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Original Article

The Association Between Uterine Leiomyoma and Hypertension: A Single Center Case-Control Study

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Abstract

Background: Cardiovascular Diseases (CVD), mainly Hypertension (HTN), is the leading cause of death among women. Uterine Leiomyomas (UL) which have been associated with hypertension in multiple studies, may be a female-specific risk factor. Fibroids have become a primary reason for myomectomy and hysterectomy, nowadays. This study aims at the relationship between HTN and fibroids.

Methods: This case-control study was conducted on patients with symptomatic UL, scheduled for surgery. Patients were studied based on Blood Pressure (BP), the number and size of fibroids, past medical conditions, and gynecological history.

Results: Four hundred patients, divided into two groups of control and case, were studied. Menometrorrhagia was the most common reason for referral in both groups (328 patients in general). The use of Oral Contraceptives (OCP) (12 *vs.* 5%), anemia (57 *vs.* 38.5%), history of infertility (11.5 *vs.* 3.5%), and abortion (38.5 *vs.* 22%) was significantly higher in patients with fibroids. 24% of patients with fibroid suffered from hypertension; which was higher in comparison to the control group (9%). Patients with UL were 4.9 times in danger of having HTN.

Conclusion: UL is associated with hypertension. It is also concluded that anemia, rate of abortion, and infertility are higher in patients with UL.

Keywords: Cardiovascular disease, Fibroid, Hypertension, Uterine leiomyoma

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Introduction

Uterine Leiomyomas or fibroids (UL) has become a public health concern and a prior indication for hysterectomy in female of reproductive age (1,2). Over 200,000 hysterectomies and a growing number of myomectomies are performed due to UL each year (3,4). UL is considered to be the most common female genital tract tumor (5). They are benign monoclonal tumors with smooth muscle origin (4,6). The etiology of this tumor is yet unknown, but they are mainly hormone-dependent, and Estrogen has an important role in fibroid growth (7-9). Although some clinical and biological studies suggest the impact of progesterone in UL development (10), age and African American ethnicity are considered to be major risk factors for UL (11). Studies have suggested that fibroids can be found in up to 70% of females but only 30% accompany by clinical features such as abdominal pain, pelvic pain, infertility, bladder or rectum obstruction, pregnancy complication, and abnormal uterine bleeding (4,7). Bimanual examination and transvaginal ultrasonography are the conventional diagnostic methods of UL (9).

As is known, Hypertension (HTN) is the most common cause of cardiovascular and kidney diseases (12,13) and the leading cause of mortality in cardiovascular diseases (1). UL and HTN can lead to smooth muscle cell alteration, linking these two diseases (14). Studies have brought up the coexistence of hypertension and fibroids. The relationship between these two is yet unknown (10). Therefore, this study aims to assess the relationship between fibroids and hypertension in a case-control study.

Materials and Methods

Study design and setting

This case-control study was conducted on patients with symptomatic UL, including menometrorrhagia, abdominal pain, and infertility, who were scheduled for surgery at the obstetrics and gynecology department of Yas Hospital, a referral center in Tehran, Iran. The study was approved by ethics committee of the Tehran University of Medical Sciences. The information about patients was collected, analyzed, and provided anonymously. The researchers adhered to the ethical principles of the Helsinki recommendations.

Participants

This study was conducted *via* patients admitted to Yas Hospital, scheduled for gynecological surgery during a three-year study period, from 2017 to 2020.

This study includes 18 to 60 years old females with a confirmed diagnosis of UL *via* clinical examination, ultrasonography, and pathology who were scheduled for myomectomy or total hysterectomy at this center, in case group. The control group includes 18 to 60-year-old females who were scheduled for a non-fibroid total hysterectomy surgery and admitted at the same center. We included patients who reported blood pressure unknown or not checked in the past 2 years and excluded women with a history of secondary hypertension, malignancy or receiving antihypertensive drug therapy. Using the reported values in previous studies (1,15), study power of 80%, the two-sided significance level of 5%, and using the sample size formula for proportional studies, the sample size for each group was calculated to be 200.

Data collection

Using a predesigned checklist, information was collected regarding demographics, Blood Pressure (BP), the number and size of fibroids, previous use of Oral Contraceptive Pills (OCP), history of infertility, diabetes, anemia, thyroid diseases, hyperlipidemia, number of abortions, number of pregnancies, and chief complaints when admitted. Blood pressure was measured twice at thirty-minute intervals in both groups. Hypertension (HTN) was defined as systolic blood pressure (SBP) ≥140 *mmHg* and/or diastolic blood pressure (DBP) ≥90 *mmHg* or a patient receiving anti-hypertensive medication (16).

Data analysis

All statistical analyses were conducted *via* the SPSS-25 (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp; 2017). Study findings were reported as frequency (%) or mean ± standard deviation (SD) for categorical and numerical variables. We reported "median and range" for data that were not normally distributed. Comparisons were performed using Chi-Square or Fisher's exact test. The mean differences in numerical variables between the two groups were compared by independent t-test. For numerical variables, Pearson's correlation and

Table 1. The baseline characteristics (N=400)

Variables		Patients with UL	Control group	p-value
Chief compliant	Menometrorrhagia	156 (78%)	172 (86%)	0.892
	Abdominal pain	38 (19%)	22 (11%)	0.291
	Infertility	6 (3%)	6 (3%)	1.000
Age		42.77±8.75	48±7.35	0.163
OCP use		24 (12%)	10 (5%)	0.019
Anemia		114 (57%)	77 (38.5%)	<0.001
Diabetes		18 (9%)	26 (13%)	0.263
Hyperlipidemia		25 (12.5%)	25 (12.5%)	1.000
Thyroid diseases		29 (14.5%)	18 (9%)	0.120
Infertility		23 (11.5%)	7 (3.5%)	0.004
Abortion		77 (38.5%)	44 (22%)	<0.001
Pregnancy		2.99±1.92	3.61±1.53	<0.001

UL (Uterine Leiomyoma).

Table 2. Associations of systolic and diastolic blood pressure in patients with UL according to their age

Variants	Patients with UL	Control group	p-value
SBP *(mmHg)*	126.68±19.67	119.23±13.96	<0.001
SBP in ages below 40 *(mmHg)*	124.23±21.2	113.9±11.45	0.049
SBP in ages above 40 *(mmHg)*	128.21±1857	119.75±14.1	<0.001
DBP *(mmHg)*	71.18±9.52	67.58±8.53	<0.001
DBP in ages below 40 *(mmHg)*	70.83±7.7	62.56±15.72	0.002
DBP in ages above 40 *(mmHg)*	71.4±10.5	68.08±7.35	0.001
HTN	24% (48)	9% (18)	<0.001
HTN in ages above 40	27.6% (34)	8.8% (16)	<0.001
HTN in ages below 40	18.42% (14)	10.52% (2)	0.288

SBP (Systolic blood pressure); DBP (Diastolic blood pressure); HTN (Hypertension); UL (Uterine Leiomyoma).

linear regression were utilized. A p-value lower than 0.05 was considered statically significant.

Results

The baseline characteristics

Four hundred patients, divided into two groups, were studied. Group one contains 200 patients with UL with a mean age of 42.77 years scheduled for surgery. Group two was the control group, with a mean age of 48.31 years scheduled for non-fibroid gynecological surgery. The baseline characteristics of both groups are thoroughly mentioned in table 1.

Menometrorrhagia was the most common reason for referral in both groups. The use of OCP, anemia, history of infertility, and abortion were significantly higher in fibroid group.

The median number and range of myomas was 2 (1-5) and the median size range was 69.6 (13-200) *mm* in patients with UL.

Blood pressure and UL

Blood pressure was measured twice at thirty-minute intervals in both groups. We documented patients' Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) separately in table 2. Hypertension was significantly higher in patients with UL (p-value< 0.001). Patients were divided into 2 groups: older than 40 years old and younger than 40 years old. The prevalence of

HTN in patients with UL older than 40 years old was the highest. Considering age, patients with UL are 4.9 times in danger of having HTN.

Factors concerning HTN in patients with UL

In order to find effective factors in blood pressure, the relationship between systolic and diastolic blood pressure and other variables was measured using Pearson's correlation test. Systolic blood pressure of patients was significantly related to age (r=0.258, p=0.026).

Anemia (r=0.194, p=0.006), hyperlipidemia (r=0.172, p=0.015), number of pregnancies (r=0.229, p=0.001), and chief complaint of abdominal pain and menometrorrhagia (r=-0.200, p=0.005) were significantly associated with higher SBP.

No significant relationship was found between blood pressure and other variables (myoma number, myoma size, OCP consumption, infertility, diabetes, thyroid diseases, and abortion) (p>0.05).

Finally, using linear regression test, the significance of the above findings (age, hyperlipidemia, anemia, number of pregnancies, reason for referral) in predicting systolic blood pressure of patients with uterine leiomyoma was measured. Only the coefficients of anemia (p=0.017) and reason for referral (chief complaint of abdominal pain and menometrorrhagia) (p=0.001) were significant in this model.

Anemia (p=0.017) and chief complaint of abdominal pain and menometrorrhagia (p=0.001) had a predicting value for higher systolic blood pressure.

Discussion

A total of 400 were studied in a case-control study to define the relationship between UL and hypertension. Studies showed that UL mostly presented in younger patients but there were no significant age differences between patients with UL and the control group.

Considering menometrorrhagia and abnormal uterine bleeding as the most common causes of referral for patients with UL, anemia can be expected as a result (17). As we can see, there was a relationship between anemia and UL in this study which was similar to previous studies (18,19). Some studies presented anemia mostly as a result of submucosal myoma (20,21). Promising theories were mentioned regarding the effect of UL on fertility. For instance, the effect of myomas on cavity distortion, the functional change of endometrium and myometrium that reduces uterine receptivity, as well as endocrine and paracrine molecular mechanisms. This can cause a hostile environment, impairing embryo implantation (22,23). In the event of pregnancy, spontaneous abortion, fetal malpresentation, preterm birth, and caesarian section are inevitable (24). In this study, pregnancy, infertility, and abortion were significantly affected by UL. Based on other studies, the location of the myomas, especially submucosal myomas, can have an important impact on this matter (10,23).

The use of OCP was significantly higher in patients with UL in our study. It is proven that OCP can be helpful in menstrual diseases in patients with UL (25). Younger age and higher infertility rate in patients with UL support the theory of sex hormone influence on UL occurrence (4,6,9,26).

Although the relationship between UL and diabetes and hyperlipidemia was not significant in this study, patients with UL displayed higher cardiovascular disease risk profiles in similar studies (2,27).

Our study proved the association between hypertension and UL as its main goal. Systolic and diastolic blood pressures were significantly higher and the frequency of hypertension was 4.9 times higher in patients with UL. The results were consistent with previous studies (1,2,8,11,14,28,29). A theory suggests the impact of hypertension on fibroid development and growth in uterine smooth similar to atherosclerotic changes in arterial smooth muscles (8). Patients referred with anemia or chief complaints of abnormal uterine bleeding and abdominal pain were accompanied by higher SBP, in this study. Patients were divided into two groups considering the importance of age in high blood pressure (30). Hypertension was mostly detected in patients diagnosed with UL older than 40 years. However, a previous study demonstrated that the incidence of UL was higher in patients affected by hypertension for at least 5 years and those diagnosed before 35 years old (10).

Limitations

The majority of researches on UL, including this study, are based on surgical cases. Therefore, selection bias and temporal bias are inevitable. Also, our control group contained no healthy individuals. African-American ethnicity is a major risk factor in patients

with UL, however ethnicity was also a limitation based on the geographical location of the study. Data regarding Myomas' location were another limitation.

Conclusion

It is confirmed that patients with UL are in danger of cardiovascular diseases mainly HTN. The prevalence of hypertension, anemia, abortion and infertility were higher in patients with UL. We recommend HTN screening in patients with UL, especially in patients with anemia, abdominal pain, and menometrorrhagia.

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Conflict of Interest

The authors declare that there are no conflicts of interest.

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References

1. Haan YC, Oudman I, de Lange ME, Timmermans A, Ankum WM, van Montfrans GA, et al. Hypertension risk in Dutch women with symptomatic uterine fibroids. Am J Hypertens 2015;28(4):487-92.

2. Haan YC, Diemer FS, Van der Woude L, Van Montfrans GA, Oehlers GP, Brewster LM. The risk of hypertension and cardiovascular disease in women with uterine fibroids. J Clin Hypertens (Greenwich) 2018;20(4):718-26.

3. Becker ER. National trends and determinants of hospitalization costs and lengths-of-stay for uterine fibroids procedures. J Health Care Finance 2007;33(3):1-16.

4. Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. Am J Obstet Gynecol 2003;188(1):100-7.

5. Cramer SF, Patel A. The frequency of uterine leiomyomas. Am J Clin Pathol 1990;94(4):435-8.

6. Rein MS, Barbieri RL, Friedman AJ. Progesterone: a critical role in the pathogenesis of uterine myomas. Am J Obstet Gynecol 1995;172(1):14-8.

7. Fields K, Neinstein L. Uterine myomas in adolescents: case reports and a review of the literature. J Pediatr Adolesc Gynecol 1996;9(4):195-8.

8. Boynton-Jarrett R, Rich-Edwards J, Malspeis S, Missmer SA, Wright R. A prospective study of hypertension and risk of uterine leiomyomata. Am J Epidemiol 2005;161(7):628-38.

9. Vitiello D, McCarthy S. Diagnostic imaging of myomas. Obstet Gynecol Clin North Am 2006;33(1):85-95.

10. 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;153(1):1-10.

11. Muawad R, Dabbagh R, Sabr Y. Association of health and lifestyle factors with uterine fibroids among Saudi women: a case–control study. J Taibah Univ Med Sci 2022 Jul 11;17(6):1039-1046.

12. Coresh J, Wei GL, McQuillan G, Brancati FL, Levey AS, Jones C, et al. Prevalence of high blood pressure and elevated serum creatinine level in the United States: findings from the third National Health and Nutrition Examination Survey (1988-1994). Arch Intern Med 2001;161(9):1207-16.

13. Staessen JA, Fagard R, Thijs L, Celis H, Arabidze GG, Birkenhäger WH, et al. Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. Lancet 1997;350(9080):757-64.

14. Stewart EA, Borah BJ. Uterine fibroids and hypertension: steps toward understanding the link. J Clin Endocrinol

Metab 2020;106(2):e1039-e41.

15. Radin R, Rosenberg L, Palmer J, Cozier Y, Kumanyika S, Wise L. Hypertension and risk of uterine leiomyomata in US black women. Hum Reprod 2012;27(5):1504-9.

16. Carretero OA, Oparil S. Essential hypertension: part I: definition and etiology. Circulation 2000;101(3):329-35.

17. Subramaniyam NK, Kandluri V, Chadeve A, Modapu D, jyothi Dumpala A, Gudise BR, et al. Prevalence of risk factors for uterine fibroids at tertiary care teaching hospital: a cross-sectional study. J Young Pharmacists 2020;12(1):86.

18. Kawano M, Okamoto M, Yano M, Kawano Y. Life-threatening anemia due to uterine fibroids: a case series. Exp Ther Med 2022;24(5):1-6.

19. Donnez J, Carmona F, Maitrot-Mantelet L, Dolmans MM, Chapron C. Uterine disorders and iron deficiency anemia. Fertil Steril 2022;118(4):615-24.

20. Puri K, Famuyide AO, Erwin PJ, Stewart EA, Laughlin-Tommaso SK. Submucosal fibroids and the relation to heavy menstrual bleeding and anemia. Am J Obstet Gynecol 2014;210(1):38. e1-. e7.

21. Yang JH, Chen MJ, Chen CD, Chen CL, Ho HN, Yang YS. Impact of submucous myoma on the severity of anemia. Fertil Steril 2011;95(5):1769-72. e1.

22. Whynott RM, Vaught KCC, Segars JH. The effect of uterine fibroids on infertility: a systematic review. Semin Reprod Med 2017 Nov;35(6):523-32.

23. Zepiridis LI, Grimbizis GF, Tarlatzis BC. Infertility and uterine fibroids. Best Pract Res Clin Obstet Gynaecol 2016;34:66-73.

24. Parazzini F, Tozzi L, Bianchi S. Pregnancy outcome and uterine fibroids. Best Pract Res Clin Obstet Gynaecol 2016 Jul;34:74-84.

25. Okolo S. Incidence, aetiology and epidemiology of uterine fibroids. Best Pract Res Clin Obstet Gynaecol 2008;22(4):571-88.

26. Wise LA, Laughlin-Tommaso SK. Epidemiology of uterine fibroids–from menarche to menopause. Clin Obstet Gynecol 2016;59(1):2.

27. Uimari O, Auvinen J, Jokelainen J, Puukka K, Ruokonen A, Järvelin M-R, et al. Uterine fibroids and cardiovascular risk. Hum Reprod 2016;31(12):2689-703.

28. Orekoya O, Kuye-Kuku T, Fabamwo A, Akinola O, Ayanbode O. Comparative plasma levels of angiotensin II in women with or without uterine fibroid in Lagos state university teaching hospital, Ikeja, Lagos, Nigeria. J Gynecol Res Rev Rep doi:org/1047363/JGRRR/2022 (4) 2022;149:11-3.

29. Ziogas A, Papadopoulou A, Kalantzi S, Lamari I, Poulopoulou D, Liasidi P, et al. 321 the correlation between uterine fibroids and hypertension: a bilateral approach. Europ J Obstetr Gynecol Reprod Biol 2022;270:e92.

30. Staessen JA, Wang J, Bianchi G, Birkenhäger WH. Essential hypertension. Lancet 2003;361(9369):1629-41.