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Analysis of Fatty Liver Prevalence in Non-Obese Women Diagnosed with Polycystic Ovary Syndrome

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ABSTRACT

Background: *Polycystic ovary syndrome (PCOS) has various causes that are largely unknown. The present study was aimed to evaluate metabolic and biochemical markers as well as body mass index (BMI) related to PCOS among two groups including patients and healthy controls.*

Methods: *A case-control study included women younger than 45 years who did not suffer from obesity. Women with male-factor infertility served as the control group, while patients detected with PCOS via the Rotterdam criteria made up the case group. There were 86 randomly selected participants in each group. Fasting blood sugar (FBS), lipid profiles, alanine aminotransferase (ALT) and other biochemical tests were gathered with demographic data, medical records, physical exams and anthropometric measurements. Ultrasound, liver enzyme levels and medical history were utilized to diagnose non-alcoholic fatty liver disease (NAFLD).*

Results: *About 172 women were selected for the research; 86 had PCOS, while the remaining 86 were healthy controls. A younger mean age and a higher BMI were found in women with PCOS. The findings showed that mild to moderate fatty liver was more prevalent in the PCOS group than the control one (P = 0.04). Although metabolic indices, liver enzymes, hematologic parameters and hormone levels did not alter significantly, the PCOS group had lower fasting blood sugar levels (P = 0.029). The correlation between total cholesterol and PCOS was still poor after adjusting for age in logistic regression analysis. Still, it became statistically insignificant after adjusting for BMI index.*

Conclusion: *Non-obese women with PCOS had a higher prevalence of fatty liver, with minor differences in metabolic parameters, and BMI partly mediated these associations.*

Keywords: non-obese, polycystic ovary syndrome, non-alcoholic fatty liver disease.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is characterized by a combination of symptoms, including irregular menstrual cycles, excess androgen (male hormone) levels and polycystic ovaries, which are enlarged ovaries containing multiple small follicles (1).

Polycystic ovary syndrome has affected about 5–10% of surveyed women (2). Heart disease, diabetes, obesity, abnormal cholesterol levels, abnormal menstrual cycles and infertility are all symptoms of this syndrome. Polycystic ovary syn-

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drome is defined by the presence of hyperandrogenism, oligoovulation and a polycystic ovarian morphology. Symptoms and possible metabolic issues vary throughout the four main classes (A–D) of these diseases (3, 4).

Findings from some relevant studies suggest that women with PCOS, especially those who exhibit hyperandrogenism, obesity, or insulin resistance, are at increased risk of developing NAFLD (5-7). Given the clinical significance of NAFLD and the prevalence of PCOS, it is imperative to identify women with PCOS who are at risk for fatty liver disease and to investigate predictive indicators for this association. Women with PCOS have varying risks of developing NAFLD contingent upon their geographical location, potentially attributable to disparities in nutrition, socioeconomic position and lifestyle choices (5-9). Moreover, steatohepatitis and fibrosis were more prevalent in women with polycystic ovarian syndrome than in the general population, especially among non-obese persons (10-12).

To address existing gaps in the literature, particularly regarding metabolic and hepatic outcomes in non-obese women with PCOS, the present study aimed to determine the prevalence of non-alcoholic fatty liver disease in non-obese women diagnosed with PCOS and to identify the metabolic and hormonal factors associated with hepatic steatosis in this population.

MATERIALS AND METHODS

Study design and population

This case-control investigation included women aged 18–45 years with a body mass index (BMI) of 30 kg/m^2 or lower who were categorized as non-obese. Participants in the case group (75 women) fulfilled the Rotterdam diagnostic criteria for PCOS. Those in the control group (75 women) were attending an infertility clinic due to male-factor infertility.

Sample size and sampling method

With an 80% test power, a 0.05 significance level and an anticipated difference between the two groups, a prior study determined that 77 people in each group would be an adequate sample size. Considering a 10% margin of error, we determined a sample size of 172 women (86 *per* group). A random sampling of women visited the infertility treatment center and the endocrinology clinic.

Instruments and data collection

A standardized questionnaire was used to gather data, which encompassed demographic, socioeconomic and ethnic details, along with medical history (including conditions like diabetes and hypertension). Additionally, biochemical testing, anthropometric quantities (such as height, weight and BMI) and a physical examination were carried out. Obesity is defined as a BMI over 30 kg/m^2. The patient's abstinence from alcohol, together with ultrasonographic anomalies and liver enzyme assessment, resulted in the diagnosis of NAFLD. Abdominal ultrasonography for the diagnosis of NAFLD was performed by an experienced radiologist with more than 10 years of clinical practice in hepatic imaging. The radiologist was blinded to the participants' clinical, hormonal, and metabolic data, as well as their case–control status. Standardized imaging criteria were applied to ensure consistency and reduce interobserver variability.

Fasting blood glucose levels, lipid profiles (total cholesterol, HDL, LDL and triglycerides) and alanine aminotransferase (ALT) measurements were included in the laboratory evaluation.

Inclusion and exclusion criteria

Participants were excluded if they had a history of alcohol consumption exceeding 20 g/day, any known liver disease such as viral hepatitis (HBV/HCV), autoimmune hepatitis, Wilson's disease, or hemochromatosis, use of hepatotoxic medications or drugs affecting liver enzymes, current pregnancy or lactation, thyroid, renal, or cardiovascular disorders, previously diagnosed diabetes mellitus or impaired glucose tolerance, or incomplete clinical, laboratory, or ultrasonographic data.

Statistical analysis

In the present study, qualitative variables were summarized as frequencies and percentages, while quantitative variables were presented as mean ± standard deviation (SD) for normally distributed data and as median with interquartile range for non-normally distributed data. The Shapiro-Wilk test was used to assess the normality of all continuous variables. Categorical varia-

Variable (unit)	Group	Minimum	Maximum	Mean	SD	P-value
Age (years)	PCOS	15	42	26.71	7.41	0.001
	Healthy	24	45	32.88	4.74	
Body mass index (kg/m²)	PCOS	19.10	24.20	22.37	1.17	<0.001
	Healthy	19.10	23.10	21.65	1.12	
FBS (mg/dL)	PCOS	71	131	92.39	10.59	0.029
	Healthy	82	130	95.85	8.62	
Triglycerides (mg/dL)	PCOS	90	408	151.96	67.98	0.930
	Healthy	95	391	152.81	56.66	
Cholesterol (mg/dL)	PCOS	62	285	186.11	33.10	0.620
	Healthy	111	245	183.80	23.93	
HDL (mg/dL)	PCOS	30	60	48.16	6.12	0.600
	Healthy	32	58	48.64	5.08	
LDL (mg/dL)	PCOS	65	191	101.96	23.39	0.960
	Healthy	69	156	102.09	15.69	
AST (U/L)	PCOS	10	43	22.05	6.29	0.970
	Healthy	16	66	22.01	6.87	
ALT (U/L)	PCOS	10	71	24.16	12.03	0.860
	Healthy	10	94	23.85	9.92	
Alkaline phosphatase (U/L)	PCOS	112	430	213.80	71.77	0.560
	Healthy	112	366	207.95	49.59	
Hemoglobin (g/dL)	PCOS	10.00	14.20	12.29	0.95	0.210
	Healthy	10.50	13.90	12.46	0.79	
Platelet count (10³/µL)	PCOS	186.60	385.00	273.64	64.30	0.460
	Healthy	147.00	406.00	266.53	54.93	
Vitamin D (ng/mL)	PCOS	9.20	145.00	27.30	17.48	0.820
	Healthy	9.50	87.00	27.91	12.59	
TSH (µIU/mL)	PCOS	0.40	5.40	2.93	1.35	0.800
	Healthy	0.88	5.40	2.89	1.20	

PCOS: polycystic ovary syndrome; SD: standard deviation; FBS: fasting blood sugar; HDL: high density lipoprotein; LDL: low density lipoprotein; ALT: alanine aminotransferase; AST: aspartate aminotransferase; TSH: thyroid-stimulating hormone

TABLE 1. Personality traits of PCOS patients and healthy controls as measured by the variables

Variables	Odds ratio (age-adjusted)	95% CI	P-value	Odds ratio (BMI-adjusted)	95% CI	P-value
LDL	1.01	0.99–1.03	0.16	1.00	0.99–1.02	0.38
HDL	0.95	0.89–1.02	0.18	0.96	0.91–1.02	0.30
Cholesterol	1.01	1.01–1.027	0.04	1.00	0.99–1.01	0.25
FBS	1.00	0.96–1.04	0.84	0.97	0.94–1.01	0.16
TG	1.00	0.99–1.01	0.18	1.001	0.99–1.00	0.67

CI: confidence interval; BMI: body mass index; HDL: high density lipoprotein; LDL: low density lipoprotein; FBS: fasting blood sugar; TG: triglycerides

TABLE 2. Relationship between PCOS and serum lipid profile following correction for age and BMI

bles were compared using the Chi-square test or Fisher's exact test, as appropriate, and continuous variables were analyzed using the independent t-test for normally distributed data or the Mann–Whitney U test for non-normal data.

To explore associations between independent variables and the primary outcome (presence of NAFLD), univariate logistic regression was first applied to identify candidate predictors ($p < 0.1$), followed by multivariate logistic regression to adjust for potential confounders and identify independent risk factors. The results of regression models are presented as odds ratios (ORs) with 95% confidence intervals (CIs). All statistical analyses were conducted using SPSS (version 26), and a two-sided p-value < 0.05 was considered statistically significant.

Ethical considerations

The Research Council of Ahvaz Jundishapur University of Medical Sciences authorized the study technique and the university's Ethics Committee produced an ethics code. The anonymity of participants was assured during the research in compliance with the standards established in the Declaration of Helsinki. The decoded information was available solely to members of the research team.

RESULTS

Women in the PCOS group were significantly younger than those in the control group (26.7 ± 7.4 *vs* 32.9 ± 4.7 years, P = 0.001). As shown in Table 1, those with PCOS exhibited a notably higher mean BMI (22.4 ± 1.2 *vs* 21.7 ± 1.1, P < 0.001) than controls.

Among the PCOS cohort, 61.3% of subjects had normal fatty liver, 32.0% presented with grade 1 fatty liver and 6.7% were classified with grade 2 fatty liver, based on the severity distribution of fatty liver. Conversely, the control group had a normal distribution: 20% grade 1 and 1.3% grade 2 fatty liver (P = 0.04).

The metabolic indices showed that the PCOS group had significantly lower fasting blood glucose (FSB) levels (92.4 ± 10.6 *vs* 95.9 ± 8.6 mg/dL, P = 0.029) as compared to the control conditions. There were no statistically significant changes (P>0.05) for the other metrics, including total cholesterol, HDL, triglycerides and LDL, between the two groups (Table 1).

As shown in Table 1, liver enzyme activities, including ALT, AST and alkaline phosphatase (ALKPH), did not differ significantly between the two groups (P > 0.05).

Table 1 further exhibits no significant changes (P > 0.05) in hematologic and hormonal measures such as mean hemoglobin levels, platelet counts, vitamin D levels and thyroid-stimulating hormone (TSH) levels.

Logistic regression research indicated that, after adjusting for age, total cholesterol remained significantly associated with PCOS (OR = 1.01, 95% CI 1.01-1.027, P = 0.04). No supplementary variables exhibited statistically significant associations. There was no significant correlation between PCOS and any metabolic markers after controlling for body mass index (Table 2). After further adjustment for BMI, this association was no longer significant, suggesting that BMI may mediate the relationship between cholesterol levels and PCOS status.

DISCUSSION

Polycystic ovary syndrome is a complicated hormonal imbalance that impacts a large percentage of reproductive-aged women. One of these effects is NAFLD, the most widespread liver condition worldwide. The exact pathophysiological mechanisms underlying the link between PCOS and NAFLD remain unidentified. The higher prevalence of NAFLD in non-obese women with PCOS likely reflects factors beyond obesity. Insulin resistance, common in PCOS even in lean women, increases free fatty acid flux to the liver and promotes hepatic fat accumulation (13). Hyperandrogenism may also contribute by altering lipid metabolism and promoting low-grade inflammation (14). Together, these mechanisms suggest that endocrine and metabolic dysregulation inherent to PCOS can drive hepatic steatosis independent of BMI.

In the present study, the PCOS group was significantly younger than the control group, which may have important implications for interpreting our findings. Age is a known determinant of metabolic risk and hepatic fat accumulation, with older age generally associated with higher insulin resistance, dyslipidemia and NAFLD prevalence. Therefore, the younger age of women with PCOS may have mitigated some metabolic differences between groups, potentially underestimating the magnitude of certain risk factors. To account for this, regression analyses were adjusted for age, allowing us to identify independent associations between PCOS status and metabolic or hepatic outcomes. These adjustments confirmed that the higher prevalence of NAFLD in non-obese PCOS women was not solely attributable to age differences. Nevertheless, the age discrepancy remains a limitation and future studies should aim to match participants more closely by age to isolate the effect of PCOS on metabolic and hepatic parameters more precisely.

The current research was designed to assess the prevalence of NAFLD among non-obese women with PCOS, using healthy women from infertility clinics as a reference population. The data demonstrated that BMI values were significantly greater in the PCOS group than the control one, which was consistent with the results of Rocha *et al*, who similarly found elevated BMI levels in women with PCOS compared to healthy participants (15).

The findings of present study indicated a correlation among PCOS and an increased likelihood of developing NAFLD, even in women without obesity. Two studies conducted by Rocha and Romanowski found a significantly higher incidence of NAFLD in women with PCOS than

those in the healthy group (15, 16). In line with these findings, Qu *et al* (17) also documented a greater frequency of NAFLD among women with PCOS.

The metabolic indices in our study showed that individuals with PCOS had significantly lower FBS levels than the control group. On the other hand, the levels of total cholesterol, triglycerides, LDL and HDL were not substantially different between the two sets of data. According to these results, lipid profile changes in this group might not be caused by PCOS alone. Nevertheless, additional research is needed to determine whether the observed discrepancy in FBS is indicative of metabolic abnormalities in PCOS individuals. Interestingly, FBS was slightly lower in the PCOS group compared with controls. This finding may reflect compensatory hyperinsulinemia commonly observed in PCOS, which helps maintain normoglycemia despite underlying insulin resistance. Additionally, the younger age of women in the PCOS group could contribute to more efficient glucose metabolism. These factors, along with the generally non-obese status of participants, may explain the observed lower FBG, highlighting the complex metabolic profile of non-obese women with PCOS (18).

There were no significant differences in serum levels of liver enzymes (AST, ALT and ALP) between the two cohorts, which was consistent with the observations made by Cappello *et al* (19). This may be attributed to the selection of non-obese women and the relatively limited study population, suggesting that early-stage or less severe hepatic disorders may present without a marked elevation in liver enzymes.

Likewise, hemoglobin, platelet count, vitamin D and TSH levels exhibited no significant variations between the groups. The results demonstrate that, within this population, PCOS did not significantly affect hematopoiesis, coagulation status, vitamin D levels, or thyroid function.

The significant age difference between groups highlights the importance of adjusting for potential confounders in interpreting our findings. After accounting for age in logistic regression analysis, the only variable significantly associated with PCOS status was total cholesterol. Thus, greater total cholesterol levels were linked to a higher chance of PCOS. Total cholesterol was associated with PCOS, but this link vanished after controlling for BMI. This suggests that BMI is a mediating variable and an important contributor to the metabolic changes associated with PCOS. These findings underscore the complex interplay of age, BMI and metabolic risk factors in non-obese women with PCOS.

Several studies have linked obesity, increased ALT, elevated fasting insulin and insulin resistance to a higher probability of NAFLD among women diagnosed with PCOS. Furthermore, elevated fasting glucose concentrations have been identified as a critical factor contributing to hepatic damage associated with PCOS, as highlighted by Paradis *et al* (20). Consistent with these findings, the current study emphasizes the significance of tracking body mass index and metabolic indices in PCOS patients who are not overweight.

Contrary to the findings by the current research, other research indicated that patients with PCOS exhibited markedly increased levels of ALT, AST and triglycerides (21). Possible causes of these variances include variations in diagnostic criteria, study populations, or sample sizes.

This study has some important limitations. The case-control design precludes any conclusions about causality between PCOS and NAFLD, due to probably improper selection related to the control group. Moreover, the diagnosis of NAFLD relied on abdominal ultrasonography, which, although non-invasive and widely used, may have limited sensitivity for detecting mild hepatic steatosis and cannot assess fibrosis accurately. Future longitudinal studies using more sensitive imaging modalities, such as MRI or transient elastography, are warranted to confirm and extend our findings. Furthermore, due to its single-center design, small sample size and significant differences in BMI between groups, this study has several important limitations. For a fuller view, it may be necessary to assess additional hormonal, inflammatory and metabolic variables. Using women with male-factor infertility as the control group may introduce selection bias, as these individuals were recruited from fertility clinics and may not fully represent the general population of healthy women. This limitation should be considered when interpreting the comparative findings of the study. Better clarification of the independent involvement of PCOS in hepatic and metabolic problems could be achieved by future research with multicenter designs and bigger more diverse populations.

CONCLUSION

The prevalence of mild to moderate fatty liver disease was higher in non-obese women with PCOS compared with controls. Fasting blood glucose was slightly lower in the PCOS group, while other metabolic, liver, hematologic and hormonal parameters did not differ significantly. Age-adjusted regression showed a small association between total cholesterol and PCOS, which became non-significant after controlling for BMI. These findings highlight the influence of BMI and age on metabolic profiles in non-obese women with PCOS. ❑

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References

1. **Akbarzadeh Morshedi M, Mohammadi M, Aminianfar A.** The effects of phytoestrogen consumption on polycystic ovary syndrome: A systematic review. *KAUMS* 2025;29:109.
2. **Bozdag G, Mumusoglu S, Zengin D, et al.** The prevalence and phenotypic features of polycystic ovary syndrome: a systematic review and meta-analysis. *Human Reproduction* 2016;31:2841-2855.
3. **Wu Z, Liang G, Zhang Y, et al.** Risk Factors for Metabolically Dysfunctional-Associated Steatotic Liver Disease in Patients With Polycystic Ovary Syndrome in East Asia: A Review and Meta-Analysis. *Endocrine Practice* 2025;31:668-676.
4. **Yang Y, Liu L, Hu N, et al.** Analysis of risk factors for depression and anxiety in women with polycystic ovary syndrome. *Frontiers in Global Women's Health* 2025;6:2025.
5. **Teng MLP, Ng CH, Huang DQ, et al.** Global incidence and prevalence of nonalcoholic fatty liver disease. *Clin Mol Hepatol* 2023;29(Suppl):S32-S42.
6. **Allen AM, Therneau TM, Ahmed OT, et al.** Clinical course of non-alcoholic fatty liver disease and the implications for clinical trial design. *J Hepatol* 2022;77:1237-1245.
7. **Pierantonelli I, Svegliati-Baroni G.** Nonalcoholic Fatty Liver Disease: Basic Pathogenetic Mechanisms in the Progression From NAFLD to NASH. *Transplantation* 2019;103:e1-e13.
8. **Younossi ZM, Golabi P, Paik JM, et al.** The global epidemiology of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH): a systematic review. *Hepatology* 2023;77:1335-1347.
9. **Shengir M, Chen T, Guadagno E, et al.** Non-alcoholic fatty liver disease in premenopausal women with polycystic ovary syndrome: A systematic review and meta-analysis. *JGH Open* 2021;5:434-445.
10. **Kim JJ, Kim D, Yim JY, et al.** Polycystic ovary syndrome with hyperandrogenism as a risk factor for non-obese non-alcoholic fatty liver disease. *Aliment Pharmacol Ther* 2017;45:1403-1412.
11. **Rathi A, Goswami D, Garg A, et al.** Prevalence and predictors of non-alcoholic fatty liver disease (NAFLD) and metabolic dysfunction-associated fatty liver disease (MAFLD) in Indian women with polycystic ovarian syndrome. *J Obstet Gynaecol Res* 2025;51:e16335.
12. **Sarkar M, Terrault N, Duwaerts CC, et al.** The Association of Hispanic Ethnicity with Nonalcoholic Fatty Liver Disease in Polycystic Ovary Syndrome. *Curr Opin Gynecol Obstet* 2018;1:24-33.
13. **Baranova A, Tran TP, et al.** Systematic review: association of polycystic ovary syndrome with metabolic syndrome and non-alcoholic fatty liver disease. *Aliment Pharmacol Ther* 2011;33:801-814.
14. **Mathur P, Kottilil S, Wilson E.** Sofosbuvir/velpatasvir/voxilaprevir: a highly effective option for retreatment of hepatitis C in difficult-to-treat patients. *Antivir The.* 2019;24:1-10.
15. **Rocha ALL, Faria L, Guimarães T, et al.** Non-alcoholic fatty liver disease in women with polycystic ovary syndrome: systematic review and meta-analysis. *J Endocrinol Invest* 2017;40:1279-1288.
16. **Romanowski MD, Parolin MB, Freitas AC, et al.** Prevalence of non-alcoholic fatty liver disease in women with polycystic ovary syndrome and its correlation with metabolic syndrome. *Arq Gastroenterol* 2015;52:117-123.
17. **Qu Z, Zhu Y, Jiang J, et al.** The clinical characteristics and etiological study of nonalcoholic fatty liver disease in Chinese women with PCOS. *Iran J Reprod Med* 2013;11:725-732.
18. **Misra S, Gada J, Dhole C, et al.** Comparative Study of Insulin Sensitivity and Resistance and Their Correlation with Androgens in Lean and Obese Women with Polycystic Ovary Syndrome. *Reprod Sci* 2024;31:754-763.
19. **Cappello M, Randazzo C, Bravatà I, et al.** Liver Function Test Abnormalities in Patients with Inflammatory Bowel Diseases: A Hospital-based Survey. *Clin Med Insights Gastroenterol* 2014;7:25-31.
20. **Paradis V, Perlemuter G, Bonvoust F, et al.** High glucose and hyperinsulinemia stimulate connective tissue growth factor expression: a potential mechanism involved in progression to fibrosis in nonalcoholic steatohepatitis. *Hepatology* 2001;34(4 Pt 1):738-744.
21. **Setji TL, Holland ND, Sanders LL, et al.** Nonalcoholic steatohepatitis and nonalcoholic Fatty liver disease in young women with polycystic ovary syndrome. *J Clin Endocrinol Metab* 2006;91:1741-1747.