

## Prevalence and Risk Factors of Uterine Fibroids in North-East Slovenia

Tina Bizjak\*, Anela Bečić Turkanović and Igor But

University Medical Centre Maribor, Department of General Gynaecology and Gynaecologic Urology, Maribor, Slovenia

### Abstract

**Objectives:** Uterine fibroids are the most common pelvic tumors in women, occurring globally with a prevalence of 21.4%. The aim of this study is to reveal the prevalence of fibroids in a patient population from the municipality of Maribor, Slovenia, and to identify associated risk factors.

**Methods:** The study was based on a random sample of 2000 women within the age group of 25 to 56 living in the municipality of Maribor, Slovenia. Participation was completely voluntary. Eligible patients had to fill out a questionnaire and would undergo a transvaginal ultrasound. The data were processed with the statistical program PASW 18, and p values < 0.05 were taken to statistically significant differences.

**Results:** Nine hundred and twenty-one of the 2,000 women (46.1%) have responded to our invitation and uterine fibroids were identified in 21.1% of them. The prevalence of fibroids was statistically significantly lower (6.7%) in the younger group (25-35 years) than in the group aged 36-45 years (prevalence of 33.3%,  $\chi^2=34.4$ ,  $p=0.0001$ ) and that of 46-56 years (prevalence of 60%,  $\chi^2=53.7$ ,  $p=0.0001$ ). The prevalence of fibroids was higher in women who had never used oral contraceptives when compared to those who had (27.0% vs. 19.7%;  $\chi^2=4.8$ ,  $p=0.028$ ). Women with fibroids had a 1.2 kg/m<sup>2</sup> (95% CI: 0.4-1.9) higher BMI ( $t=-3.0$ ,  $p=0.003$ ). Other previously described risk factors did not appear of significance.

**Conclusion:** Fibroids represent an important gynecologic pathology in women due to its relatively high prevalence and their probable impact on patient's quality of life.

**Keywords:** Fibroids; Prevalence; Risk factors; Age; Contraceptive pills; Body mass index; Smoking

### Introduction

Uterine fibroids (i.e. myomas or leiomyomas), benign tumors of the uterus, are the most common pelvic tumors in women [1,2]. According to Italian Seveso Women's Health Study (SWHS), 21.4% of women aged 30 to 60 years were diagnosed with fibroids, which provide one of the best prevalence estimated for fibroids in a European population [3].

Because of their frequency, fibroids represent an important pathology, hence can be the cause of abnormal uterine bleeding, pelvic pain/pressure and may have reproductive effects on infertility and adverse pregnancy outcomes [4].

The etiology of uterine fibroids is poorly understood. Previous studies suggest multiple risk factors for developing fibroids, such as: age, African ethnicity, early age at menarche, reduced fertility, frequent alcohol and caffeine consumption, obesity, consumption of red meat, hypertension, diabetes mellitus, previous pelvic inflammatory disease and genetics [5-11]. Protective factors are prolonged menstrual cycles, (multi)parity, prolonged use of oral contraceptives, late age at first birth, breast feeding, post menopause, smoking and vegetarian food [11,12].

There is little known about fibroids prevalence in Europe and therefore, the aim of this study was to assess the prevalence of fibroids in our population of women and to discover possible risk factors for the occurrence of this common gynecological pathology.

### Methods

This study was performed in the year 2010 based on a random sample of 2000 women aged between 25 and 56 years who were living in the Municipality of Maribor, Slovenia. This random sample of women was provided by the Statistical Office of the Republic of Slovenia. We mailed to all women invitations where we explained the aim of the

study in detail and asked for their cooperation. We also informed them that their participation in the study was completely voluntary. Those who responded were scheduled for examination. On the examination day all participants signed an Informed Consent Form and filled out the 45-item questionnaire. In addition to basic information regarding the age, height, weight, and education, the questionnaire also asked about smoking, alcohol and caffeine consumption, nutrition, sexual and reproductive life, participant's health status (hypertension, diabetes mellitus) and about the family history of the disease (fibroids).

After completing the questionnaire, the participants were invited to an ultrasonography office where the screening for uterine fibroids was performed by certified gynecologists trained in transvaginal ultrasonography. For this purpose, the Medison Accuvix XQ ultrasound machine with the EC4-9IS endovaginal probe was used. During an ultrasound examination, uterine dimensions and structure were assessed and the number, location and size of largest fibroid defined.

The data was analyzed with the statistical program PASW 18 (SPSS Inc., Chicago, Illinois, USA). Numeric variables were represented by the arithmetic mean and standard deviation and descriptive variables were presented with frequencies. The relationship between descriptive

**\*Corresponding author:** Tina Bizjak, University Clinical Centre Maribor, Division of Gynecology and Perinatology, Ljubljanska 5, 2000 Maribor, Slovenia, Tel: +386 2 321 2178; E-mail: [tina.bizjak20@gmail.com](mailto:tina.bizjak20@gmail.com)

**Received** December 23, 2015; **Accepted** January 18, 2016; **Published** January 20, 2016

**Citation:** Bizjak T, Turkanović AB, But I (2016) Prevalence and Risk Factors of Uterine Fibroids in North-East Slovenia. Gynecol Obstet (Sunnyvale) 6: 350. doi:10.4172/2161-0932.1000350

**Copyright:** © 2016 Bizjak T, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

variables was analyzed with the »Pearson chi-square test« or »Fisher's exact test of independence« by testing equality between the observed and expected frequencies. The differences in the average value of the numeric variables were assessed using t-test for independent samples or one-way analysis of variance (ANOVA). The multiple comparisons as "a post hoc" analysis were performed using Bonferroni error correction of the first type. The limit of statistical significance was at  $p < 0.05$ . This study was approved by the Institutional Review Board at the University Medical Centre Maribor.

## Results

921 out of 2000 randomly selected women have responded to our invitations (46.1% response rate). The mean age of the participants was 42.4 years. Fibroids were found in 21.2% of participants (195 women), of these 63.6% were newly discovered (124 women). The results of the fibroids characteristics such as number, location and volume are presented in Table 1.

Fibroid incidence showed statistically significant correlation with age. In the age group of 25-35 years, the incidence of fibroids was significantly lower (6.7%), than in the latter two groups: 33.3% in the 36-45 years of age ( $\chi^2=34.4$ ,  $p=0.0001$ ) and 60% in the 46-56 years of age group ( $\chi^2=53.7$ ,  $p=0.0001$ ).

732 women (79.5%) were using hormonal contraception pills this contraception at some point of their life. In women who have never used these pills, the prevalence of fibroids was higher (27.0%), than in women who have used hormonal contraception pills (19.7%) ( $\chi^2=4.8$ ,  $p=0.028$ ). In women who have used combined oral contraceptives a lower prevalence of fibroids was observed (13.3%) as compared to those who have used only gestagens (33.3%) ( $\chi^2=4.3$ ,  $p=0.038$ ).

Average body mass index (BMI) of women with fibroids detected in our study was 25.8 kg/m<sup>2</sup>, while BMI of women without fibroids was 24.7 kg/m<sup>2</sup>. Women with fibroids had a 1.2 kg/m<sup>2</sup> (95% CI: 0.4-1.9) higher BMI than women without fibroids ( $t(919) = -3.0$ ,  $p=0.003$ ). Women were divided into four categories based on their BMI score; comparison of individual categories of BMI showed that women with a BMI of 25 kg/m<sup>2</sup> to 29.9 kg/m<sup>2</sup> had a higher prevalence of fibroids (27.4%), than women with a BMI of 18.5 kg/m<sup>2</sup> to 24.9 kg/m<sup>2</sup> (17.6%) ( $\chi^2=9.6$ ,  $p=0.002$ ).

We found that gynecological history (age at menarche, menstrual cycle, spontaneous abortion, previous pelvic inflammatory disease, positive family history of fibroid), lifestyle (smoking, alcohol and caffeine consumption, dietary habits as vegetarian diet and consumption of red meat) and medical history (high blood pressure, diabetes) were not statistically significant associated with fibroids. Results are presented in Table 2.

Although the connection between fibroids and spontaneous abortions was proved to be non-significant, we found that women with subserosal fibroids had spontaneous abortions at lower rates (14.5%), than women with intramural fibroids (34.3%) ( $\chi^2=9.6$ ,  $p=0.002$ ).

## Discussion

Uterine fibroids represent an important gynecological pathology, however, the data on their prevalence in European female population is lacking. The only relatively recent study, published in 2004, was performed in Italy where a screening was made in population of women aged between 30 and 60 years and the prevalence of fibroids was found to be 21,4% [13,3]. Older sources suggest that fibroids occur in 70% of women but are believed to be symptomatic in only 30% of women older than 30 years of age [14].

Therefore, the aim of the present study was to assess the prevalence and risk factors for uterine fibroids in our population of randomly selected women. The results of our study showed the prevalence of uterine fibroids of 21.2%, which is similar to the results of Seveso Women's Health Study (21.4%). The response rate of patients in our study was less than 50%, however, we believe that it was still relatively high (46.1%) bearing in mind that a participation of women was voluntary and the examination was very intimate. Namely, the transvaginal ultrasound examinations were performed by different gynecologists with whom patients were not familiar. Usually, Slovenian women are examined and followed once yearly by their chosen gynecologist to whom they are used to and whom they trust.

Participants in our research were on average 42.4 years old, which means that they were somewhat younger than the average age of Slovenian women (43.1 years) and female citizens of the Maribor city (45.6 years) [13]. Despite the fact that the data obtained during the survey to a lesser extent deviates from the data applicable to the entire female population in Slovenia, we believe that the data can be extrapolated to the entire Slovenian population (around 2 million), since the sample was wide enough and can be generalized to similar women, at least in Slovenia.

The average volume of fibroids was 8.87 cm<sup>3</sup>. The majority of fibroids were intramural (53.8%).

In our study the most important and significant risk factors associated with fibroids were age, the use oral hormonal contraception and BMI. All the other risk factors previously described in literature proved to be non-significant.

Age of the patients was significantly associated with the prevalence of fibroids. The prevalence of fibroids was lower in women who were younger than 35 years. The prevalence of fibroids increased from 6.7% in patient from the young group (<35 years) to 33.3% in women between 36-45 years of age and to 60% in the age group of 46-56 years. We were also able to confirm that the prevalence of fibroids decreased significantly after age of 50. In our sample the peak of detected fibroids was at the age of 49, after which the prevalence of fibroids was decreasing until the age of 56 where we did not find any fibroid. The most likely explanation is that growth of fibroid is hormone-

Number of fibroids	1	57.9 %
	2-4	42.1 %
	5+	3.6 %
Location	Subserosal	42.1 %
	Intramural	53.8 %
	Submucosal	4.1 %
Volume	Smallest	3 mm <sup>3</sup>
	Average	517.1 mm <sup>3</sup>
	Largest	5312 mm <sup>3</sup>

Table 1: Properties of myomas identified by vaginal ultrasound.

Risk factor	Statistical significance
Smoking	$\chi^2 = 0.04$ $p = 0.835$
Alcohol	$\chi^2 = 1.68$ , $p = 0.195$
Caffeine	$\chi^2 = 1.30$ , $p = 0.255$
Red meat consumption	$\chi^2 = 1.38$ , $p = 0.240$
Regular green vegetables consumption	$\chi^2 = 0.17$ , $p = 0.682$
Age at menarche	$\chi^2 = 3.64$ , $p = 0.162$
Menstrual cycle duration	$t(918)=0.23$ , $p=0.817$
Arterial Hypertension	$\chi^2 = 1.11$ , $p = 0.293$
Diabetes Mellitus	$\chi^2 = 1.63$ , $p = 0.212$

Table 2: Factors which were not significantly connected to prevalence of fibroids.

dependent; therefore, the prevalence is different among age groups [12]. Furthermore, women in menopause are exposed to lower levels of female sex hormones; accordingly, fibroids may significantly reduce their size during this period [15].

Oral contraceptives may affect the development and growth of fibroids with the time-dependent fashion [16,17]. Beneficial effect is attributed to the progestagen components of a combined oral contraceptive. It was found that the higher the dose of progesterone norethisterone acetate at the same amount of ethinylestradiol, the lower the incidence of fibroids. In contrast, all the prescriptions containing gestagen ethynodioldiacetate irrespective of the quantity and type of estrogen, increased the incidence of fibroids [7,18]. Our results showed a protective role of contraceptives on the prevalence of fibroids. The prevalence of fibroid was higher in women who have never used contraceptives (27.0%), than in women who have used contraceptive pills at some point of their live (19.7%), from which we could conclude that taking birth control pills might have a protective role in the occurrence of fibroids. Additionally, our results showed that the occurrence of fibroids is dependent of the type of contraceptives. In women who used combined oral contraceptives fibroids occurred less often (13.3%) than in women who used gestagen tablets (33.3%). In contrast to some reports in the literature the duration of the oral contraceptive pills was not found to be statistically important for the occurrence of fibroids in our patients.

It was observed that fibroids are more frequent in obese women (body mass index – BMI > 30 kg/m<sup>2</sup>). Body weight of 70 kg or more represents a nearly three-fold increased risk of incidence of fibroids compared with a body weight of 50 kg [18]. Similar results were obtained by monitoring the BMI. In a case-control study from Thailand, a 6% increase in risk was observed for each unit increase in BMI [18,19]. Our results showed that BMI in women with fibroids was in average 1.2 kg/m<sup>2</sup> higher compared to women without fibroids. Elevated BMI has a greater impact on the risk of the incidence of fibroids after the age of 18, if it is higher than 20 kg/m<sup>2</sup>. Its greatest impact has been seen between 27.5 kg/m<sup>2</sup> and 29.9 kg/m<sup>2</sup> [9,20]. Our results showed that the prevalence of fibroids was higher (27.4%) in women with BMI between 25 and 29.9 kg/m<sup>2</sup> than in women with a BMI between 18.5 to 24.9 kg/m<sup>2</sup> (17.6%). These results are consistent with reports in the literature.

In our study we also assessed the importance of the other risk factors which might have a possible role in the occurrence of fibroids. Three major groups of risk factors were analyzed: gynecological history, lifestyle and medical history. Although early age at menarche showed to be important in association with fibroids development, we did not find any significance [14,21]. Moreover, we did not find any significant correlation between some of the lifestyle habits, like cigarette smoking, consumption of alcohol, consumption of red meat, vegetarian diet, and occurrence of fibroids, even though some authors describe these features as significant [6,10,22]. Some reports in the literature showed fibroids to be more frequent in women who experience arterial hypertension and diabetes [17,23], however our results do not support this association.

There are some studies that show connection between different types of fibroids and reproductive outcomes [24]. Results from our study showed that intramural fibroids are associated with greater risk for spontaneous abortion. This may be important for those fertile women who are trying to get pregnant and experience asymptomatic intramural fibroids.

Our study was limited to Caucasian women, since in Slovenia there is mostly Caucasian race present in the population. Thus, this result

could be generalized to the Slovenian population; other countries with diverse races could have other results of similar studies.

## Conclusion

The prevalence of uterine fibroids in our population of women was found to be 21.1%. We found that the significant risk factors for fibroid development were higher BMI and the age between 35 and 50 years, whereas the oral contraceptive pills use has a protective role. The two strengths of our study were the use of a stratified random sample and use of transvaginal ultrasound examination performed by skillful gynecology specialists. However, the possible drawback of our study may be somewhat lower response rate of the participants (46.1%) what still seems to be acceptable bearing in mind that the transvaginal examination is a very intimate examination. Future studies are needed to evaluate whether some lifestyle habits and chronic diseases are associated with fibroids.

## Acknowledgments

The study was independent and was not sponsored by any companies.

## Conflict of Interest

All authors declare no conflicts of interest.

## References

1. Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM (2003) High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. *Am J Obstet Gynecol* 188: 100-107.
2. Serden SP, Brooks PG (1991) Treatment of abnormal uterine bleeding with the gynecologic resectoscope. *J Reprod Med* 36: 697-679.
3. Marino JL, Eskenazi B, Warner M, Samuels S, Vercellini S, et al. (2004) Uterine leiomyoma and menstrual cycle characteristics in a population-based cohort study. *Hum Reprod* 19: 2350-2355.
4. Lippman SA, Warner M, Samuels S, Olive D, Vercellini P, et al. (2003) Uterine fibroids and gynecologic pain symptoms in a population-based study. *Fertil Steril* 80: 1488-1494.
5. Catherino WH, Eltoukhi HM, Al-Hendy A (2013) Racial and ethnic differences in the pathogenesis and clinical manifestations of uterine leiomyoma. *Semin Reprod Med* 31: 370-379.
6. Wise LA, Palmer JR, Harlow BL, Spiegelman D, Stewart EA, et al. (2004) Risk of uterine leiomyomata in relation to tobacco, alcohol and caffeine consumption in the Black Women's Health Study. *Hum Reprod* 19: 1746-1754.
7. Wise LA, Palmer JR, Harlow BL, Spiegelman D, Stewart EA, et al. (2004) Reproductive Factors, Hormonal Contraception, and Risk of Uterine Leiomyomata in African-American Women: A Prospective Study. *Am J Epidemiol* 159: 113-123.
8. Wise LA, Palmer JR, Spiegelman D, Harlow BL, Stewart EA, et al. (2005) Influence of body size and body fat distribution on risk of uterine leiomyomata in U.S. black women. *Epidemiology* 16: 346-354.
9. Lobel MK, Somasundaram P, Morton CC (2006) The genetic heterogeneity of uterine leiomyomata. *Obstet Gynecol Clin North Am* 33: 13-39.
10. Chiaffarino F, Parazzini F, La Vecchia C, Chatenoud L, Di Cintio E, et al. (1999) Diet and uterine myomas. *Obstet Gynecol* 94: 395-398.
11. Evans P, Brunsell S (2007) Uterine fibroid tumors: Diagnosis and treatment. *Am Fam Physician* 75: 1503-1508.
12. Terry KL, De Vivo I, Hankinson SE, Missmer SA (2010) Reproductive characteristics and risk of uterine leiomyomata. *Fertil Steril* 94: 2703-2707.
13. Slovenia S.O.O.R.O (2010) Rapid reports, in Population.
14. Vitiello D, McCarthy S (2006) Diagnostic imaging of myomas. *Obstet Gynecol Clin North Am* 33: 85-95.
15. Blake RE (2007) Leiomyomata uteri: hormonal and molecular determinants of growth. *J Natl Med Assoc* 99: 1170-1184.
16. Payson M, Leppert P, Segars J (2006) Epidemiology of Myomas. *Obstet Gynecol Clin North Am* 33: 1-11.

17. Ross RK, Pike MC, Vessey MP, Bull D, Yeates D, et al. (1986) Risk factors for uterine fibroids: reduced risk associated with oral contraceptives. *Br Med J* 293: 359-362.
18. Flake GP, Andersen J, Dixon D (2003) Etiology and pathogenesis of uterine leiomyomas: a review. *Environ Health Perspect* 111: 1037-1054.
19. Lumbiganon P, Ruggao S, Phandhu-fung S, Laopaiboon M, Vudhikamraksa N, et al. (1996) Protective effect of depot-medroxyprogesterone acetate on surgically treated uterine leiomyomas: a multicentre case-control study. *Br J Obstet Gynaecol* 103: 909-914.
20. Marshall LM, Spiegelman D, Manson JE, Goldman MB, Barbieri RL, et al. (1998) Risk of uterine leiomyomata among premenopausal women in relation to body size and cigarette smoking. *Epidemiology* 9: 511-517.
21. Gupta S, Manyonda IT (2009) Acute complications of fibroids. *Best Pract Res Clin Obstet Gynaecol* 23: 609-617.
22. Parazzini F, Negri E, La Vecchia C, Rabaiotti M, Luchini L, et al. (1996) Uterine myomas and smoking. Results from an Italian study. *J Reprod Med* 41: 316-320.
23. Okolo S (2008) Incidence, aetiology and epidemiology of uterine fibroids. *Best Pract Res Clin Obstet Gynaecol* 22: 571-588.
24. Pritts EA, Parker WH, Olive DL (2009) Fibroids and infertility: an updated systematic review of the evidence. *Fertil Steril* 91: 1215-1223.