

## Comparing the Serum Lipid Profile Levels in Women Suffering From Endometriosis With Healthy Women

Fariba Almassinokiani<sup>1</sup>; Abolfazl Mehdizadehkashi<sup>1</sup>; Jila Amirkhani<sup>2,\*</sup>; Peyman Akbari<sup>3</sup>; Kobra Tahermanesh<sup>1</sup>; Fahimeh Soheilipour<sup>1</sup>; Sara Asadolla<sup>4</sup>

<sup>1</sup>Minimally Invasive Surgery Research Center, Rasoul-e-Akram Hospital, Iran University of Medical Sciences, Tehran, IR Iran

<sup>2</sup>Department of Gynecology, Islamic Azad University, Tehran Medical Branch, Tehran, IR Iran

<sup>3</sup>Department of Basic Science, Tehran University of Medical Sciences, Tehran, IR Iran

<sup>4</sup>Department of Gynecology, Iran University of Medical Sciences, Tehran, IR Iran

\*Corresponding author: Jila Amirkhani, Department of Gynecology, Islamic Azad University, Tehran Medical Branch, Tehran, IR Iran. Tel: +98-2166509283, Fax: +98-2166509283, E-mail: research\_center88@yahoo.com

Received: April 29, 2014; Accepted: June 10, 2014

**Background:** Endometriosis is a prevalent disease that can disable the patient and its etiology is not clear. Since simvastatin and similar drugs were successful in regressing endometrial implants, perhaps the serum lipid levels may be important in endometriosis.

**Objectives:** The aim of this study was to compare the serum lipid profile levels of women suffering from endometriosis with healthy women.

**Materials and Methods:** In a cross sectional study, after at least 12 hours of fasting, we measured serum lipid profile levels (including Triglyceride, Low Density Lipoprotein, High Density Lipoprotein and Total Cholesterol ) in all patients before laparoscopy. According to the visual evidences of laparoscopy done for all patients, we compared the lipid profile levels of women suffering from endometriosis with healthy women.

**Results:** We had 25 patients in endometriosis group and 50 in non-endometriosis. Two groups were matched for age, parity and Body Mass Index. In endometriosis group 64% had moderate to severe endometriosis. Only total cholesterol levels had significant difference between the two groups ( $P = 0.004$ ) and it was higher in patients with endometriosis.

**Conclusions:** Some other small studies have proved that statins were effective in regression of endometriosis implants and we have also proved that the levels of serum lipid profile was higher in patients suffering from endometriosis, perhaps higher levels of lipid profile has a significant etiologic role in pathogenesis of endometriosis.

**Keywords:** Cholesterol; Endometriosis; Laparoscopy; Serum

### 1. Background

The presence of endometrial glandular and stromal cells outside the uterine cavity is called endometriosis, which can be diagnosed by laparoscopy. Endometriosis is a chronic gynecological disease that its common manifestations are chronic pelvic pain and infertility and can affect the quality of life of the patients. In women with pelvic pain or infertility symptoms, prevalence of endometriosis is reported at 20-90 percent (1). Etiology of endometriosis is poorly understood. One of the recent proposed causes of endometriosis is the role of angiogenic genes that can be inhibited by Atorvastatin (2). Statins are potent inhibitors of cholesterol biosynthesis and reduce serum cholesterol in patients with hyperlipidemia. Statins act by inhibiting 3-Hydroxy-3-Methyl Glutaryl Coenzyme A (HMG-CoA) to block the conversion of HMG-CoA to L-mevalonate, a rate-limiting step in cholesterol synthesis. Statins were also effective in inhibiting the mechanisms of cell proliferation and angiogenesis in experimental models for the development of endometri-

osis-like tissue. Simvastatin could inhibit proliferation and the contractility of human of endometrial stromal cells invitro and can also decrease the number and size of endometrial implants in mice (3, 4). Statins can inhibit angiogenesis in endometrial culture (5).

### 2. Objectives

As proved in some studies, statins were effective in regression of endometriosis implants; perhaps lipid profile of women suffering from endometriosis is different from non-endometriosis women. So we decided to compare the lipid profile between these two groups.

### 3. Materials and Methods

In this cross sectional study from Feb 2012 to Oct 2013 women of reproductive age who underwent laparoscopy for different reasons like infertility, ovarian cysts and tubal ligation were recruited. Five cc of venous blood sample were gathered from all of them after 12 hours fasting for routine tests and lipid profile the day before operation.

After laparoscopy and according to the American Society of Reproductive Medicine for endometriosis criteria (1), we included the patients suffering from endometriosis to E group (n = 25) and the rest to non-endometriosis group (NE) (n = 50). Two groups were matched for age and body mass index (BMI) and none had history of hyperlipidemia. Exclusion criteria included: Hypothyroidism, pregnancy, BMI more than 30 kg/m<sup>2</sup>, alcoholism, smoking, use of hormonal contraception or hormonal medications, history of hyperlipidemia and any systemic diseases (like diabetes or hypertension). All patients approved the written informed consent and the project was approved by ethics committee of minimally invasive surgery research center. Lipid profile analysis included total cholesterol (TC), LDL, HDL and triglyceride (TG). Statistical analysis was performed by SPSS 13. We used the K-S test (one sample Kolmogorov-Smirnov test) for normality of data distribution and unpaired t-tests for equality of means for comparing quantitative normal data between two groups. According to K-S test, we compared the normal quantitative data by non-parametric Mann-Whitney U test between two groups.

#### 4. Results

We had 25 patients in E group and 50 in NE group. The mean age in E group was 29.04 ± 7.4 and in NE group was 29.22 ± 7.7 years. The age range in E group was 21-46 years and in NE was 21- 47. Most of the patients in two groups were nulliparous (64% in E group and 54% in NE group). BMI in two groups did not have significant difference (22.44 ± 3.03 in E group and 24.44 ± 4.5 in NE group). 64% of patients with endometriosis had moderate to severe endometriosis; moderate endometriosis were noticed in 8 patients (32%) and severe in 8 (32%). The mean level of LDL, HDL and triglyceride in two groups did not have significant difference, but the mean cholesterol level in two groups had significant difference (P = 0.004) and was higher in E group. The different criteria in patients are compared in Table 1.

**Table 1.** Comparison of Different Criteria in Patients with Endometriosis and Without Endometriosis <sup>a,b</sup>

Criteria	Endometriosis	Non Endometriosis	P Value
Age, y	29.04 ± 7.4	29.22 ± 7.7	0.924
Nuliparity	16 (64)	27 (54)	0.165
BMI, kg/m <sup>2</sup>	22.44 ± 3.03	24.4 ± 4.5	0.052
LDL, mg/dl	100.12 ± 21	96 ± 42.5	0.563
HDL, mg/dl	41.1 ± 10.1	45.9 ± 24.6	0.426
Cholesterol, mg/dl	160.9 ± 29.5	140.9 ± 20.4	0.004
Triglyceride, mg/dl	110.7 ± 56	110.7 ± 54	0.314

<sup>a</sup> BMI, Body Mass Index; LDL, Low Density Lipoprotein; HDL, High Density Lipoprotein.

<sup>b</sup> Data are presented as Mean ± SD or No. (%).

#### 5. Discussion

In our study the only significant difference between E and NE group was in serum cholesterol level that was higher in E group. Endometriosis is a common and disabling disease with pain and infertility as its most important manifestations. As proved in some small in vitro studies statins were successful in regression of endometriosis implants (2-8), so the difference between serum lipids of women suffering from endometriosis in comparison with healthy women may have an important role in progression of the treatment of this disease. In another study on patients of reproductive age endometriotic cyst wall tissue was obtained by biopsy from endometrioma of 13 patients and in the secretory phase of patients without endometriosis. 20 µmol/L Atorvastatin had no effect on the viability of endometriotic stromal cells in 24 hours. However higher doses led to decreased viability at 48 hours and 72 hours. So Atorvastatin was able to inhibit cell proliferation of endometriotic stromal cells (2). In another study human endometrial stromal cells (HES) were collected from 9 subjects (18-45 years). After enzymatic digestion of endometrial fragments, HES cells apoptosis were evaluated. Then the HES cells were cultured without and with Simvastatin (10-30 µM) for 6-48 hours. Apoptotic cells were morphologically identified based on disrupted or disorganized F-actin filaments. The experiment was repeated 3 times using endometriotic samples obtained from 3 patients. Exposure to Simvastatin at either concentration had no significant effect at 6 and 12 hours. But after 24 hours had significant effect. Simvastatin induces a wave of apoptosis and morphological changes including cell shrinkage and derangement of the cytoskeleton (8). Different hormonal treatments, like Medroxyprogesterone acetate or Danazole in patients with endometriosis can have adverse effects on serum lipids. So long term treatments with these agents may reduce the beneficial effects of these agents on endometriosis. In a study on comparison of serum lipid profile of women suffering from endometriosis with healthy women, there were no differences between lipid profiles of these two groups (9). In a cross sectional study on serum lipid profile, in women with endometriosis (n = 40) the serum level of LDL, HDL, TC and TG were higher than control group (n = 80). But HDL/TC ratio was lower and LDL/TC was higher than control group and the authors reached to this point that patients with endometriosis have an unfavorable lipid profile compared with healthy women and may have a greater predisposition to atherogenesis (6). The limitation of this study is that the patients were not matched for physical activity, the patients who were taking hormonal medications were not excluded and patients in NE group were diagnosed only by history and not by laparoscopy. Larger studies need to be done to evaluate the role of serum lipid profile in pathogenesis and treatment of endometriosis.

## Authors' Contributions

Study concept and design: Dr. Almassinokiani; Acquisition of data: Dr. Almassinokiani, Mehdizadehkashi, Soheilipour, Amirkhani, Peyman Akbari, Kobra Tahermanesh; Analysis and interpretation of data: Sara Asadolla, Dr. Almassinokiani; Drafting of the manuscript: Dr. Almassinokiani; Critical revision of the manuscript for important intellectual content: Dr. Almassinokiani, and Amirkhani; Statistical analysis: Sara Asadolla; Administrative, technical, and material support: Dr. Almassinokiani; Study supervision: Dr. Almassinokiani.

## Funding/Support

This study was supported by Iran University of Medical Sciences (IUMS).

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