

Evaluation of cardiovascular disease risk and renal function in women with uterine fibroids

R. Alice¹, P. Shanmugasundaram^{2*}

ABSTRACT

Objective: Recent studies have found a positive association of uterine fibroids with hypertension. However, other cardiovascular disease (CVD) risk factors and renal function have not been evaluated. Accordingly, we aimed to investigate the CVD risk factors and renal function in women with uterine fibroids. **Materials and Methods:** A total of 77 reproductive-aged women (18–60 years) were enrolled in the study and were divided into case group ($n = 37$) women with uterine fibroids and control group ($n = 40$) without fibroids. The following clinical and demographic parameters such as age, body mass index (BMI), hypertension, diabetes mellitus, hyperlipidemia, and further renal function markers (urea and creatinine) were recorded at baseline and 3-month follow-up period and compared between the groups. **Results:** Comparison of CVD risk factors between women with and without uterine fibroids revealed that the presence of hypertension (29 [78%] vs. 8 [20%], $P = 0.003$), diabetes mellitus (5 [13.5%] vs. 1 [2.5%], $P = 0.04$), and hyperlipidemia (4 [10.8%] vs. 2 [5%], $P = 0.03$) was significantly higher in patients with uterine fibroids than in the control group. **Conclusion:** Uterine fibroids were associated with a significant elevated risk of hypertension, diabetes mellitus, and hyperlipidemia.

KEY WORDS: Cardiovascular disease risk, Hypertension, Renal function, Uterine fibroids

INTRODUCTION

Uterine fibroids (also known as myomas or leiomyomata) are the most common benign tumor that arises in the smooth muscle of the uterus and affect women reproductive age.^[1] Uterine fibroids contribute to impaired fertility, pregnancy complication, and other adverse obstetric outcomes.^[1,2] They are found to be clinically apparent in 25% of the reproductive age women, with an incidence of 70% by the age of 50 years. However, the true incidence and prevalence of uterine fibroids are unknown.^[1,3,4]

However, cardiovascular disease (CVD) remains the number one cause of approximately 30% of all female deaths, wherein hypertension remains the main risk factor for CVD.^[5-8] Several reports indicate that uterine fibroids remain the common female-specific risk factor for hypertension compared to other female

risk factors such as polycystic ovary syndrome, contraceptive use, and pre-eclampsia.^[7,9]

Other CVD risk factors such as diabetes mellitus and lipid disorders are also associated with uterine fibroids.^[4,7,10] Uterine fibroids also can cause obstructive renal impairment with mechanical obstruction/compression of the pelvic uterus.^[11]

In the present study, patient-specific CVD risk assessment score (Framingham risk score) was investigated to assess the metabolic risk for future cardiovascular events in both the groups.

MATERIALS AND METHODS

This prospective study was conducted on reproductive-aged women (18–60 years), who were admitted in employee state corporation multispecialty hospital between November 2018 and May 2019. The study was approved by local Institutional Review Ethics Committee and informed consent was obtained from all the participants. During the study period, a total

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of 77 women were included in the study and were divided into two groups, as the case group ($n = 37$) composed of women who were diagnosed with uterine fibroids by ultrasonography and the control group ($n = 40$) without uterine fibroids, who come for routine gynecological checkups. Any patients with a history of hypertension, diabetes mellitus, hyperlipidemia, other CVDs, known case of renal and hepatic failure, polycystic ovarian syndrome, malignancy, pregnant and lactating women, and systemic illness that restricts the participation were excluded from the study.

The following clinical and demographic parameters such as age, body mass index (BMI), hypertension, diabetes mellitus, hyperlipidemia, and further renal function markers (urea and creatinine) were recorded and compared between the groups. BMI of each patient was calculated by dividing the body weight by the squared height (kg/m^2). Hypertension was defined as systolic blood pressure ≥ 140 mmHg and diastolic blood pressure ≥ 90 mmHg. Blood samples were collected for total cholesterol level, high-density lipoprotein, glycated hemoglobin (HbA1c), blood urea nitrogen (BUN), and serum creatinine levels. Baseline characteristics and follow-ups were recorded and compared between groups.

Outcome

The primary outcome of the study is to determine the major CVD risk factors (hypertension, obesity, diabetes mellitus, and hyperlipidemia). As a secondary outcome, we assessed the renal function BUN and serum creatinine.

Statistical Assessment

Results are expressed as mean \pm SD and in percentages. The difference between the two groups was tested for significance by independent sample *t*-tests. Differences were considered statistically significant at $P < 0.05$. The statistical analyses were performed by GraphPad Prism version 8 and SPSS software.

RESULTS

The study included 77 patients with a mean age of 40.32 ± 6.74 years in the case group and 39.71 ± 8.54 years in the control group ($P = 0.7214$). The BMI was calculated 24.76 ± 2.73 in the case group and 22.53 ± 4.005 in the control group ($P < 0.006$). Comparison of cardiovascular risk factors between two groups revealed the presence of hypertension (29 [78%] vs. 8 [20%], $P = 0.003$), diabetes mellitus (5 [13.5%] vs. 1 [2.5%], $P = 0.04$), hyperlipidemia (4 [10.8%] vs. 2 [5%], $P = 0.03$), and CVD risk was significantly higher in patients with uterine fibroids than in the control group.

DISCUSSION

Uterine fibroids most common female reproductive tract tumors being unicellular greatly affect reproductive

health and well-being. The pathophysiology and epidemiology are poorly understood.^[5] The main finding of our study is that cardiovascular risk factors such as [Figures 1 and 2] hypertension, [Figure 3] diabetes mellitus, and [Figure 4] hyperlipidemia have positive association with uterine fibroids [Table 1].

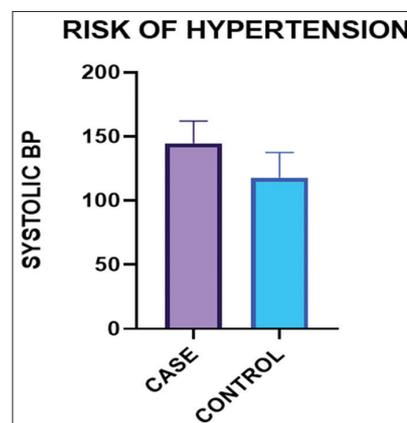


Figure 1: Comparison of systolic blood pressure between the case and control group

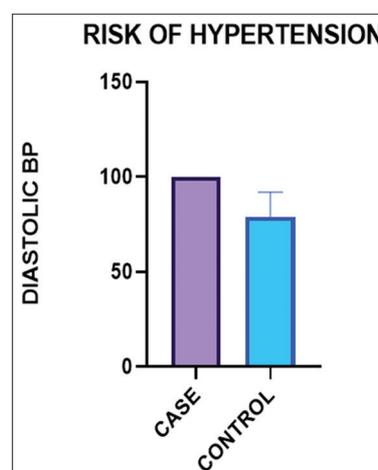


Figure 2: Comparison of diastolic blood pressure between the case group and control group

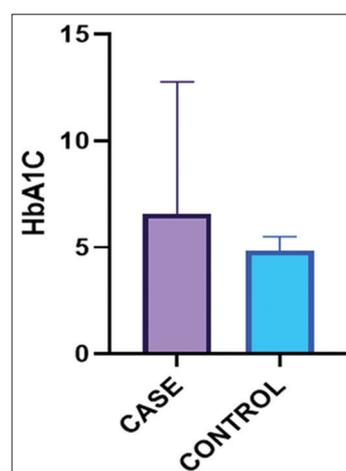


Figure 3: Comparison of diabetes mellitus between the case group and control group

Table 1: Mean reduction in hypertension, diabetes mellitus and hyperlipidemia compared to baseline

Variables	Uterine fibroids	No fibroids	P-value
	(n=37)	(n=40)	
Systolic BP (mmHg)			
Baseline	119.74±11.35	118.07±0.87	<0.0001
3 months	144.72±17.27	117.87±19.70	<0.0001
Diastolic BP (mmHg)			
Baseline	79.23±6.23	78.09±5.51	<0.065
3 months	92.43±12.67	79±12.91	<0.0001
Diabetes mellitus			
HbA1c (%)			
Baseline	5.05±0.67	5.42±0.56	0.094
3 months	6.55±6.20	4.84±0.65	0.0559
Hyperlipidemia			
Serum cholesterol (mg/dl)			
Baseline	186.55±19.66	160.52±23.22	0.0042
3 months	186.21±33.61	163.87±31.9	0.0038

Table 2: Mean reduction in renal profile compared to baseline

Variables	Uterine fibroids	No fibroids	P-value
	(n=37)	(n=40)	
Renal function			
BUN			
Baseline	18.43±1.82	18.24±2.01	0.072
3 months	19.72±1.95	18.87±2.04	0.064
Serum creatinine			
Baseline	0.68±0.89	0.7±0.19	0.092
3months	0.88±0.23	0.79±0.23	0.08

Table 3: Mean reduction in Framingham risk score compared to baseline

Framingham risk score	Uterine fibroids	No fibroids	P-value
	(n=37)	(n=40)	
Baseline	7.34±2.80	6.17±1.98	<0.004
3 months	8.48±2.28	6.35±2.01	<0.001

The association of uterine fibroids with hypertension is that large tumors can cause urinary tract obstruction and may cause hypertension. Another explanation includes the circulating renin–angiotensin (AT) system can play a role in fibrosis and in the pathogenesis of hypertension.^[10,12] AT II receptors found in various tissues including the uterine myometrium and vascular smooth muscle cells are influenced by estrogen and progesterone and show proliferative action and hypertrophy of uterus by inducing some proto-oncogenes and autocrine growth factors.^[10] The AT II-mediated effects through AT receptors may cause vasoconstriction, endothelial dysfunction and are associated with progressive fibrosis. In addition to hypertension, we also found the association of diabetes mellitus in uterine fibroids.^[10,13] However, hyperinsulinemia can cause uterine fibroids by means of myometrial smooth muscle proliferation or by increasing circulating ovarian hormones. Hyperinsulinemia and insulin resistance have been a possible mechanism in connecting the

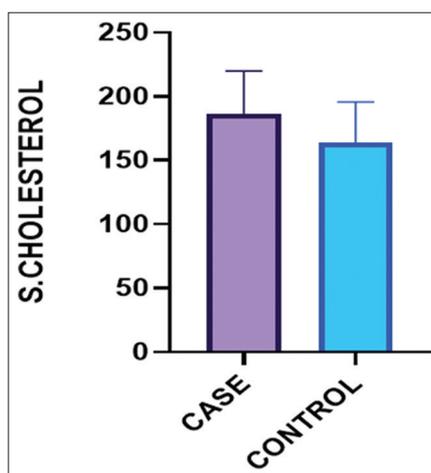


Figure 4: Comparison of hyperlipidemia between the case and control group

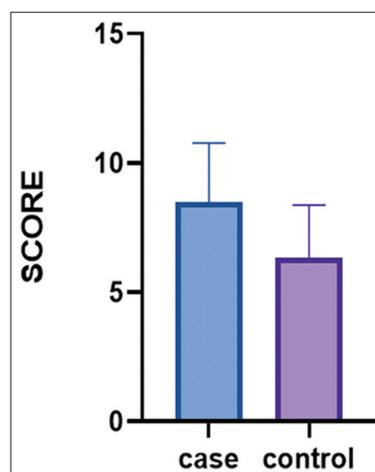


Figure 5: Comparison of Framingham risk score between the case group and control group

pathophysiologic pathways of obesity, diabetes mellitus, and hyperlipidemia.^[10,12-15]

Uterine fibroids also can cause obstructive renal impairment with mechanical obstruction/compression

of the pelvic uterus.^[11,15] No statistically significant association has been observed between uterine fibroids and renal impairment in this study [Table 2]. Framingham risk score showed higher metabolic risk in women with uterine fibroids [Table 3 and Figure 5].

CONCLUSION

The results of the study showed that major cardiovascular risk factors, namely, hypertension, diabetes mellitus, and hyperlipidemia are significantly and independently associated with uterine fibroids. Therefore, further studies should be done in wider participation to confirm these findings.

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