History of Medicine, 2023, 9(1): 1151–1161
DOI: 10.17720/2409-5834.v9.1.2023.136

Estimation of Interleukin 17A Gene Polymorphism in Patients with Polycystic Ovary Syndrome

Haneen Kareem Khalaf Rawdhah[1]*, Abeer Thaher Naji Al-Hasnawi[1], Zainab Jaber hadi[2], Amal Mounir Mubarki[3]

№College of Medicine, University of Karbala, Karbala, Iraq
EM: haneenkareemkhalaf@gmail.com
ICollege of Medicine, University of Kufa, Najaf, Iraq,
iAl-sader Teaching Hospital, AL-Zahraa Teaching Hospital, Najaf, Iraq

*Corresponding author: Haneen Kareem Khalaf Rawdhah (haneenkareemkhalaf@gmail.com)

Received: 20 January 2023 **Accepted:** 15 April 2023

Citation: Rawdhah HKK, Al-Hasnawi ATN, hadi ZJ, Mubarki AM (2023) Estimation of Interleukin 17A Gene Polymorphism in Patients with Polycystic Ovary Syndrome. History of Medicine 9(1): 1151−1161. https://doi.org/10.17720/2409-5834.v9.1.2023.136

Abstract

Background: Polycystic ovary syndrome (PCOS) is a prevalent endocrine disorder with a vital genetic component and is characterized by polycystic ovaries, hyperandrogenemia, and menstrual irregularity. Methods: A case-control study includes 50 PCOS-affected women and 50 healthy women as a control group. Whole blood was used for DNA extraction. DNA extraction was used to detect Interleukin-17A gene polymorphism (rs2275913) usingReal-Time Polymerase Chain Reaction (RT-PCR). Results: Regarding the genotypes of IL-17A gene (rs2275913) polymorphism, there were no significant differences between the studied group (P=0.421).The AG genotype was at a higher frequency in patients compared with control (50% vs. 42%, respectively); also, the AA genotype was elevated in patients compared with control (16% vs. 12%, respectively).In the alleles frequency, there were no significant differences between the studied group (P=0.307). Conclusion:The result of this study has shown that the IL-17A gene (rs2275913) polymorphism maybe have a protective role in PCOS.Further studies are requiredto demonstrate the role of this polymorphism in PCOS disease.

Keywords
Polycystic ovary syndrome, Interleukin17A gene (rs2275913) polymorphism

Polycystic ovary syndrome (PCOS) is a common disorder in women that is characterized by hyperandrogenism, ovulatory dysfunction and polycystic ovarian morphology (Azziz et al., 2016).
Chronic anovulation, increased androgen, and insulin resistance are all symptoms of PCOS. PCOS is frequently associated with hypertension, obesity,and type II diabetes (Karabulut et al., 2012).
Globally, the geographic variations in PCOS prevalence have been studied. The prevalence of PCOS has been shown to range between 2% and 26%. Among the likely descriptions of significant geographic variations in the prevalence rate were differences in diagnostic criteria, sample heterogeneity, socioeconomic level, medical care availability, the prevalence of important risk factors, health, and education (Deswal et al., 2020).
PCOS is characterized by increased androgen production by the ovaries. Most affected people have metabolic dysfunction defined by insulin resistance and consequent hyperinsulinemia. PCOS raises the chances of developing type 2

diabetes, gestational diabetes, and other pregnancy-related problems, venous thromboembolism, cerebrovascular and cardiovascular events, and endometrial cancer (Azziz et al., 2016).

It is frequently associated with psychological problems like depression and other mood disorders. Most PCOS women are also overweight or obese, which increases androgen secretion while compromising metabolic and reproductive systems and potentially favoring the development of the PCOS phenotype. The definition of PCOS has resulted in a significant increase in scientific interest in this illness, which should be directed further toward improving customized clinical methods and, as a result, therapeutic options (Pasquali et al., 2011).

Factors contributing to difficulties in diagnosing PCOS include the coexistence of multiple diagnostic criteria for PCOS, limitations with standardization of clinical and biochemical hyperandrogenism definitions, the presence of multiple phenotypes, and changes in presentation depending on the patient's age and ethnicity (Dokras et al., 2017). PCOS is marked by increased luteinizing hormone (LH) secretion compared to follicle-stimulating hormone (FSH), increased LH-dependent ovarian testosterone (T), recurrent adrenal androgen excess, significant insulin resistance, dysglycemia, and obesity (Chang and Dunaif, 2021).

The etiological factors related to PCOS are currently unclear and being debated. Numerous reasons may contribute to the etiology of PCOS, including genetic, metabolic, environmental, and immunological factors. Many genes have been identified as essential contributors to PCOS; however, none of these factors have been identified as the primary cause (Abbott, Dumesic, and Franks, 2006). Extensive research suggests that the etiology of PCOS involves an interaction betweenenvironmental factors and gene variants. However, it has been suggested that genetic factorscontribute less than 10% to disease susceptibility(Parker et al., 2022).

The polycystic ovarian syndrome is a chronic inflammatory disease. Several studies have discovered that people with Polycystic ovarian syndrome had more significant amounts of circulating inflammatory molecules. It is unknown whether their rise is due to Polycystic ovary syndrome or obesity and abdominal adiposity (Chang and Dong, 2011). Interleukin-17 (IL-17) is a T cell-derived inflammatory cytokine primarily supplied by Th17 cells and T cells and neutrophils. IL-17 is often referred to as IL-17A (Chaudhari et al., 2016). IL-17 also stimulates the production of other proinflammatory cytokines and chemokines, which mediate immune responses. The human interleukin-17A (IL-17A) gene is located on chromosome 6p12.2 and encodes IL-17A, a major proinflammatory cytokine. IL-17A regulates diverse immune functions, such as promoting the production of other proinflammatory cytokines and cooperating with other cytokines. The rs2275913, a single nucleotide polymorphism (SNP) located at the promoter region of the IL-17A gene, is associated with the activation of the nuclear factor of activated T cell.In addition, several studies found that rs2275913 affects an individual's risk of developing different diseases (Zou et al., 2022).

Materials and Methods

The study had 100 participants divided into two groups: 50 PCOS as patients group, who attended a private clinic at a gynecological clinic in Najaf city, AL-Sader Teaching Medical City, and AL-Zahraa Teaching Hospital and were diagnosed by specialized gynecologists based on The Rotterdam Consensus (2003).The patients must have PCOS and have no history of immunological problems such as autoimmunity, immune deficits, or malignancy. The second group is the control group, which consists of 50 healthy females with no history of pregnancy-related illnesses and at least one successful delivery. Women with no family history of PCOS were chosen for the control group. Patients with PCOS are the exclusion criteria. The number of patients, Type 2 diabetes, family history of diabetes, family history of infertility, lack of physical exercise, high blood pressure, depression, sleep apnea, Cardiovascular disease, and phone numbers were collected from eachparticipant. A disposable syringe and a sterilizing procedure were used to collect 10 ml of blood from the veins of 100 individuals (patients and controls). For the hematological and molecular tests, three milliliters of blood

were distributed into two EDTA tubes (1.5 milliliters of blood in each tube) and stored at -20 ˚C for RT-PCR to evaluate the presence or absence of IL-17A gene polymorphism in the research blood samples. The remaining 7 ml of blood was allowed to coagulate before the serum was separated by centrifugation at 3000 rpm for 5 minutes. The serum was collected in an Eppendorf tube and stored at -20 ˚C for hormonal evaluation.MINI VIDAS® was used to assess the LH, FSH, TSH, and prolactin concentrations.

Detection of IL-17A gene by PCR:

Peripheral blood samples from each patient and healthy control werecollected in sterilized EDTA vacutainers and kept at -20 ˚C until DNA extraction. Moreover, according to the procedure of the FAVORGEN Biotech Corp, Taiwan, genomic DNA was extracted from the nucleated cells of the study groups. Evaluation of DNA extracts quality and integrity as shown in (figure-1).

Five microlitersof genomic DNA was added to a 25 microliter PCR mixture that already included 12.5 microliter ready-to-use Go Taq® Promega Green Master Mix 2x (Promega), 2 microliter of 10 pmol of each of forward- and reverse specific primers of the gene, and 3.5 microliters of nuclease-free water.

Using primers:

Forward:

5-'GCCAAGGAATCTGTGAGGAA-3'

Reverse

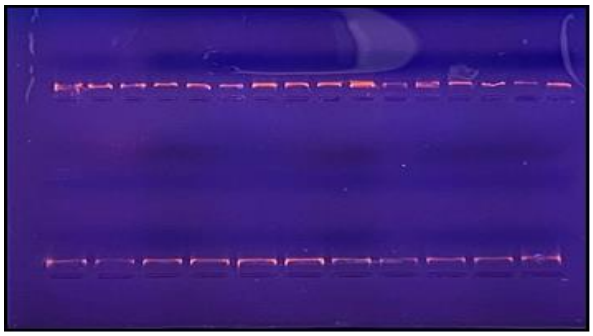

Figure (1): Evaluation of DNA extract quality and integrity. 1.5% agarose gel electrophoresis of genomic DNA in 80 volts at 15 minutes.

5'-TGCCTGCTATGAGATGGACA-3'

To amplify the polymorphism of the IL-17A gene (rs2275913) (Hesampour et al., 2019). The amplification conditions were as follows: Initial Denaturation at 95 ˚C for 5 minutes with one cycle,followed by 29 cycles of, Denaturationat 95 ˚C for 30 s, Annealing at54 ˚C for 60 s, Extension at 72 ˚C for 60 s and Final Extension at 72 ˚C for 5 minutesthen hold at 4˚Con the applied Biosystems thermal cycler. Agarose gel electrophoresis at a concentration of 1.5% was used to confirm the PCR product's presence and integrity, as shown in figure-2.

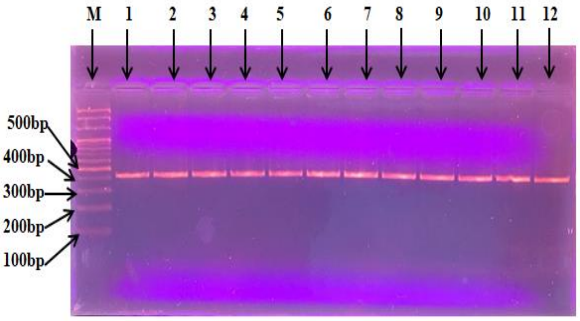

Figure (2): Gel electrophoresis for PCR product of IL-17A gene. 400bp with DNA ladder 100bp (M) on agarose gel 1.5% in 80 volts, 1hour, and detection of the result by UV documentation system.

Detection of IL-17A gene (rs2275139) polymorphism by RT-PCR:

Performing RT-PCR using Sacace, Italy instrument. 4 microliters genomic DNA was added to 10 µL TaqMan® Genotyping Master Mix and0.5 µL from 20X SNP Genotyping Assay (already diluted to be ready to use) into a sterile tube and 5.5 microliters of nuclease-free water. The amplification conditions were as follows: Enzyme activation at 94 ˚C for 15 minutes, Denaturation 40 cycles at 95 ˚C for 15 seconds, and Annealing/ Extension at 60 ˚C for 1 minute.

Statistical analysis

SPSS, a statistical software for the social sciences, was used to conduct the statistical analysis (version 20.0 for windows, SPSS, Chicago, IL, USA). The mean, standard deviation, and range depict quantitative data. The Student's t-test was performed to compare differences between the two groups.A P value of 0.05 was regarded as statistically significant.

Results

PCOS patients with a family history of infertility 4 (8.0%), and the patients that did

not have a family history of infertility 46 (92.0%). In the control group, the number of women with a family history of infertility was 0 (0.00%) while the number of women that did not have a family history of infertility reached 50 (100%). There was no significant difference between PCOS patients and control (P=0.117).

PCOS patients were with a lack of exercise 17 (34.0%) and the patients that did not have a lack of exercise were 33 (66.0%). In the control group, the number of women with a lack of exercise was 0 (0.0%) while the number of women with no lack of exercise reached 50 (100%). There was a significant difference between PCOS patients and control (P=0.005).

PCOS patients were with a hypertension3 (6.0%) and the patients that did not have hypertension were 47 (94.0%). In the control group, the number of women with hypertension was 0 (0.0%) while the number of women that did not have hypertension reached 50 (100%). There was no significant difference between PCOS patients and control (P=0.242).

In PCOS patients, the number of depressed women was 11 (22.0%) and the number of non-depressed women reached 39 (78.0%), while in the control group, the number of depressed women was 0 (0.0%) and non-depressed women 50 (100%). There was a significant difference between PCOS patients and control (P=0.001).

In PCOS patients, the number of women with sleep apnea was 9 (18.0%) and the number of women that did not have sleep apnea reached 41 (82.0%), while in the control group, the number of women with sleep apnea was 0 (0.0%) and the number of women that did not have sleep apnea was 50 (100%). There was a significant difference between PCOS patients and control (P=0.003).

In PCOS cases, the number of women with cardiovascular disease (CVD) was 0 (0.0%) and the number of women that did not have CVD reached 50 (100%), while in the control group, the number of women with CVD was 2 (4.0%) and the number of women that did not have CVD were 48 (96.0%). There was no significant difference between PCOS patients and control (P=0.242), as shown in table-1.

Table (1): Distribution of family history of infertility, lack of exercise, hypertension, depression, sleep apnea, and CVD characteristics of the studied subjects.

Variables		Group				P value
		Patient		Control		
		Count	%	Count	%	
Family history of infertility	Yes	4	8.0%	0	0.0%	0.117**
	No	46	92.0%	50	100.0%	
Lack of exercise	Yes	17	34.0%	0	0.0%	0.005*
	No	33	66.0%	50	100.0%	
Hypertension	Yes	3	6.0%	0	0.0%	0.242**
	No	47	94.0%	50	100.0%	
Depression	Yes	11	22.0%	0	0.0%	0.001*
	No	39	78.0%	50	100.0%	
Sleep apnea	Yes	9	18.0%	0	0.0%	0.003*
	No	41	82.0%	50	100.0%	
Cardiovascular disease (CVD)	Yes	0	0.0%	2	4.0%	0.242**
	No	50	100.0%	48	96.0%	
*P value is significant, **P value is non-significant (Chi-Square test)						

FSH, LH, TSH, Prolactin, WBC, and lymphocyte means of the patients and control groups:

The mean of follicle-stimulating hormone(FSH) in PCOS cases was (7.11) and in control was (5.71). However, the association was non-significant (P=0.402) between PCOS patients and control.The mean of luteinizing hormone (LH) in PCOS cases was (5.46) and in control was (4.53), the association was non-significant (P=0.429) between PCOS patients and control.The mean of thyroid stimulating hormone (TSH) in PCOS cases was (1.86) and in control was (2.79).There was a significant difference in TSH between patients and control (P=0.004).The mean of prolactin in PCOS cases was (25.24) and in control was (20.93), the association was non-significant (P=0.111) between PCOS patients and control.

In the current study, the mean white blood cell count (WBC) in PCOS cases was (7.12)

and in control was (7.57). However, the association was non-significant (P=0.230) between PCOS patients and control. Also, the mean of lymphocytes in PCOS cases was (31.81) and in control was (33.67), the association was non-significant (P=0.231) between PCOS patients and control, as demonstrated in table -2.

Table (2): Determination of FSH, LH, TSH, Prolactin, WCC, and lymphocyte characteristics of the studied subjects.

Variables	Group				P value
	Patient		Control		
	Mean	SD	Mean	SD	
Follicle Stimulating Hormone (FSH)	7.11	10.88	5.71	3.34	0.402**
Luteinizing Hormone (LH)	5.46	6.75	4.53	3.88	0.429**
Thyroid-stimulating Hormone (TSH)	1.86	1.03	2.79	2.03	0.004*
Prolactin	25.24	15.57	20.93	10.75	0.111**
White cell count (WCC)	7.12	1.94	7.57	1.92	0.230**
Lymphocyte	31.81	7.50	33.67	8.78	0.231**
*P value is significant, **P value is non-significant (Student's t-test), SD: Standard Deviation					

The IL-17A gene (rs2275913) polymorphism in patients and control:

Genetic polymorphism of the IL-17A gene (rs2275913) was observed with three genotypes (AG, GG, and AA) in PCOS patients and control. The "G" allele was elevated in control compared with patients (67% vs 59%, respectively) whereas, the "A" allele was elevated in patients compared with control (41% vs 33%, respectively) as shown in the table (3). In the alleles, there was no significant difference with the studied group (P=0.307). The AG genotype was found to be at a higher frequency in patients compared with control (50% vs 42%, respectively), the GG genotype was found to be at a higher frequency in control compared with patients (46% vs 34%, respectively) and the AA genotype was elevated in patients compared with control (16% vs 12%, respectively), as shown in the table-3. In the genotype, there was no significant difference between the studied groups (P=0.421).

Table (3): Genotypes and allele frequency distribution of IL-17A gene polymorphism in patients and control.

Variables		Group				P value
		Patient		Control		
		Count	%	Count	%	
Alleles	G	59	59%	67	67%	0.307*
	A	41	41%	33	33%	
IL-17A genotypes	AG	25	50.0%	21	42.0%	0.421*
	GG	17	34.0%	23	46.0%	
	AA	8	16.0%	6	12.0%	
*P value is non-significant (P> 0.05), (Chi-Square test).						

Discussion

In this study, there was no significant (P=0.117) association between a family history of infertility and PCOS patients compared with healthy control. This result is slightly lower than the result found in the study by Shan et al., (2015), who reported that 41(14.4%) of PCOS patients had a family history of infertility and 244 (85.6%) doesn't have, while the control group only 4 (0.7%) had a family history of infertility and 576 (99.3%) had not, with (P=0.000). The present study result is incompatible with the study by Hussein and Alalaf, (2013) who found there were 106 women in the PCOS group and 214 in the non-PCOS group, the family history of PCOS patients was 40(37.7%) which is slightly higher than in the non-PCOS were 67 (31.3%). In addition, a study by Al-Musawy, Al-Saimary, and Flaifil,(2018), demonstrated out of 73 PCOS cases 50 (68.5%) had a history of infertility and out of 73 fertile control 0 (0.0%) had a history of infertility.

Also, the present study showed a significant association (P=0.005) between lack of exercise and PCOS patients compared with healthy control. This result was agreed with several studies such as the study by Shan et al.,(2015), in which lack of exercise PCOS cases were 159 (27.4%) and the patients that did not have a lack of exercise were 421 (72.6%), while the control in the same study with lack of exercise were 43 (15.1%) and those without lack of exercise 242 (84.9%). Lack of physical exercise, leading to uneven distribution of

body fat, is an important risk factor of centripetal obesity. One study advises proper diet and regular physical exercise to obese PCOS patients to achieve significant alleviation of symptoms like excessive hair and irregular menstruation (Le Donne et al., 2012).

Hypertension develops in some women with PCOS during their reproductive years and sustained hypertension may develop in later-life women with the disorder,reduce vascular compliance and vascular endothelial dysfunction were noted in most,but not all (Wesen,2008). The current study showed no significant difference between PCOS patients and control (P=0.242). These results disagreed with another study conducted by Chen et al., (2007), in which, the high bioavailable testosterone levels (free androgen index: ≥ 19%) in women with PCOS increased the risk of elevated blood pressure (SBP ≥ 130 mm Hg and/or DBP ≥ 85 mm Hg) with (P=0.029) after adjustment for age, anthropometric measures, and metabolic profiles. And a study by Joham et al., (2015) in which Hypertension prevalence was 5.5% (95% CI: 3.3−7.7) in women reporting PCOS and 2.0% (95% CI: 1.6−2.3) in women not reporting PCOS (P <0.001). Other studies agreed with the current result such as the study by Meyer, McGrath, and Teede,(2005) which demonstrated no difference in 24-hour ambulatory BP between women with PCOS and control despite evidence of increased arterial stiffness and endothelial dysfunction.

The present study showed a significant difference between PCOS patients and control (P=0.001) regardingdepressed women. This result is compatible with the study by Chaudhari, Mazumdar, and Mehta, (2018) who found in 70 females studied, 27 were found to be suffering from anxiety disorders, while 18 were found to be suffering from depressive disorders. The prevalence of anxiety disorders was 38.6%, and the prevalence of depressive disorders was 25.7%. A study by Cinar et al. (2011) reported 28.6% of PCOS women versus 4.7% of control women had clinical depression scores indicating an 8.1-fold increased risk of depression in PCOS (P =0.001). Also, a study accomplished by Anitha, SubhaRevathi, and Kalaivani, (2017) revealed that depression scores were significantly increased in the PCOS group compared to the control (P < 0.001). PCOS patients with menstrual irregularities have been linked to higher rates of depression. These irregularities mean these women have brief fertile periods and emotional changes like anger, irritability, and signs of stress are seen in these periods, the emotional changes are linked to the hormonal changes in those fertile periods (Balikci et al., 2014).

The prevalence of obstructive sleep apnea (OSA) in the general population varies considerably between studies, mainly due to differences in the populations studied, study designs, and the methods and criteria used to diagnose OSA (Tahrani, 2015). In the present study, there was a significant difference between PCOS patients and control (P=0.003) regardingsleep apnea. Vgontzas et al., (2001) assessed the prevalence of OSA in 53 premenopausal women with PCOS as compared to 452 control women. The authors found that PCOS women were 30 times more likely to have OSA than control and that the difference between the two groups remained significant even after controlling for BMI. In an independent study published in the same year, a comparison of 18 overweight women with PCOS with 18 age- and weight-matched control, showed that PCOS women were significantly more likely to suffer from symptomatic OSA (based on an apnea-hypopnea index (AHI) >5 and the presence of excessive daytime sleepiness) than control women (44.4% vs 5.5%) (Fogel et al., 2001). Finally, survey assessments of the prevalence of sleep apnea risk (using the Berlin questionnaire) in a cohort of 40 women with PCOS, revealed that three of four women were at high risk for sleep apnea.

In women with PCOS, the role of hyperandrogenism per se in Cardiovascular disease (CVD) development has been difficult to distinguish from the effect of obesity and IR. CVD in PCOS may be related to IR, as cardiac and endothelial dysfunction, greater carotid intima-media thickness test (cIMT), and dyslipidemia are associated with IR in adults (Robinson et al., 1996; Yaralı et al., 2001; Orio et al., 2004; Vural et al., 2005). In the current study, there was no significant

difference between PCOS patients and control (P=0.242). This result was agreed with a study by Lakhani et al., (2000) which reported beneficial internal carotid artery flow parameters consistent with reduced vascular tone in women with PCOS, another cohort of 309 women with PCOS and 343 control with a mean (SD) follow-up time of 23.7 (13.7) years, women with PCOS had no increase in adverse cardiovascular outcomes in midlife even though they weighed more compared to control, for example, adjusted HR for MI and stroke were 0.74 [(0.32−1.72); p = 0.48]and 1.05 [(0.28−3.92); P= 0.94], respectively (Iftikhar et al., 2012).

Regarding follicle-stimulating hormone (FSH), in the current study, there was a non-significant association (P=0.402) between PCOS patients compared with healthy control. This result is consistent with other studies such as a study by Anwary, Alfazzaman, and Begum, (2010) in which fifty subfertile women suffering from PCOS were recruited for evaluation in which serum FSH range was 2.30-13.10 mlU/ml (mean±SD 6.10±1.94). In only 1 patient (2%) serum FSH level was low <2.8 mlU/ml and normal (2.8-21.0) in the rest 49 (98%) patients and another study by Desforges-Bullet et al. (2010) in which 22 PCOS women had serum FSH was range 2.8−9 IU/L (mean 5.9) and control range 4.8−10.6 lU/L (mean 7.3) with (P=0.06). The present study disagreed with the study by Mehde and Resan, (2014) in which sixty patients with PCOS and thirty healthy control have participated in this study FSH in PCOS cases with mean±SD (5.03±0.77) and control had mean±SD (6.00±0.95) with (P=0.045). Determinations of FSH, however, are characterized by many difficulties. One quite obvious problem is the inconvenience of required blood draw on day 2 or 3 of menses. The second issue of concern is the degree of cycle-to-cycle fluctuation in baseline FSH levels (Hehenkamp et al., 2006). Regardingluteinizing hormone (LH) level, the association was non-significant (P=0.429) between PCOS patients and control. A study by Anwary, Alfazzaman, and Begum, (2010), reported that serum LH was normal (1.1-14.7 mIU/ml) in 22 (44%) women and raised (>14.7 mIU/ml) in 28 (56%) cases. The mean (±SD) serum LH level was (15.02±3.66 mIU/ml) (range 6.70-25.50). Another study by Mehde and Resan,(2014), in which LH in PCOS cases with mean±SD (12.68±3.57) and control had mean±SD (6.96±0.99) with (P=0.0008).The mean LH level was observed at (12.79±7.1mIU/ml) in a study by Begum, (2009) as well as a study by Nahar et al., (2017). Other studies by Timpatanapong and Rojanasakul, (1997), Codner et al., (2007), and Kumar et al., (2016) found that serum LH was (8.68±5.5, 8.1±3.0 and 9.3±5.0 mIU/ml) respectively.

Concerning thyroid stimulating hormone (TSH), the present study showed a significant association (P=0.004) between PCOS patients compared with healthy control. This result agreed with some studies such as a study by Anwary, Alfazzaman, and Begum, (2010), in which the mean (±SD) of TSH serum level was 2.35±0.82 μIU/ml (range 0.94-4.20); 49 (98%) women had normal level (0.4-4.0 μIU/ml) and 1 (2%) had raised value (>4.0 μIU/ml) and a study by Christodoulopoulou et al. (2016) whose found FSH serum level about (2.39±1.63). Also, a study by Nahar et al., (2017) in which the mean serum TSH was 3.4±1.28 μIU/ml. IslamPathan and Ahmed, (2015) found hypothyroidism in 11.4% of PCOS patients.

Regarding prolactin level, the association was non-significant (P=0.111) between PCOS patients and control. This result agreed with a study by Nahar et al. (2017) in which the mean serum prolactin level was found (315.15±80.5) μIU/ml with a reference range 204-412 μIU/ml and a study by Anwary, Alfazzaman, and Begum, (2010), in which serum prolactin was normal (1.9-25.0 ng/ml) in 43 (86%) and raised (>25 ng/ml) in 7 (14%) women; mean (±SD) was (23.52±46.96 ng/ml) (range 5.60-315.18) but Begum, (2009) found it higher (415.15±180.5) in another group of Bangladeshi women and study by Mehde and Resan,(2014) found a highly significant increase in serum prolactin (P>0.001). Islam, Pathan, and Ahmed, (2015) in another Bangladeshi study observed hyperprolactinemia in 18.6% of cases of PCOS.

In addition, there was no significant association (P=0.230) between white blood

cell (WBC) count in PCOS patients compared with healthy control in this study. This result agreed with some studies such as a study by Patel et al.,(2017) in which the mean of WBC in PCOS cases was (7.95±1.50) and in control was(6.87 ± 2.84) with (P=0.156). In Contrary, a study by Orio et al. (2005) this study evaluated 150 women with PCOS and 150 control matched for age and BMI. Median WBC in the PCOS and control groups was 7,260 and 5,220 cells/mm^3 respectively with (P<.0001) and in a study by Herlihy et al. (2011) the mean WCC was higher in the PCOS group compared with the non-PCOS-group ($8.9Ч10^9$/L vs $7.4Ч10^9$/L P=0.002).

Regarding lymphocyte count, the association was non-significant (P=0.231) between PCOS patients and control groups. The current study result is compatible with a study by Yilmaz, Duran, and Basaran, (2016) in which the mean lymphocyte count was (31.04±6.42) in the patient group and (34.4±6.69) for the control group with (P=0.036). In contrary, a study by Almaeen et al.,(2022), in which the mean of lymphocyte count was (38.77±10.74) in the patients' group and (46.99±1.63) in the control with significantassociation(P=0.000). Significant elevation of lymphocytes and monocytes was also found in a study reported by Orio et al.,(2005).

Regarding genetic polymorphism of the IL-17A gene (rs2275913), there were no significant differences between the studied groups regarding alleles frequency (P=0.307) and the genotypes (P=0.421).This result disagreed with a study conducted by Hesampour et al. (2019), which showed that the distribution of rs2275913 SNP in IL-17A was different between Iranian women complicated with PCOS and healthy women. Both the GG genotype and G allele were found in a higher proportion in the PCOS group compared with the control. Which is considered the first study to report the relationship between IL-17A gene rs2275913 and PCOS. And also a study by Zou et al. (2022) in which the distribution of rs2275913 in the control group and the PCOS group was statistically different. The multivariate logistic regression model showed that (rs2275913) could increase the risk of PCOS occurrence.

Conclusion

Our study found that IL-17A gene (rs2275913) polymorphism maybe have a protective role in PCOS. Further studies with large samples size need for recognizing the role of this polymorphism in PCOS patients.

Reference

ABBOTT, D., DUMESIC, D. & FRANKS, S. 2006. Developmental origin of polycystic ovary syndrome. J. Endocrinol.(in the press).

ALMAEEN, A. H., ALDURAYWISH, A. A., NABI, M., SHAH, N. N., SHAIK, R. & TANTRY, B. A. 2022. Quantitative Changes in White Blood Cells: Correlation with the Hallmarks of Polycystic Ovary Syndrome. Medicina, 58, 535.

AL-MUSAWY, S. H. H., AL-SAIMARY, I. E. & FLAIFIL, M. S. 2018. Levels of cytokines profile in polycystic ovary syndrome. Medical Journal of Babylon, 15, 124.

ANITHA, B., SUBHAREVATHI, K. & KALAIVANI, S. 2017. Prevalence of depression among women with polycystic ovarian syndrome. Indian Journal of Basic and Applied Medical Research, 6, 84-91.

ANWARY, S. A., ALFAZZAMAN, M. & BEGUM, N. 2010. A clinical study on PCOS patients in a Tertiary Hospital. Medicine today, 22, 34-37.

AZZIZ, R., CARMINA, E., CHEN, Z., DUNAIF, A., LAVEN, J. S., LEGRO, R. S., et al. YILDIZ, B. O. 2016. Polycystic ovary syndrome. Nature reviews Disease primers, 2, 1-18.

BALIKCI, A., ERDEM, M., KESKIN, U., ZINCIR, S. B., GUELSUEN, M., OEZCELIK, F., et al. ERGUEN, A. 2014. Depression, anxiety, and anger in patients with polycystic ovary syndrome. Nцro Psikiyatri Arşivi, 51, 328.

BEGUM, F. 2009. Clinical and hormonal profile of polycystic ovary syndrome. Journal of SAFOG, 1, 22-25.

CHANG, S. & DUNAIF, A. 2021. Diagnosis of polycystic ovary syndrome: which criteria to use and when? Endocrinology and Metabolism Clinics, 50, 11-23.

CHANG, S. H. & DONG, C. 2011. Signaling of interleukin-17 family cytokines in immunity and inflammation. Cellular signalling, 23, 1069-1075.

CHAUDHARI, A. P., MAZUMDAR, K. & MEHTA, P. D. 2018. Anxiety, depression, and quality of life in women with polycystic ovarian syndrome. Indian journal of psychological medicine, 40, 239-246.

CHAUDHARI, H. L., WARAD, S., ASHOK, N., BAROUDI, K. & TARAKJI, B. 2016. Association of Interleukin-17 polymorphism (-197G/A) in chronic and localized aggressive periodontitis. Brazilian oral research, 30.

CHEN, M.-J., YANG, W.-S., YANG, J.-H., CHEN, C.-L., HO, H.-N. & YANG, Y.-S. 2007. Relationship between androgen levels and blood pressure in young women with polycystic ovary syndrome. Hypertension, 49, 1442-1447.

CHRISTODOULOPOULOU, V., TRAKAKIS, E., PERGIALIOTIS, V., PEPPA, M., CHRELIAS, C., KASSANOS, D. & PAPANTONIOU, N. 2016. Clinical and biochemical characteristics in PCOS women with menstrual abnormalities. Journal of Family & Reproductive Health, 10, 184.

CINAR, N., KIZILARSLANOGLU, M. C., HARMANCI, A., AKSOY, D. Y., BOZDAG, G., DEMIR, B. & YILDIZ, B. O. 2011. Depression, anxiety and cardiometabolic risk in polycystic ovary syndrome. Human Reproduction, 26, 3339-3345.

CODNER, E., ICHGUEZ, G. N., VILLARROEL, C., LOPEZ, P., SOTO, N. S., SIR-PETERMANN, T., et al. REY, R. A. 2007. Hormonal profile in women with polycystic ovarian syndrome with or without type 1 diabetes mellitus. The Journal of Clinical Endocrinology & Metabolism, 92, 4742-4746.

DESFORGES-BULLET, V., GALLO, C., LEFEBVRE, C., PIGNY, P., DEWAILLY, D. & CATTEAU-JONARD, S. 2010. Increased anti-Mьllerian hormone and decreased FSH levels in follicular fluid obtained in women with polycystic ovaries at the time of follicle puncture for in vitro fertilization. Fertility and sterility, 94, 198-204.

DESWAL, R., NARWAL, V., DANG, A. & PUNDIR, C. S. 2020. The prevalence of polycystic ovary syndrome: a brief systematic review. Journal of Human Reproductive Sciences, 13, 261.

DOKRAS, A., SAINI, S., GIBSON-HELM, M., SCHULKIN, J., COONEY, L. & TEEDE, H. 2017. Gaps in knowledge among physicians regarding diagnostic criteria and management of polycystic ovary syndrome. Fertility and sterility, 107, 1380-1386. e1.

FOGEL, R. B., MALHOTRA, A., PILLAR, G., PITTMAN, S. D., DUNAIF, A. & WHITE, D. P. 2001. Increased prevalence of obstructive sleep apnea syndrome in obese women with polycystic ovary syndrome. The Journal of Clinical Endocrinology & Metabolism, 86, 1175-1180.

HEHENKAMP, W. J., LOOMAN, C. W., THEMMEN, A. P., DE JONG, F. H., TE VELDE, E. & BROEKMANS, F. J. 2006. Anti-Mullerian hormone levels in the spontaneous menstrual cycle do not show substantial fluctuation. The Journal of Clinical Endocrinology & Metabolism, 91, 4057-4063.

HERLIHY, A., KELLY, R., HOGAN, J., O'CONNOR, N., FARAH, N. & TURNER, M. 2011. Polycystic ovary syndrome and the peripheral blood white cell count. Journal of Obstetrics and Gynaecology, 31, 242-244.

HESAMPOUR, F., JAHROMI, B. N., TAHMASEBI, F. & GHARESI-FARD, B. 2019. Association between interleukin-32 and interleukin-17A single nucleotide polymorphisms and serum levels with polycystic ovary syndrome. Iranian Journal of Allergy, Asthma and Immunology, 91-99.

HUSSEIN, B. & ALALAF, S. 2013. Prevalence and characteristics of polycystic ovarian syndrome in a sample of infertile Kurdish women attending IVF infertility center in maternity teaching hospital of Erbil City. Open Journal of Obstetrics and Gynecology, 2013.

IFTIKHAR, S., COLLAZO-CLAVELL, M., ROGER, V., SAUVER, J. S., BROWN JR, R., CHA, S. & RHODES, D. 2012. Risk of cardiovascular events in patients with polycystic ovary syndrome. The Netherlands journal of medicine, 70, 74.

ISLAM, S., PATHAN, F. & AHMED, T. 2015. Clinical and Biochemical Characteristics of Polycystic Ovarian Syndrome among Women in Bangladesh. Mymensingh medical journal: MMJ, 24, 310-318.

JOHAM, A. E., BOYLE, J. A., ZOUNGAS, S. & TEEDE, H. J. 2015. Hypertension in reproductive-aged women with polycystic ovary syndrome and association with obesity. American journal of hypertension, 28, 847-851.

KARABULUT, A., YAYLALI, G. F., DEMIRLENK, S., SEVKET, O. & ACUN, A. 2012. Evaluation of body fat distribution in PCOS and its association with carotid atherosclerosis and insulin resistance. Gynecological Endocrinology, 28, 111-114.

KUMAR, A. N., NAIDU, J. N., SATYANARAYANA, U., RAMALINGAM, K. & ANITHA, M. 2016. Metabolic and endocrine characteristics of Indian women with polycystic ovary syndrome. International journal of fertility & sterility, 10, 22.

LAKHANI, K., CONSTANTINOVICI, N., PURCELL, W., FERNANDO, R. & HARDIMAN, P. 2000. Internal carotid artery haemodynamics in women with polycystic ovaries. Clinical Science, 98, 661-665.

LE DONNE, M., ALIBRANDI, A., GIARRUSSO, R., MONACO, L. & MURACA, U. 2012. Dieta, metformina e inositolo in donne sovrappeso e obese con sindrome dell'ovaio policistico: effetti sulla composizione corporea. Minerva Ginecol, 64, 23-9.

MEHDE, A. A. & RESAN, A. K. 2014. Study of several biochemical features in sera of patients with polycystic ovaries and compared with the control group. Australian Journal of Basic and Applied Sciences, 8, 620-627.

MEYER, C., MCGRATH, B. P. & TEEDE, H. J. 2005. Overweight women with polycystic ovary syndrome have evidence of subclinical cardiovascular disease. The Journal of Clinical Endocrinology & Metabolism, 90, 5711-5716.

NAHAR, K., MAHFUZA, G., BEGUM, S. A., KHATUN, K. & ISLAM, M. R. 2017. Clinical, biochemical and hormonal profile of polycystic ovary syndrome. Journal of National Institute of Neurosciences Bangladesh, 3, 94-98.

ORIO JR, F., PALOMBA, S., CASCELLA, T., DI BIASE, S., MANGUSO, F., TAUCHMANOVA, L., et al. RUSSO, T. 2005. The increase of leukocytes as a new putative marker of low-grade chronic inflammation and early cardiovascular risk in polycystic ovary syndrome. The Journal of Clinical Endocrinology & Metabolism, 90, 2-5.

ORIO JR, F., PALOMBA, S., SPINELLI, L., CASCELLA, T., TAUCHMANOVA, L., ZULLO, F., et al. COLAO, A. 2004. The cardiovascular risk of young women with polycystic ovary syndrome: an observational, analytical, prospective case-control study. The Journal of Clinical Endocrinology & Metabolism, 89, 3696-3701.

PARKER, J., O'BRIEN, C., HAWRELAK, J. & GERSH, F. L. 2022. Polycystic ovary syndrome: An evolutionary adaptation to lifestyle and the environment. International Journal of Environmental Research and Public Health, 19, 1336.

PASQUALI, R., STENER-VICTORIN, E., YILDIZ, B. O., DULEBA, A. J., HOEGER, K., MASON, H., et al. TAPANAINEN, J. S. 2011. PCOS Forum: research in polycystic ovary syndrome today and tomorrow. Clinical endocrinology, 74, 424-433.

PATEL, S. S., TRUONG, U., KING, M., FERLAND, A., MOREAU, K. L., DOROSZ, J., et al. MAAHS, D. M. 2017. Obese adolescents with polycystic ovarian syndrome have elevated cardiovascular disease risk markers. Vascular Medicine, 22, 85-95.

ROBINSON, S., HENDERSON, A., GELDING, S., KIDDY, D., NITHTHYANANTHAN, R., BUSH, A., et al. FRANKS, S. 1996. Dyslipidaemia is associated with insulin resistance in women with polycystic ovaries. Clinical endocrinology, 44, 277-284.

SHAN, B., CAI, J.-H., YANG, S.-Y. & LI, Z.-R. 2015. Risk factors of polycystic ovarian syndrome among Li People. Asian Pacific journal of tropical medicine, 8, 590-593.

TAHRANI, A. A. 2015. Diabetes and sleep apnea. International textbook of diabetes mellitus, 316-336.

TIMPATANAPONG, P. & ROJANASAKUL, A. 1997. Hormonal profiles and prevalence of polycystic ovary syndrome in women with acne. The Journal of dermatology, 24, 223-229.

VGONTZAS, A. N., LEGRO, R. S., BIXLER, E. O., GRAYEV, A., KALES, A. & CHROUSOS, G. P. 2001. Polycystic ovary syndrome is associated with obstructive sleep apnea and daytime sleepiness: role of insulin resistance. The Journal of Clinical Endocrinology & Metabolism, 86, 517-520.

VURAL, B., CALISKAN, E., TURKOZ, E., KILIC, T. & DEMIRCI, A. 2005. Evaluation of metabolic syndrome frequency and premature carotid atherosclerosis in young women with polycystic ovary syndrome. Human Reproduction, 20, 2409-2413.

WESEN, A. 2008. Hormonal Changes in Polycystic Ovarian Syndrome As Related to Metabolic Syndrome in Iraqi Women. Department of Chemistry, College of Science for Women, University of Baghdad.

YARALı, H., YıLDıRıR, A., AYBAR, F., KABAKCı, G., BUKULMEZ, O., AKGUL, E. & OTO, A. 2001. Diastolic dysfunction and increased serum homocysteine concentrations may contribute to increased cardiovascular risk in patients with polycystic ovary syndrome. Fertility and sterility, 76, 511-516.

YILMAZ, M., DURAN, C. & BASARAN, M. 2016. The mean platelet volume and neutrophil to lymphocyte ratio in obese and lean patients with polycystic ovary syndrome. Journal of Endocrinological Investigation, 39, 45-53.

ZOU, L., CHENG, Y., YANG, L., ZHANG, F., ZHAO, H., NIAN, L., et al. FENG, Y. 2022. Association of IL-17A gene polymorphism rs2275913 with the polycystic ovary syndrome in Yunnan Province, China. European Journal of Obstetrics & Gynecology and Reproductive Biology, 271, 27-30.