

A comparative study of premenopausal women with fibroids and Lipid profile

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Abstract

Background: Uterine fibroids are common benign tumors of uterus. There is sharing in patterns between uterine fibroids and atherosclerosis development. Aim: To study the relationship between lipid profile and uterine fibroids among premenopausal women. Patients & methods: A cross sectional study conducted in Gynecological Outpatients Clinic at Erbil Maternity Teaching Hospital-Governmental region of Iraq through the period from 1st of April, 2015 to end of March, 2016 on convenient sample of 60 women with fibroids 60 control women free of fibroids. Lipid profile of both groups was checked in hospital laboratory. Results: Mean age of women with fibroids was 38.3 ± 5.4 years. A highly significant association was observed between women with fibroids and higher level of high density lipoprotein cholesterol ($p < 0.001$). No significant differences were observed between fibroids women and controls regarding serum cholesterol, serum triglycerides and serum low density lipoprotein cholesterol levels. Conclusions: This study found a protective effect of fibroids for women regarding lipids risk.

Keywords: Fibroid, High density lipoprotein, Premenopausal.

Introduction

Uterine fibroids (derived from Latin fibra) are common benign tumors of human uterus smooth muscle and it is the main indication of hysterectomy 1. It is clinically obvious among 30–70% of women in reproductive age and in Iraq, it was estimated as 17.7% 2. Women have uterine fibroid are diagnosed by different methods and clinically asymptomatic in at least 50% of cases while in symptomatic women characterized with heavy menses, pelvic pain and sometimes with infertility and bad obstetric outcome 3.

The pathogenesis of uterine fibroids is not well clear. Some authors documented multiple risk factors as an etiology of fibroids like; reproductive age, black race, low fertility, obesity, hypertension, diabetes mellitus and genetics 4, 5. It was shown that uterine fibroids are hormone dependent disease 6.

In premenopausal women, the estrogen is uniquely related to uterine fibroid growth 7. The mechanism of action for estrogen and its receptor can accelerate the growth of uterine fibroid 8. The estrogens have been reported to protect against cardiovascular disease. Previous studies stated that estrogen

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replacement therapy play an important role in the prevention of ischemic heart disease in women 9. Many large prospective studies as the Women's Health Initiative (WHI) and the Heart and Estrogen/Progestin Replacement study (HERS) revealed that estrogen is not preventive for cardiovascular diseases 10, 11. These studies showed an improvement in lipid profile 10. Other authors suggested strong relationship between sex hormone and antioxidant system which had cardiac protective effect but disrupted at menopause 12. Estrogens regulated serum lipids, inflammatory markers and the coagulant factors. They had a direct vasodilatory effect by α and β receptors in the vessel wall 13. During menopause, estrogens alter plasma levels of low density lipoproteins (LDL) and high density lipoproteins (HDL). They modify the plasma LDL:HDL ratio which had a cardiovascular preventive effect, however, recent evidence indicates that these play a minor role 14.

The uterine fibroids and metabolic syndrome might be shared in pathogenesis with proved relevance regarding hypertension and diabetes¹⁴ with unclear effect of lipids. For that, this work was aimed to study the

relationship between lipid profile and uterine fibroids among premenopausal women.

Patients & Methods

The study design is cross sectional study conducted in Gynecological Outpatients Clinic at Erbil Maternity Teaching Hospital -Governmental region of Iraq through the period from 1st of April, 2015 to end of March, 2016. All women presented to Gynecological clinic with uterine fibroids were study population. Inclusion criteria were premenopausal age (18-45 years) diagnosed with uterine fibroids. Exclusion criteria were menopause, pregnancy, women on hormonal therapy, history of cardiovascular diseases, hyperlipidemia, hypertension and diabetes mellitus. A convenient sample of 60 women with fibroids was included as a case group and convenient sample of 60 healthy women free of fibroids was selected as control group from women relatives to patients presented to the clinic. Informed oral consent was taken from women of both groups before inclusion in the study and this study was approved by Scientific Committee of

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Medical College/Hawler Medical University.

The data were collected by the researcher through direct interview and filling of prepared questionnaire. After taking full history and gynecological examination, the women were examined by pelvic ultrasonography done by Specialist in Radiology in the hospital. Fibroids diagnosis was confirmed by Specialist in Gynecology in the outpatient clinic. The questionnaire included the followings: Sociodemographic characteristics, weight & height, blood group, gynecological & obstetrical history, ultrasound finding and lipid profile results as total cholesterol, triglycerides, HDL and LDL.

The weight and height were measured by the researcher using Seca scale weighing and tape. BMI was categorized as normal if BMI (kg/m²) was <25, overweight if BMI was 25–29.9, and obese if BMI was ≥30. All studied women were referred to laboratory of Erbil Maternity Teaching Hospital for checking their lipid profile. Five ml of venous blood was taken from each woman after overnight fasting during 2-5 days of menstrual cycle. After centrifuge, serum concentrations of total cholesterol and

triglycerides were determined by enzymatic methods (Biomeiurex, France). The serum concentration of high density lipoprotein cholesterol (HDL-c) was also determined after precipitation of low density lipoprotein cholesterol (LDL-c) with phosphotungstate and magnesium.

All patients' data entered using computerized statistical software; Statistical Package for Social Sciences (SPSS) version 20 was used. Descriptive statistics presented as means, frequencies and percentages. Kolmogorov Smirnov analysis verified the normality of the data set. Multiple contingency tables conducted and appropriate statistical tests performed, Chi-square used for categorical variables and Independent-sample t-test was used to compare between two means. In all statistical analysis, level of significance (p value) set at ≤ 0.05. Statistical analysis of the study was done by Community Medicine Specialist

Results

As shown in Table 1, no significant differences were found between fibroid women and healthy control women regarding sociodemographic

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characteristics and BMI except the educational level as women with fibroids were significantly had low educational level. In same way, there was highly significant association between women with fibroids and housewife employment ($p < 0.001$).

As shown in Table 2, no significant difference was detected between women with fibroids and control women ($p = 0.4$). Irregular menstrual history was significantly reported among women with fibroids ($p = 0.04$). There was a highly significant association between fibroids women and heavy menses ($p < 0.001$).

As shown in Table 3 and Figure 1, menses duration mean was significantly higher among women with fibroids ($p < 0.001$). There was a significant association between fibroids women and younger age at menarche ($p = 0.002$). A highly significant association was observed between women with fibroids and higher HDL level ($p < 0.001$). No significant differences were observed between fibroids women and controls regarding parity, serum cholesterol,

serum triglycerides and serum LDL levels.

Discussion

Uterine fibroid is the most gynecological neoplasm. Limited research attention was appointed to relationship between lipid profile and uterine fibroids in younger women 15. Premenopausal women were found to have low risk of atherosclerosis development as compared to age-matched males, however, this effect diminished after menopause 16.

Present study showed significantly higher HDL level among women with fibroids in comparison to control women ($p < 0.001$). This finding is consistent with results of Sersam and Hmaili study in Iraq 17 which stated that women with uterine fibroid have lower atherogenic index and higher HDL level compared to women without uterine fibroid. Leiomyomas are dependent on ovarian hormones especially estrogens. They have a preventive effect on lipid profile; they decrease LDL level and increase HDL level 18. Estrogens mechanism of action on HDL cholesterol is by lowering hepatic triglycerides lipase

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activity that catabolizes HDL 13. HDL is good cholesterol and an independent risk factor of coronary heart diseases. Despite this effect, combination hormone therapy had no effect in reducing coronary heart diseases events among premenopausal women¹⁹. This is confirmed by He et al 1 which reported that uterine fibroids might have an increased risk of subclinical atherosclerosis although they found that HDL was inversely related to fibroids among premenopausal women.

Current study found no significant difference in LDL between women with fibroids and women without fibroids. This finding is consistent with Kong et al 15 study in China. However, this finding is inconsistent with results of Sadlonova et al 20 study in Czech that reported significant decrease in LDL of women with fibroids. This inconsistency might be due to differences in sample size and study design. Previous studies proved a negative correlation between LDL and estrogen level related the activity of LDL receptors in liver. Estrogen had a potential role in catabolism of LDL in liver 21. Total serum cholesterol and

triglycerides levels in this study were not significantly different between two groups of studied women. This is similar to results of Swarnalatha and Ebrahim study in India 9.

Our study showed that women with fibroids were significantly associated lower educational level and housewife employment. These findings coincide with results of previous Chinese study 22. Younger age at menarche in present study was significantly risk factor for women with fibroids ($p=0.002$). Many authors had shown that early age at menarche as a common risk factor for the development of uterine fibroids 23, 24. This relationship might be attributed to a multiple factors such as high estrogen level, genetic, environmental and lifestyle factors. Present study revealed that women with fibroids had significantly more irregular menstrual history ($p=0.04$), heavier menses ($p<0.001$) and longer menses duration ($p<0.001$) than healthy women. These findings are similar to results of Mahmood and Ali study in Iraq 2. The explanation of these symptoms is due to ovarian

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hormones disturbances mostly the estrogens.

References

1. He Y, Zeng Q, Li X, Liu B, Wang P. The Association between Subclinical Atherosclerosis and Uterine Fibroids. Biondi-Zoccai G, ed. PLoS ONE 2013; 8(2):e57089.
2. Mahmood MK, Ali ZMA. The relationship between the presence of uterine fibroid and symptoms in women 20-40 years old. Karbala J Med 2014; 7 (1): 1793-1796.
3. Okolo S. Incidence, aetiology and epidemiology of uterine fibroids. Best Practice & Research in Clinical Obstetrics & Gynaecology 2008; 22: 571–588.
4. Catherino WH, Eltoukhi HM, Al-Hendy A. Racial and ethnic differences in the pathogenesis and clinical manifestations of uterine leiomyoma. Semin Reprod Med 2013; 31: 370-379.
5. Evans P, Brunzell S. Uterine fibroid tumors: Diagnosis and treatment. Am Fam Physician 2007; 75: 1503-1508.
6. Walker CL, Stewart EA. Uterine fibroids: the elephant in the room. Science 2005; 308: 1589–1592.
7. Islam MS, Protic O, Stortoni P, Grechi G, Lamanna P, Petraglia F, et al. Complex networks of multiple factors in the pathogenesis of uterine leiomyoma. Fertility and Sterility 2013; 100: 178-193.
8. Laughlin SK, Schroeder JC, Baird DD. Semin Reprod Med. New Directions in the Epidemiology of Uterine Fibroids 2010; 28: 204-217.
9. Swarnalatha PK, Ebrahim NKC. A correlative study of estrogen and lipid profile in premenopausal and postmenopausal women. International Journal of Biochemical and Advanced Research 2012; 3 (11): 818-822.
10. Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML, et al. Risks and benefits of

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- estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. *JAMA* 2002; 288:321–333.
11. Shlipak MG, Chaput LA, Vittinghoff E, Lin F, Bittner V, Knopp RH, et al. Lipid changes on hormone therapy and coronary heart disease events in the Heart and Estrogen/progestin Replacement Study (HERS). *Am Heart J* 2003; 146:870 –875.
 12. Pejić S, Todorović A, Stojilković V, Gavrilović L, Popović N, Pajović SB. Antioxidant status in women with uterine leiomyoma: relation with sex hormones. *An Acad Bras Cienc* 2015; 87(3):1771-1782.
 13. Auda FM. A Biochemical Study to Evaluate Lipid Profiles and Sex Hormone In Sera of Females Patients Suffering CHD. *Journal of Kufa for Chemical Science* 2013; 8: 22-34.
 14. Takeda T, Sakata M, Isobe A, Miyake A, Nishimoto F, et al. Relationship between metabolic syndrome and uterine leiomyomas: a case-control study. *Gynecologic & Obstetric Investigation* 2008; 66: 14–17.
 15. Kong S, Hou J, Xia M, Yang Y, Xu A, Tang Q. Association of Hyperglycemia, Hyperlipemia with the Risk of Uterine. *Cancer Cell Research* 2014: 37-41. Available on: <http://www.cancerellresearch.org/>
 16. Perrella J, Berco M, Cecutti A, Gerulath A, Bhavnani BR. Potential role of the interaction between equine estrogens, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) in the prevention of coronary heart and neurodegenerative diseases in postmenopausal women. *Lipids in Health and Disease* 2003; 2:4.
 17. Sersam LW, Hmaili SA. Study of Lipid Profile in Patients with Uterine Fibroid. *The Iraqi Postgraduate Medical Journal* 2012; 11 (2): 274-279.

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18. Usoro CAO, Adikwuru CC, Usoro IN, Nsonwu AC. Lipid Profile of Postmenopausal Women in Calabar, Nigeria. *Pakistan J Nutrition* 2006; 5 (1): 79-82.
19. Shlipak MG, Chaput LA, Vittinghoff E, Lin F, Bittner V, Knopp RH, Hulley SB; Heart and Estrogen/progestin Replacement Study Investigators. Lipid changes on hormone therapy and coronary heart disease events in the Heart and Estrogen/progestin Replacement Study (HERS). *Am Heart J* 2003; 146(5):870-875.
20. Sadlonova J, Kostal M, Smahelova A, Hendl J, Starkova J, Nachtigal P. Selected metabolic parameters and the risk for uterine fibroids. *Int J Gynaecol Obstet* 2008; 102(1):50-54.
21. Ganz.P. Vasomotor and vascular effects of hormone replacement therapy. *Am J Cardiol* 2002; 90 (1A): 11-16.
22. He Y, Zeng Q, Dong S, Qin L, Li G, Wang P. Associations between uterine fibroids and lifestyles including diet, physical activity and stress: a case-control study in China. *Asia Pac J Clin Nutr* 2013; 22(1):109-117.
23. Dragomir AD, Schroeder JC, Connolly A, Kupper LL, Hill MC, Olashan AF, et al. Potential risk factors associated with subtypes of uterine leiomyomata. *Reprod Sci.* 2010; 17(11):1029–1035.
24. Johnson G, MacLehose RF, Baird DD, Laughlin-Tommaso SK, Hartmann KE. Uterine leiomyomata and fecundability in the Right from the Start study. *Human Reproduction* (Oxford, England) 2012; 27(10):2991-2997.

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Table 1: Distribution of women general characteristics according to fibroid cases and controls.

| Variable | Fibroid | | Control | | Total | P |
|--------------------------|---------|-------|---------|-------|-------|---------|
| | No. | % | No. | % | No. | |
| Maternal age | | | | | | 0.2 |
| <30 years | 1 | 16.7 | 5 | 83.3 | 6 | |
| 30-39 years | 31 | 50.8 | 30 | 49.2 | 61 | |
| 40-45 years | 28 | 52.8 | 25 | 47.2 | 53 | |
| Marital status | | | | | | 0.5 |
| Married | 46 | 51.7 | 43 | 48.3 | 89 | |
| Unmarried | 14 | 45.2 | 17 | 54.8 | 31 | |
| Educational level | | | | | | <0.001* |
| Primary | 29 | 78.4 | 8 | 21.6 | 37 | |
| Secondary | 25 | 54.3 | 21 | 45.7 | 46 | |
| College | 6 | 16.7 | 30 | 83.3 | 36 | |
| Occupation | | | | | | <0.001* |
| Housewife | 52 | 62.7 | 31 | 37.3 | 83 | |
| Employed | 8 | 25.8 | 23 | 74.2 | 31 | |
| Student | 0 | - | 6 | 100.0 | 6 | |
| Blood group | | | | | | 0.1 |
| O +ve | 11 | 61.1 | 7 | 38.9 | 18 | |
| A +ve | 40 | 46.0 | 47 | 54.0 | 87 | |
| B +ve | 5 | 45.5 | 6 | 54.5 | 11 | |
| AB +ve | 4 | 100.0 | 0 | - | 4 | |
| BMI | | | | | | 0.07 |
| Normal | 12 | 52.2 | 11 | 47.8 | 23 | |
| Overweight | 28 | 41.8 | 39 | 58.2 | 67 | |
| Obese | 20 | 66.7 | 10 | 33.3 | 30 | |

*Significant.

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Table 2: Distribution of women gynecological characteristics according to fibroid cases and controls.

| Variable | Fibroid | | Control | | Total No. | P |
|--------------------------|---------|-------|---------|------|--------------|-------------------|
| | No. | % | No. | % | | |
| Contraceptive use | | | | | | 0.4 |
| Yes | 12 | 57.1 | 9 | 42.9 | 21 | |
| No | 48 | 48.5 | 51 | 51.5 | 99 | |
| Menstrual history | | | | | | 0.04* |
| Regular | 56 | 48.3 | 60 | 51.7 | 116 | |
| Irregular | 4 | 100.0 | 0 | - | 4 | |
| Menses amount | | | | | | <0.001* |
| Normal | 30 | 33.3 | 60 | 66.7 | 90 | |
| Heavy | 30 | 100.0 | 0 | - | 30 | |

*Significant.

Table 3: Distribution of obstetrical history and lipid profile means according to fibroid cases and controls.

| Variable | Fibroid | Control | P |
|------------------------|------------|------------|-------------------|
| | Mean±SD | Mean±SD | |
| Parity | 4±2 | 3±2 | 0.1 |
| Menses duration (day) | 7.1±1.9 | 5.9±1.1 | <0.001* |
| Age at menarche (year) | 12.5±0.6 | 12.9±0.5 | 0.002* |
| Cholesterol (mg/dl) | 165.1±35.7 | 152.9±39.6 | 0.07 |
| Triglycerides (mg/dl) | 115.4±43.1 | 122.9±40.5 | 0.3 |
| HDL (mg/dl) | 60.3±13.3 | 43.6±11.5 | <0.001* |
| LDL (mg/dl) | 56.9±25.2 | 62.6±24.0 | 0.2 |

*Significant.

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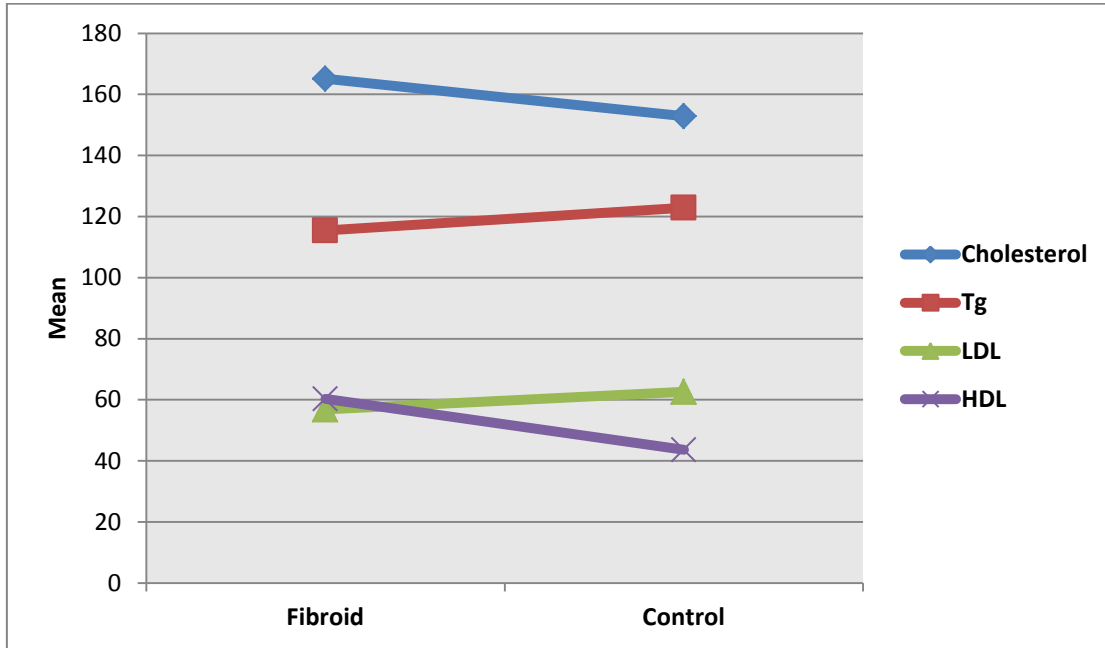


Figure 1: Lipid profile distribution according to fibroid cases and controls.