ORIGINAL ARTICLE

The Characteristics of Uterine Leiomyoma and Metabolic Syndrome in the Multiparous Overweight Women in Northern Iran

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ABSTRACT

Background: some Studies have shown that the incidence of Uterine Leiomyoma (U.L) is associated with obesity and hypertension as the components of metabolic syndrome .Therefore, authors aimed to investigate the relationship between incidence of U.L and their characteristics with metabolic syndrome and its components in women referring to Al-Zahra hospital in Rasht.

Methods: This study was conducted in two groups (N=144) with and without U.L. Demographic, anthropometric, smoking, past medical history, serum lipids and blood glucose levels, U.L features including size, number, location of U.L and clinical symptoms were recorded. Data were analyzed in version21SPSS.

Results: Results showed that there was no significant difference between the components of metabolic syndrome including waist circumference, systolic and diastolic blood pressure, fasting blood sugar and HDL levels in the groups (P> 0.05). There was no significant difference regarding the occurrence of metabolic syndrome in the groups (P> 0.05). However, individuals had U.L without metabolic syndrome were 28.9% asymptomatic, but in individuals with metabolic syndrome, this finding was decreased to 8.2 (P <0.001). Also the incidence of U.L (4.9%) in patients with metabolic syndrome was lower than those who didn't have metabolic syndrome (21.7%) (P = 0.014).

Conclusion: The incidence of U.L in this study did not correlate with metabolic syndrome and its components, but those with metabolic syndrome were more likely to have abnormal uterine bleeding. The most common bleeding pattern was menometrorrhagia, and their U.L were less submucosal predominantly.

Key words: Leiomyoma; Metabolic syndrome; Hypertension

INTRODUCTION

Uterine leiomyoma is the most common benign tumor in the reproductive age and causes two thirds of hospitalization and is the main reason of hysterectomy[1,2,3]. U.L can itself cause menstrual irregularities, infertility, recurrent abortion, preterm labor, and abnormal presentations of fetus. Considering the high prevalence of U.L in women of northern Iran (50%), the importance of examining and identifying the risk factors of this benign tumor becomes more significant[4]. Epidemiologic studies have shown that U.L is associated with factors such as age, race, body mass index(BMI), hereditary, reproductive factors, sexual hormones, obesity, lifestyle (smoking cigarette and alcohol, diet, physical activity and stress), blood pressure and infection[1,2,3,5-14]. Some studies have shown that obesity, increased BMI, inactivity, and insulin resistance, all of which are components of metabolic syndrome, can be associated with an increased incidence of U.L. This topic led to researchers toward this thinking metabolic syndrome could be associated with the development of this benign tumor[15].

The metabolic syndrome includes a set of risk factors such as abdominal obesity, dyslipidemia, decreased level of high-density lipoprotein cholesterol, high serum triglyceride, hypertension and insulin resistance, which may increase the risk of cardiovascular disease, type 2 diabetes and finally high cardiovascular mortality rates[16].

Probably following the incidence of metabolic syndrome, excess body fat may change the metabolism of steroid hormones and insulin resistance and decrease in the level of steroid hormones binding globulin in premenopausal women and it leads to an increase in the incidence of U.L[13,15]. On the other hand, hyperinsulinemia caused by insulin resistance in women with metabolic syndrome increases the expression of insulin-like factor 1 and increases the level of epidermal growth factor. These two factors can lead to U.L growth by increasing ovarian hormones secretion or increasing cell proliferation directly[15].

Recently, a study on female rats have found that insulin resistance affect sex hormones and can cause Myometer growth[15]. Takeda et al showed that overweight

and hypertension are directly linked to an increased risk of uterine leiomyoma[17]. But Tak et al stated that there was no significant relation between metabolic syndrome and the incidence of U.L[15]. Generally, both studies, as well as Mon et al found significant association between some components of metabolic syndrome such as abdominal obesity, hypertension, hypertriglyceridemia with the incidence of U.L[15,17,18].

Considering the aforementioned studies, different anthropometric patterns of Iranians and the genetic dimensions affecting the incidence of U.L, investigators aimed to assess the association of U.L with metabolic syndrome and its components in women referred to the clinic of Al-Zahra hospital in Rasht, Iran.

MATERIALS AND METHODS

In this case-control study, 288 patients who were referred to the clinic of Al-Zahra hospital in Rasht in 2018 had been requested for transvaginal ultrasonography (TVS) and were selected by convenient sampling method. Investigators assessed women with a history of pregnancy that have not been menopause yet. This study was approved by the Ethics Committee of Guilan University of Medical Sciences (the code IR.GUMS.REC.1397.177). Informed consents were obtained from all participants. Menopause women with an amenorrhea for 12 months or more, nulliparous, and patients with cancer, or consumers of any type of drug that can affect the production or secretion of ovarian hormones in the last 12 months and, individuals with a history of hysterectomy were excluded in this study.

In this study, women with U.L (case group) were matched in the term of age and parity with women without U.L (control group). The control groups were women that referred to clinic of Al-Zahra hospital and undergone TVS.

Tools and data gathering: Vaginal ultrasounds were performed by an experienced radiologist and based on the ultrasound results, participants were divided into two groups with and without U.L. Also, complete medical history and anthropometric features including waist circumference, height and weight, and BMI were assessed for each participant .All participant were given researcher questionnaires , in which they were asked demographic characteristics (age, cigarette consumption, history of hypertension (the drug was prescribed frequently)), diabetes or dyslipidemia, frequency of miscarriage and symptoms (abnormal uterine bleeding was considered as menorrhagia, menometrorrhagia and spotting between the cycles). Abnormal uterine bleeding means any abnormalities in menstrual periods based on the volume of vaginal bleeding or prolonged menstruation (more than 8 days), the age of the menarche, the age at the first birth, parity, and the use of oral contraceptives and IUDs.

Blood pressure was taken in two sessions after 15 minutes rest at least .The average of pressure was calculated and recorded. Height and weight were measured with a digital tool in a bare foot and light clothing. The BMI was also calculated by dividing the weight (in kilograms) by height squared (in meters). The waist circumference was calculated in the meter at the top of the posterior upper Iliac crest, and was reported in millimeters.In all patients, the blood sample was taken from an Anticoagulant vein and sent to the reference laboratory in a plastic tube after 12 hours of fasting from 6 in the afternoon to 8 in the morning. The lipid profile (triglyceride, HDL, LDL, cholesterol) was subjected to auto-analysis (Hitachi 747, Japan). Glucose was also evaluated by the Glucose oxidase method.

Metabolic syndrome was defined based on the following definition in Iran (16): Female waist circumference >80 cm, triglycerides ≥150, HDL < 50, blood pressure ≥ 130 mm Hg systolic and ≥85 mm Hg/ diastolic and fasting blood sugar > 100 mg/dL. The existence of three or more of these parameters in each individual indicated metabolic syndrome.

Uterine evaluation: The diagnosis of U.L was performed with TVS that has a sensitivity of 99% and a 95% specificity, and comparable to pathology (15). Finally, the number of U.L and their sizes and locations (submucosal-interamural and subserous) were recorded. If more than one U.L were observed, the largest diameter would record.

Statistical analysis: All data were entered into the SPSS version 22. The normal distribution of quantitative data was examined by Kolmogorov-Smirnov test. Qualitative data were reported as frequency, percentages, and quantitative data were reported as mean and standard deviation.

In order to investigate the relationship between qualitative variables, the chi-square test was used. Independent t-test and Mann-Whitney test were used respectively for comparing the parametric and nonparametric quantitative variables. Considering the estimation of odds ratio (OR) between dependent and independent variables and controlling variables, one-dimensional and multivariate logistic regression analysis were also used. P-value<0.05 indicated statistical significance.

RESULTS

Results showed that 50% of participants aged> 45 years. More than 80% of the participants had a body mass index >25. Most of the patients had waist circumference above 80 centimeters. More than one-third of the participants had triglycerides above 150, and in more than two-thirds of the participants, HDL was below 50. In more than 85% of cases, systolic and diastolic blood pressures were within normal range. 44.4% of the participants had metabolic syndrome (42.2% in the U.L group versus 46.6% in the control group) which was not statistically significant (Table 1).

Results showed that, despite the high mean and median of waist circumference, weight and body mass index in the case group, this difference was not statistically significant. Also, no significant difference was noted regarding other variables as well (p>0.05). Also, the median of HDL was less than 50 in the group with U.L, which was not statistically significant. Other triglyceride variables, FBS, cholesterol and hypertension (systolic and diastolic), and LDL were higher in case group, but no statistically significant difference was noted. Furthermore, there was no significant difference between the history of diabetes, hypertension, physical activity and smoking in two groups (P> 0.05). Results showed that none of the

components of metabolic syndrome including weight, waist circumference, BMI, FBS, triglyceride and HDL levels, and systolic and diastolic blood pressures were not correlated significantly with the size of U.L.

Regarding the characteristics of U.L based on the presence or absence of metabolic syndrome, the data are summarized in Table 1. There is a significant relationship between metabolic syndrome and U.L location (P-value = 0.014).

In participants with metabolic syndrome, the prevalence of submucosal leiomyoma was lower than that of the non-metabolic syndrome group. On the other hand, although there was no significant relationship between metabolic syndrome with single or multiple U.L (P-value = 0.548), there was a significant relation between metabolic syndrome and symptomatic U.L in the case group, meaning that most of the participants with U.L and metabolic syndrome were symptomatic. Half of the participants had abnormal vaginal bleeding (91% versus 71% without metabolic syndrome) (P-value = 0.002). It was found that 91.8% of people with metabolic syndrome also had symptomatic U.L. also, his study showed that there was a significant difference between metabolic syndrome and type of vaginal bleeding (P <0.001), whereas participants with metabolic syndrome had more menometrorrhagia and participants without metabolic syndrome more likely had menorrhagia. (Table 2)

Using Logistic regression, the relationship between each of the variables and U.Lwas examined and for each of the variables, the odds ratio was calculated independently and no relation was found between the two variables in the case and control groups. Variables such as age, age of menarche, age of first pregnancy, delivery and contraceptive methods were considered as confounding variables. First, variables were entered separately in the model 1 with the same conditions for the age. Considering the OR, they did not have any significant difference. The second model was used under the same conditions of age and other confounding variables including the age of the menarche, the age of the first pregnancy, delivery, and contraceptive method. Each variable was entered into the model separately and there was no significant correlation in this model as well (P-value <0.05).(Table 3)

Table 1: Demographic characteristics in two the groups

Variable name	**Without leiomyoma**	**leiomyoma**	**p-value**
	Mean ± SD median(min-max)	**Mean ± SD median(min-max)**	
Age (yr)	43(23-53)	43.5(23-53)	0.861**
Waist circumference(cm)	109.59±12.54	110.77±13.92	0.455*
Body Mass Index	28.56(18.8-60.5)	29.34(19.2-48.8)	0.489**
Weight(kg)	74(46.8_140)	74(50-125)	0.625**
Height (cm)	160(1.06_1.74)	158(1.4_1.88)	0.416**
HDL	47(26_81)	45(22_74)	0.255**
TG	130.5(32_389)	130.5(48_431)	0.657**
Cholesterol	172(88_334)	168.5(100_336)	0.217**
LDL	100(42_225)	93.5(44_227)	0.292**
FBS	95(65_157)	94(72_179)	0.777**
systolic blood pressure	120(100_150)	120(100_160)	0.253**
diastolic blood pressure	80(60_100)	80(60_95)	0.256**
Menarche age	13(14_35)	20(9_17)	0.694**
Age in first pregnancy	20(14_35)	20(13_30)	0.088**
parity	2(1_5)	2()1_6)	0.931**
Number of Abortion	0(0_3)	0(0_5)	03.663**
Gravidity	2(1_8)	2(1_9)	0.866**
*Independent T-test **Mann-Whitney U-test			

G: Triglyceride HDL: High-density lipoprotein LDL: Low-density lipoprotein FBS: Fasting Blood Sugar

Table 2: Characteristics of U.L based on the occurrence or absence of metabolic syndrome

Variable			**Without metabolic syndrome**	**metabolic syndrome**	**p-value**
			N(%)	**N(%)**	
U.L	NO		77(53.5)	67(46.5)	0.477
	YES	Total	83(57.6)	61(42.4)	0.780
		Single	51(59.3)	32(55.2)	
		Multiple	35(40.7)	26(44.8)	
location of U.L	Intramural		49(59)	47(77)	0.014
	Subserosal		16(19.3)	11(18)	
	Submucosa		18(21.7)	3(4.9)	
Number of U.L			1(0_4)	0(0_5)	0.548
U.L	Non-asymptomatic		24(28.9)	5(8.2)	0.002
	Asymptomatic	Total	59(71.1)	56(91.8)	
		menorrhagia	34(41)	22(36.1)	0.001
		menometrorrhagia	25(30.1)	34(55.7)	

*chi-square test

Table 3: Determination of the odds ratio of the variables in the development of U.L by controlling the confounding variables

Variable	B	SE	OR CRUDE (95% CI)	Or Adj Model (95% CI)	Or Adj Model 2(95% CI)	P-VALUE	P-Value Model 1	P-VALUE 2
FBS	0.007	0.009	1.006(-0.989-1.024)	1.006(-0.989-1.024)	1.006(-0.989-1.024)	470.7	0.477	0.438
Cholesterol	-0.003	0.003	0.996(-0.990_1.003)	0.996(-0.990_1.003)	0.996(-0.990_1.003)	240.1	0.231	0.369
TG	0.000	0.002	0.999(-0.995-1.003)	0.999(-0.995-1.003)	0.999(-0.996-1.003)	580.3	0.581	0.737
HDL	-0.014	0.012	0.988(-0.967-1.010)	0.988(-0.967-1.010)	0.986(-0.964-1.009)	290.3	0.287	0.228
LDL	-0.003	0.004	0.997(-0.989-1.004)	0.997(-0.989-1.004)	0.997(-0.990-1.005)	370.2	0.370	0.505
systolic blood pressure	-0.011	0.011	0.987(-0.967-1.008)	0.987(-0.967-1.008)	0.989(-0.967-1.011)	230.8	0.227	0.319
dystonic blood pressure	-0.016	0.014	0.983(-0.957-1.010)	0.983(-0.957-1.010)	0.984(-0.957-1.012)	220.6	0.212	0.264
Body Mass Index	0.001	0.02	1.001(-0.962-1.041)	1.001(-0.962-1.041)	1.001(-0.962-1.042)	970.7	0.977	0.960
Waist circumference(cm)	0.007	0.009	1.007(-0.989-1.025)	1.007(-0.989-1.025)	1.007(-0.989-1.025)	440.9	0.448	0.430
Metabolic syndrome	-0.146	0.243	0.845(-0.530-1.345)	0.845(-0.530-1.345)	0.864(-0.537-1.391)	470.7	0.477	0.548

TG: Triglyceride HDL: High-density lipoprotein LDL: Low-density lipoprotein FBS: Fasting Blood Sugar

DISCUSSION

As it was mentioned in this study, there was no statistically significant association between metabolic syndrome and its components withU.L, but significant relationship was found between metabolic syndrome and symptomatic U.L with abnormal uterine bleeding (p = 0.002). Women with metabolic syndrome had more menomethrorrhagia and Women without metabolic syndrome had more menorrhagia (P = 0.001). Also, there was a significant association between the metabolic syndrome and the location of U.L, and in non-diabetic subjects, the prevalence of submucosal U.L was lower in patients with metabolic syndrome (P = 0.014)

The frequency of metabolic syndrome was 42.4% in the U.L group and 46.6% in the non-leiomyoma group, and the majority of patients were overweight and obese and had waist circumference > 80 cm. There was a similar distribution for frequency of fasting blood sugar ≥ 100, triglyceride ≥150 and above, HDL < 50, and blood pressure > 120 / 85 in the both groups.

The frequency ofU.L varies according to various factors in different societies. Age, race, body mass index, heritability, reproductive factors, sexual hormones, obesity, lifestyle (diet, caffeine, alcohol use, physical activity and stress), environmental factors and underlying diseases (hypertension and infection) are influencing factors[19]. In this study, a combination of these risk factors which is called metabolic syndrome, has been addressed. Factors such as BMI, waist circumference, hypertension, lipid profile and serum glucose, as the components of metabolic syndrome, have been reported as the effective factors for the occurrence of U.L.[19]

Tak et al and our studies are the only studies that assessed the size and number of U.L .Tak et al stated that there was a linear correlation between age, BMI and fasting blood sugar with U.L size. By adjusting the data based on the age, the only direct correlation remained with the body mass index. Also, considering the presence of U.L based on the presence of metabolic syndrome showed that participants with multiple U.L were more likely to have metabolic syndrome than patients with single U.L. They also showed that in case of eliminating the effect of age, people with more than 3 U.L had higher BMI, body fat, systolic blood pressure, fasting blood sugar and triglyceride levels, as well as lower HDL than women who had only one lesion[15]. Dendulo et al showed although BMI had a significant correlation with U.L, it did not correlate with the size of U.L[20]. In our study, there was no significant relationship between the components of the metabolic syndrome with the size of the lesions. There was also no significant difference between the number of lesions and metabolic syndrome. Further studies are required on the relationship between metabolic syndrome and the size and number of U.L.

In this study, results showed that the frequency of symptomatic U.L was higher in patients with metabolic syndrome (91.8%). However, there is no study which assesses the clinical symptoms of U.L in the patients with metabolic syndrome. They were evaluated for the first time in this study. Results showed that menorrhagia was the most common type of bleeding in patients without metabolic syndrome, but menometrorrhagia was the most common form of abnormal uterine bleeding in patients with metabolic syndrome.

The most common pattern of abnormal uterine bleeding in women with U.L was menorrhagia, which usually occurs with submucosal and intramural U.L. In spite of the fact that the prevalence of submucosal U.L was higher in women with metabolic syndrome, it is expected that the incidence of abnormal uterine bleeding in this group was higher. But higher symptomatic U.L with abnormal uterine bleeding in patients with metabolic syndrome was noted (91.8% vs. 71.1%, p = 0.002). The bleeding pattern in most women with metabolic syndrome comparing without metabolic syndrome was menometrorrhagia (55/7% Vs. 30.1%, p = 0.001). It is concluded that menometrorrhagia in women with U.L may have other causes and mechanisms. The most important

cause is hyperstrogenism and subsequent endometrial hyperplasia. It is worth mentioning that endometrial hyperplasia following hyperstrogenism associated with obesity, overweight and diabetes can be adjustable in women with metabolic syndrome.

On the other hand, this study examined the association of metabolic syndrome with the location of U.L for the first time. In this study, 77% of U.L in patients with metabolic syndrome were intramural and subserosal. Only 4.9% occurred in submucosal location. But in patients without metabolic syndrome, 59% were in intramural and subserosal. However, 21.7% of lesions were submucosal. The frequency of submucosal U.L in patients without metabolic syndrome were 4 times higher than patients with metabolic syndrome (21.7% vs. 4.9%), because submucosal U.L is more important than intramural and subserosal U.L regarding the development of clinical symptoms including abnormal uterine bleeding and other consequences such as abortion and infertility.

For logistical justification manifest difference between two groups. Can the other reasons and mechanisms except for parity, age and obesity or hyperstrogenism be effective in the incidence of submucosal U.L? Although some studies have reported the association between U.L with infection and inflammation, there is no adequate data about the association between location of U.L and infection.

Some studies have shown that inflammation and chronic infection cause elevated cellular extracellular Matrix and cell proliferation (13, 21,22). In this study, the incidence of U.L was higher in women with a history of PID, IUD, and chlamydia[14]. In another study, results showed that infiltration of Macrophages in submucosal U.L was more than intermural and subserousal U.L and justified that the presence of submucosal U.L could be associated with infertility due to the underlying infection[23]. Regarding the high prevalence of genital infections and the fact that the Endometrial cavity is a susceptible environment for infection such as STDs. Uterine infections and inflammations may be the underlying cause of submucosal U.L. To prove this subject, further studies are required. Inflammation and infections are mechanisms that can be modified, thus if this hypothesis would be supported by other researchers, an opportunity to focus on U.L prevention could be created.

The relationship between obesity and the growth of U.L is quite contradictory[7,24]. Some epidemiological studies have shown that there is an increased risk of U.L due to obesity and diabetes[7,24,25,26]. The common cause of this association is insulin resistance, which is believed to be a risk for U.L in obese women as a result of increased levels of IGF-I and Androgen[7]. Okolo et al also stated that obesity and diabetes were associated with an increased risk of uterine U.L[7]. On the other hand, Parasini et al did not observe any association between BMI and the risk of U.L[27]. In this study, there was no significant correlation between BMI and incidence of U.L.As mentioned this difference may be related to the race of individual. In our study, in both groups case study, overweight and obesity noted in> 80% of the population. The important point was the high prevalence of overweight and obesity. Obesity has been shown to play an important role in determining Estrogen level, which could be due to the aromatizing role of Androgens in the fatty cells. In 2007, Takeda et al examined the association between metabolic syndrome with the incidence of U.L in Japan. Takeda et al observed that in the group with and without U.L, BMI (22.9 vs. 21.5 units), systolic (123 vs 114 mmHg) and diastolic (1/75 vs. 68.5 mmHg) blood pressures, triglyceride level (86.5 vs. 72.6 kg / dL) and fasting blood sugar (93.2 vs. 89.5 mmg / dl) was statistically different (P <0.05)

Takeda et al assessed the risk factors of metabolic syndrome and showed that if the OR was evaluated in detail, overweight and hypertension were directly related to increased risk of uterine leiomymoa (2/11: 0.79 – 5.61 and 2/55: 0.050 – 13.03). Also,they assessed the risk factors for metabolic syndrome in a cluster and cumulative manner and showed that by increasing the risk factors from zero to three, OR increased significantly. However, they stated that many patients did not have complete criteria for metabolic syndrome, and therefore they cumulatively assessed these factors[17].

In this study, the level of blood sugar and triglyceride in patients was in normal range and the median of waist circumference was not reported. Tak et al studied the association between the occurrence of metabolic syndrome and the incidence of U.L. They stated that only 7% (86) of their patients had metabolic syndrome. They showed that women with U.L had significantly higher waist circumference, body fat, systolic and diastolic pressure and LDL levels than women without U.L. Although there was no significant difference in blood sugar and insulin levels in two groups, diabetes was more common in the group with U.L. However, there was no significant association between the prevalence of metabolic syndrome and the incidence of U.L (7.5% vs. 8.3%, P = 0.052)[15]. In this study, there was no difference between the metabolic syndrome and its components with U.L. Although similar to this study, Takeda et al and Tak et al, did not observe a significant relation between metabolic syndrome with U.L, but they found significant relation in components of this syndrome[15,17].

Although findings suggested that metabolic syndrome and its components did not affect the incidence of female U.L, most people with metabolic syndrome had symptomatic U.L with abnormal uterine bleeding.

CONCLUSION

The results of this study showed that there was no statistically significant association between metabolic syndrome and its components with uterine U.L, but there was a significant relationship between the metabolic syndrome and symptomatic U.L with abnormal uterine bleeding. Although Participants with metabolic syndrome had more menometrorrhagia , those without metabolic syndrome had more menorrhagia, respectively. In addition, there was a significant association between the metabolic syndrome and the location of U.L, the prevalence of submucosal U.L was higher in patients with metabolic syndrome.

Limitations: This study has some limitations: There are different reason why this study doesn't have the relationship between U.L and metabolic syndrome and its

components The study population was multiparous and overweight, and the mean BMI in the group without U.L was 28.56 and in the group with U.L was 29.34, which was different from other studies. An average of BMI in the study of Tau was 22.8 .Control group were subjected to ultrasound for another cause such as abnormal uterine bleeding. Abnormal uterine bleeding can be due to other causes such as anovulation, endometrial hyperplasia and endometrial polyps, which are more common in women of high age and overweight with metabolic syndrome. Therefore, if the participants in the control group were completely normal without gynecologic problems or abnormal bleeding, the results of the study might vary.

Suggestions: It's recommended to study higher sample size for assessing the relationship between between metabolic syndrome and the size and number of U.L.

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REFERENCES

1. Sparic R. Uterine myomas in pregnancy, childbirth and puerperium. Srp Arh Celok Lek. 2014 Jan-Feb;142(1-2):118-24. PubMed PMID: 24684044.
2. Downes E, Sikirica V, Gilabert-Estelles J, Bolge SC, Dodd SL, Maroulis C, et al. The burden of uterine fibroids in five European countries. Eur J Obstet Gynecol Reprod Biol. 2010 Sep;152(1):96-102. PubMed PMID: 20598796.
3. Sparic R, Hudelist G, Berisava M, Gudovic A, Buzadzic S. Hysterectomy throughout history. Acta Chir Iugosl. 2011;58(4):9-14. PubMed PMID: 22519184.
4. Asgharnia M, Faraji R, Mir Hagh Jou SN, Karimi M. Frequency of Uterine fibroids and related risk factors in women with hysterectomy. Journal of Holistic Nursing and Midwifery. 2013;23(1):1-6 {Text in Pesion}. eng.
5. Evans P, Brunsell S. Uterine fibroid tumors: diagnosis and treatment. Am Fam Physician. 2007 May 15;75(10):1503-8. PubMed PMID: 17555142.
6. Goldman MB, Troisi R, Rexrode KM. Women and health. 2nd ed. Amsterdam: Elsevier/Academic Press; 2013. xxxi, 1581 p. p.
7. Okolo S. Incidence, aetiology and epidemiology of uterine fibroids. Best Pract Res Clin Obstet Gynaecol. 2008 Aug;22(4):571-88. PubMed PMID: 18534913.
8. Somigliana E, Vercellini P, Daguati R, Pasin R, De Giorgi O, Crosignani PG. Fibroids and female reproduction: a critical analysis of the evidence. Hum Reprod Update. 2007 Sep-Oct;13(5):465-76. PubMed PMID: 17584819.
9. Tinelli A, Hurst BS, Hudelist G, Tsin DA, Stark M, Mettler L, et al. Laparoscopic myomectomy focusing on the myoma pseudocapsule: technical and outcome reports. Hum Reprod. 2012 Feb;27(2):427-35. PubMed PMID: 22095838.
10. Tinelli A, Malvasi A, Rahimi S, Negro R, Cavallotti C, Vergara D, et al. Myoma pseudocapsule: a distinct endocrino-anatomical entity in gynecological surgery. Gynecol Endocrinol. 2009 Oct;25(10):661-7. PubMed PMID: 19526398.
11. Luoto R. Re: "Risk factors for uterine leiomyoma: a practice-based case-control study. II. Atherogenic risk factors and potential sources of uterine irritation". Am J Epidemiol. 2002 Jan 15;155(2):187-8. PubMed PMID: 11790683.
12. Sharami, SH, Zahiri, Z, Ghanaie M. Risk Factors of Uterine Leiomyoma in Women of Reproductive Ages. Journal of Babol University Of Medical Sciences. 2009;11(4):54-61. eng.
13. Faerstein E, Szklo M, Rosenshein NB. Risk factors for uterine leiomyoma: a practice-based case-control study. II. Atherogenic risk factors and potential sources of uterine irritation. Am J Epidemiol. 2001 Jan 01;153(1):11-9. PubMed PMID: 11159140.
14. Faerstein E, Szklo M, Rosenshein N. Risk factors for uterine leiomyoma: a practice-based case-control study. I. African-American heritage, reproductive history, body size, and smoking. Am J Epidemiol. 2001 Jan 01;153(1):1-10. PubMed PMID: 11159139.
15. Tak YJ, Lee SY, Park SK, Kim YJ, Lee JG, Jeong DW, et al. Association between uterine leiomyoma and metabolic syndrome in parous premenopausal women: A case-control study. Medicine (Baltimore). 2016 Nov;95(46):e5325. PubMed PMID: 27861360. Pubmed Central PMCID: PMC5120917.
16. Kasper DL. Harrison's principles of internal medicine. 19th edition / editors, Dennis L. Kasper, MD, William Ellery Channing, Professor of Medicine, Professor of Microbiology, Department of Microbiology and Immunobiology, Harvard Medical School, Division of Infectious Diseases, Brigham and Women's Hospital, Boston, Massachusetts and five others . ed. New York: McGraw Hill Education; 2015. 1 volume (various pagings) p.
17. Takeda T, Sakata M, Isobe A, Miyake A, Nishimoto F, Ota Y, et al. Relationship between metabolic syndrome and uterine leiomyomas: a case-control study. Gynecol Obstet Invest. 2008;66(1):14-7. PubMed PMID: 18230910.
18. Moon K-H, Ryu S-K, Kim K-K, Suh H-S, Hwang IC. Relationship between Metabolic Syndrome and Uterine Fibroids in Premenopausal Korean Women. Korean J Fam Pract. 2013;3(4):437-41.
19. Sparic R, Mirkovic L, Malvasi A, Tinelli A. Epidemiology of Uterine Myomas: A Review. Int J Fertil Steril. 2016 Jan-Mar;9(4):424-35. PubMed PMID: 26985330. Pubmed Central PMCID: PMC4793163.
20. Dandolu V, Singh R, Lidicker J, Harmanli O. BMI and uterine size: is there any relationship? Int J Gynecol Pathol. 2010 Nov;29(6):568-71. PubMed PMID: 20881854.
21. Manta L, Suciu N, Toader O, Purcărea R, Constantin A, Popa F. The etiopathogenesis of uterine fibromatosis. Journal of medicine and life. 2016;9(1):39.
22. Wegienka G. Are uterine leiomyoma a consequence of a chronically inflammatory immune system? Medical hypotheses. 2012;79(2):226-31.
23. Miura S, Khan KN, Kitajima M, Hiraki K, Moriyama S, Masuzaki H, et al. Differential infiltration of macrophages and prostaglandin production by different uterine leiomyomas. Human reproduction. 2006;21(10):2545-54.
24. Wise LA, Palmer JR, Stewart EA, Rosenberg L. Polycystic ovary syndrome and risk of uterine leiomyomata. Fertil Steril. 2007 May;87(5):1108-15. PubMed PMID: 17241625. Pubmed Central PMCID: PMC1876794.
25. Lethaby AE, Vollenhoven BJ. Fibroids (uterine myomatosis, leiomyomas). BMJ Clin Evid. 2007 May 1;2007. PubMed PMID: 19454074. Pubmed Central PMCID: PMC2943812.
26. Parker WH. Etiology, symptomatology, and diagnosis of uterine myomas. Fertil Steril. 2007 Apr;87(4):725-36. PubMed PMID: 17430732.
27. Parazzini F, La Vecchia C, Negri E, Cecchetti G, Fedele L. Epidemiologic characteristics of women with uterine fibroids: a case-control study. Obstet Gynecol. 1988 Dec;72(6):853-7. PubMed PMID: 3186092