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PCOS and Its Correlation to Insulin Resistance and Dyslipidemia

Sukhmani Batra K[1] and Jay Shubrook H[2]*

[1]*College of Osteopathic Medicine at Touro University California, Vallejo, CA, USA*

[2]*Department of Clinical Sciences and Community Health, College of Osteopathic Medicine at Touro University California, Vallejo, CA, USA*

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***Corresponding author:** Jay Shubrook, Department of Clinical Sciences and Community Health, College of Osteopathic Medicine at Touro University California, Vallejo, CA, USA, Email: jshubroo@touro.edu

Abstract

Context: Polycystic Ovarian Syndrome (PCOS) is a common endocrine disorder associated with significant metabolic complications. Many people with PCOS often only consider the reproductive implications. Insulpatientse (IR) and dyslipidemia are two distinct metabolic markers found in PCOS patients but remain relatively unaddressed in-patient care.

Objectives: To analyze the correlation between polycystic ovarian syndrome and metabolic markers, including IR and free fatty acid metabolism impairment.

Methods: PubMed was searched using the terms PCOS, IR, biomarkers, genetics, lifestyle modification, free fatty acid metabolism, and dyslipidemia. A total of 2600 articles were identified. After removing duplicates and non-full text articles, 340 articles remained, which were assessed for eligibility. Articles were excluded due to a lack of focus on IR, impaired free fatty acid metabolism, or dyslipidemia in PCOS patients. Articles that described genetic predisposition, biomarkers, or lifestyle modifications in PCOS patients without a specific focus on their association with IR were also excluded. Identification, screening, and selection of articles were conducted by one reviewer (SKB).

Results: A total of 68 articles were reviewed to analyze the prevalence and association of IR and dyslipidemia in PCOS patients. Genetic susceptibility, biomarkers, and lifestyle modification indicated that IR plays a crucial role in the pathophysiology of PCOS. Dyslipidemia was also found to be closely associated with PCOS.

Conclusion: PCOS has profound metabolic complications that are associated with the presence of IR and dyslipidemia in PCOS patients. IR and dyslipidemia should be addressed as a part of PCOS treatment.

Keywords: Insulin resistance; polycystic ovarian syndrome; Clinical implications; DNA methylation; Reproductive disorder

Abbreviations: PCOS: Polycystic Ovarian Syndrome; IR: Insulin Resistance; CVD: Cardiovascular Disease; AMH: Anti-Mullerian Hormone; CEBPS: CCAAT/Enhancer-Binding Protein; LMNA; Lamin A; miRNAs: microRNAs; OxLDLs: Oxidized LDLs; NEFAs: Non-Esterified Fatty Acids; OA: Oleic Acid

Introduction

Polycystic ovarian syndrome (PCOS) is a common endocrine disorder that impacts 3-15% of all women [1]. It is often diagnosed using the Rotterdam criteria, which requires two of the following symptoms: abnormal ovulation, hyperandrogenism, and polycystic ovaries [1]. PCOS can often manifest through hormonal, reproductive, and mental health presentations. With hyperandrogenism, PCOS patients will likely experience hirsutism and acne due to an altered hormonal profile [2]. Menstrual complications are common in PCOS and can lead to infertility complaints [1]. Studies have also shown a correlation between PCOS and depression, eating disorders, and anxiety [2]. While commonly characterized by its gynecologic features, PCOS has significant endocrine and metabolic implications. Often accompanied by metabolic abnormalities, including IR and impaired lipid metabolism [3], PCOS has been identified as a precursor to metabolic syndrome, which increases the risk of type 2 diabetes and cardiovascular disease (CVD) [1]. Due to serious clinical implications, recent research has focused on the metabolic implications of PCOS. This systematic review examines the genetic

mechanisms, biomarkers, and effect of lifestyle modification on IR in PCOS patients, as well as dyslipidemia's involvement in the pathophysiology and treatment of PCOS.

Methods

PubMed was searched from inception, including terms - PCOS, IR, biomarkers, genetics, lifestyle modification, free fatty acid metabolism, and dyslipidemia. Articles were restricted using PubMed's filters for "Free Full Text." All article types were included except "Books and Documents." Duplicate and non-English articles were excluded. The identified studies were screened with the title and abstract. Studies that discussed IR or dyslipidemia were eligible for inclusion. Studies that analyzed biomarkers, genetics, and lifestyle modification and their association with IR in PCOS patients were included. Studies were excluded if the study discussed IR or dyslipidemia without a specific focus on PCOS patients. Studies were also excluded if free fatty acid metabolism or dyslipidemia were analyzed without a particular emphasis on PCOS patients. Searches, screening, and selection were conducted by one reviewer (SKB) from February 21, 2023, to July 14, 2023(Figure 1).

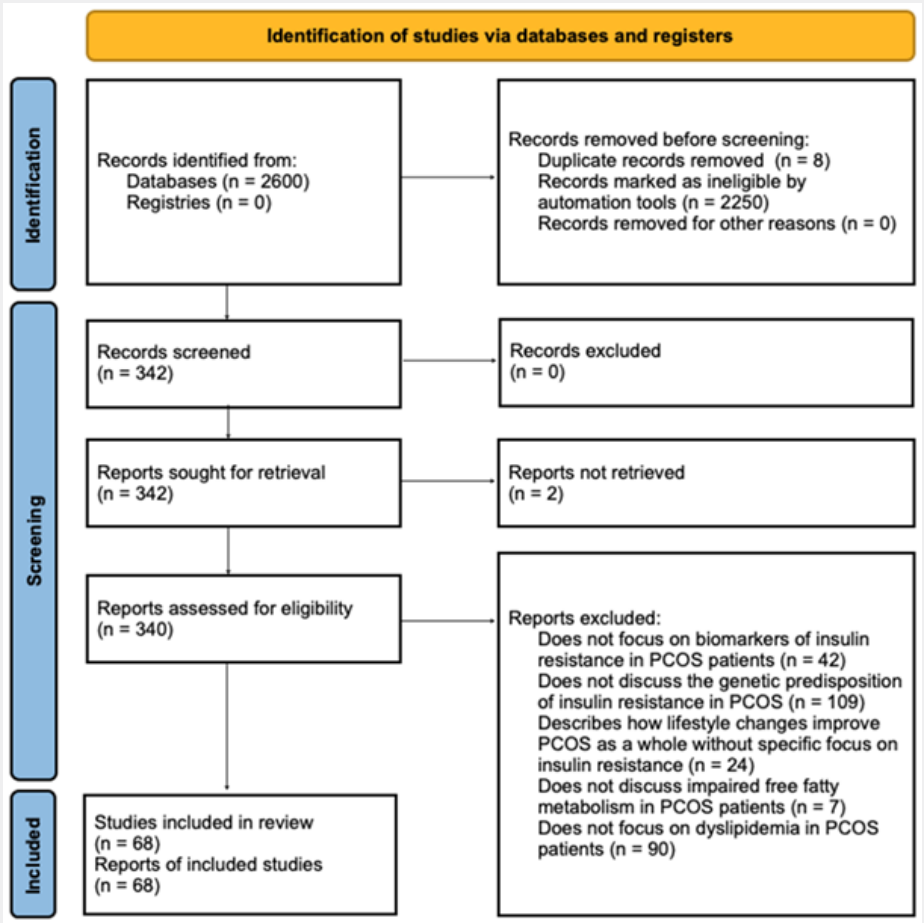

Figure 1: PRISMA Diagram for Article Selection a.

Results

Insulin Resistance (IR)

Recent research has shown a high prevalence of IR in PCOS patients. While the etiology of IR in PCOS is unclear, there are several proposed mechanisms. One mechanism is intrauterine growth restriction, which leads to changes in adipose tissue development at the fetal stage, which can promote IR in adulthood [5]. Changes in insulin function and the hormonal profile may be another mechanism of IR in PCOS patients [5]. In some PCOS patients, auto-phosphorylation of receptors is abnormal, while in other PCOS patients, there are defects in post-binding receptor events [5]. Both mechanisms contribute to insulin function changes, leading to IR [5]. Moreover, hyperandrogenism can change insulin sensitivity by modifying visceral fat or secretion of adiponectin, resulting in hyperandrogenemia-induced IR [5].

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Genetics

PCOS and IR correlations can be identified through several genetic mechanisms. Many genes involved in insulin signaling or metabolic regulation are altered in people with PCOS [5]. Many of these genes are also identified as risk genes for diabetes and other metabolic disorders (Table 1) [5-18]. While genetic polymorphisms have been heavily studied, epigenetic theories about IR in PCOS patients are now being explored. Fetal development is an area of focus for epigenetics in PCOS and IR. One theory is that a fetus' exposure to excess androgens may increase susceptibility to PCOS due to the known correlation between androgens and the polycystic morphology of ovaries, hyperandrogenism, and IR [2]. Several animal studies have shown consistent results to support this theory [2]. Another theory focuses on the anti-Mullerian hormone (AMH), which is responsible for fetal sex differentiation [2]. An increase in AMH can lead to a reduction in estradiol, which may contribute to both the polycystic morphology and the rise in testosterone, as seen in animal studies [2]. The increase in testosterone may lead to metabolic abnormalities seen in PCOS patients, including IR [2].

Table 1: Genetic Polymorphisms Identified in IR in PCOS.

Gene	Function	Polymorphism	Impact on IR and PCOS	References
ADIPOQ	Encodes for Adiponectin, which regulates insulin sensitivity	rs1501299	Risk factor for IR in PCOS patients	[5]
		G276T	Strong risk predictor of IR and metabolic abnormalities with decreased risk for PCOS	[5]
AR	Encodes for androgen receptors	CAG Repeats in N Terminal	Increases IR due to androgen-induced IR	[6-9]
CAPN10	Encodes for Calpain protein, which processes pro-insulin and is involved in insulin secretion and action	UCSNP-19	Found in PCOS patients with IR	[5, 6, 10]
		UCSNP-45		
		UCSNP-63		
CYP17	Encodes for Cytochrome P450, which is a rate-limiting enzyme for androgen formation	T/C	Increases IR in PCOS patients	[7-9, 11, 12]
INS	Encodes for Insulin	Variable Number of Tandem Repeats in Promoter Region	Correlated with PCOS	[10, 11]
			No associations	[5, 13]
INSR	Encodes an insulin receptor	C/T in Tyrosine Kinase Region	Strongly associated with IR in metabolic tissues in PCOS	[5, 6, 10, 11, 13-15]
		rs2059807		[5, 10, 15]
		rs1799817		
IRS-1	Encodes for insulin receptor substrate 1	Decreased Phosphorylation	Increased susceptibility to IR	[5, 10]
		Gly972Arg	Risk factor for IR	[5, 6, 10, 15, 16]
IRS-2	Encodes for insulin receptor substrate 2	Increased phosphorylation	Increased susceptibility to IR	[5, 10]
		Gly1057Asp	Risk factor for IR	[10, 16]
MNTR1A	Encodes melatonin receptor 1A	rs2119882	Associated with metabolic abnormalities in PCOS	[5]
MNTR1B	Encodes melatonin receptor 1B	rs10830963	Correlated with IR and lower B-cell function in Chinese PCOS patients	[5]
PPAR-y	Involved in differentiation of adipocytes and modification of insulin sensitivity	Pro12Ala	Has a protective effect on IR	[5, 6, 16, 17]
THADA	Encodes for Thyroid-Adenoma associated protein.	rs13429458	May modify insulin secretion in PCOS patients	[5]
		rs7563201	Associated with IR in PCOS patients	[18]

However, some research has found that maternal AMH is not present until 36 weeks of gestation, which suggests that AMH may not be a contributing factor during fetal development [2]. With both theories, the excess androgens that result are expected to have an epigenetic effect on developing ovaries, increasing susceptibility to IR [2]. DNA methylation is another epigenetic mechanism closely associated with PCOS and its metabolic effects [19]. Researchers detected changes in DNA methylation in 78 genes when comparing PCOS patients with IR to those without [19]. Significant alterations have been found in DNA methylation in the CCAAT/enhancer-binding protein (CEBPS) gene, which can also indirectly regulate the ODC1 gene [19]. Both genes are

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known to contribute to IR when modified. Lamin A (LMNA) gene mutations and hypermethylation have also been shown to cause IR and other metabolic abnormalities in PCOS patients [19]. DNA methylation of insulin signaling pathway genes, like INSR, has also been implicated in the development of IR in PCOS patients [19].

Biomarkers

IR in PCOS patients can be identified through the presence of several biomarkers. Several hormones [20,21], proteins and peptides [22-25] have been implicated in PCOS and IR. Additionally, PCOS has been associated with chronic inflammation primarily due to excess adipose tissue, so inflammatory biomarkers have been an essential area of research [26]. Moreover microRNAs (miRNAs), small RNAs that regulate gene expression post-transcriptionally, have been found in the blood, serum, plasma, and follicular fluid of PCOS patients and are being investigated as potential biomarkers of IR in PCOS [27]. Also, vitamin D deficiency is a common feature in PCOS and may be a potential biomarker for IR in PCOS (Table 2) [21-39].

Table 2: Biomarkers Associated with PCOS.

Biomarker	Correlation with IR and insulin signaling in PCOS patients	References
Hormones		
AMH	Positively correlated with indirect measurements of IR	[21]
Androgens	Correlated to increased HOMA-IR	[20]
Proteins and Peptides		
Copeptin	Positively correlated to IR	[29]
Galectin-3	Positively correlated to IR	[24]
Ghrelin	Limited association with IR	[29]
Gremlin	Positively correlated to IR	[24]
Irisin	Positively correlated to IR	[29]
Kisspeptin	Limited association with IR	[29]
Leptin	Limited association with IR	[29]
Lipocalin-2	Currently under consideration	[24]
Myonectin	Inversely correlated with IR	[24]
Nefastin-1	Inconsistent correlation findings	[24]
Neudesin	Currently under consideration	[24]
Neureglin-4	Positively correlated to IR	[24]
Omentin-1	Inversely correlated with IR	[24]
Plasminogen Activator Inhibitor-1	Positively correlated to IR	[29]
Preptin	Associated with elevated HOMA-IR	[24, 30]
	Serum level not correlated with IR markers	[24]
Retinol Binding Protein-4	Inconsistent correlation findings	[29, 31]
SHBG	Good indicator of insulin sensitivity	[23,25]
	Not good indicator of intensity of IR	[22]
Vaspin	Positively correlated to IR	[29]
Visfatin	Limited association with IR	[29]
Xenin	Currently under consideration	[24]
Xenopsin-1	Positively correlated to IR	[24]
Zonulin	Currently under consideration	[29]
Inflammatory Markers		
Adiponectin	Negatively correlated with IR but may be modified by other factors including diet and body composition	[29,32-34]
CXCL-14	Protective effects against IR	[33]
IL-6	Positively correlated with IR independent of obesity	[35]
Resistin	Positive correlation with HOMA-IR	[25]
TNF-α	Positively correlated with fasting insulin and HOMA-IR	[29,34,36]

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Micro-RNAs		
miR-93	Inversely correlated with insulin sensitivity	[27,37]
miR-133	Inversely correlated with insulin sensitivity	[37]
miR-123	Possible role in insulin signaling	[37]
miR-143	Possible role in insulin signaling	[37]
miR-144	Possible role in insulin signaling	[37]
miR-233	Inversely correlated with insulin sensitivity	[37]
miR-320	Possible role in promoting IR in PCOS patients	[27]
Other		
Vitamin D	Deficiency correlated to IR	[38]
	Inversely correlated with HOMA-IR only in obese PCOS patients	[28, 39]

Lifestyle Modification

Lifestyle modification, a common treatment for PCOS patients, has improved both IR and other non-related symptoms of PCOS. Key recommendations for lifestyle changes include weight reduction, diet, and exercise [40,41]. Weight reduction is often recommended to PCOS patients as a therapeutic option. It has been shown that weight loss may decrease the magnitude of hyperinsulinemia and help scale down menstrual irregularities and infertility [41]. Weight reduction may specifically benefit obese PCOS women by decreasing adiposity, reducing androgen and insulin levels, improving ovulatory function, increasing fertility, and decreasing the risk of metabolic complications like CVD [41]. It has been reported that a minor weight reduction of 5-10% could significantly improve metabolic and reproductive dysfunction in PCOS patients [42-45]. Nutritional interventions have also been assessed as a treatment for PCOS. With PCOS' association with IR and other metabolic complications, a low glycemic index diet has been considered [41,46]. One meta-analysis showed improved menstrual irregularities and decreased IR with a low glycemic diet [41]. Another meta-analysis showed that a low glycemic diet decreased androgen levels and reduced IR [47]. Some research has also looked at low or reduced carbohydrate diets and found beneficial metabolic effects, including weight reduction, decreased adiposity, decreased insulin levels, improvement in fertility, and normalization of the hormonal profile [41]. A ketogenic Mediterranean diet reduced serum insulin, blood glucose levels, and weight [41]. Low-calorie diets improved insulin sensitivity and promoted weight loss in PCOS patients [46]. A pulse-based diet has also improved insulin sensitivity and lipid profiles in PCOS patients [43].

Additionally, increasing intake of fiber-rich food can help regulate insulin levels and promote weight loss [46]. Plant-based foods, which promote glycemic control, also have phytochemicals that can reduce hyperglycemia and improve insulin sensitivity and acute insulin response [46]. Limiting simple sugar, salt, and processed food intake can also help improve insulin sensitivity and reduce the risk of PCOS's metabolic complications [46]. Saturated fat has been found to worsen IR, and unsaturated fatty acids have been found to improve IR [46]. Omega-3 fatty acids have also been found to enhance insulin sensitivity in PCOS patients [46]. Physical activity is another therapeutic option for PCOS patients. Benefits of exercise include weight loss, reduced IR, decreased androgen concentrations, and restored fertility [46]. Moderate-intensity aerobic exercise was found to reduce menstrual dysfunction and contribute to weight loss and reduced IR in PCOS patients [41]. Vigorous aerobic exercise decreased IR significantly in PCOS patients [45]. Some research has found that vigorous aerobic exercise and resistance training improve insulin sensitivity and androgen concentrations in PCOS patients [45]. Moreover, it has been reported that a reduction in insulin levels can improve hirsutism, acne, and the menstrual cycle, all of which are symptoms of PCOS [44]. Yoga has been found to be effective in improving ovarian morphology, mood, and hormonal profiles but is ineffective in regulating IR [44].

Other lifestyle modifications have been shown to have positive effects. Sleep deprivation has been found to increase risk of IR, obesity, and type 2 diabetes in PCOS patients, so sufficient, high-quality sleep is essential for PCOS patients [15,45]. Additionally, IR is independently associated with depression in PCOS, so psychological care is another key therapeutic option for PCOS patients [15]. Avoidance of smoking is essential in PCOS patients because smoking can decrease insulin sensitivity and increase the risk of CVD in PCOS patients [48]. The gut microbiome has also been studied for its connection to PCOS and IR. It has been established that PCOS patients have an altered gut microbiome [49,50]. It has been found that alterations in the gut microbiome are more distinct in PCOS patients with IR than those without [49]. It is believed that altered gut microbiota may contribute to the development of IR in PCOS patients [49]. It is proposed that an imbalance of gut microbiota can activate chronic low-grade inflammation, disrupting that insulin signaling pathway leading to IR [49]. This mechanism has been supported through preliminary studies [49]. Another plausible mechanism suggests that increased Bacteroides species in the gut microbiome decrease ghrelin and peptide YY levels, leading to IR [49]. It is known that diet, probiotics, and prebiotics can change the gut microbiome,

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so these may be potential targeted therapeutic options for PCOS patients [49,50]. Several studies have looked at the benefits of lifestyle modification and medication as combined therapy, but data remains inconclusive [51,52].

Dyslipidemia

In addition to IR, dyslipidemia, an imbalance of lipids, is another common metabolic abnormality in PCOS patients [53]. Dyslipidemia is seen in both obese and non-obese PCOS patients [54]. One meta-analysis has found an increased prevalence of dyslipidemia in mothers and fathers of PCOS patients, which suggests there may be a partial genetic causality for dyslipidemia in PCOS patients [55]. The typical lipid profile of a PCOS patient consists of an increase in VLDL, LDL-C, and triglycerides and a decrease in HDL-C [1,53,56]. The most common pattern of dyslipidemia in PCOS patients is reported to be classic atherogenic dyslipidemia (increased triglycerides, increased LDL-C, and low HDL-C) which is linked to IR, while the elevated LDL-C is suggested to be due to the excess of androgens in PCOS patients [56]. Moreover, apolipoprotein concentrations were found to be modified in PCOS patients. Apo-AI levels are significantly reduced in PCOS patients, with no difference in Apo-B levels, due to obesity and hyperandrogenism [53]. It has also been reported that Apo-CI levels are increased in both lean and obese PCOS patients and may be early indicators of lipid abnormalities in PCOS patients [53]. Levels of lipoprotein a, an independent risk factor for CVD, were also significantly higher in some PCOS phenotypes and may be a focus of future research [53].

Recent studies have found a correlation between dyslipidemia and hyperandrogenism in PCOS patients. One study found that liver fat was strongly associated with hyperandrogenism [3]. It has also been reported that hyperandrogenism is related to fat distribution, specifically intra-abdominal fat deposition [3]. Additionally, the reduced Apo-AI levels in the granulosa cells of PCOS patients could hamper the conversion of testosterone to estradiol, which may account for the elevated testosterone concentrations observed in PCOS patients [3]. Dyslipidemia has also been associated with anovulation in PCOS patients. It has been reported that anovulatory PCOS patients have higher total cholesterol, triglycerides, and LDL-C levels and lower HDL-C levels than ovulatory PCOS patients [3]. It has also been found that high levels of triglycerides, free fatty acids, and oxidized LDLs (oxLDLs) result in mitochondrial dysfunction, which increases ROS, leading to ovarian damage and follicular atresia [3]. Additionally, oxLDLs can activate receptors, which cause apoptosis of granulosa cells and impaired ovulation [3]. Specific lipid abnormalities have also been investigated for their association with PCOS. A few studies found that concentrations of prostaglandins and metabolites of arachidonic acid, via the COX pathway, were elevated in the ovarian tissue of the PCOS group compared to the control group [57,58]. In humans, a significant increase was found in concentrations of 9-HODE and 13-HODE, both derivatives of linoleic acid [58].

Non-esterified fatty acids (NEFAs), associated with lipotoxic effects, have also been associated with PCOS [59]. Increased mitochondrial NEFA β-oxidation has been shown to increase serine phosphorylation of insulin receptors in PCOS skin fibroblasts [59]. Additionally, TNF-α, a NEFA metabolite, has been associated with PCOS [59]. Moreover, palmitate, a saturated fatty acid, increases androgen biosynthesis in animal models, which may model lipids promoting androgen overproduction in PCOS patients (59). It was also found that PPAR-y activation reduces androgen hyperresponsiveness in PCOS by upregulating genes that decrease circulating NEFA concentrations [59]. Unsaturated fatty acids are also implicated in PCOS pathophysiology. Elevated concentrations of oleic acid (OA) have been found in the follicular fluid of PCOS patients and are thought to contribute to adverse pregnancy outcomes [57]. OA also regulates transcriptional factors necessary for synthesizing female hormones, which may contribute to excess androgens [57]. Dyslipidemia is also believed to increase the risk of CVD in PCOS patients [60-63]. Dyslipidemia is an important factor in intensifying atherosclerosis, leading to cardiovascular events. While PCOS is linked to vascular impairment and cardiovascular risk [62, 64], data connecting dyslipidemia to CVD in PCOS patients is limited and unclear [60,65].

Treatments for dyslipidemia have shown positive effects in treating PCOS [66]. In addition to improving the lipid profile, simvastatin was found to reduce testosterone, with a proposed mechanism of inhibiting cholesterol production, which is needed for testosterone synthesis [3,66]. It also improved hirsutism, acne, and the hormonal profile [3,66]. Moreover, simvastatin was seen to be cardioprotective, with lower pro-inflammatory markers [66]. Atorvastatin has also been found to improve the lipid profile, decrease hyperandrogenism, and reduce IR in PCOS patients. Other treatments have also been investigated for their potential as a therapeutic option for dyslipidemia in PCOS patients. Omega-3 fatty acid supplementation has improved serum adiponectin levels, IR, serum lipids, the overall lipid profile [3,67], and other metabolic dysfunction [68] in PCOS patients. One study found that vitamin D supplementation resulted in significant improvement in total cholesterol, triglycerides, LDL-C, and VLDL-C [69], while other research found no therapeutic effect on the lipid profile [39]. Additionally, metformin has shown improvement in lipid profiles and IR, but data is inconsistent due to several confounding factors [64].

Discussion

IR and dyslipidemia are integral metabolic manifestations of PCOS that require a greater clinical focus and should be regularly assessed in all PCOS patients. Dyslipidemia profoundly affects PCOS pathogenesis, prognosis, and treatment and should be monitored regularly. PCOS' status as a precursor to metabolic syndrome highlights a critical need to gain further insight into PCOS as a metabolic disorder, especially for patient awareness. Further studies should include greater emphasis on biomarkers

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of IR and dyslipidemia in PCOS and their clinical applicability. Additionally, research should focus on treatment options that target IR and dyslipidemia in addition to the symptoms of PCOS. More research is needed to determine dyslipidemia's role in PCOS pathogenesis and cardiovascular risk. There are several limitations in the literature review. Only one database, PubMed, was searched for relevant articles, which may reduce the available research. One reviewer identified, screened, and selected articles, which may have introduced selection bias. Articles were screened at the title and abstract level, which may have brought selection bias.

Conclusion

PCOS is often identified as a reproductive disorder, but its metabolic and endocrine significance is too important to ignore. PCOS has profound metabolic effects, including IR and dyslipidemia, which lead to significant metabolic complications. It is important to recognize the relationship between PCOS, IR, and dyslipidemia as they are vital to treating PCOS and managing patient care.

References

1. Bednarska S, Siejka A (2017) The pathogenesis and treatment of polycystic ovary syndrome: What's new?. Adv Clin Exp Med 26(2): 359-667.
2. Raperport C, Homburg R (2019) The Source of Polycystic Ovarian Syndrome. Clin Med Insights Reprod Health 13: 1179558119871467.
3. Liu Q, Xie YJ, Qu LH, Zhang MX, Mo ZC (2019) Dyslipidemia involvement in the development of polycystic ovary syndrome. Taiwan J Obstet Gynecol 58(4): 447-453.
4. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, et al. (2021) The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 372: n71.
5. Shaaban Z, Khoradmehr A, Amiri-Yekta A, Nowzari F, Jafarzadeh Shirazi MR, et al. (2021) Pathophysiologic Mechanisms of Insulin Secretion and Signaling-Related Genes in Etiology of Polycystic Ovary Syndrome. Genet Res (Camb) 2021: 7781823.
6. Diamanti-Kandarakis E, Piperi C, Spina J, Argyrakopoulou G, Papanastasiou L, et al. (2006) Polycystic ovary syndrome: the influence of environmental and genetic factors. Hormones (Athens) 5(1): 17-34.
7. Dadachanji R, Shaikh N, Mukherjee S (2018) Genetic Variants Associated with Hyperandrogenemia in PCOS Pathophysiology. Genet Res Int 2018: 7624932.
8. Bogari NM (2020) Genetic construction between polycystic ovarian syndrome and type 2 diabetes. Saudi J Biol Sci 27(10): 2539-2543.
9. Saddick SY (2020) Identifying genes associated with the development of human polycystic ovary syndrome. Saudi J Biol Sci 27(5): 1271-1279.
10. Nautiyal H, Imam SS, Alshehri S, Ghoneim MM, Afzal M, Alzarea SI, et al. (2022) Polycystic Ovarian Syndrome: A Complex Disease with a Genetics Approach. Biomedicines 10(3): 540.
11. Diamanti-Kandarakis E, Dunaif A (2012) Insulin resistance and the polycystic ovary syndrome revisited: an update on mechanisms and implications. Endocr Rev 33(6): 981-1030.
12. Rosenfield RL, Ehrmann DA (2016) The Pathogenesis of Polycystic Ovary Syndrome (PCOS): The Hypothesis of PCOS as Functional Ovarian Hyperandrogenism Revisited. Endocr Rev 37(5): 467-520.
13. Lakkakula BV, Thangavelu M, Godla UR (2013) Genetic variants associated with insulin signaling and glucose homeostasis in the pathogenesis of insulin resistance in polycystic ovary syndrome: a systematic review. J Assist Reprod Genet 30(7): 883-895.
14. Crespo RP, Bachega T, Mendonça BB, Gomes LG (2018) An update of genetic basis of PCOS pathogenesis. Arch Endocrinol Metab 62(3): 352-361.
15. Zhao H, Zhang J, Cheng X, Nie X, He B (2023) Insulin resistance in polycystic ovary syndrome across various tissues: an updated review of pathogenesis, evaluation, and treatment. J Ovarian Res 16(1): 9.
16. Chen Y, Fang SY (2018) Potential genetic polymorphisms predicting polycystic ovary syndrome. Endocr Connect 7(5): R187-R195.
17. He J, Wang L, Liu J, Liu F, Li X (2012) A meta-analysis on the association between PPAR-γ Pro12Ala polymorphism and polycystic ovary syndrome. J Assist Reprod Genet 29(7): 669-677.
18. Day F, Karaderi T, Jones MR, Meun C, He C, et al. (2018) Large-scale genome-wide meta-analysis of polycystic ovary syndrome suggests shared genetic architecture for different diagnosis criteria. PLoS Genet 14(12): e1007813.
19. Liu YN, Qin Y, Wu B, Peng H, Li M, et al. (2022) DNA methylation in polycystic ovary syndrome: Emerging evidence and challenges. Reprod Toxicol 111: 11-19.
20. Yang R, Yang S, Li R, Liu P, Qiao J, Zhang Y (2016) Effects of hyperandrogenism on metabolic abnormalities in patients with polycystic ovary syndrome: a meta-analysis. Reprod Biol Endocrinol 14(1): 67.
21. Łebkowska A, Kowalska I (2017) Anti-Müllerian hormone and polycystic ovary syndrome. Endokrynol Pol 68(1): 74-78.
22. Dahan MH, Goldstein J (2006) Serum sex hormone-binding globulin levels show too much variability to be used effectively as a screening marker for insulin resistance in women with polycystic ovary syndrome. Fertil Steril 86(4): 934-941.
23. Qu X, Donnelly R (2020) Sex Hormone-Binding Globulin (SHBG) as an Early Biomarker and Therapeutic Target in Polycystic Ovary Syndrome. Int J Mol Sci 21(21): 8191.
24. Kruszewska J, Laudy-Wiaderny H, Kunicki M (2022) Review of Novel Potential Insulin Resistance Biomarkers in PCOS Patients-The Debate Is Still Open. Int J Environ Res Public Health 19(4): 2099.
25. Xing C, Zhang J, Zhao H, He B (2022) Effect of Sex Hormone-Binding Globulin on Polycystic Ovary Syndrome: Mechanisms, Manifestations, Genetics, and Treatment. Int J Womens Health 14: 91-105.
26. Dabravolski SA, Nikiforov NG, Eid AH, Nedosugova LV, Starodubova AV, et al. (2021) Mitochondrial Dysfunction and Chronic Inflammation in Polycystic Ovary Syndrome. Int J Mol Sci 22(8): 3923.
27. Sørensen AE, Wissing ML, Salö S, Englund AL, Dalgaard LT (2014) MicroRNAs Related to Polycystic Ovary Syndrome (PCOS). Genes (Basel) 5(3): 684-708.
28. Morgante G, Darino I, Spanò A, Luisi S, Luddi A, et al. (2022) PCOS Physiopathology and Vitamin D Deficiency: Biological Insights and Perspectives for Treatment. J Clin Med 11(15): 4509.
29. Polak K, Czyzyk A, Simoncini T, Meczekalski B (2017) New markers of insulin resistance in polycystic ovary syndrome. J Endocrinol Invest 40(1): 1-8.

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30. Sobhan Bahreiny S, Harooni E, Reza Dabbagh M, Ebrahimi R (2023) Circulating serum preptin levels in women with polycystic ovary syndrome: A systematic review and meta-analysis. Int J Reprod Biomed 21(5): 367-378.

31. Yildizhan R, Ilhan GA, Yildizhan B, Kolusari A, Adali E, et al. (2011) Serum retinol-binding protein 4, leptin, and plasma asymmetric dimethylarginine levels in obese and nonobese young women with polycystic ovary syndrome. Fertil Steril 96(1): 246-250.

32. Groth SW (2010) Adiponectin and polycystic ovary syndrome. Biol Res Nurs 12(1): 62-72.

33. García-Beltran C, Cereijo R, Quesada-López T, Malpique R, López-Bermejo A, et al. (2020) Reduced circulating levels of chemokine CXCL14 in adolescent girls with polycystic ovary syndrome: normalization after insulin sensitization. BMJ Open Diabetes Res Care 8(1): e001035.

34. Van Der Ham K, Louwers YV, Laven JSE (2022) Cardiometabolic biomarkers in women with polycystic ovary syndrome. Fertil Steril. 117(5): 887-896.

35. Peng Z, Sun Y, Lv X, Zhang H, Liu C, et al. (2016) Interleukin-6 Levels in Women with Polycystic Ovary Syndrome: A Systematic Review and Meta-Analysis. PLoS One 11(2): e0148531.

36. Thathapudi S, Kodati V, Erukkambattu J, Katragadda A, Addepally U, et al. (2014) Tumor necrosis factor-alpha and polycystic ovarian syndrome: a clinical, biochemical, and molecular genetic study. Genet Test Mol Biomarkers 18(9): 605-609.

37. Vitale SG, Fulghesu AM, Mikuš M, Watrowski R, D'Alterio MN, et al. (2022) The Translational Role of miRNA in Polycystic Ovary Syndrome: From Bench to Bedside-A Systematic Literature Review. Biomedicines 10(8): 1816.

38. Dastorani M, Aghadavod E, Mirhosseini N, Foroozanfard F, Zadeh Modarres S, et al. (2018) The effects of vitamin D supplementation on metabolic profiles and gene expression of insulin and lipid metabolism in infertile polycystic ovary syndrome candidates for in vitro fertilization. Reprod Biol Endocrinol 16(1): 94.

39. Javed Z, Papageorgiou M, Deshmukh H, Kilpatrick ES, Mann V, et al. (2019) A Randomized, Controlled Trial of Vitamin D Supplementation on Cardiovascular Risk Factors, Hormones, and Liver Markers in Women with Polycystic Ovary Syndrome. Nutrients 11(1): 188.

40. Tan WC, Yap C, Tan AS (2001) Clinical management of PCOS. Acta Obstet Gynecol Scand 80(8): 689-696.

41. Abdalla MA, Deshmukh H, Atkin S, Sathyapalan T (2020) A review of therapeutic options for managing the metabolic aspects of polycystic ovary syndrome. Ther Adv Endocrinol Metab 11: 2042018820938305.

42. Saleem F, Rizvi SW (2017) New Therapeutic Approaches in Obesity and Metabolic Syndrome Associated with Polycystic Ovary Syndrome. Cureus 9(11): e1844.

43. Kazemi M, McBreairty LE, Chizen DR, Pierson RA, Chilibeck PD, et al. (2018) A Comparison of a Pulse-Based Diet and the Therapeutic Lifestyle Changes Diet in Combination with Exercise and Health Counselling on the Cardio-Metabolic Risk Profile in Women with Polycystic Ovary Syndrome: A Randomized Controlled Trial. Nutrients 10(10): 1387.

44. Abdolahian S, Tehrani FR, Amiri M, Ghodsi D, Yarandi RB, et al. (2020) Effect of lifestyle modifications on anthropometric, clinical, and biochemical parameters in adolescent girls with polycystic ovary syndrome: a systematic review and meta-analysis. BMC Endocr Disord 20(1): 71.

45. Gu Y, Zhou G, Zhou F, Wu Q, Ma C, Zhang Y, et al. (2022) Life Modifications and PCOS: Old Story But New Tales. Front Endocrinol (Lausanne) 13: 808898.

46. Han Y, Wu H, Sun S, Zhao R, Deng Y, Zeng S, et al. (2023) Effect of High Fat Diet on Disease Development of Polycystic Ovary Syndrome and Lifestyle Intervention Strategies. Nutrients 15(9): 2230.

47. Kazemi M, Hadi A, Pierson RA, Lujan ME, Zello GA, et al. (2021) Chilibeck PD Effects of Dietary Glycemic Index and Glycemic Load on Cardiometabolic and Reproductive Profiles in Women with Polycystic Ovary Syndrome: A Systematic Review and Meta-analysis of Randomized Controlled Trials. Adv Nutr 12(1): 161-178.

48. Krysiak R, Okopień B, Gdula-Dymek A, Herman ZS (2006) Update on the management of polycystic ovary syndrome. Pharmacol Rep 58(5): 614-625.

49. Giampaolino P, Foreste V, Di Filippo C, Gallo A, Mercorio A, et al. (2021) Microbiome and PCOS: State-of-Art and Future Aspects. Int J Mol Sci 22(4): 2048.

50. Rizk MG, Thackray VG (2021) Intersection of Polycystic Ovary Syndrome and the Gut Microbiome. J Endocr Soc 5(2): bvaa177.

51. Kim CH, Chon SJ, Lee SH (2020) Effects of lifestyle modification in polycystic ovary syndrome compared to metformin only or metformin addition: A systematic review and meta-analysis. Sci Rep 10(1): 7802.

52. Shah A, Dodson WC, Kris-Etherton PM, Kunselman AR, Stetter CM, et al. (2021) Effects of Oral Contraception and Lifestyle Modification on Incretins and TGF-ß Superfamily Hormones in PCOS. J Clin Endocrinol Metab 106(1): 108-119.

53. Kim JJ, Choi YM (2013) Dyslipidemia in women with polycystic ovary syndrome. Obstet Gynecol Sci 56(3): 137-142.

54. Zhu S, Zhang B, Jiang X, Li Z, Zhao S, et al. (2019) Metabolic disturbances in non-obese women with polycystic ovary syndrome: a systematic review and meta-analysis. Fertil Steril 111(1): 168-177.

55. Yilmaz B, Vellanki P, Ata B, Yildiz BO (2018) Metabolic syndrome, hypertension, and hyperlipidemia in mothers, fathers, sisters, and brothers of women with polycystic ovary syndrome: a systematic review and meta-analysis. Fertil Steril 109(2): 356-364.

56. Wild RA, Rizzo M, Clifton S, Carmina E (2011) Lipid levels in polycystic ovary syndrome: systematic review and meta-analysis. Fertil Steril 95(3): 1073-1079.

57. Baddela VS, Sharma A, Vanselow J (2020) Non-esterified fatty acids in the ovary: friends or foes? Reprod Biol Endocrinol 18(1): 60.

58. Szczuko M, Kikut J, Komorniak N, Bilicki J, Celewicz Z, et al. (2020) The Role of Arachidonic and Linoleic Acid Derivatives in Pathological Pregnancies and the Human Reproduction Process. Int J Mol Sci 21(24): 9628.

59. Connolly A, Leblanc S, Baillargeon JP (2018) Role of Lipotoxicity and Contribution of the Renin-Angiotensin System in the Development of Polycystic Ovary Syndrome. Int J Endocrinol 2018: 4315413.

60. Ramezani TF, Behboudi GS, Rostami DM, Farahmand M, Minooee S, et al. (2018) Reproductive Assessment: Findings from 20 Years of the Tehran Lipid and Glucose Study. Int J Endocrinol Metab 16(Suppl 4): e84786.

61. Osibogun O, Ogunmoroti O, Michos ED (2020) Polycystic ovary syndrome and cardiometabolic risk: Opportunities for cardiovascular disease prevention. Trends Cardiovasc Med 30(7): 399-404.

62. Gomez JMD, VanHise K, Stachenfeld N, Chan JL, Merz NB, Shufelt C (2022) Subclinical cardiovascular disease and polycystic ovary syndrome. Fertil Steril 117(5): 912-923.

63. Sangaraju SL, Yepez D, Grandes XA, Talanki Manjunatha R, Habib S (2022) Cardio-Metabolic Disease and Polycystic Ovarian Syndrome (PCOS): A Narrative Review. Cureus 14(5): e25076.

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64. Duleba AJ (2012) Medical management of metabolic dysfunction in PCOS. Steroids 77(4): 306-311.

65. Wekker V, Van Dammen L, Koning A, Heida KY, Painter RC, et al. (2020) Long-term cardiometabolic disease risk in women with PCOS: a systematic review and meta-analysis. Hum Reprod Update 26(6): 942-960.

66. Kodaman PH, Duleba AJ (2008) Statins in the treatment of polycystic ovary syndrome. Semin Reprod Med 26(1): 127-138.

67. Mohammadi E, Rafraf M, Farzadi L, Asghari-Jafarabadi M, Sabour S (2012) Effects of omega-3 fatty acids supplementation on serum adiponectin levels and some metabolic risk factors in women with polycystic ovary syndrome. Asia Pac J Clin Nutr 21(4):511-518.

68. Salek M, Clark CCT, Taghizadeh M, Jafarnejad S (2019) N-3 fatty acids as preventive and therapeutic agents in attenuating PCOS complications. Excli J 18: 558-575.

69. Luo J, Li T, Yuan J (2021) Effectiveness of vitamin D supplementation on lipid profile in polycystic ovary syndrome women: a meta-analysis of randomized controlled trials. Ann Palliat Med 10(1): 114-129.

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