Three-Dimensional Ultrasonography Compared with Histopathology for the Diagnosis of Adenomyosis: A Prospective Study

Original Article

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ABSTRACT

Objective: Evaluation the accuracy of 3D-TVS in the diagnosis of adenomyosis compared with histopathologic finding after hysterectomy.

Patients and Method: This prospective case controlled study was performed at Obstetrics & Gynecology department Mansoura University Hospitals between January 2019 to march 2022, including 53 women ≥40 years complaining of menorrhagia, dysmenorrhea or chronic pelvic pain, showing one or more of The 2D-TVS features of adenomyosis and requiring hysterectomy. Initially, 2D TVS was done evaluating the pelvic organs, then signs suggestive of adenomyosis was assessed. Subsequently, the 3D ultrasound of the uterus was obtained, thin hysterectomy specimens was subjected to histopathological assessment with focusing on specific areas determined by 3D-TVS. Data was regestrated for statistical analyses.

Results: Our study shows that mean age of the cases is 46.11 years. 64.2% of the cases are multipara. 56.6% of the cases have early menarche and 22.6% past oral COC use. The presenting symptoms of the cases; 83% heavy menstrual bleeding, 79.2% chronic pelvic pain, 69.8% tender uterus, 60.4% uterine enlargement, 41.5% dyspareunia and the least frequent symptoms was infertility. 50 (94.0%) of the studied cases have adenomyosis by histopathology examination and 3 cases no adenomyosis (6%). Number of cases with adenomyosis as detected by 2D TVS was 53 cases with adenomyosis, by 3 D TVS was 48 cases and by histopathology is 50 cases *p value* (0.021).

Conclusions: Our results suggest that 3D-TVS is more accurate than is conventional 2D imaging to detect adenomyosis, as 3D TVS enables accurate diagnosis of adenomyosis and its specific location.

Key Words: 3DTVS, adenomyosis, histopathology.

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INTRODUCTION

Adenomyosis is the presence of ectopic endometrial glands and stroma surrounded by hyperplastic smooth muscle within the myometrium[1]. The general consensus is that adenomyosis occurs when there is a disruption of the normal boundary between the endometrial basal layer and the myometrium[2]. Adenomyosis has two forms, the diffuse type and the focal type known as adenomyoma[3]. Around 80% of cases of adenomyosis affect woman between 40 and 50 years and the most frequent symptoms are menorrhagia, dysmenorrhea and chronic pelvic pain. Hysterectomy is the standard line of treatment[3].

Hysterectomy is also the definitive diagnostic method for adenomyosis[3]. Currently, the two-dimensional transvaginal ultrasound (2D TVS) represents the primary screening tool for adenomyosis. The TVS features considered to be typical of adenomyosis are asymmetry of the myometrial walls, the presence of myometrial cysts, myometrial hyperechoic islands, subendometrial echogenic linear striations and irregular or interrupted junctional zone(JZ)[4]. However, the JZ, that is adjacent to the basal endometrium, is better defined by MR imaging with an accurate diagnosis of adenomyosis if thickening of the JZ ≥ 12mm, and ratio of the maximum thickness of the JZ (JZ max)/total maximum myometrial thickness > 40%[5].

Three-dimensional (3D) TVS allows more accurate evaluation of JZ than 2D-TVS. The 3D TVS markers for detection of adenomyosis are thickening of the JZ ≥ 8m, JZ difference ≥ 4mm and JZ infiltration. Total accuracy for 3D TVS in the diagnosis of adenomyosis was 89%,

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similar to accuracy reported in MRI studies[6]. Currently, there is a paucity of data concerning 3D-TVS evaluation of JZ compared with histopathology in the diagnosis of adenomyosis. So, this point warrants more attention and evaluation.

PATIENTS AND METHOD

This prospective observational study was conducted from January 2019 to march 2022 at Obstetrics & Gynecology department Mansoura University Hospitals. Approval of the local ethical committee was obtained before starting our research. Informed consent was obtained from all patients participating in the study after explaining to the patients the benefits and the potential risks involved.

The study group including, women, complaining of menorrhagia, dysmenorrhea or chronic pelvic pain, showing one or more of the 2D-TVS features of adenomyosis and requiring hysterectomy. We exclude, menopausal women, ongoing pregnancy, genital tract cancer, any condition affecting the accuracy of JZ measurements e.g. submucousor intramural myomas > 4cm or > 3intramural myomas larger than 3 cm.

With 85% expected accuracy of 3D-TVS in the diagnosis of adenomyosis, a sample size of 53 participants was required for the study with 5% level of significance and 80% power of the study, using G power sample size calculator program.

All patients subjected to; full history taken, through clinical examination, then, 2D TVS was done evaluating the pelvic organs (uterus and adenxae), then signs suggestive of adenomyosis was assessed. Subsequently, the 3D volume of the uterus was obtained commencing with the sagittal plane. Then, the uterine cavity was assessed after obtaining a mid-coronal view. Thickening of the JZ ≥ 8 mm, JZ difference ≥ 4 mm, and JZ alteration was identified and its location within the uterus was reported. Other lesions e.g. myometrial asymmetry, myometrial cysts, hyperechoic striation, heterogenous myometrium was also reported. Hysterectomy specimens will be subjected to histopathological assessment with focusing on specific areas determined by 3D-TVS.

All data was collected in prepared sheet that was entered into an electronic spreadsheet (Microsoft Excel) and transferred into SPSS (Statistical Package for Social Sciences) program.

Statistical analysis was conducted using SPSS 22 system (SPSS Inc., Chicago, IL, United States). Continuous data was expressed as the mean ±SD, and categorical variables expressed as percentage. Sensitivity, Specificity, diagnostic accuracy, positive and negative predictive values, and positive and negative likelihood ratios of 3D TVS was calculated compared with histopathological findings as the gold standard for the diagnosis of adenomyosis.

RESULTS

The present study is methodological study that is carried out on 53 females attending Mansoura University hospitals at obstetrics & gynecology department complaining of menorrhagia, dysmenorrhea, chronic pelvic pain to assess validity of 3D TVUS in diagnosing adenomyosis as compared to histopathological results (Gold standard). As regard socio-demographic, medical and obstetric history of the studied cases (Table 1) main age was 46.11±3.79, main body mass index was34.24 ±4.25. 34 patients (64.2%) were multipara, 15 patients (28.6%) were low parity, 4patients (7.5%) were nullipara. 14 patients were diabetics(26.4%), 18 patients (34%) were hypertensive. As regard to the risk factors and the presenting symptoms (Table 2) demonstrates that 56.6% of the studied cases have early menarche and 22.6% past oral COC use. Among presenting symptoms of the studied cases; 83% heavy menstrual bleeding, 79.2% chronic pelvic pain, 69.8% tender uterus, 60.4% uterine enlargement, 41.5% dyspareunia and the least frequent symptoms is infertility. Regarding to post hysterectomy histopathology (Table 3) shows that 50 (94.0%) of the studied cases have adenomyosis by histopathology examination and 3 cases no adenomyosis (6%). (Table 4) shows that there is statistically significant relation between histopathological findings and 3 D ultrasound findings as regard presence of adenomyosis among studied cases. Number of cases with adenomyosis as detected by 2D TVS is 53 cases with adenomyosis, by 3 D TVS 48 cases and by histopathology is 50 cases p value (0.021). (Table 5) illustrates that 47 cases are true positive, 2 cases true negative while comparing results of3D TVUS with histopathology yielding sensitivity of 97.9%, specificity of 66.7%, positive predictive value of 97.9% negative predictive value 40% and total accuracy 92.5%.

Table 1: Socio-demographic, medical and obstetric history of the studied cases

	total number=53	%
age/years mean±SD (Min-Max	46.11±3.79 (38-53)	
BMI(Kg/m2) mean±SD (Min-Max)	34.24±4.25(27.68-50.78)	
Parity		
Nullipara	4	7.5
Low parity	15	28.6
Multi parity	34	64.2
Associated comorbidities		
DM	14	26.4
Hypertension	18	34.0

Table 2: Distribution of the studied cases according to risk factors and presenting symptoms.

	Total no 53	%
Risk factors		
Early menarche	30	56.6
past oral COC use	12	22.6
Presenting symptoms		
Heavy menstrual Bleeding	44	83.0
Chronic pelvic pain	42	79.2
Dyspareunia	22	41.5
Uterine enlargement	32	60.4
Tender uterus	37	64.8
Infertility	5	9.4

Table 3: Distribution of the studied cases according to results of Post hysterectomy histopathology.

Histopathology	total number=53	%
No adenomyosis	3	5.7
Adenomyosis	50	94.3

Table 4: Distribution of 2D and 3 D findings in relation to histopathological findings

TVS	Histopathology		
	no adenomyosis n=3(%)	Adenomyosis n=50(%)	*P value*
2D			
-ve (n=0)	0	0	p=1.0
+ve(n=53)	3(100)	50(100)	
3D			
-ve (n=5)	2(66.7)	3(6.0)	0.021*
+ve (n=48)	1(33.3)	47(94.0)	

Table 5: Validity of 3DTVUS in diagnosing adenomyosis

	TP	TN	%Sensitivity	%Specificity	%PPV	%NPV	%Accuracy
TVS	47	2	97.9	66.7	97.9	40.0	92.5

TP: True positive, TN: True negative, PPV: Positive predictive value, NPV: Negative predictive value

DISCUSSION

The sonographic findings of adenomyosis generally involve alterations of the myometrium, such as; presence of myometrial hypoechoic striations or myometrial cysts or heterogeneous areas, asymmetry of the myometrial walls, diffuse vascularity and globular uterine configuration[7]. Coronal section of the uterus, obtained with 3D TVS, can visualize the JZ more clearly with certain postprocessing arrangements[8]. So, our study was carried out to evaluate the accuracy of 3D-TVS in the diagnosis of adenomyosis compared with histopathologic finding from hysterectomy specimens.

In the current study, the mean age of the studied cases is 46.11 years ranging from 38 to 53 years and mean body mass index is 34.24 kg/m2 ranging from 27.68 to 50.78 kg/m2, Associated comorbidities of the studied cases is distributed as following; 34% hypertensive and 26.4% are diabetic.

(Puente et al., 2016) found that mean BMI was significantly lower among women with adenomyosis (20.9 ± 4.5) than among women without adenomyosis (21.8 ± 3) (P = 0.003), which was different from our study, as high BMI in our locality is a result of socioeconomic factors and lifestyle[9].

Exacoustos et al. (2011) found that adenomyosis tend to occur in low parity, although there was no statistically significant difference in the mean gravidity or parity between adenomyosis group and the group without adenomyosis[6]. In our study, we found an increased incidence of adenomyosis in multiparous (64.2% of the cases were multiparas, 28.6% had low parity and 7.5% were nulliparas), in concordance with (Taran et al., 2012, Weiss et al., 2009) studies, which reported that a high percentage of women with adenomyosis were multiparous[10,11]. This is because of that the invasive nature of the trophoblast during pregnancy allow adenomyotic foci to be included on the myometrial fibers[11]. Also, childbirth-related trauma, may cause disruption of the barrier between basal endometrium and the myometrium. Also, pregnancy hormones especially estrogen may help in the development of islands of ectopic endometrium. Alternatively, hysterectomy more accepted in multiparous women[12].

On the other hand, (Puente et al., 2016) reported an increases incidence of adenomyosis with nulliparity, as they found that 94 % of women with adenomyosis were nulliparous. they stated that adenomyosis is linked to infertility, but the mechanisms behind this relationship are not clearly established[9].

In our study, past oral COC use was risk factors in development of adenomyosis, similar to (Templeman et al., 2008) who reported that past oral contraceptive use was a risk factor for the development of adenomyosis (80% of women with adenomyosis were past COC users), thus suggesting an association between adenomyosis and estrogen exposure[13]. Nevertheless, (Schindler, 2010) stated that hormonal contraceptives as estrogen/progestogen combinations (monophasic, progestogendominant) or progestogen-only preparations provide control of symptoms and can lead to the regression of adenomyosis[14]. It is not clear if contraceptive use is a risk factor for adenomyosis, or if women were prescribed a COC to manage symptoms of dysmenorrhea and heavy menstrual bleeding, which are common symptoms in patients with adenomyosis.

In our study, early menarche was risk factors for development of adenomyosis. Similar to (Templeman et al., 2008) who reported that women with early menarche (10 years or younger) had a greater risk for an adenomyosis

than women with later menarche.13 Also, in line with our results, (Missmer et al., 2004) found an increased risk of endometriosis in women who had experienced early age menarche[15].

(Parazzini et al., 1997, Vercellini et al., 2006) stated that there was no association between early menarche and adenomyosis diagnosed at the time of hysterectomy[16,17]. Our findings of early age at menarche suggest that increased exposure to menstrual blood increase the risk of adenomyosis. This finding also accepted by (TakahasHi et al., 1989) who shown that estradiol levels was higher in menstrual blood in patients with adenomyosis than in those with endometriosis or in disease-free control women[18]. Struble etal,(2016), concluded that estrogen metabolism in the endometrium of patients with adenomyosis differs from that in women without adenomyosis, these changes result in a hyperestrogenic environment that increase the risk of the disease in susceptible patients[3].

In our study, the presenting symptoms were heavy menstrual bleeding in 83% of cases, chronic pelvic pain in 79.2%, tender uterus in 69.8%, uterine enlargement in 60.4%, dyspareunia in 41.5% and the least frequent symptoms is infertility. Abnormal uterine bleeding and pelvic pain are two of the most commonly reported symptoms in our study, similarly, (Exacoustos et al., 2011) stated that pain and bleeding are symptoms typical of adenomyosis, although that many women remain asymptomatic[6]. In concordance with our results, Cheng et al., 2012 also found that the most common presentation was menorrhagia in 53.7% of cases, followed by dysmenorrhea in 17.9%, and multiple symptoms in 17.9%[19].

In line with our results, (Luciano et al., 2013) reported that adenomyosis mainly diagnosed clinically, and the most common symptoms, were dysmenorrhea, menorrhagia, abnormal bleeding, and pelvic pain[20]. they also stated that, a preoperative diagnosis based solely on symptoms is accurate only about 25% of the . Also, (Elkattan et al., 2016) reported that the most common presentation in their study was menorrhagia in 73% of cases followed by dysmenorrhea in 8% and multiple symptoms in14.6%[21]. (Hashad et al., 2017) noted that the major symptoms were, abnormal uterine bleeding in 62.33% patients, pain in 18.18% and both in 19.48%[22]. Conversely, (Sammour et al., 2002) found that the major symptoms of adenomyosis were pelvic pain (p=.02) and dysmenorrhea (p=.01) but not associated with heavy menstrual bleeding or dyspareunia[23]. Also, in contrast to our results (Chen et al., 2019) found that pain was the most common clinical presentation in 72% of cases followed by bleeding in 68% of cases[24].

These symptoms are due to hyperplasia and hypertrophy of smooth muscle cells of the myometrium surrounding the adenomyotic foci. Dysmenorrhea, heavy menstrual bleeding, and infertility most probably results of inflammation, neurogenesis, angiogenesis, and contractile abnormalities in the endometrial and myometrial components[25].

Our study results have revealed that 50 (94.0%) of the studied cases have adenomyosis by histopathology examination and 3 cases no adenomyosis (6%).

In our study, 3D-TVS found to be 92.5% accurate in the diagnosis of adenomyosis, with 97.9% sensitivity, 66.7 specificity, NPV of 40 and PPV of 93.18%. Similar results, obtained by (Gaafar et al., 2014) in their study on 100 premenopausal women having abnormal uterine bleeding who underwent TAH after a preoperative assessment by 3D TVUS. They found that, the diagnostic accuracy of 3D ultrasonography versus uterine pathology was sensitivity and specificity (90% and 92.8%) respectively, a PPV and NPV (69.2% and 98.1%) respectively with overall accuracy 92.42% in diagnosis of adenomyosis. The cause of difference from our study may be due to we include patients having abnormal uterine bleeding, chronic pelvic pain or combined symptoms[26]. Also, our results comes with positive correlation to results obtained by (Andres et al., 2018), in a systematic evaluation of the literature in the last 10 years to determine the accuracy of 3D TVUS for the diagnosis of adenomyosis, pooled sensitivity and specificity for all combined imaging characteristics was 88.9% and 56.0% respectively[27]. Poor definition of junctional zone showed the highest pooled sensitivity (86%) and the highest pooled specificity (56.0%) for the diagnosis of adenomyosis with 3D TVUS. Also, (Tellum et al., 2020) metanalysis, reported that the pooled 3DTVUS had a sensitivity of 84% and specificity of 84% for diagnosing adenomyosis[28]. they stated that 3D-TVUS improved the diagnostic quality for diagnosing adenomyosis compared to 2D-TVUS and can detect changes in the JZ, which was one of the best performing diagnostic determinants.

Adenomyosis is most likely caused by invasion of endometrial tissue across the JZ and into the myometrium, so evaluation of the JZ by 3D-TVS could detect early adenomyosis. However, (Hashad et al., 2017) concludes that 3D TVUS is found to be sensitive (95.8 %) but not specific (27.6 %) in diagnosis of adenomyosis. Therefore, evaluation of the JZ and its alterations by non-invasive imaging could be very important in diagnosis of adenomyosis[29]. TVS is the imaging technique most commonly available in gynecological offices and therefore it is the first line diagnostic tool for the diagnosis of adenomyosis[30]. One of the strengths of our study is that it included only the patients who had hysterectomy, which allow us to exclude double pathology and give more accurate results after histopathologic examination of the uterus. The pitfalls in our study the was that our study group comes from patients requiring hysterectomy, who tend to be older and symptomatic, and in whom adenomyosis is likely to be

more advanced. A second potential limitation of this study was that histological biopsies were not performed using an ultrasound-guided approach, so it was not possible to ascertain whether the JZ alterations seen on TVS were really due to adenomyosis, as the diagnostic accuracy when examining the entire uterus could be overestimated.

CONCLUSION

Our results suggest that 3D-TVS is easy, non invasive, with high accuracy diagnostic imaging to detect adenomyosis, and we recommend its use to evaluate patients in early stages of the disease, especially in young patients in whom histological diagnosis is difficult to perform, as 3D TVS enables accurate diagnosis of adenomyosis and its specific location more than conventional TVS decreasing the need for MRI.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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