Study of Lipid Profile in Patients with Uterine Fibroid

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ABSTRACT:

BACKGROUND:

Leiomyomas are the most common gynaecological neoplasms. Despite the major public health impact of leiomyomas, little is known about their cause. As fibroids are hormone-dependent tumours and their development can be promoted by estrogens, an inverse association between hypercholesterolemia and fibroids should be observed as well as direct association between high-density lipoprotein cholesterol (HDL-C) levels and the presence of fibroids.

OBJECTIVE:

To investigate the lipid profile in patients with uterine fibroids and to compare it with the lipid profile of women without fibroids.

METHODS:

A case-control study was conducted in the Department of Obstetrics and Gynaecology at Al-Yarmouk Teaching Hospital during the period from May 2008 to May 2009. Participants were one-hundred twenty pre-menopausal women aged between 18 and 45 years who were recruited during their visit to the gynaecological outpatient clinic and were not taking hormonal therapy. Cases consisted of 60 women with uterine fibroids, and controls were 60 women visiting the same gynaecological outpatient clinic for routine reasons. Thorough history and examination was done for each participant. Body Mass Index (BMI) was measured in kg/m^2. All patients underwent a baseline ultrasound examination and classified into two groups according to the presence or absence of uterine fibroids. All women where scheduled to undergo blood test at the beginning (2^{nd} -5^{th} day) of their next menstrual cycle. Fasting venous blood glucose and lipid profile were determined in blood samples taken for each patient. Atherogenic index was also calculated.

RESULTS:

Women with uterine fibroids were found to have significantly higher levels of serum HDL-C compared to the controls (P=0.0001). A significantly lower levels of total serum cholesterol, low-density lipoprotein cholesterol (LDL-C) were also found in women with uterine fibroids compared to the controls (P=0.0001). Atherogenic index was significantly lower in fibroid group compared with controls (P=0.0001). There was a significant positive correlation between largest fibroid volume and HDL-C level (P<0.0001).

CONCLUSION:

Women with uterine fibroid have lower atherogenic index compared to women without uterine fibroid. Larger volume of fibroid is associated with higher level of HDL-C.

***KEYWORDS*:** Lipid profile, uterine fibroid.

INTRODUCTION:

Uterine fibroids are the most common benign tumours arising from the myometrium of the uterus, also called leiomyomatas [(1)]. They are apparent clinically in up to 25 percent of women [(2)]. They are frequent indication for gynaecological surgery, most commonly hysterectomy [(3)], and are considered a major public health concern [(4)]. There are suggestions in the literature of a similarity between smooth muscle cell tumours (ie, fibroids) and atherosclerotic plaque [(5-7)]. Both conditions are of monoclonal origin [(8)]. Faerstein *et al*. [(6)] reported no association between fibroids and a history of diabetes, however, they quoted a non significant 2-fold adjusted excess risk for diabetes requiring medication. An association between uterine fibroids and hypertension has also been reported. Luoto *et al*. [(9)] found a statistically significant association between fibroids and hypertension, and Faerstein *et al*. [(6)] found an increased risk for fibroids in patients with hypertension compared with normotensive controls. It has been established

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that uterine leiomyomas development is absolutely dependent on steroid hormones and that sensitivity / responsiveness to estrogen is enhanced in tumours and tumour-derived cell lines [10]. Further more, fibroids have higher estrogen concentrations, bind more estrogen, have more estrogen receptors and convert estradiol (a more active form of estrogen) to estrone (a less active form of estrogen) more slowly than normal myometrium [10]. Several authors have demonstrated that leiomyomas over-express aromatase P450, an estrogen synthetase, which catalyses androgens to estrogens, and that *in situ* estrogen synthesized in leiomyoma may play a role in the promotion of leiomyoma growth in an autocrine/paracrine mechanism [11-13]. It has been reported that estrogen levels are inversely related to cholesterol levels [14]. As fibroids are estrogen-related tumours, an inverse association between hyperlipidemia and the risk for fibroids should be observed. Sadlonova *et al.* [4] found that women with fibroids had significantly higher levels of serum HDL-C compared with control patients. The latter study also reported a negative association between some parameters of metabolic syndrome and fibroid volume [4].

The aim of the present study was to investigate the lipid profile in patients with uterine fibroids and to analyze the possible associations between dyslipidemia with uterine fibroids.

PATIENTS AND METHODS:

A Case-control study was conducted on 120 women who were attending the Gynaecological outpatient clinic in the Department of Obstetrics and Gynaecology at Al-Yarmouk Teaching Hospital, Baghdad, Iraq – during the period from May 2008 till May 2009. The study was approved by hospital's ethics committee, and all the women involved gave their informed consent to participate. The participants consisted of 60 women with uterine fibroids in the case group, and 60 women without fibroids in the control group. Exclusion criteria were women who were postmenopausal, pregnant, less than 18 years old, and patients with a diagnosis of hypertension, diabetes mellitus or thyroid disease, women undergoing hormonal therapy or having family history of hyperlipidemia were also excluded from the study. Anthropometric examinations were performed and body mass index was calculated (BMI, the weight in kilograms divided by height in meters squared). All participants underwent a baseline ultrasound examination using the ultrasound device "Siemens real-time scanning system" of 3.5 MHz frequency and were assigned to either the case or control group based on the results. Fibroids were defined as hypoechogenic solid masses on ultrasound examination. The volume of the uterus and each identified fibroid was calculated using the formula for a prolate ellipsoid ($D1 \times D2 \times D3 \times 0.5233$ cm^3, where D1, D2, and D3 are the largest dimensions in perpendicular planes). Participants were scheduled to undergo blood tests at the beginning (2^{nd} to 5^{th} day) of their next menstrual cycle. During this visit 5cc of venous blood were collected by venipuncture after an overnight fasting for the measurement of fasting glucose and lipid profile which included: total serum cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG). Blood samples were put in a plane tube without anticoagulant, the serum was prepared after centrifugation for 10 minutes and analyzed. Total serum cholesterol and serum triglyceride concentrations were measured by enzymatic method with commercially available kit (Bio-Merieux, France). Total serum cholesterol and total serum triglycerides were measured spectrophotometrically at 500nm. High-density lipoprotein cholesterol was measured by enzymatic method with commercially available kit (Bio-Merieux, France), the principle of this method is to precipitate the chylomicrons and lipoprotein of very low-density (VLDL-C) and low-density lipoprotein (LDL-C) by the addition of phosphotengstic acid in the presence of magnesium ion. High-density lipoprotein cholesterol was determined spectrophotometrically at 500nm. Atherogenic index was calculated by using the following equation: (total cholesterol – HDL-C/HDL-C).

Statistical analysis:

Data were analyzed using the computer facility with the available statistical package of SPSS-15 (Statistical Package for Social Science-version 15.0) software package. Data were presented in simple measure of number, percentage, mean, standard deviation and range. Significance of difference between two quantitative variables was measured using independent t-test. P value ≤ 0.05 was considered as the level of significance.

RESULTS:

Table 1 shows the characteristics of the study groups. The mean age of the patients with uterine fibroid was (33.22±5.59) years (range 25-43 years) compared to the mean age of women without uterine fibroid which was (34.25±5.16) years (range 25-43 years) which was statistically not significant. The mean weight of patients with

uterine fibroid was (76.30±8.05) kg (range 59-90 kg) compared to the control group where the mean weight was (74.10±7.28) kg (range 65-90 kg) which was statistically not significant. The mean BMI in patients with uterine fibroid was (30.13±2.93) kg/m^2 (range 22-35 kg/m^2) compared to the mean BMI in women without uterine fibroid which was (29.47±2.37) kg/m^2 (range 26-35 kg/m^2) which was statistically not significant. Table 2 shows the distribution of age, BMI and parity of the study groups which where matched to each other to avoid possible effects of these variables on the level of lipid profile. Table 3 shows the lipid profile in the study groups. The mean serum cholesterol level in patients with uterine fibroid was (4.54±0.48) mmol/l compared to the control group where mean serum cholesterol level was (5.51±0.74) mmol/l which was statistically significant (*P*=0.0001). The mean HDL-C level in the fibroid group was (2.09±0.26) mmol/l compared to the control group level (1.38±0.14) mmol/l which was statistically significant. The mean LDL-C level was lower in the fibroid group compared to the control group which was statistically significant (*P*=0.0001). Atherogenic index was lower in the fibroid group compared to the control group which was statistically significant (*P*=0.0001). Figure 1 shows the correlation between the largest fibroid volume and HDL-C level.

Table 1: Characteristics of the study groups

	Fibroid	Control	P value
	Mean±SD (Min-Max)	Mean±SD (Min-Max)	
Age (years)	33.22±5.59 (25.00-43.00)	34.25±5.16 (25.00-43.00)	0.295
Weight (Kg)	76.30±8.05 (59.00-90.00)	74.10±7.28 (65.00-90.00)	0.119
Height (meter)	1.57±0.06 (1.50-1.67)	1.57±0.05 (1.50-1.67)	0.667
BMI (Kg/m2)	30.13±2.93 (22.00-35.00)	29.47±2.37 (26.00-35.00)	0.173
Fasting blood sugar (mmol/l)	4.48±0.75 (3.50-6.10)	4.39±0.68 (3.40-6.00)	0.502

*Significant difference using t-test for two independent means at 0.05 level of significance

Table 2: Distribution of age, BMI and parity in the study groups

		Fibroid		Control		
		No	%	No	%	P value
Age	19-29 years	11	18	1	1.7	
30-39		40	67	52	86.7	0.19
40-49		9	15	7	11.7	
BMI	Normal (18.5-24.9)	2	3.3	1	1.7	
	Overweight (25-29.9)	24	40.0	31	51.7	0.537
	Obese (30-34.9)	30	50.0	26	43.3	
	Morbid obesity (>35)	4	6.7	2	3.3	
Parity	Para 0	9	15.0	8	13.3	
	Para 1	15	25.0	8	13.3	
	Para 2	13	21.7	16	26.7	1.174
	Para 3	15	25.0	11	18.3	
	Para 4 & more	8	13.3	17	28.3	

*Significant difference using t-test for two independent means at 0.05 level of significance

Table 3: Lipid profile in the study groups

	Fibroid	Control	P value
	Mean±SD (Min-Max)	Mean±SD (Min-Max)	
Cholesterol (mmol/l)	4.54±0.48 (3.80-5.50)	5.51±0.74 (4.30-6.50)	0.0001*
HDL-C (mmol/l)	2.09±0.26 (1.70-2.50)	1.38±0.14 (1.10-1.70)	0.0001*
LDL-C (mmol/l)	2.61±0.53 (1.90-3.70)	3.29±0.76 (2.00-4.50)	0.0001*
TG (mmol/l)	1.14±0.46 (0.40-1.90)	1.06±0.49 (0.30-1.90)	0.338
Atherogenic index	1.216±0.508 (0.520-2.200)	3.023±0.815 (1.600-4.700)	0.0001*

*Significant difference using t-test for two independent means at 0.05 level of significance

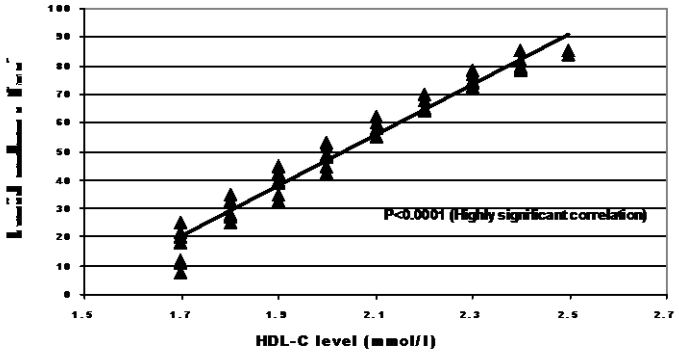

Figure 1: The correlation between largest fibroid volume and HDL-C level in patients included in the study.

This scatter diagram shows strong direct significant correlation between largest fibroid volume (cc^3) and HDL-C level (mmol/l).

DISCUSSION:

Uterine leiomyomas are the most common gynaecological tumours and are a significant health concern for many women. Although the exact etiology of these tumours is unknown, epidemiological and experimental evidence has established an essential role for ovarian hormones in the pathogenesis of this disease [15]. Uterine leiomyomas develop during the reproductive years and regress after menopause, indicating ovarian steroid-dependent growth potential [16]. Our study was designed to investigate the lipid profile of patients with uterine fibroids and to compare it with the lipid profile of women without uterine fibroids. In the present study both groups were comparable in their age, parity and BMI in order to avoid possible bias caused by the effect of these variables on lipid profile.

There have been few studies published that investigated the lipid profile of patients with uterine fibroid. Parazzini *et al.* [17] did not observe an association between hyperlipidemia and fibroids. In a study conducted in the United States in 1982, no relation between serum cholesterol levels and the presence of uterine fibroids was observed [5]. Both studies derived their data from medical records and subject interviews, moreover, neither study contained information on HDL-C, LDL-C or the atherogenic index.

Our results are somewhat different from the cited studies: women with uterine fibroids reported hypercholesterolemia significantly less often than women without fibroids. In the present study, measurement of total serum cholesterol was significantly lower in patients with fibroids compared with controls (4.54±0.48 vs. 5.51±0.74; *P*=0.0001). This was somewhat different from the findings reported by Sadlonova *et al.* [4] who have found no significant difference in measurement of total serum cholesterol between women with fibroids and their control group, although lower levels of total serum cholesterol were reported in women with fibroids. In our study women with

uterine fibroids had significantly lower LDL-C levels than comparative control patients (2.61±0.53 vs. 3.29±0.76; *P*=0.0001), while Sadlonova *et al*. [4] reported that LDL-C was not significantly increased in women without fibroids of all ages, but was significantly increased in the subgroup of women without fibroids aged 30-45 years. In relation to HDL-C, the results of our study confirmed a significantly higher levels of serum HDL-C in women with fibroids compared with controls (2.090.26 vs. 1.38±0.14; *P*=0.0001). This comes in agreement with findings reported by Sadlonova *et al*. [4] in 2008. Regarding total serum triglycerides, a non-significant difference was reported in our study between the two groups. This observation is consistent with same findings, elsewhere [4].

In this study atherogenic index was significantly lower in fibroid group compared with controls (1.216±0.508 vs. 3.023±0.815; *P*=0.0001). This finding corresponds to the estrogenic effects on lipid profile. Our results partially agree with those observed by Sadlonova *et al*. [4] in 2008 who reported a lower atherogenic index in women with uterine fibroids, although the association was not significant.

Interestingly, our study revealed an important relation between serum levels of HDL-C and largest fibroid volume with strong direct significant correlation between largest fibroid volume and HDL-C level. This finding was somewhat similar to Sadlonova *et al*. [4] who reported that in the subgroup aged 30-45 years, patients with higher levels of HDL-C tended to have larger fibroids.

In the present study, all these findings (more favourable lipid profile in fibroid group, lower atherogenic index and the strong direct positive correlation between volume of the largest fibroid and serum HDL-C level) correspond to the estrogen theory in myomatosis.

CONCLUSION:

In patients with uterine fibroids lipid profile differs from that in women without uterine fibroids. Women with uterine fibroid have lower atherogenic index compared to women without uterine fibroid. Larger volume of fibroid is associated with higher level of HDL-C.

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