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Alterations in lipid profile among women with premature ovarian failure

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Abstract
Background: Premature ovarian failure (POF), also termed premature ovarian insufficiency, is characterized by the cessation of ovarian activity before the age of 40 years. Beyond infertility and hormonal symptoms, POF is associated with adverse metabolic changes and increased cardiovascular risk. Dyslipidemia is a central mechanism through which estrogen deficiency contributes to vascular disease.
Objective: This study aimed to evaluate alterations in lipid profiles among women with POF compared to healthy age-matched controls.
Methods: A cross-sectional comparative study was conducted between March and July 2025 at Maternity and Children's Teaching Hospital. Seventy-five women aged 30-40 years were enrolled, including 35 with confirmed POF and 40 healthy controls. Diagnosis of POF was based on amenorrhea lasting more than four months and elevated serum follicle-stimulating hormone (> 25 IU/L on two occasions). Sociodemographic and clinical data, including body mass index (BMI) and smoking status, were recorded. Fasting venous blood samples were collected and analyzed for triglycerides (TG), total cholesterol (TCH), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) using enzymatic colorimetric assays.
Results: The POF group reported significantly higher smoking exposure compared with controls (P=0.021). Lipid analysis revealed significantly higher TCH (4.55±0.58 vs 3.71±0.75 mmol/L; P=0.0001) and LDL-C (2.31±0.69 vs 1.95±0.61 mmol/L; P=0.02) among POF women. Conversely, TG levels were lower in POF patients (1.15±0.22 vs 1.73±0.79 mmol/L; P=0.0001). No significant difference was observed in HDL-C levels (P=0.5).
Conclusion: Women with POF demonstrate significant dyslipidemia, characterized by elevated atherogenic lipids, which may predispose them to premature cardiovascular disease. Smoking emerged as a notable risk factor. Early screening, lifestyle modification, and tailored hormone therapy should be prioritized to mitigate long-term cardiometabolic consequences.

Keywords: Lipid profile, women, premature, ovarian, failure

Introduction

Premature ovarian failure, currently referred to as Premature Ovarian Insufficiency (POI), is a clinical condition characterized by the cessation of ovarian function before the age of 40 years. It affects approximately 1-4% of women worldwide and is associated with infertility, hypoestrogenism, and increased long-term health risks [1]. Beyond reproductive implications, POI has significant systemic consequences due to early estrogen deficiency, including reduced bone density, psychological distress, and notably, increased cardiovascular morbidity and mortality [2].

Cardiovascular Disease (CVD) is the leading cause of death in women, and dyslipidemia is one of the major modifiable risk factors contributing to its development. A growing body of evidence suggests that women with POI exhibit alterations in their lipid profiles, which may explain their heightened cardiovascular risk [3]. Several systematic reviews and meta-analyses have shown higher serum concentrations of Total Cholesterol (TC), Low-Density Lipoprotein Cholesterol (LDL-C), and Triglycerides (TG) among women with POI compared to age-matched controls [4, 5]. While findings regarding High-Density Lipoprotein Cholesterol (HDL-C) remain inconsistent, the overall trend suggests a more atherogenic lipid pattern in affected women [6].

The pathophysiological mechanisms linking POI to dyslipidemia are primarily attributed to estrogen deficiency. Estrogen is known to enhance hepatic LDL receptor activity, promote favorable lipid metabolism, and exert anti-inflammatory vascular effects [7]. Loss of ovarian estrogen before the expected age of menopause leads to an earlier and prolonged exposure to adverse lipid changes, thereby accelerating the risk of subclinical atherosclerosis and overt cardiovascular disease [8]. Furthermore, studies have suggested that POI is associated with other metabolic disturbances, including central adiposity, insulin resistance, and impaired glucose metabolism, which collectively compound the cardiovascular burden [9]. Given these findings, international guidelines recommend early cardiovascular risk assessment and regular monitoring of lipid profiles in women diagnosed with POI [10]. Hormone Therapy (HT) has been shown to partially restore lipid balance by reducing LDL-C and raising HDL-C, though treatment decisions must be individualized based on age, comorbidities, and contraindications [11]. Nevertheless, the literature remains limited by small sample sizes, heterogeneity in diagnostic criteria, and underrepresentation of diverse populations. This study aims to investigate alterations in lipid profiles among women with premature ovarian failure compared to healthy controls. By characterizing these differences, the study contributes to a better understanding of the metabolic consequences of POI and underscores the need for targeted preventive strategies to mitigate cardiovascular risk in this population.

Methods

Study Design and Setting

This was a cross-sectional comparative study conducted at Maternity and Children's Teaching Hospital between March 2025 to July 2025]. The purpose was to assess alterations in lipid profiles among women diagnosed with premature ovarian failure (POF) compared with healthy controls. The study received approval from the Institutional Ethics Committee (Approval No. 144, dated 1-4-2025). Written informed consent was obtained from all participants prior to enrollment.

Study Population

Seventy-five women aged 30-40 years were recruited and divided into two groups: 40 healthy controls and 35 patients with POF. The diagnosis of POF was confirmed by the presence of amenorrhea for more than four months and elevated serum follicle-stimulating hormone (FSH > 25 IU/L on two occasions at least four weeks apart). Women with chronic systemic illness, diabetes mellitus, hepatic or renal disease, or those receiving lipid-lowering drugs or hormonal therapy within the last three months were excluded.

Data Collection

Socio-demographic data, body mass index (BMI), and smoking history were recorded for each participant using structured interviews and clinical examination. Venous blood samples were collected in the morning after 10-12 hours of overnight fasting.

Laboratory Analysis

Serum was separated and analyzed for lipid profile parameters, including triglycerides (TG), total cholesterol (TCH), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C). Measurements were performed using standard enzymatic colorimetric methods with an automated biochemical analyzer (e.g., Roche Cobas system). Internal quality control procedures were applied throughout the analysis to ensure accuracy.

Statistical Analysis

Data were analyzed using SPSS version 24. Continuous variables were presented as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. The independent Student's *t*-test was used to compare mean values between POF patients and controls. A p-value < 0.05 was considered statistically significant.

Results

Table 1 compares age, BMI, and smoking state between the control group (N=40) and women with Premature Ovarian Failure (POF, N=35).

- **Age:** The mean age of the control group was 33.88±2.57 years, while the POF group had a slightly higher mean age of 34.46±2.85 years. The difference was not statistically significant (P=0.3), suggesting that age was relatively matched between the groups and is unlikely to confound the outcomes.
- **BMI:** Controls had a higher mean BMI (30.85±5.09 kg/m²) compared to the POF group (25.15±3.14 kg/m²). Although the difference appears clinically meaningful (with the control group averaging in the obese category while POF patients averaged in the overweight range), the p-value (0.3) indicates that it was not statistically significant. This implies that, within the study population, BMI differences did not reach the threshold of statistical importance, though the trend could still be biologically relevant.
- **Smoking State:** A notable finding was that the POF group reported higher smoking exposure (5.61±0.32) compared to the control group (4.39±0.40). This difference was statistically significant (P=0.021), suggesting a potential association between increased smoking habits and POF. Cigarette smoking has been well-documented as a risk factor for diminished ovarian reserve and earlier onset of menopause, and the findings here reinforce this relationship.

So smoking appears to be a significant differentiating factor between women with POF and controls, while age and BMI did not show significant differences. This suggests that lifestyle factors such as tobacco exposure may play an important role in the pathogenesis of POF.

Table 1: Differences mean of age, BMI, smoking state according to study group

Variable	Control (N=40)	POF (N=35)	P-Value
Age (years)	33.88±2.57	34.46±2.85	0.3
BMI (kg/m²)	30.85±5.09	25.15±3.14	0.3
Smoking State	4.39±0.4	5.61±0.32	0.021

Table 2 presents the differences in lipid profile parameters (TG, HDL, TCH, LDL) between the two groups.

- **Triglycerides (TG):** The control group had significantly higher TG levels (1.73±0.79 mmol/L) compared to the POF group (1.15±0.22 mmol/L), with a highly significant p-value (P=0.0001). This indicates that POF patients may have reduced circulating triglycerides, which could reflect altered lipid metabolism associated with ovarian insufficiency.
- **High-Density Lipoprotein (HDL):** Mean HDL was slightly higher in the control group (1.73±0.28 mmol/L) than in the POF group (1.51±0.27 mmol/L), but this difference was not statistically significant (P=0.5). Since

HDL is considered a protective lipid, its lack of significant reduction in POF patients suggests that not all aspects of lipid metabolism are uniformly affected.

- **Total Cholesterol (TCH):** Women with POF had significantly higher TCH levels (4.55±0.58 mmol/L) compared to controls (3.71±0.75 mmol/L), with a highly significant difference (P=0.0001). Elevated cholesterol in POF patients may predispose them to increased cardiovascular risks, which aligns with existing literature linking early menopause and ovarian insufficiency to adverse cardiometabolic outcomes.
- **Low-Density Lipoprotein (LDL):** Similarly, LDL cholesterol was higher in POF patients (2.31±0.69 mmol/L) than controls (1.95±0.61 mmol/L), and the difference was statistically significant (P=0.02). This reinforces the pattern of dyslipidemia in POF, with elevations in atherogenic lipids that could accelerate vascular aging.

Table 2: Differences mean of lipid profile according to study group

Variable	Control (N=40)	POF (N=35)	P-Value
TG (mmol/L)	1.73±0.79	1.15±0.22	0.0001
HDL (mmol/L)	1.73±0.28	1.51±0.27	0.5
TCH (mmol/L)	3.71±0.75	4.55±0.58	0.0001
LDL (mmol/L)	1.95±0.61	2.31±0.69	0.02

Discussion

The present study investigated lipid profile alterations among women with Premature Ovarian Failure (POF) compared with healthy controls. The findings demonstrated that women with POF had significantly higher total cholesterol (TCH) and Low-Density Lipoprotein Cholesterol (LDL-C) levels, while triglycerides (TG) were significantly lower. No significant difference was observed in high-density lipoprotein cholesterol (HDL-C). These results provide further evidence that POF is associated with metabolic disturbances that may contribute to long-term cardiovascular risk. The significant elevation of TCH and LDL-C among POF patients is consistent with previous meta-analyses and systematic reviews, which have reported a more atherogenic lipid profile in women with ovarian insufficiency [12, 13]. Estrogen deficiency is a key driver of these changes, as it reduces hepatic LDL receptor expression, leading to increased circulating LDL-C and promoting cholesterol accumulation in vascular walls [14]. This mechanistic pathway may explain the increased incidence of premature atherosclerosis and cardiovascular morbidity observed in women with early ovarian failure [15]. Interestingly, our study found that TG levels were significantly lower in the POF group compared with controls, a finding that contrasts with some reports suggesting hypertriglyceridemia in estrogen-deficient states [16]. One possible explanation may relate to differences in body composition, as women with POF in our sample had a lower mean BMI than controls, despite the difference not reaching statistical significance. Obesity is strongly associated with elevated TG, and therefore, lower BMI in POF patients might have contributed to reduced TG concentrations [17]. This highlights the complexity of interactions between ovarian function, adiposity, and lipid metabolism. Although HDL-C levels were slightly lower in the POF group, the difference was not statistically significant. Prior studies have shown inconsistent results regarding HDL-C, with some reporting reductions in POF and others finding no significant change [18]. This variability may reflect differences in study design, sample size, ethnicity, and lifestyle-related factors such as diet, smoking, and physical activity. Our findings on smoking are noteworthy, as POF women reported significantly higher smoking exposure than controls. Cigarette smoking is a well-documented risk factor for reduced ovarian reserve and early menopause, largely through mechanisms involving oxidative stress and follicular depletion [19]. Furthermore, smoking independently contributes to dyslipidemia and vascular dysfunction, compounding the adverse metabolic profile observed in POF [20]. Overall, these results emphasize the importance of early cardiovascular risk assessment in women with POF. Current international guidelines recommend lipid screening at diagnosis and regular follow-up, with consideration of hormone therapy (HT) to mitigate estrogen deficiency and improve lipid metabolism when not contraindicated [21, 22]. Future studies should explore longitudinal changes in lipid profiles over the disease course, as well as the role of lifestyle modification and tailored HT regimens in reducing cardiovascular burden among women with POF.

Conclusion

Women with premature ovarian failure exhibit significant alterations in their lipid profiles, characterized by elevated total cholesterol and LDL-C, alongside reduced triglycerides, compared with healthy controls. These changes highlight an increased risk of cardiovascular disease in this population. Smoking was found to be a significant associated factor, reinforcing its role in ovarian dysfunction and metabolic imbalance. Early screening, lifestyle modification, and individualized hormone therapy may help mitigate long-term cardio metabolic risks.

Conflicts of Interest

Not available

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