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Hysteroscopy in the Evaluation of Recurrent First Trimesteric Miscarriages

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ABSTRACT

Background: Recurrent pregnancy loss (RPL) is one of the most painful and difficult areas of reproductive medicine since the explanation is often unknown. RPL is caused by uterine factors (both acquired and congenital). Hysteroscopy is the gold standard for evaluating the endometrial cavity because it allows direct sight of the endometrium.

Objective: This study aimed to evaluate the role of hysteroscopy in the assessment of cases with recurrent first trimesteric miscarriage.

Methods: This prospective cohort study was conducted on 164 women with recurrent first trimesteric miscarriages, who were referred to Early Cancer Detection Unit (ECDU) to undergo diagnostic hysteroscopy for various complaints. Women were asked to attend postmenstrual within 3-6 months following abortion. Hysteroscopy was done under local anesthesia. Before operation, all cases were subjected to full history taking, clinical examination and laboratory investigations as random blood glucose level, serum thyroid stimulating hormone (TSH), serum prolactin, anticardiolipin (IgG, IgM), follicle-stimulating hormone (FSH) and luteinizing hormone (LH).

Results: Abnormal hysteroscopic study was found in 53.0% of cases with recurrent first trimesteric miscarriages. Acquired uterine abnormalities were found in 27.4% of cases and it was more common than congenital uterine anomalies that were found in 25.6% of cases. The most common congenital uterine anomaly was uterine septum that was found in 20% of cases, while the most common acquired abnormality was uterine polyp (s) that was found in 11% of cases. 20% of these anatomical abnormalities were corrected hysteroscopically.

Conclusion: Hysteroscopy is safe, sensitive and reliable tool of diagnosis and could be performed at outpatient bases without anesthesia.

Keywords: Hysteroscopy, Pregnancy loss, Recurrent first trimesteric miscarriages.

INTRODUCTION

When a pregnancy spontaneously ends three times in a row, either before 20 weeks of pregnancy or before the foetus weighs 500 g, the condition is known as recurrent miscarriage [(1)]. Recurrent pregnancy loss has a significant impact on a couple's psycho-social status. Recurrent pregnancy losses can occur in up to 3% of women, and in about 50% of those cases, the underlying cause is idiopathic [(2)].

The aetiology of recurrent pregnancy loss can be divided into potentially treatable and currently untreatable etiologies based on their treatment potential. There are several possibly curable causes, including structural flaws, endocrine issues (luteal phase deficiency), thrombotic pregnancies (thrombophilia or autoantibodies), and immunological issues (immunoglobulins and immunization). Idiopathic etiologies and genetic anomalies are the situations that are now incurable [(3)].

Hysteroscopy is quite helpful in interpreting ambiguous results from other diagnostic modalities. Additionally, it improves accuracy in the evaluation of intrauterine anomalies and allows direct visualisation of the cervical canal and uterine cavity [(4)].

Uterine malformations can be acquired (such as submucous myomas, endometrial polyps, and adhesion) or congenital (such as Mullerian anomalies) [(5)]. Eight to ten percent of women who experience recurrent miscarriage have Mullerian defects, with uterine septum being the most frequent. The majority of the flaws can be fixed [(6)].

High rates of conception are reported following hysteroscopic metroplasty in septate uteri or hysteroscopic cutting of intrauterine adhesion, with a postoperative conception rate of 87% [(7)]. This work aimed to evaluate the role of hysteroscopy in the assessment of cases with recurrent first trimesteric miscarriage.

PATIENTS AND METHODS

This prospective cohort study was carried out on 164 women with recurrent (3 or more), first trimester miscarriage planned to undergo office (diagnostic) hysteroscopy to assess the uterine cavity. They attended to Ain shams University Maternity Hospital Early Cancer Detection Unit through the period from July 2018 to December 2018.

Inclusion criteria: Women with normal transvaginal ultrasound scan, lupus anticoagulants, anticardiolepin antibodies, complete blood count, sedimentation rate, progesterone level in the luteal phase were enrolled in

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the study. In addition, none of the patients was carrier of Neisseria gonorrhea, chlamydia trachomatis or syphilis and all husbands had a spermiogram within normal limits.

Exclusion criteria: Women with induced therapeutic abortion, proved cause (s) for RPL, acute or recent pelvic infection, suspected or confirmed pregnancy, uterine cavity pathology previously known to the examiner. Also, patients who had uncontrolled or undetected endocrinological conditions like diabetes or hypothyroidism or who were known to be carriers of balanced chromosomal abnormalities.

Study procedure:

All study participants were questioned about their personal history, including their full name, place of employment, and residence, as well as their obstetric history, including their date of marriage, parity, mode of delivery, number of miscarriages, length of each gestation, and whether or not it ended in a complete, incomplete, or missed abortion, and whether curettage was performed.

Complete gynecological history was taken including menstrual history as cycle regularity, last menstrual period, history of vaginal discharge, itching, dyspareunia, postcoital bleeding or any symptoms of sexually transmitted diseases.

We also asked all cases about their past surgical and medical histories as previous operations, hypertension, diabetes mellitus, thyroid dysfunction and thrombophilia weather congenital or acquired.

All tools were set up on a sterile tray so that the responsible consultant could conveniently reach them while the women were evaluated in the lithotomy posture. The consultant was sat on a chair with wheels for mobility.

Karl Storz, Tuttlingen, Germany produced the employed hysteroscopic apparatus, which included a rigid telescope and a 30o Hamou II hysteroscope (model 26157BT, with a Hopkins II lens system).

The Xenon Nova, model 20131520, produced by Storz, has a fiberoptic light source with a 5 mm outside diameter (Karl Storz).

Saline solution was the diversion medium. Hamou endomat infusion, model 26331020, 50 mL/min, 80 mmHg, and 0.2 psi of suction (pound per square inch).

The camera was a Karl Storz-endoskope with a Storz 20232020 telecom DXpal type. To display and record the hysteroscopic occurrences, use a TVCR LG plasma monitor at 50 Hz and AC 100-270 V.

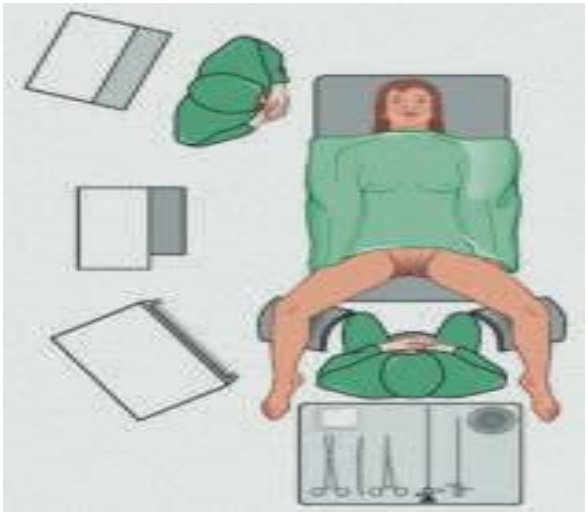


Figure (1): Patient, surgeon, and equipment placement in the operating room.

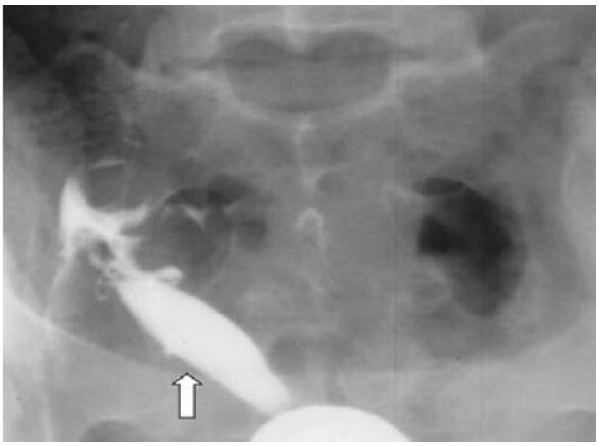
Figure (2): Telescope with in-out sheath with a side channel 4.5 mm (Storz, Tuttlingen, Germany), Early Cancer Detection Unit, Ain Shams Maternity Hospital.

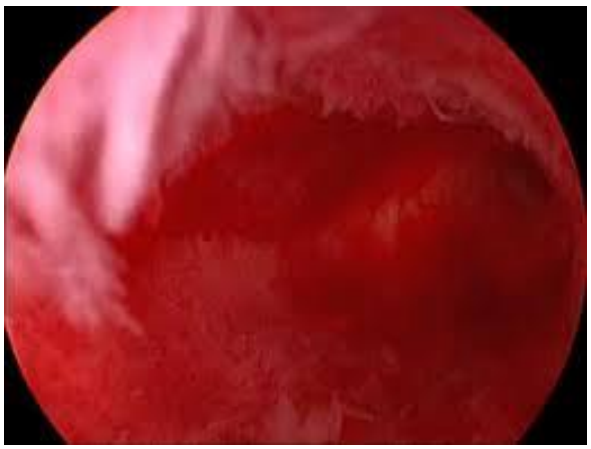
Figure (3): "Continuous suction irrigation pump "Endomat", Early Cancer Detection Unit, Ain Shams Maternity Hospital.

The hysteroscope was introduced without anesthesia, using saline as distension media, the patients sometimes expressed some pain ranging from mild, moderate, to severe, that was one of the obstacles for our study because this may make proper evaluation of the uterine cavity difficult.

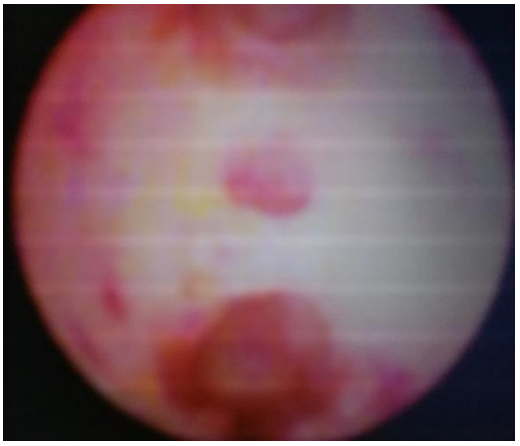
Vaginoscopy was done to assess any vaginal pathology and find the ectocervical os to be entered then evaluation of cervical canal for adhesions, polyps, stenosis and fibroid or any other unexpected pathology can be seen, then from endocervix to the uterine cavity, assessment of endometrium, uterine fundus and tubal ostia for any pathology was done.

Some cases required a vaginoscopic examination, while others required the use of a cervical volcellum and Sim's speculum. According to the table of attendance for each patient in the study, there were many operators to perform the hysteroscopy for them.





Case (1): 24 years old, nulliparous, 65 kg weight and 1.59 m height, BMI 26, married for 6 years with 4 recurrent first trimester abortions, all terminated by missed abortion, HSG showed unilateral spilling, and hysteroscopy showed solitary uterine horn with single tubal ostia.



Case (2): 30 years, 72 kg, 1.58 m height, married for 11 years, para1 circulage done and delivered normally, followed by 3 recurrent first trimester miscarriages, 2 ended by missed miscarriage and 1 ended by complete miscarriage, then 2 second trimester miscarriages ended by missed abortion, HSG showed subseptate versus bicornuate uterus, hysteroscopy showed uterine septum dividing the uterine cavity to a distance.

Confidentiality

Only the patient's number and initials were entered on the case report form, and the investigators were required to maintain patient confidentiality if the patient's name appeared on any other document (such as an imaging scan report). In order to enable records to be identified, the investigator kept a personal patient identification list (patient numbers with the matching patient names).

Ethical consent: This study was approved by Ain Shams University Ethical Committee. Informed written consents were obtained from all included women after explanation. This study was conducted in accordance with the local ethical committee regulations and according to the Declaration of Helsinki.

Statistical analysis

Statistical Package for Social Sciences (SPSS) version 22 for Windows was used to code, process, and analyse the obtained data (IBM SPSS Inc., Chicago, IL, USA). Using the Shapiro Walk test, the distribution of the data was examined for normality.

Frequencies and relative percentages were used to depict qualitative data. Quantitative data were presented as mean ± SD (Standard deviation).

In order to evaluate the effectiveness of real-time fibrosis prediction among patient groups, ROC curve analysis was built. Two independent groups of normally distributed variables were compared using the independent samples t-test (parametric data). P value ≤ 0.05 was regarded as significant.

RESULTS

The mean of age for our patients was 32 years, and the mean of BMI was 25.7 kg/m^2 **(Table 1).**

Table (1): Demographic characteristics of the whole study population

					Percentiles		
Variable	Min.	Max.	Mean	SD	25th p.	50th p.	75th p.
Age (years)	17	45	32	7	27	31	37
Weight (kg)	46	85	66	9	59	67	73
Height (m)	1.49	1.75	1.61	.05	1.57	1.61	1.64
BMI (kg/m^2)	18.3	34.6	25.7	3.5	23.1	25.7	27.9

The mean of parity was 1, and the mean of previous abortions was 5 **(Table 2).**

Table (2): Frequency of previous deliveries and abortions in the study population

					Percentiles		
Variable	Min.	Max.	Mean	SD	25th p.	50th p.	75th p.
Frequency of previous deliveries	0	5	1	1	0	0	1
Frequency of previous abortions	3	33	5	4	3	4	5

The largest proportion of our study population was 45.1% had three miscarriages **(Table 3)**.

Table (3): Frequency of previous abortions in the study population

Variable		**Frequency**	**Percent**	**Cumulative Percent**
Frequency of previous abortions	3 abortions	74	45.1	45.1
	4 abortions	33	20.1	65.2
	5 abortions	19	11.6	76.8
	6 abortions	12	7.3	84.1
	7 abortions	7	4.3	88.4
	8 abortions	6	3.7	92.1
	9 abortions	2	1.2	93.3
	10 abortions	5	3.0	96.3
	≥11 abortions	6	3.7	100.0

Normal hysteroscopic examination was the highest percentage 47% of the participants in our study, and the women who experienced repeated first trimester losses had the highest incidence of the uterine septum **(Table 4)**.

Table (4): Results of hysteroscopic examination

Variable		Frequency	Percent
Hysteroscopic findings	Normal	77	47.0%
	Uterine septum	33	20.1%
	Endometrial polyp(s)	18	11.0%
	Submucous fibroid	10	6.1%
	Bicornuate uterus	4	2.4%
	Adhesion(s)	16	9.8%
	Arcuate uterus	4	2.4%
	Cervical polyp	1	0.6%
	Unicornuate uterus	1	0.6%
Ultimate result of hysteroscopic examination	Normal hysteroscopic findings	77	47.0%
	Abnormal hysteroscopic findings	87	53.0%

34 cases (20.8%) underwent hysteroscopy assisted interventions, 17 cases (10.4%) underwent septal resection, 8 cases (4.0%) underwent adhesiolysis, 6 cases (3.7%) underwent polypectomy and 3 cases (1.8%) underwent myomectomy **(Table 5)**.

Table (5): Rate of performing hysteroscopy-assisted interventions in the whole study population

Variable	Frequency	Percentage
Interventional hysteroscopy	34	20.8%
Septal resection	17	10.4%
Adhesiolysis	8	4.0%
polypectomy	6	3.7%
myomectomy	3	1.8%

Patients with abnormal hysteroscopic findings had significantly fewer number of previous miscarriages compared to those with normal hysteroscopy (median [IQR] = 3 [3 to 5] versus 4 [3 to 6], respectively, p-value = 0.025) **(Table 6)**.

Table (6): Comparison of the frequency of previous deliveries and abortions in patients with normal or abnormal hysteroscopy findings

	Normal hysteroscopic findings (n=77)			**Abnormal hysteroscopic findings (n=87)**			
Variable	Median	IQR	Mean rank	Median	IQR	Mean rank	p-value*
Frequency of previous deliveries	1	0 to 1	86.4	0	0 to 1	79.1	0.286
Frequency of previous abortions	4	3 to 6	90.9	3	3 to 5	75.1	**0.025**

The results of receiver-operating characteristic (ROC) curve analysis for discrimination between patients with normal or abnormal hysteroscopic findings using the frequency of previous abortions. The frequency of previous abortions had modest diagnostic value as a predictor for abnormal hysteroscopy findings with an area under the ROC curve of 0.596 (95% CI = 0.517 to 0.672, p-value = 0.023). The best cut-off criterion was a frequency of ≤ 5 abortions, which had a sensitivity of 85.1%, specificity of 32.5%, positive predictive value (+PV) of 58.7% and negative predictive value (-PV) of 65.8% **(Table 7)**.

Table (7): Receiver-operating characteristic (ROC) curve analysis for discrimination between patients with normal or abnormal hysteroscopic findings using the frequency of previous abortions

Variable	Value	95% CI
Area under the ROC curve (AUC)	0.596	0.517 to 0.672
z statistic	2.272	
P-value (AUC0=0.5)*	**0.023**	
Youden index J	0.1753	
Associated cutoff criterion	≤5	
Sensitivity	85.1%	75.8% - 91.8%
Specificity	32.5%	22.2% - 44.1%
Positive likelihood ratio (+LR)	1.26	1.1 - 1.5
Negative likelihood ratio (-LR)	0.46	0.3 - 0.8
Positive predictive value (+PV)	58.7%	54.4% - 63.0%
Negative predictive value (-PV)	65.8%	51.4% - 77.7%

DISCUSSION

Our study found that hysteroscopy has a major role in detection of possible uterine causes of miscarriage in women with recurrent first trimesteric miscarriages like (uterine septum, endometrial polyp(s), submucous fibroid, bicornuate uterus, intrauterine adhesion(s), arcuate uterus, cervical polyp and unicornuate uterus).

One of the challenges we encountered was the lack of a single operator assigned to perform hysteroscopy on the entire study population. Instead, doctors performed it in accordance with the attendance chart in the unit, and occasionally it was challenging to perform vaginoscopy, necessitating the use of Sims speculum and volcellum.

In this study we found that, the mean maternal age of our study population was 32 ± 7 years. This is consistent with **De souza *et al.*** [8] and **Bohlmann *et al.*** [9] who found that it was 31-39 and 32.95 ± 4.46 years respectively. We disagree with **Ventolini *et al.*** [10] and **Alobaidy *et al.*** [11] who reported that mean maternal age was 28.1 and 27.9 ± 3.4 respectively that might be attributed to racial and social factors.

In this study, the mean BMI was 25.7 ± 3.5 kg/m^2. This agrees with **Alobaidy *et al.*** [11] where it was 26.3 ± 2.3 and disagrees with **De souza *et al.*** [8] where it was 23.4 that might be attributed to higher prevalence of obesity in our population.

In this study, major proportion of the patients were nulliparous 84 cases (51.2%), with mean number of previous deliveries of 1 ± 0.2. The following studies found almost same results, **Bohlmann *et al.*** [9] found that 54.5% where nullipara, and **De souza *et al.*** [8] study had a mean of previous deliveries of 0.5 ± 1. While **Alobaidy *et al.*** [11] found different results with 68% nulliparity, **Elsokkary *et al.*** [12] also disagrees with 88% nulliparity. In **Weiss *et al.*** [13] the mean of previous deliveries of 5.08 ± 2.29 was much higher than ours this could be due to decreased awareness of antenatal care in our patients.

Our cases had a history of previous miscarriages at the mean of 5 ± 3 with minimum of 3 and maximum of 28 abortions, most of the patients (45.1%) had 3 abortions. This is consistent with **Elsokkary *et al.*** [12] in which the mean of previous miscarriages was (3-5), **Bohlmann *et al.*** [9] with mean of 3.74 ± 1.09, and **Camuzcuoglu *et al.*** [14] with mean of 3.62. **De souza *et al.*** [8] reported a mean of 3**,** and **Alobaidy *et al.*** [11] showed a mean of 3.2 ± 1.1. However the higher number of previous abortions in our study population might be attributed to late obstetric consultation.

In our study, patients with abnormal hysteroscopy findings had significantly fewer number of previous abortions compared to those with normal hysteroscopy (IQR=3 versus 4 respectively, p-value=0.025).

The frequency of prior abortions has a modest diagnostic value as a predictor for abnormal hysteroscopy findings, according to the receiver operating characteristic (ROC) curve analysis for discrimination between patients with normal or abnormal hysteroscopic findings using the frequency of prior abortions, with an area under the ROC curve of 0.596 (95% confidence interval =0.517 to 0.672).

Hysteroscopic work up of our study population showed that 77 cases (47%) of our patients had normal hysteroscopy of endometrial cavity, cervical canal and tubal ostia apart from some variations and abnormalities in endometrial thickness, which could be dysfunctional. **Bohlmann *et al.*** [9]**, Elsokkary *et al.*** [12] and **Moiety *et al.*** [15] nearly found similar results (54.5%), (42.9%) and (43.8%) of study population had abnormal hysteroscopic findings respectively. Whereas, **De souza *et al.*** [8]**, Ventolini *et al.*** [10]**,** **Weiss *et al.*** [13]**,** and **Camuzcuoglu *et al.*** [14]

found different results with 33.3%, 39.1%, 31% and (70.8%) of their study cases had abnormal hysteroscopic findings respectively.

In our study the uterine septum was the most common uterine anomaly affecting 33 cases (20.1%) of our cases with recurrent first trimesteric abortions. This result is similar to **Bohlmann *et al.*** [9], **Elsokkary *et al.*** [12], **Weiss *et al.*** [13] and **Moiety *et al.*** [15]. While, in **Ventolini *et al.*** [10] and **Camuzcuoglu *et al.*** [14] the uterine adhesion(s) were the most common.

Although the exact process by which a septate uterus results in pregnancy loss is unknown, one theory suggests that insufficient blood flow to the septum causes poor implantation [16].

Endometrial polyp (s) were the second most common uterine anomaly found in 18 cases (11.0%) of our study population. This agrees with **Al Chami and Saridogan** [17] and **El-bareg *et al.*** [18] and disagrees with **De souza *et al.*** [8], **Ventolini *et al.*** [10] and **Weiss *et al.*** [13]**.** Endometrial polyps are uterine mucosa focused growths made up of stroma, blood vessels, and endometrial glands. According to **Clark *et al.*** [19]**,** 10% of all females are thought to have uterine polyps. The best method for determining whether a woman has endometrial polyps is still hysteroscopy. Additionally, hysteroscopy enables concurrent treatment for endometrial abnormalities such polyps and tiny submucous fibroids [17].

Intrauterine adhesions in our study population was found in 16 cases (9.8%). This is consistent with **Bohlmann *et al.*** [9] and **Weiss *et al.*** [13] where adhesions were found in (9.8%) and (11%) respectively. Endometritis, curettage, surgical removal of myomas, repair of uterine structural deformities, and caesarian section are the most common causes of intrauterine adhesions. Abortion can result from a decrease in the endometrial surface area available for embryo implantation or from problems with uterine growth [20].

In our study submucous myoma (s) were present in 10 cases (6.1%). **Bohlmann *et al.*** [9] agrees with us 7.6% and 5% in **El-bareg *et al.*** [18]. There is much discussion about the role that polyps and myomas play in the development of abortion. The mere entry of one of them into the uterine cavity can negatively impact fertility and implantation by fostering an unfavourable environment [17]. In spite of the fact that myomas are typically asymptomatic during pregnancy, there is evidence linking them to a higher risk of infertility, spontaneous abortion, and preterm labour. According to estimates, about (41%) of women with myomas, particularly sub mucous ones, may experience an abortion [21].

Bicornuate uterus was found in 4 cases (4.5%), because it mostly causes second trimester miscarriages.

Also we had arcuate cavity in 4 cases 2.4% and unicornuate uterus in 1case (0.6%). Of these 164 women with recurrent first trimester miscarriage, 34 cases (20.8%), underwent hysteroscopic assisted interventions, in 17 cases (10.4%) septal resection was done, in 8 cases (4.0%) adhesiolysis was achieved, in 6cases (3.7%) polypectomy was done and sent for histopathology and in 3 cases (1.8%) myomectomy was done. These results agree with **Elsokkary *et al.*** [12]**.**

CONCLUSION

Hysteroscopy is a reliable, sensitive, and safe diagnostic technique that can be used as an outpatient procedure without the need for general anaesthesia. The most reliable technique for evaluating the uterine cavity is hysteroscopy. Possible uterine reasons of recurrent miscarriage may be diagnosed and occasionally treated by hysteroscopy. Atypical hysteroscopic findings were present in 53% of the study population with recurrent first trimester miscarriages. Women who experienced repeated first-trimester miscarriages may be caused by uterine morphological anomalies, which are mostly uterine septum.

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REFERENCES

1. **Trojano G, Malvasi A, Caroli Casavola V *et al.* (2018):** Outpatient hysteroscopy in recurrent pregnancy loss. Hysteroscopy, 18: 211-21.
2. **El Sayed M, Ahmed A, Sultan E (2022):** Office Hysteroscopy in Recurrent Abortion. Al-Azhar International Medical Journal, 3 (9): 38-43.
3. **Elmandooh M (2016):** Validity of hysteroscopy in detection of uterine cavity abnormalities in women with recurrent pregnancy loss. Journal of Gynecological Research and Obstetrics, 2 (1): 26-30.
4. **Gkrozou F, Tsonis O, Dimitriou E *et al.* (2020):** In women with chronic or subclinical endometritis is hysteroscopy suitable for setting the diagnosis? A systematic review. Journal of Obstetrics and Gynaecology Research, 46 (9): 1639-50.
5. **Kinkel K, Ascher S, Reinhold C (2018):** Diseases of the Abdomen and Pelvis 2018-2021: Diagnostic Imaging - IDKD Book, Pp: 21-33. https://www.ncbi.nlm.nih.gov/books/NBK543803/

6. **Schlegel P, Sigman M, Collura B *et al.* (2020):** Diagnosis and Treatment of Infertility in Men: AUA/ASRM Guideline part II. Fertil Steril., 115 (1): 62-69.
7. **Corroenne R, Legendre G, May-Panloup P *et al.* (2018):** Surgical treatment of septate uterus in cases of primary infertility and before assisted reproductive technologies. Journal of Gynecology Obstetrics and Human Reproduction, 47 (9): 413-8.
8. **Souza C, Schmitz C, Genro V *et al.* (20**
9. **11):** Office hysteroscopy study in consecutive miscarriage patients. Journal of the Brazilian Medical Association, 57: 404-8.
10. **Bohlmann M, von Wolff M, Luedders D *et al.* (2010):** Hysteroscopic findings in women with two and with more than two first-trimester miscarriages are not significantly different. Reproductive Biomedicine Online, 21 (2): 230-6.
11. **Ventolini G, Zhang M, Gruber J (2004):** Hysteroscopy in the evaluation of patients with recurrent pregnancy loss: a cohort study in a primary care population. Surgical Endoscopy, 18 (12): 1782-4.
12. **Alobaidy E (2018):** Comparison the diagnostic accuracy of hysterosalpingography and hysteroscopy in the detection of intrauterine abnormality in recurrent pregnancy loss. Journal of Pharmaceutical Sciences and Research, 10 (4): 900-2.
13. **Elsokkary M, Elshourbagy M, Labib K *et al.* (2018):** Assessment of hysteroscopic role in management of women with recurrent pregnancy loss. The Journal of Maternal-Fetal & Neonatal Medicine, 31 (11): 1494-504.
14. **Weiss A, Shalev E, Romano S (2005):** Hysteroscopy may be justified after two miscarriages. Human Reproduction, 20 (9): 2628-31.
15. **Camuzcuoglu H, Yildirim Y, Sadik S *et al.* (2005):** Comparison of the accuracy of hysteroscopy and hysterosalpingography in evaluation of the uterine cavity in patients with recurrent pregnancy loss. Gynecological Surgery, 2 (3): 159-63.
16. **Moiety F, Agameya A, Saleh H (2018):** Recurrent Miscarriage: Hysteroscopy-Assisted Management. Open Journal of Obstetrics and Gynecology, 8 (05): 425-30.
17. **Bashiri A, Halper K, Orvieto R (2018):** Recurrent Implantation Failure-update overview on etiology, diagnosis, treatment and future directions. Reprod Biol Endocrinol., 16 (1): 121. doi: 10.1186/s12958-018-0414-2.
18. **Al Chami A, Saridogan E (2017):** Endometrial polyps and subfertility. The Journal of Obstetrics and Gynecology of India, 67 (1): 9-14.
19. **Elbareg A, Elmahashi M, Essadi F (2015):** Evaluation of intrauterine pathology: efficacy of diagnostic hysteroscopy in comparison to histopathological examination. Reprod Syst Sex Disord., 4 (149): 2. http://dx.doi.org/10.4172/2161-038X.1000149
20. **Clark P, Walker I, Langhorne P *et al.* (2010):** SPIN (Scottish Pregnancy Intervention) study: a multicenter, randomized controlled trial of low-molecular-weight heparin and low-dose aspirin in women with recurrent miscarriage. The Journal of the American Society of Hematology, 115 (21): 4162-7.
21. **Alamo L, Vial Y, Denys A *et al.* (2018):** MRI findings of complications related to previous uterine scars. European Journal of Radiology Open, 5: 6-15.
22. **Lee H, Norwitz E, Shaw J (2010):** Contemporary management of fibroids in pregnancy. Reviews in Obstetrics and Gynecology, 3 (1): 20-27.