hysteroscopy for diagnosis of uterine abnormalities in infertile women with less costs and complications.^[1]

Uterine and endometrial abnormalities are only present in few patients presented to the infertility clinics. Obese women are commonly presented with subfertility^[8] this can be linked to anovulation and disturbances of hypothalamo-pituitary-ovarian axis presented as polycystic ovary syndrome (PCOS) which is the commonest one. Other causes related to aberrant BMI and subfertility is the thyroid dysfunction which is shown to have a negative impact upon ovum quality during intracytoplasmic sperm injection (ICSI) procedures.^[9]

This study aims to address the detection rate of uterine abnormalities (using 3 dimensional U/S) including Müllerian duct anomalies, uterine fibroids, endometrial polyps, and irregularities among infertile women undergoing assisted reproductive techniques (ART) 3 dimensional U/S is preferred as a non-invasive accurate easily accessible tool.

MATERIALS AND METHODS

A prospective cross-sectional observational study involved 211 subfertile women who were arranged for different assisted reproductive techniques ART for management of their infertility, informed verbal consent obtained from all women before enrolment in this study.

Detailed history and complete general and gynecological clinical examination were performed, and then transvaginal ultrasonography was performed between 7 and 11 days of menstrual cycle in dorsal position after bladder emptying using trans-vaginal volume probe RIC5-9A-RS—Voluson S10 (GE Medical Systems, Korea) ultrasound machine with dedicated 3D imaging software); all the U/S examinations were done by single sonographer.

Examination was started with conventional 2D scan in order to assess the size, orientation, texture of myometrium, and measurement the endometrial thickness in longitudinal view and for any abnormalities including masses as fibroids, polyps, other lesion as scar, calcification, and recording of these lesions. Then assessing both ovaries and adnexa for any lesion then the assessment was completed using the 3D scan for more detailed view of the uterus and endometrium.

After completing the U/S examination for those with detected endometrial abnormalities the probe will be removed, then a sterile speculum inserted into the vagina and external part of cervix is disinfected with antiseptic solution. Catheter (intrauterine insemination (IUI) catheter) will be inserted into the uterine cavity and the transvaginal probe will be re-inserted into the vaginal canal. Sterile saline will then be injected through the catheter into the uterine cavity and whereas saline fills the endometrial cavity, ultrasound examination continued to assess the distention of cavity and any abnormalities including masses as fibroids, polyps, scars, calcifications, and other abnormalities, the detected lesions with both 2D and 3D scans were saved by captured pictures (the final diagnosis with hysteroscopic and histopathological examination for confirmation of ultrasound finding). Tubal patency was assessed by fluid accumulation in the pouch of Douglas during saline infusion sonography (SIS) examination.

Whereas those with detected uterine shape anomalies by 2D U/S their assessment further completed by three-dimensional volume images to assess the shape of uterus by obtaining coronal views, detection of any abnormality in the corpus of uterus was according to Congenital Uterine Malformation by Expert Classification (CUME) classification which consider the best cut-off values for measuring septate uterus are: depth of indentation ≥ 10 mm, angle of indentation $< 140^\circ$, and ratio of indentation to wall thickness $> 110\%$.^[10]

Statistical analysis

SPSS version 25.0 (SPSS Inc., Chicago, Illinois) was utilized for statistical analysis. Data were expressed as frequencies and percentages for Categorical variables, and level of significance was looked for using Fisher's exact or

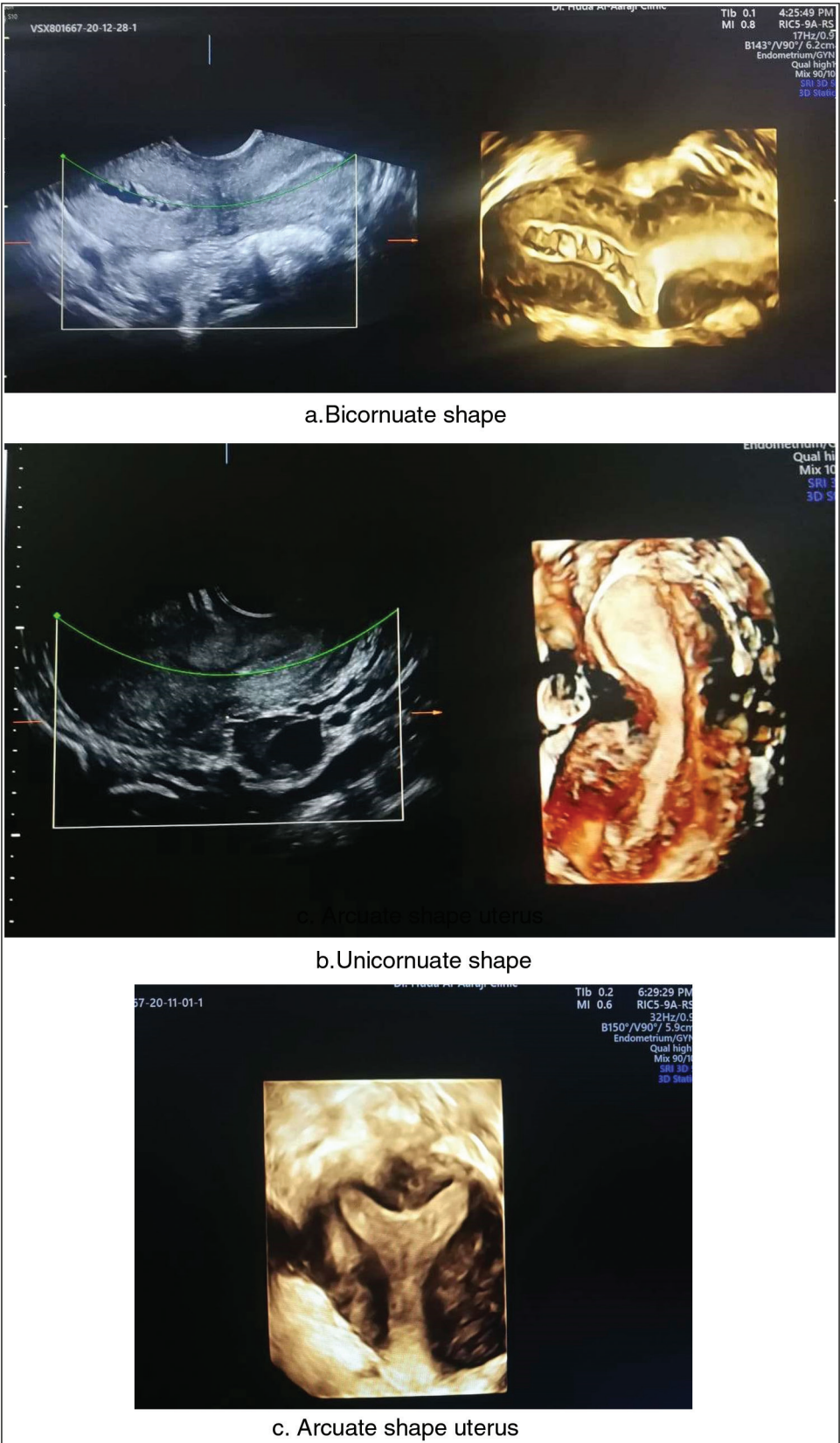


Figure 1: Uterine shape abnormalities using 3D U/S examination (A. bicornuate, B. unicornuate, C. arcuate shape)

Chi square tests accordingly, with a P value of 0.05 or less was considered significant.

Ethical approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients verbal and analytical approval before sample was taken. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee according to the document number (16) in October 21, 2021.

RESULTS

Uterine shape

Three-dimensional ultrasonographic findings of uterine shape [Figure 1].

Regarding uterine shape shown by 3D U/S, 203 patients were with normal shaped uterus whereas eight were with abnormal shaped uterus distributed as 4 arcuate, 3 bicornuate, and 1 unicornuate uterus, as demonstrated in Table 1.

Endometrial cavity

Three-dimensional ultrasonographic findings of endometrial cavity

Table 2 demonstrates the three-dimensional U/S findings of endometrial cavity of 211 infertile patients enrolled in this study and the results showed 164 (77.7%) normal findings and 47 (22.3%) abnormal findings distributed as single polyps (8.1%), multiple polyps (6.6%), single fibroid

(3.8%), endometrium compressed by fibroid (1.4%), and (0.5%) for each of other abnormalities, that is, multiple fibroids, mixed fibroid and polyps, Osseous metaplasia, endometrial calcification and irregular cavity surface, as shown in Table 2 and Figures 2 and 3.

Comparison of endometrial 3D ultrasonographic findings between different age groups

Women were divided into four groups of 10 years interval according to their ages, the comparison of endometrial 3D sonographical findings in different age groups demonstrated higher frequencies of normal findings at age of less 20 years old (100%) and single fibroid after age of 40 years (12.0%). Single polyps (9.5%) and multiple polyps (10.5%) were predominantly seen in women aged between 30 and 39 years. There were also no significant differences regarding the rest of endometrial findings between the four age groups, as showed in Table 3.

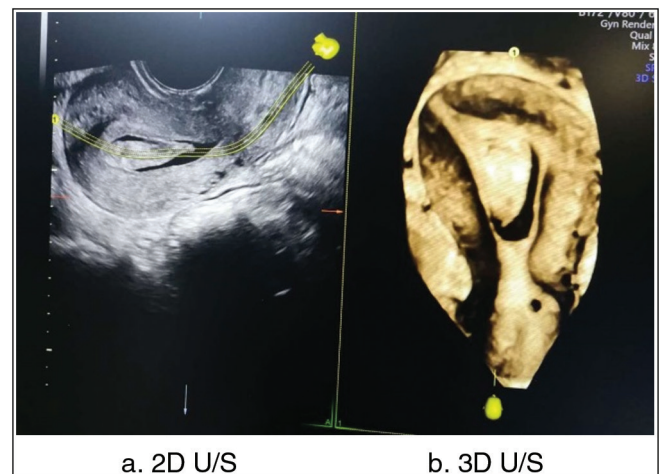


Figure 2: 2D and 3D U/S finding of endometrial polyp (A. 2D U/S, B. 3D U/S)

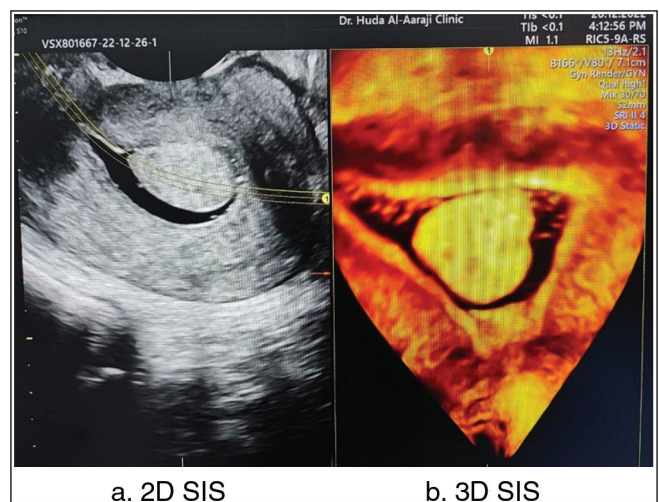


Figure 3: Endometrial polyp by saline infusion sonography (SIS) using 2D and 3D U/S (A. 2D U/S, B. 3D U/S)

Table 1: Shape of the uterus by 3D U/S

Uterine shape	Patients $n = 211$ (%)
Normal	203 (96.2%)
Arcuate uterus	4 (1.9%)
Bicornuate uterus	3 (1.4%)
Unicornuate uterus	1 (0.5%)

Table 2: Frequency of endometrial cavity findings as detected by 3D U/S

Endometrial cavity finding by 3D U/S	Patient no. ($n = 211$)	%
Normal	164	77.7%
Single polyp	17	8.1%
Multiple polyps	14	6.6%
Single fibroid	8	3.8%
Compressed by fibroid	3	1.4%
Multiple fibroid	1	0.5%
Mixed (fibroid and polyps)	1	0.5%
Osseous metaplasia	1	0.5%
Endometrial calcification	1	0.5%
Irregular cavity	1	0.5%

Table 3: Comparison of 3D U/S findings of endometrial cavity indifferent age groups

Endometrial cavity finding by 3D U/S	Patients' age groups				Total no.	P value
	<20 years n = 11	20–29 years n = 80	30–39 years n = 95	>40 years n = 25		
Normal	11 (100%)	67 (83.8%)	67 (70.5%)	19 (76.0%)	164	0.052
Single polyp	0 (0%)	7 (8.8%)	9 (9.5%)	1 (4.0%)	17	0.609
Multiple polyps	0 (0%)	3 (3.8%)	10 (10.5%)	1 (4.0%)	14	0.216
Single fibroid	0 (0%)	1 (1.3%)	4 (4.2%)	3 (12.0%)	8	0.089
Compressed by fibroid	0 (0%)	1 (1.3%)	1 (1.1%)	1 (4.0%)	3	0.693
Multiple fibroids	0 (0%)	0 (0%)	1 (1.1%)	0 (0%)	1	0.747
Mixed (fibroid and polyps)	0 (0%)	0 (0%)	1 (1.1%)	0 (0%)	1	0.747
Osseous metaplasia	0 (0%)	0 (0%)	1 (1.1%)	0 (0%)	1	0.747
Calcification	0 (0%)	1 (1.3%)	0 (0%)	0 (0%)	1	0.649
Irregular surface	0 (0%)	0 (0%)	1 (1.1%)	0 (0%)	1	0.747

Table 4: Comparison of 3D U/S findings of endometrial cavity in women with primary or secondary infertility

Endometrial cavity finding by 3D U/S	Type of infertility		Total no.	P value
	Primary infertility n = 89	Secondary infertility n = 122		
Normal	67 (75.3%)	97 (79.5%)	164	0.466
Single polyp	8 (9.0%)	9 (7.4%)	17	0.671
Multiple polyps	7 (7.9%)	7 (5.7%)	14	0.540
Single fibroid	3 (3.4%)	5 (4.1%)	8	0.785
Compressed by fibroid	2 (2.2%)	1 (0.8%)	3	0.387
Multiple fibroids	1 (1.1%)	0 (0%)	1	0.241
Mixed (fibroid and polyps)	1 (1.1%)	0 (0%)	1	0.241
Osseous metaplasia	0 (0%)	1 (0.8%)	1	0.392
calcification	0 (0%)	1 (0.8%)	1	0.392
Irregular	0 (0%)	1 (0.8%)	1	0.392

Comparison of endometrial 3D ultrasonographic findings between primary and secondary infertility

No significant differences were observed among patients presented with primary or secondary infertility regarding endometrial abnormalities detected by 3D U/S [Table 4].

DISCUSSION

Three-dimensional ultrasonography is highly accurate imaging modality for detection of aberrant development of Mullerian system with sensitivity and specificity as high as that of magnetic resonance imaging which is considered as the gold standard for the diagnosis of uterine structural defects.^[11,12] using three-dimensional ultrasonography can provide a clear sight of both interior and exterior aspects of uterine contour with a least costly and non-invasive tool^[12] of comparable accuracy to hysteroscopy and other investigating approaches.^[11,13,14]

Uterine congenital abnormalities are ranging from 0.1% to 3% in the general population with an average of 0.4%, whereas 4% in the infertile population;^[11,15,16] these reach up to 24.5% in infertile couples suffering from miscarriage.^[17]

A study done by Prior *et al.*^[18] found that prevalence of uterine anomalies among infertile women undergoing ART using the three-dimensional ultrasonography is as

high as 18.2% of the studied group, and most of them have arcuate uterus with a percentage as high as 16.3%, whereas in the current study, the rate of uterine anomalies in total was 8 (3.8%) and arcuate uterus 4 (1.9%) of the studied group [Table 1]. None of them had septate or subseptate uterus, as this may be due to larger sample size of Prior *et al.* study or due to different classification system used by them. Prior *et al.* used a system proposed by Salim *et al.* which state that “If the external contour of the uterus was uniformly convex or had an indentation of <10mm, but there was a cavity indentation, it was defined as arcuate or septate. Arcuate uterus was further defined as the presence of a concave fundal indentation with a central point of indentation at an obtuse angle. Subseptate uterus was defined as the presence of a septum, not extending to the cervix, with the central point of the septum at an acute angle; if the septum is extended to the internal cervical, then the uterus will be defined as septate”. This classification is known as the modified American Fertility Society (AFS) classification of uterine congenital malformation,^[19] whereas in our study, we used the classification of CUME which considers the best cut-off values for measuring septate uterus that are depth of indentation ≥ 10 mm, angle of indentation $< 140^\circ$, and ratio of indentation to wall thickness $> 110\%$.^[10]

CUME classification got rid of the overestimation of septate uterus using the European Society of Human Reproduction and Embryology-European Society for Gynecologic Endoscopy (ESHRE-ESGE) classification that not taking into account the type of an arcuate uterus which it classifies as a subtype of septate.^[10,17]

The prevalence of uterine anomalies was studied by different researchers using different tools of varying levels of accuracy of detection and diagnosis.^[20] Saravelos *et al.* critically appraised in their e four previously published review articles with different methods for the detection and diagnosis of uterine anomalies (using 3D U/S), and they classified 3D ultrasonography as one of the highest accuracy tools in the diagnosis of such anomalies with sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) as high as 100%. Their finding showed the prevalence of total number of uterine anomalies in (4521) women was 305 (6.7%) in the general population, 1 (0.03%) is unicornuate, 10 (0.3%) bicornuate, 68 (2.0%) septate, and 170 (4.9%) arcuate uteri.

On the other hand, in infertile population the most predominant abnormality is the septate uterus whereas the arcuate uterus has the same prevalence as in the general population indicating its benign behavior with pregnancy on the opposite for septate and unicornuate uterus which are associated with infertility and recurrent miscarriage.^[20] In our study, eight women were presented with infertility having congenitally abnormal uterus, half of them with arcuate uteri, and none of them had septate uterus.

Uterine cavity abnormalities and endometrial pathologies have negative impact on fertility and implantation and frequently linked to subfertility and/or recurrent miscarriage, in the current study the endometrial cavity was assessed using 3D ultrasound aided by saline infusion for better delineation of the endometrial cavity details which further confirmed by hysteroscopic assessment and histological examination. Three-dimensional saline sonohysterography is recommended as a 1st choice for accurate detection and diagnosis of intra-cavitary masses and endometrial polyps (100% detection rate) even it can determine the site of attachment of polyp with accuracy approaching 87.5% which is much higher than that of magnetic resonance imaging (MRI).^[21] 3D SIS is not only helpful in detection but also it can tell the type whether sessile or pedunculated, and telling the number of polyps in the cavity with confidence,^[22] so by inspecting these promising findings, it can be said that 3D ultrasonography and 3D SIS may substitute and replace the 2D ultrasonography and 2D SIS in the workup of women with subfertility and even replace the need for diagnostic hysteroscopy.^[23]

In the current study 47 (22.3%) of the studied group have uterine cavity abnormalities and/ or endometrial pathologies as shown in Table 2. A total of 31 (14.7%)

patients diagnosed with endometrial polyps whether single 17 (8.1%) or multiple 14 (6.6%) with higher percentage in the age group between 30 and 39 years old [Table 3]. Intra-cavitary lesions apply a major clinical challenge and producing considerable stress to infertile patients, in studies which depend on hysteroscopy. They stated the prevalence of intra-cavitary abnormalities, detected via hysteroscopy before ART is between (11%) and (45%)^[24,25] with the polyp representing the most common intra-cavitary disorder reported in (32%) 323/1000 patients undergoing IVF,^[24] whereas others reported in 41/678 (6%) of similar patients.^[26]

Other cause distorting uterine cavity is leiomyoma. It appears either hypo or iso-echoic relative to the muscle of the uterus (myometrium) in U/S examination. Submucous leiomyoma can be detected by SIS easily by seeing its echogenicity, the broad-based appearance during examination, and also proportion of protrusion of fibroid into the uterine cavity.^[27] Leiomyoma is commonly occurring benign tumor of female genital tract. It may have an impact on women fertility and conception according to its size and location, and it is detected in more than 20% of reproductive-aged women.^[28] In the current study eight (3.8%) of total patients have single fibroid, in three (12%) of patients aged ≥ 40 years, and in three (1.4%) patients myoma was compressing the endometrium.

CONCLUSION

3D ultrasonography represents an excellent tool for investigating subfertile women undergoing ART to explore uterine shape and endometrial cavity abnormalities that have deleterious impact on ART outcome when untreated. Uterine shape abnormalities especially the arcuate are the most common abnormalities followed by the bicornuate, yet none of the patients had septate uterus. On the other hand, endometrial polyp visualized by SIS 3D U/S was the most common endometrial abnormalities followed by uterine fibroid whether single or multiple, or intramural or submucosal.

Consent for publication

All authors gave their consent for publication.

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Conflicts of interest

There are no conflicts of interest.

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