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Original Research Article

STUDY OF LIPOPROTEINS A AND LIPID PROFILE IN POLYCYSTIC OVARIAN SYNDROME CASES IN TERTIARY CARE HOSPITAL

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Abstract

Background: Lipoprotein(a) [Lp(a)] is a modified form of LDL with a distinct metabolism and genetically determined levels that remain stable over a person's lifetime. Changes in plasma lipid and Lp(a) levels increase the risk of CVD. Elevated Lp(a) levels represent an independent risk factor for cardiovascular events, including myocardial infarction, stroke, and coronary heart disease. Early screening for modifiable cardiovascular risk factors may aid in preventing CVD development. **Materials and Methods:** This study was conducted in the Department of Biochemistry in Patna Medical College, Patna, Bihar, India. This case-control study comprised a total of 100 participants, with 50 individuals diagnosed with PCOS and 50 control subjects included in the analysis. The duration of study was over a period of one year. **Result and Conclusion:** This study concludes that the elevated Lipoprotein (a) was prevalent among the majority of PCOS cases examined in this study. These observed abnormalities suggest that polycystic ovarian syndrome may contribute to the emergence of an atherogenic lipid profile, thereby increasing the patient's susceptibility to future metabolic syndrome.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a prevalent endocrine disorder, impacting approximately 6 to 22% of women globally. Its primary characteristics consist of irregular ovulation, heightened androgen levels (hyperandrogenism), and the presence of ovarian cysts.[1-3] Typically diagnosed during the reproductive years, women with PCOS often experience fertility issues, irregular menstrual cycles, and symptoms such as acne, hair loss, and excessive hair growth due to androgen excess.[4] Additionally, dyslipidemia is becoming increasingly prevalent among young adult females with PCOS. Studies, both retrospective and prospective, suggest a heightened risk of coronary artery disease in individuals with PCOS. However, there's a lack of comprehensive research on the potential interactions between endocrine dysfunctions, metabolic abnormalities, and lipid profiles in PCOS patients.[5] Factors like hyperandrogenism, insulin resistance, glucose metabolism disorders, and obesity may independently or collectively influence circulating lipid levels, necessitating further investigation into the underlying mechanisms.[6-8]

Insulin resistance, hyperandrogenism, and dyslipidemia are believed to be the primary risk factors for cardiovascular diseases (CVD) in women with PCOS. Insulin resistance and dyslipidemia are thought to play significant roles in the cardiovascular risk associated with PCOS, although the extent of dyslipidemia's contribution to this risk remains unclear.[9] Typically, dyslipidemia in PCOS is characterized by elevated triglycerides and low levels of high-density lipoprotein (HDL) cholesterol, although hypertriglyceridemia is relatively uncommon compared to low HDL cholesterol.[10,11] Conversely, the classic lipid alteration indicative of cardiovascular risk, an increase in low-density lipoprotein (LDL) cholesterol, is not universally common in all PCOS populations. Beyond LDL cholesterol levels, the quality of LDL may directly influence cardiovascular risk. While PCOS has long been known to be associated with reproductive issues and an increased risk of conditions like diabetes mellitus, ovarian, and endometrial cancer, recent research has highlighted an elevated cardiovascular risk in women with PCOS.[12] Lipoprotein(a) [Lp(a)] is a modified form of LDL with a distinct metabolism and genetically determined levels that remain stable

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over a person's lifetime. Changes in plasma lipid and Lp(a) levels increase the risk of CVD. Elevated Lp(a) levels represent an independent risk factor for cardiovascular events, including myocardial infarction, stroke, and coronary heart disease. Early screening for modifiable cardiovascular risk factors may aid in preventing CVD development. Thus, our study aims to investigate elevated Lp(a) levels and dyslipidemia in PCOS. The objective of the study is to evaluate Lp(a) and lipid profile levels in women with PCOS.[13]

MATERIALS AND METHODS

Study Area: This study was conducted in the Department of Biochemistry in Patna Medical College, Patna, Bihar, India.

Study Population: This case-control study comprised a total of 100 participants, with 50 individuals diagnosed with PCOS and 50 control subjects included in the analysis.

Study Duration: The duration of study was over a period of one year.

Data collection: For data collection, we enrolled 50 PCOS cases with prior diagnosis and 50 healthy individuals as controls. A comprehensive history, including menstrual patterns, was obtained. Baseline information such as age, body mass index (BMI; kg/m2), detailed medical history, clinical examination findings, and relevant investigations were documented. Serum samples were isolated from a five mL peripheral venous blood draw obtained via venipuncture from both the patients and controls following a 12-hour overnight fast. Serum Lipoprotein (a) levels were quantified using the immunonephelometric technique. Total cholesterol (TC), serum triglycerides (TG), HDL cholesterol, fasting blood glucose, blood urea, and serum creatinine were measured using commercial kits on the Erba Chem 7 Semi-Automatic Biochemistry Analyzer. Friedewald's method was employed to derive serum very-low-density lipoprotein (VLDL) cholesterol and LDL cholesterol from TC, TG, and HDL cholesterol values. Additionally, ratios of TC/HDL cholesterol and LDL cholesterol/HDL cholesterol were computed in this study.

Data Analysis: Data were analysed by using Microsoft Excel & SPSS software.

RESULTS

This study comprised two cohorts: one consisting of participants with PCOS and the other serving as the control group, with each group comprising 50 individuals. Both cases and controls were categorized into four age brackets. The highest number of cases was observed in the age groups of 25 - 30 years (22 cases) and 21-25 years (20 controls). In terms of BMI scores, the study revealed that 24 individuals in the PCOS group and 30 in the control group had scores ranging from 18.0 to 25.0, while 20 individuals in the PCOS group and 14 in the control group had scores from 25.1 to 30.0. BMI scores exceeding 30.0 were found in 6 individuals in both the PCOS and control groups. Analysis of lipid profile variation between cases and controls is presented in Table 3. The mean total cholesterol levels among cases were 208.5 ± 35.67 mg/dl. Among the cases, 60% had levels below 200 mg/dl, while 40% exceeded this threshold. The mean cholesterol levels were significantly higher in cases compared to controls ($p < 0.05$). Distribution of Serum Low-Density Lipoproteins (LDL) among Cases and Controls, with 92% of cases and 98% of controls falling within the normal range (≤129 mg/dl). Similarly, Distribution of Serum Very Low-Density Lipoprotein (VLDL) among Cases and Controls indicated that 88% of cases and 96% of controls were within the normal range (≤40 mg/dl). Regarding Serum High-density Lipoprotein (HDL), 96% of cases and 92% of controls had levels below 40 mg/dl [Table 3]. Although cases exhibited a higher mean Lp(a) compared to controls, the difference was not statistically significant ($p > 0.05$). However, when considering Lp(a) distribution, 20% of cases had values ≥ 30mg/dl [Table 3].

Table 1: Distribution of age group among PCOS cases and control group

Age group	PCOS cases	Control
15-20	6	6
21-25	16	20
25-30	22	16
31-35	6	8
Total	50	50

Table 2: Distribution of BMI score among PCOS cases and control group

BMI score Kg/m2	PCOS cases	Control
18.0-25.0	24	30
25.1-30.0	20	14
>30.0	6	6

Table 3: Lipid profile and lipoprotein A profile among PCOS cases and control group

Lipid profile	PCOS cases (mean±SD)	Control (mean±SD)
Cholesterol (mg/dl)	208.5±35.6	175.9±18.1
Triglycerides (mg/dl)	165.3±50.3	135.4±22.3
LDL (mg/dl)	125.2±25.6	120.2±15.6

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HDL (mg/dl)	38.9±8.5	43.2±7.2
VLDL (mg/dl)	25.7±6.6	23.1±6.5
Lp(a) (mg/dl)	22.1±12.1	17.5±6.8

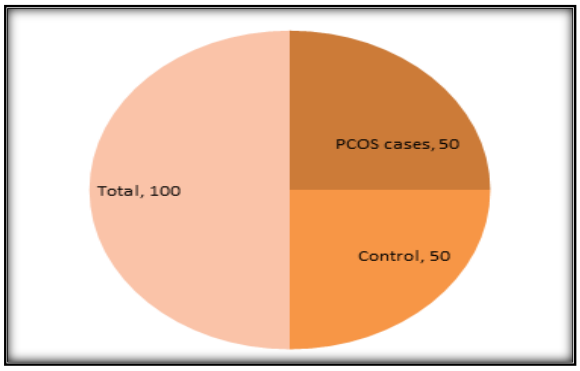

Figure 1: Distribution of cases and control among all population

DISCUSSION

Polycystic ovary syndrome (PCOS) stands as the foremost endocrine disorder impacting women, marked by manifestations such as hyperandrogenism, amenorrhea, oligomenorrhea, and infertility among women of reproductive age. Key indicators of PCOS encompass chronic anovulation, clinical or biochemical hyperandrogenism, obesity, and the presence of polycystic ovaries. Hyperandrogenism is closely associated with oligomenorrhea or amenorrhea, with potential clinical signs such as hirsutism or acne. Most studies investigating dyslipidemia and PCOS have primarily concentrated on levels of cholesterol and triglycerides (TGs). Women diagnosed with PCOS exhibit a lipid profile characterized by elevated TG levels and reduced levels of high-density lipoprotein-cholesterol (HDL-C).[14] These changes align with the typical lipid profile often linked to insulin resistance. Insulin resistance has long been acknowledged for its impact on lipid metabolism. Elevated plasma triglyceride (TG) concentrations result from increased liver secretion of very-low-density lipoprotein (VLDL) particles. Subsequently, cholesteryl ester (CE) transfer protein activity facilitates the exchange of TGs for cholesteryl esters (CE). As a consequence of this process, triglyceride-enriched high-density lipoprotein (HDL) particles degrade more rapidly, while CE-enriched VLDL particles transform into small, dense low-density lipoprotein (LDL) particles.[15] Insulin resistance is responsible for reducing plasma levels of HDL-C and apoprotein (apo) A-I, while simultaneously increasing apo B levels. In women diagnosed with PCOS, alterations in lipid metabolism may result not only from insulin resistance but also from ovarian and/or adrenal steroid production. Sex steroids, comprising both androgens and estrogens, exert a multifaceted influence on lipid metabolism. Hyperandrogenism, for instance, has been linked to heightened hepatic lipase (HL) activity.[16-18] This enzyme, crucial in the breakdown of HDL particles, displays sexual dimorphism, with exogenous androgens elevating its activity and estrogens diminishing it.[19] In our investigation, PCOS subjects exhibited higher mean levels of total cholesterol (TC), triglycerides (TG), and low-density lipoprotein (LDL) compared to controls. These findings are consistent with similar research conducted by Olivier et al., who observed an increase in triglycerides, cholesterol, and LDL-C, alongside a decrease in HDL-C and apo A-I.[20,21] Berneis et al. found that low HDL-C is common among PCOS patients, although hypertriglyceridemia is uncommon. Interestingly, they noted that the most prevalent lipid alteration associated with cardiovascular risk, namely an increase in LDL-C, is not universally present in all PCOS groups. Additionally, besides overall LDL-C levels, the quality of LDL may directly influence cardiovascular risk. The Adult Treatment Panel III of the National Cholesterol Education Program recognizes that small, dense LDL carries a 3-fold higher risk of coronary artery disease and is classified as an emerging cardiovascular risk factor. Our study revealed that PCOS patients exhibited lower HDL-C levels compared to controls, while PCOS patients had higher mean VLDL levels. These findings are consistent with those of Wild et al., who observed that women with PCOS had elevated triglycerides and VLDL-C, along with reduced HDL2-C and A1:A2 ratios. Researchers also observed decreased levels of HDL2 cholesterol and increased levels of apolipoprotein B in PCOS patients.[22]

Compared to the control group, we observed a notably higher proportion of patients with Lp(a) levels exceeding 30 mg/dl. Despite the fact that the average Lp(a) levels in cases were higher than those in controls, this disparity did not reach statistical significance. Our results align with those reported by Berneis et al,[23] who similarly noted elevated levels of circulating asymmetric dimethylarginine (ADMA), total homocysteine, hsCRP, Lp(a), and fibrinogen in PCOS patients compared to healthy controls.

CONCLUSION

Based on the constraints of the present study, it is evident that PCOS patients consistently exhibited higher levels of total cholesterol, triglycerides, low-density lipoproteins, and very-low-density lipoproteins compared to the normal control group. Moreover, elevated Lipoprotein (a) was prevalent among the majority of PCOS cases examined in this study. These observed abnormalities suggest that polycystic ovarian syndrome may contribute to the emergence of an atherogenic lipid profile, thereby increasing the patient's susceptibility to future metabolic syndrome.

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