sciendo

ENDOCRINE REGULATIONS, Vol. 58, No. 2, 83–90, 2024

doi:10.2478/enr-2024-0009

Association of lipid profile and obesity in patients with polycystic ovary syndrome

Sadaf Parveen [1], Saba Khan [1], Mohammad Mustufa Khan [2], Bhavana Gupta [3], Ausaf Ahmad [4], Roshan Alam [1]

[1]Department of Biochemistry, Integral Institute of Medical Sciences & Research (IIMSR), Integral University, Lucknow, Uttar Pradesh- 226026, India; [2]Department of Basic Medical Sciences, Integral Institute of Allied Health Sciences & Research (IIAHSR), Integral University, Lucknow, Uttar Pradesh-226026, India; [3]Department of Obstetrics and Gynaecology, Integral Institute of Medical Sciences & Research (IIMSR), Integral University, Lucknow, Uttar Pradesh-226026, India; [4]Department of Community Medicine, Integral Institute of Medical Sciences & Research (IIMSR), Integral University, Lucknow, Uttar Pradesh-226026, India
E-mail: profroshanalam@gmail.com

Objective. Abnormal lipid profile and obesity increase the risk of polycystic ovary syndrome (PCOS). PCOS patients may have a greater risk of infertility, metabolic syndrome (MetS) and cardiovascular disease (CVD) due to abnormal lipid profile and obesity. The aim of the study was to find the association between abnormal lipid profile and obesity in patients with PCOS.

Methods. In this case-control study, a total of 102 female subjects (51 diagnosed PCOS and 51 age-matched healthy controls) were enrolled, aged between 20–40 years. Biochemical parameters such as total cholesterol (TC), triglycerides (TG), low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), very low-density lipoprotein-cholesterol (VLDL-C), luteinizing hormone (LH), and follicle-stimulating hormone (FSH) were estimated. Anthropometric parameters such as body mass index (BMI), waist circumference (WC), hip circumference (HC), and waist-to-hip ratio (WHR) were recorded. A $p<0.05$ was considered statistically significant.

Results. Mean of BMI, WC, WHR, LH, FSH, TC, TG, LDL-C, and VLDL-C was found significantly elevated in patients with PCOS as compared to controls ($p<0.01$). However, the mean of HDL-C was found significantly reduced in patients with PCOS as compared to controls ($p<0.01$). BMI has shown a significant positive correlation with WC ($r=0.562$, $p<0.01$) and WHR ($r=0.580$, $p<0.01$) among PCOS patients. LH has shown a significant positive correlation with FSH ($r=0.572$, $p<0.01$) among PCOS patients. TC has shown a significant positive correlation with TG ($r=0.687$, $p<0.01$), LDL-C ($r=0.917$, $p<0.01$), and VLDL-C ($r=0.726$, $p<0.01$) among PCOS patients.

Conclusion. The results showed that abnormal lipid profile and obesity have a significant association with PCOS patients. Regular monitoring and treatment of PCOS patients are required to reduce the risk of infertility, MetS, and CVD.

Key words: body mass index, lipid profile, polycystic ovarian syndrome, waist circumference

Polycystic ovarian syndrome (PCOS) is a common endocrine condition that affects 6–22% of women worldwide (Stener-Victorin and Deng 2021; Zhu et al. 2021). Its primary symptoms include ovulatory dysfunction, hyperandrogenism, and polycystic changes in the ovaries (Mimouni et al. 2021). Due to the improper functioning of reproductive hormones such as luteinizing hormone (LH), follicle-stimulating hormone (FSH), estrogen, and testosterone, the normal menstrual cycle is disrupted, resulting in

Corresponding author: Dr. Roshan Alam, Professor & Head, Department of Biochemistry, Integral Institute of Medical Sciences & Research (IIMSR), Integral University, Lucknow, Uttar Pradesh-226026, India; e-mail: drroshan@iul.ac.in; profroshanalam@gmail.com.

irregularities, like oligomenorrhea and amenorrhea. This multifaceted syndrome primarily affects adolescents, who are predisposed to developing a range of comorbidities such as obesity, type 2 diabetes, infertility, cardiovascular disorders, and mental disorders (El Hayek et al. 2016).

Obesity, one of the major modifiable risk factors for cardiometabolic disease, frequently co-occurs with PCOS: around half of those with PCOS women are obese (Glueck et al. 2005; Rojas et al. 2014). However, there is no clear evidence that obesity causes PCOS (Legro 2012). Obesity and PCOS are both associated with an increased risk of metabolic syndrome (MetS) and cardiovascular disease (CVD), however, there is conflicting data about whether these are separate correlations (Karabulut et al. 2012). Insulin clamp investigations have revealed that women with PCOS exhibit intrinsic insulin resistance that is independent of weight. This implies a greater risk of type 2 diabetes, even in the absence of obesity (Cassar et al. 2016). This insulin resistance has a significant impact on the phenotype of PCOS patients and may play a dominant role in the physiopathology of hyperandrogenism, persistent anovulation, and the metabolic system. Obesity is linked to infertility, MetS, and an increased risk of CVD (Costa et al. 2012). A study found that obese women with PCOS were more likely to develop hyperandrogenism, insulin resistance, hypercholesterolemia, hypertriglyceridemia, and elevated reactive protein C (CRP) compared to women with normal weight (Baldani et al. 2012).

Dyslipidemia is becoming more common in young adult women with PCOS (Wekker et al. 2020). Several retrospective and prospective studies have shown an increased risk of coronary atherosclerotic cardiopathy in PCOS patients (Mani et al. 2013; Gunning and Fauser 2017; Anagnostis et al. 2018). However, not much research has been done on the effects of endocrine diseases and metabolic abnormalities on lipid profiles in PCOS patients. Hyperandrogenism, insulin resistance, impaired glucose metabolism, and obesity all have independent and interrelated effects on circulating lipid profiles, and the underlying mechanism needs further explanation.

In this study, we aimed to determine the association between abnormal lipid profile and obesity in patients with PCOS.

Materials and Methods

Subjects. This case-control study was conducted in the Department of Biochemistry, Integral Institute of Medical Sciences and Research (IIMSR), Integral University, Lucknow in association with the Department of Obstetrics and Gynaecology, IIMSR, Integral University, Lucknow. All procedures performed in the study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (IEC Approval No. IEC/IIMS&R/2022/74) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

A total of 102 female subjects between the age of 20–40 years were divided equally into two groups: 51 women diagnosed with PCOS and 51 age-matched healthy controls. All participants who met the inclusion criteria provided informed written consent, and institutional ethics review committee approval was obtained prior to the commencement of the study. The women's medical history, including their chief complaints, presenting illness, demographic information, menstrual history, obstetric, past medical and surgical history, and personal history, were documented in detail. Additionally, a general physical examination was conducted, with a focus on identifying features of hirsutism, acne, and acanthosis nigricans.

Inclusion criteria for cases. All female participants of age group 20–40 years who meet the Rotterdam criteria, 2003 like oligomenorrhea/anovulation, clinical and/or biochemical signs of hyperandrogenism and polycystic ovaries were included.

Inclusion criteria for selection of controls. Regular menstrual cycle, no menstrual abnormalities, absence of hirsutism, alopecia, and acne age-matched control for case.

Exclusion criteria. Women under treatment for diabetes mellitus, renal diseases, thyroid disorders, hypertension, cardiovascular diseases, pregnant or lactating women, women on drugs, like oral contraceptives or lipid-lowering drugs, hypoglycemic agents and hormonal medicines, within six weeks were excluded from the study. None of the subjects were alcoholics or smokers.

Sample collection. Venous blood samples of 3 ml were collected in a plain vial after 12 h of overnight fasting to investigate biochemical and endocrine parameters. The samples were then centrifuged to separate the serum.

Endocrine parameters. Serum LH and FSH levels were measured using commercially available Human LH ELISA kit (Calbiotech, Catalog No.: LH231F) and Human FSH ELISA kit (Calbiotech, Catalog No.: FS232F). A sensitivity for LH and FSH ELISA kits was 3.1 mIU/ml and 5 mIU/ml, respectively.

Biochemical parameters. The lipid profile was analyzed using commercially available ERBA kits and the Erba chem7semiautoanalyzer. High-density lipoprotein-cholesterol (HDL-C) was measured directly, whereas low-density lipoprotein-cholesterol (LDL-C) and very low-density lipoprotein-cholesterol (VLDL-C) were calculated using the Friedewald equation:

LDL-C = Total cholesterol – [HDL-C + (0.46 × triglycerides)] (Prajapati 2023).

The values are expressed in mg/dL. According to the Adult Treatment Panel III, LDL-C levels below 100 mg/dL are considered optimal, while levels between 100–129 mg/dL are considered near optimal. For triglycerides (TG), levels below 150 mg/dL are normal, while for total cholesterol (TC), levels below 200 mg/dL are desirable. For women, HDL-C levels equal to or greater than 50 mg/dL are considered normal.

In dyslipidemia, LDL-C levels are categorized as borderline high (130–150 mg/dL), high (160–189 mg/dL), and very high (greater than or equal to 190 mg/dL). Similarly, TG levels are categorized as borderline high (150–199 mg/dL), high (200–499 mg/dL), and very high (greater than 500 mg/dL). Additionally, TC levels are categorized as borderline high (200–239 mg/dL) or high (greater than or equal to 240 mg/dL). In women, HDL-C levels below 50 mg/dL are considered a risk factor (Cheung et al. 2008).

Anthropometric parameters. Anthropometric measurements were taken in all participants. Body weight was measured using the same calibrated digital scale and height was also measured by a standard stadiometer with the participant wearing no shoes. Body mass index (BMI) was calculated using the most recent weight (kg) documented in the medical record divided by the height (m^2). Cut-off values for underweight BMI <18.5kg/m^2, normal weight 18.5–22.9 kg/m^2, overweight 23–24.9 kg/m^2, and obese, ±25 kg/m^2 (Khan et al. 2017).

Waist circumference (WC) was measured using flexible tapes on a horizontal plane, midway between the lower border of the ribs and the iliac crest. Hip circumference (HC) was taken in cm around the widest portion of the buttocks, with tape parallel to the floor. The threshold cut-off values adapted for BMI were ≥25 kg/m^2 for overweight and ≥30 kg/m^2 for obesity, WC ≥80 cm, waist hip ratio (WHR/WHIPR) ≥0.85 (Status 1995).

Statistical analysis. Statistical analysis was performed using the Statistical Package for the Social Sciences trial version 20.0 software (SPSS Inc., Chicago, IL, United States) and MS Excel 2007 spreadsheet. Pearson's correlation coefficient was calculated to see the correlation between anthropometric parameters and lipid profile. For all statistical analyses, p-value <0.05 was considered statistically significant.

Results

Mean values of BMI, WC, WHR, LH, FSH, TC, TG, LDL-C, and VLDL-C were found significantly elevated in patients with PCOS compared to controls (p<0.01). However, the mean value of HDL-C was found significantly reduced in patients with PCOS compared to controls (p<0.01) (Table 1).

BMI showed a significant positive correlation with WC (r=0.562, p<0.01) and WHR (r=0.580, p<0.01) among PCOS patients (Figure 1A). WC showed a significant positive correlation with HC (r=0.747, p<0.01) and WHR (r=0.513, p<0.01) among PCOS patients. LH showed a significant positive correlation with FSH (r=0.572, p<0.01) among PCOS patients (Figure 1B). TC showed a significant positive correlation with TG (r=0.687, p<0.01), LDL-C (r=0.917, p<0.01), and VLDL-C (r=0.726, p<0.01) among PCOS patients. Similarly, TG showed a significant positive correlation with LDL-C (r=0.441,

Table 1
Baseline characteristics of cases and controls

Parameters	Case (n=51)	Control (n=51)	p-value
Age (years)	23.90±3.69	24.41±3.92	0.5003
BMI (kg/m^2)	25.04± 3.50	23.07 ± 2.51	0.0015*
WC (cm)	79.74 ± 10.76	71.08 ± 8.17	0.0429*
HC (cm)	99.01±12.89	91.56±9.16	0.0011*
WHR (cm)	0.80±0.06	0.76±0.07	0.0025*
LH (mIU/ml)	14.97±2.30	6.41±2.31	0.0001*
FSH (mIU/ml)	6.05±0.90	5.36±1.43	0.0044*
TC (mg/dL)	220.97±55.62	140±36.93	0.0001*
TG (mg/dL)	155.46±43.07	136.13±34.16	0.0108*
LDL-C (mg/dL)	102.2±46.14	66.15±32.05	0.0001*
HDL -C(mg/dL)	46.02± 9.46	53.82±9.24	0.0001*
VLDL-C (mg/dL)	33.55±13.09	28.23± 9.09	0.0190*

Abbreviations: BMI – body mass index; HC – hip circumference; HDL-C – high-density lipoprotein-cholesterol; LDL-C – low-density lipoprotein-cholesterol; TC – total cholesterol; TG – triglyceride, VLDL-C – very low-density lipoprotein-cholesterol; WC – waist circumference; WHR – waist-to-hip ratio. Data are represented as mean±SD (standard deviation). *p<0.05 was considered statistically significant.

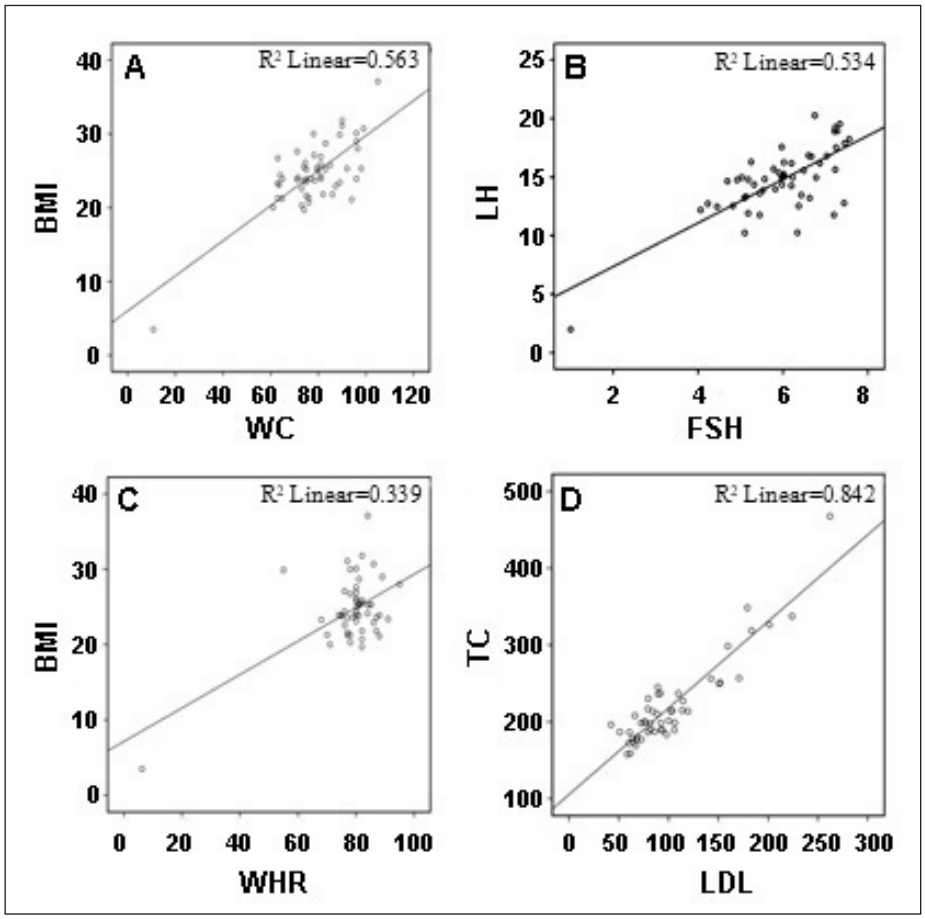

Figure 1. Correlation between **(A)** body mass index (BMI) and waist circumference (WC), **(B)** luteinizing hormone (LH) and follicle-stimulating hormone (FSH), **(C)** BMI and waist-to-hip ratio (WHR), and **(D)** total cholesterol (TC) and low-density lipoprotein-cholesterol (LDL-C).

Table 2
Correlation of anthropometric and biochemical parameters among PCOS patients

Parameters	BMI	WC	HC	WHR	LH	FSH	TC	TG	HDL-C	LDL-C	VLDL-C
BMI	1	0.562**	**0.580****	0.063	–0.200	0.039	0.065	–0.078	0.120	0.120	–0.082
WC		1	**0.747****	0.513**	–0.201	0.093	–0.113	0.007	0.171	–0.150	–0.031
HC			1	–0.173	–0.076	0.110	–0.122	–0.145	0.155	–0.114	–0.136
WHR				1	–0.220	–0.009	–0.028	0.206	0.072	–0.105	0.132
LH					1	**0.572****	0.015	0.005	–0.030	0.041	–0.011
FSH						1	–0.040	–0.157	0.025	–0.011	–0.122
TC							1	0.687**	0.080	**0.917****	**0.726****
TG								1	0.057	**0.441****	**0.918****
HDL-C									1	–0.073	–0.048
LDL-C										1	0.500**
VLDL-C											1

Abbreviations: BMI – body mass index; FSH – follicle-stimulating hormone; HC – hip circumference; HDL-C – high-density lipoprotein-cholesterol; LDL-C – low-density lipoprotein-cholesterol; LH – luteinizing hormone; PCOS – polycystic ovarian syndrome; TC – total cholesterol; TG – triglyceride; VLDL-C – very low-density lipoprotein-cholesterol; WC – waist circumference; WHR – waist-to-hip ratio. **Correlation is significant at the 0.01 level (2-tailed).

p<0.01) and VLDL-C (r=0.918, p<0.01) among PCOS patients. LDL-C showed a significant positive correlation with VLDL-C (r=0.500, p<0.01) among PCOS patients, as shown in Table 2.

Discussion

PCOS is a lifelong multisystem condition that causes reproductive and metabolic symptoms (Kaluzna et al. 2022). MetS is a condition characterized by dyslipidemia and obesity (Teede et al. 2018). Irrespective of BMI, lipid abnormalities are common in PCOS patients (Vekic et al. 2019).

The results of this study demonstrate that patients with PCOS have significantly higher levels of TC, TG, LDL-C, and VLDL-C, and significantly lower levels of HDL-C, compared to healthy individuals (p<0.01). This suggests that patients with PCOS are at an increased risk of developing CVD and associated mortality in the future. Dyslipidemia, which is characterized by elevated levels of LDL-C and decreased levels of HDL-C, is an independent risk factor for atherosclerosis in patients with PCOS. Insulin resistance is the key factor in the pathophysiology of PCOS and is associated with increased adiposity and the development of MetS (Wild et al. 2011).

The study results indicate that patients with PCOS have elevated levels of TC, TG, and LDL-C, and low levels of HDL-C, which supports the findings of previous studies which indicated that dyslipidemia is prevalent in women with PCOS (Naidu et al. 2013; Kumar et al. 2016). Furthermore, several studies have suggested that the TG/HDL-C and TC/HDL-C ratios in PCOS women are excellent preliminary predictors of insulin resistance (Kheirollahi et al. 2020). The correlation of TC with LDL-C in the patient group showed a significant positive correlation (r=0.842, p<0.01) (Figure 1D). Young women with PCOS have an increased risk of dyslipidemia and MetS. The link between PCOS and MetS could be due to both inherent insulin resistance, which is part of the pathophysiology of PCOS, and lifestyle-related insulin resistance, which is linked to an increased risk of overweight/obesity in PCOS (Cooney and Dokras 2018).

Hyperinsulinemia is the root cause of excess androgens since insulin directly mimics the action of LH and indirectly raises gonadotropin-releasing hormone (GnRH) (Puttabyatappa and Padmanabhan 2018). Lower sex hormone-binding globulin (SHBG) levels result in higher levels of free androgens, which cause clinical symptoms such as hirsutism, alopecia, and acne (Rojas et al. 2014). Insulin resistance can lead to dyslipidemia, and PCOS patients are at a higher risk of CVD and diabetes (McCartney and Marshall 2016; Bulsara et al. 2021). The prevalence of PCOS in women with type 1 diabetes is 19%, 37%, and 41% according to NIH criteria, AE-PCOS definition, and ESHRE/ASRM criteria, respectively (Escobar-Morreale and Roldan-Martin 2016). In a recent analysis of 41 studies, the increased risk of MetS persisted in studies that were age- and BMI-matched or adjusted for age and BMI (OR 2.6, 95% CI 1.3–5.5; 11 studies; PCOS: n=2,033) (Behboudi-Gandevani et al. 2018).

Although there is sufficient data that indicates an elevated risk of subclinical atherosclerosis in women of reproductive age, the prevalence of CVD events must be determined to counsel women and implement prevention methods. Several meta-analyses have been conducted to investigate the relationship between PCOS and the risk of myocardial infarction or stroke (Anderson et al. 2014; Zhao et al. 2016). A recent study compared the incidence of stroke and myocardial infarction among women with PCOS and control women (PCOS: n=136; age>45 years). The study found no significant differences between the two groups in terms of stroke or myocardial infarction. However, it should be noted that the diagnostic criteria for PCOS included obesity and infertility, which limits the generalizability of the findings (Lunde and Tanbo 2007).

Obesity has been linked to abnormalities in the hypothalamic-pituitary-ovarian (HPO) axis function, leading to PCOS (Legro 2012). In our study and other investigations (Yuan et al. 2016; Kaluzna et al. 2020), PCOS women had higher BMI compared to control groups. Obesity is also associated with hyperinsulinemia, which increases the lipid profile and glucose intolerance in PCOS patients. After analyzing the correlation of BMI with anthropometric parameters of the case group, we found that there is a significant association between BMI and WC (r=0.563, p<0.01) as well as WHR (r=0.339, p<0.01) among women with PCOS (Figures 1A, B). The WC and waist-to-hip ratio (WHTR) have been found to predict lipid abnormalities and MetS in Brazilian women with PCOS (Costa et al. 2012). A study found that American women with PCOS had higher BMI and lipid profiles than Italian women (Essah et al. 2008).

Women with PCOS having high WC and WHTR were found to be linked to composite CVD risk variables (Gateva and Kamenov 2012). Another study found that women with PCOS commonly experience obesity and lipid abnormalities similar to the present findings (Thathapudi et al. 2014). Variations in body

weight and composition may not entirely explain the disparities in dyslipidemia among women with PCOS from various racial and geographical backgrounds. These discrepancies are likely to be caused by environmental and genetic factors, such as diet and physical activity level. In trials conducted by Crosignani et al. (2003), a low-calorie diet and physical exercise promoted weight loss in women with PCOS, which was associated with significant improvement in anthropometric parameters.

The condition of obesity leads to an increase in androgen production by activating LH, which leads to a state of hyperandrogenism (Glueck and Goldenberg 2019). Leptin, which is an adipokine that controls appetite, has a direct impact on the neuroendocrine and reproductive function of women with PCOS who are also obese (Barber et al. 2006; Rojas et al. 2014). Moreover, elevated levels of leptin have been associated with a decrease in ovarian follicular growth (Barber et al. 2006; Rojas et al. 2014).

The study found that patients with PCOS have significantly higher levels of LH and FSH compared to healthy individuals ($p<0.01$). This could be due to the overproduction of androgens caused by the malfunctioning of the theca cells and/or the HPO axis. Hyperandrogenism leads to abnormal GnRH pulsation and gonadotropin secretion through the faulty negative or positive feedback of progesterone and estrogen.

The abnormal gonadotropin secretion is characterized by a high LH/FSH ratio, which causes ovarian dysfunction and the hypersecretion of androgens. Furthermore, women with PCOS have high levels of anti-Müllerian hormone (AMH), which is secreted by pre-/small antral follicles that accumulate in the ovaries. This high concentration of AMH worsens ovarian dysfunction by negatively affecting the follicular microenvironment and/or GnRH pulsation (Harada 2022). Women with PCOS have AMH levels that are two to three times higher than non-PCOS women, and the increased AMH level is correlated with the severity of PCOS (Sahmay et al. 2018).

Conclusion

The study found a significant association between lipid profile and obesity in patients with PCOS. It is recommended to regularly monitor and treat PCOS patients to reduce the risk of infertility, MetS, and CVD. Early treatment of dyslipidemia and obesity should be prioritized to prevent future cardiometabolic complications in women with PCOS.

Acknowledgement

We are grateful to Prof. (Dr.) Abha Chandra, Dean, Integral Institute of Medical Sciences & Research (IIMSR), Integral University, Lucknow, India-226026 for the invaluable help and suggestions to write this article without any hindrance. I would like to acknowledge Integral University, Lucknow, India (IU/R&D/2024-MCN0002400).

Conflict of interest: *The authors declared no conflict of interest.*

References

Anagnostis P, Tarlatzis BC, Kauffman RP. Polycystic ovarian syndrome (PCOS): Long-term metabolic consequences. Metabolism 86, 33–43, 2018.

Anderson SA, Barry JA, Hardiman PJ. Risk of coronary heart disease and risk of stroke in women with polycystic ovary syndrome: a systematic review and meta-analysis. Int J Cardiol 176, 486–487, 2014.

Baldani DP, Skrgatic L, Goldstajn MS, Zlopasa G, Oguic SK, Canic T, Piljek AN. Clinical and biochemical characteristics of polycystic ovary syndrome in Croatian population. Coll Antropol 36, 1413–1418, 2012.

Barber TM, McCarthy MI, Wass JA, Franks S. Obesity and polycystic ovary syndrome. Clin Endocrinol (Oxf) 65, 137–145, 2006.

Behboudi-Gandevani S, Amiri M, Bidhendi Yarandi R, Noroozzadeh M, Farahmand M, Rostami Dovom M, Ramezani Tehrani F. The risk of metabolic syndrome in polycystic ovary syndrome: A systematic review and meta-analysis. Clin Endocrinol (Oxf) 88, 169–184, 2018.

Bulsara J, Patel P, Soni A, Acharya S. A review: Brief insight into polycystic ovarian syndrome. Endocr Metab Sci 3, 100085, 2021.

Cassar S, Misso ML, Hopkins WG, Shaw CS, Teede HJ, Stepto NK. Insulin resistance in polycystic ovary syndrome: a systematic review and meta-analysis of euglycaemic–hyperinsulinaemic clamp studies. Hum Reprod 31, 2619–2631, 2016.

Cheung LP, Ma RC, Lam PM, Lok IH, Haines CJ, So WY, Tong PC, Cockram CS, Chow CC, Goggins WB. Cardiovascular risks and metabolic syndrome in Hong Kong Chinese women with polycystic ovary syndrome. Hum Reprod 23, 1431–1438, 2008.

Cooney LG, Dokras A. Beyond fertility: polycystic ovary syndrome and long-term health. Fertil Steril 110, 794–809, 2018.

Costa EC, Sa JC, Soares EM, Lemos TM, Maranhao TM, Azevedo GD. Anthropometric indices of central obesity how discriminators of metabolic syndrome in Brazilian women with polycystic ovary syndrome. Gynecol Endocrinol 28, 12–15, 2012.

Crosignani PG, Colombo M, Vegetti W, Somigliana E, Gessati A, Ragni G. Overweight and obese anovulatory patients with polycystic ovaries: parallel improvements in anthropometric indices, ovarian physiology and fertility rate induced by diet. Hum Reprod 18, 1928–1932, 2003.

El Hayek S, Bitar L, Hamdar LH, Mirza FG, Daoud G. Polycystic ovarian syndrome: an updated overview. Front Physiol 7, 124, 2016.

Escobar-Morreale HF, Roldan-Martin MB. Type 1 diabetes and polycystic ovary syndrome: systematic review and meta-analysis. Diabetes Care 39, 639–648, 2016.

Essah PA, Nestler JE, Carmina E. Differences in dyslipidemia between American and Italian women with polycystic ovary syndrome. J Endocrinol Invest 31, 35–41, 2008.

Gateva A, Kamenov Z. Anthropometric indices of visceral obesity and cardiovascular risk factors in patients with polycystic ovarian syndrome. In Endocrine Abstracts 29, P900, 2012.

Glueck CJ, Dharashivkar S, Wang P, Zhu B, Gartside PS, Tracy T, Sieve L. Obesity and extreme obesity, manifest by ages 20–24 years, continuing through 32–41 years in women, should alert physicians to the diagnostic likelihood of polycystic ovary syndrome as a reversible underlying endocrinopathy. Eur J Obstet Gynecol Reprod Biol 122, 206–212, 2005.

Glueck CJ, Goldenberg N. Characteristics of obesity in polycystic ovary syndrome: Etiology, treatment, and genetics. Metabolism 92, 108–120, 2019.

Gunning MN, Fauser BCJM. Are women with polycystic ovary syndrome at increased cardiovascular disease risk later in life? Climacteric 20, 222–227, 2017.

Harada M. Pathophysiology of polycystic ovary syndrome revisited: Current understanding and perspectives regarding future research. Reprod Med Biol 21, e12487, 2022.

Kaluzna M, Czlapka-Matyasik M, Wachowiak-Ochmanska K, Moczko J, Kaczmarek J, Janicki A, Piatek K, Ruchala M, Ziemnicka K. Effect of central obesity and hyperandrogenism on selected inflammatory markers in patients with PCOS: a WHtR-matched case-control study. J Clin Med 9, 3024, 2020.

Kaluzna M, Czlapka-Matyasik M, Kompf P, Moczko J, Wachowiak-Ochmanska K, Janicki A, Samarzewska K, Ruchala M, Ziemnicka K. Lipid ratios and obesity indices are effective predictors of metabolic syndrome in women with polycystic ovary syndrome. Ther Adv Endocrinol Metab 13, 20420188211066699, 2022.

Karabulut A, Yaylali GF, Demirlenk S, Sevket O, Acun A. Evaluation of body fat distribution in PCOS and its association with carotid atherosclerosis and insulin resistance. Gynecol Endocrinol 28, 111–114, 2012.

Khan MM, Sonkar GK, Alam R, Mehrotra S, Khan MS, Kumar A, Sonkar SK. Validity of Indian Diabetes Risk Score and its association with body mass index and glycosylated hemoglobin for screening of diabetes in and around areas of Lucknow. J Family Med Prim Care 6, 366–373, 2017.

Kheirollahi A, Teimouri M, Karimi M, Vatannejad A, Moradi N, Borumandnia N, Sadeghi A. Evaluation of lipid ratios and triglyceride-glucose index as risk markers of insulin resistance in Iranian polycystic ovary syndrome women. Lipids Health Dis 19, 235, 2020.

Kumar AN, Naidu JN, Satyanarayana U, Ramalingam K, Anitha M. Metabolic and endocrine characteristics of Indian women with polycystic ovary syndrome. Int J Fertil Steril 10, 22–28, 2016.

Legro RS. Obesity and PCOS: implications for diagnosis and treatment. Semin Reprod Med 30, 496–506, 2012.

Lunde O, Tanbo T. Polycystic ovary syndrome: a follow-up study on diabetes mellitus, cardiovascular disease and malignancy 15-25 years after ovarian wedge resection. Gynecol Endocrinol 23, 704–709, 2007.

Mani H, Levy MJ, Davies MJ, Morris DH, Gray LJ, Bankart J, Blackledge H, Khunti K, Howlett TA. Diabetes and cardiovascular events in women with polycystic ovary syndrome: a 20-year retrospective cohort study. Clin Endocrinol (Oxf) 78, 926–934, 2013.

McCartney ChR, Marshall JC. Polycystic ovary syndrome. N Engl J Med 375, 1398–1399, 2016.

Mimouni NE, Paiva I, Barbotin AL, Timzoura FE, Plassard D, Le Gras S, Ternier G, Pigny P, Catteau-Jonard S, Simon V, Prevot V, Boutillier AL, Giacobini P. Polycystic ovary syndrome is transmitted via a transgenerational epigenetic process. Cell Metabol 33, 513–530, 2021.

Naidu JN, Swapna GN, Kumar AN, Krishnamma M, Anitha M. Importance of elevated insulin resistance, dyslipidemia and status of antioxidant vitamins in polycystic ovary disease. Free Rad Antiox 3, 17–19, 2013.

Prajapati P. A lipid profile study in polycystic ovary syndrome women. Int J Reprod Contracept Obstet Gynecol 12, 234–239, 2023.

Puttabyatappa M, Padmanabhan V. Ovarian and extra-ovarian mediators in the development of polycystic ovary syndrome. J Mol Endocrinol 61, R161–R184, 2018.

Rojas J, Chavez M, Olivar L, Rojas M, Morillo J, Mejias J, Calvo M, Bermudez V. Polycystic ovary syndrome, insulin resistance, and obesity: navigating the pathophysiologic labyrinth. Inter J Reprod Med 2014, 719050, 2014.

Sahmay S, Aydogan Mathyk B, Sofiyeva N, Atakul N, Azemi A, Erel T. Serum AMH levels and insulin resistance in women with PCOS. Eur J Obstet Gynecol Reprod Biol 224, 159–164, 2018.

Status WP. The use and interpretation of anthropometry. WHO technical report series 854, 1995.

Stener-Victorin E, Deng Q. Epigenetic inheritance of polycystic ovary syndrome—Challenges and opportunities for treatment. Nat Rev Endocrinol 17, 521–533, 2021.

Teede HJ, Misso ML, Costello MF, Dokras A, Laven J, Moran L, Piltonen T, Norman RJ; International PCOS Network. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Hum Reprod 33, 1602–1618, 2018.

Thathapudi S, Kodati V, Erukkambattu J, Katragadda A, Addepally U, Hasan Q. Anthropometric and biochemical characteristics of polycystic ovarian syndrome in South Indian women using AES-2006 criteria. Int J Endocrinol Metab 12, e12470, 2014.

Vekic J, Zeljkovic A, Stefanovic A, Jelic-Ivanovic Z, Spasojevic-Kalimanovska V. Obesity and dyslipidemia. Metabolism 92, 71–81, 2019.

Wekker V, van Dammen L, Koning A, Heida KY, Painter RC, Limpens J, Laven JSE, Roeters van Lennep JE, Roseboom TJ, Hoek A. Long-term cardiometabolic disease risk in women with PCOS: a systematic review and meta-analysis. Hum Reprod Update 26, 942–960, 2020.

Wild RA, Rizzo M, Clifton S, Carmina E. Lipid levels in polycystic ovary syndrome: systematic review and meta-analysis. Fertil Steril 95, 1073–1079.e1–11, 2011.

Yuan C, Liu X, Mao Y, Diao F, Cui Y, Liu J. Polycystic ovary syndrome patients with high BMI tend to have functional disorders of androgen excess: a prospective study. J Biomed Res 30, 197–202, 2016.

Zhao L, Zhu Z, Lou H, Zhu G, Huang W, Zhang S, Liu F. Polycystic ovary syndrome (PCOS) and the risk of coronary heart disease (CHD): a meta-analysis. Oncotarget 7, 33715–33721, 2016.

Zhu T, Cui J, Goodarzi MO. Polycystic ovary syndrome and risk of type 2 diabetes, coronary heart disease, and stroke. Diabetes 70, 627–637, 2021.