International Journal of Chemical and Biochemical Sciences
(ISSN 2226-9614)

Journal Home page: www.iscientific.org/Journal.html

Ultrasound estimation of Uterine Vascularity in Uterine Adenomyosis and Its Relation to Pain and Bleeding as the Primary Clinical Presentation

Rehab Lotfy Abdel Kader, Mostafa Seleem, Rasha Ahmed Mostafa Kamel, Mazen Anas Abdellatif Ahmed Wahdan

Department of Obstetrics and Gynecology, Faculty of Medicine, Cairo University, Egypt.

Abstract

Adenomyosis is a prevalent gynecological disorder. According to reports, roughly 20% of adenomyosis instances include women under the age of 40, with the remaining 80% occurring in women aged 40 to 50**.** To correlate the severity of symptoms in patients with uterine adenomyosis to their ultrasound estimated uterine vascularity. This observational cross-sectional study was conducted on eighty-one Patients with uterine adenomyosis at Kasr Alaini hospitals between January 2021 and January 2022. There was significant positive correlation between the ultrasound estimation of uterine vascularity using a subjective color score [by applying power Doppler] and the following: the visual analogue scale scores for pelvic pain p= 0.019, reported dyspareunia p= 0.002, reported heavy menstrual cycle pattern p<0.001and menstrual pictogram scores. And no significant correlation was found with any of the following: reported dysmenorrhea p=0.129, reported frequent micturition, reported long cycle pattern p=0.364 or pelvic heaviness. There was significant positive correlation between the ultrasound estimation of uterine vascularity using the flow index and the following: reported dyspareunia, reported heavy menstrual cycle pattern and menstrual pictogram scores. The three-dimensional ultrasound assessment of uteri of adenomyosis allowed deeper evaluation the vascularity. The increase of uterine vascularity is associated with an increase in the amount of uterine bleeding, pelvic pain scores and dyspareunia.

Keywords: Ultrasound estimation of uterine vascularity, uterine adenomyosis, pain, bleeding

Full-length article

*Corresponding Author, e-mail: Mazen.medk@gmail.com

1. Introduction

Adenomyosis is a prevalent gynecological disorder, according to reports, roughly 20% of adenomyosis instances include women under the age of 40, with the remaining 80% occurring in women aged 40 to 50. The elder group is connected with the most severe symptoms. In around a third of patients, adenomyosis can be asymptomatic. Menorrhagia, dysmenorrhea and metrorrhagia are the most common symptoms in the remaining two-thirds. Dyspareunia is another possible problem [1]. The improper placement of endometrial glandular tissue inside the uterine myometrium in cases of adenomyosis is typically related with cyclical uterine pain, dyspareunia, abnormal uterine bleeding (AUB) such as menorrhagia, spotting or bleeding before and after menses, and infertility [2]. Imaging investigations, particularly pelvic ultrasonography, are increasingly revealing signs indicative of adenomyosis, such as a globular enlarged uterus, ambiguous or uneven endometrial myometrial junction, heterogeneous myometrium, and myometrial cysts, among others [3]. Three-dimensional Ultrasound has largely improved our diagnosis and assessment of adenomyosis, and the use of its obtained data can be further helpful if it can be correlated to the clinical symptoms of the patients [4]. The aim of this study was to correlate the severity of symptoms in patients with uterine adenomyosis to their ultrasound estimated uterine vascularity.

2. Patients and methods

This was an observational cross-sectional study conducted on eighty-one Patients with uterine adenomyosis at Kasr Alaini hospitals in the period between January 2021 and January 2022.

Inclusion criteria: Women with ultrasound criteria of uterine adenomyosis. Age between 18 years and 45 years old.

Exclusion criteria: women who were having any congenital uterine malformation, having uterine, adnexal, or pelvic masses, Uncontrolled hypertensive, Suffering from psychiatric illness, Pregnant or puerperal. Using a

contraceptive method or hormonal treatment. With known coagulopathy or endocrinal disorders. Having associated endometrial polyps.

2.1. Sample size

According to our knowledge after review of the literature, this study has not been attempted before and therefore a proper sample size could not be calculated. So we recruited all the patients that meet the inclusion criteria during the study period and analyzed their data for the intended outcomes. During this process, a total of eighty-one patients from the gynecology outpatient clinic at kasr Alaini hospitals during the study period were suspected to have uterine adenomyosis according to their clinical presentation. After being screened by pelvic ultrasonography, only fifty-seven of them met the ultrasound criteria of adenomyosis according to MUSA approach, the number of eligible patients after applying the inclusion and exclusion criteria were thirty-eight, 8 patients dropped out and the data of thirty patients was tabulated and statistically analyzed [5].

Interventions done: Diagnostic intervention and Pelvic ultrasound.

2.2. Potential risks: None.

2.3. Confidentiality of data

All patients were assigned codes and all personal and medical information were related to the code not the name of the patient.

2.4. Methods

All patients underwent full history taking, physical examination and screening pelvic ultrasound assessment to recruit eligible patients meeting the inclusion and exclusion criteria of the study, and they had the aim and the method of the study been explained to them in order to obtain their informed consent. The patients were then brought for data collection immediately postmenstrual. Assessment of the severity of their symptoms was done using the following validated objective measures of quantification. To quantify pelvic pain, the Visual Analogue Scale was used. To quantify the degree of menstrual loss, Larsen's menstrual pictogram was used [6]. The patients were also asked to fill a questionnaire to stand on the type of pelvic pain experienced whether it is in the form of dyspareunia, dysmenorrhea, or pelvic heaviness, also to determine the pattern of abnormal uterine bleeding whether it is in the form of heavy cycle or prolonged cycle or both. Each item was given a score that was used during the statistical analysis. Two dimensional transvaginal ultrasound assessment of pelvic organs was first performed, ensuring again that the patient meets the inclusion criteria of the study with no exclusion criteria, then power Doppler was applied on the uterine corpus to evaluate the degree of vascularization, Doppler gain was set to 8 cm/s, then subjective color scoring was done, with a color score of 1 representing no color and a score of 4 representing abundant color signals. The color score was assigned taking into account the myometrium as a whole, but in lesions with uneven internal vascularization (e.g. because of cystic areas), the score reflected the degree of vascularization in the solid parts of the lesion. Vascularization index (VI) and flow index (FI)were also used to objectively assess the vascularity, VI measures the number of color voxels in the region of myometrium denoting the vessels in the tissue and is expressed as a percentage; FI indicates the mean color value in the color voxels and denotes the average intensity of flow[7].

2.5. Statistical analysis

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA). Data was summarized using mean, standard deviation, median, minimum and maximum. Comparisons between quantitative variables were done using the non-parametric Kruskal-Wallis and Mann-Whitney tests [8]. Correlations between quantitative variables were done using Spearman correlation coefficient [8]. P-values less than 0.05 were considered as statistically significant.

3. Results

There was no significant difference regarding their age, body mass index (BMI), gravidity, parity, or the number of previous cesarean sections. (Table1). Regarding to statistical analysis of obtained data of all patients. Dyspareunia was (1.07±0.78), Dysmenorrhea (1.20±0.61), Heaviness (1.17±0.75), Frequency (1.23±0.82), VAS (60.80±28.80), Vascularity score (2.30±1.09). (Table 2). The statistical analysis of the results showed significant positive correlation between the ultrasound estimation of uterine vascularity using a subjective color score [by applying power Doppler] and the following: the visual analogue scale scores for pelvic pain p= 0.019, reported dyspareunia p= 0.002, reported heavy menstrual cycle pattern p<0.001and menstrual pictogram scores. And no significant correlation was found with any of the following: reported dysmenorrhea p=0.129, reported frequent micturition, reported long cycle pattern p=0.364 or pelvic heaviness. (Table 3)

The statistical analysis of the results showed significant positive correlation between the ultrasound estimation of uterine vascularity using the vascularization index and the following: visual analogue scale scores for pelvic pain P value=0.011, reported dyspareunia p=0.002, reported heavy menstrual cycle pattern p<0.001 and menstrual pictogram scores. And no significant correlation was found with any of the following: reported dysmenorrhea p=0.126, reported frequent micturition, reported long cycle pattern p=0.277 or pelvic heaviness. (Table 4). The statistical analysis of the results showed significant positive correlation between the ultrasound estimation of uterine vascularity using the flow index and the following: reported dyspareunia, reported heavy menstrual cycle pattern and menstrual pictogram scores. And no significant correlation was found with any of the following: visual analogue scale scores for pelvic pain p= 0.085, reported pelvic heaviness p=0.872, reported dysmenorrhea p=0.358, reported frequent micturition or reported long cycle pattern p= 0.178.

4. Discussion

We found that the degree of increase of uterine vascularity evaluated by the subjective scoring system was associated with an increase in the amount of uterine bleeding, global pelvic pain and dyspareunia, but not the complaints of pelvic heaviness, dysmenorrhea or frequent micturition episodes. Some other studies showed results suggesting a relationship between general change of uterine volume and the severity of clinical symptoms of the patients.

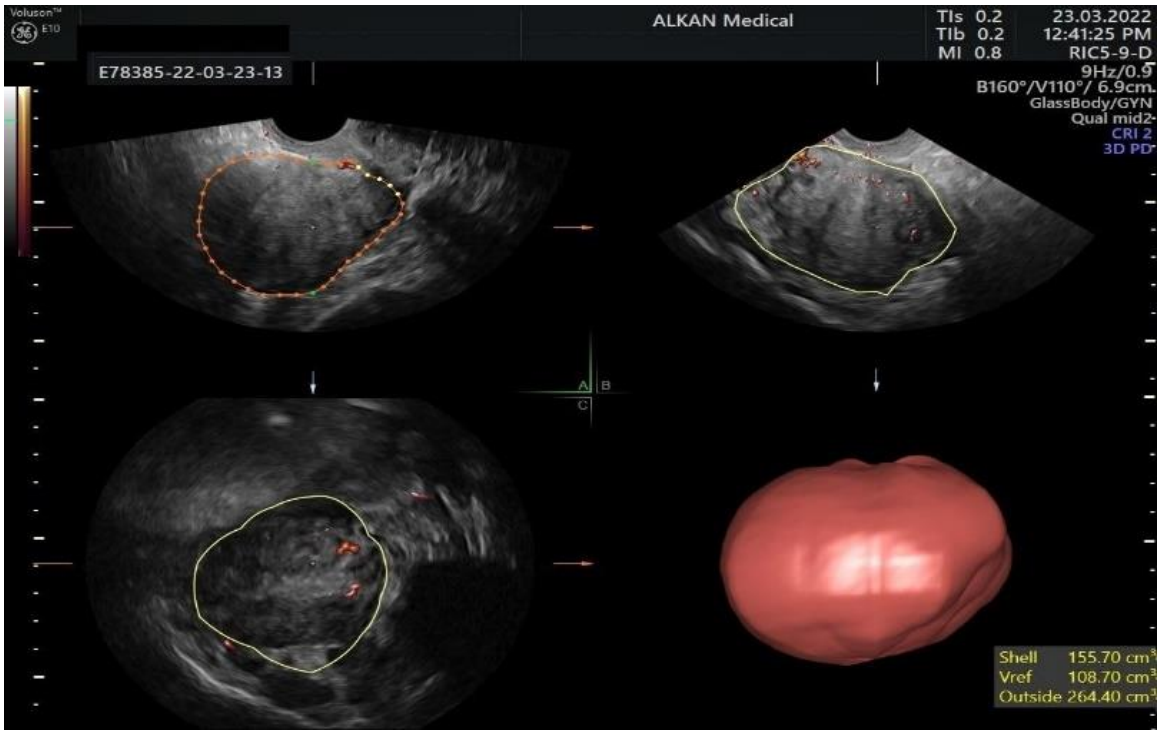

Figure 1. Three dimentional volumetric aquestation

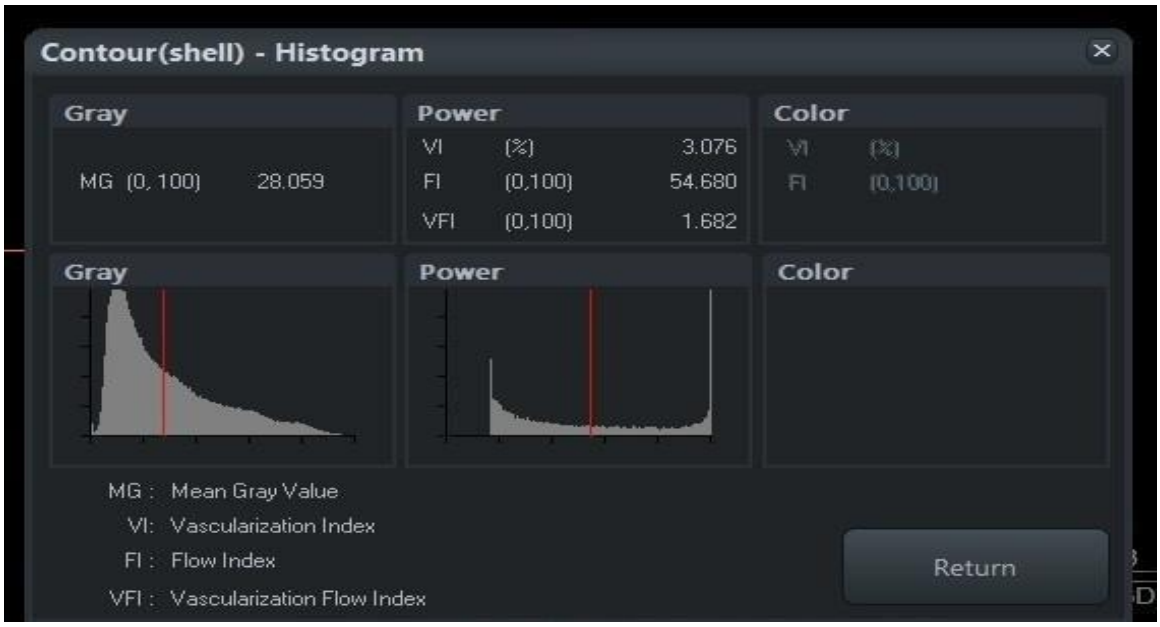

Figure 2. Vascularization and flow indices

Table 1. Baseline characteristics of all patients

	Mean	SD	Median	Minimum	Maximum
BMI	30.23	3.58	29.50	24.00	38.00
Gravidity	4.77	1.61	5.00	1.00	9.00
Parity	3.80	1.30	4.00	1.00	6.00
Cesarean sections	0.97	1.47	0.00	0.00	5.00
Age	41.80	2.93	42.00	36.00	48.00

Table 2. Statistical analysis of obtained data of all patients

	Mean	SD	Median	Minimum	Maximum
Dyspareunia	1.07	0.78	1.00	0.00	2.00
Dysmenorrhea	1.20	0.61	1.00	0.00	2.00
Heaviness	1.17	0.75	1.00	0.00	2.00
Frequency	1.23	0.82	1.00	0.00	2.00
Heavy cycles	1.13	0.78	1.00	0.00	2.00
Long cycles	1.17	0.75	1.00	0.00	2.00
VAS	60.80	28.80	63.13	0.00	100.00
MP	105.20	62.94	95.00	20.00	240.00
Vascularity score	2.30	1.09	2.00	1.00	4.00
VI	3.02	1.30	2.87	1.30	5.70
FI	47.41	7.10	48.30	35.20	59.60

Table 3. Subjective vascularity scoring correlation to symptoms

	Vascularity score		
	Correlation Coefficient	P value	N
VAS score	0.424	0.019	30
MP score	0.767	<0.001	30
Dyspareunia score	0.566	0.002	27
Dysmenorrhea score	0.284	0.129	30
Heaviness score	0.203	0.282	30
Frequency score	0.148	0.436	30
Heavy cycles score	0.772	<0.001	30
Long cycles score	0.172	0.364	30

Table 4. Vascularization index correlation to symptoms

	VI		
	Correlation Coefficient	**P value**	**N**
VAS score	0.459	0.011	30
MP score	0.773	<0.001	30
Dyspareunia score	0.558	0.002	27
Dysmenorrhea score	0.286	0.126	30
Heaviness score	0.131	0.491	30
Frequency score	0.144	0.449	30
Heavy cycles score	0.818	<0.001	30
Long cycles score	0.205	0.277	30

Table 5. Flow index correlation to symptoms

	FI		
	Correlation Coefficient	**P value**	**N**
VAS score	0.320	0.085	30
MP score	0.688	<0.001	30
Dyspareunia score	0.456	0.017	27
Dysmenorrhea score	0.174	0.358	30
Heaviness score	0.031	0.872	30
Frequency score	0.096	0.613	30
Heavy cycles score	0.738	<0.001	30
Long cycles score	0.252	0.178	30

Li et al. found that large uterine size was independently linked to both bothersome lower urinary tract symptoms (LUTS) and HMB, but not to dysmenorrhea [9]. Focusing on the lower urinary tract symptoms (LUTS) which are common complaints in people with adenomyosis, he stated that these symptoms are associated to uterine volume alterations. Between July 2016 and November 2016, a study was carried out to ascertain the prevalence of (LUTS) and variables influencing the severity of these symptoms in women with adenomyosis. Two hundreds and eighty age-matched controls and 298 patients with untreated symptomatic adenomyosis were participated in the study. The following information was logged: demographics, LUTS, pain symptoms, ultrasonographic uterine size, and serum CA125 level.

They discovered that having a big uterine volume may be a risk factor for developing moderate to severe LUTS [9]. According to Gordts et al. a typical sign of adenomyosis is abnormal uterine hemorrhage. In form of excessive menstruation that can cause significant anaemia. This hemorrhage is greatly believed to be due to the expansion of the uterine volume and how adenomyosis lesions affect the contraction of the uterine muscle fibers [10]. According to our knowledge after reviewing the literature a similar study to ours has not been attempted before, we found no studies that correlated the change in severity of specific symptoms to certain ranges of change in uterine vascularity. The literature showed efforts to classify the severity of symptoms based on other parameters.

Van den Bosch proposed that the degree of severity of adenomyosis can be graded based on the ultrasound estimated proportion of the uterine corpus that is affected by adenomyosis, thus the severity of the disease was defined as mild if 25 percent is affected, moderate if 25–50 percent is affected, or severe if > 50 percent is affected [5]. Pinzauti et al. studied the disease distribution [either diffuse or focal] as another parameter for classification and found that women with diffuse adenomyosis experienced a greater average load of symptoms than those who do not [11]. For focal adenomyosis, Kishe et al. studied the position of lesions within the myometrium using MRI, to use this as parameter for classification but discovered no differences in HMB or pain scores for dysmenorrhea, dyspareunia, or CPP [12].

Our use of uterine vascularity in adenomyosis can help in selection of treatment lines and predicting the response to them, for example; the use of the levonorgestrel intrauterine device (LNG-IUD), which released 20 mcg of levonorgestrel per day, acts directly on adenomyotic deposits. It causes a down-regulation of the oestrogen receptors, at least for the first year of use. As a result, the size of the adenomyotic deposits decreases. In numerous trials, this shrinkage was linked to an improvement in the symptoms of adenomyosis [13]. The effectiveness of LNG-IUS in reducing uterine volume and vascularity was demonstrated by a comprehensive review and meta-analysis of 10 prospective studies (n = 551) that concurrently reduced the pain score, endometrial thickness, and menstrual flow [14]. When using a GnRH antagonist to treat adenomyosis, the flare-up effect is avoided, and hormone output returns to normal after quitting the medication. Theoretically, they could lessen uterine vascularity, lessen the likelihood of ectopic endometrial implants in the myometrium, lessen pain brought on by adenomyosis **[**15].

In a retrospective cohort research carried out at Musashikosugi Hospital of Nippon Medical School. 28 women in all were identified as having adenomyosis during this investigation using magnetic resonance imaging. For around 16 weeks, patients received treatment with dienogest (DNG group), a low-dose oestrogen and progestin combination, or a gonadotropin-releasing hormone agonist (GnRHa group).They come to the conclusion that GnRHa is useful in uterine vascularity reduction and ought to be taken into account when recommending hormone therapy for adenomyosis [16]. Along with this GnRH-a effectiveness in reducing adenomyoma vascularity in women with adenomyosis, patients reported improvements in heavy menstrual flow and pelvic pain. Then later, after stopping the dose of GnRH-a, reversal of these changes and a return of symptoms was observed [17].

Another illustration is the research by Jacques et al. who discovered that linzagolix, when taken at a dose of 200 mg per day enhanced clinically significant symptoms[18]. Dienogest is a selective synthetic oral progestin that has been used to treat adenomyosis and shown to lessen persistent pelvic discomfort, dysmenorrhea, and dyspareunia. The therapeutic impact is thought to be connected to the reduced uterine blood flow during treatment [19]. In most women with therapy-resistant adenomyosis, according to De Bruijn et al. Uterine artery embolization induced a noticeable improvement in overall quality of life scores as it alleviated dysmenorrhea, lessened menstrual volume, and ameliorated anaemia symptoms [20].

5. Conclusions

The three-dimensional ultrasound assessment of uteri of adenomyosis allowed deeper evaluation the vascularity. The increase of uterine vascularity is associated with an increase in the amount of uterine bleeding, pelvic pain scores and dyspareunia. The change in uterine vascularity isn't associated with significant change in degree of pelvic heaviness, dysmenorrhea, or frequent micturition episodes.

References

[1] K. UPSON, S.A. Missmer. (2020). Epidemiology of adenomyosis. In: Seminars in Reproductive Medicine, 333 Seventh Avenue, 18th Floor, New York, NY 10001, USA: Thieme Medical Publishers, Inc. 089-107.

[2] Harada, T., Khine, Y. M., Kaponis, A., Nikellis, T., Decavalas, G., & Taniguchi, F. (2016). The Impact of Adenomyosis on Women's Fertility. *Obstetrical & gynecological survey*, *71*(9), 557–568

[3] Yu, O., Schulze-Rath, R., Grafton, J., Hansen, K., Scholes, D., & Reed, S. D. (2020). Adenomyosis incidence, prevalence and treatment: United States population-based study 2006-2015. *American Journal of Obstetrics and Gynecology*, *223*(1), 94.e1–94.e10.

[4] Andres, M. P., Borrelli, G. M., Ribeiro, J., Baracat, E. C., Abrão, M. S., & Kho, R. M. (2018). Transvaginal Ultrasound for the Diagnosis of Adenomyosis: Systematic Review and Meta-

Analysis. *Journal of minimally invasive gynecology*, *25*(2), 257–264.

[5] Van den Bosch, T., de Bruijn, A. M., de Leeuw, R. A., Dueholm, M., Exacoustos, C., Valentin, L., Bourne, T., Timmerman, D., & Huirne, J. A. F. (2019). Sonographic classification and reporting system for diagnosing adenomyosis. *Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology*, *53*(5), 576–582.

[6] Larsen, L., Coyne, K., & Chwalisz, K. (2013). Validation of the menstrual pictogram in women with leiomyomata associated with heavy menstrual bleeding. *Reproductive sciences (Thousand Oaks, Calif.)*, *20*(6), 680–687.

[7] Wang, W., Tian, X., Zhang, T., Wang, Y., Han, Z., & An, R. (2015). Characteristics of Three-Dimensional Power Doppler in Gestational Trophoblastic Disease. *Disease markers*, *2015*, 917687.

[8] Chan Y. H. (2003). Biostatistics 104: correlational analysis. *Singapore medical journal*, *44*(12), 614–619.

[9] Li, Q., Huang, J., Zhang, X. Y., Feng, W. W., & Hua, K. Q. (2021). Dysmenorrhea in patients with adenomyosis: A clinical and demographic study. *Journal of gynecology obstetrics and human reproduction*, *50*(3), 101761.

[10] Gordts, S., Brosens, J. J., Fusi, L., Benagiano, G., & Brosens, I. (2008). Uterine adenomyosis: a need for uniform terminology and consensus classification. *Reproductive biomedicine online*, *17*(2), 244–248.

[11] Pinzauti, S., Lazzeri, L., Tosti, C., Centini, G., Orlandini, C., Luisi, S., Zupi, E., Exacoustos, C., & Petraglia, F. (2015). Transvaginal sonographic features of diffuse adenomyosis in 18-30-year-old nulligravid women without endometriosis: association with symptoms. *Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology*, *46*(6), 730–736.

[12] Kishi, Y., Suginami, H., Kuramori, R., Yabuta, M., Suginami, R., & Taniguchi, F. (2012). Four subtypes of adenomyosis assessed by magnetic resonance imaging and their specification. *American journal of obstetrics and gynecology*, *207*(2), 114.e1–114.e1147.

[13] Habiba, M., Gordts, S., Bazot, M., Brosens, I., & Benagiano, G. (2020). Exploring the challenges for a new classification of adenomyosis. *Reproductive biomedicine online*, *40*(4), 569–581.

[14] Abbas, A. M., Samy, A., Atwa, K., Ghoneim, H. M., Lotfy, M., Saber Mohammed, H., Abdellah, A. M., El Bahie, A. M., Aboelroose, A. A., El Gedawy, A. M., Mostafa, M., Elsenity, M. A., Samy, M., Safwat, S., Abdelrahman, R. M., Salah El Din, A. S., Badran, E., Abdelkader, A. M., & Abdallah, A. (2020). The role of levonorgestrel intra-uterine system in the management of adenomyosis: A systematic review and meta-analysis of prospective studies. *Acta obstetricia et gynecologica Scandinavica*, *99*(5), 571–581.

[15] Donnez, J., Taylor, R. N., & Taylor, H. S. (2017). Partial suppression of estradiol: a new strategy in endometriosis management?. *Fertility and sterility*, *107*(3), 568–570.

[16] Matsushima, T., Akira, S., Fukami, T., Yoneyama, K., & Takeshita, T. (2018). Efficacy of Hormonal Therapies for Decreasing Uterine Volume in Patients with Adenomyosis. *Gynecology and minimally invasive therapy*, *7*(3), 119–123.

[17] M. Fawzy, Y. Mesbah. (2015). Comparison of dienogest versus triptorelin acetate in premenopausal women with adenomyosis: a prospective clinical trial. Archives of Gynecology and Obstetrics. 292: 1267-1271.

[18] J. Donnez, C.A. Stratopoulou, M.M. Dolmans. (2021). Uterine adenomyosis: from disease pathogenesis to a new medical approach using GnRH antagonists. International Journal of Environmental Research and Public Health. 18(19): 9941.

[19] Y. Fan, S. Zhu, X. Liang. (2022). Conservative surgical and drug therapies for adenomyosis Medicine. Reproductive Biology. 22(3): 100664.

[20] A.M. de Bruijn, et al. (2017). Uterine artery embolization for symptomatic adenomyosis: 7-year clinical follow-up using UFS-Qol questionnaire. Cardiovascular and Interventional Radiology. 40: 1344-1350.