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Original Article

Biochemistry Section

Serum Lipid Profile in Uterine Fibroids Patients Attending a Tertiary Healthcare: A Cross-sectional Study

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ABSTRACT

Introduction: Uterine leiomyoma, also called uterine fibroids, is the most common benign tumour of the female genital tract. Symptomatic uterine fibroids cause significant morbidity and are the most common indication for hysterectomy. Steroid hormones such as oestrogen and progesterone are considered to be the most important links in the pathophysiology of uterine fibroids. Simultaneously, oestrogen affects several aspects of lipid metabolism. Therefore, there might be a possible association between dyslipidaemia and uterine fibroids.

Aim: To determine and compare the serum lipid profile in women with and without uterine fibroids.

Materials and Methods: The present cross-sectional study was conducted in the Department of Biochemistry in collaboration with the Department of Obstetrics and Gynaecology at the Regional Institute of Medical Sciences (RIMS), Imphal, Manipur, India, from January 2021 to October 2022. Fifty women with uterine fibroids (cases) and 50 women without uterine fibroids (controls), who fulfilled the inclusion and exclusion criteria, were conveniently recruited. Their blood samples were taken and analysed for serum lipid profile. The data were analysed using Statistical Package for the Social Sciences (SPSS) version 21.0. For continuous variables, an independent t-test was used, while for categorical variables, the Chi-square test was employed to compare cases and controls. Pearson's correlation was used to find the correlation between the variables. A p-value of <0.05 was considered statistically significant.

Results: The mean age of the cases was 44 years, while that of the controls was 42 years. However, no statistical significance was observed (p-value >0.05) among the groups for age. The mean levels of serum total cholesterol (193.06±18.11 mg/dL), triglycerides (179.70±28.45 mg/dL), and Low-Density Lipoprotein Cholesterol (LDL-C) (152.72±17.70 mg/dL) in uterine fibroid cases were significantly higher compared to the controls (176.60±15.17 mg/dL, 160.96±32.89 mg/dL, 132.04±19.97 mg/dL), respectively (p-value <0.001, p-value <0.01, p-value <0.001, respectively). High-Density Lipoprotein Cholesterol (HDL-C) was significantly lower in cases (38.94±6.53 mg/dL) compared to the controls (45.22±7.76 mg/dL) (p-value <0.001).

Conclusion: Dyslipidaemia in women is associated with the risk of uterine fibroids. Hence, early interventions such as dietary lifestyle modifications might help to control dyslipidaemia and prevent uterine fibroids.

Keywords: Dyslipidaemia, High density lipoprotein, Hysterectomy, Leiomyoma

INTRODUCTION

Uterine leiomyoma, also referred to as uterine fibroids, are monoclonal tumours of the smooth muscle cells of the myometrium [1]. The prevalence of uterine fibroids is over 50% in women aged over 45 years, making them the most common benign tumours of the female genital tract [2]. The prevalence rate of uterine fibroids increases with age during the reproductive years and then declines after menopause [3]. According to a study conducted among South Indian women, the prevalence of uterine fibroids was found to be 37.65% [4].

The exact cause of uterine fibroids is still not known. However, several risk factors have been implicated in their development, such as age, premenopausal status, black race, hypertension, obesity and a family history of uterine fibroids [5]. Symptomatic uterine fibroids adversely affect the quality of life of women of reproductive age and impact both physical and mental wellbeing. Menorrhagia, infertility, iron deficiency anaemia and chronic pelvic pain are some of the attributes of fibroids that negatively affect women's quality of life [6]. Given the multifactorial origin of uterine fibroids, there are currently no specific methods of prevention [7]. Uterine fibroids are among the leading reasons for hysterectomy or myomectomy [8]. Medical treatments, on the other hand, are typically used for short-term therapy and there is a lack of evidence regarding the risks and benefits of long-term treatment [9]. Several studies have suggested an association between dyslipidaemia and uterine fibroids [4, 10-12].

Uterine fibroids are oestrogen- and progesterone-sensitive tumours that originate from a single progenitor myocyte [13]. The local uterine tissue concentrations of hormones and hormone receptors, such as estradiol, aromatase, progesterone receptor and oestrogen receptor, differ between uterine fibroids and healthy myometrial tissue [14]. Oestrogen and progesterone play important roles in fibroid growth and maintenance [15], and steroids like cholesterol serve as precursors to other steroid hormones such as oestrogen [3]. Dyslipidaemia is linked to uterine fibroids, as oestrogen, which is known to affect lipid metabolism, is also involved in the development of these oestrogen-dependent tumours [16]. Hyperlipidaemia is also associated with the escape of free radicals from the mitochondrial electron transport chain due to the altered physical properties of cellular membranes [17]. Reactive Oxygen Species (ROS) cause oxidative stress, leading to cellular tissue damage [18]. These ROS also promote cell proliferation, inhibit cell apoptosis and favour extracellular matrix deposition, which represents key events in the development of uterine fibroids [19].

Similar studies have been conducted in Southern India and in neighbouring countries like Bangladesh [4,20]. However, to the best of our knowledge, such studies have not been conducted in the northeastern part of India. Therefore, the objective of this study was to determine and compare serum lipid profile levels in women with and without uterine fibroids.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Biochemistry in collaboration with the Department of Obstetrics and Gynaecology at RIMS, Imphal, Manipur, India. The study was carried out from January 2021 to October 2022. Ethical clearance was obtained from the RIMS Ethical Board, with IEC approval number (A/206/REB-comm (SP/RIMS/2015/678/20/202).

Inclusion criteria: Cases included women aged 18 years or older diagnosed with uterine fibroids within the last six months or more. Controls included apparently healthy women aged 18 years or older.

Exclusion criteria: Pregnant women, lactating mothers, menopausal women and women who were on lipid-lowering medication during the recruitment process or in the six months prior to recruitment were excluded. Additionally, women with diabetes, hypertension, chronic kidney disease, liver disease and malignant conditions were also excluded from the study.

Sample size: Sample size was calculated using the formula $n=\frac{(u+v)^2 s_1^2+s_2^2}{(m_1-m_2)^2}$ as per study conducted by Singh V et al., where

n=sample size, u=2.32 at 99% power, v=2.58 at 99% confidence interval, S1=(standard deviation of Group 1), S2=(standard deviation of Group 2), m1=(mean of Group 1), and m2=(mean of Group 2) [21]. Taking m1=10.81 and S1=6.18 for serum vitamin D levels (mg/dL) among participants with uterine fibroids, and m2=22.91 and S2=16.18 for serum vitamin D levels (mg/dL) among healthy female participants without uterine fibroids, the sample size was determined to be 50.

The study population consisted of 50 diagnosed cases of uterine fibroids who attended the gynaecology OPD or were admitted to the gynaecology ward (cases), and 50 age-matched normal healthy women without uterine fibroids who attended RIMS hospital (controls).

Data collection: Written informed consent was obtained from the participants before the study, and confidentiality was maintained. The particulars of participants, such as age, body weight, height and Body Mass Index (BMI), were recorded using a predesigned proforma.

Method: A 5 mL venous blood sample was drawn into a plain vial and allowed to clot for 20 minutes. The vial was then centrifuged for 10 minutes at 3000 rpm in a centrifuge machine. The serum was immediately stored at -20ºC until analysis. Serum lipid profiles were measured using the RANDOX Rx IMOLA autoanalyser.

Parameters analysed and cut-off values:

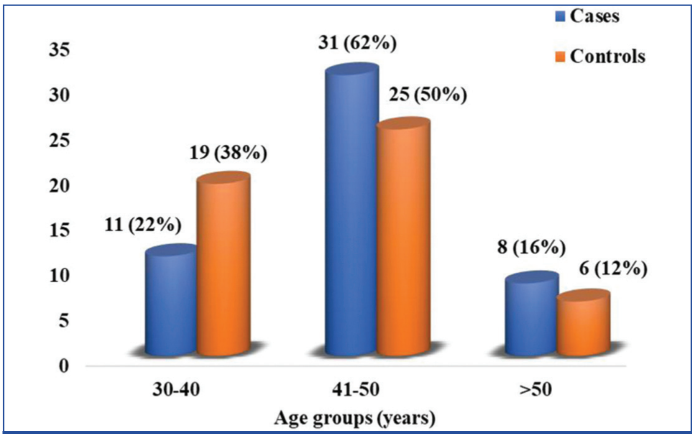
- Cholesterol: desirable (<200 mg/dL), borderline-high (200-239 mg/dL), high (≥240 mg/dL) [22];
- Triglycerides: desirable (<200 mg/dL), borderline-high (200-399 mg/dL), high (≥400 mg/dL) [23];
- LDL: desirable (<130 mg/dL), borderline-high (130-159 mg/dL), high (≥160 mg/dL) [24];
- HDL: prognostically favourable (>65 mg/dL), standard risk level (45-65 mg/dL), risk indicator (<45 mg/dL) [25].

STATISTICAL ANALYSIS

The collected data were analysed using IBM SPSS version 21.0. Continuous variables were reported as mean±SD, and the Independent sample t-test was employed to compare the cases and controls. Categorical variables were reported as numbers and percentages and the Chi-square test was used to compare the cases and controls. A p-value of <0.05 was considered statistically significant.

RESULTS

The results and observations of the study are presented as follows. [Table/Fig-1] shows that almost two-thirds, 31 (62%) of the cases and half of the controls, 25 (50%), were aged between 41 and 50 years, while 8 (16%) of the cases and 6 (12%) of the controls were in the age group of over 50 years.



[Table/Fig-1]: Bar diagram showing distribution of age groups among cases and controls (N=100).

[Table/Fig-2] indicates that the mean±SD age of the cases was 44.78±6.04 years, compared to 42.62±7.05 years for the controls, which was statistically insignificant (p-value=0.061). The BMI of the cases was significantly lower (22.25±2.75) compared to the controls (24.05±2.07), with a p-value of 0.016.

Variable	Cases	Control	p-value*
Age (years)	44.78±6.04	42.62±7.05	0.061
BMI (kg/m²)	22.25±2.75	24.05±2.07	0.016
Duration of disease	≥6 months	Nil	NA
Co-morbidity	Nil	Nil	NA

[Table/Fig-2]: Comparison of the mean age and BMI between the cases and controls. (N=100).
*Independent samples t-test

The mean levels of serum total cholesterol, triglycerides, and LDL were significantly higher in cases compared to controls (p-value <0.01). Conversely, the mean levels of serum HDL were found to be significantly lower in cases than in controls (p-value <0.01) [Table/Fig-3].

Variables	Cases (Mean±SD)	Controls (Mean±SD)	p-value*
Total cholesterol (mg/dL)	193.06±18.11	176.60±15.17	**<0.001**
Triglycerides (TG) (mg/dL)	179.70±28.45	160.96±32.89	**<0.01**
Low Density Lipoprotein-Cholesterol (LDL-C) (mg/dL)	152.72±17.70	132.04±19.97	**<0.001**
High Density Lipoprotein-Cholesterol (HDL-C) (mg/dL)	38.94±6.53	45.22±7.76	**<0.001**

[Table/Fig-3]: Comparison of the mean levels of serum lipid profile between the cases and controls (N=100).
*Independent samples t-test

[Table/Fig-4] shows that a greater number of controls had desirable levels of LDL and triglycerides compared to cases. In terms of cholesterol, more cases fell into the high category than controls.

Variables	Cut-offs (mg/dL)	Cases N (%)	Controls N (%)
Cholesterol-	Desirable (<200)	15 (30)	25 (50)
	Borderline-high (200-239)	20 (40)	15 (30)
	High (≥240)	15 (30)	10 (20)
Triglyceride-	Desirable (<200)	20 (40)	35 (70)
	Borderline-high (200-399)	15 (30)	10 (20)
	High (≥400)	15 (30)	5 (10)
HDL	Prognostically favourable (>65)	15 (30)	30 (60)
	Standard risk level (45-65)	20 (40)	10 (20)
	Risk indicator (<45)	15 (30)	10 (20)

LDL	Desirable (<130)	20 (40)	30 (60)
	Borderline-high (130-159)	15 (30)	10 (20)
	High (≥160)	15 (30)	10 (20)

[Table/Fig-4]: Distribution of lipid profile in cases and controls according to the cut-off values.

Regarding HDL, the majority of cases had standard risk levels, whereas most controls had prognostically favourable levels.

DISCUSSION

In this study, the age of the respondents ranged from 30 to 56 years. It is evident from [Table/Fig-1] that almost two-thirds (62%) of the cases and half of the controls (50%) belonged to the age group of 41 to 50 years, followed by 22% of cases and 38% of controls in the age group of 30 to 40 years, and 16% of cases and 12% of controls in the age group over 50 years. However, no statistical significance was observed (p-value>0.05). These findings were similar to a study conducted by Magda AF et al., who observed that the majority of women with uterine fibroids (i.e., 75%) were in the age group of 41 to 50 years, followed by 25% in the age group of 30 to 40 years [11]. The difference in mean age between the cases and controls was found to be statistically insignificant (p-value=0.061). Therefore, both groups were comparable with respect to age. The occurrence of uterine leiomyomas is common during the reproductive years and regresses after menopause, which could be due to age-related hormonal changes, namely oestrogen and progesterone [20].

The mean levels of serum total cholesterol, triglycerides and LDL were found to be significantly (p-value <0.01) higher in cases (193.06±18.11 mg/dL, 179.70±28.45 mg/dL, and 152.72±17.70 mg/dL, respectively) compared to controls (176.60±15.17 mg/dL, 160.96±32.89 mg/dL, and 132.04±19.97 mg/dL, respectively). The mean serum HDL was found to be significantly (p-value<0.001) higher in controls (45.22±7.76 mg/dL) compared to cases (38.94±6.53 mg/dL). These findings are consistent with a study conducted by Afruza S et al., in which they found that women with uterine fibroids had significantly higher levels of serum total cholesterol, triglycerides and LDL (198.56±34.94 mg/dL vs 165.52±20.08 mg/dL, 173.8±112.13 mg/dL vs 109.22±51.73 mg/dL, and 128.66±32.86 mg/dL vs 101.42±21.12 mg/dL, respectively) and significantly lower levels of serum HDL (39.46±10.51 mg/dL (case) vs 44.92±11.57 mg/dL (control)) when compared with women without uterine fibroids (p-value<0.05) [12]. Since cholesterol is important in the formation of sexually active hormones, Vignini A et al., also found lower levels of HDL-C (45.4±8.3 vs 57.2±13.4 mg/dL; p-value=0.017) and higher levels of LDL-C (92.3±21.5 vs 72.0±14.6 mg/dL; p-value=0.007) [26].

Oestrogen is thought to stimulate the development of uterine fibroids because it triggers physiological responses in target cells after binding to oestrogen receptors. Both oestrogen receptor and oestrogen receptor mRNA expression levels are greater in fibroids than in normal myometrium. The physiology of the myometrium and the development of uterine fibroids are profoundly influenced by oestrogen and its receptor [10].

Limitation(s)

The limitation of the study was that due to the cross-sectional study design, the causal relationship between serum lipid profiles and uterine fibroids could not be determined.

CONCLUSION(S)

The present study suggested that there may be a high prevalence rate of dyslipidaemia among women in the age group of 41 to 50 years, which could be a potential risk factor in the development of uterine fibroids (leiomyoma) and could contribute to an increased risk of cardiovascular disease. Women with uterine fibroids have higher lipid profile markers compared to women without uterine fibroids, with the exception of HDL. Therefore, maintaining desirable serum lipid profile levels may reduce the risk of developing uterine fibroids. Additionally, further research is needed to explore the mechanisms linking dyslipidaemia with uterine fibroid formation, which could lead to targeted prevention strategies. Encouraging early intervention and personalised care plans that address both metabolic and reproductive health may ultimately lower the burden of fibroid-related complications and cardiovascular risks in this population.

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