

Evaluation of the compatibility of ultrasound and hysteroscopic findings and histopathological results in women with abnormal uterine bleeding (AUB)

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ABSTRACT

Background and aim: This study aimed to determine the compatibility of ultrasound and hysteroscopy findings and histopathological results in women with abnormal uterine bleeding. Due to the high prevalence of cesarean section in our country and since less attention has been paid to cesarean section defects (isthmocoele) as a cause of abnormal uterine bleeding, even in cases where hysteroscopy findings and ultrasound are not fully matched, in the present study, the presence of isthmocoele during hysteroscopy and its compliance with the ultrasound reports is examined.

Material and method: In this cross-sectional study, 913 women with abnormal uterine bleeding who met the inclusion criteria, were studied. After obtaining written consent from the patients, hysteroscopy was performed under local or general anesthesia, and ultrasonography was also performed. If polyps or myoma were observed, the resection was performed using scissors or a resect scope. The site of cesarean section defects was also examined by hysteroscopy. In the absence of focal lesions, endometrial curettage was performed, and all samples were sent for pathological examination. Data were entered into SPSS software, version 23, and analyzed.

Results: The study included 913 patients with abnormal uterine bleeding (AUB) with an average age of 41.13±9.22. The mean duration of AUB in patients was 10.97±14.61 months. The most common form of bleeding was intermenstrual spotting, which was seen in 27.7% of patients, followed by menorrhagia in 26.4% and menometrorrhagia in 21.1%. In ultrasonography findings, the most common findings were polyp and then myoma in 38.1% and 20.0% of patients, respectively. In hysteroscopy, the most common findings were polyp, myoma, and normal evaluation, respectively. A positive and significant correlation was found between the presence of isthmocoele in ultrasonography and the number of cesarean sections (CC=0.189, p-value=0.0001) and the duration of bleeding (CC =0.086, p-value=0.009), and there was also a positive and significant correlation between isthmocoele finding in hysteroscopy with the number of cesarean sections (CC=0.566, p-value=0.0001) and parity (CC=0.200, p-value=0.0001). An inverse and significant correlation was also observed between the age of patients and abnormal pathological findings in ultrasonography and hysteroscopy. Based on the kappa coefficient (19.2%), hysteroscopy was a more appropriate method in diagnosing patients with AUB.

Conclusion: The ultrasound and hysteroscopy diagnostic methods demonstrated appropriate sensitivity in investigating cases of abnormal uterine bleeding. However, the hysteroscopy was actually useful in diagnostic experiments of AUB.

Keywords: ultrasound, hysteroscopy, histopathology, abnormal uterine bleeding, isthmocoele

INTRODUCTION

Abnormal uterine bleeding (AUB) is one of the most common gynecological problems in premenopausal women [1, 2]. It is one of the most common causes of women's referral to a gynecologist [3]. This problem affects about 20% of women of reproductive age and causes almost two-thirds of all hysterectomy cases [4].

On the other hand, gynecologists are often unable to identify the cause of abnormal bleeding after histopathological and clinical examinations [5, 6]. Different causes of abnormal uterine bleeding include pregnancy problems, infections, vaginal and cervical problems, benign and malignant neoplasms, coagulation disorders, endocrine problems, trauma, foreign body, systemic diseases leading to bleeding, and the use of some drugs. It should be noted that diagnostic evaluations and treatment methods for this problem have been evolving [7, 8].

Dilatation and curettage (D&C) is a conventional evaluation to investigate the causes of abnormal uterine

bleeding from the past to present [5, 6]. This is an invasive procedure and endometrial tissue must be sent to a laboratory for pathology evaluation, and the pathologist's accuracy and skill are also critical [7]. On the other hand, this method causes discomfort to the patient and imposes additional costs on the patient and the health care system [8].

It has been shown that prop and high-resolution ultrasound waves provide reliable information about the pelvic organs and allow for rapid assessment of the uterus and adnexa. It is known to have no adverse effects and can, therefore, be repeated several times [9].

Abnormal uterine bleeding has recently been identified and described as one of the gynecological consequences of isthmocoele [1, 10]; therefore, isthmocoele should be explicitly considered in cases where other causes have been ruled out in women with abnormal uterine bleeding and a history of cesarean section [10, 11].

Today, hysteroscopy is the best way to diagnose cesarean section defects and also allows for surgical treatment. In this regard, studies have been conducted outside of Iran; for instance, Wanderley et al. [12] evaluated the accuracy of transvaginal and hysteroscopy ultrasound and uterine curettage in endometrial pathology. Based on hysteroscopy results, the diagnostic accuracy of this method is higher than 90 % for all problems. In comparison, the diagnostic accuracy of transvaginal ultrasound is 65.9% for polyps, 78.1% for myoma, and 63.2% for endometrial hyperplasia.

Due to the high prevalence of cesarean section in our country [13] and since less attention has been paid to cesarean section defects (isthmocele) as a cause of abnormal uterine bleeding, even in cases where hysteroscopy findings and ultrasound are not fully matched [2, 14, 15], in the present study, the presence of isthmocele during hysteroscopy and its compliance with the ultrasound report is examined. Accordingly, this study aimed to determine the compatibility of ultrasound and hysteroscopy findings and histopathological results in women with abnormal uterine bleeding.

MATERIALS AND METHODS

The purpose of this descriptive study and cross-sectional analysis is to evaluate the compliance of ultrasound and hysteroscopy findings with the results of histopathology in women with AUB. This study was performed in Arash Women's Hospital, after receiving the necessary permits and approval of the ethics committee of Tehran University of Medical Sciences.

Inclusion criteria: All women in reproductive ages and over 18 years of age, and postmenopausal women who had abnormal uterine bleeding or abnormal ultrasound findings, including polyps, myoma, or increased endometrial thickness (more than 5 mm in menopausal women and more than 15 mm in reproductive age) and were candidates for hysteroscopy, were included in the study.

Exclusion criteria: Exclusion criteria included coagulation disorders [12], pelvic inflammatory diseases [16], or patients with a previous diagnosis of endometrial carcinoma [13] or under treatment for endometrial hyperplasia [4].

Study method: The study included 913 women with abnormal uterine bleeding, who met the inclusion criteria of the study. After obtaining written consent from the patients, explaining the purpose of the study, and full examination and recording the history of patients, hysteroscopy was performed under local or general anesthesia with a 30-degree (Karl Storz hysteroscope) and a diameter of 5 mm using normal saline media, and ultra-sonography was also performed. If polyps or myoma were observed, the resection was performed using scissors or a resect scope.

In the absence of focal lesions, endometrial curettage was performed, and all samples were sent for pathological examination. Also, in patients with a history of previous cesarean section, during the hysteroscopy, the site of the cesarean scar was observed in terms of the presence of isthmocele (defect at the site of the cesarean section) and, if necessary, hysteroscopic resection was performed.

The findings of ultrasound were compared with the observations made during hysteroscopy and the histopathological results of the samples. In this study, the pathological results of secretory/proliferative/atrophic endometrium were considered as normal results, and the results of simple or complex hyperplasia / with or without atypia, carcinoma, polyps, and myoma were considered as abnormal results.

Statistical Analysis: Data were entered into SPSS software, version 23, and analyzed. Clinical features and results of imaging studies in patients were described by descriptive methods, including frequency distribution and percentage, as well as tables and graphs. The statistical methods of T-test and chi-Square were also used to compare the groups. Using the Kappa coefficient test, the value of the agreement between the two methods of ultrasound and hysteroscopy was evaluated, and finally, based on the pathological results, the two methods were compared with each other. The correlation between total cases with isthmocele in ultra-sonographic findings and age, parity, number of cesarean, polyp, myoma time of bleeding, type of pathology (normal/abnormal), and total cases with isthmocele in hysteroscopic findings was investigated with Spearman's correlation test. A p-value of less than 0.05 was considered significant.

RESULTS

The study included 913 patients with abnormal uterine bleeding (AUB) with a mean age of 41.13 ± 9.22 years old, with a minimum age of 18 years and a maximum age of 73 years. The mean duration of abnormal uterine bleeding in patients was 10.97 ± 14.61 months. The lowest bleeding time was 15 days and the longest period was 5 years.

Among patients, 131 people (14.3%) had no history of pregnancy at all; 25.6% and 35.3% of patients had a history of one and two pregnancies, respectively. The other number of pregnancies is shown in Figure 1.

Patients were also examined for the number of cesarean sections and among them, 492 (53.9%) patients had no history of cesarean section, while 21.7% had 1 C/S, 18.4% had two, and 5.4% had a history of cesarean section for three times (Table 1). Also, according to Table 1 and Figure 2, the most common form of bleeding was intermenstrual Spotting, which was seen in 27.7% of patients, followed by menorrhagia in 26.4% and menometrorrhagia in 21.1%.

The findings of ultrasonography and hysteroscopy obtained from patients with AUB showed that the most common findings were polyp (38.1% and 34.1%, respectively) and then myoma (20.0% and 15.6%, respectively). It should be noted that in ultrasonography and hysteroscopy, 27 cases (3%) and 162 cases (17.7%) of patients with isthmocele were found, respectively (Table 2).

Based on Table 3 and Figure 3, the frequency of pathological findings was also investigated and the most common pathological findings were polyp (48.08%) and myoma (16.4%), respectively.

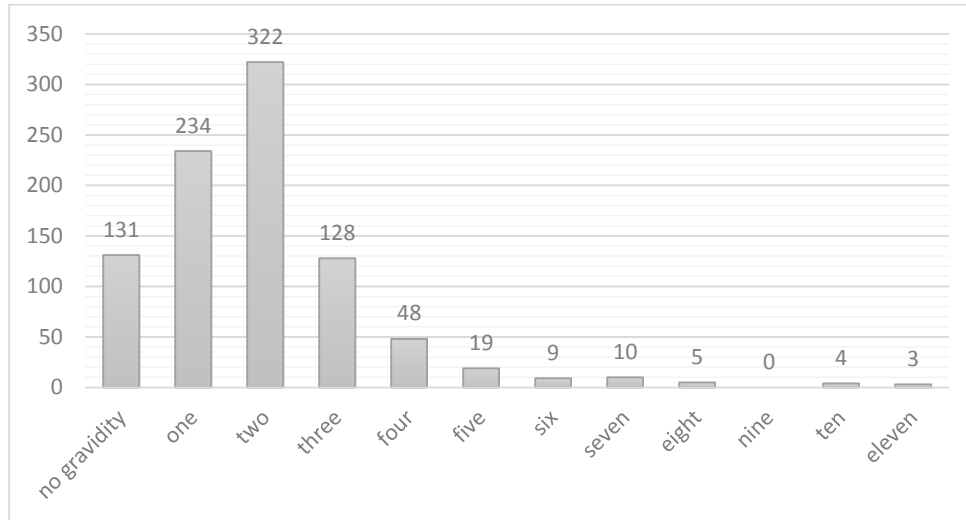


Figure 1. Frequency of gravidity in patients with abnormal uterine bleeding (AUB)

Table 1. frequency of cesarean section history and AUB pattern in patients

variable		N	%
History of cesarean section	no	492	53.9
	1	198	21.7
	2	168	18.4
	3	49	5.4
	4	5	0.5
	5	1	0.1
AUB pattern	polymenorrhagia	32	3.5
	oligomenorrhea	29	3.2
	menorrhagia	241	26.4
	metrorrhagia	75	8.2
	menometrorrhagia	193	21.1
	intermenstrual Spotting	253	27.7
	postmenopausal bleeding	90	9.9

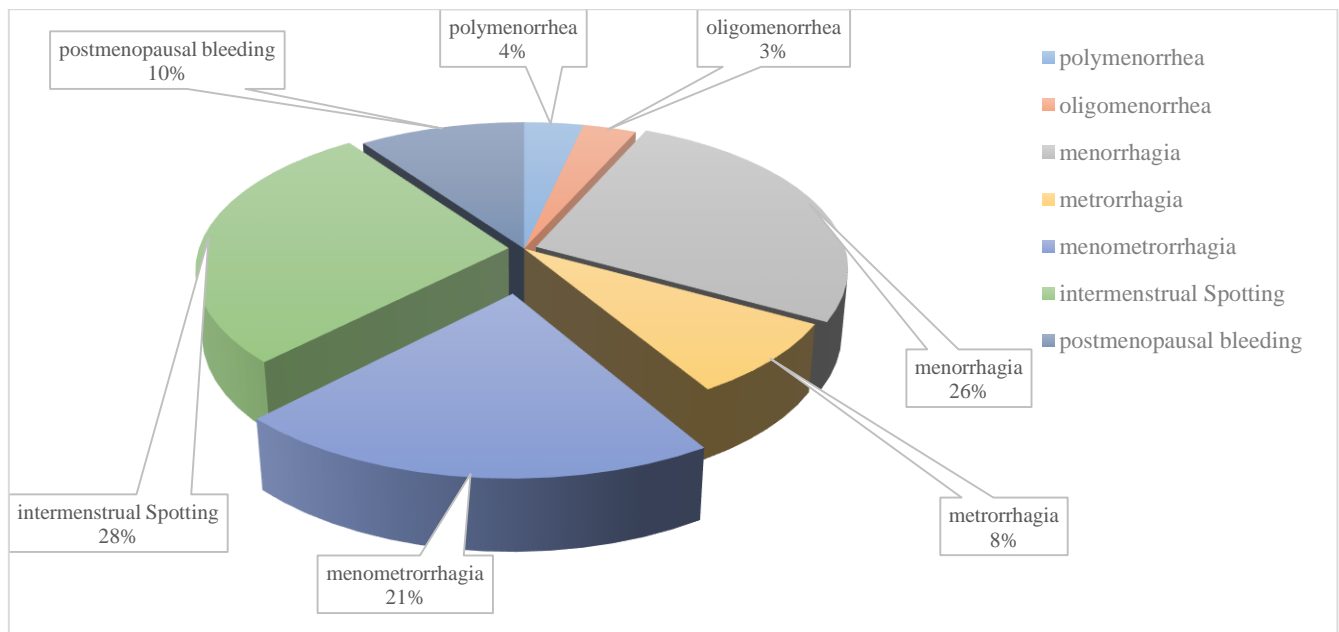


Figure2. Frequency pattern of AUB in patients

Table 2. Frequency of ultrasonography and hysteroscopy findings obtained from patients with AUB

Variable	Findings	N	%
Ultrasonography findings	Normal evaluation	109	11.9
	myoma	183	20.0
	polyp	348	38.1
	hyperplasia	108	11.8
	residual pregnancy tissue	71	7.8
	Isthmocele	27	3.0
	Polyp +myoma	67	7.3
Total		913	100.0
Hysteroscopy findings	Normal evaluation	134	14.7
	myoma	142	15.6
	polyp	311	34.1
	hyperplasia	84	9.2
	residual pregnancy tissue	56	6.1
	Isthmocele	162	17.7
	Polyp +myoma	24	2.6
Total		913	100.0

Table 3. Frequency of pathologic findings and type of pathologic findings obtained from patients with AUB

Variable	findings	N	%
pathologic findings	secretory Endometria	80	8.8
	proliferative Endometria	106	11.6
	atrophic Endometria	7	.8
	hyperplasia simple or complex/with or without atypia	39	4.3
	Carcinoma	9	1.0
	Myoma	150	16.4
	Polyp	439	48.08
	residual pregnancy tissue	65	7.1
Total	Normal evaluation	6	.7
Total		913	100.0
Type of pathologic findings	Normal	259	28.4
	Abnormal	654	71.6

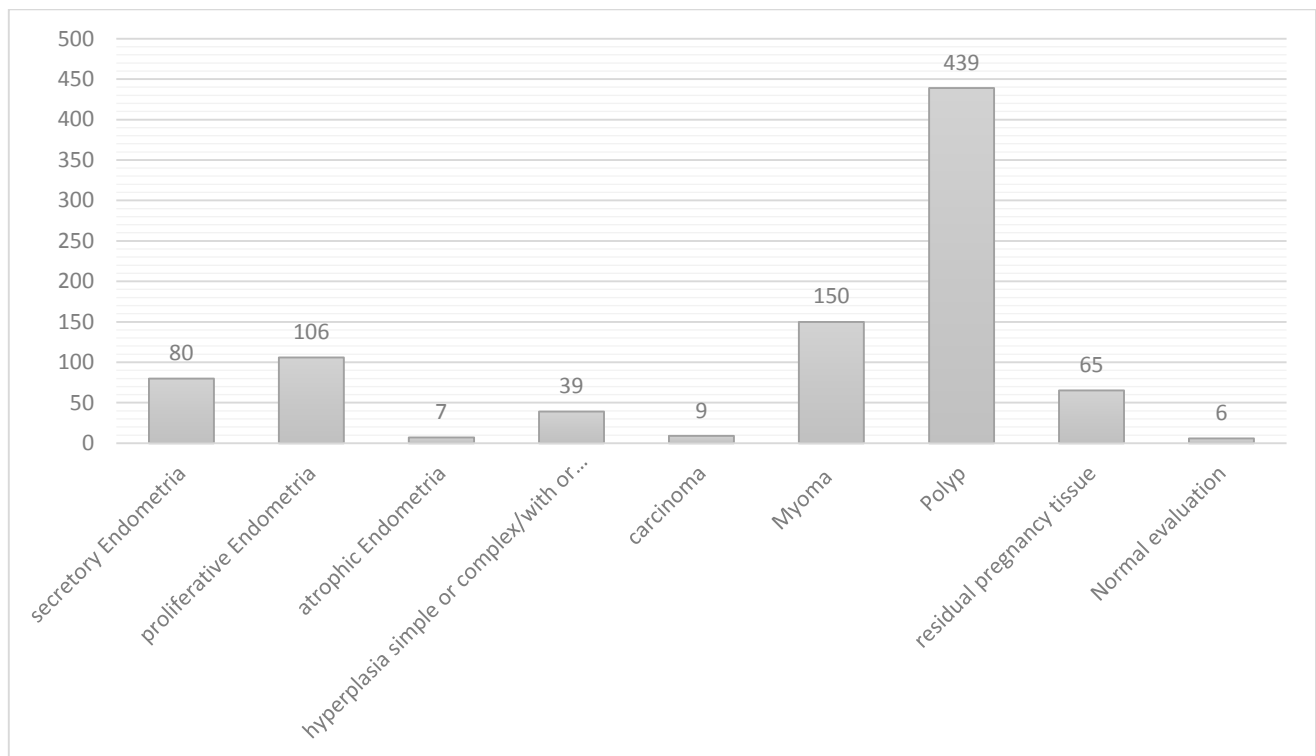


Figure-3. Frequency of pathologic findings obtained from patients with AUB

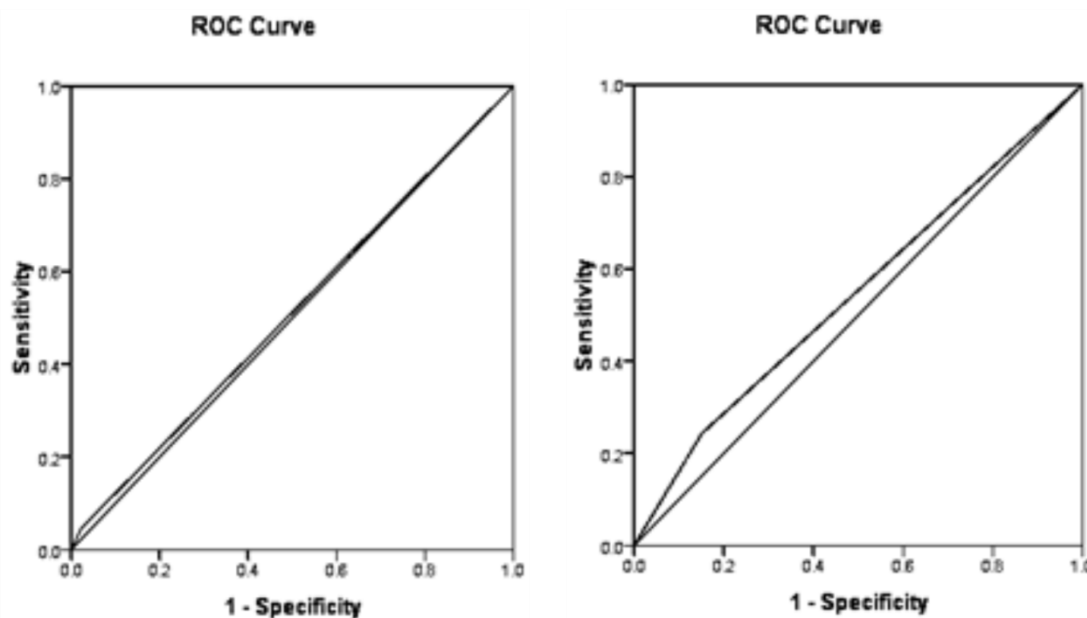
Table 5. Spearman's correlation between Total cases with isthmocele in ultra-sonographic findings and Total cases with isthmocele in Hysteroscopy findings with age, parity, cesarean, Time of Bleeding, Type of pathology

Spearman's rho	Correlations		Age	parity	C/S	Time Of Bleeding	Type of pathology (normal/abnormal)	Total cases with isthmocele in ultra-sonographic findings	Total cases with isthmocele in Hysteroscopy findings
		Total cases with isthmocele in ultrasonographic findings	Correlation Coefficient	-0.089	0.021	0.189	0.086	-0.062	1.000
		Sig. (2-tailed)	0.007	0.530	0.0001	0.009	0.060	.	0.0001
	Total cases with isthmocele in Hysteroscopy findings	Correlation Coefficient	0.017	0.200	0.566	0.020	-0.108	0.291	1.000
		Sig. (2-tailed)	0.608	0.0001	0.0001	0.536	0.001	0.0001	.

Table 5. Kappa test for ultra-sonographic and Hysteroscopy in isthmocele finding Cross tabulation

Variable		isthmocele in Hysteroscopy		p-value=0.0001
		no	yes	
isthmocele in ultra-sonographic	No	number	746	140
		% in ultra-sonographic	84.2%	15.8%
		% in Hysteroscopy	99.3%	86.4%
	Yes	number	5	22
		% in ultra-sonographic	18.5%	81.5%
		% in Hysteroscopy	0.7%	13.6%

Figure 4. Roc curves were drawn to determine the sensitivity and susceptibility of two ultra-sonographic (A), hysteroscopy (B) methods in the diagnosis of isthmocele with normal pathological findings.



The correlation between total cases with isthmocele in ultrasonographic and hysteroscopic findings has been shown in Table 4. A positive and significant correlation was found between the presence of isthmocele in ultrasonography and the number of cesarean sections (CC=0.189, p-value=0.0001) and the duration of bleeding (CC =0.086, p-value=0.009). There was also a positive and significant correlation between isthmocele finding in hysteroscopy and the number of cesarean sections (CC=0.566, p-value=0.0001) and parity (CC=0.200, p-value=0.0001). On the other hand, an inverse and significant correlation have been observed between age and abnormal pathological findings, (CC=-0.108, p-

value=0.0001) in ultrasonographic and hysteroscopic findings, which means that with the increase in age, the findings of isthmocele in hysteroscopy will decrease.

Kappa coefficient test has been used to investigate the agreement between ultrasonographic and hysteroscopy methods in finding cases of isthmocele in patients with AUB. Based on the results shown in Table 5, the significance level of this test was p = 0.0001, which means that both of the diagnostic methods mentioned are reliable. Although considering the Kappa coefficient (19.2%), hysteroscopy is more useful than any other method in diagnosing patients with AUB.

In this study, the sensitivity and specificity of ultrasonography in cases of isthmocele that are consistent with normal pathological findings were investigated using the ROC curve method. According to the results obtained from the ROC curve, area under the curve was 0.512, which demonstrated that ultrasonography method was reliable, and the sensitivity and specificity of this method were 64% and 20%, respectively. Also, the results obtained from the ROC curve showed that hysteroscopy method was reliable and the area under the curve was 0.503; Sensitivity and specificity were 75% and 19%, respectively, for hysteroscopy method in patients with isthmocele findings that have normal pathology.

DISCUSSION

The problem of abnormal uterine bleeding is a common complaint in gynecological diseases, and about a third of women's outpatient visits are due to this complaint [12]. Causes of AUB include a wide range of systemic, localized diseases and drug-related factors [16, 17]. Therefore, the purpose of this study was to evaluate the compatibility of ultrasound and hysteroscopy findings and histopathological results in women with abnormal uterine bleeding. In addition, since one of the causes of AUB in women can be isthmocele, and it is one of the risk factors for cesarean section, another goal of this study was to investigate isthmocele in the study population, also, to determine the sensitivity and specificity of the two diagnostic methods and the degree of their compatibility with each other.

The study included 913 AUB patients with an average age of 41.13. The mean duration of abnormal uterine bleeding in patients was 10.97 months. In this study, most patients experienced two pregnancies. Among the studied patients, 131 (14.3%) had no history of pregnancy at all, and 492 (53.9%) patients had no history of cesarean section, while 21.7% had one C/S, 18.4% had two C/S, and 5.4% had a history of cesarean section for three times.

In our study, the most common form of bleeding was intermenstrual Spotting, which was seen in 27.7% of patients, followed by menorrhagia and menometrorrhagia, respectively.

In both ultrasonography and hysteroscopy findings, the most common findings were polyp and myoma, and the most common pathological finding was polyp (48.08%).

In a study by Dueholm 2017 [17] on 50 patients with abnormal uterine bleeding using transvaginal ultrasound and diagnostic hysteroscopy, the most common histopathology finding was proliferative endometrium. However, the sample size was much more abundant in our study. Consistent with the results of our study, Sinha et al. [18], reported that polyps were the most common abnormal pathological finding (16.1%). This difference in percentage may be due to the smaller number of samples in their study (47 cases). In another study by Reznak and Kudela [19], which was performed on 95 patients, only polyps were identified. The success rate for polyp prediction by ultrasound was 65.1%. Although the number of patients studied in this study was much lower than our study, the agreement between the findings of ultrasound and hysteroscopy and histopathology was 72%.

Moreover, in our study, isthmocele were found in ultrasonography and hysteroscopy of 3% and 17.7% of

patients, respectively. In addition, since few studies have examined this defect in the cesarean section, one of the strengths of our study has been that it has evaluated this agreement for cases of isthmocele. Therefore, according to the results of this study, the cases of isthmocele that have been found using hysteroscopy were more than ultrasonography, indicating greater hysteroscopy diagnostic accuracy. In a review study conducted by Tower et al. [20], the prevalence of symptomatic or clinical cesarean section defects was 19.4% to 88%. Also, because there is no accepted guideline for the diagnostic criteria for cesarean section defects, the presence of a defect in the myometrium in the form of a hypochoic triangular area was recommended in transvaginal ultrasound as a definition of cesarean section scar defect. However, our study shows a hysteroscopy advantage in diagnosing cesarean section defects. Sharma et al. [21], also showed in a study of 50 patients that hysteroscopy was a reliable method to assess abnormal uterine bleeding and it can be used as a first-line diagnostic method for benign lesions such as isthmocele. Borges et al. [22] showed that patients with a history of previous cesarean section and complaints of abnormal bleeding in the form of postmenopausal spotting have a high prevalence of cesarean section defects and these conditions can be detected by hysteroscopy.

In our study, the agreement between ultrasonography and hysteroscopy methods in finding cases of isthmocele in patients with abnormal uterine bleeding (AUB) was investigated. Based on our results, that the diagnostic methods mentioned were reliable. Although considering the Kappa coefficient, hysteroscopy was far more useful than any other method in diagnosing patients with AUB.

In a study by Mathlouthi et al. [23]. comparison of ultrasound and hysteroscopy findings and histological results were performed to determine the diagnostic value of transvaginal ultrasound and hysteroscopy in determining the cause of postmenopausal bleeding. The results of this study showed that the sensitivity and specificity were 75%, 87.5%, respectively, for ultrasound, and in the other part, hysteroscopy performed better in diagnosing intrauterine disorders, whereas the sensitivity and specificity were 100% and 95.83%, respectively.

Also, it should be emphasized that these sensitivities and specificities in this study have been present in all findings, and our study specifically examined cesarean section defects in patients as the cause of bleeding, which shows the superiority of a hysteroscopy procedure in our study because the studies in this regard are scarce. Also, it should be noted that in this study the patients had postmenopausal bleeding, but our study included a wide range of ages in patients.

Vitner et al. conducted a study [24] to compare ultrasound and hysteroscopy in the diagnosis of uterine pathologies, and the results showed that hysteroscopy is more sensitive and can potentially detect residual pregnancy products. Although hysteroscopy has a higher predictive value in the diagnosis of uterine polyps, this compliance and agreement were not statistically significant between the two methods. The results were consistent with our study, except that only polyps were evaluated in this study.

In another study that had contrary results to the findings of our study, Dimitrijevic et al. [16] compared the findings of hysterosonography and hysteroscopy to determine the sensitivity and efficacy of hysterosonography to diagnose the cause of abnormal bleeding in premenopausal women. The study results showed that hysterosonography in the diagnosis of submucosal myomas, endometrial hyperplasia, and endometrial polyps is an excellent, easy, and less invasive screening method. In contrast, hysteroscopy has been superior in our study, and this difference may be due to the difference in the study community, sample size, and design of the study.

In our study, a positive and significant correlation was found between the presence of isthmocele in ultrasonography and the number of cesarean sections, and the duration of bleeding. Also, there was a positive and significant correlation between the presence of isthmocele in hysteroscopy and the number of cesarean sections and parity, which means that by increasing cesarean and parity cases, and increasing total cases with isthmocele in ultrasonographic findings, the isthmocele findings in hysteroscopy will increase.

In our study, the findings of correlation analysis showed a positive and very significant correlation between ultrasonography and hysteroscopy in lesion diagnosis. In a similar study, Borges (2010) examined and compared the accuracy of transvaginal ultrasound, sono-hysteroscopy, and hysteroscopy in the diagnosis of uterine pathologies. The results showed an excellent correlation between sono-hysteroscopy and diagnostic hysteroscopy in the diagnosis of focal lesions. Moreover, hysteroscopy provides more information on the diagnosis of pathologies within the uterine cavity than transvaginal ultrasound. However, hysteroscopy has the advantage that occupational therapy can be performed on the patient at the same time as the focal lesion is diagnosed[22].

In our study, the sensitivity and specificity of ultrasonography in detecting isthmocele in patients with normal pathological findings were 64% and 20%, respectively. Also, the sensitivity and specificity of hysteroscopy were 75% and 19%, respectively. In a study by Parul Sinha et al. [25] it was demonstrated that sensitivity and specificity of TVS for this defect are 77.7% and 56%, respectively, but in this study, the relative supremacy of SIS over TVs in the diagnosis of uterine abnormalities in cases of abnormal uterine bleeding was concluded.

In a study by Wanderley et al. [26], based on hysteroscopy results, the diagnostic accuracy was above 90% for all pathologies, while the diagnostic accuracy for transvaginal ultrasound was 65.9% for polyps, 78.1% for myoma, and 63.2% for endometrial hyperplasia. However, in addition to the pathological findings, this diagnostic accuracy was also evaluated in terms of isthmocele findings in our study, but the sensitivity of hysteroscopy was higher in the present study, and it has found more isthmocele findings than sonography.

In general, few studies have been conducted to evaluate the diagnostic accuracy and compatibility of these two methods in finding isthmocele defects. Moreover, few studies have evaluated all uterine pathologies and paid attention to this cesarean section defect, which is one of

the causes of abnormal uterine bleeding. Therefore, our study is rare and notable, and further studies in this regard are needed in the future.

CONCLUSION

According to the results of this study, it can be concluded that ultrasound and hysteroscopy diagnostic methods have good sensitivity in investigating cases of abnormal uterine bleeding. However, in the evaluation of uterine defects such as isthmocele, pathological findings such as polyp and myoma, hysteroscopy have a relative advantage and can be used as the first line of diagnostic methods and as a treatment for patients, and it should be emphasized that further studies in this field with a greater sample size are needed.

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