Original Article

Association of High Levels of Testosterone and Ferritin with Overweight in Women with PCOS

Barartabar Z[1,2], Danesh H[1,2], Mazloomi S[1,2], Alizadeh N[3], Pilehvari SH[4,5*]

1. Students Research Committee, Hamadan University of Medical Sciences, Hamadan, Iran.
2. Department of Clinical Biochemistry, Faculty of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran
3. Department of Obstetrics and Gynaecology, Shariati Hospital, Alborz University of Medical Sciences, Alborz, Iran
4. Department of Obstetrics and Gynaecology, Faculty of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran
5. Endometrium and Endometriosis Research Center, Hamadan University of Medical Sciences, Hamadan, Iran

Received: 11 Jan 2021 Accepted: 21 Apr 2021

Abstract

Background & Objective: The present study was conducted to determine testosterone and ferritin levels in women with polycystic ovary syndrome (PCOS) and investigate its relationship with body mass index (BMI)

Materials & Methods: In this case-control study, 104 PCOS cases and 99 controls were included. The concentration of testosterone, ferritin, lipid profile, insulin, glucose, and androgen was measured in fasting blood samples.

Results: Testosterone level was equal to 1.08 ± 0.50 and 0.85 ± 0.42 in the case and control groups, respectively (P< 0.001). Values of ferritin (123.45 ± 18.21ng/dl vs. 92.14 ± 17.74 ng/dl in control group, p< 0.001), insulin (11.41 ± 3.84 µU/ml vs. 7.02 ± 3.29 µU/ml in control group, p< 0.001), and insulin resistance (11.41 ± 3.84 vs.7.02 ± 3.29 in control group, p< 0.001) was also measured. There was a significant relationship between serum concentration of testosterone and ferritin with BMI (p<0.001). The role of ferritin to predict PCOS was significant (ß:-1.1, P< 0.001).

Conclusion: According to the findings of the present study, the levels of testosterone and ferritin were increased in patients with PCOS. Although elevated testosterone levels are effective in PCOS, ferritin concentration is an important factor in predicting and exacerbating the disease.

Keywords: Testosterone, Ferritin, PCOS, Insulin .

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women, affecting about 6 - 20 % of women of childbearing age (1). In this syndrome, abnormalities of reproductive glands, such as amenorrhea, infertility, hirsutism, and acne caused by the increased androgen and metabolic disorders including central obesity, insulin resistance, and metabolic syndrome are seen (2). Recently, the etiology of PCOS has been shown to be multifactorial due to genetic and environmental factors (3). An increase in the level of androgens is one of the main causes of PCOS (4). Androgens are synthesized in a variety of tissues. Synthesis of androstenedione in the adrenal, gonad, and peripheral

*** Corresponding Author: Pilehvari Shamim,** Department of Obstetrics and Gynaecology, Faculty of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran
Email: sh.pilehvari@yahoo.com
https://orcid.org/0000-0002-2639-2941

[DOR: 20.1001.1.22285105.2021.11.2.9.8]

[DOI: 10.18502/jabs.v11i2.8781]

tissues, and synthesis of testosterone mainly occur in the ovaries, as well as in adipose and other peripheral tissues (5). Increased serum testosterone levels are associated with obesity, especially abdominal obesity, insulin resistance, and increased glucose tolerance testing, as a result, increased androgen and insulin resistance in the patients with PCOS increases testosterone synthesis in the ovaries (6).

Studies have shown that about 50 % of women with PCOS are overweight or obese (7). It has also been shown that the distribution of fat changes in women with PCOS and the amount of fat is higher in visceral tissues (8). Increased levels of androgens are associated with abdominal fat (9). Contradictory findings have been reported regarding androgen production in obese and non-obese people. In some studies, levels of testosterone and androstenedione, were similar in obese and non-obese people with PCOS, and in others, the rate of testosterone was increased in the obese patients with PCOS, and some researchers have shown a reduction in the androstenedione levels in the obese people with PCOS (10).

Ferritin is an intracellular protein involved in regulating iron homeostasis (11). Ferritin is a part of insulin resistance syndrome and increases in abdominal obesity (12). Studies have shown that increased levels of androgens and menstrual disorders are associated with ferritin (13). Studies have also indicated that serum ferritin levels increase in women with PCOS as well as obese patients with PCOS (14).

Testosterone testing is important in the diagnosis and management of PCOS, and there is a possibility of an increased level of ferritin in obese people and patients with PCOS. Therefore, this study was conducted to evaluate the level of testosterone and ferritin in people with PCOS and investigate its relationship with body mass index (BMI).

Materials & Methods

Two hundred and three women aged between 18 – 40 years old, including 104 patients recently diagnosed with PCOS, and 99 healthy women were included in the study as the case and control groups, respectively. The patients were outpatients of the Gynecology Clinic of Fatemieh Hospital affiliated with Hamadan University of Medical Sciences. Individuals were matched in terms of cultural and social issues and lifestyles. PCOS was diagnosed according to the Rotterdam Criteria. The subjects did not have any acute or chronic inflammatory disease and regarding the role of metabolic factors in the development of the disease, the two groups were matched in terms of age and BMI. Information on demographic characteristics and clinical presentations was collected by questionnaire. This study was approved by the Ethics Committee of Hamadan University of Medical Sciences with the ethics code of IR.UMSHA.REC.1399.041. Informed written consent was obtained from all the subjects before participating in the project.

Measurements

Bodyweight was tested to the closest 0.1kg while wearing light clothing by a balanced-beam scale. Moreover, height was computed by a stadiometer to the nearest 0.5 cm. BMI was computed based on the following formula: [weight (kg) / [height (m)] ^{2}. Waist circumferences between the lowest rib and iliac crest in umbilicus level were handled in duplicate to the nearest mm utilizing an adaptable tape. Blood samples were taken between days 3 and 6 of an unconstrained menstrual cycle from all the women after night fasting (8-12 h) and then, serum samples were collected by centrifugation for 15 min at 3000 rpm. The serum was elucidated and stored at -80°C for the next steps. In order to the laboratory blinded in terms of control and case, the samples were numbered and laboratory experts did not know the nature of the samples. The serum concentration of testosterone was measured using the Monobind kit and enzyme-linked immunosorbent assay (ELISA) method. Sensitivity of the ELISA kit was equal to 0.038 ng / ml. The serum concentration of ferritin was measured using the Biovendor kit by ELISA method. The sensitivity of the ELISA kit was equal to 0.44 ng / ml. Insulin concentration in the serum samples was measured using the chemiluminescent immunoassay (CLIA) method and the LIAISON apparatus. Serum glucose concentration and lipid profile were determined using the Pars Azmoon kit.

[DOR: 20.1001.1.22285105.2021.11.2.9.8]

[DOI: 10.18502/jabs.v11i2.8781]

Insulin resistance was measured by the following formula:

HOMA-IR (fasting plasma insulin (mU/l) ×fasting plasma glucose (mmol/l)/22.5) for insulin resistance were calculated. Insulin resistance was considered as HOMA index value of more than 2.1.

Statistical data analysis was done in SPSS software (version 20). Descriptive statistics were expressed as mean ± standard deviation and percentage for quantitative and qualitative variables, respectively. Proportions were contrasted utilizing the Chi-Square test. The differences between the two groups were studied using the Student's t-test and Mann-Whitney U test. The Pearson and Spearman correlation coefficients were utilized to survey the correlations between the variables. A bivariate correlation survey (calculation of the Pearson coefficient) was utilized to evaluate the relationship of serum levels of testosterone, ferritin, and insulin with every parameter. Multiple logistic regression analyses were used to assess the independent effect of ferritin on the odds for PCOS after adjustment for confounding factors. Statistical significance was set at $P<0.05$.

Results

Description of the Patients

In the present study, 104 patients with PCOS (average age: 25.82 ± 4.16years old; average BMI: 26.84 ± 3.48) and 99 healthy individuals (average age: 26.05 ± 4.85 years old; average BMI: 26.43 ± 3.82) were evaluated. Table 1 shows the general characteristics of women with PCOS and healthy controls. As can be seen, the studied women were matched in terms of age ($p=0.775$). Also, regarding the effect of weight interference on the cause of the disease, the study groups were matched in terms of BMI. Although the two groups did not differ significantly in terms of BMI, waist circumference was much larger in the PCOS group than in the control group. LH and lipid profile were necessarily higher in the healthy controls than the subjects with PCOS. Serum insulin and HOMA-IR levels were significant in the control and case groups ($p<0.001$). Serum testosterone levels were evaluated between the patients with PCOS and healthy individuals. According to the results, there was a statistically significant difference in the serum testosterone levels between the patients with PCOS and healthy individuals ($p<0.001$). The groups were divided into two subgroups with normal weight and overweight based on BMI, Table 2 showed the serum ferritin level in women with PCOS was significantly higher in overweight and obese individuals than in normal-weight individuals ($p<0.001$). Although both testosterone and ferritin in the presence of BMI had an effect on the incidence of PCOS, after the removal of the BMI factor, the only increase in ferritin increased the chance of developing PCOS by 1.1 times, Table 3 and Table 4. The data also showed that there is a direct relationship between ferritin and testosterone with BMI ($p<0.001$).

Discussion

PCOS is an important disease as it affects fertility and is the most common cause of ovarian dysfunction (15). PCOS is the most common cause of infertility in approximately 5 - 10% of women of childbearing age. According to the research conducted on PCOS, the outcomes of dysfunction are not limited to a local defect or a specific center because, the previous findings have shown that several hormonal changes, such as androgens and 17 alpha-hydroxyprogesterone also play a role in the development of this syndrome (16). There are similar reports on elevated serum lutein levels in the women with PCOS (17). Increased secretion of luteinizing hormone (LH), expressed as the ratio of follicle-stimulating hormone (FSH) to LH is correlated with an increase in the level of free estradiol (18). Serum concentrations of FSH in non-ovulatory women with PCOS are similar to those in the middle follicular phase of the normal menstrual cycle but, they are less in women who are in the early stages of follicular development (19). This difference may be related to the mechanism of infertility and is unlikely to be the main cause (20). Serum concentrations of testosterone and androstenedione are 50 – 150 % higher in women with PCOS than normal women but, like LH, there are individual differences in the women (21). More than half of women with PCOS are

[DOR: 20.1001.1.22285105.2021.11.2.9.8]

[DOI: 10.18502/jabs.v11i2.8781]

Table1. Biochemical indexes and clinical characteristics of the women with PCOS and their control group (mean±SD).

Variable	Control group (n=99)	PCOS group (n=104)	*p*-value
Age(year)	26.05±4.85	25.82±4.16	0.775
BMI[b](Kg/m^2)	26.43±3.82	26.84±3.48	0.420
Waist(cm)	86.44±10.95	91.57±11.12	0.003
TC(mg/dl)	162.99±34.26	172.63±33.85	0.044
TG(mg/dl)	124.18±22.96	151.21±58.34	0.002
LDL(mg/dl)	92.76±22.53	101.34±22.04	0.007
HDL(mg/dl)	48.77±9.36	47.33±9.34	0.261
FBS(mg/dl)	82.75±7.18	84.03±5.82	0.163
Testosterone(ng/dl)	0.85±0.42	1.08±0.50	< 0.001
Ferritin(ng/dl)	92.14±17.74	123.45±18.21	< 0.001
Insulin(µU/ml)	7.02±3.29	11.41±3.84	< 0.001

BMI: Body Mass Index; FBS: Fasting Blood Sugar; TC:Total Cholesterol,TG: Triglyceride; LDL : Low Density Lipoprotein, HDL: High Density Lipoprotein; FSH: Follicle-Stimulating, Hormone; LH: Luteinizing Hormone. The results are reported as mean ± SD and statistical

Table2. Differences in Waist, Insulin and HOMA-IR, Ferritin, Testosterone in the subjects with and without PCOS based on their BMI

Parameter	Case group (n = 104)			Control group (n = 99)		
	Normal Weight(28)	Overweight(76)	p	Normal Weight(39)	Overweight(60)	p
WC(cm)	80.00 ± 6.08	95.62 ± 9.52	0.001	79.92 ± 7.79	90.68 ±10.66	0.001
Insulin(µU/ml)	9.06 ± 3.24	12.23 ± 3.72	0.001	6.23 ± 2.52	7.54 ± 3.64	0.037
HOMA-IR	1.82 ± 0.66	2.57 ± 0.79	0.001	1.26 ± 0.56	1.58 ± 0.81	0.019
Ferritin(ng/dl)	105.61 ± 12.25	130.01 ± 15.47	0.001	90.45± 17.24	93.23± 18.12	0.443
Testosterone(ng/dl	0.71 ± 0.18	1.21 ± 0.51	0.001	0.69 ± 0.29	0.95 ± 0.45	0.002

significance was set at P<0.05.

WC, Waist circumference; The results are reported as mean ± SD and statistical significance was set at P<0.05.

[DOR: 20.1001.1.22285105.2021.11.2.9.8]

[DOI: 10.18502/jabs.v11i2.8781]

Table3. logistic regression analyses of BMI and other confounding variables to predict PCOS.

Dependent Variables	independent Variables	Odds Ratio (Exp (β))	CI for Exp (β)	P-value
PCOS	BMI	0.847	0.743 - 0.967	0.014
	Ferritin	1.100	1.069 - 1.132	0.001
	Testosterone	2.385	0.880 - 6.468	0.088
	Insulin	0.678	0.295 - 1.559	0.360
	HOMA-IR	43.548	0.138 - 13782.272	0.199

BMI: body mass index; HOMA index: homeostasis model assessment index

Table 4. logistic regression analyses of ferritin and other confounding variables to predict PCOS.

Dependent Variables	independent Variables	Odds Ratio (Exp (β))	CI for Exp (β)	P-value
PCOS	Ferritin	1.094	1.064 - 1.124	0.001
	Testosterone	2.385	0.880 - 6.468	0.088
	Insulin	0.677	0.290 - 1.577	0.366
	HOMA-IR	40.034	0.116 - 13824.142	0.216

HOMA index: homeostasis model assessment index

[DOR: 20.1001.1.22285105.2021.11.2.9.8]

[DOI: 10.18502/jabs.v11i2.8781]

obese and have an extra burden of insulin resistance due to their excess fat (22). Most studies have supported the prevalence of obesity in this disease. Obesity, especially central obesity, is specifically identified as the cause of insulin resistance in PCOS because; obesity worsens the endocrine and metabolic profile in this disease, and leads to the increased levels of androgens including total testosterone through various mechanisms and may reduce the response to treatment (19). Free testosterone levels also increase in obese people with PCOS due to the decreased level of sex hormone-binding globin (SHBG) (23). On the other hand, insulin inhibits SHBG production in the liver and thus, hyperinsulinemia directly increases testosterone secretion from the ovaries (24). Amate et al., reviewed and analyzed clinical findings, sex hormones, fasting glucose, hemostatic model of insulin resistance, and insulin-sensitive index by studying 130 patients with PCOS. PCOS women with hirsutism had significantly higher levels of testosterone, free testosterone, DHEA-s, and 4-androstenedione. They had similar BMI and were significantly less sensitive to insulin than the women without hirsutism (5). In our study, people with PCOS showed a significant difference in their testosterone levels compared to the control group. The relationship between testosterone and BMI was also studied and these two parameters were significantly related to each other.

Thozhukat Sathyapalan et al., (2017) measured testosterone and androstenedione levels in the saliva of healthy women and those with PCOS in the UK. Salivary testosterone and androstenedione levels were significantly higher in people with PCOS than normal people (P < 001) (25). Elisabeth Lerchbaum et al., (2014) studied the relationship between levels of androstenedione, testosterone, and free testosterone, and metabolic parameters in the patients and healthy controls in Australia. The results showed that women with PCOS had higher levels of free testosterone (26). In our study, people with PCOS showed significant testosterone levels compared to the controls. The relationship between testosterone and BMI was also studied and these two parameters were significantly related to each other.

Recent studies have shown that the body's iron stores determined by serum ferritin levels are part of the insulin resistance syndrome. Serum ferritin level is associated with abdominal obesity and other obesity criteria (27). Iron levels are also associated with the incidence of type 2 diabetes, gestational diabetes, and metabolic syndrome (28). Increased iron stores have also been reported in overweight or obese women with polycystic ovaries. The elevated level of iron in these patients can lead to insulin resistance and dysfunction of pancreatic beta cells (14). Iron has a significant effect on oxidative stress. Oxidative stress is higher in patients with PCOS. Oxidative stress increases the synthesis of ferritin. However, the increase in the level of ferritin in the body of these patients prevents further oxidative damage by neutralizing highly toxic iron. Iron deposition in some tissues increases insulin resistance, which in turn increases ferritin production, thus completing a vicious cycle of iron deficiency, exposing the patients to the impaired glucose tolerance and metabolic syndrome (29).

However, elevated serum iron in patients with PCOS may not be a primary phenomenon. Insulin resistance-induced hyperinsulinemia in these patients can influence food intake and increase absorption of iron from the intestine by increasing the activity of some intestinal factors, such as hypoxia-inducible factor-1 (30). Decreased blood flow due to complete cessation or reduction of normal menstrual frequency in these patients can also be effective in increasing their iron stores (14).

Agnieszka Adamska et al., (2020) investigated the relationship between serum concentration of ferritin and visceral (abdominal) fat in women with PCOS. The results showed that in women with PCOS, serum concentration of ferritin ($p = 0.002$), basal insulin $p = 0.03$), insulin resistance test ($p = 0.03$), visceral fat content ($p = 0.0001$) were higher than the control group. There was a relationship between ferritin concentration and basal insulin concentration and insulin resistance and a correlation was observed between serum concentration of ferritin and visceral adipose tissue (VAT). They found that the increased serum concentration of ferritin is associated with insulin resistance as well as visceral fat and body fat in the women with

[DOR: 20.1001.1.22285105.2021.11.2.9.8]

[DOI: 10.18502/jabs.v11i2.8781]

PCOS and may be a sign of metabolic dysfunction(31). In our study, an increase was observed in the serum concentration of ferritin in the patients with PCOS, also a significant relationship was observed between serum concentration of ferritin and BMI, ferritin was found to be an effective factor in predicting and exacerbating the disease. our result showed that ferritin was higher in women with PCOS and overweight.

Po-Chun Ko et al., (2015) in a review study investigated serum ferritin levels and complications associated with PCOS in obese and non-obese women. They demonstrated that elevated serum ferritin levels are associated with the increased insulin resistance and risk of diabetes in obese women, and high serum concentrations of ferritin are associated with an increased risk of hyperglyceridemia in obese and non-obese women. Therefore, the elevated level of triglycerides in women with PCOS may be associated with iron metabolism (32).

Faranak Sharifi et al., (2011) measured BMI, waist circumference, blood pressure, androgen, gonadotropin, insulin, glucose, cholesterol, triglyceride, C-reactive protein (CRP), and ferritin in healthy women and those with PCOS in Iran. In women with PCOS, serum ferritin (P = 0.03) and insulin (P = 0.017) levels were increased compared to control women. No association was found between ferritin, BMI, blood pressure, waist circumference, fasting glucose, and CRP confirming the results of our study (33).

In our study, concentrations of ferritin, blood sugar, cholesterol, insulin, HDL-C, and triglyceride were measured in the patients with PCOS and were compared with a control group of similar age, sex, and BMI. In these patients, the mean level of serum ferritin and serum testosterone was higher than the control group. This increase was statistically significant. The relationship between both parameters and BMI was investigated. There was a significant relationship between serum concentration of testosterone and BMI with P = 0.047, but no significant relationship was found between ferritin level and BMI with P = 0.987.

Although the present study for the first time showed that high ferritin is more effective on PCOS independent of BMI, but taking into account the limitations present in our study, we believe that measurement of ferritin-dependent analytes, such as iron, transferrin, and hemosiderin, may strengthen the results.

Conclusion

The results of the present study showed that PCOS is associated with high serum concentrations of testosterone, ferritin, insulin, and insulin resistance. A significant correlation was observed between serum concentration of testosterone and ferritin with BMI. The increase in the ferritin level may be due to the increased levels of insulin and insulin resistance. In this study, it was first observed that ferritin is a more aggravating factor in polycystic ovary syndrome than testosterone.

Conflicts of Interest

The authors have no conflicts of interest relevant to this paper.

Acknowledgments

This study was supported by Students Research Center of Hamadan University of Medical Sciences and Alborz University of Medical Sciences. All authors have nothing to declare and also this work was supported by Students Research Center of Hamadan University of Medical Sciences [grant NO. 9705022569]

Refrences

1.Teede HJ, Joham AE, Paul E, Moran LJ, Loxton D, Jolley D, et al. Longitudinal weight gain in women identified with polycystic ovary syndrome: results of an observational study in young women. Obesity. 2013;21(8):1526-32.

2.Ehrman DA, Barnes RB, Rosenfield RL. Polycystic ovary syndrome as a form of functional ovarian hyperandrogenism due to dysregulation of androgen secretion. Endocrine reviews. 1995;16(3):322-53.

3.Driscoll DA. Polycystic ovary syndrome in adolescence. Annals of the New York Academy of Sciences. 2003;997(1):49-55.

4.Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, et al. Criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic syndrome: an androgen excess society guideline. The Journal of Clinical Endocrinology & Metabolism. 2006;91(11):4237-45.

[DOR: 20.1001.1.22285105.2021.11.2.9.8]

[DOI: 10.18502/jabs.v11i2.8781]

5.Amato MC, Galluzzo A, Merlino S, Mattina A, Richiusa P, Criscimanna A, et al. Lower insulin sensitivity differentiates hirsute from non-hirsute Sicilian women with polycystic ovary syndrome. European journal of endocrinology. 2006;155(6):859-65.
6.Wehr E, Möller R, Horejsi R, Giuliani A, Kopera D, Schweighofer N, et al. Subcutaneous adipose tissue topography and metabolic disturbances in polycystic ovary syndrome. Wiener Klinische Wochenschrift. 2009;121(7-8):262-9.
7.Glueck CJ, Goldenberg N. Characteristics of obesity in polycystic ovary syndrome: etiology, treatment, and genetics. Metabolism. 2019;92:108-20.
8.Jena D, Choudhury AK, Mangaraj S, Singh M, Mohanty BK, Baliarsinha AK. Study of visceral and subcutaneous abdominal fat thickness and its correlation with cardiometabolic risk factors and hormonal parameters in polycystic ovary syndrome. Indian journal of endocrinology and metabolism. 2018;22(3):321.
9.Escobar-Morreale HF. Iron metabolism and the polycystic ovary syndrome. Trends in Endocrinology & Metabolism. 2012;23(10):509-15.
10.Acién P, Quereda F, Matallín P, Villarroya E, López-Fernández JA, Acién M, et al. Insulin, androgens, and obesity in women with and without polycystic ovary syndrome: a heterogeneous group of disorders. Fertility and sterility. 1999;72(1):32-40.
11.Rajpathak SN, Crandall JP, Wylie-Rosett J, Kabat GC, Rohan TE, Hu FB. The role of iron in type 2 diabetes in humans. Biochimica et Biophysica Acta (BBA)-General Subjects. 2009;1790(7):671-81.
12.Hramiak IM, Finegood DT, Adams PC. Factors affecting glucose tolerance in hereditary hemochromatosis. Clinical and investigative medicine. 1997;20(2):110-8.
13.Martínez-García MÁ, Luque-Ramírez M, San-Millán JL, Escobar-Morreale HF. Body iron stores and glucose intolerance in premenopausal women: role of hyperandrogenism, insulin resistance, and genomic variants related to inflammation, oxidative stress, and iron metabolism. Diabetes care. 2009;32(8):1525-30.
14.Escobar-Morreale HF, Luque-Ramírez M, Álvarez-Blasco F, Botella-Carretero JI, Sancho J, San Millán JL. Body iron stores are increased in overweight and obese women with polycystic ovary syndrome. Diabetes care. 2005;28(8):2042-4.
15.Oki T, Douchi T, Mori A, Yamamoto S, Matsumoto T, Nakamura Y, et al. Primary amenorrhea and hirsutism associated with hyperinsulinemia type A. Nihon Sanka Fujinka Gakkai Zasshi. 1992;44(4):387-90.
16.Fritz MA, Speroff L. Clinical gynecologic endocrinology and infertility: lippincott Williams & wilkins; 2012.
17.FRANKS S. Polycystic ovary syndrome: a changing perspective. Clinical endocrinology. 1989;31(1):87-120.
18.LOBO RA, GRANGER L, Goebelsmann U, MANASCO PK, LINSELL C, PEART WS. Elevations sin unbound serum estradiol as a possible mechanism for inappropriate gonadotropin secretion in women with PCO. The Journal of Clinical Endocrinology & Metabolism. 1981;52(1):156-8.
19.Holte J, Bergh T, Berne C, Wide L, Lithell H. Restored insulin sensitivity but persistently increased early insulin secretion after weight loss in obese women with polycystic ovary syndrome. The Journal of Clinical Endocrinology & Metabolism. 1995;80(9):2586-93.
20.Franks S. Polycystic ovary syndrome. New England Journal of Medicine. 1995;333(13):853-61.
21.Escobar-Morreale HF, Luque-Ramírez M, San Millán JL. The molecular-genetic basis of functional hyperandrogenism and the polycystic ovary syndrome. Endocrine reviews. 2005;26(2):251-82.
22.Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, et al. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report. Fertility and sterility. 2009;91(2):456-88.
23.Martínez-García MÁ, Gambineri A, Alpañés M, Sanchón R, Pasquali R, Escobar-Morreale HF. Common variants in the sex hormone-binding globulin gene (SHBG) and polycystic ovary syndrome (PCOS) in Mediterranean women. Human reproduction. 2012;27(12):3569-76.
24.Committee AAoCEPOSW. American Association of Clinical Endocrinologists Position Statement on Metabolic and Cardiovascular Consequences of Polycystic Ovary Syndrome. Endocrine practice: official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists. 2005;11(2):126.
25.Sathyapalan T, Al-Qaissi A, Kilpatrick ES, Dargham SR, Adaway J, Keevil B, et al. Salivary testosterone measurement in women with and without polycystic ovary syndrome. Scientific Reports. 2017;7(1):1-9.
26.Lerchbaum E, Schwetz V, Rabe T, Giuliani A, Obermayer-Pietsch B. Hyperandrogenemia in polycystic ovary syndrome: exploration of the role of free testosterone and androstenedione in metabolic phenotype. PLoS One. 2014;9(10):e108263.
27.Fernández-Real JM, López-Bermejo A, Ricart W. Cross-talk between iron metabolism and diabetes. Diabetes. 2002;51(8):2348-54.
28.Jehn M, Clark JM, Guallar E. Serum ferritin and risk of the metabolic syndrome in US adults. Diabetes care. 2004;27(10):2422-8.
29.Gillum R. Association of serum ferritin and indices of body fat distribution and obesity in Mexican American men—the Third National Health and Nutrition Examination Survey. International journal of obesity. 2001;25(5):639-45.
30.McCarty M. Hyperinsulinemia may boost both hematocrit and iron absorption by up-regulating activity of hypoxia-inducible factor-1α. Medical hypotheses. 2003;61(5-6):567-73.

31.Adamska A, Łebkowska A, Krentowska A, Adamski M, Kowalska I. The association between serum ferritin concentration and visceral adiposity estimated by whole body DXA scan in women with polycystic ovary syndrome. Frontiers in Endocrinology. 2019;10:873.
32.Chao K-C, Chang C-C, Chiou H-Y, Chang J-S. Serum ferritin is inversely correlated with testosterone in boys and young male adolescents: A cross-sectional study in taiwan. PLoS One. 2015;10(12):e0144238.
33.Sharifi F, Mazloomi S, Mousavinasab N. High Serum Ferritin Concentrations in Polycystic Ovary Syndrome Is Not Related to Insulin Resistance. Iranian journal of diabetes and obesity 2011;3(2):47-53

[DOR: 20.1001.1.22285105.2021.11.2.9.8]

[DOI: 10.18502/jabs.v11i2.8781]