

ORIGINAL ARTICLE

Prevalence and Risk Factors of Sonographically Detected Uterine Fibroid among Iraqi Women in Medical Baghdad City, Baghdad, Iraq

Abdul Sattar Arif Khammas^{1*}, Safwan Saeed Mohammed¹, Sarah Qahtan Mohammed Salih², Danmaigoro Abubakar³

¹ Department of Radiological Techniques, College of Health and Medical Technology, Middle Technical University, Baghdad, Iraq

² Computer Center, College of Health and Medical Technology, Middle Technical University, Baghdad, Iraq

³ Faculty of Veterinary Medicine, Usmanu Danfodiyo University, Sokoto, Nigeria

*Corresponding author's email: abdulsattar.arif@mtu.edu.iq

Received: 15 August 2021

Accepted: 6 January 2022

Published: 31 May 2022

DOI: <https://doi.org/10.51200/bjms.vi.3334>

Keywords: *uterine fibroid, sonography, Iraqi women, risk factors*

ABSTRACT

Uterine fibroid (uterine myoma or leiomyoma) is the most common benign tumour of the women's pelvic. This study aimed to determine the prevalence and risk factors associated with uterine fibroid among Iraqi women in Baghdad, Iraq. A cross-sectional study was prospectively carried out in this survey. Women aged 13 years old and above were randomly recruited based on a systematic sampling method. The participants' personal and history information were collected using a structured self-administered questionnaire (SSAQ). In addition, a trans-abdominal ultrasound with both B-mode and Doppler was used to detect uterine fibroid. Transabdominal ultrasound was performed on 127 women with a mean age of 36.3 ± 11.5 years old. Among those, 43 (33.9%) women were reported to have a uterine fibroid. However, uterine fibroid was statistically associated with age ($X^2 = 35.3, P < 0.001$), BMI ($X^2 = 11.2, P = 0.011$), family history of uterine fibroid ($X^2 = 8.1, P = 0.005$), and age at first menstruation ($X^2 = 12.9, P = 0.005$). The prevalence of uterine fibroid detected by ultrasound was alarming among Iraqi women aged 49 to 60 years old. Being overweight, obese, having a positive family history of uterine fibroid, and early menarche increases the risk of developing uterine fibroid.

INTRODUCTION

Uterine fibroid, also referred to as uterine myoma or leiomyoma, is the most common benign tumour of the women's pelvic (Serden & Brooks, 1991; Baird et al., 2003; Pavone et al., 2018). Histologically, it is a benign tumour of the myometrium due to hormonal disruption

during early development growth (Cramer & Patel, 1990; Flake et al., 2003). It was reported that about 40 to 60% of all hysterectomies result from fibroid, and 30% of them are from young women between 18 and 44 years old (Merrill, 2008). Therefore, uterine fibroid considers a major indication for hysterectomy (Farquhar & Steiner, 2002; Merrill, 2008). Clinically, it is characterized by irregular menstrual bleeding associated with pelvic pains leading to chronic anaemia (Pérez-López et al., 2014). Although this condition rarely can cause death, it is considered the leading cause of morbidity (Baird et al., 2015).

The risk factors that induce tumorigenesis are still not apparent. However, oestrogen and progesterone have a critical role in growth (Bulun, 2013). Although the healthcare and morbidity costs are correlated with uterine fibroid, few studies determined its risk factors and possible strategy prevention. In this context, age, ethnicity, age of menarche, and parity are the most risk factors replicated (Laughlin et al., 2010).

However, the initiating factors of the uterine fibroid are still poorly understood, although previous studies demonstrated that age advances, obesity, smoking, earlier menstrual period, uterine infections, hypertension and diabetes mellitus, hormonal imbalance, and nulliparous are important risk factors for developing uterine fibroid (Laughlin et al., 2010; Pavone et al., 2018). The actual time of the commencement of fibroid growth is not usually known since no clinical manifestation is revealed at the early growth stage (Pavone et al., 2018). Ultrasound is widely used in detecting uterine fibroids since it is safe (non-ionizing radiation and readily available at a meagre cost compared to other diagnostic radiological modalities such as computed tomography (CT) and magnetic resonance imaging (MRI). Although this condition is considered a public health burden, no previous study in Iraq has been conducted to periodically screen uterine fibroid with

ultrasound to detect its prevalence and risk factors (Baird et al., 2015). Thus, this study aimed to determine the prevalence and risk factors associated with uterine fibroid detected using ultrasound among Iraqi women.

MATERIALS AND METHODS

Study Design and Population

A prospective cross-sectional study was used in this study. The participants consisted of Iraqi women who attended the radiology department in Medical Baghdad City and were enrolled for 6 months from July 2019 to December 2019. Participants aged 13 years old and above at enrollment with an intact uterus were randomly selected using systematic sampling techniques. Women aged 18 years old and above signed the informed consent form before enrollment into this study. However, for those below 18 years old, the consent form was signed by their parents. Variables such as demographic information, medical history, family history of the disease, and menstrual period schedules were obtained using a structured self-administered questionnaire (SSAQ) and interview. However, participants diagnosed with uterine fibroid, uterine cancer, or under chemotherapy/ radiotherapy or premenstrual period were excluded from the study. Ethical approval was obtained from the College of Health and Medical Technology with reference number 3/11/1654.

Sample Size Calculation

The sample size calculation was carried out using KC Lun and Peter Chiam software based on hypothesis tests for two population proportions (two-sided test). The differences between the two proportions having uterine fibroids (P1 and P2) were calculated. P1 was the larger population and P2 was the smaller. An α error of 0.05 and a power of 0.90 was used for sample size calculation. Thus, the sample size for the uterine fibroid group was calculated to be 53 patients and for the

group without uterine fibroid was 53 subjects. Therefore, a minimum total sample size for the present study was estimated to be 106 subjects. However, the sample size recruited and analyzed in this study was 127 subjects.

Anthropometric Data Acquisition

A weighing scale (COPY, max 180 kg/ 396 lbs) was used to measure body weight, whereas an elastic tape measure was used to measure body height, and then a body mass index (BMI) (kg/m^2) was calculated. BMI was classified based on a global database on BMI in adults as follows: BMI $< 18.5 \text{ kg}/\text{m}^2$ was described as underweight, $18.5 - 24.9 \text{ kg}/\text{m}^2$ was described as normal, $25.0 - 29.9 \text{ kg}/\text{m}^2$ was defined as overweight, BMI $\geq 30.0 \text{ kg}/\text{m}^2$ was described as obese (World Health Organization [WHO], 2000). Blood pressure was measured by using a standardized sphygmomanometer. The participants were considered to have hypertension if they had systolic blood pressure $\geq 140 \text{ mmHg}$ or diastolic blood pressure $\geq 90 \text{ mmHg}$, had taken antihypertensive medication(s), and had a self-reported history of hypertension (National Cholesterol Education Program [NCEP], 2002). Similarly, the women were considered to have diabetes mellitus (DM) if they had fasting blood glucose (FBG) $\geq 126 \text{ mg}/\text{dL}$ and glycosylated haemoglobin (HbA1c) $\geq 6.5 \%$, had taken antidiabetic medication (s), or had a self-reported history of DM (NCEP, 2002).

Sonography of Uterine Fibroid

This study used a GE LOGIQ 6 ultrasound machine equipped with a convex probe (3.5 MHz) for pelvic scanning. Radiologists carried out ultrasound examinations with more than 10-year work experience. Transabdominal ultrasound was performed to detect and evaluate uterine fibroids. Each participant was informed to drink water even if her bladder became full to make a good window for pelvic organs such as the uterus. The participant was informed to lie supine; then, both longitudinal

and transverse scans were applied. A B-mode grayscale and Doppler study were performed in each scan. Since uterine fibroid is an overgrowth of the smooth muscle in the uterine wall, its echogenicity always appears similar to myometrium but sometimes echoic with acoustic shadowing. In addition, fibroid causes the uterus to be bulky and may be irregular in shape.

When the colour Doppler study was applied, there was no internal vascularity within the fibroid, but peripheral vascularity was shown. However, lack of vascularity was monitored if the necrotic or torsion was diagnosed within the fibroid. Colour Doppler of the uterine blood flow is mainly dependent on the quality of the ultrasound machine, parity and age of the women. For instance, in postmenopausal women, myometrium and endometrium of the uterus have shown hypovascularity in colour Doppler study.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) software version 22.0 was used to analyze the data. The descriptive statistics were used to find the percentages and frequencies for categorical variables and mean \pm SD for the continuous variables. A Chi-square was used to determine an association between factors and uterine fibroid, where a P-value of less than 0.05 was considered statistically significant.

RESULTS

The characteristics of the study population are illustrated in Table 1. However, 127 consecutive women enrolled were scanned and included in the statistical analysis. The mean age of our study population was 36.3 ± 11.5 years old. Out of 127 participants, 43 (33.9%) women were reported to have fibroids, with 50.4 % of the women being overweight and 88.2% married. Non-smoking was overwhelming (96.9%) among our study population. In terms of the medical history of diseases, most of our study

population had normotensive and normal blood sugar (78.8% and 93.7%, respectively). Our results also reported that only 4 (3.1%) women were found to have a family history of fibroid. The premenopausal women (those who are still menstruating) had a higher percentage (81.1%) than postmenopausal women (18.9%). The women who had taken oral and hormonal contraceptives were less common than those without contraceptives (26.4% vs 73.6%). The number of women who had an abortion was lower than those who never had an abortion (32.7% vs 67.3). The majority of the women (38.6%) had their first menstrual cycle at 12 years old. Furthermore, the highest percentage of women was found among those who had delivered 3 children and above (46.4%), followed by 2 children (19.6%). In contrast, those who had delivered 1 child or never had parity were the lowest and equally in per cent (17.0%). The majority of the women had (53.8%) their first delivery between 14 and 20 years of age, whereas a high percentage of women (55.9%) had a final delivery between 24 and 31 years of age.

Table 1 Distribution of the study population (n = 127 subjects)

Variables	Mean ±SD	n (%)
Age	36.3 ± 11.5	
Marital status		
Single		15 (11.8)
Married		112 (88.2)
Smoking		
No		123 (96.9)
Yes		4 (3.1)
BMI categories		
Underweight		0 (0.0)
Normal		22 (17.3)
Overweight		64 (50.4)
Obese		41 (32.3)
Hypertension		
No		100 (78.8)
Yes		27 (21.3)
DM		
No		119 (93.7)
Yes		8 (6.3)

Family history of fibroid		
No		123 (96.9)
Yes		4 (3.1)
Menstruation status		
Premenopausal state		103 (81.1)
Postmenopausal state		24 (18.9)
Contraceptives use		
No		81 (73.6)
Yes		29 (26.4)
Abortion		
No		74 (67.3)
Yes		36 (32.7)
Presence of fibroid		
No		84 (66.1)
Yes		43 (33.9)
Age of 1st menstruation (Age of menarche)		
≥ 11 years		18 (14.2)
12 years		49 (38.6)
13 years		33 (26.0)
≥ 14 years		27 (21.3)
Parity		
None		19 (17.0)
1		19 (17.0)
2		22 (19.6)
≥ 3		52 (46.4)
Age of the 1st delivery		
14 – 20 years		50 (53.8)
21 – 27 years		38 (40.9)
28 – 34 years		4 (4.3)
≥ 35 years		1 (1.1)
Age of the last delivery		
16 – 23 years		21 (22.6)
24 – 31 years		52 (55.9)
32 – 39 years		15 (16.1)
≥ 40 years		5 (5.4)

Distribution of Fibroids and Association With Their Locations

Of those with uterine fibroid, 29 women (67.4%) had multiple fibroids, while 14 women (32.6%) had solitary fibroid (Figure 1). Our results also revealed that most of the women, 29 (67.4%), were noted to have fibroid in the fundus followed by corpus with 6 (13.9%), cervix with 4 (9.3%), fundus and cervix with 3 (7.0%), and fundus and corpus with 1 (2.3%) (Figure 2). The overall number of fibroids was counted to be 95 and was distributed as follows: 59 (62.1%) in the fundus, 15 (15.8%) in the fundus and cervix, 13 (13.7%), 5 (5.3%) in the cervix and 3 (3.1%) in fundus and corpus (Figure 3).

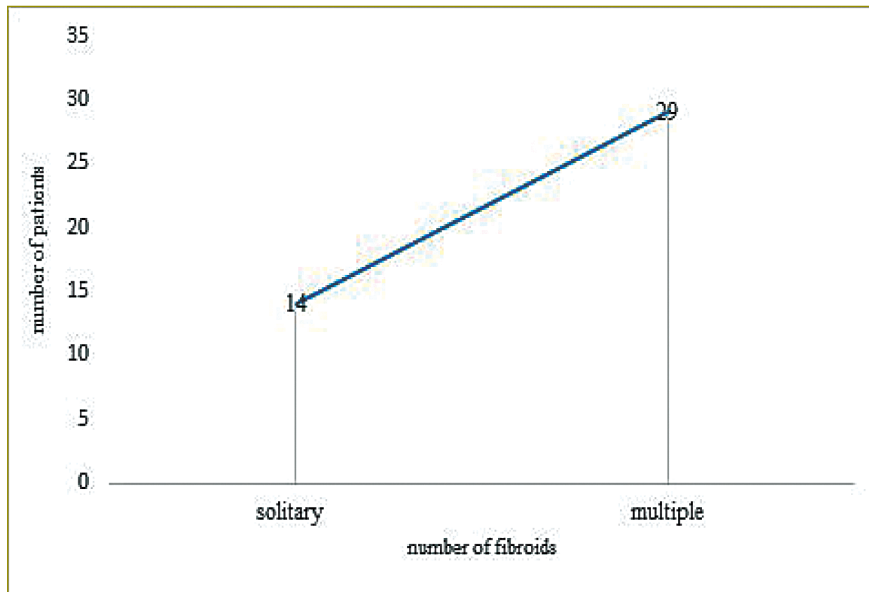


Figure 1 Distribution of the number of fibroids among women with uterine fibroid

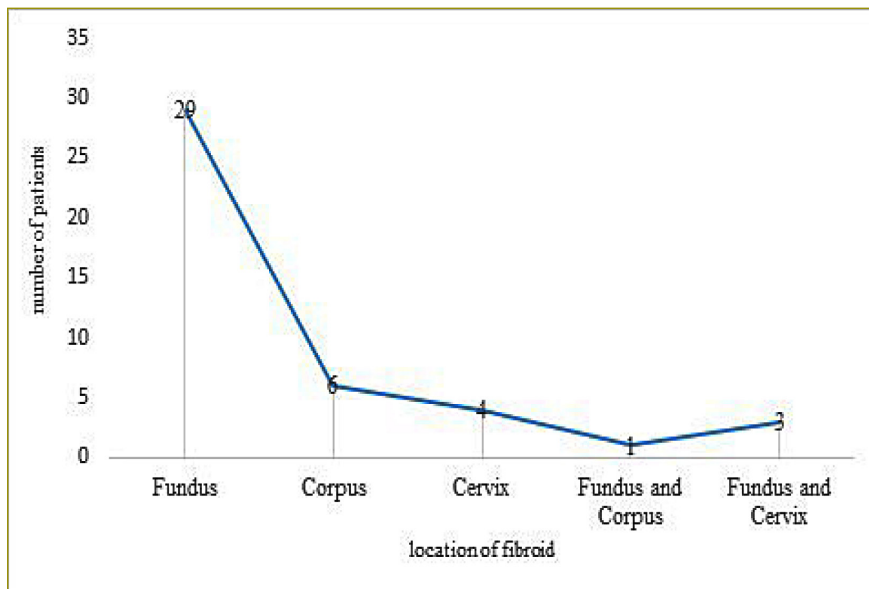


Figure 2 Distribution of uterine fibroids according to their locations within the uterus

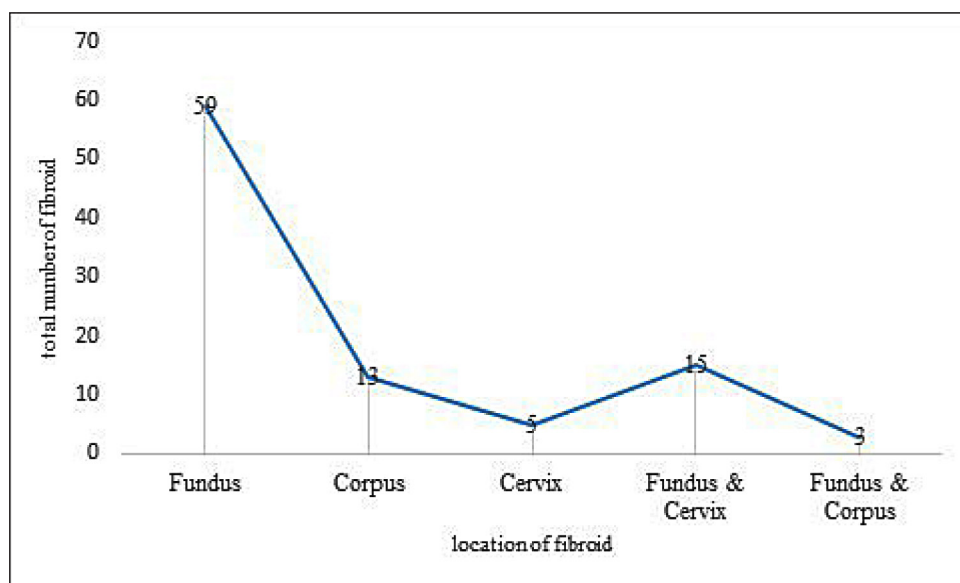


Figure 3 Distribution of the total number of uterine fibroids according to their locations within the uterus

Factors Associated with Uterine Fibroid

As shown in Table 2, the results of this study revealed that the 49 – 60 years old age group had the highest fibroid prevalence, whereas the 13 – 24 years old age group had the lowest prevalence. Age was significantly associated with the uterine fibroid ($X^2 = 35.3, P < 0.001$). Similarly, the women who were overweight and obese had more frequent uterine fibroid than those with normal BMI. This indicated a significant association between BMI and uterine fibroid ($X^2 = 11.2, P = 0.011$). In addition, the highest prevalence of uterine fibroid (56.3%) was noted in women who had

their first menstruation at 11 years old and below. So, a significant association between the age at first menstruation and uterine fibroid was reported ($X^2 = 12.9, P = 0.005$). The findings reported that women with a family history of uterine fibroid were more likely to have the disease than those without. Thus, an association between a family history of uterine fibroid and the disease itself was significant ($X^2 = 8.1, P = 0.005$). On the contrary, our results revealed no significant associations between marital status, smoking, hypertension, DM, menstruation status, parity, contraception, abortion, and first and last delivery with the uterine fibroid ($P < 0.05$).

Table 2 Association between the fibroid and some factors

Variables	Presence of fibroid		X ²	P-value
	Yes	No		
Age group (years)			35.3	< 0.001
13 – 24	1 (6.7)	14 (93.3)		
25 – 36	9 (16.1)	47 (83.9)		
37 – 48	22 (59.5)	15 (40.5)		
49 – 60	10 (76.9)	3 (23.1)		
≥ 61	1 (16.7)	5 (83.3)		
Marital status			3.2	0.074
Single	9 (52.9)	8 (47.1)		
Married	34 (30.9)	76 (69.1)		
Smoking			0.48	0.488

No	41 (33.3)	82 (66.7)		
Yes	2 (50.0)	2 (50.0)		
BMI categories			11.2	0.011
Underweight	0 (0.0)	0 (0.0)		
Normal	2 (9.1)	20 (90.9)		
Overweight	25 (39.1)	39 (60.9)		
Obese	16 (39.0)	25 (61.0)		
Family history of fibroid			8.1	0.005
No	39 (31.7)	84 (68.3)		
Yes	4 (100.0)	0 (0.0)		
Hypertension			1.7	0.190
No	12 (44.4)	69 (69.0)		
Yes	31 (31.0)	15 (55.6)		
DM			0.9	0.319
No	39 (32.8)	80 (67.2)		
Yes	4 (50.0)	4 (50.0)		
Menstruation status			1.0	0.309
Premenopausal state	37 (35.9)	66 (64.1)		
Postmenopausal state	6 (25.0)	18 (75.0)		
Age of 1st menstruation (Age of menarche)			12.9	0.005
≤ 11 years	10 (55.6)	8 (44.4)		
12 years	22 (44.9)	27 (55.1)		
13 years	6 (18.2)	27 (81.8)		
≥ 14 years	5 (18.5)	22 (81.5)		
Parity			5.9	0.113
0	2 (11.8)	15 (88.2)		
1	4 (21.1)	15 (78.9)		
2	7 (31.8)	15 (68.2)		
≥ 3	21 (40.4)	31 (59.6)		
Contraceptives use			0.2	0.652
No	26 (32.1)	55 (67.9)		
Yes	8 (27.6)	21 (72.4)		
Abortion			2.9	0.089
No	19 (25.7)	55 (74.3)		
Yes	15 (41.7)	21 (58.3)		
Age group of the 1st delivery			2.1	0.559
14 – 20 years	17 (34.0)	33 (66.0)		
21 – 27 years	13 (34.2)	25 (65.8)		
28 – 34 years	1 (25.0)	3 (75.0)		
≥ 35 years	1 (100.0)	0 (0.0)		
Age group of the last delivery			3.1	0.381
16 – 23 years	6 (28.6)	15 (71.4)		
24 – 31 years	16 (30.8)	36 (69.2)		
32 – 39 years	7 (46.7)	8 (53.3)		
≥ 40 years	3 (60.0)	2 (40.0)		

DISCUSSION

Uterine fibroid is the most gynaecological benign tumour in women. A total of 127 women underwent transabdominal ultrasounds and were included in the analysis. The main limitation of some studies is based on the clinical diagnosis of fibroid by uterine palpation. However, when sonography was performed in these studies, most cases were confirmed to have fibroid (Parazzini, 2006). A recent study from Italy showed that the prevalence of uterine fibroid among women aged 30 – 60 years old was 21.4% (Marino et al., 2004). Moreover, a study from Ghana showed that the prevalence of uterine fibroid among Ghanaian women was 36.9% (Sarkodie et al., 2016). Our study found that the overall prevalence of uterine fibroid among our study population was 33.9%.

A previous study stated that age increases the risk of fibroid. The incidence of fibroid pathologically increases with age advances; even it reaches its peak at 50 years of age. The same study also showed that fibroids did not occur before maturity (Marshall et al., 1997). Likewise, a previous review from the United Kingdom showed that women over 40 years old were more likely to have uterine fibroid four times than those under 40 years old (Selo-Ojeme et al., 2008). Our study revealed that an increase in age was significantly associated with the incidence of uterine fibroid. Our subjects in the age group of 49 to 60 years old had the highest prevalence of uterine fibroid others. According to marital status, Chen et al. (2001) from the United States found no significant association between marital status and uterine fibroid. However, although the present study revealed that single women had a higher incidence of having uterine fibroid than married women, an association between marital status and uterine fibroid was not significant.

The relationship between smoking and the uterine fibroid is still controversial (Chiaffarino et al., 2016). Early results

showed that smoking was a protective factor for uterine fibroid (Parazzini et al., 1996; Templeman et al., 2009). Nevertheless, the subsequent study suggested an increased risk of uterine fibroid (Dragomir et al., 2010), whereas others did not find an association (Wise et al., 2004). Smoking leads to decreased levels of oestrogen bioavailability where it inhibits the enzyme aromatase, which plays a vital role in transforming androgens to estrone and shifting estradiol (E2) metabolism toward 2-hydroxylation pathways as the result of reducing circulating estrogen (Biegon et al., 2012). Moreover, smoking may also exert oestrogen-related effects on the uterus, inducing cell growth (Ohtake et al., 2003; Marom-Haham & Shulman, 2016; Helle et al., 2017). The present study documented no significant association between smoking and uterine fibroid even though the incidence of uterine fibroid was higher among smoking women than non-smoking women.

In terms of anthropometrics, a recent study conducted in 2016 by Wise and Laughlin-Tommaso was consistent with our study. Both confirmed that high BMI was closely associated with uterine fibroid. In the present study, the prevalence of uterine fibroid was higher among overweight and obese women than those with a normal BMI. A case-control study from Japan showed that hypertension could increase the risk of uterine fibroid by five folds (Takeda et al., 2008). Furthermore, a systematic review demonstrated that DM was considered a potential risk factor for inducing uterine fibroid (Stewart et al., 2017). A significant association between hypertension and DM with uterine fibroid was not observed in this study.

Genetically, uterine fibroid risk was high in women with a positive family history of fibroid (Lumbiganon et al., 1996). This result was in line with our results. We identified a high significant prevalence of uterine fibroid (100%) in women with a family history of uterine fibroid compared to those without fibroid (31.7%).

Several epidemiological studies showed that the premenopausal state was significantly associated with uterine fibroid risk (Flake et al., 2003; Samadi et al., 1996; Templeman et al., 2009). Unexpectedly, our study revealed no significant association between menstruation status and risk of uterine fibroid despite the role of female gonadal steroid hormones in inducing uterine fibroid growth (Flake et al., 2003). In their prospective study, Marshall et al. (1998) observed an inverse association between early age of menstruation and uterine fibroid. Incompatible with this finding, the present study found a higher prevalence of uterine fibroid in women with earlier age of menarche (55.6% at ≤ 11 years and 44.9% at 12 years) than in women with late age of menarche (18.2% at 13 years and 18.5% at ≥ 14 years). Thus, the risk of developing uterine fibroid was significantly increased with the early age of menarche in this study.

Several previous studies confirmed that an increase in parity was considered a protective factor against progressing uterine fibroid (Chen et al., 2001; Sato et al., 2002). This could cause infertility or subfertility, subsequently decreasing parity itself. However, we did not identify an association between parity and uterine fibroid development. Numerous studies documented a protective effect of oral contraceptive use on uterine fibroid development (Chiaffarino et al., 1999; Lumbiganon et al., 1996; Marshall et al., 1998). Nonetheless, our study was not compatible with these studies since we did not find a significant association between contraceptives and uterine fibroid, even though the incidence of the uterine fibroid was lower in women who used contraceptives than in those who did not use them. Previous studies also discussed the association between abortion and uterine fibroid. For instance, a study done by Parrizzini et al. (1996) revealed that abortion promoted the risk of uterine fibroid development. However, our study was in line with a study done by Bizjak et al. (2016), which both reported that abortion was not significantly associated with uterine fibroid.

In 2016, Sarkodie et al. found that the last age of delivery was significantly associated with uterine fibroid. The authors observed that the late age of last delivery increases the risk of uterine fibroid. In the light of that, Sarkodie and colleagues agreed with our findings in which a significant association between the first age of delivery and uterine fibroid was not reported.

According to fibroid location within the uterus parts, a study from the US by Baird et al. (2015) reported that the majority of uterine fibroids were located in the corpus (72%), whereas 46% of them were located in the fundus and only 8% located at the lower uterine segment.

The limitations of this study are that our data were obtained from single centres where they were not representative of the general population. Some of our data were dependent on the history of the self-report, which could be affected by recall bias. Besides, the trans-pelvic ultrasound frequently results in overestimation of incidence as it is not a specific or sensitive test.

CONCLUSION

The high prevalence of uterine fibroid among Iraqi women in Baghdad is alarming. The 49 – 60 years old age group, overweight and obese, positive family history of fibroid, and early age of having a first menstrual period (≤ 11 years old) were strongly associated with increased risk of uterine fibroid. However, marital status, smoking, hypertension, DM, menstruation status, parity, contraceptive use, abortion, and age at the first and last delivery were not associated with uterine fibroid development. A large based-population study is recommended for future studies. In addition, a broad spectrum of factors with a case-control design should be taken into account in determining the risk factors of uterine fibroids.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this article.

ACKNOWLEDGMENTS

The authors would like to acknowledge the help of all radiologists and staff in radiological departments in Medical Baghdad City.

REFERENCES

- Baird, D. D., Dunson, D. B., Hill, M. C., Cousins, D., & Schectman, J. M. (2003). High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. *American Journal of Obstetrics and Gynecology*, 188 (1), 100 – 107. <https://doi.org/10.1067/mob.2003.99>
- Baird, D. D., Harmon, Q. E., Upson, K., Moore, K. R., Barker-Cummings, C., Baker, S., Cooper, T., & Wegienka, G. (2015). A prospective, ultrasound-based study to evaluate risk factors for uterine fibroid incidence and growth: Methods and results of recruitment. *Journal of Women's Health*, 24 (11), 907 – 915. <https://doi.org/10.1089/jwh.2015.5277>
- Biegon, A., Alia-Klein, N., & Fowler, J. S. (2012). Potential contribution of aromatase inhibition to the effects of nicotine and related compounds on the brain. *Frontiers in Pharmacology*, 3, 185. <https://doi.org/10.3389/fphar.2012.00185>
- Bizjak, T., Bečić, A., & But, I. (2016). Prevalence and risk factors of uterine fibroids in North-East Slovenia. *Gynecol Obstet (Sunnyvale)*, 6, 350. <https://doi.org/10.4172/2161-0932.1000350>
- Bulun, S. E. (2013). Uterine fibroids. *New England Journal of Medicine*, 369 (14), 1344 – 1355. <https://doi.org/10.1056/NEJMra1209993>
- Chen, C. R., Buck, G. M., Courey, N. G., Perez, K. M., & Wactawski-Wende, J. (2001). Risk factors for uterine fibroids among women undergoing tubal sterilization. *American Journal of Epidemiology*, 153 (1), 20 – 26. <https://doi.org/10.1093/aje/153.1.20>
- Chiapparino, F., Parazzini, F., La Vecchia, C., Marsico, S., Surace, M., & Ricci, E. (1999). Use of oral contraceptives and uterine fibroids: Results from a case-control study. *BJOG: An International Journal of Obstetrics & Gynaecology*, 106 (8), 857 – 860. <https://doi.org/10.1111/j.1471-0528.1999.tb08409.x>
- Chiapparino, F., Ricci, E., Cipriani, S., Chiantera, V., & Parazzini, F. (2016). Cigarette smoking and risk of uterine myoma: systematic review and meta-analysis. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 197, 63 – 71. <https://doi.org/10.1016/j.ejogrb.2015.11.023>
- Cramer, S. F., & Patel, A. (1990). The frequency of uterine leiomyomas. *American Journal of Clinical Pathology*, 94 (4), 435 – 438. <https://doi.org/10.1093/ajcp/94.4.435>
- Dragomir, A. D., Schroeder, J. C., Connolly, A., Kupper, L. L., Hill, M. C., Olshan, A. F., & Baird, D. D. (2010). Potential risk factors associated with subtypes of uterine leiomyomata. *Reproductive Sciences*, 17 (11), 1029 – 1035. <https://doi.org/10.1177/19337191110376979>
- Farquhar, C. M., & Steiner, C. A. (2002). Hysterectomy rates in the United States 1990–1997. *Obstetrics & Gynecology*, 99 (2), 229 – 234. [https://doi.org/10.1016/s0029-7844\(01\)01723-9](https://doi.org/10.1016/s0029-7844(01)01723-9)
- Flake, G. P., Andersen, J., & Dixon, D. (2003). Etiology and pathogenesis of uterine leiomyomas: A review. *Environmental Health Perspectives*, 111 (8), 1037 – 1054. <https://doi.org/10.1289/ehp.5787>
- Helle, J., Keiler, A. M., Zierau, O., Dörfelt, P., Vollmer, G., Lehmann, L., Chittur, S. V., Tenniswood, M., Welsh, J., & Kretzschmar, G. (2017). Effects of the aryl hydrocarbon receptor agonist 3-methylcholanthrene on the 17 β -estradiol regulated mRNA transcriptome of the rat uterus. *The Journal of Steroid Biochemistry and Molecular Biology*, 171, 133 – 143. <https://doi.org/10.1016/j.jsbmb.2017.03.004>
- Houston, K. D., Hunter, D. S., Hodges, L. C., & Walker, C. L. (2001). Uterine leiomyomas: mechanisms of tumorigenesis. *Toxicologic Pathology*, 29 (1), 100 – 104. <https://doi.org/10.1080/019262301301418900>
- Laughlin, S. K., Schroeder, J. C., & Baird, D. D. (2010). New directions in the epidemiology of uterine fibroids. *Seminars in Reproductive Medicine*, 28 (3), 204 – 217. <https://doi.org/10.1055/s-0030-1251477>
- Lumbiganon, P., Ruggao, S., Phandhu-fung, S., Laopaiboon, M., Vudhikamraksa, N., & Werawatakul, Y. (1996). Protective effect of depot-medroxyprogesterone acetate on surgically treated uterine leiomyomas: A multicentre case-control study. *BJOG: An International Journal of Obstetrics & Gynaecology*, 103 (9), 909 – 914. <https://doi.org/10.1111/j.1471-0528.1996.tb09911.x>

- Marino, J. L., Eskenazi, B., Warner, M., Samuels, S., Vercellini, P., Gavoni, N., & Olive, D. (2004). Uterine leiomyoma and menstrual cycle characteristics in a population-based cohort study. *Human Reproduction*, 19 (10), 2350 – 2355. <https://doi.org/10.1093/humrep/deh407>
- Marom-Haham, L., & Shulman, A. (2016). Cigarette smoking and hormones. *Current Opinion in Obstetrics and Gynecology*, 28 (4), 230 – 235. <https://doi.org/10.1097/GCO.0000000000000283>
- Marshall, L. M., Spiegelman, D., Barbieri, R. L., Goldman, M. B., Manson, J. E., Colditz, G. A., Willett, W. C., & Hunter, D. J. (1997). Variation in the incidence of uterine leiomyoma among premenopausal women by age and race. *Obstetrics & Gynecology*, 90 (6), 967 – 973. [https://doi.org/10.1016/s0029-7844\(97\)00534-6](https://doi.org/10.1016/s0029-7844(97)00534-6)
- Marshall, L. M., Spiegelman, D., Goldman, M. B., Manson, J. E., Colditz, G. A., Barbieri, R. L., Stampfer, M. J., & Hunter, D. J. (1998). A prospective study of reproductive factors and oral contraceptive use in relation to the risk of uterine leiomyomata. *Fertility and Sterility*, 70 (3), 432 – 439. [https://doi.org/10.1016/s0015-0282\(98\)00208-8](https://doi.org/10.1016/s0015-0282(98)00208-8)
- Merrill, R. M. (2008). Hysterectomy surveillance in the United States, 1997 through 2005. *Medical Science Monitor*, 14 (1), CR24 – CR31. PMID: 18160941
- National Cholesterol Education Program (NCEP). (2002). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation*, 106 (25), 3143 – 3421.
- Ohtake, F., Takeyama, K. I., Matsumoto, T., Kitagawa, H., Yamamoto, Y., Nohara, K., Tohyama, C., Krust, A., Mimura, J., Chambon, P., Yanagisawa, J., Fujii-Kuriyama, Y., & Kato, S. (2003). Modulation of oestrogen receptor signalling by association with the activated dioxin receptor. *Nature*, 423 (6939), 545 – 550. <https://doi.org/10.1038/nature01606>
- Parazzini, F. (2006). Risk factors for clinically diagnosed uterine fibroids in women around menopause. *Maturitas*, 55 (2), 174 – 179. <https://doi.org/10.1016/j.maturitas.2006.01.013>
- Parazzini, F., Negri, E., La Vecchia, C., Rabaiotti, M., Luchini, L., Villa, A., & Fedele, L. (1996). Uterine myomas and smoking. Results from an Italian study. *The Journal of Reproductive Medicine*, 41 (5), 316 – 320. PMID: 8725755
- Parazzini, F., Negri, E., La Vecchia, C., Chatenoud, L., Ricci, E., & Guarnerio, P. (1996). Reproductive factors and risk of uterine fibroids. *Epidemiology*, 7 (4), 440 – 442. <https://doi.org/10.1097/00001648-199607000-00018>
- Pavone, D., Clemenza, S., Sorbi, F., Fambrini, M., & Petraglia, F. (2018). Epidemiology and risk factors of uterine fibroids. *Best Practice & Research Clinical Obstetrics & Gynaecology*, 46, 3 – 11. <https://doi.org/10.1016/j.bpobgyn.2017.09.004>
- Pérez-López, F. R., Ornat, L., Ceausu, I., Depypere, H., Erel, C. T., Lambrinouadaki, I., Schenck-Gustafsson, K., Simoncini, T., Tremollieres, F., Rees, M., & EMAS. (2014). EMAS position statement: Management of uterine fibroids. *Maturitas*, 79 (1), 106 – 116. <https://doi.org/10.1016/j.maturitas.2014.06.002>
- Samadi, A. R., Lee, N. C., Flanders, W. D., Boring 3rd, J. R., & Parris, E. B. (1996). Risk factors for self-reported uterine fibroids: a case-control study. *American Journal of Public Health*, 86 (6), 858 – 862. <https://doi.org/10.2105/ajph.86.6.858>
- Sarkodie, B. D., Botwe, B. O., Adjei, D. N., & Ofori, E. (2016). Factors associated with uterine fibroid in Ghanaian women undergoing pelvic scans with suspected uterine fibroid. *Fertility Research and Practice*, 2 (9), 1 – 7. <https://doi.org/10.1186/s40738-016-0022-9>
- Sato, F., Mori, M., Nishi, M., Kudo, R., & Miyake, H. (2002). Familial aggregation of uterine myomas in Japanese women. *Journal of Epidemiology*, 12 (3), 249 – 253. <https://doi.org/10.2188/jea.12.249>
- Selo-Ojeme, D., Lawal, O., Shah, J., Mandal, R., Pathak, S., Selo-Ojeme, U., & Samuel, D. (2008). The incidence of uterine leiomyoma and other pelvic ultrasonographic findings in 2,034 consecutive women in a north London hospital. *Journal of Obstetrics and Gynaecology*, 28 (4), 421 – 423. <https://doi.org/10.1080/01443610802149863>
- Serden, S. P., & Brooks, P. G. (1991). Treatment of abnormal uterine bleeding with the gynecologic resectoscope. *The Journal of Reproductive Medicine*, 36 (10), 697 – 699. PMID: 1835500
- Stewart, E. A., Cookson, C. L., Gandolfo, R. A., & Schulze-Rath, R. (2017). Epidemiology of uterine fibroids: a systematic review. *BJOG: An International Journal of Obstetrics & Gynaecology*, 124 (10), 1501 – 1512. <https://doi.org/10.1111/1471-0528.14640>

- Takeda, T., Sakata, M., Isobe, A., Miyake, A., Nishimoto, F., Ota, Y., Kamiura, S., & Kimura, T. (2008). Relationship between metabolic syndrome and uterine leiomyomas: a case-control study. *Gynecologic and Obstetric Investigation, 66* (1), 14 – 17. <https://doi.org/10.1159/000114250>
- Templeman, C., Marshall, S. F., Clarke, C. A., Henderson, K. D., Largent, J., Neuhausen, S., Reynolds, P., Ursin, G., & Bernstein, L. (2009). Risk factors for surgically removed fibroids in a large cohort of teachers. *Fertility and Sterility, 92* (4), 1436 – 1446. <https://doi.org/10.1016/j.fertnstert.2008.08.074>
- Wise, L. A., & Laughlin-Tommaso, S. K. (2016). Epidemiology of uterine fibroids—from menarche to menopause. *Clinical Obstetrics and Gynecology, 59* (1), 2 – 24. <https://doi.org/10.1097/GRF.0000000000000164>
- Wise, L. A., Palmer, J. R., Harlow, B. L., Spiegelman, D., Stewart, E. A., Adams-Campbell, L. L., & Rosenberg, L. (2004). Risk of uterine leiomyomata in relation to tobacco, alcohol and caffeine consumption in the Black Women’s Health Study. *Human Reproduction, 19* (8), 1746 – 1754. <https://doi.org/10.1093/humrep/deh309>
- World Health Organization (WHO). (2000). Global database on body mass index, BMI classification, adapted from WHO, 1995, WHO 2000 and WHO 2004.