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Comparison between Hysteroscopy and 3D Ultrasound for Assessment of Uterine Cavity in Patient with Recurrent Pregnancy Loss

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Abstract:

Background: Recurrent pregnancy loss (RPL) affects 1%–3% of couples and has multifactorial etiology like uterine abnormalities, thrombophilia, and immune factors but often is unexplained. Uterine abnormalities are common in Recurrent pregnancy loss and can cause implantation and placental growth problems but have a very good prognosis after surgical treatment. Diagnostic modalities like 3D transvaginal ultrasound are more accurate than 2D US in evaluating uterine abnormalities. Aim: The primary objective was to assess the diagnostic accuracy of hysteroscopy and 3D US in detecting uterine cavity abnormalities, specifically partial septate uterus, in patints with RPL. **Patients and methods:** This prospective investigation at Benha University Hospital comprised 36 patints of RPL with partial septate uterus, divided based on the uterine indentation angle. All underwent clinical examination, laboratory investigations, and imaging with 2D and 3D transvaginal US. Diagnostic hysteroscopy, being the gold standard, was noted to be beneficial for detecting subtle uterine anomalies that were missed by the other methods. **Results:** there was a significant agreement was observed between 3D US and hysteroscopy outcomes (Kappa = 0.833, $p < 0.001$). Hysteroscopy showed high accuracy in predicting outcomes consistent with 3D US, with an AUC of 0.917, sensitivity of 88.9%, and specificity of 94.4%. **Conclusion:** Hysteroscopy is a highly accurate and reliable tool for diagnosing partial septate uterus in RPL, with excellent concordance with 3D US. It was found to be exquisitely sensitive and specific, as good as advanced imaging. Hysteroscopy is especially useful in low-resource settings both as a diagnostic and therapeutic tool.

Key words: Partial Septate Uterus, Hysteroscopy, 3D Transvaginal Ultrasound, Uterine Anomalies

Introduction

Recurrent pregnancy loss (RPL) is commonly defined as the occurrence of three or more consecutive pregnancy losses [1].

The etiology of RPL is diverse and multifactorial. Known contributing factors include congenital and acquired structural abnormalities of the uterus, hormonal and endocrine dysfunctions, immunologic conditions, infections, parental chromosomal abnormalities, and maternal autoimmune diseases. Despite comprehensive evaluation, the underlying cause remains idiopathic in approximately 50–60% of cases [2].

During pregnancy, physiological adaptations lead to a shift in the coagulation system toward a prothrombotic state. This hypercoagulability is believed to serve a protective function, compensating for the hemostatic challenges associated with placental separation and delivery. Elevated levels of clotting factors—including fibrinogen (factor I), factor VII, factor VIII, and von Willebrand factor—are observed in normal pregnancy. Furthermore, biomarkers indicative of coagulation activation, such as D-dimer and prothrombin fragments, are also elevated during gestation, contributing to a state of acquired thrombophilia that, if dysregulated, may adversely affect placental perfusion and increase miscarriage risk [3]

In addition to hematologic and systemic causes, several structural and acquired uterine factors have been implicated in RPL. These include submucosal fibroids, intrauterine adhesions resulting from previous surgical interventions such as myomectomy or cesarean section, and Asherman's syndrome. These conditions can lead to distortion of the uterine cavity and compromise its vascular integrity, thereby impairing embryo implantation or sustaining pregnancy beyond the early gestational period [4]

Congenital uterine anomalies are among the most frequently identified structural causes of RPL, with a reported prevalence of approximately 13.3%. [5]

Histologically, the septal tissue is distinct from normal endometrial tissue. It tends to be poorly vascularized and contains a higher proportion of fibrous connective tissue. These histological and functional deficiencies can interfere with successful embryo implantation and may compromise placental development [6].

Accurate diagnosis of uterine anomalies relies on imaging modalities that allow precise localization and morphological assessment. Currently, ultrasonography, particularly 3D TVUS, and diagnostic hysteroscopy are regarded as the primary tools for evaluating uterine septa [7].

The primary objective was to compare the diagnostic accuracy of hysteroscopy and 3D TVUS in detecting intrauterine anomalies, specifically partial septate uterus, among women with RPL. Secondary objectives include evaluating the concordance between these two modalities and determining the sensitivity and specificity of hysteroscopy relative to 3D TVUS outcomes.

Patients and Methods

This prospective comparative investigation, which was performed from October 2023 to October 2024 at Benha University Hospitals, involved 36 females with unexplained RPL and partial septate uterus. The aim was the comparison of hysteroscopy and 3D transvaginal ultrasound (3D US) accuracy in uterine abnormalities diagnosis. The authors were also curious about finding the correlation between the two procedures and the diagnostic value of hysteroscopy on the basis of 3D US as a gold standard. The ethical committee approval **(MS 27-3-2022).**

Ethical clearance was achieved and informed consent from all participants was attained. They were explained thoroughly the objectives of the investigation, hazards,

and the right to withdraw at any moment, following ethical research and patient autonomy guidelines.

Cases were divided into two equal groups based on uterine indentation angle: Group A with obtuse angles and Group B with acute angles of < 90°, both fulfilling criteria for partial septate uterus. Only women with documented partial septum and unexplained RPL were recruited; women with known etiology for RPL or complete septum were excluded.

Each of the cases underwent a complete medical evaluation and an exhaustive panel of laboratory tests. Imaging was commenced with 2D transvaginal US, and it was followed by 3D US on a Voluson P8 scanner, which produced good coronal images required to identify uterine anomalies.

All women then underwent diagnostic hysteroscopy without anesthesia, using a small-diameter scope through a vaginoscopic approach. Pre-procedure medication was given for cervical preparation and to prevent discomfort. Direct, systematic examination of the uterine cavity was possible through the procedure, and findings were recorded.

The investigation reconfirmed that hysteroscopy remains a very precise diagnostic method for partial septate uterus in RPL women and can also serve as a therapeutic and diagnostic modality. Its usefulness is especially in settings where there is no facility for advanced imaging, and thus it finds application in management of unexplained pregnancy losses.

Statistical analysis

Data analysis was conducted using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). The Shapiro–Wilk test, along with visual inspection of histograms, was employed to assess the normality of data distribution. Quantitative variables following a normal distribution were expressed as mean ± standard deviation (SD), while categorical variables were summarized as frequencies and percentages. A two-tailed p-value < 0.05 was considered indicative of statistical significance.

Results

Table 1 shows that the average age in group A ranged from 25 to 36 with an average age of 31.1 ± 3.9 years old and in group B ranged from 24 to 37 with average age of 30.5 ± 3.9 years old. The BMI in group A ranged from 23.8 to 34.4 with average BMI of 30.4 ± 3.5 kg/m^2 and in group B ranged from 21.6 to 34.8 with an average BMI of 28.6 ± 4.1 kg/m^2. The age of menarche in group A ranged from 9 to 12 years old with average age of 10.4 ± 1.1 years old, and in group B ranged from 8 to 14 with average age of 10.3 ± 1.5 years old. There was only 2 (11%) smokers in group A and none in group B. There was no significant difference in baseline characteristics (age, BMI, age of menarche, and smoking) between the enrolled cases.

Table 2 shows that the gravidity in group A ranged from 3 to 7 with a median value of 6 (4.25 - 7), and in group B ranged from 3 to 7 with a median value of 6 (5 - 6). The parity in group A ranged from 1 to 4 with a median value of 2 (2 - 3) and in group B ranged from 1 to 4 with a median value of 2 (1.25 - 2.75). Regarding the number of abortions, it ranged from 2 to 5 times with median value of 3 (2 - 4) in group A, and ranged from 2 to 6 with a median value of 3 (2.25 - 4) in group B.

The number of females who suffered from irregular menstruations in group A was 5 (28%) females in group B was 8 (44%) females. while there was no significant difference in gravidity, parity, number of abortions, and history of irregular menstruation between the enrolled cases.

Table 3 shows that the number of females who suffered from HTN, DM, thyroid disease, liver diseases and kidney diseases in group A were 2 (11.1%), 2 (11.1%), 3 (16.7%), 0 (0%), and 0 (0%) females respectively, and in group B were 0 (0%),

4 (22.2%), 6 (33.3%), 1 (5.6%), and 0 (0%) females respectively.

The history of parents' consanguinity was positive in 7 (38.9%) females in group A and in 9 (50%) females in group B.The signs of endocrinopathy was present in 3 (16.7%) females in group A and in 5 (27.8%) females in groups B.And there was no significant difference in medical history, consanguinity, and signs of endocrinopathy between the enrolled cases.

Table 4 shows that hysteroscopy showed the same results as 3D US in 16 (88.9%) females in group A and in 17 (94.4%) females in group B. There was no significant difference in the outcomes of 3D US and hysteroscopy in the enrolled cases.

Table 5 shows that there was a significant almost perfect agreement in the outcomes (Kappa =0.833, p <0.001) between 3D US and hysteroscopy.

Table 6 shows that their hysteroscopy can significantly predict the same outcome as 3D US (AUC: 0.917, p <0.001) with a sensitivity of 88.9% and specificity of 94.4%. **Figure 1**

Table 1: Baseline characteristics of the enrolled cases

		Group A (n =18)	**Group B (n =18)**	**P**
Age (year)	**Mean ± SD**	31.1 ± 3.9	30.5 ± 3.9	**0.642**
	Range	25 - 36	24 - 37	
BMI (kg/m^2)	**Mean ± SD**	30.4 ± 3.5	28.6 ± 4.1	**0.158**
	Range	23.8 - 34.4	21.6 - 34.8	
Age of menarche	**Mean ± SD**	10.4 ± 1.1	10.3 ± 1.5	**0.061**
	Range	9 - 12	9 - 14	
Smoking	**Yes**	2 (11%)	0 (0%)	**0.486**
	No	16 (89%)	18 (100%)	

SD: Standard deviation

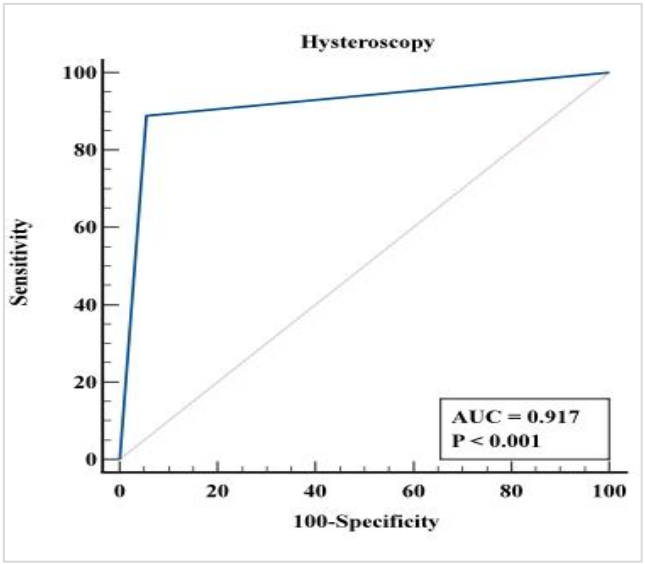

Figure (1): ROC curve analysis of the ability of hysteroscopy to predict the same outcome as 3D US

Table 2: Pregnancy and menstrual data among the enrolled cases

		Group A (n =18)	Group B (n =18)	P
Gravidity	**Median (IQR)**	6 (4.25 - 7)	6 (5 - 6)	0.535
	Range	3 - 7	3 - 7	
Parity	**Median (IQR)**	2 (2 - 3)	2 (1.25 - 2.75)	0.473
	Range	1 - 4	1 - 4	
Abortion	**Median (IQR)**	3 (2 - 4)	3 (2.25 - 4)	0.899
	Range	2 - 5	2 - 6	
Irregular menstruation	**Yes**	5 (28%)	8 (44%)	0.489
	No	13 (72%)	10 (56%)	

IQR: Interquartile range.

Table 3: Personal and family history among the enrolled cases

		Group A (n =18)	Group B (n =18)	P
Medical history	**HTN**	2 (11.1%)	0 (0%)	0.486
	DM	2 (11.1%)	4 (22.2%)	0.658
	Thyroid disease	3 (16.7%)	6 (33.3%)	0.443
	Liver disease	0 (0%)	1 (5.6%)	1.000
	Kidney disease	0 (0%)	0 (0%)	-
Consanguinity	**Yes**	7 (38.9%)	9 (50%)	0.738
	No	11 (61.1%)	9 (50%)	
Signs of endocrinopathy (hirsutism, galactorrhea)	**Yes**	3 (16.7%)	5 (27.8%)	0.691
	No	15 (83.3%)	13 (72.2%)	

HTN: Hypertension, DM: Diabetes mellites.

Table 4: Outcome of hysteroscopy among the enrolled cases

		Group A (n =18)	Group B (n =18)	P
Confirmation of 3D US diagnosis by hysteroscopy	**Yes**	16 (88.9%)	17 (94.4%)	1.000
	No	2 (11.1%)	1 (5.6%)	

US: Ultrasound.

Table 5: Agreement between hysteroscopy and 3D US outcomes among the studied females

	Kappa value	SE	95% CI	P
Methods agreement	**0.833**	**0.091**	**0.653 – 1.000**	**<0.001***

SD: Standard deviation.

Table 6: ROC curve analysis of the ability of hysteroscopy to predict the same outcome as 3D US

	Sen.	Spe.	AUC	P
Hysteroscopy	**88.9%**	**94.4%**	**0.917**	**<0.001***

SD: Standard deviation.

Discussion

RPL affecting approximately 2–4% of couples, has traditionally been defined as the occurrence of three or more consecutive miscarriages; however, clinical assessment is now often initiated after two losses, reflecting evolving diagnostic and management practices. Despite a wide range of possible causes—including uterine anomalies, genetic issues, and immune dysfunction—up to two-thirds of cases remain unexplained. Diagnostic tools like 3D ultrasound and hysteroscopy play crucial roles in detecting correctable uterine abnormalities, a common factor in RPL [8].
Therefore, this investigation aimed to compare hysteroscopy and 3D ultrasound for assessing uterine cavity in RPL.

This prospective comparative investigation took place at the Obstetrics and Gynecology Department, Benha University Hospitals, and included 36 cases with recurrent pregnancy loss (RPL) diagnosed with partial septate uterus. Participants were divided into two groups based on the angle of the central indentation: acute angle (<90°) and obtuse angle. After obtaining informed consent, a detailed history, general and local examinations, and various routine laboratory investigations were performed to exclude other causes of RPL, such as antiphospholipid syndrome and endocrine disorders. Imaging included initial TV 2D US followed by TV 3D US to detect uterine anomalies. Diagnostic hysteroscopy, a gold-standard technique for direct visualization and management of uterine abnormalities, was emphasized for its ability to identify subtle anomalies missed by conventional imaging techniques.

Our investigation revealed that there is perfect agreement in the outcomes (Kappa = 0.833, p <0.001) between 3D US and hysteroscopy.

These findings are consistent with a research conducted by Abd Elkhalek and colleagues [12], which compared the diagnostic accuracy of three-dimensional saline infusion sonohysterography (3D SIS) and hysteroscopy in detecting intracavitary uterine abnormalities in premenopausal women with abnormal uterine bleeding. The investigation demonstrated agreement between the two methods in 40 cases, including 18 true negatives and 22 true positives, while discrepancies were noted in 10 cases [12].

Confirming our results, El-Darwish and colleagues [10], assessed the diagnostic accuracy of TVUS versus hysteroscopy in identifying intrauterine abnormalities among women with unexplained infertility. The analysis revealed a moderate level of agreement between TVUS and hysteroscopy, with a kappa coefficient (κ) of 0.484 and a statistically significant p-value of 0.027, indicating a meaningful correlation between both diagnostic methods [10].

Our investigation found that hysteroscopy can significantly predict the same outcome as 3D US (AUC: 0.917, p <0.001) with a sensitivity of 88.9% and specificity of 94.4%.

These findings align with those reported in a investigation conducted by Haemila and colleagues [11], which aimed to evaluate the diagnostic accuracy of 3D US in detecting endometrial and intramyometrial lesions, using hysteroscopy as the reference standard. In this investigation, all 70 participants underwent 3D US followed by hysteroscopy. The results of both procedures were compared to evaluate the diagnostic performance of 3D US. In 70 cases with AUB, 3D US showed a sensitivity of 63.16%, specificity of 80.77%, PPV of 54.55%, NPV of 85.71%, and overall accuracy of 76.1%. These findings differ notably from our observations [11].

Furthermore, Sousa and colleagues [12] aimed to assess and compare the diagnostic performance of TVUS and

hysteroscopy in the evaluation of women presenting with postmenopausal bleeding. The investigation, which spanned from January 1, 1998, to June 30, 1999, included a total of 88 outpatient women who were systematically assessed using both diagnostic modalities. The findings revealed that TVUS exhibited a sensitivity of 77.8%, a specificity of 93.3%, PPV of 63.6%, and NPV of 96.6% in identifying endometrial pathology. In contrast, hysteroscopy demonstrated superior diagnostic accuracy, with a sensitivity of 88.9%, specificity of 98.3%, PPV of 88.9%, and NPV of 98.3%. Importantly, when the two methods were used in combination, the diagnostic yield improved further. The combined approach achieved a sensitivity of 100%, a specificity of 91.7%, a PPV of 64.3%, and an NPV of 100% [(12).]

In line with these outcomes, Midan and colleagues [(13)] conducted a investigation at Al-Azhar University Maternity Hospital in Damietta to compare the diagnostic accuracy of 3DUS and office hysteroscopy in evaluating uterine cavity abnormalities in infertile women. A total of 100 cases were examined during the research. The diagnostic accuracy of 3DUS was found to be 97.57%, slightly surpassing that of hysteroscopy, which was 93.71%. The authors concluded that 3DUS is particularly advantageous in identifying Müllerian anomalies due to its superior capability in evaluating uterine surface contours and the myometrium. Conversely, hysteroscopy was more effective in detecting intracavitary lesions [(13).]

Similarly, Loverro and colleagues [(14)] assessed the diagnostic performance of TVUS compared to hysteroscopy in recognizing uterine cavity abnormalities among infertile women. Conducted at the Institute of Obstetrics and Gynaecology, University of Bari, this investigation included 134 women who underwent both TVUS and hysteroscopy, alongside endometrial biopsy in all cases. With hysteroscopy considered the reference standard, TVUS demonstrated a sensitivity of 84.5%, specificity of 98.7%, PPV of 98.0%, and NPV of 89.2% [(14).]

Congenital uterine anomalies represent a significant contributing factor to RPL. Among women diagnosed with Müllerian anomalies—such as unicornuate, bicornuate, didelphys, or septate uterus—approximately 20–25% experience compromised reproductive outcomes, including difficulty in conceiving, heightened risk of miscarriage, and particularly RPL. These structural abnormalities of the uterus can interfere with normal implantation, placentation, and fetal development, ultimately impacting pregnancy viability. Notably, 2nd-trimester pregnancy losses are more frequently associated with uterine fusion defects, such as those observed in bicornuate or didelphys uteri. These anomalies result from incomplete fusion or resorption of the Müllerian ducts during embryogenesis and often lead to poor reproductive prognosis if left uncorrected. Therefore, early identification and appropriate management of uterine anomalies are critical in women presenting with RPL, particularly when losses occur in the mid-trimester [(15).]

The incidence of spontaneous abortion varies across different types of Müllerian anomalies. Reported rates include 48% in women with a unicornuate uterus, 43% in those with uterine didelphys, 35% in cases of bicornuate uterus, and as high as 67% in cases with a septate uterus. Prompt and accurate diagnosis is essential for guiding appropriate treatment. While hysteroscopy enables direct visualization and diagnosis of intrauterine abnormalities, distinguishing between septate and bicornuate uteri often requires the complementary use of laparoscopy to evaluate external uterine morphology. For cases with RPL and a confirmed septate uterus, hysteroscopic septum resection is considered an effective therapeutic intervention. However, in diagnostic

settings, 3D USG has demonstrated sufficient accuracy to be used as a standalone diagnostic tool in RPL cases involving uterine anomalies [16].

Further supporting these findings, a prospective cohort investigation conducted by Abd Elmonsef et al[17] aimed to assess and compare 3D USG and hysteroscopy diagnostic validity in the recognition of intrauterine abnormalities among women experiencing recurrent miscarriage. A total of 200 cases were enrolled in the research. The results demonstrated that 3D USG was capable of effectively distinguishing between normal and abnormal findings confirmed by endometrial biopsy. Specifically, 3D USG got an AUC of 0.793, with a sensitivity of 58.6%, a specificity of 100.0%, PPV of 100.0%, NPV of 85.5%, and an overall diagnostic accuracy of 88%. Comparatively, hysteroscopy also achieved an AUC of 0.793 but demonstrated superior sensitivity at 75.9%, while maintaining the same high levels of specificity (100.0%) and PPV (100.0%). Additionally, hysteroscopy showed a higher NPV of 91.0% and a greater overall diagnostic accuracy of 93%. These results suggest that while both modalities offer excellent specificity and predictive value, hysteroscopy may provide more reliable sensitivity in detecting endometrial pathology in cases with RPL [17].

Hysteroscopy is most commonly carried out in an outpatient clinical setting and, in most cases, exceeding 90%, does not require the administration of either general or local anesthesia. One of the primary advantages of this minimally invasive procedure lies in its capability to offer direct, real-time visualization of the uterine cavity. This enables clinicians not only to observe and assess intrauterine conditions with precision but also to perform diagnostic biopsies and simultaneously remove any identified endometrial abnormalities. As a result, hysteroscopy serves a dual function, acting effectively as both a diagnostic tool and a therapeutic intervention [18]. In a large-scale investigation involving 1,500 females, hysteroscopy demonstrated high diagnostic accuracy in detecting endometrial pathology, with reported sensitivity of 94.2%, specificity of 88.8%, PPV of 83.1%, and NPV of 96.3%, underscoring its effectiveness in differentiating between normal and abnormal endometrium [19].

Complication rates associated with diagnostic hysteroscopy are relatively low, with an overall incidence of below 4%. Among these, uterine perforation and cervical trauma are the highest frequently encountered, occurring in approximately 0.7% to 2.7% of cases, primarily during cervical dilation [11]. Although hysteroscopy is an operative procedure, its complication profile remains favorable. According to Castaing and colleagues [20], the rates of uterine perforation, hemorrhage, and metabolic disturbances were 4.8%, 0.6%, and 5.5%, respectively. Notably, most metabolic complications were asymptomatic. The investigation further noted a higher perforation rate in procedures addressing intrauterine synechiae, with complication risk correlating with the surgeon's level of experience [20].

Postoperative bleeding is the 2nd most frequent adverse event, with an incidence of 0.25%, and is most frequently associated with hysteroscopic myomectomy, which carries a complication rate of 2–3%. Persistent postoperative bleeding can be managed initially with intrauterine tamponade using a Foley catheter balloon inflated with fifteen to thirty mL of fluid. If bleeding remains uncontrolled, more advanced interventions such as administration of vasopressin or misoprostol, uterine artery embolization, or, in rare and severe cases, hysterectomy may be necessary. [21].

Conclusion

Hysteroscopy is a highly accurate and reliable tool for diagnosing partial septate uterus in cases with recurrent pregnancy loss, showing significant agreement with 3D ultrasound outcomes. Over the investigation period, hysteroscopy demonstrated excellent sensitivity and specificity in predicting uterine anomalies, matching the performance of advanced imaging techniques. These results suggest that hysteroscopy can serve as an effective diagnostic and therapeutic tool for optimizing outcomes in cases with RPL, particularly in settings where 3D ultrasound is less accessible**.**

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