The association between curcumin and polycystic ovarian syndrome.

Kirthika Venkatesan[1], Nisha Nigil Haroon[2*]

[1]Department of Endocrinology, Caribbean Medical University School of Medicine, Willemstad, Curacao

[2]Department of Endocrinology and Internal Medicine, Northern Ontario School of Medicine, Ontario, Canada

Received: *08-November-2021, Manuscript No. AAGGS-21-46932;* ***Editor assigned:*** *12-November-2021, PreQC No. AAGGS-21-46932;* ***Reviewed:****26-November-2021, QC No. AAGGS-21-46932;* ***Revised:*** *25-August-2022, Manuscript No. AAGGS-21-46932; QI No. AAGGS-21-46932;* ***Published:*** *22-September-2022, DOI:10.35841/2591-7994-6.4.120*

Abstract

Background: Curcumin is the active ingredient in turmeric known to have several benefits in women diagnosed with Polycystic Ovarian Syndrome (PCOS).

Objective: In this systematic review, we aim to provide a brief review of the existing literature on the association between curcumin and PCOS.

Methods: Available published papers relevant to the topic were obtained through extensive search using major databases. Inclusion criteria included studies that investigated PCOS and turmeric/ curcumin. Exclusion criteria included studies that investigated curcumin and other gynecological disorders, infertility, rodent studies, and any investigations that do not meet the diagnostic criteria for PCOS.

Results: We found a total of 14 articles and only five studies were incorporated based on our exclusion criteria. The main findings were that curcumin supplementation can aid in improvements in lipid and glycemic profile, along with weight reductions and lower androgen levels.

Conclusion: Curcumin supplementation is beneficial for women with PCOS and offers good cholesterol and glycemic improvement along with weight reduction. However, further research is required to investigate the interaction between curcumin and ovulation/reproduction and hyperandrogenism.

Keywords: Turmeric, Polycystic ovarian syndrome, Transvaginal, Curcumin.

Introduction

PCOS is the most common endocrine disorder and is the leading cause of infertility among women of reproductive age with an incidence rate between 4% to 12% globally [1]. The incidence of PCOS has been increasing in the U.S.A by almost close to 18%. There are no racial or ethnic differences in the prevalence of PCOS [2]. However, there are differences in the severity of PCOS presentation between ethnicities. For example, Hispanic women with PCOS present with the most severe phenotype whereas, non-Hispanic Black women have an overall milder presentation.

Risk factors for PCOS include menstrual cycle irregularities, family history of diabetes, family history of infertility, bad mood, and lack of physical exercise [3]. Women with PCOS are at an increased risk of Type 2 diabetes or dysglycemia, infertility, obesity, hypertension, obstructive sleep apnea, dyslipidemia, and non-alcoholic fatty liver [4]. The combination of dyslipidemia, hyperglycemia and obesity predisposes women to coronary artery disease [5].

Clinical features of PCOS include oligomenorrhea, acne, hirsutism, and obesity [6]. Laboratory features include high, normal or borderline free testosterone levels, mildly elevated prolactin, impaired oral glucose tolerance test, or elevated lipids. Transvaginal ultrasound may show multiple follicular cysts on the ovaries. PCOS is a diagnosis of exclusion. According to the Rotterdam criteria, PCOS diagnosis involves the presence of two of the following three findings- hyperandrogenism, ovulatory dysfunction, and polycystic ovaries [7].

First-line treatment for PCOS includes weight loss and lifestyle modifications necessary to decrease insulin resistance in those who are overweight. If the patient desires fertility, metformin, clomiphene citrate, or letrozole can be used. Research shows that letrozole results in greater live births and ovulation compared to clomiphene citrate [8]. If fertility is not desired, hormonal contraception and intrauterine devices may be prescribed. To target hirsutism, spironolactone, eflornithine, or flutamide may be used. These medications are useful to target hormonal acne as well.

Curcumin is the active ingredient found in turmeric. It has anti-inflammatory and anti-oxidant properties exerting effects through gene expression and cellular signalling [9]. Several studies have documented that curcumin has potent antimicrobial effects against chronic diseases such as cancer, diabetes, pulmonary, neurological, cardiovascular, and autoimmune diseases [10]. In addition, curcumin is found to have several pharmacologic benefits in patients with PCOS. In this systematic review, we aim to provide a brief review of the existing evidence on the association between PCOS and

curcumin and address potential barriers and prospective studies.

Materials and Methods

The search was limited to human studies published in English. No limitations were applied regarding the geography of participants. Only randomized clinical trials were incorporated in this study. One author conducted the literature search while another one verified the data. All published papers relevant to the topic from inception to July 2021 were obtained through extensive search using databases such as Google Scholar, PubMed, and ScienceDirect, using any relevant keywords in different orders: "Polycystic Ovarian Syndrome", "PCOS", "turmeric", "nano curcumin", and "curcumin". The search strategy is outlined in Figure 1.

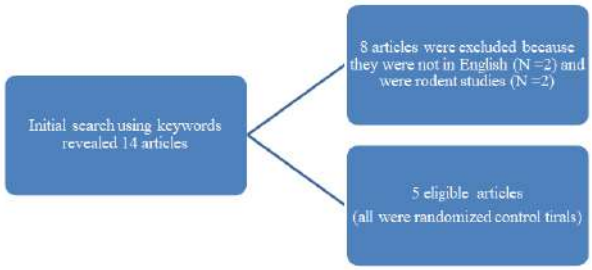

***Figure 1**: Search strategy for eligible studies.*

The relevance of the article was determined by reading the abstract. Inclusion criteria included studies that investigated PCOS and turmeric or curcumin. Exclusion criteria included studies that investigated curcumin and other gynecological disorders, infertility, rodent studies, and any studies that do not meet the diagnostic criteria for PCOS. Parameters investigated were glycemic control, lipid profile, and hyperandrogenism. The Newcastle-Ottawa Scale was used to address the quality of the eligible studies and the Jadad scale to assess the quality of the randomized control trials.

Results

The initial search revealed 14 articles. Two articles were excluded as it was not in English. Based on our exclusion criteria, six articles were excluded. Only six articles were used in this review [11-16]. The studies were conducted in Iran. The sample sizes varied from 60 to 100 women with PCOS. The curcumin dose ranged from 80 mg to 1500 mg per day with treatment periods ranging from 6 weeks to 12 weeks. Results from these studies are evident in Table 1.

***Table 1.** Characteristics of included studies.*

Name of study	Sample size and study design	Objective and procedure	Results	Conclusion
1. Effects of curcumin on body weight, glycemic control and serum lipids in women with polycystic ovary syndrome: A randomized, double-blind, placebo-controlled trial [11].	Randomized double-blinded, placebo-controlled clinical trial.	Participants were randomly allocated to take 500 mg/day curcumin (N=24) or placebo (N=26) for 12 weeks. Glycemic control and serum lipids were measured at baseline and after the 12-week intervention. Using the RT-PCR method, gene expression related to insulin and lipid metabolism was assessed.	Curcumin significantly decreased weight and BMI, reduced fasting glucose, serum insulin, insulin, and significantly increased insulin sensitivity compared to placebo.	Curcumin administration for 12 weeks to women with PCOS can have beneficial effects on body weight, glycemic control, serum lipids except for triglycerides and VLDL-cholesterol levels, and gene expression of PPARy and LDLR.
	N=50 (18-40 years of age) women with PCOS in Arak, Iran		Curcumin was associated with a significant reduction in total cholesterol, LDL-cholesterol and total-/HDL-cholesterol ratio and a significant increase in HDL-cholesterol PPARy levels compared with the placebo.	
			Curcumin up-regulated gene expression of PPARy and LDL receptor compared to placebo.	
2. Effects of Curcumin Supplementation on Blood Glucose, Insulin Resistance and Androgens in Patients with Polycystic Ovary Syndrome: A Randomized Double-Blind Placebo-Controlled Clinical Trial [12].	Randomized double-blind placebo-controlled trial.	Participants were treated with curcumin (500 mg thrice daily) or placebo for 12 weeks. Primary outcome measures were fasting plasma glucose, fasting insulin, sex hormone levels, and hirsutism. Secondary outcomes included anthropometric measurements.	Mean fasting plasma glucose levels and DHEAS levels were significantly lower in the intervention group compared to the placebo group.	Curcumin might be a safe and useful supplement to reduce PCOS-associated hyperandrogenemia and hyperglycemia.
	N=67 (18-49 years of age) women with PCOS in Tehran, Iran			
3. Therapeutic Effect of Curcumin in Women with Polycystic Ovary Syndrome Receiving Metformin: A Randomized Controlled Trial [13].	Randomized clinic trial.	Evaluated the effects of curcumin nanomicelle on PCOS with and without concomitant metformin use.	Fasting insulin, insulin resistance, LDL-C and total testosterone were significantly lower in group 2 than in group 1. HDL-C levels increased in group 2. Total cholesterol and triglycerides decreased in group 2.	Combined treatment with metformin and curcumin can lead to improvement in insulin resistance and lipid profile in patients with PCOS.
		Group 1: 50 received 500 mg metformin TID. Group 2: 50 received 80 mg/day capsule of curcumin nanomicelle and metformin 500 mg TID for 3 months		

	N=100 women with PCOS in Iran	Fasting insulin, total testosterone, HDL-C, LDL-C, triglycerides, AST and ALT levels were assessed.		
4. The effects of curcumin supplementation on oxidative stress, Sirtuin-1 and peroxisome proliferator-activated receptor coactivator 1a gene expression in Polycystic Ovarian Syndrome (PCOS) patients: A randomized placebo-controlled clinical trial [14].	Randomized double-blind clinical trial N=67 women with PCOS [34 received curcumin 1500 mg TID, and 33 received placebo for 3 months] in Tehran, Iran	Gene expression of SIRT1, PGC1a and serum activity of Glutathione Peroxidase (Gpx) and Superoxide Dismutase (SOD) enzymes were evaluated at the beginning of the trial and a 3-month follow-up.	Curcumin supplementation significantly increased gene expression of PGC1 alpha and activity of the Gpx enzyme. Curcumin. There was a non-significant increase in gene expression of SIRT1 and activity of the SOD enzyme.	Curcumin is an efficient reducer of oxidative stress-related complications in patients with PCOS
5. Effects of Curcumin on Glycemic Control and Lipid Profile in Polycystic Ovary Syndrome: Systematic Review with Meta-Analysis and Trial Sequential Analysis [15].	Systematic Review with Meta-analysis.	The objective was to investigate the effects of curcumin on glycemic control in patients with PCOS, which is assessed by fasting glucose, fasting insulin, Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), and quantitative insulin sensitivity check index (QUICKI).	In terms of glycemic control, there was an improvement in fasting glucose and fasting insulin, and a significant increase in HOMA-IR, and QUICKI in those taking curcumin compared to placebo.	Curcumin may improve glycemic control and lipid metabolism in patients with PCOS and metabolic abnormality without significant adverse effects.
		The secondary aim was to investigate the effects of curcumin on lipid profile, assessed by plasma High-Density Lipoprotein (HDL), Low-Density Lipoprotein (LDL), triglyceride, and total cholesterol	In terms of lipid control, HDL levels increased and total cholesterol levels decreased in those taking curcumin. There was no statistically significant improvement in LDL and triglycerides in those taking curcumin compared to placebo.	
	A total of 177 studies were identified using major databases. Based on exclusion criteria only three studies were included in the meta-analysis.	Dosage of curcumin across the studies ranged from 500 mg to 1500 mg per day and the treatment period ranged from 6 weeks to 12 weeks.		
6. The effects of curcumin supplementation on glycemic status, lipid profile and hs-CRP levels in overweight/obese women with polycystic ovary syndrome: A randomized, double-blind, placebo-controlled clinical trial [16].	Randomized double-blind clinical trial N=51 (Intervention group: N=27, Curcumin (500 mg/d) or placebo twice daily for 6 weeks; Placebo group: N=24) in Isfahan, Iran	This study aimed to assess the effects of curcumin supplementation on glycemic status, lipid profile and high sensitivity C-reactive protein serum levels in women with PCOS.	Serum insulin and Quantitative Insulin Sensitivity Check Index (QUICKI) were improved significantly, while Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) improved marginally in the curcumin-treated group	Curcumin supplementation might be beneficial for improving serum insulin and QUICKI. No significant changes in FBS, serum insulin, HOMA-IR, and QUICKI were seen. Serum hs-CRP level was not affected by curcumin supplementation

Lipid profile

Lipid profile was investigated at baseline and after curcumin supplementation. Two studies showed a reduction in total cholesterol and LDL [17,18]. Three studies showed that the improvement in HDL cholesterol [19-22] after three consecutive months of curcumin use compared to placebo or concomitant metformin use [23].

Glcemic control

In terms of glycemic control, the majority of the studies reported an improvement in fasting glucose, insulin resistance and sensitivity [24-29]. Two studies reported improvement in the Quantitative Insulin Sensitivity Check Index (QUICKI) [30,31].

Weight management

Only one study reported a statistically significant decrease in weight and BMI with 12 weeks of curcumin supplementation. Two studies did not demonstrate a statistically significant difference in BMI/weight after curcumin supplementation. The remaining three studies did not measure BMI/weight changes as an outcome of curcumin supplementation.

Hyperandrogenism

Four studies did not investigate hyperandrogenism as an outcome in the study [32]. There was a non-statistically significant increase in estradiol in the intervention group compared to the placebo group. Furthermore, there were no significant changes between the two groups for other hormones such as LH and FSH [33].

Discussion

This systematic review documented six studies investigating the association between curcumin and PCOS. The main findings from this review are that women with PCOS who take curcumin supplementation have improved glycemic control, lipid profile, hyperandrogenism, and reduction in weight/BMI compared to those taking placebo. Specifically, there is a decrease in insulin resistance, DHEAS, LDL and total cholesterol, improvement in fasting glucose, HDL, HOMA-IR and QUICKI.

Curcumin has pharmacological properties such as antioxidant, anti-inflammatory, immunomodulatory, hepatoprotective, nephroprotective, neuroprotective, anti-cancer, anti-atherosclerotic, and anti-diabetic properties. The dosage and route of curcumin administration can influence serum levels.

Glcemic control and lipid profile

The interaction between lipids, glycemic control and curcumin is complex. Curcumin stimulates insulin-mediated glucose uptake by the phosphatidylinositol 3-kinase pathway. This, in turn, upregulates the translocation of glucose transporter 4 to the membrane of skeletal muscle and adipocytes, leading to an increase in glucose uptake, thereby decreasing serum glucose levels.

Curcumin also activates glucose transporter 2 and glucokinases in the liver by increasing the transcription of PPARγ. PPARγ expression can improve glucose homeostasis, insulin sensitivity which can help prevent progression to overt diabetes in patients with PCOS.

SIRT1 can promote insulin secretion and increase insulin sensitivity. Decreases in SIRT1 expression or its activity can lead to the onset of insulin resistance diseases such as PCOS. A rodent study reported that SIRT1 expression in ovaries was lower in PCOS rats compared to controls, suggesting a decline in SIRT1 expression may be associated with local insulin resistance in the ovary. Nevertheless, further research is required to investigate the interaction between SIRT1, curcumin supplementation, and PCOS.

We found promising improvements in LDL, triglycerides, total cholesterol, and increases in HDL. They reported that after 12 weeks of curcumin supplementation, there was a significant improvement in HDL-C, LDL, and triglycerides; however, glycemic status and weight did not change.

Curcumin upregulates LDL receptors and inhibits cholesterol and triglyceride synthesis in hepatocytes in addition to promoting cholesterol metabolism and fecal elimination of bile acids. Another mechanism by which curcumin reduces cholesterol and glucose is through its anti-inflammatory properties. Curcumin is known to reduce tumour necrosis factor-alpha and interleukin-6 which improves insulin sensitivity and decreases obesity-related insulin resistance. Women with PCOS have increased levels of tumour necrosis factor-alpha and other inflammatory cytokines. Hence, curcumin supplementation can help reduce pro-inflammatory cytokines and oxidative stress in women with PCOS.

Hyperandrogenism

Elevations of various androgens including testosterone, androstenedione and DHEAS are observed in women with PCOS. Hyperandrogenism in patients with PCOS is due to excessive activity from the stimulation of luteinizing hormone and failed downregulation of thecal androgen production. This can lead to the appearance of mild to severe acne and hirsutism which can cause significant distress in patients. Theca cells from polycystic ovaries display dysregulation of steroid hormone production. These cells overproduce steroidogenic enzymes, especially cytochrome P450C17. In addition, hyperinsulinemia can lead to aggravation of androgen production as they reduce sex hormone-binding globulin levels leading to an increase in free androgens.

Curcumin is known to have gonado-protective effects due to its antioxidant, anti-inflammatory, anti-carcinogenic, and anti-apoptotic properties, in addition to its ability to modify androgen and estrogen regulation. There have been anecdotal reports of long-term topical application of turmeric leading to slowing or stopping hair growth. Further research is required in this area.

PPARγ agonists can help reduce androgen secretion and enhance ovulation rates in both obese and non-obese women with PCOS. In the ovaries, PPARγ production is found primarily in granulosa cells of developing follicles, theca cells, and the corpus luteum. After the LH surge of the menstrual cycle, PPARγ expression decreases in follicles. The use of PPARγ agonists such as glitazones can decrease the secretion of androgens in the ovaries and can modulate the secretion of certain hormones and immunochemical such as tumour necrosis factor-alpha, reducing androgen production.

Weight management

One of the primary treatments for PCOS is weight reduction. This aids in reducing insulin resistance and regulating menstrual cycles. The mechanism of weight gain may be a result of insulin resistance, decreased insulin sensitivity, impaired glucose and lipid control, and oxidative stress. Obese women with PCOS may experience severe comorbidities such as higher degrees of insulin resistance, hyperandrogenism and hyperinsulinemia. Hence, weight loss is recommended as one of the first management options for these patients.

Once appropriate glycemic and lipid control is achieved, there may be a sufficient reduction in weight. Exercise and diet also play a role in PCOS. It is suggested that women with PCOS limit their intake of gluten and dairy products, and engage in slow-weighted exercises as opposed to high-intensity workouts. The use of curcumin can help reduce weight and BMI. This effect can be a direct result of improvement in glycemic and lipid control or an increase in metabolism.

Prospective studies

The majority of studies of PCOS have been performed on rodents. Future studies should investigate the effects of curcumin on ovulation and reproduction. There is also limited research on the interaction between androgens and curcumin. Prospective studies may also investigate if there are ethnic variations in response to curcumin in women with PCOS. In addition, since most of these studies were done in Iran, future studies can investigate if similar results are evident in women from other countries.

Conclusion

In conclusion, there is a firm association between curcumin and PCOS. The use of curcumin supplements is strongly associated with improvements in glycemic control, lipid and weight management. Incorporating curcumin intake daily for at least three months may improve health outcomes in women with PCOS. Further research is required to understand the interaction between curcumin and ovulation/menstruation and fertility.

References

1. Franik S, Kremer JA, Nelen WL, et al. Aromatase inhibitors for subfertile women with polycystic ovary syndrome. Cochrane Database Syst Rev. 2014;2.
2. Wolf WM, Wattick RA, Kinkade ON, et al. Geographical prevalence of polycystic ovary syndrome as determined by region and race/ethnicity. Int J Environ Res. 2018;15(11): 2589.
3. Shan B, Cai JH, Yang SY, et al. Risk factors of polycystic ovarian syndrome among Li People. Asian Pac J Trop Med. 2015;8(7):590-93.
4. Sartor BM, Dickey RP. Polycystic ovarian syndrome and the metabolic syndrome. Am J Med Sci. 2005;330(6): 336-42.
5. Meier RK. Polycystic ovary syndrome. Nurs Clin North Am. 2018;53(3):407-20.
6. Yau TT, Ng NY, Cheung LP, et al. Polycystic ovary syndrome: A common reproductive syndrome with long-term metabolic consequences. Hong Kong Med J. 2017;23(6):622-34.
7. Williams T, Mortada R, Porter S. Diagnosis and treatment of polycystic ovary syndrome. Am Fam Physician. 2016;94(2):106-13.
8. Legro RS, Brzyski RG, Diamond MP, et al. Letrozole *vs* clomiphene for infertility in the polycystic ovary syndrome. N Engl J Med. 2014;371:119-29.
9. Kunnumakkara AB, Bordoloi D, Padmavathi G, et al. Curcumin, the golden nutraceutical: Multitargeting for multiple chronic diseases. Br J Pharmacol. 2017;174(11): 1325-48.
10. Aggarwal BB, Yuan W, Li S, et al. Curcumin-free turmeric exhibits anti-inflammatory and anticancer activities: Identification of novel components of turmeric. Mol Nutr Food Res. 2013;57(9):1529-42.
11. Jamilian M, Foroozanfard F, Kavossian E, et al. Effects of curcumin on body weight, glycemic control and serum lipids in women with polycystic ovary syndrome: A randomized, double-blind, placebo-controlled trial. Clin Nutr ESPEN. 2020;36:128-133.
12. Heshmati J, Moini A, Sepidarkish M, et al. Effects of curcumin supplementation on blood glucose, insulin resistance and androgens in patients with polycystic ovary syndrome: A randomized double-blind placebo-controlled clinical trial. Phytomedicine: Int J Phyto Phytopharmacol. 2020;80:153395.
13. Sohrevardi SM, Heydari B, Azarpazhooh MR, et al. Therapeutic effect of curcumin in women with polycystic ovary syndrome receiving metformin: A randomized controlled trial. Adv Exp Med Biol. 2021;1308:109-117.
14. Heshmati J, Golab F, Morvaridzadeh M, et al. The effects of curcumin supplementation on oxidative stress, Sirtuin-1 and peroxisome proliferator activated receptor γ coactivator 1α gene expression in Polycystic Ovarian Syndrome (PCOS) patients: A randomized placebo-controlled clinical trial. Diabetes Metab Syndr. 2020;14(2):77-82.
15. Chien YJ, Chang CY, Wu MY, et al. Effects of curcumin on glycemic control and lipid profile in polycystic ovary syndrome: Systematic review with meta-analysis and trial sequential analysis. Nutrients. 2021;13(2):684.
16. Sohaei S, Amani R, Tarrahi MJ, et al. The effects of curcumin supplementation on glycemic status, lipid profile and hs-CRP levels in overweight/obese women with polycystic ovary syndrome: A randomized, double-blind, placebo-controlled clinical trial. Complement Ther Med. 2019;47:102201.
17. Arun N, Nalini N. Efficacy of turmeric on blood sugar and polyol pathway in diabetic albino rats. Plant Foods Hum Nutr. (Dordrecht, Netherlands). 2002;57(1): 41-52.
18. Den Hartogh DJ, Gabriel A, Tsiani E, et al. Antidiabetic properties of curcumin I : Evidence from *in vitro* studies. Nutrients. 2020;12(1):118.
19. Lin J, Zheng S, Chen A, et al. Curcumin attenuates the effects of insulin on stimulating hepatic stellate cell activation by interrupting insulin signaling and attenuating oxidative stress. Lab Invest. 2009;89(12):1397-1409.
20. Jacob A, Wu R, Zhou M, et al. Mechanism of the anti-inflammatory effect of curcumin: PPAR-γ activation. PPAR Res. 2008.
21. Kim HI, Ahn YH. Role of peroxisome proliferator-activated receptor-γ in the glucose-sensing apparatus of liver and β-cells. Diabetes. 2004;53:S60-S65.
22. Janani C, Kumari BR. PPAR gamma gene-A review. diabetes and metabolic syndrome: Clinic Res Rev. 2015;9(1):46-50.
23. Tao X, Zhang X, Ge SQ, et al. Expression of SIRT1 in the ovaries of rats with polycystic ovary syndrome before and after therapeutic intervention with exenatide. Int J Clin Exp. 2015;8(7):8276-8283.
24. Yang YS, Su YF, Yang HW, et al. Lipid lowering effects of curcumin in patients with metabolic syndrome: A randomized, double blind, placebo controlled trial. Phytother Res. 2014;28(12):1770-77.
25. Kim M, Kim Y. Hypocholesterolemic effects of curcumin *via* up-regulation of cholesterol 7a-hydroxylase in rats fed a high fat diet. Nutr Res Pract. 2010;4(3):191-5.
26. Peschel D, Koerting R, Nass N, et al. Curcumin induces changes in expression of genes involved in cholesterol homeostasis. J Nutr Biochem. 2007;18(2):113-19.
27. Rao DS, Sekhara NC, Satyanarayana MN, et al. Effect of curcumin on serum and liver cholesterol levels in the rat. J Nutr. 1970;100(11):1307-1315.

28. Gao L, Gu Y, Yin X, et al. High serum tumor necrosis factor-alpha levels in women with polycystic ovary syndrome: A meta-analysis. PloS one. 2016;11(10):e0164021.
29. Gilling Smith C, Story H, Rogers V, et al. Evidence for a primary abnormality of thecal cell steroidogenesis in the polycystic ovary syndrome. Clin Endocrinol. 1997;47(1): 93-99.
30. Rodriguez Paris V, Bertoldo MJ, et al. The mechanism of androgen actions in PCOS etiology. Med Sci. 2019;7(9):89.
31. Kadasi A, Maruniakova N, Stochmalova A, et al. Direct effect of curcumin on porcine ovarian cell functions. Anim Reprod Sci. 2017;182:77-83.
32. Froment P, Touraine P. Thiazolidinediones and fertility in polycystic ovary syndrome. PPAR Res. 2006;73986.
33. Morales AJ, Laughlin GA, Bützow T, et al. Insulin, somatotropic, and luteinizing hormone axes in lean and obese women with polycystic ovary syndrome: Common and distinct features. J Clin Endocrinol Metab. 1996;81(8): 2854-64.

*Correspondence to:

Dr. Nisha Nigil Haroon

Department of Endocrinology and Internal Medicine

Northern Ontario School of Medicine

Ontario

Canada

E-mail: drnishanigilendo@gmail.com