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# Association between dyslipidemia and uterine fibroid growth: A comparative case-control study

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#### Abstract

**Background:** Uterine fibroids (UFs) are the most prevalent benign gynecologic tumors among reproductive-aged women. Emerging evidence suggests a possible association between dyslipidemia and fibroid pathogenesis.

**Aim:** This study aimed to evaluate lipid profile alterations, atherogenic risk, and their associations with fibroid size, number, and clinical manifestations.

**Methods:** A case-control study was conducted at Tikrit Teaching Hospital between November 2024 and June 2025. Ninety women aged 18-45 years were enrolled and allocated into two groups: 45 patients with ultrasonographically confirmed uterine fibroids and 45 age-matched controls without fibroids. Detailed demographic, reproductive, and clinical data were recorded. Fasting lipid profiles were measured (TC, LDL-C, HDL-C, TG), and the Atherogenic Index of Plasma (AIP) was calculated. Statistical comparisons were made using t-tests and chi-square tests; significance was set at p < 0.05.

**Results:** The fibroid group exhibited significantly higher levels of total cholesterol (198.56 $\pm$ 34.94 vs. 165.52 $\pm$ 20.08 mg/dL; p = 0.001), LDL-C (128.66 $\pm$ 32.86 vs. 101.42 $\pm$ 21.12 mg/dL; p = 0.001), triglycerides (173.80 $\pm$ 112.13 vs. 109.22 $\pm$ 51.73 mg/dL; p = 0.004), and AIP (4.30 $\pm$ 1.41 vs. 2.86 $\pm$ 0.97; p = 0.001), while HDL-C was significantly lower (39.46 $\pm$ 10.51 vs. 44.92 $\pm$ 11.57 mg/dL; p = 0.015). Menorrhagia (57.78% vs. 6.67%), pelvic pain (44.44% vs. 8.89%), and anemia (33.33% vs. 4.44%) were more prevalent among fibroid patients (all p<0.001). Among fibroid cases, elevated lipid levels were significantly associated with clinical symptoms and fibroid characteristics. For instance, raised total cholesterol was significantly associated with menorrhagia (66.67%), pelvic pain (75.00%), and fibroid size  $\geq$ 5 cm (77.78%) (all p<0.05). Larger fibroid size (>5 cm) was significantly linked to high TG (88.89%), low HDL (83.33%), and high LDL (72.22%). Multiple fibroids were associated with higher prevalence of dyslipidemia than single fibroids (raised TC: 72.73% vs. 47.83%; p = 0.034).

**Conclusion:** This study confirms a significant association between uterine fibroids and dyslipidemia, particularly elevated atherogenic index and lipid fractions. Lipid abnormalities were closely linked to fibroid burden (size and multiplicity) and symptom severity. These findings underscore the importance of incorporating lipid screening into the clinical assessment of women with fibroids to identify cardiometabolic risks and strategies support individualized management.

Keywords: Uterine fibroids, dyslipidemia, lipid profile, atherogenic index, fibroid size

### 1. Introduction

In the uterus, uterine fibroids, also known as leiomyoma or myoma, are prevalent benign masses that develop when one or more smooth muscle cells in the myometrium undergo cancerous transformation. Comprised of proteoglycans, fibronectins, and collagen, they are all components of the extracellular matrix (ECM). In the uterus, fibroids may be located in various regions and may vary in size. They are in the corpus the majority of the time [1]. Uterine fibroids, which are also known as leiomyoma or myoma, are common tumors in the uterus that are not harmful. They grow when one or more smooth muscle cells in the myometrium become cancerous. Collagen, fibronectins, and proteoglycans make them up. These are all parts of the extracellular matrix (ECM). There are various fibroid sizes and locations in the uterus [2]. Myomectomy, uterine artery embolization, and endometrial ablation are examples of conservative treatments that are only considered when cancer is no longer a chance. Fibroids in the uterus are hormone-sensitive tumors that began from a single source myocyte. 14 There are different amounts of hormones and hormone receptors in uterine tissue that has uterine fibroids compared to tissue that is healthy. Some of these are progesterone receptor (PR), estrogen receptor- $\alpha$  (ER- $\alpha$ ), and estradiol [3].

Corresponding Author: Marwa Mahdi Lefta Department of Obstetrics & Gynecology, College of Medicine, Tikrit University, Salaheddin, Iraq Estrogen and progesterone are crucial for the development and sustenance of fibroid tumors. Estrogen establishes an environment characterized by elevated estrogen levels, but progesterone assumes a more complex role by modulating various growth factors and anti-apoptotic proteins [4]. Hormones function by directly activating or inhibiting growth factor pathways, including aromatase, growth factors such as basic fibroblast growth factor (bFGF), and hormone receptors including estrogen receptor (ER) and progesterone receptor (PR). They accomplish this by altering the transcription of growth factors and their corresponding receptors. The International Federation of Gynecology and Obstetrics (FIGO) classifies fibroids by quantity and location. The classifications extend from 0 (pedunculated intracavitary) to 8 (other types, including cervical or parasitic) [5].

Lipids are fundamental chemicals present in all living beings. They are insoluble in water but soluble in non-polar solvents, including fats, oils, phospholipids, waxes, and steroids. These molecules are essential for energy storage, insulation, absorption of fat-soluble vitamins, and the formation of cell membranes. Steroids, including cholesterol, are essential for the synthesis of other steroid hormones and for modulating cell membrane fluidity. Lipids are conveyed in the bloodstream by lipoproteins, comprising triglycerides, cholesterol, phospholipids, and apolipoproteins [6,7].

Lipid transport occurs through two pathways: the exogenous pathway, which carries dietary lipids from the small intestine, and the endogenous pathway, which transports lipids synthesized in the liver and other tissues to the bloodstream. Abnormal lipid levels in the blood—referred to as hyperlipoproteinemia or hypolipoproteinemia—are associated with cardiovascular diseases and serve as markers for identifying individuals at risk [8,9].

Dyslipidemia has been associated with uterine fibroids, as estrogen, a crucial regulator of lipid metabolism, promotes the growth of these estrogen-dependent tumors. Lipid-lowering agents, including statins, impede steroidogenesis, thereby diminishing estradiol and progesterone concentrations [10]. Statins are being investigated as potential therapies for uterine fibroids owing to their capacity to impede cellular proliferation and interrupt the cell cycle. Their utilization has been linked to a diminished chance of developing uterine fibroids and accompanying symptoms, indicating a twofold advantage for women with both uterine fibroids and hypercholesterolemia [11, 12].

# 2. Methods

### 2.1 Clinical Evaluation and Data Collection

A structured form for data collection shall be used to source information concerning

- 1. Demographic data: Age, BMI
- **2. Reproductive history data:** Parity, history of contraception, regularity of menstruation

**3. Gynecologic evaluation data:** Clinical symptoms, uterine size, and fibroid characteristics by ultrasound (site and number and size, if applicable).

Ultrasound confirmation of fibroids will be carried out as per standard diagnostic criteria using transabdominal and/or transvaginal imaging by an experienced sonographer or gynecologist.

### 2.2 Biochemical Investigations

All participants will have an overnight fast for at least 8 hours, following which venous blood sampling will be performed. Lipid profile parameters shall be determined by standard enzymatic colorimetric methods for:

- Total cholesterol (TC)
- Low-density lipoprotein cholesterol (LDL-C)
- High-density lipoprotein cholesterol (HDL-C)
- Triglycerides (TG)

The technologists shall carry out all assays in the hospital central laboratory using an automated biochemistry analyzer. The quality control protocol shall be stringently followed to ascertain the reliability of test results.

### 2.3 Atherogenic Index Calculation

Calculation of the Atherogenic Index of Plasma (AIP) will be done individually for each study subject by using the given formula:

$$A the rogenic \ Index = \log_{10} \left( \frac{TG \ (mg/dl)}{HDL\text{-}C \ (mg/dl)} \right)$$

Since the AIP is a novel surrogate marker for cardiovascular risk, it has gained recognition in gynecological and metabolic research. An elevated AIP would mean a higher chance of pro-atherogenic dyslipidemia that could share its pathophysiological basis with fibroid formation

## 2.4 Statistical Analysis

The data will be entered into SPSS (Statistical Package for Social Science), version 26. Continuous variables (such as TC, HDL-C, LDL-C, TG, and AIP) will be given as mean $\pm$ standard deviation (Mean  $\pm$  SD) and compared between groups using the Student's t-test for independent samples. In addition, categorical variables will be given as frequencies and percentages and compared using the Chisquare test. The p-value for the assessment of statistical significance will be taken as <0.05.

#### 3. Results

# 3.1 General characteristics of study participants

Age-related means and BMI were slightly higher in the fibroid group but were statistically nonsignificant. The irregularities in the menstrual function were more common among cases (35.56%) than in controls (17.78%), yielding a significant p-value of 0.037. Table 3.1

**Table 1:** General characteristics of study participants

Variable	Fibroid group $(n = 45)$	Control group (n = 45)	p-value
Age (years)	34.2±5.8	33.6±6.1	0.521
BMI (kg/m²)	27.1±3.5	26.3±3.2	0.231
Parity (median)	2 (1-4)	2 (0-3)	0.408
Menstrual Regularity (irregular%)	16 (35.56%)	8 (17.78%)	0.037

#### 3.2 Clinical characteristics of study participants

Symptoms related to fibroids were significantly more common among women with fibroids than among the controls: menorrhagia (57.78%), pelvic pain (44.44%), and anemia (33.33%) (All p<0.001). Table 3.2

**Table 2:** Clinical characteristics of study participants

Clinical Characteristic	Fibroid group $(n = 45)$	Control group (n = 45)	p-value
Fibroid Size ≥5 cm	18 (40.00%)	0 (0.00%)	< 0.001
Multiple Fibroids	22 (48.89%)	0 (0.00%)	< 0.001
Menorrhagia	26 (57.78%)	3 (6.67%)	< 0.001
Pelvic Pain	20 (44.44%)	4 (8.89%)	< 0.001
Anemia (Hb <12 g/dL)	15 (33.33%)	2 (4.44%)	< 0.001

# 3.3 Atherogenic index comparison between the studied groups

The study showed that the mean atherogenic index was significantly higher in women with uterine fibroids

(4.30±1.41) compared to those without fibroids (2.86±0.97), with a P-value of 0.001. This suggests a greater atherogenic risk among fibroid patients. Table 3

Table 3: Atherogenic index comparison between the studied groups

Variable	Group	Mean	SD	SD P-value	
Atherogenic Index	With Fibroid	4.30	1.41	0.001	
Atherogenic Index	Without Fibroid	2.86	0.97		

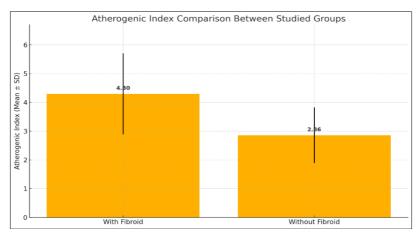


Fig 1: Atherogenic index comparison between the studied groups

# 3.4 Atherogenic index comparison between the studied groups

The study showed that total cholesterol was higher in fibroid women (198.56 $\pm$ 34.94 mg/dL) than in those who were not (165.52 $\pm$ 20.08 mg/dL), owing to a very highly significant P-value of 0.001. HDL-C, the protective fraction, was significantly lower in fibroid women (39.46 $\pm$ 10.51 mg/dL) than in the control group (44.92 $\pm$ 11.57 mg/dL), (P = 0.015).

LDL-C levels, on the contrary, were much higher in fibroid women (128.66 $\pm$ 32.86 mg/dL) compared to women not having fibroids (101.42 $\pm$ 21.12 mg/dL), with again a very strong association at P = 0.001. Triglycerides were also higher than those of the controls in fibroid women (173.80 $\pm$ 112.13 mg/dL) (109.22 $\pm$ 51.73 mg/dL) at P = 0.004. Table 4

Table 4: Lipid profile comparison between women with and without uterine fibroids

Lipid Parameter	Group	Mean (mg/dL)	SD	P-value
Total Cholesterol	With Fibroid	198.56	34.94	0.001
Total Cholesterol	Without Fibroid	165.52	20.08	0.001
HDL-C	With Fibroid	39.46	10.51	0.015
HDL-C	Without Fibroid	44.92	11.57	0.015
I DI G	With Fibroid	128.66	32.86	0.001
LDL-C	Without Fibroid	101.42	21.12	0.001
Trighyaaridas	With Fibroid	173.80	112.13	0.004
Triglycerides	Without Fibroid	109.22	51.73	0.004

# 3.5 Association between clinical Features and lipid profile among fibroid group

Table 3.5 shows a significant association between some of the clinical features of lipid profile abnormalities in women with uterine fibroids. Menorrhagia was significantly higher among those with raised cholesterol (66.67%), triglycerides (81.48%), low HDL (71.43%), and LDL (65.38%), all with p-values less than 0.05. Likewise, pelvic pain was significantly associated with raised cholesterol (75.00%), triglycerides (85.00%), low HDL (80.00%), and high LDL

(70.00%). Similarly, fibroid size  $\geq 5$  cm was significantly associated with atherogenic lipid disturbances, raised cholesterol (77.78%), triglycerides (88.89%), low HDL

(83.33%), and high LDL (72.22%), all with p-values less than 0.05.

**Table 5:** Association between clinical Features and lipid profile among fibroid group

CP-1-1 F-4	Cholesterol		
Clinical Feature	Raised (>200 mg/dL)	Normal(≤200 mg/dL)	p-value
Menorrhagia	18 (66.67%)	9 (33.33%)	0.032
Pelvic Pain	15 (75.00%)	5 (25.00%)	0.018
Fibroid Size ≥5 cm	14 (77.78%)	4 (22.22%)	0.009
	Trigly	yceride	
	Raised (≥150 mg/dL)	Normal (<150 mg/dL)	
Menorrhagia	22 (81.48%)	5 (18.52%)	0.007
Pelvic Pain	17 (85.00%)	3 (15.00%)	0.004
Fibroid Size ≥5 cm	16 (88.89%)	2 (11.11%)	0.002
	HDL		
	Low (<40 mg/dL)	Normal (≥40 mg/dL)	
Menorrhagia	20 (71.43%)	8 (28.57%)	0.014
Pelvic Pain	16 (80.00%)	4 (20.00%)	0.005
Fibroid Size ≥5 cm	15 (83.33%)	3 (16.67%)	0.003
	L	DL	
	Raised (≥130 mg/dL)	Normal (<130 mg/dL)	
Menorrhagia	17 (65.38%)	9 (34.62%)	0.026
Pelvic Pain	14 (70.00%)	6 (30.00%)	0.031
Fibroid Size ≥5 cm	13 (72.22%)	5 (27.78%)	0.012

# 3.6 Association between fibroid Size and lipid abnormalities among fibroid group

Fibroid size and the prevalence of lipid abnormalities among women with fibroids maintain an unmistakable and statistically significant association, which Table 4.6 clearly presents. As the size of the fibroids increases, the percentage of dyslipidemic patients also increases substantially. There were 77.78% with high cholesterol, 88.89% with raised

triglycerides, 83.33% with low HDL levels, and 72.22% with raised LDL levels in patients with fibroids above 5 cm of size. In comparison, these lipid abnormalities were less frequent with smaller fibroids (<3 cm). The intermediate group (3-5 cm) recorded moderate elevations. The p-value (ranging from 0.001 to 0.004) further affirms that these are statistically significant associations.

Table 6: Association between fibroid Size and lipid abnormalities among fibroid group

	Fibroid Size Category	Raised Cholesterol n (%)	Raised TG n (%)	Low HDL n (%)	High LDL n (%)	p-value
	<3 cm	5 (27.78%)	6 (33.33%)	7 (38.89%)	6 (33.33%)	0.002
ĺ	3-5 cm	8 (44.44%)	10 (55.56%)	11 (61.11%)	10 (55.56%)	0.004
ĺ	>5 cm	14 (77.78%)	16 (88.89%)	15 (83.33%)	13 (72.22%)	0.001

# 3.7 Association between multiple fibroids and lipid abnormalities among fibroid group

According to Table 3.7, a statistically significant association was found between lipid abnormalities and the presence of multiple fibroids in the study population. Women bearing multiple fibroids were more likely to have dyslipidemia than those with a single fibroid. Raised total cholesterol was

found in 72.73% of women with multiple fibroids as compared to 47.83% with a single fibroid (p = 0.034). In parallel, multiple fibroids were linked to raised triglycerides (77.27% vs. 56.52%, p = 0.041), lower HDL (81.82% vs. 52.17%, p = 0.029), and increased LDL (77.27% vs. 47.83%, p = 0.037) more commonly.

Table 7: Association between multiple fibroids and lipid abnormalities among fibroid group

Lipid Abnormality Multiple Fibroids (n = 22)		Single Fibroid (n = 23)	p-value
Raised TC	16 (72.73%)	11 (47.83%)	0.034
Raised TG	17 (77.27%)	13 (56.52%)	0.041
Low HDL	18 (81.82%)	12 (52.17%)	0.029
High LDL	17 (77.27%)	11 (47.83%)	0.037

#### 4. Discussion

This case-control study was conducted to investigate the associations between uterine fibroids and lipid abnormalities among women aged 18-45 years. During the study, it became evident that women suffering from uterine fibroids showed significant changes in their lipid profile when compared with age-matched controls and that these abnormalities were correlated with certain clinical features,

including fibroid size, fibroid number, and degree of symptom severity.

Our analysis showed no significant differences in age, BMI, or parity between the two study groups, which suggests that associations observed between these factors and fibroid presence were absent. However, irregular menstruation was significantly more common in the fibroid group (35.56%) vs. controls (17.78%) and concurs with earlier reports

linking fibroids with menstrual disorders due to impaired endometrial functions and vascularity [13].

Lipid analysis demonstrated significantly increased levels of total cholesterol, LDL-C, and triglycerides, yet significantly decreased HDL-C in women being diagnosed with fibroids. Furthermore, the atherogenic index, an independent cardiovascular risk marker, was notably higher in the fibroid group (4.30 vs. 2.86; p = 0.001), supporting the notion that lipid dysregulation may contribute to the development or progression of uterine fibroids. In the same way, Shahzadi Afruza *et al.* [14] reported lipid abnormalities in fibroid patients, supporting the importance of dyslipidemia in uterine smooth muscle proliferation.

Additional evidence comes from Turkey and Rubayae (2023), who observed a significant link between high cholesterol and fibroid size, noting that large fibroids (>5 cm) were more common in women with raised LDL and triglyceride levels. This follows the same pattern as our results, where women with fibroids  $\geq$ 5 cm demonstrated significantly greater frequencies of dyslipidemia in all lipid parameters. Along similar lines, Duan *et al.* indicated a probable mechanistic link between lipid metabolism and the formation of uterine fibroids via inflammatory mediators and oxidative stress pathways [15].

Association between clinical parameters and lipid parameters opens a new dimension in fibroid risk stratification. It was observed that symptomatic women, i.e., those with menorrhagia or pelvic pain, were more likely to have an abnormal or deranged lipid profile. For instance, out of all patients with menorrhagia, 81.48% had raised triglycerides, and 71.43% had low HDL-C. This reflects a probable relationship between the metabolic environment and the symptomatic burden of fibroids. Several studies brought molecular perspectives to this by identifying lipid-regulating genes with altered expression in fibroid tissues, placing a genetically inclined predisposition [16].

Another finding was that women with multiple fibroids showed more lipid abnormalities than patients with single fibroids, thereby reinforcing the hypothesis that a more disturbed lipid environment may favor multicentric fibroid growth, with more raised cholesterol, low HDL, and raised LDL in the population affected by multiple fibroids. We further noted a strong positive correlation between the atherogenic index and serum triglycerides, LDL-C, and total cholesterol, while HDL-C was negatively correlated. This pattern corresponds to studies that found the atherogenic index a very sensitive indicator for both cardiovascular and gynecological disorders, including fibroids Contradictory results have been reported as well. For instance, the 2012 Baghdad study suggested a lower atherogenic risk profile for women with fibroids, showing lower LDL-C and raised HDL-C [18]. These differences could be explained in terms of local dietary habits, varied sample sizes, or some untreated confounders such as physical activity levels and hormonal therapy use. Lin et al. and Parazzini et al. also found no significant link between lipid levels and fibroid risk [19]. Such inconsistencies warrant large-scale longitudinal cohort studies controlling for lifestyle and components of metabolic syndrome. Of recent interest is the association of uterine fibroids with cardiovascular disease risk. A nationwide population-based cohort from South Korea revealed that women with fibroids were at increased risk of myocardial infarction and stroke due to what seems to be common pathway mechanisms such

as dyslipidemia, estrogen dominance, and vascular remodeling <sup>[20]</sup>. This fact, again, helps support the view of fibroids not being mere localized uterine growths but systemic manifestations of metabolic imbalance.

### 5. Conclusion

- A strong association was observed in the study between uterine fibroids and dyslipidemia, whereby women with fibroids showed significantly higher levels of total cholesterol, LDL-C, triglycerides, and atherogenic index.
- HDL-C levels were significantly lower in the fibroid group, further giving credence to the atherogenic dyslipidemia pattern.
- From a clinical perspective, symptoms such as menorrhagia, pelvic pain, and anemia prevailed more in women with fibroids and were correlated with abnormal lipid profiles.
- Larger fibroid size and presence of multiple fibroids were both significantly correlated with more profound lipid disturbances, thereby indicative of a dose-response relationship.
- The link between irregular menstruation and uterine fibroids points to a possible hormonal-metabolic connection in the pathogenesis of fibroids.
- These findings lend support to the hypothesis that metabolic factors, especially lipid abnormalities, might have an effect on the development, growth, or symptom-evaluating severity of uterine fibroids.

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