

## Accuracy of Ultrasound in the Diagnosis of Uterine Fibroids and Malignant Uterine Lesions among Saudi Women

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### Abstract

**Background:** Uterine fibroids, the most frequent benign uterus tumors, often cannot be distinguished from malignant uterine tumors using clinical criteria. Due to their potential overlapping characteristics, imaging differentiation between both entities is commonly challenging. This study aims to evaluate the diagnostic accuracy of ultrasound (US) in the diagnosis of uterine fibroids and malignant uterine lesions among Saudi women.

**Methods and Results:** Eighty Saudi women aged between 20 and 70 years were retrospectively collected from two different centers in Riyadh, Saudi Arabia. All patients were subjected to a presurgical US scan, and the diagnosis was histopathologically proven. The US accurately detected uterine fibroids in 43 (53.75%) of cases with different locations. Intramural fibroids [62.8% (27/43)] were the most common, followed by subserosal fibroids [25.6% (11/43)], submucosal fibroids [7.0% (3/43)], and pedunculated fibroids [4.6% (2/43)]. Signs of endometrial cancer were US found in 7 (8.75%) cases that were histologically proven. Ultrasound features suspicious of uterine cancer were found in 30 (37.5%) cases that were not confirmed by histopathological examination. The sensitivity and specificity of ultrasound for uterine cancer diagnosis were 100% (95% CI: 59.04% to 100.00%) and 58.9% (95% CI: 46.77% to 70.29%), respectively. Cancer incidence was more frequent among postmenopausal patients (n=5) compared to premenopausal patients (n=2) ( $P=0.028$ ).

**Conclusion:** The US is a good and accurate diagnostic method in differentiating types of uterine fibroids in Saudi women. The sensitivity and specificity of ultrasound in diagnosing uterine cancer are 100% and 58.9%, respectively. The incidence of cancer is higher among postmenopausal patients compared to premenopausal patients. (*International Journal of Biomedicine*. 2024;14(3):469-473.)

**Key words:** uterine fibroids • ultrasound imaging • malignant tumors • diagnosis

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### Introduction

In women of reproductive age, uterine fibroids (also called leiomyomas) are the most frequent benign uterus neoplasm and a significant source of morbidity, affecting up to 68.6% of women.<sup>(1,2)</sup> Globally, high uterine fibroid prevalence significantly affects healthcare costs.<sup>(1)</sup> Most women with

leiomyoma are asymptomatic, and about a third of cases have significant symptoms such as pelvic pain, secondary anemia, abnormal uterine bleeding, menorrhagia, dysmenorrhea, and infertility.<sup>(3,4)</sup> The treatment of uterine fibroid cases should be individualized based on the nodule characteristics (e.g., location and size), the patient's desire to preserve the uterus or fertility, the patient's age, and the symptoms, as well as the therapy availability and the physician's experience.<sup>(5)</sup>

In this context, the US is considered the initial test of choice for fibroids diagnosis in symptomatic patients, mainly due to its high specificity and sensitivity, cost-effectiveness, ease of use, and broad availability.<sup>(6,7)</sup> To accurately describe

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and identify all fibroids, US examinations should be performed by specially trained physicians.<sup>(8)</sup> Other aspects that are important in the therapy choice are the location and size of the fibroids, coexistence of deep endometriosis or adenomyosis, vascular supply, relationship with and proximity to the endometrial cavity, proximity to the uterine serosa, penetration of the myometrial component and the submucosal component presence that easily detected and can be characterized by using transvaginal US.<sup>(6,8,9)</sup>

In clinical practice, uterine tumors are the most common gynecologic malignancies and are a challenge encountered by each gynecologist.<sup>(10)</sup> There were about an estimated 3.6% (65,620 cases) of all new tumor cases and 2.1% (12,590 deaths) of all tumor-related deaths accounted for uterine cancer.<sup>(11)</sup> In patients with sonographic suspicion of benign leiomyoma, most uterine malignant tumors diagnosis is incidentally carried out at pathology or during surgery.<sup>(12)</sup> The accurate differential diagnosis between sarcoma and benign myoma is mandatory for a correct surgical treatment.<sup>(10)</sup> Degenerating uterine fibroids often cannot be distinguished from malignant uterine tumors based on clinical criteria alone.<sup>(13)</sup> Furthermore, due to their potential overlapping features, imaging differentiation between both entities is commonly challenging.<sup>(13)</sup> It should be noted that ultrasound's accuracy in the differential diagnosis of uterine leiomyoma and in detecting uterine sarcoma in various populations remains relevant. This study aimed to evaluate the diagnostic accuracy of ultrasound in the diagnosis of uterine fibroids and malignant uterine lesions among Saudi women.

## Materials and Methods

### Patients

This retrospective study was conducted at the College of Health and Rehabilitation Sciences, Nourah bint Abdulrahman University. Patients were collected, and their demographic data was coded at two hospitals: Al-Yamamah Hospital, Riyadh, Saudi Arabia, and Riyadh Care, Riyadh, Saudi Arabia. The inclusion criteria were Saudi women aged 20-70 years, the ability to communicate with the physician, patients with clear and identified uterine fibroids with diameters of 3-8 cm, and patients with histologically proven uterine malignant tumors who had previous fibroids. The exclusion criteria were ongoing or recent pelvic inflammatory disorder, patients who underwent hysterectomy, and current pregnancy. In all eligible cases (n=80), the patient underwent US before enrollment. The patients' height, weight, and age were recorded.

### Sample Size

The final sample size of this study was 80 cases, which was calculated using the following formula:<sup>(14)</sup>  $n = Z^2 \times P \times (1-P) / e^2$ , where n = the needed sample size, Z at a 95% CI = 1.96, P = the prevalence of uterus cancer in Saudi Arabia, and e = the margin of error (5%).

### Ultrasound Examination

One hour before the transabdominal US examination,<sup>(15)</sup> patients were asked to drink 24 ounces of clear water to fill the bladder. A US device (GE VolusonE10, USA) was used to examine the abdomen. For routine uterus scanning, a transabdominal convex array probe (low frequency: 3-5 MHz)

was selected to identify the bilateral appendage, uterine wall thickness, contour, size, position, and other surrounding uterus tissues. Unaware of the pathological results, three experienced radiologists reviewed the final diagnosis individually to reduce the error.

Before the transvaginal US examination,<sup>(15)</sup> the patient was told to empty the bladder. During the examination, the lithotomy position of the patient's bladder was taken. The tip of the high frequency (5-7.5 MHz) transvaginal transducer probe of the US diagnostic device was inserted into the vagina of the subject and placed in the vagina's external cervical opening. By using tilt and rotation, the uterus was explored in several sections. Uterine muscle wall thickness, presence of mass, endometrial abnormalities, edge characteristics, position, shape, size, and other information were observed.

### Fibroids and Malignant Tumor Assessment

In the US examination, fibroids appear as well-defined solid masses. Usually, they have similar echogenicity to the myometrium and may appear hypoechoic. They cause the uterus to appear bulky or may cause distortion of the normal uterine contour. Calcified fibroids have posterior acoustic shadowing; even non-calcified fibroids often show a degree of posterior acoustic shadowing. Degenerate fibroids with cystic change may have a complex appearance. Doppler ultrasound commonly shows circumferential vascularity; however, necrotic or undergone torsion fibroids show the absence of flow.<sup>(16-18)</sup>

Images from the transvaginal US may reveal if the uterus contains a mass or if the endometrium is thicker than usual, which can be a sign of endometrial cancer. Histopathological Examination

During the operation, tissue specimens of the uterus were collected from each patient and sent for examination. The samples were placed in a neutral formaldehyde fixative solution (10%). After sectioning, dehydration, and hematoxylin-eosin staining, the diagnosis results were obtained by microscopic examination.

Statistical analysis was performed using the statistical software package SPSS version 20.0 (SPSS Inc, Armonk, NY: IBM Corp). Baseline characteristics were summarized as frequencies and percentages for categorical variables and as mean (M) ± standard deviation (SD) for continuous variables. For data with normal distribution, inter-group comparisons were performed using Student's t-test. Group comparisons with respect to categorical variables were performed using the chi-square test or, alternatively, Fisher's exact test. A probability value of  $P < 0.05$  was considered statistically significant.

## Results

Eighty Saudi female patients aged between 20 and 70 years were included in this study. Patient characteristics are presented in Table 1. Regarding menopause age, patients were divided into 2 groups: Group 1 included 55 patients at the age of ≤ 50 years and Group 2 included 25 patients over 50 (Table 1). According to the histopathological examination, 73 patients were proven to have uterine fibroids and 7 with uterine cancer.

**Table 1.****Baseline patient characteristics.**

Variable	Value
Total number of patients	80
Age (years)	42.25±12.17
≤50 years	55 (68.75%)
>50 years	25 (31.25%)
Height (cm)	161.11±8.91
Weight (kg)	71.44±17.12

The US accurately detected uterine fibroids in 43 (53.75%) of cases with different locations. Intramural fibroids [62.8% (27/43)] were the most common, followed by subserosal fibroids [25.6% (11/43)], submucosal fibroids [7.0% (3/43)], and pedunculated fibroids [4.6% (2/43)]. Signs of endometrial cancer were US found in 7 (8.75%) cases that were histologically proven. Ultrasound features suspicious of uterine cancer were found in 30 (37.5%) cases that were not confirmed by histopathological examination.

The sensitivity and specificity of ultrasound for uterine cancer diagnosis were 100% (95% CI: 59.04% to 100.00%) and 58.9% (95% CI: 46.77% to 70.29%), respectively (Table 2). Cancer incidence was more frequent among postmenopausal patients (n=5) compared to premenopausal patients (n=2) ( $P=0.028$ ) (Table 3).

**Table 2.****Ultrasound preoperative diagnosis of uterine lesions against the final histology diagnosis.**

			Histology Uterine cancer		P-value
			Absent	Precent	
			n=73	n=7	
US	Fibroids	n=43	43	0	0.003
	Suspicious of UC	n=37	30	7	

UC, uterine cancer

**Table 3.****Cancer incidence among women by age.**

	≤50 years	>50 years	Total	Mean age
Cancer	2	5	7	60.29±13.96
Non-Cancer	53	20	73	43.81±11.01
P-value	0.028			<0.001

## Discussion

Uterine fibroids are smooth muscle benign tumors that originate from the myometrium, or outer uterus muscular layer, and they are the most frequent uterus neoplasms.<sup>(19)</sup> They constitute the primary cause of hysterectomies, representing about 40% of all hysterectomies.<sup>(19)</sup> Given that uterine fibroids

may be managed with minimally invasive therapy, it is specifically urgent to distinguish them preoperatively from confounding uterine malignant entities.<sup>(13,20)</sup>

Although uterine malignant sarcomas are rare women tumors, these types of tumors have a poor prognosis, and the vast majority of cases have no specific signs (about 25% of cases are asymptomatic).<sup>(21)</sup> The preoperative detection of uterine malignant tumors is challenging because of the similarity of symptoms to those of uterine fibroids and their nonspecific clinical manifestations.<sup>(22)</sup> The US examination is the first approach because the US scan is low-cost, requires no preparation, and is easy to perform.<sup>(23)</sup> Accordingly, this study aimed to evaluate US diagnostic accuracy in the detection of uterine fibroids and in predicting uterine suspicious malignant tumors among Saudi female patients.

According to their location, fibroids are classified into intramural, subserosal, pedunculated, or submucosal.<sup>(24)</sup> In this study, US accurately differentiated and detected different locations of uterine fibroids and revealed that intramural fibroids (62.5%) were the most common, followed by subserosal fibroids (25%), submucosal fibroids (8.75%) and pedunculated fibroids (3.75%). Other studies in Saudi Arabia have also reported that intramural fibroids are the most common uterine fibroids. For example, Muawad et al., among patients from 2 different medical centers in Riyadh, Saudi Arabia, reported that the most common uterine fibroids type was intramural (64.4%), followed by intramural subserosal (15.9%), subserosal (15.5%), submucosal (2.9%) and intramural submucosal (1.3%).<sup>(25)</sup>

Based on many ultrasonographic results, some reports have demonstrated that uterine malignant tumors were likely to appear as solid masses with enhanced vascularity and heterogeneous echogenicity<sup>(26,27)</sup> and that Doppler assessment of the resistance index may be a useful diagnostic approach.<sup>(28)</sup> Nevertheless, limited data from a small number of studies supported that issue. In this study, as confirmed by histopathological examination after surgical intervention, a presurgical US scan successfully detected all patients with suspicious cancer lesions (7/7, sensitivity =100 %). However, there were other 30 patients that were falsely diagnosed by US scan to be with malignant lesions.

Kim et al.<sup>(27)</sup> found that no definite clinical symptoms were helpful in misdiagnosed sarcomas, and a thorough US evaluation is necessary to rule out uterine malignant tumors. They found that ultrasonography showed irregular cystic degeneration and heterogeneous echogenicity in these patients. Exacoustos et al.<sup>(29)</sup> demonstrated that the US can differentiate uterine leiomyosarcoma from benign leiomyoma. They found that sarcomas were associated with large size ( $\geq 8$  cm), degenerative cystic, and elevated central and peripheral vascularity. In agreement, Ludovisi et al.<sup>(26)</sup> also described that sarcomas are solitary and large lesions, even if they may coexist in the same uterus with benign fibroids. In half of the cases, the malignant tumors are solid masses with inhomogeneous echogenicity, irregular cystic areas, and irregular borders.<sup>(26)</sup>

In general, and on the malignant spectrum, uterine malignant tumors are pathologically diagnosed and tend to occur in postmenopausal older women after surgery.<sup>(27,30)</sup> Another important finding of our study is that cancer incidence

was more frequent among postmenopausal patients (71.4%) compared to premenopausal patients (28.6%). The positive relation between uterine fibroids and age agreed with results from other studies conducted in different world regions, some estimated that 60-70% of women have one or more uterine fibroids by age 50.<sup>(31,32)</sup> In women, this association may be due to the accumulation of hormonal changes during the reproductive lifespan. A remarkable characteristic of uterine fibroids is their dependency on ovarian steroids, progesterone, and estrogen.<sup>(33)</sup> During the reproductive years, clinical and experimental studies have suggested that progesterone and estrogen stimulate uterine fibroid growth.<sup>(33,34)</sup>

**In conclusion**, the US is a good and accurate diagnostic method in differentiating types of uterine fibroids in Saudi women. The sensitivity and specificity of ultrasound in diagnosing uterine cancer are 100% and 58.9%, respectively. The incidence of cancer is higher among postmenopausal patients compared to premenopausal patients.

## Ethical Considerations

The study was conducted in accordance with ethical principles of the Declaration of Helsinki<sup>(35)</sup> and approved by the Ethics Committee at Princess Nourah bint Abdulrahman University. All participants provided written informed consent.

## Competing Interests

The authors declare that they have no competing interests.

## References

1. Lou Z, Huang Y, Li S, Luo Z, Li C, Chu K, Zhang T, Song P, Zhou J. Global, regional, and national time trends in incidence, prevalence, years lived with disability for uterine fibroids, 1990-2019: an age-period-cohort analysis for the global burden of disease 2019 study. *BMC Public Health*. 2023 May 19;23(1):916. doi: 10.1186/s12889-023-15765-x. PMID: 37208621; PMCID: PMC10199532.
2. Giuliani E, As-Sanie S, Marsh EE. Epidemiology and management of uterine fibroids. *Int J Gynaecol Obstet*. 2020 Apr;149(1):3-9. doi: 10.1002/ijgo.13102. Epub 2020 Feb 17. PMID: 31960950.
3. Keizer AL, van Kesteren PJM, Terwee C, de Lange ME, Hehenkamp WJK, Kok HS. Uterine Fibroid Symptom and Quality of Life questionnaire (UFS-QOL NL) in the Dutch population: a validation study. *BMJ Open*. 2021 Nov 23;11(11):e052664. doi: 10.1136/bmjopen-2021-052664. PMID: 34815284; PMCID: PMC8611425.
4. Stewart EA, Laughlin-Tommaso SK, Catherino WH, Lalitkumar S, Gupta D, Vollenhoven B. Uterine fibroids. *Nat Rev Dis Primers*. 2016 Jun 23;2:16043. doi: 10.1038/nrdp.2016.43. PMID: 27335259.
5. Management of Symptomatic Uterine Leiomyomas: ACOG Practice Bulletin, Number 228. *Obstet Gynecol*. 2021 Jun 1;137(6):e100-e115. doi: 10.1097/AOG.0000000000004401. PMID: 34011888.
6. Palheta MS, Medeiros FDC, Severiano ARG. Reporting

- of uterine fibroids on ultrasound examinations: an illustrated report template focused on surgical planning. *Radiol Bras*. 2023 Mar-Apr;56(2):86-94. doi: 10.1590/0100-3984.2022.0048. PMID: 37168038; PMCID: PMC10165971.
7. Pereira AEMM, Franco J, Machado FS, Geber S. Accuracy of Transvaginal Ultrasound in the Diagnosis of Intrauterine Lesions. *Rev Bras Ginecol Obstet*. 2021 Jul;43(7):530-534. doi: 10.1055/s-0041-1732462. Epub 2021 Aug 30. PMID: 34461663; PMCID: PMC10305154.
  8. Liu YH, Qiu YH, Ru Y, Liu YQ, Wang D, Zhang PA. Selection of different surgical methods for uterine fibroids: Protocol for a retrospective clinical study. *Medicine (Baltimore)*. 2021 Dec 23;100(51):e28378. doi: 10.1097/MD.00000000000028378. PMID: 34941163; PMCID: PMC8702229.
  9. Metwally M, Raybould G, Cheong YC, Horne AW. Surgical treatment of fibroids for subfertility. *Cochrane Database Syst Rev*. 2020 Jan 29;1(1):CD003857. doi: 10.1002/14651858.CD003857.pub4. PMID: 31995657; PMCID: PMC6989141.
  10. Wojtowicz K, Góra T, Guzik P, Harpula M, Chechliński P, Wolak E, Strykowska-Góra A. Uterine Myomas and Sarcomas - Clinical and Ultrasound Characteristics and Differential Diagnosis Using Pulsed and Color Doppler Techniques. *J Ultrason*. 2022 Apr 27;22(89):100-108. doi: 10.15557/JoU.2022.0017. PMID: 35811590; PMCID: PMC9231509.
  11. Chelmos D, Brooks R, Cavens A, Huber-Keener K, Scott DM, Sheth SS, Whetstone S, Worly B, Burke W. Executive Summary of the Uterine Cancer Evidence Review Conference. *Obstet Gynecol*. 2022 Apr 1;139(4):626-643. doi: 10.1097/AOG.0000000000004711. Epub 2022 Mar 10. PMID: 35272316; PMCID: PMC8936160.
  12. Giunchi S, Perrone AM, Tesei M, Bovicelli A, De Crescenzo E, Dondi G, et al. Sonographic imaging in uterine sarcoma: a narrative review of literature. *Gynecol Pelvic Med*. 2021;5:14.
  13. Sun S, Bonaffini PA, Nougaret S, Fournier L, Dohan A, Chong J, Smith J, Addley H, Reinhold C. How to differentiate uterine leiomyosarcoma from leiomyoma with imaging. *Diagn Interv Imaging*. 2019 Oct;100(10):619-634. doi: 10.1016/j.diii.2019.07.007. Epub 2019 Aug 16. PMID: 31427216.
  14. Pourhoseingholi MA, Vahedi M, Rahimzadeh M. Sample size calculation in medical studies. *Gastroenterol Hepatol Bed Bench*. 2013 Winter;6(1):14-7. PMID: 24834239; PMCID: PMC4017493.
  15. Qi H, Zhou C, Huang Z, Yang N, Wu Q. Value of Transabdominal Combined Transvaginal Color Doppler Ultrasonography in the Distinguish between Uterine Adenomyoma and Uterine Fibroids. *Biomed Res Int*. 2022 Jul 7;2022:9599571. doi: 10.1155/2022/9599571. Retraction in: *Biomed Res Int*. 2023 Nov 29;2023:9876769. doi: 10.1155/2023/9876769. PMID: 35845931; PMCID: PMC9283036.
  16. Woźniak A, Woźniak S. Ultrasonography of uterine leiomyomas. *Prz Menopauzalny*. 2017 Dec;16(4):113-117. doi: 10.5114/pm.2017.72754. Epub 2017 Dec 30. PMID: 29483851; PMCID: PMC5824679.
  17. De La Cruz MS, Buchanan EM. Uterine Fibroids: Diagnosis and Treatment. *Am Fam Physician*. 2017 Jan 15;95(2):100-107. PMID: 28084714.
  18. Khan AT, Shehmar M, Gupta JK. Uterine fibroids: current perspectives. *Int J Womens Health*. 2014 Jan 29;6:95-114.

- doi: 10.2147/IJWH.S51083. PMID: 24511243; PMCID: PMC3914832.
19. George JW. The burden of uterine fibroids: an overview. *J Histotechnol.* 2023 Dec;46(4):153-155. doi: 10.1080/01478885.2023.2265185. Epub 2023 Nov 27.
20. Mori KM, Abaid LN, Mendivil AA, Brown JV 3rd, Beck TL, Micha JP, Epstein HD, Goldstein BH. The incidence of occult malignancy following uterine morcellation: A ten-year single institution experience retrospective cohort study. *Int J Surg.* 2018 May;53:239-242. doi: 10.1016/j.ijvs.2018.03.075. Epub 2018 Apr 3. PMID: 29621658.
21. Cheng G, Hu Y, Gong Y. Clinical manifestations and prognosis of unexpected uterine sarcoma of uterine fibroids in Tianjin China. *BMC Womens Health.* 2022 Dec 6;22(1):495. doi: 10.1186/s12905-022-02077-2. PMID: 36474216.
22. Zhu M, Chen S. Clinical features of uterine sarcomas presenting mainly with uterine masses: a retrospective study. *BMC Womens Health.* 2023 Jul 26;23(1):394. doi: 10.1186/s12905-023-02517-7. PMID: 37496042; PMCID: PMC10373283.
23. Liu S, Wang Y, Yang X, Lei B, Liu L, Li S X., et al. Deep Learning in Medical Ultrasound Analysis: A Review. *Engineering.* 2019; 5: 261-275.
24. Bulun SE. Uterine fibroids. *N Engl J Med.* 2013 Oct 3;369(14):1344-55. doi: 10.1056/NEJMra1209993. PMID: 24088094.
25. Muawad R, Dabbagh R, Sabr Y. Association of health and lifestyle factors with uterine fibroids among Saudi women: A case-control study. *J Taibah Univ Med Sci.* 2022 Jul 11;17(6):1039-1046. doi: 10.1016/j.jtumed.2022.06.005. PMID: 36212583; PMCID: PMC9519786.
26. Ludovisi M, Moro F, Pasciuto T, Di Noi S, Giunchi S, Savelli L, Pascual MA, Sladkevicius P, Alcazar JL, Franchi D, Mancari R, Moruzzi MC, Jurkovic D, Chiappa V, Guerriero S, Exacoustos C, Epstein E, Frühauf F, Fischerova D, Fruscio R, Ciccarone F, Zannoni GF, Scambia G, Valentin L, Testa AC. Imaging in gynecological disease (15): clinical and ultrasound characteristics of uterine sarcoma. *Ultrasound Obstet Gynecol.* 2019 Nov;54(5):676-687. doi: 10.1002/uog.20270. Epub 2019 Oct 7. PMID: 30908820.
27. Kim JH, Kim HJ, Kim SH, Shin SA, Park SY, Kim DY, Lee SR, Chae HD, Kang BM. Sonographic and Clinical Characteristics of Uterine Sarcoma Initially Misdiagnosed as Uterine Fibroid in Women in the Late Reproductive Age. *J Menopausal Med.* 2019 Dec;25(3):164-171. doi: 10.6118/jmm.19007. PMID: 32307942; PMCID: PMC6952706.
28. Szabó I, Szánthó A, Csabay L, Csapó Z, Szirmai K, Papp Z. Color Doppler ultrasonography in the differentiation of uterine sarcomas from uterine leiomyomas. *Eur J Gynaecol Oncol.* 2002;23(1):29-34. PMID: 11876388.
29. Exacoustos C, Romanini ME, Amadio A, Amoroso C, Szabolcs B, Zupi E, Arduini D. Can gray-scale and color Doppler sonography differentiate between uterine leiomyosarcoma and leiomyoma? *J Clin Ultrasound.* 2007 Oct;35(8):449-57. doi: 10.1002/jcu.20386. PMID: 17636502.
30. Aviram R, Ochshorn Y, Markovitch O, Fishman A, Cohen I, Altaras MM, Tepper R. Uterine sarcomas versus leiomyomas: gray-scale and Doppler sonographic findings. *J Clin Ultrasound.* 2005 Jan;33(1):10-3. doi: 10.1002/jcu.20075. PMID: 15690441.
31. Donnez J, Dolmans MM. Uterine fibroid management: from the present to the future. *Hum Reprod Update.* 2016 Nov;22(6):665-686. doi: 10.1093/humupd/dmw023. Epub 2016 Jul 27. PMID: 27466209; PMCID: PMC5853598.
32. Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. *Am J Obstet Gynecol.* 2003 Jan;188(1):100-7. doi: 10.1067/mob.2003.99. PMID: 12548202.
33. Wise LA, Laughlin-Tommaso SK. Epidemiology of Uterine Fibroids: From Menarche to Menopause. *Clin Obstet Gynecol.* 2016 Mar;59(1):2-24. doi: 10.1097/GRF.000000000000164. PMID: 26744813; PMCID: PMC4733579.
34. Cermik D, Arici A, Taylor HS. Coordinated regulation of HOX gene expression in myometrium and uterine leiomyoma. *Fertil Steril.* 2002 Nov;78(5):979-84. doi: 10.1016/s0015-0282(02)03366-6. PMID: 12413981.
35. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA.* 2013 Nov 27;310(20):2191-4. doi: 10.1001/jama.2013.281053. PMID: 24141714.
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