

Transvaginal Ultrasound versus Saline Infusion Ultrasound for the Characterization of Intrauterine Lesions in Premenopausal Women with Abnormal Uterine Bleeding

Rana Hatem Matrood Alkhazraji ^{*1}, Mohammed Habeeb Hachim ² and Alaq Saeed Abdulhussain ³

^{1,3} College of Medicine, University of Al-Qadisiyah, Al-Diwaniyah province, Iraq

²Al-Diwaniyah Teaching hospital, Department of radiology, Al-Diwaniyah province

Email: rana.hatem@qu.edu.iq

ABSTRACT

Background: Abnormal uterine bleeding is among common health issues seen in premenopausal women. The use of invasive techniques such as hysteroscopy and dilatation and curettage are associated with surgical risks, use of anesthesia, severe post-operative pain and are costly. Therefore, the use of non-invasive technique is preferred by both patients and the treating clinicians. Although, transvaginal sonography has been proved to be good diagnostic tool in categorizing causes of abnormal uterine bleeding, saline infusion sonography nowadays gains better reputation because of better endometrial surface visualization.

Aim of the study: The current study was aiming at comparing the sensitivity and specificity of saline infusion sonography to transvaginal sonography.

Patients and methods: The current prospective study was carried out between 1st of January 2018 and 30th of June 2019 at the gynecological outpatient clinic in maternity and children teaching hospital/ Al-Diwaniyah. At the end of the study, authors were able to recruit 80 women with abnormal uterine bleeding with an age range of 25 to 45 years. Women with obvious infection, pregnant women, those with known adnexal abnormality and those who fail to complete both saline infusion and transvaginal ultrasound procedures were excluded from the study. All women were subjected to transvaginal sonography, saline infusion sonography and dilatation and curettage. **Results:** When endometrial biopsy was considered as the gold standard, no abnormal pathology (36.25%), polypoid lesion (35%), endometrial hyperplasia (8.75%), submucosal leiomyoma (20%) were found among our study population. With reference to pathological results, and when compare TVS & SIS; we found that SIS was more sensitive and highly specific than TVS with sensitivity of 79.56 and specificity of 98.85 respectively, and it was statistically significant.

Conclusion: saline infusion sonography is more sensitive, more specific and more accurate than transvaginal sonography in characterizing organic pathology in premenopausal women with abnormal uterine bleeding.

Keywords: Transvaginal ultrasound saline infusion ultrasound premenopausal women

Correspondence:

Rana Hatem Matrood Alkhazraji

College of Medicine, University of Al-Qadisiyah, Al-Diwaniyah province, Iraq

Email: rana.hatem@qu.edu.iq

INTRODUCTION

The highly orchestrated interaction between endometrium and regulatory factors causes the regular menstrual shedding in a cyclic fashion. Disturbance of such interaction may result in abnormal uterine bleeding. A number of causes have been identified for such abnormal bleeding including hormonal disturbances, trauma of reproductive tract, coagulopathies, pregnancy related complications, infectious disorders and neoplastic conditions (Farrukh *et al.*, 2015; Cheong *et al.*, 2017; Sun *et al.*, 2018). One of common health issues seen during daily gynecological practice is abnormal uterine bleeding which affects women of all age groups (Dickerson *et al.*, 2018; Elmaogullari and Aycan, 2018). Women at premenopausal period frequently seek medical advice for an abnormal bleeding per vagina (Pennant *et al.*, 2017). Benign organic lesions, such as endometrial polyp and submucosal fibroid, are often seen in women during premenopausal period with abnormal vaginal bleeding. Endometrial polyps are seen in approximately 13 to 50 % (Nijkang *et al.*, 2019); whereas submucosal fibroid accounts to 14 to 25% (Sun *et al.*, 2018) of premenopausal women with abnormal uterine bleeding.

The primary aim of diagnostic workup in any women with abnormal uterine bleeding is to exclude malignant

neoplasm. In addition, the diagnostic work up aims also to identify the exact cause so that proper treatment is going to be followed. The evaluation of a patient with abnormal uterine bleeding has evaluated with advances in technology and the primary tools available nowadays are ultrasound, hysteroscopy and endometrial biopsy (Telner and Jakubovicz, 2007). The main goal has been always to exclude endometrial carcinoma of which approximately 90% of women are going to present with abnormal uterine bleeding (Clarke *et al.*, 2018; Masciullo *et al.*, 2010).

Endometrial biopsy following dilatation and curettage has gain wide acceptance among clinicians to categories causes of abnormal uterine bleeding; however, this approach is associated with patients' dissatisfaction because of post-operative pain, need for general anesthesia and associated surgical risk. Therefore, the search for other less invasive approaches was necessary to ensure patients compliance. False negative results frequently associate endometrial sampling because of inadequate sampling or mis-targeting or involved tissue (Kolhe, 2018; Gan *et al.*, 2013; Yarandi *et al.*, 2010). Modification of conventional D&C has been evaluated such as the use of metal curettes and flexible plastic samplers, but these were also accompanied by several disadvantages (Chun *et al.*, 2017). Hysteroscopy is more accurate than

performing blind D & C, but again the invasive nature of the technique and the need for anesthesia limit its value (Sinha *et al.*, 2018).

Transvaginal ultrasound has been increasingly used in characterization of causes of abnormal uterine bleeding and has been proved of acceptable sensitivity in identifying organic lesions such as uterine fibroid, endometrial hyperplasia, endometrial polyp and endometrial carcinoma (Veena and Shivalingaiah, 2014). It relies on measuring endometrial thickness; however, the dependence on endometrial thickness is non-specific (Wheeler and Goldstein, 2017). The saline infusion ultrasound provided recent advance in evaluation of endometrial cavity in women complaining of abnormal uterine bleeding, in which the uterine cavity is better evaluated because of distension permitting better assessment of endometrial lining surface with high sensitivity and specificity (Moradan *et al.*, 2019). The current study was aiming at comparing the sensitivity and specificity of saline infusion sonography to transvaginal sonography.

PATIENTS AND METHODS

The current prospective study was carried out between 1st of January 2018 and 30th of June 2019 at the gynecological outpatient clinic in maternity and children teaching hospital/ Al-Diwaniyah. At the end of the study, authors were able to recruit 80 women with abnormal uterine bleeding with an age range of 25 to 45 years. Women with obvious infection, pregnant women, those with known adnexal abnormality and those who fail to complete both saline infusion and transvaginal ultrasound procedures were excluded from the study.

A questionnaire form was prepared to include details about obstetric, gynecologic and menstrual history. Women were also subjected to adequate physical examination and Pap smear investigation. This was followed by a Transvaginal sonography with a transvaginal probe (6.5 MHz) by General Electric Medical Systems, Milwaukee, WI, USA. Assessment of endometrium and myometrium was carried out in transverse and longitudinal planes. Eight mm was the "the accepted threshold maximum thickness of the endometrium examined" at time of early or mid-proliferative phases. Measurements less than these values were regarded normal. An endometrial polyp was defined as "a smooth margined, echogenic mass with homogeneous texture and of variable size and shape". A submucosal leiomyoma was defined as "a solid, circular structure of mixed echogenicity, arising from the myometrium and protruding into the uterine cavity; it should be covered by intact epithelium". The saline infusion ultrasound was carried out while the woman is in the dorsal lithotomy position. Insertion of a standard bivalve speculum was performed, and the cervix was sterilized using povidone iodine antiseptic solution. A 15

cm long and 2 mm width disposable sterile catheter was introduced through the cervical os till reaching the uterine fundus. The transvaginal ultrasound (6.5 MHz) probe was then introduced after withdrawal of the speculum. The adequate amount of infused normal saline was in the range of 5 to 10 ml; however, an amount up to 20 ml was sometimes needed. A case record form was used to observe the size and location of any abnormalities related to the uterus. Endometrial thickness at the thickest region, both anterior and posterior, was estimated in transverse and longitudinal planes from fundus to cervix. In order to get the entire endometrial thickness, both anterior and posterior portions were added together. The following criteria were used to describe results obtained following either ultrasound technique: normal cavity, endometrial hypertrophy (single-layer endometrial thickness > 6 mm), endometrial atrophy (single-layer endometrial thickness < 2 mm), endometrial polyp (hyperechogenic lesion with a pedunculated attachment to the endometrium) and submucosal leiomyoma (lesion of mixed echogenicity disrupting the endometrial continuity).

Later on women underwent D&C and proper endometrial sampling was carried out followed by histopathological assessment. Obtained results from histopathology were contrasted to those obtained from ultrasound techniques. The ethical approval of the current study of the current study was issued by the ethical approval committee of the institute and a verbal consent was obtained for all participants. Statistical analysis was carried out using Statistical Package for the Social Science (SPSS) software version 23 (SPSS Inc., Chicago, IL). Continuous data were expressed as mean and SD. Calculation of sensitivity, specificity, positive predictive value, negative predictive value and accuracy of two tests (TVS and SIS), with histological result used as reference standard. Chi square test used for comparison between TVS and SIS. The level of significance was considered at $P \leq 0.05$.

RESULTS

Eighty women were enrolled in this study. The mean age of patients was 38 ± 9.6 years (range 25-45 years). Twenty-seven of sample (33%) were multiparous, twenty-eight of sample (35%) were ≥ 40 , as shown in table 1. All women underwent TVS, SIS, and D&C. The results obtained from TVS; SIS were compared in relation to histopathological results as shown in table 2&3. When endometrial biopsy was considered as the gold standard, no abnormal pathology (36.25%), polypoid lesion (35%), endometrial hyperplasia (8.75%), submucosal leiomyoma (20%) were found among our study population as shown in table 4. With reference to pathological results, and when compare TVS & SIS; we found that SIS was more sensitive and highly specific than TVS with sensitivity of 79.56 and specificity of 98.85 respectively, and it was statistically significant as shown in table 5.

Table 1: Demographic characteristics of study group according to histopathology and ultrasound examination

		n	TVS		SIS		Histopathology	
			Normal	Abnormal	Normal	Abnormal	Normal	Abnormal
Age (years)	25-29	12	5	7	9	3	11	1
	30-34	18	4	14	7	11	8	10
	35-39	22	8	14	5	17	6	16
	≥ 40	28	2	26	3	25	4	24

	Total	80	19	61	24	56	29	51
Parity	P0	12	3	9	2	10	3	9
	P1	16	3	13	3	13	5	11
	P2	11	2	9	6	5	5	6
	P3	14	5	9	5	9	7	7
	≥ P4	27	6	21	8	19	9	18
	Total	80	19	61	24	56	29	51

TVS: transvaginal sonography; SIS: saline infusion sonography

Table 2: Comparison of TVS findings with pathological results

TVS	Pathology				Total
	Normal	EH	Fibroid	Polyp	
Normal	10	2	2	5	19
EH	3	1	0	6	10
Fibroid	1	0	17	4	22
Polyp	4	1	0	24	29
Total	18	4	19	39	80

TVS: transvaginal sonography; EH: endometrial hyperplasia

Table 3: Comparison of SIS findings with pathological results

SIS	Pathology				Total
	Normal	EH	Fibroid	Polyp	
Normal	23	1	0	0	24
EH	4	5	0	2	11
Fibroid	1	0	13	1	15
Polyp	1	1	3	25	30
Total	29	7	16	28	80

SIS: saline infusion sonography; EH: endometrial hyperplasia

Table 4: Findings reported following histopathological examination

Pathology	N	%
Normal	29	36.25
EH	7	8.75
Fibroid	16	20
Polyp	28	35
Total	80	100

EH: endometrial hyperplasia

Table 5: Diagnostic parameters of SIS and TVS in reference to pathological finding

Characteristic	SIS	TVS
Sensitivity	79%	56%
Specificity	98%	85%
Positive predictive value (PPV)	96%	53%
Negative predictive value (NPV)	89%	87%
Accuracy	91%	79%
Statistical significance	0.002 **	

SIS: saline infusion sonography; TVS: transvaginal sonography; PPV: Positive predictive value; NPV: Negative predictive value; **: highly significant at $P \leq 0.01$

DISCUSSION

The aim of the current study is to find evidence about which tool is more accurate in detecting intrauterine pathologies associating abnormal uterine bleeding, transvaginal sonography or saline infusion sonography. Advantages attributed to transvaginal ultrasound included excellent visualization of endometrium, the relatively low cost, being less invasive and painless procedure and can be performed as an outpatient procedure (Atalabi *et al.*, 2012). However, a number of disadvantages have been linked to transvaginal sonography such as the production of equivocal results and the inability to exclude all abnormal uterine growths, myomas or polyps (Schwarzle *et al.*, 1998). In addition, further investigation may be needed to reach the final diagnosis in a substantial proportion of patients. Intramural fibroid that impinge upon the uterine cavity is sometimes difficult to be distinguished from submucosal fibroid. In the current study we were able to identify the intramural nature of misleadingly appearing submucosal fibroid by transvaginal sonography following performance of saline infusion sonography.

Previous reports have shown that saline infusion sonography was superior to transvaginal ultrasound in terms of sensitivity and specificity in diagnosing endometrial polyps and leiomyoma when pathological reports were taken as a reference (Erdem *et al.*, 2007; Schwarzle *et al.*, 1998). In the present study, the sensitivity, specificity, PPV and NPV of TVS were 65.2%, 87.9%, 81.0% and 76.1%, respectively, in detecting endometrial polyps and 89%, 91.0%, 77% and 96%, respectively in detecting fibroids. Vercellini *et al.*, in 1997 has found in a large series, that TVS possesses 69% specificity and 80% sensitivity for detecting fibroids that are submucosal. In addition, it has been shown that transvaginal sonography is sensitive for uterine fibroid, but, it has poor capacity to relate these lesions to the uterine wall. Goldstein *et al.* in 1997 also reported that minor anatomical pathologies may be easily undetected and that it is difficult to differentiate between myometrial abnormalities and endometrial lesions by TVS; in addition, it was suboptimal in differentiating between endometrial hyperplasia and dysfunctional uterine bleeding. In the current study, the use of transvaginal ultrasound, interpreted some cases of endometrial polyps as normal endometrium. Current study results confirmed that, transvaginal ultrasound was insufficient tool for evaluation of causes of abnormal uterine bleeding because of its low sensitivity.

Better results were obtained when both saline infusion sonography was combined with that of transvaginal sonography in the current study. Further management steps rely on accurate diagnosis, for example proceeding with D&C yields better results when the underlying pathology is already than doing it blindly. The performance of saline infusion sonography permits choosing the ideal surgical approach (Mihm *et al.*, 2002). In a systematic review and meta-analysis of 24 studies, de Kroon *et al.* (2003) found SIS to be both feasible and accurate in the evaluation of the uterine cavity in pre and postmenopausal women. The results obtained from a previous meta-analysis have shown that combined saline infusion sonography and aspiration biopsy is optimum in premenopausal and postmenopausal women with abnormal uterine bleeding to accurately categorize

pathological lesions (Mihm *et al.*, 2002). Transvaginal sonography has been shown to be a sensitive technique in the detection abnormalities of endometrium in women during postmenopausal period (Emanuel *et al.*, 1995), nevertheless, differentiating between a number of benign lesions and endometrial hyperplasia is somewhat uneasy. However, transvaginal ultrasound has been shown to possess high specificity and sensitivity in diagnosing endometrial hyperplasia, especially in women with uterine bleeding during postmenopausal period (Giusa-Chiferi *et al.*, 1996), but, saline infusion sonography is more efficient than transvaginal sonography because the later often fails to differentiate among polyps, endometrial hyperplasia and submucosal leiomyoma (Gaucherand *et al.*, 1995). Moreover, the exact site of the growths or polyps is difficult to be judged based on transvaginal sonography. In view of previous reports and data obtained from the current study, it is concluded that saline infusion sonography is more sensitive, more specific and more accurate than transvaginal sonography in characterizing organic pathology in premenopausal women with abnormal uterine bleeding.

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