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Original Research Article

Possible association between lipid profile and uterine fibroid size

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ABSTRACT

Background: Uterine fibroid is the most common benign tumor in reproductive age group, arising from single smooth muscle cell of the uterus. Steroid hormones, estrogen, and progesterone are considered to be the most important links in the pathophysiology of uterine fibroid; meanwhile estrogens influence several aspects of lipid metabolism; so it's possible to theorize a relationship between uterine fibroid size and dyslipidemia. Aim of the study was to evaluate possible association of lipid profile with uterine fibroid size.
Methods: This was a cross sectional study performed in Babylon Teaching Hospital for Maternity and Pediatrics during the period from 1st of March 2020- 1st of December 2020. This study included one hundred women diagnosed with uterine fibroid using abdominal and/or transvaginal ultrasound, fifty patients with large uterine fibroids ≥5cm^3, and fifty patients with small uterine fibroid<5cm^3. Serum lipid profile was measured in both groups in fasting state for comparison.
Results: The most common complaint was abnormal uterine bleeding in both groups. body mass index were 20-29.9; and significant difference between group1 that showed a lower levels of high-density lipoprotein 40.82±9.4, higher levels of low-density lipoprotein 94.79±35.07 and total serum cholesterol 155.7±43.63 and group 2 that showed higher level of high density lipoprotein 50.7±6.55, lower level of low density lipoprotein 51.49±15.2 and total cholesterol 123.2±14.18 with p value <0.001.while non-significant difference between the two groups in term of very low density lipoprotein with p value 0.878 and triglyceride with p value 0.879.
Conclusions: Dyslipidemia in the form of low high density lipoprotein, high low density lipoprotein and high cholesterol was significantly associated with increased size of uterine fibroid.

Keywords: Association, Lipid profile, Size, Uterine fibroid

INTRODUCTION

Uterine fibroids, also known as leiomyoma or myoma, are common benign uterine tumors that arise from the neoplastic transformation of single smooth muscle cells in the myometrium.[1] They are composed of extracellular matrix (ECM) containing collagen, fibronectins, and proteoglycans.[2] Fibroids vary in size and location, and are most commonly found in the corpus of the uterus.[3] The incidence of fibroids increases with age and is influenced by various risk factors, such as age, race, obesity, diet and exercise, caffeine and alcohol intake, menarche, genetic factors, parity, and hormone replacement therapy.[4-10] Environmental factors, such as smoking, also play a role in fibroid development, with smoking decreasing the risk.[11] Conservative treatments, including myomectomy, uterine artery embolization, and endometrial ablation, are considered only after malignancy has been excluded.[12,13] uterine fibroids are estrogen and progesterone-sensitive tumors derived from a single progenitor myocyte.[14] Local uterine tissue concentrations of hormones and hormone receptors, such as estradiol, aromatase, progesterone receptor (PR), and estrogen receptor-α (ER-α), differ between uterine fibroids and healthy myometrial tissue.[15]

Estrogen and progesterone play crucial roles in fibroid growth and maintenance, with estrogen creating a hyper-estrogenic environment and progesterone having a more complex role involving upregulation and downregulation of various growth factors and anti-apoptotic proteins.[16,6] Hormones mediate their effects through transcriptional activation or suppression of growth factors and their receptors, as well as through direct activation or suppression of growth factor pathways, such as aromatase, growth factors like basic fibroblast growth factor (bFGF), and hormone receptors like ER and PR.[4] Fibroids are classified numerically based on their location, with categories ranging from 0 (pedunculated intracavitary) to 8 (other, e.g., cervical, parasitic) according to the International Federation of Gynecology and Obstetrics (FIGO) system.[17] Lipids, insoluble in water but soluble in non-polar organic solvents, are present in all living organisms and include fats and oils, phospholipids, waxes, and steroids.[1] They play essential roles in energy storage, insulation, absorption of fat-soluble vitamins, and as components of cell membranes.[1]

Steroids like cholesterol act as precursors to other steroid hormones and influence cell membrane fluidity.[1] Lipoproteins, consisting of triglycerides, cholesterol, phospholipids, and apolipoproteins, transport lipids in plasma.[1] Lipid transport occurs through two routes: the exogenous path, involving the transport of dietary lipids from the small intestine, and the endogenous system, where lipids travel from the liver and non-intestinal tissues into circulation.[1] Abnormal levels of lipids in the blood, termed hyperlipoproteinemia and hypolipoproteinemia, are associated with cardiovascular diseases and serve as risk indicators.[18] Dyslipidemia is linked to uterine fibroids, as estrogens, which are known to influence lipid metabolism, are also implicated in the development of these estrogen-dependent tumors.[19] Lipid-lowering agents, such as statins, inhibit steroidogenesis, leading to decreased estradiol and progesterone levels, and are considered potential treatments for uterine fibroids.[19] Statins inhibit cell proliferation and cell cycle progression, and studies have shown that their use is associated with a reduced risk of uterine fibroids and related symptoms.[20,21] This suggests that statins could have a dual benefit for women with both uterine fibroids and hyperlipidemia.[23] We aimed to evaluate the possible association between uterine fibroid size and lipid profile.

METHODS

A study was conducted as a cross- sectional study in the Department of Obstetrics and Gynecology in Babylon Maternity and Pediatric Teaching Hospital, during the period from 1st of March 2020 to 1st of December 2020.after approval by Iraqi Board of Medical Specializations and after confirmed verbal consent from all studied women. The study included 100 pre-menopausal, non-pregnant women aged 20-45 years, all of whom had ultrasound-confirmed uterine fibroids and experienced fibroid-related symptoms such as heavy menstrual bleeding, dysmenorrhea, abdominal distention, and other symptoms. Abdominal and/or endo-vaginal ultrasound was performed to assess fibroid details, including number, size, and location. Based on uterine fibroid size, patients were divided into two groups: 50 with small-sized fibroids (<5 cm³) and 50 with large fibroids (≥5 cm³).

Exclusion criteria

Exclusion criteria for the study were as follows pregnancy, endometriosis, adenomyosis, active neoplastic disease or history of malignancy, use of medications for fibroids, such as hormonal or non-hormonal therapy, medical conditions such as ischemic heart disease, hypertension, diabetes mellitus, or thyroid disease, women undergoing hormonal therapy, or those with a family history of hyperlipidemia, treatment with lipid-lowering agents at the time of the study.

Patient selection began with obtaining detailed history, including demographic criteria (age, marital status, parity, occupation, and residence), patient complaints such as menstrual disturbance, pelvic pain, infertility, or asymptomatic, gynecological history such as age of menarche, menstrual cycle details, contraception use, subfertility, obstetrical history such as gestations, parities, abortions, live or dead babies, past medical history to exclude other causes of heavy menstrual bleeding or other conditions, past surgical history, drug history including hormone replacement, contraception, or anti-lipid drugs, smoking and herbal use

Physical examination included height measured with a wall-mounted stadiometer, weight measured with a portable digital scale, BMI calculated and categorized, abdominal examination for masses or distention, pelvic examination to assess for enlarged uterus or mass.

Patients underwent abdominal or transvaginal sonography at Babylon maternity and pediatric teaching hospital to measure and record uterine fibroid size, number, and anatomical subtypes. Fibroid sizes were classified as large if they measured ≥5cm³.

Blood samples were collected after overnight fasting to measure lipid profiles. Samples were processed and stored at -20°C until analysis. Total serum cholesterol, HDL-C, LDL-C, and triglycerides were calculated using the Friedewald formula. Statistical analysis was performed using SPSS version 26. Continuous data were expressed as means±SD, while categorical variables were presented as absolute numbers and percentages. The Kolmogorov-Smirnov test determined data normality distribution. Continuous variables were analyzed using Independent Samples T Test or Mann-Whitney U Test, and categorical variables with Pearson's chi-squared test. A p-value of less than 0.05 was considered significant.

RESULTS

Table 1 showed the demographic features of the subjects and that was: the mean age of the women was (35.38±7.04) range (22-45), BMI mean±SD 26.18±2.96 range 20-29, and fibroid size (cm^3) mean±SD 5.78±4.6 range 2-62.

Table 2 showed the women with large UFs aged 20-29 were 24%, aged 30-39 were 30%, aged 40-49 were 52% and women with small UFs aged 20-29 were 36%, aged 30-39 were 30% and women aged 40-49 were 34% The p value 0.181 which was statistically non-significant.

Table 1: Demographic criteria groups (n = 100).

Parameters	Total patients mean±SD	Range
Age/years	35.38±7.04	22-45
BMI (kg/m^2)	26.18±2.96	20-29
Fibroid size (cm)	5.78±4.6	2-62

Table 2: Comparison of demographic criteria in women with small and large UFs.

Parameters		Large fibroid size group 1, N (%)	Small fibroid size group 2, N (%)	*P value
Age/years	20-29	12 (24)	18 (36)	0.181
	30-39	12 (24)	15 (30)	
	40-49	26 (52)	17 (34)	
BMI (kg/m^2)	Normal (18.5-24.9)	10 (20)	18 (36)	0.075
	Overweight (25-29.9)	40 (80)	32 (64)	
Parity	para 0	5 (10)	3 (6)	0.001
	para 1-3	29 (58)	13 (26)	
	para 4 and more	16 (32)	34 (68)	
Total no.		50	50	

*Pearson's chi-squared test

Regarding the BMI, women that had large UFs with normal weight 20%, over weight were 80% and that had small UFs with normal weight 36% and overweight were 46% with p value 0.075 which was statistically non-significant as in Figure 1. Regarding parity group 1 there were 5 women (10%) nulliparous, and 16 women (28%) were multiparous, and group 2 there were 3 women (6%) nulliparous and 34 women (68 %) were multiparous the difference statistically significant using Pearson's chi-squared test with p value <0.001 as shown in Figure 2.

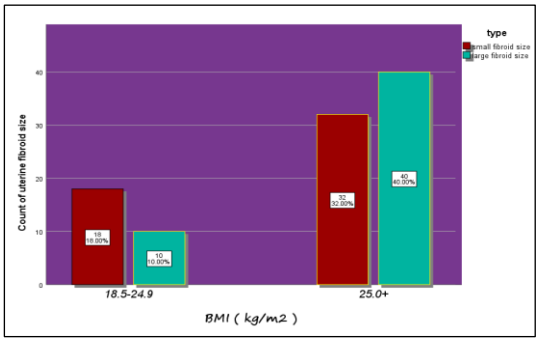

Figure 2: Comparison between women with small UF and large UF according to body mass index.

Table 3 showed comparison of lipid profile between two groups. The mean total HDL-C was 40.82±9.4mg/dl in group 1 and 50.7±6.55mg/dl in group 2 using independent samples T test p value <0.001 which was statistically significant. Total cholesterol (TC) was 155.7±43.63mg/dl in group 1 and 123.2±14.18mg/dl in group 2 the difference were statistically significant p value <0.001, mean total LDL-C was 94.79±35.07 mg/dl in group 1 and 51.49±15.2 mg/dl in group 2. The difference were statistically significant p value <0.001 between two groups using Mann-Whitney U Test. The mean total TG was 100.5±55.4 mg/dl in group 1 and 105±58.66 mg/dl in group 2. The difference statistically non-significant p value 0.879, the mean VLDL 20.1±11 (mg/dl) in group 1 and 21±11.73 mg/dl in group 2. The difference were statistically non-significant p value 0.878 between two groups as shown in Figure 3.

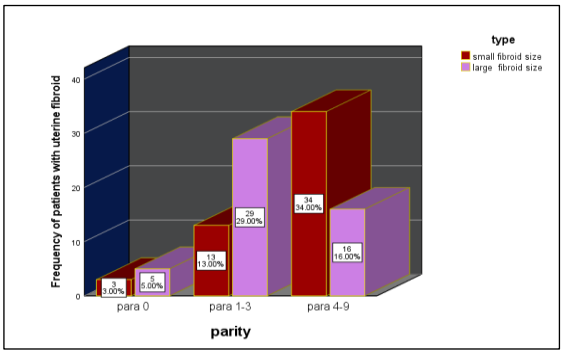

Figure 3: Comparison of parity in women with small and large uterine fibroid.

Table 3: Comparison of lipid profile in women with large uterine fibroid (≥ 5 cm^3) and small uterine fibroid (< 5 cm^3).

Parameters	Large fibroid size group 1 (n = 50) mean±SD	Small fibroid size group 2 (n = 50) mean±SD	*P* value
LDL (mg/dl)	94.79±35.07	51.49±15.2	< 0.001*
HDL (mg/dl)	40.82±9.4	50.7±6.55	< 0.001**
TG (mg/dl)	100.5±55.4	105±58.66	0.879*
Cholesterol (mg/dl)	155.7±43.63	123.2±14.18	< 0.001*
VLDL (mg/dl)	20.1±11	21±11.73	0.878*
***Mann-Whitney U Test**			
**Independent Samples T Test			

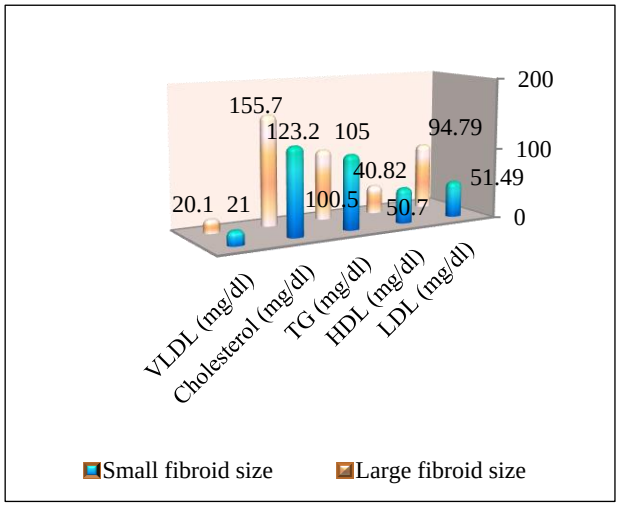

Figure 4: Lipid profile according UFs size.

DISCUSSION

Uterine fibroids are the most common benign neoplasm affecting women in reproductive age, which can cause significant morbidity and may adversely impact fertility. In present study we compare the women with large uterine fibroids ≥5cm^3 and women with small uterine fibroids <5cm^3 as taken by Shavell et al 2012, and Ciavattini et al 2014, to find the potential association between the lipid profile (HDL, LDL, VLDL, TG, total cholesterol) and size of UFs.[23,24] In present study, we took women with large and small UFs matched for age and weight in order to avoid possible bias caused by the effect of these variables on lipid profile. In our study the larger uterine fibroid correlate positively with null-parity up to para three and smaller size with multi-parity and this agree with Sarkodie et al 2016; but inconsistent with Sharami et al 2019, this explained by the effect of the gestation or labor on the uterus.[25-27] In this study, it was observed that total cholesterol positively correlates with UFs size and this consistent with Sharami et al 2019; Afruza et al 2020.[28,29] Since cholesterol is crucial in the creation of sexually active hormones. Oestrogens are thought to stimulate the development of UFs because they trigger physiological responses in their target cells after binding to ER- and E receptor-(ER-). Both ER- and ER- protein and mRNA expression levels are greater in fibroids than in normal myometrium. Myometrial physiology and the development of uterine fibroids are profoundly influenced by oestrogens and their receptors, but this inconsistent with Vignini et al 2017.[28,30] Regarding the HDL-C we found a negative relationship between the size of UFs and HDL-C level, this was consistent with Vignini et al 2017 and Afruza et al 2020, in contrast although Sersam et al (2012) and Sadlonova et al (2008) found higher HDL-C levels, these findings may have been the product of a limited sample size or an inadequately adjusted research group.[29,30,28,31] Consistent with the findings of Afruza et al (2020) and Sharami et al (2019), we identified a positive correlation between LDL-C and the size of uterine fibroids in our investigation; Akinlua et al 2013 Vignini et al (2017) and Parazian et al (2004) initially found a significant relationship between LDL-C levels and UFs, the latter two studies were retrospective studies that drew their data from medical records and subject interviews, and the former study did not include any information on HDL-C or LDL-C.[26,29,32,33] However, only high-density lipoprotein (HDL-C) was correlated adversely with UFs in a multivariate analysis.[30] In our study, the triglyceride and VLDL had no significant correlation with fibroids size and this was consistent with Vignini et al 2017 and Swarnaltha et al 2012 but inconsistent with Afruza et al 2020 and Kong et al 2014 that reported all the patients in their research reached operational criteria, which indicated that the amount of fibroid tissue was significant enough or had produced substantial symptoms, suggesting a possible association between triglycerides and the beginning of uterine leiomyoma.[30,34,28]

CONCLUSION

Serum low-density lipoprotein (LDL) and total cholesterol levels were significantly higher in patients with larger UF s. The blood HDL level was significantly correlated with size.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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