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Research Article

SIGNIFICANCE OF MONOCYTE CHEMOATTRACTANT PROTEIN-1, THYROID HORMONES AND OTHER CLINICAL MANIFESTATIONS IN IRAQI PATIENTS WITH POLYCYSTIC OVARIAN SYNDROME

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ABSTRACT

Objective: Polycystic ovarian syndrome (PCOS) is a complex disease occurred throw genital period of women depends on the age, genetic factors, and ethnicity. Monocyte Chemoattractant Protein-1 (MCP-1) has been implicated in the metabolic disturbances and menstrual irregularities.

Methods: In the biochemical test, the blood was collected in plain tubes then separated by centrifugation. Serum was collected in test tubes then, MCP, haemoglobin (Hb), packed cell volume (PCV), fasting blood glucose (FBG), urea, creatinine, prolactin, testosterone, luteinizing hormone (LH), follicle stimulating hormone (FSH), T3, T4, and thyroid-stimulating hormone (TSH) were determined by enzyme-linked immune-sorbent assay and relevant clinical features were collected simultaneously in all subjects.

Results: The results showed no significant increased in means of age, body mass index in PCOS women (patients) when compared with healthy subjects (control groups) also there was no significant decreased in levels of Hb, PCV while increased in FBG, urea and creatinine in PCOS women when compared with healthy subjects. In addition, mean of LH and 17 β-Estradiol were no significant increased except the significantly increased in the ratio of LH/FSH, prolactin, and testosterone, while FSH was significantly decreased in PCOS women when compared with healthy subjects. Levels of triiodothyronine (T3) and thyroxine (T4) were found significantly decreased while an increased level of TSH when compared with healthy subjects. Finally, MCP-1 was showed significantly increased in PCOS women when compared with healthy subjects.

Conclusions: It can be concluded that PCOS women might suffer from changes in the levels of MCP-1(an inflammation marker). Besides, it was detected that TSH might be responsible related metabolic disturbances could be related to TSH and MCP which can be considered as relevant features in such disturbances.

Keywords: Polycystic ovarian syndrome, Reproductive hormones, Thyroid hormones, Monocyte chemoattractant protein-1.

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INTRODUCTION

Polycystic ovarian syndrome (PCOS) is endocrine disease causes infertility, acne, hirsutism, and irregular periods, with insulin resistance [1,2]. The follicles in each ovarian outside about 10–15 with most of them generally small or immature than average caused infertility [3]. Many factors are thought to be responsible for its pathophysiology such as ethnicity, genetic, multiple endocrine, and metabolic abnormalities [4,5]. In addition to, environmental factors such as physical activity, lifestyle, and diet [6]. Insulin resistance, hyperandrogenemia, and PCOS are associated with pro-inflammatory status caused by oxidative stress [7]. The production of reactive oxygen species is increased by hyperglycemia associated with PCOS [8] Elevated androgen which leads to overproduction of gonadotropins particularly luteinizing hormone (LH) [9] together with high insulin level leads to follicular growth arrest that initiates anovulation [10]. Anovulation in PCOS women is often associated with estradiol (E_2) secretion and progesterone production [11]. PCOS women present with phenotypes according to ESHRE guidelines [12] endocrine irregularities including abnormally high levels of LH, follicle stimulating hormone (FSH), FSH/ LH, prolactin, estradiol, testosterone, and insulin resistance [13,14]. Moreover, PCOS women may be presented with nodular goiter associated with this syndrome [15,16]. Many studies showed disorder in tri-iodothyronine (T3) level and anti-thyroid peroxidase antibody in PCOS patients [17]. Hypothyroidism has been associated increase of sex hormone-binding globulin levels [18] these actions effected on the osteoblast cells [19]. The treatment aimed in the regulation of menses and recover of fertility [20]. The first-line therapy is the lifestyle modification, oral pharmacological agents such as clomiphene and metformin, which lower the level of insulin resistance and induce ovulation [21]. Besides, it was found that Vitamin D and metabolic modulations [22]. Monocyte chemoattractant protein-1 (MCP-1) and Macrophage inflammatory protein-1 closely related to metabolic syndrome presence of chronic low-grade inflammation in women with this syndrome are emerging [23]. MCP-1 is expressed and secreted by adipocyte, which has been reported to be involved in the recruitment and activation of peripheral blood leukocytes in adipose tissue and the induction of systemic insulin resistance [24].

PATIENTS AND METHODS

About 25 PCOS women (patients) and 25 healthy subjects (control group) were enrolled in this study. Blood was collected from Kamal- Al SamarraiHospital/Baghdad. In the biochemical test, the blood was separated by centrifugation then in test tubes which were marked with names of patients and control group then frozen at −20°C. Then, MCP, hemoglobin (Hb), packed cell volume (PCV), fasting blood glucose (FBG), urea, creatinine, prolactin, testosterone, LH, FSH, T3, T4, and thyroid-stimulating hormone (TSH) were determined by enzyme-linked immune-sorbent assay and relevant clinical features were collected simultaneously in all subjects.

Statistical analysis

The results were expressed as Mean±standard deviation with $p<0.05$ indicated that there was a significant difference when comparing between PCOS women and healthy subjects using SPSS-18 program

Microsoft. Correlation coefficients test was done between groups; the significant correlation between values was expressed as $p<0.05$.

RESULTS AND DISCUSSION

Patients with PCOS suffered irregularity in a menstrual cycle which usually either amenorrhea or oligomenorrhea, patients with PCOS suffered from symptoms such as depression, acne, and hirsutism in varying intensity as shown in Table 1.

In this study, the results showed no significant increase in the means of age and body mass index in patients when compared with healthy subjects as shown in Table 2.

There was no significant decrease in the serum levels of Hb and PCV while no significant increase in FBG, urea, and creatinine in PCOS patients when compared with the control group as shown in Table 3.

In addition, mean of LH and 17 β-Estradiol were no significantly increased except the significant increase in the ratio of LH/FSH, prolactin, and testosterone, while FSH was significantly decreased in PCOS women when compared with healthy subjects as shown in Table 4.

Levels of triiodothyronine (T3), thyroxine (T4) were found to be significantly decreased, however, a significant increase in the level of TSH was found in patients when compared with healthy subjects. Finally, a significant increase was detected in the level of MCP-1 in patients when compared with healthy control as shown in Table 5 and Fig. 1.

Table 1: General description of PCOS women

Symptoms	n (%)
Amenorrhea	7 (28)
Oligomenorrhea	14 (56)
Menstrual irregularity	21 (84)
Acne	14 (56)
Depression	16 (64)
Hirsutism	20 (80)

PCOS: Polycystic ovarian syndrome

Table 2: Clinical characteristics for PCOS women and control groups

Parameters	Mean±SD		p
	Controls	Patients	
Age	24.9±5.646	29.4±5.680	0.6
BMI (Kg/m^2)	23.884±2.306	25.101±4.546	0.8

Significant using SPSS for two independent means of significance *(p≤0.05), **(p≤0.01). PCOS: Polycystic ovarian syndrome, SD: Standard deviation, BMI: Body mass index

Table 3: PCV, Hb, FBG, urea, and creatinine levels in PCOS and control groups

Parameters	Mean±SD		p
	Controls	Patients	
PCV (%)	39.933±1.830	38.8±3.707	0.45
Hb	13.493±0.705	12.933±0.983	0.16
FBG mmol/l	4.763±0.370	5.066±0.601	0.82
Urea mmol/l	21.266±1.624	23.41±4.017	0.08
Creatinine mg/dl	0.980 0.1321	1.008±0.164	0.64

Significant using SPSS for two independent means of significance * (p≤0.05), ** (p≤0.01). PCOS: Polycystic ovarian syndrome, SD: Standard deviation, PCV: Packed cell volume, Hb: Hemoglobin, FBG: Fasting blood glucose

There was a significant correlation between MCP-1 and other clinical markers demonstrated in Table 6 and Fig. 2-5.

The increased risk of Type 2 diabetes mellitus (DM) among women with PCOS was clarified in a study which was demonstrated to be higher compared with healthy subjects, impaired glucose tolerance, insulin resistance of tissues (adipose tissue, liver, and skeletal muscle), and metabolic syndrome in PCOS women, all these together with irregularities in the menstrual cycle (amenorrhea or oligomenorrhea) [25,26]. PCOS can be considered a genetic disorder just like T2 DM [27], and it has been occurred in one of each five women within the reproductive age [28,29]. On the other hand, it was found that high Estradiol levels may affect the thyroid cells [30]. In hyperandrogenemia, Testosterone level measurement is very important [31]. Besides, it was predicted that perpubertal obese girls with hyperandrogenemia had abnormal fasting insulin [32], in addition obese patients have higher estrogens levels which lead to hirsutism and FSH inhibition because excess adipose tissue in those patients can convert androstenedione to estrone and testosterone to estradiol through its aromatase enzyme [33]. Mec Cartney demonstrated that women with PCOS having higher LH pulse abundance and frequency in addition to abnormal LH secretions. Other studies found that high insulin levels in 75% of PCOS women may lead to hypothalamic pituitary-ovarian axis abnormalities which may result in an elevation in LH levels in those patients. On the other hand, it was demonstrated that FSH levels in those patients were significantly lower than in healthy subjects, these findings agree with some other studies, where it is thought that adipose tissue in PCOS patients by increasing androstenedione levels, it will lead to LH stimulation and FSH inhibition at the same time [34]. In women at the reproductive age who had thyroid

Table 4: Testosterone, FSH, LH, prolactin, and estradiol levels in PCOS and Control groups

Parameters	Mean±SD		p
	Controls	Patients	
LH mlU/ml	5.233±5.744	6.966±2.315	0.3
FSH mlU/ml	7.74±4.347	4.212±2.478	0.009**
LH/FSH	0.720±0.649	1.925±1.217	0.005**
Prolactin ng/ml	14.084±11.836	20.821±5.270	0.01**
17 β-estradiol pg/ml	31.733±14.598	38.28±6.924	0.13
Testosterone ng/ml	0.21±0.107	3.990±5.853	0.026*

Significant using SPSS for two independent means of significance *(p≤0.05), **(p≤0.01). LH: Luteinizing hormone, FSH: Follicle stimulating hormone

Table 5: T3, T4, TSH, MCP levels in PCOS and control groups

Parameters	Mean±SD		p
	Controls	Patients	
T_3 nmol/ml	1.243±0.248	1.013±0.199	0.02*
T_4 nmol/ml	94.190±9.755	81.786±15.19	0.01**
TSH mulu/ml	1.268±0.655	2.128±1.106	0.02*
MCP-1 ng/l	1.975±0.716	3.115±0.681	0.007**

Significant using SPSS for two independent means of significance *(p≤0.05), **(p≤0.01). MCP: Monocyte chemoattractant protein, TSH: Thyroid-stimulating hormone, PCOS: Polycystic ovarian syndrome

Table 6: Correlation coefficient between clinical markers in patients with PCOS

Variable	Correlation	Sig.(2-tail)
Testosterone and MCP	0.752	0.002**
17 β-Estradiol and T4	−0.654	0.03*
17 β-Estradiol and Prolactin	−0.606	0028*
Creatinine and urea	0.758	0.001**

Significant using SPSS for two independent means of significance *(p≤0.05), **(p≤0.01)

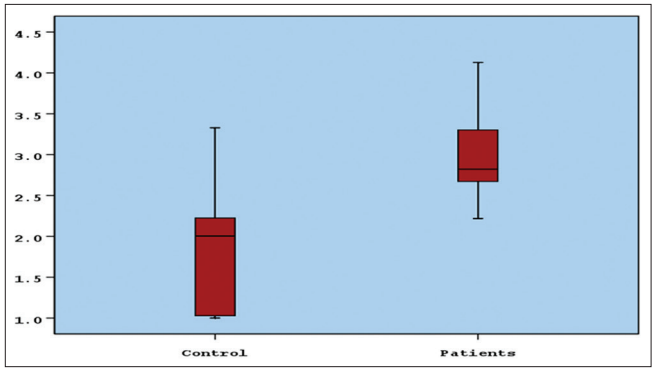

Fig. 1: The boxplot graph of monocyte chemoattractant protein of controls and patients

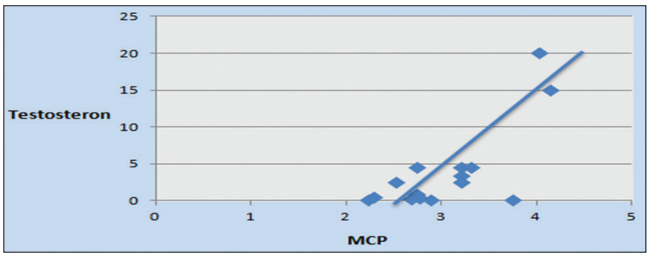

Fig. 2: Relationship between monocyte chemoattractant protein and testosterone in women with polycystic ovarian syndrome

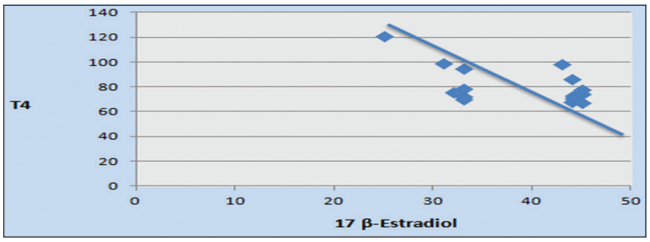

Fig. 3: Relationship between 17 β-Estradiol and T4 in women with polycystic ovarian syndrome

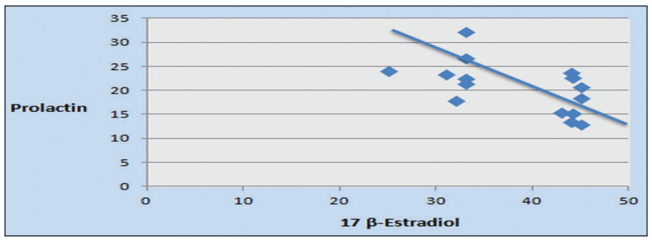

Fig. 4: Relationship between17 β-estradiol and prolactin in women with polycystic ovarian syndrome

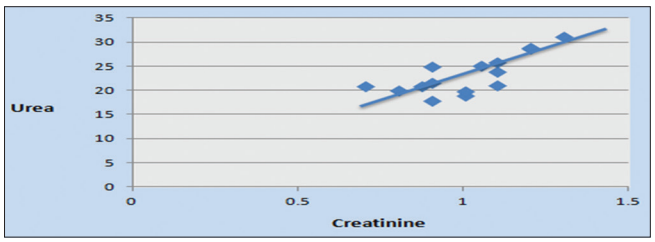

Fig. 5: Relationship between creatinine and urea in women with polycystic ovarian syndrome

disorders, LH/FSH ratio was higher due to the presence of thyroid antibody, which may interact with the ovaries through both direct effects on ovarian function and autoimmune pathways besides chromosome X abnormalities [35]. A profound relationship was found between thyroid dysfunction (thyroid volume) and PCOS [36]. The mechanism for this relationship is still unclear; however, it might be due to the changes occur in LH levels that increased about 50% of PCOS women while FSH levels were either normal or decreased [37]. A recent study demonstrated that metabolic changes responsible for the significant increment in total thyroxine (TT4), total triiodothyronine (TT3), and TSH, besides, it was found that total testosterone and TSH levels were significantly increased in those patients compared with healthy controls [38,39]. This high level of TSH may lead to disorder of FSH receptor [40]. Those PCOS women with higher TSH show metabolic syndrome complications [41]. On the other hand, recent findings found that ovarian cysts may be produced by hypothyroidism and that polycystic behavior of the ovaries was relieved by treatment with thyroxine, so, as a conclusion, primary hypothyroidism can lead to PCOS-like ovaries [42]. One of the mechanisms that lead to the infiltration of leukocytes into sites of inflammatory responses is the production of chemotactic molecules that diffuse out from the site of release and form concentration gradient to which leukocytes respond and migrate, serum from women with PCOS, when compared to serum from controls, induced significantly increased expression of MCP-1 in THP-1 human monocyte cell line. Several reviews concerning the role of MCP-1 in the pathogenesis of many inflammatory diseases are already available elsewhere. Macrophages play important roles in defense by presenting Ag to lymphocytes or by participating in efferent limb immune responses as effecter or secreting cytokines. Macrophages infiltrating sites of inflammation are derived from blood monocytes, which are attracted by chemotactic factors produced at inflammatory sites [43].

CONCLUSION

From the current study, it can be concluded that PCOS women might suffer from low-grade chronic inflammation as a result of changes in the levels of MCP-1(an inflammation marker). Besides, it was detected that TSH might be responsible for all of the irregularities in the levels of sex hormones in such patients. Furthermore, PCOS-related metabolic disturbances could be related to TSH and MCP which can be considered as relevant features in such disturbances.

Recommendations

In subjects who have high risk of developing PCOS at a very young age, it is important to keep in mind all the abnormalities that could be occurred in metabolic (such as adiposity and hyperinsulinemia) and endocrine (includes adrenal and ovarian) functions during this disease and to find reliable markers that can give a clear diagnosis of such disorders in early childhood prior the development of PCOS.

AUTHOR'S CONTRIBUTIONS

ISRAA BURHAN RAOOF
1. Write the Introduction, Patients and Methods and Conclusion
2. Measurement of parameters in hospital.

ASEEL GHASSAN DAOUD

1. Work of Turn tin of article
2. Sample collection; Write the Results and Discussion and Recommendation

RAGHAD ABDULMAHDI MOHSIN

1. Work of Statistical analysis of article
2. Complete collection of sample; write Abstract and Arrangement of References.

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