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# Association of body mass index & android obesity with uterine leiomyoma among premenopausal women: A case–control study

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**Abstract**

Uterine leiomyomas (ULs) or uterine fibroids are the primary genital tumors in women of reproductive age. Obesity and increased visceral fat, and the production of inflammatory mediators might be risk factors for ULs. This study aimed to assess the correlation between ULs and body fat distribution among Iranian women. This case-control study involved 280 women of reproductive age with ULs and without myoma in 2020. They referred to three women's clinics in Shiraz (Shahid Faghihi, Zeinabieh, and Motahhari clinics). The sample size for each group consisted of at least 140 subjects selected via consumptive sampling methods. A gynecologist pre-diagnosed ULs based on the findings of vaginal ultrasound. We recorded and compared both groups' demographic information, fertility and ULs histories, body mass index (BMI), and android obesity. We used chi-square and t-tests to analyze the data. Most patients with ULs (64 people, 45.7%) were 41-50 years old. Most of them (126, 90%) were housewives, and the level of education of most patients (74 people, 52.9%) was under high school diploma. The mean BMI in women with myoma was 26.05±5.32 and 25.81 ±4.38 in women without myoma. There was no significant difference in the mean scores of BMI between the two groups, but the Android fat obesity was higher in patients with ULs. Few studies have attempted to identify specific risk factors for this tumor. Preventing weight gain and obesity and lifestyle modification can prevent Uterine leiomyoma.

**Keywords:** gynecology, premenopausal, uterine leiomyoma, women, body mass index, android obesity

## 1. Introduction

Uterine leiomyomas (ULs), or uterine fibroids, of the most common myometrial muscle cell tumors of benign pelvic origin (1), are benign steroid monoclonal tumors that stimulate the smooth muscle (myometrium) of the uterus (2). It is estimated that up to 77% (25-77%) of all women suffer from ULs during their life, and 15-30% suffer from significant symptoms (3-5). ULs are a common cause of menstrual irregularities, pelvic discomfort, menorrhagia, dysmenorrhea, anemia, recurrent pregnancy loss, preterm labor, incontinence, and infertility (4). Ekin et al. (2014) reported that the frequency of genital symptoms, urinary incontinence, including stress urinary incontinence, urgency and frequency of urination, and painful intercourse were higher in women with ULs. Women with ULs greater than 5 cm had more urinary incontinence than other women during physical activity and travel (6).

These seemingly benign tumors can be associated with abnormalities in preterm labor and infertility and recurrent miscarriages. The prevalence of abortion in such women is also twice as high as in other myoma-free pregnancies (7, 8). ULs are also the most common significant cause of uterine resection, which causes several complications for the patient (5, 9). The exact causes of ULs remain unknown, but two hypotheses propose genetics and hormones to be the cause (10, 11). Risk factors for ULs' development are obesity, reproductive factors such as nulliparity, young age in the first pregnancy, premature menarche, menstrual cycle length of more than 30 days and bleeding duration of more than six days, diabetes, and hypertension (12-16). A case-control study by Giri et al. (2017) (539 cases and 794 controls) entitled "African genetic ancestry interacts with body mass index to modify risk for uterine fibroids." reported that race, especially African race, and obesity are important risk factors for ULs and create suitable conditions for ULs growth (17). Obesity decreases the 2-hydroxylation of estrone to catechol estrogens and an increase in 16-alpha-hydroxylation of

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estrone to estriol. Eventually, it produces estrogens with more uterotropic activity (18, 19). Other studies in a white population had contradictory results regarding the association between BMI and uterine leiomyoma (20-24). Some studies showed a positive correlation (20, 22, 23) or an inverse correlation (21, 24), while others showed no correlation between BMI and uterine leiomyoma (5, 25, 26). There are different conclusions about the effect of obesity on UL incidence, some of which may be related to disease definitions and climatic and geographical differences. Prompt diagnosis and early commencement of treatment of GHD are of great importance in children's reaching target heights (5, 7, 8). Patients started on GH therapy must be followed up in terms of efficacy (9). Growth velocity and IGF-1 and IGFBP-3 levels can be evaluated in terms of the effectiveness of treatment in these cases (10).

We conducted this case-control study to investigate the BMI and Android obesity in women with and without ULs among the population referred to the gynecological clinics of Shiraz University of Medical Sciences. With the knowledge of these predictive risk factors, appropriate strategies can be taken to determine the etiology of this tumor and design preventive measures.

## 2. Materials and Methods

### 2.1. Study design

This case-control study involved 280 women of reproductive age with ULs (symptomatic and asymptomatic) and without Uls referred to Shiraz Women's Clinics (Shahid Faghihi, Zeinabieh and Motahhari Clinics) in 2020.

### 2.2. Study size, setting and search strategy

We determined the sample size by a statistical expert using the Medcalc software according to a similar previous study (27) considering 90% power, first type error of 5%, the mean difference of 0.19 and the standard deviation of 0.46 and 0.52 for the two groups. Using the convenience sampling method based on inclusion criteria, we involved at least 140 people in the study.

### 2.3. Participants

The case group included people with symptomatic or asymptomatic ULs who were pre-menopausal, and the control group also included all women referred to clinics to receive periodic care for ULs and Endometriosis for other reasons.

### 2.4. Inclusion and exclusion criteria

**Inclusion criteria:** Married women with Iranian citizenship, pre-menopausal age and myoma (from the age of 15 until menopause, when the average age of menopause is 51 years), any hormonal drug affecting the size of the myoma from the beginning to one month after completion, signing the informer written consent form, not attending any classes or programs that affect the quality of life and lifestyle such as relaxation, yoga, meditation, and no history of endometriosis in the myoma group.

**Exclusion criteria:** Not using special diets during the study, taking any drug that affects the quality of life and lifestyle from three months before the study, and patients' unwillingness to continue the study.

### 2.6. Research tools

Research tools: Demographic information questionnaire including demographic characteristics of subjects such as age, weight, height, abdominal circumference, blood pressure, history of hypertension, education, age of marriage, economic status, number of pregnancies, number of abortions and stillbirths, age of onset of the first menstrual period, the history of myoma and the impact of myoma on quality of life, the history of myoma in the first-degree family, menstrual order and bleeding rate, smoking or alcohol consumption, and contraception. BMI is determined by dividing weight by the square of height and classified into lean (less than 18.5), normal (18.5 to 24.9), overweight (25 to 29.9), obese (30 to 39.9), and very obese (greater than or equal to 40) (95). Android obesity is calculated by dividing abdominal circumference by hip circumference and interpreted as low risk (equal to or less than 0.8) and moderate risk (0.81 to 0.89), and high risk (equal to or more than 0.9). We recorded the weight of all individuals in a fixed state using a digital scale (Camry, I.R. Iran) with an accuracy of 100 grams. We measured the heights with an accuracy of 0.5 cm using a tape measure in a standing position with the head was straight, the legs together, the knees straight, and the four points of the heel, buttocks and shoulders attached to the wall without any footwear or headwear.

### 2.7. Statistical tests

It was done by SPSS statistical software v.22. We used the independent t-test to evaluate the mean scores of body mass index and Android obesity in the two groups with and without myoma. We used a Chi-square test to compare the frequency of Android obesity in the two groups with and without myoma.

### 2.8. Ethical considerations

The Ethics Committee of Shiraz University of Medical Sciences confirmed the research (grant No: 20735-98, ethics code: (18120-98, IR.SMS-TEC1398-989). All participants signed written informed consent. We designed the protocol per the Helsinki principles of ethics.

## 3. Results

### 3.1. Clinical characteristics of the study subjects

Out of the 140 people in the ULs group, 53 (37.9%) were from Motahhari Hospital and 87 (62.1%) from Zeinabieh Hospital. Sixty-four (45.7%) were in the 41-50 years age range, 126 (90%) were housewives, and 74 (52.9%) had an educational level under high school diploma (Table 1).

**Table 1.** Frequency distribution and comparison of the studied variables in two groups with myoma and without myoma

| Variable | | Group Myoma N (%) | Without Myoma N (%) | P-value |
|---|---|---|---|---|
| Age | 20-30 | 10 (7.1) | 24 (17.1) | 0.054† |
| | 31-40 | 60 (42.9) | 61 (43.6) | |
| | 41-50 | 64 (45.7) | 50 (35.7) | |
| | >51 | 6 (4.3) | 5 (3.6) | |
| Job | housewife | 126 (90) | 124 (88.6) | 0.722* |
| | Employee | 12 (8.6) | 12 (8.6) | |
| | Free | 2 (1.4) | 4 (2.9) | |
| Education | Less than a diploma | 74 (52.9) | 60 (42.9) | 0.083† |
| | Diploma | 44 (31.4) | 54 (38.6) | |
| | Associate Degree | 18 (12.9) | 15 (10.7) | |
| | Bachelor and higher | 4 (2.9) | 11 (7.9) | |
| Number of Pregnant | once | 14 (11) | 32 (26.7) | 0.057† |
| | Twice | 39 (30.7) | 42 (35) | |
| | three times | 34 (26.8) | 23 (19.1) | |
| | Four times | 27 (21.25) | 14 (11.7) | |
| | Five times and above | 13 (10.25) | 9 (7. 5) | |
| Number of Abortion | once | 35 (25.8) | 25 (19.25) | 0.055† |
| | Twice | 3 (2.2) | 12 (9.25) | |
| | Three times and more | 2 (1.5) | 5 (3.9) | |
| | Have not | 96 (70.5) | 88 (67.6) | |
| Number of child | once | 21 (17) | 35 (29.4) | 0.059† |
| | Twice | 42 (33.8) | 49 (41.2) | |
| | three times | 35 (28.2) | 20 (16.8) | |
| | Four times | 18 (14.5) | 8 (6.7) | |
| | Five times and above | 8 (6.5) | 7 (5.9) | |

†:Chi-Square Test, *: Fisher's Exact Test

### 3.2. Obesity and UL correlation

We used an independent t-test to evaluate the mean scores of BMI in with and without ULs. Comparing the means, the calculated T-statistic value was 0.412 with a degree of freedom of 278, and considering that the significance level was 0.681, there was no significant difference between the mean scores of BMI between the two groups (Table 2).

**Table 2.** Comparison of mean body mass index between myoma and non-myoma groups

| Variable | Group | N | Mean ± SD | Test statistics | P-value * |
|---|---|---|---|---|---|
| BMI | Myoma | 140 | 26.05 ± 5.32 | 0.42 | 0.675 |
| | Without Myoma | 140 | 25.81 ± 4.38 | | |

**Independent T-test*

We used a Chi-square test to compare the frequency of Android obesity in the two groups with and without ULs. Considering the significance level of the Chi-square test of 0.05, which was less than the assumed error in this study, there was a statistically significant difference in the observed frequencies of Android obesity between participants with and without ULs (Table 3). We used an independent t-test to evaluate the mean scores of Android obesity in the two groups. Comparing the means, the value of the T statistic was -5.88 with a degree of freedom of 278, and according to the value of the significance level of 0.001, there was a significant difference in the mean scores of Android obesity between the two groups, and Android obesity was higher in the non-myomas group (Table 4).

**Table 3.** Descriptive results of Android obesity scores in two groups with and without myoma

| | | Android Obesity | | | total |
|---|---|---|---|---|---|
| | | Low | Moderate | High | |
| Group | Myoma | 21 | 23 | 96 | 140 |
| | Without Myoma | 33 | 36 | 71 | 140 |
| Total | | 54 | 59 | 167 | 280 |

**Table 4.** Comparison of mean scores of Android obesity in case group with control

| Variable | Group | N | Mean ± SD | Test statistics | P-value* |
|---|---|---|---|---|---|
| Android Obesity | Myoma | 140 | 0.98 ± 0.16 | -5.88 | 0.001 |
| | Without Myoma | 140 | 0.91 ± 0.16 | | |

*Independent t-test

## 4. Discussion

Our results showed that the mean scores of BMI were not significantly different between the two groups with and without ULs. Takeda et al.'s study (16), which compared 213 women with and 159 without ULs, reported that ULs was significantly associated with obesity and HTN and the presence of several risk factors associated with ULs increased the risk of metabolic syndrome in patients. In a prospective study in the US, Marshall et al. (27) found that the risk of ULs increases with BMI and ULs are associated with weight gain. Sharmi et al. (2009) examined the risk factors associated with uterine fibroids in a case-control study on 990 women of reproductive age in Rasht, Iran. They asked about myoma family history, fertility history, BMI and the contraceptive method in their questionnaire. The results showed a statistically significant relationship between uterine fibroids and BMI higher than 5 (28). Their results were inconsistent with the present study, which can be due to the type of information collected, the face-to-face interview method, or the large size of their study population (990 people). He et al. (2013) also showed that BMI significantly increased the risk of uterine myoma in pre-menopausal women (29). Their obtained results were inconsistent with the present study. This could be due to the difference in the study population and the racial differences between Iran and China. They studied pre-menopausal women with a mean age of 45-555, while our study involved women 31-40 years old. Another debatable point is that the mean BMI of patients with myoma and non-patients was 26.05 and 25.81, respectively, indicating that the study population was only slightly overweight. In contrast, several reported studies showed no association between UL incidence and obesity (24, 26), consistent with the present study.

In our study, the mean scores of Android obesity in the case group were significantly greater than that of the control group. In a case study, Chen et al. (2001) reported that BMI, hip circumference, waist-to-height ratio, waist circumference (WC), body fat content, and body fat percentage were

positively associated with uterine fibroids. Women with high BMI and waist-to-thigh ratio had the most significant uterine fibroids risk. Also, women with a body fat percentage of higher than 30% were comparatively prone to uterine fibroids, and uterine fibroids could be associated with overweight and central obesity (5), which is consistent with some of the findings of the present study. In a study by Tak et al., the WC and body fat were significantly greater in the ULs group. These outcomes are consistent with previous reports showing a positive correlation between obesity and the occurrence of ULs (15). In another study, visceral fat area (VFA), BMI, WC, body fat percentage, waist-to-height ratio, and waist-to-pelvic ratio were positively associated with uterine fibroids (30). Boclin et al. (2015) examined the association between adult weight gain and uterine myomas among Brazilian women. The results showed no significant relationship in the presence of uterine myomas among people with weight gain (31). Their results were inconsistent with our study. This difference might be due to the study population and the racial differences between Iran and Brazil. They studied 1560 Brazilian women whose weight gain had been continuously studied.

Studies show that the estrone to estradiol conversion in uterine fibroids is significantly lesser than the normal muscle tissue, and the estrogen receptors' concentration in fibroids is obviously greater than in peripheral muscle tissue. Thus, the pathogenesis of uterine fibroids might be related to the level of sex hormones (32). Obesity can lead to metabolic disorders, leading to local tissues creating an unusually great estrogen environment. This mechanism contains the following: 1) Androstenedione secreted through the adrenal glands could be converted to estrone via aromatase in adipose tissue, and plasma estrone levels increase with increased adipose tissue, hence causing a continuous effect of estrogen. 2) Obesity causes a periodic lack of regulation of progesterone; therefore, the endometrium is over-stimulated in an environment where no progesterone has an estrogen antagonist (33, 34). Uterine fibroids may develop in an abnormal environment with high estrogen. Therefore, obesity can be a risk factor for uterine fibroids.

Evidence shows that the levels of SHBG are lower in women with central obesity, and they have altered estrogen metabolism and hyperinsulinemia that are anticipated to stimulate the growth of UL (14, 23). However, a clear link between obesity and UL is connected to the hormonal effects associated with obesity. For instance, obesity increases with increased circulating adrenal androgens to estrones conversion due to adipose tissue accumulation (15). In addition, hepatic SHBR production is reduced, leading to more unrestricted physiologically active estrogen (35), which can cause a comparatively hyperestrogenic state. Previous studies have shown increased levels of estrogen and adipokines due to extreme fat accumulation and raised systemic inflammatory cytokines levels that may raise the tumorigenesis risk (36, 37).

Considering the above issues, it can be concluded that various factors are involved in the development of fibroids, and its true etiology remains unknown but understanding the risk factors associated with fibroids can be effective in providing preventive measures in the development of the disease. Preventing weight gain during fertility and lifestyle modification can be one of the preventative measures.

In conclusion, there was no significant difference in the mean scores of BMI between the case and control groups, but the Android fat index was higher in patients with myoma. Preventing weight gain during the reproductive period and improving lifestyle can be one of the preventive ways. Providing nutritional tips, changing diets, and exercising are essential steps to preventing uterine fibroids.

One of the study's limitations was that it was conducted during the COVID-19 pandemic in hospitals and public centers. As a result, a series of protocols were observed during the presence of participants, and completing the questionnaires, including maintaining the physical distance, necessitated a longer time than stated in the proposal. Furthermore, because only Iranian women participated in the study, our findings could not be generalized to other ethnicities or geographies.

**Conflict of interest**

All authors have no financial or personal conflict of interest.

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**Authors' contributions**

MA and ZK prepared the first draft of the manuscript, and MA &SA made critical revisions to the paper and responded to the reviewers. FN helped the Surge Articles and Clinical Research.

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