Al-Mustansiriyah Journal of Science
ISSN: 1814-635X (print), ISSN:2521-3520 (online) Volume 34, Issue 1, 2023 DOI: http://doi.org/10.23851/mjs.v34i1.1299

Research Article **Open Access**

Evaluation of Adiponectin and Hepcidin with some Biochemical Parameters in Sera of Women with Polycystic Ovary Syndrome

Sura. M. Kadhim[1,*], Falah. S. Al-Fartusie[1], Nisred K. Klichkhanov[2]

[1]Department of Chemistry, College of Science, Mustansiriyah University, 10052 Baghdad, IRAQ.
[2]Department of Biochemistry, College of Biology, Dagestan State University, Dagestan, RUSSIA.

Correspondent contact: surabiochem@yahoo.com

Article Info

Received
01/02/2023

Accepted
20/02/2023

Published
30/03/2023

ABSTRACT

Polycystic ovarian syndrome (PCOS) is the most recorded endocrinological condition that impacts women throughout their fertile years and causes a variety of clinical symptoms. The study included 60 women with PCOS and 60 women who were matched for age and body mass index (BMI) and excluded the participants refrain from vigorous exercise and drink anything with alcohol or caffeine. were tested levels for IR, insulin, Hepcidin, Adiponectin, lipids profile in control and PCOS. and found Reduced levels (non sig.) of adiponectin have been documented in Iraqi patients with Polycystic Ovary Syndrome. There was an inverse relationship between IR and hepcidin levels in both groups meaning increase in IR (0.001) and decrease in hepcidin (0.001) levels may increase the risk of PCOS. well found that lipid profile (HDL, LDL, TG) that is non-significant but cholesterol high significant 0.001 in patients.

KEYWORDS: PCOS; adiponectin; IR; BMI; Hepcidin.

الخلاصة

متلازمة تكيس المبايض (PCOS) هي أكثر حالات الغدد الصماء التي تم تسجيلها والتي تؤثر على النساء طوال سنوات الخصوبة وتسبب مجموعة متنوعة من الأعراض السريرية. اشتملت الدراسة على 60 امرأة مصابة بمتلازمة تكيس المبايض و60 امرأة تمت مطابقتهن من حيث العمر ومؤشر كتلة الجسم (BMI) واستبعدت المشاركين الامتناع عن ممارسة التمارين الرياضية القوية وشرب أي شيء مع الكحول أو الكافيين. تم اختبار مستويات الأشعة تحت الحمراء والأنسولين وHepcidin وAdiponectin ونسبة الدهون في السيطرة وPCOS. ووجدت أن مستويات منخفضة من الأديبونكتين (non sig.) قد تم توثيقها في المرضى العراقيين الذين يعانون من متلازمة تكيس المبايض، وكانت هناك علاقة عكسية بين مستويات الأشعة تحت الحمراء والهيبسيدين في كلا المجموعتين مما يعني زيادة في الأشعة تحت الحمراء (0.001) وانخفاض في مستويات الهيبسيدين (0.001). قد يزيد من خطر الإصابة بمتلازمة تكيّس المبايض. وجد أن محتوى الدهون (HDL، LDL، TG) غير مهم ولكن نسبة الكوليسترول عالية معنوية 0.001 في المرضى.

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is the most recorded endocrinological condition that impacts women throughout their fertile years and causes a variety of clinical symptoms. Women with PCOS usually demonstrate hyperandrogenism, and the underlying genesis of PCOS is likely complex [1]. The increase of insulin resistance (IR) is a fundamental property associates with PCOS, which does not relate to the body mass index (BMI). Metabolic syndrome characteristics include abdominal obesity, which is frequent in PCOS patients, and hyperinsulinemia. Metabolic syndrome impacts one in every five persons and increases the chance of heart disease and type 2 diabetes. It is frequently observed in middle-ages of females. In addition to the classic signs of PCOS such as

hirsutism, acne, and anovulatory infertility, PCOS patients have been shown to have cardiology and endothelial issues [2].

In addition to storing a significant amount of fat for use as fuel [3], adipose tissue (AT) simultaneously encodes genes for secretory proteins [4]. The mammalian adipose most abundant gene transcript 1 (apM1), which is only produced in white AT, has recently been discovered [5]. human adiponectin is encoded by the apM1 gene. It consists of a protein of 244 amino acids [6]. Peroxisome proliferator-activated receptor enhance adiponectin [7]. Despite the fact that adiponectin's physiological function in PCOS is uncertain, recent studies indicate that it is a type of protein encoded with prospective anti-inflammatory and anti-atherosclerotic properties [8]. The metabolic and neuroendocrine problems linked to obesity and obesity-related illnesses like PCOS may be caused by adiponectin, a fat cell protein that is generated in the circulation. Adiponectin is exclusively generated in AT; however, its circulating levels are less in obese individuals than in non-obese individuals [9]. The reduction of adiponectin levels when BMI is elevated [10], demonstrating that adiposity inhibits adiponectin expression in ATs [11]. Additionally, circulating concentrations of low-density lipoprotein (LDL) cholesterol and triglycerides (TGs) as well as circulating adiponectin concentrations were negatively associated to the degree of IR [12, 13]. The majority of this peptide is generated by liver cells, namely hepcidin. Hepcidin, an antimicrobial peptide that is produced in reaction to inflammation, hypoxia, and an increased blood iron concentration, is one of the factors that contribute to the pathophysiology of PCOS [14]. Hepcidin is directly controlled by insulin, according to Wang et al., and it is crucial for iron overload in diabetic rats [15].

Patients with PCOS had lower circulatory hepcidin concentrations than healthy volunteers [16,17-18]. Hepcidin levels rise in inflammatory circumstances and fall in cases of hyperandrogenism, IR, and both [19-20]. Consequently, because of PCOS's elevated inflammatory condition, IR, and hyperandrogenism [20]. In order to determine whether there is a relationship between adiponectin concentrations, hepcidin levels, insulin production, and sensitivity, this study was conducted on Baghdad women with PCOS.

MATERIALS AND METHODS

In this experiment, 120 specimens were collected from females between the ages of 18 and 40. Of these, 60 specimens were from PCOS patients (the patients' group), while the remaining 60 samples came from healthy participants (control group). With the assistance of qualified doctors, the specimens were obtained at Kamal Al-Samarrai for Fertility and Infertility Hospital, which is situated in Baghdad city. The ladies were divided into two groups: one with PCOS (N = 60) and the other as a control group (N = 60) without PCOS. In vacutainer tubes, fasting blood specimens were taken on the second through seventh day of menstruation or during amenorrhea (BD-Becton Dickinson, Plymouth, UK). Participants who had been fasting for 12 hours had blood drawn. For 48 hours, we excluded the participants refrain from vigorous exercise and drink anything with alcohol or caffeine.

The amounts of TGs and cholesterol (total, LDL, HDL, and VLDL) in the blood were measured using spectrophotometric kits. Adiponectin, hepcidin, and insulin were assessed by using ELISA kits (Bio Vision). Two-way analysis of variance was used to investigate the impact of PCOS and body fat percentage (ANOVA). The Student Newman-Keuls test was used to make post hoc comparisons. When p value <0.05, the differences were statistically significant.

RESULTS AND DISCUSSION

Table 1 shows distribution of samples under investigation. The results indicate that no significant change in the mean of age, BMI and

WHR between patients and control groups at P≤0.001*

Table 1. Demographic presentation of the study subjects.

Parameters	Controls (n=60)	PCOS (n=60)	*p value*<
HOMA-IR	2.45 ± 0.45	5.18 ± 1.19	0.001*
Insulin (µIU/mL)	11.38 ± 1.3	16.14 ± 2.3	0.001*
Hepcidin (ng/mL)	22.68±2.17	15.05±0.85	0.001*
Adiponectin (ng/mL)	8.98 ± 0.85	8.85± 1.13	NS

PCOS women had increased fasting insulin and HOMA-IR indexes than the control group. The HOMA-IR index was used to evaluate IR as an indirect methodology. The mean hepcidin level was 15.05±0.85 ng/ml in the patients and 22.68±2.17 ng/ml in the control groups. The statistical comparison has indicated a significant variance in hepcidin concentration between the groups (p=0.001), as shown in Table 2.

This study revealed that IR is common in Iraqi PCOS women, regardless of their weight. Furthermore, more research is needed to understand the pathophysiologic role of IR in PCOS.

Table 2. HOMA-IR, Insulin (µIU/mL), Hepcidin (ng/mL) and Adiponectin (ng/mL) features measurements distributed among PCOS patients' group and control group.

Parameters	Controls (n=60)	PCOS (n=60)	*p value*>
Age (years)	24.6±4.7	29.8±4.5	0.413
BMI (kg/m^2)	26.7±2.9	28.76±1.17	0.001*
WHR	0.76 ± 0.05	0.89 ± 0.19	0.001*

Table 3 shows the distribution of lipid profile such as HDL, LDL, triglyceride (TG), and cholesterol between PCOS patients and the control group. Total cholesterol and TGs were substantially greater in PCOS patients than in controls.

Table 3. Lipid profile parameters which distributed between patients of PCOS as compared to control group.

Parameters (mg/dL)	Controls (n=60)	PCOS (n=60)	*p value*
HDL	59.15 ± 1.93	49.07 ± 2.5	NS
LDL	71.43 ± 2.5	95.40 ± 1.79	NS
Triglycerides	97.84 ± 1.11	115.05 ± 8.24	NS
cholesterol	137.15 ± 6.73	178.50 ± 3.81	0.001*

DISCUSSION

PCOS is usually linked to IR, which results in compensatory hyperinsulinemia [21]. In this research, women with PCOS had higher HOMA-IR scores than normal controls, signifying elevated IR. These outcomes are in line with those of the Amer et al. research, which found that using the same measure, cases were more insulin resistant than controls [22]. Furthermore, doh et al. discovered a poor degree of insulin sensitivity in fourteen Cameroonian women with PCOS using the standard technique for assessing insulin sensitivity including the euglycemic, hyper insulinemic and clamp [23]. The PCOS group showed significantly higher insulin release than the controls, indicating that this group had hyperinsulinemia as expected. Although basal insulin production is increased in PCOS patients, insulin production feedbacks to a glucose concentration are frequently inadequate, leading to a poorer glucose disposition score compared to controls with same age and BMI [24]. Adiponectin levels in PCOS women were comparable to those in controls, falling within the average limits of 8.63 to 3.75 g/mL [25]. Similar outcomes have been reported in other investigations of in BMI-matched PCOS and controls [26,27]. However, patients with PCOS had serum hepcidin concentrations reduced than healthy controls and was no significant changes were detected in adiponectin between two groups. [28][29].

Research by Sam et al. [30] found that systemic hepcidin concentrations and IR had a strong negative connection, which was similar with the outcomes of the current investigation. Conversely, research done on rats found that insulin directly controlled the level of hepcidin, which reduced when the insulin signal was lost [15]. In other words, greater levels of HOMA-IR

and lower concentrations of hepcidin raise the risk of PCOS since there is a positive association between HOMA-IR and PCOS and an inverse link between the two.

The localization of fat and the variable amounts of subcutaneous and visceral fat were connected to these changes [31]. Between PCOS patients and control volunteers, there were no substantial differences in LDL cholesterol, HDL cholesterol, or TG levels. However, compared to controls, people with PCOS had reduced HDL cholesterol and greater LDL cholesterol. In comparison to controls, PCOS patients exhibited increased mean HDL and LDL cholesterol [32]. In this study, low HDL (below 50 mg/dL) was demonstrated to be a dyslipidemia determinant in patients. This is in line with research in the South Indian demographic, where 93.3 % of PCOS patients had low HDL levels. Dyslipidemia in PCOS might be caused by high circulating levels of insulin and androgens. Adipocytes were able to release free fatty acids into the circulation as a result of catecholamine's accelerated lipolysis. Through the reverse cholesterol transfer mechanism, hypertriglyceridemia raises LDL cholesterol levels and lowers HDL cholesterol. In this study, the clinical characteristics of controls and PCOS-positive women were comparable, and the variation was statistically insignificant. In our PCOS study, nonobese women had significantly higher total cholesterol and TGs than patient controls. These results are consistent with those of Pagotto et al. [33], who discovered that even though HDL, LDL, and VLDL were not substantially differing between the two groups, serum overall cholesterol and serum TGs were greater in PCOS than in the control group in both studies. These results also agree with those of Khomami et al., who discovered that while TGs and serum HDL did not alter statistically significantly in PCOS patients compared to controls, total cholesterol and LDL did statistically significantly increase. In this study, we discovered that total cholesterol levels were higher in obese women.

In comparison to the non-PCOS group, the PCOS group had higher TGs and LDL, and this variation was statistically significant ($P<0.01$) for LDL and the statistics were tremendously significant ($P<0.001$) for total cholesterol and TGs. There was a considerable difference between the HDL and VLDL groups even though there was no statistically considerable variation between the two groups. This research supports the conclusions of Khomami et al. [34]. Furthermore, Jones et al. [35], found that the obese women with PCOS have higher level of cholesterol and TGs while they had statistically lower HDL level than that in lean PCOS patients and control groups. Jayasekara et al. [36], found substantial increases in blood cholesterol, LDL, and TGs, whereas serum HDL was lower in PCOS. According to their findings, PCOS serum cholesterol and LDL rose considerably when compared to control. The rise in TGs among PCOS patients was not significant statistically, which according to Goldstein et al. [32], a disagreement was found in which they reported that the lipid profile in the PCOS women observed with a statistically considerable elevation in VLDL ($P<0.01$) and TGs ($P<0.05$) in comparison to the control group.

CONCLUSIONS

According to the findings of this research, there is a quite link between adiponectin level and IR in women with PCOS. This may be can play a key role as a pathway to the consequences of PCOS. Hence, adiponectin can be used as a biomarker for monitoring the health condition of women with PCOS. Hepcidin, on the other hand, had shown a reduction in PCOS patients. The use of hepcidin test as a prognostic biomarker is recommended, yet, there is a need for more information of its physiological effects in PCOS.

ACKNOWLEDGMENT

Mustansiriyah University supported this study.

Disclosure and conflict of interest: The authors declare that they have no conflicts of interest.

REFERENCES

[1] Norman RJ, Dewaill D, Legro RS, Hickey TE. Polycystic ovary syndrome. Lancet 2007; 370(9588): 685-97.

[2] Kuçu NK, Var A. Oxidative stress but not endothelial dysfunction exists in non-obese, young group of patients with polycystic ovary Syndrome. Acta Obstet Gynecol Scand 2009; 88(5): 6127.

[3] Trayhurn P, Beattie JH 2001 Physiological role of adipose tissue: white adipose tissue as an endocrine and secretory organ. Proc Nutr Soc 60:329–339

[4] Maeda K, Okubo K, Shimomura I, Mizuno K, Matsuzawa K 1997 Analysis of an expression profile of genes in the human adipose tissue. Gene 190:227–235.

[5] Saito K, Tobe T, Minoshima S, Asakawa S, Sumiya J, Yoda M, Nakano Y, Shimizu N, Tomita M 1999 Organization of the gene for gelatin-binding protein (GBP28). Gene 229:67–73.

[6] Halleux CM, Takahashi M, Delporte ML, Detry R, Funahashi T, Matsuzawa Y, Brichard SM 2001 Secretion of adiponectin and regulation of apM1 gene expression in human visceral adipose tissue. Biochem Biophys Res Commun 2:1102-1007

[7] Yang WS, Leng CY, Wu TJ, Tanaka S, Funahashi T, Matsuzawa Y, Wang JP, Chen CL, Tai TY, Chuang LM 2002 Synthetic peroxisome proliferator-activated receptor agonist, rosiglitazone, increases plasma levels of adiponectin in type 2 diabetic patients. Diabetes Care 25:376–380

[8] Yang WS, Lee WJ, Funahashi T, Tanaka S, Matsazawa Y, Chao CL, Chen CL, Tai TY, Chuang LM 2001 Weight reduction increases plasma levels of an adipose-derived anti-inflammatory protein, adiponectin. J Clin Endocrinol Metab 86:3815–3819

[9] Arita Y, Kihara S, Ouchi N, Takahashi M, Maeda K, Miyagawa JI, Hotta K, Shimomura I, Nakamura T, Miyaoka K, Kuriyama H, Nishida M, YamashitaS, Okubo K, Matsubara K, Muraguchi M, Ohmoto Y, Funahashi T, Matsu- zawa Y 1999 Paradoxical decrease of an adipose-specific protein, adiponectin, in obesity. Biochem Biophys Res Commun 257:79–83

[10] Yang WS, Lee WJ, Funahashi T, Tanaka S, Matsazawa Y, Chao CL, Chen CL, Tai TY, Chuang LM 2001 Weight reduction increases plasma levels of an adipose-derived anti-inflammatory protein, adiponectin. J Clin Endocrinol Metabol86:3815–3819.

[11] Matsubara M, Maruoka S, Katayose S 2002 Decreased plasma adiponectin concentrations in women with dyslipidemia. J Clin Endocrinol Metab 87:2764– 2769.

[12] Kondo H, Shimomura I, Matsukawa Y, Takahashi M, Matsuda M, Ouchi N, Kihara S, Kanamoto T, Sumitsuji S, Funahashi T, Matsuzawa Y 2002 Association of adiponectin mutation with type 2 diabetes. Diabetes 51:2325–2328.

[13] Kazumi T, Kawaguchi A, Sakai K, Hirano T, oshino G 2002 Young men with high-normal blood pressure have lower serum adiponectin, smaller LDL size, and higher elevated heart rate than those with optimal blood pressure. Dia betes Care 25:971–976.

[14] Castagna A, Campostrini N, Zaninotto F, Girelli D.Hepcidin assay in serum by SELDI-TOF-MS and other approaches. J Proteomics 2009; 73:527-36.

[15] Wang H, Li H, Jiang X, Shi W, Shen Z, Li M. Hepcidin is directly regulated by insulin and plays an important role in iron overload in streptozotocin-induced diabetic rats. Diabetes 2014; 63:1506-18

[16] Luque-Ramírez M, Álvarez-Blasco F, Alpañés M, Escobar-Morreale HF. Role ofdecreased circulating hepcidin concentrations in the iron excess of women with the polycystic ovary syndrome. J Clin Endocrinol Metab 2011; 96:846-52.

[17] Sam AH, Busbridge M, Amin A, Webber L, White D,Franks S, et al. Hepcidin levels in diabetes mellitus andpolycystic ovary syndrome. Diabet Med 2013; 30:1495-9.

[18] Datz C, Felder TK, Niederseer D, Aigner E. Iron homeostasis in the metabolic syndrome. Eur J Clin Invest 2013; 43:215-24.

[19] Luque-Ramírez M, Alvarez-Blasco F, Botella-CarreteroJI, Sanchón R, San MillánJL, Escobar-Morreale HF.Increased body iron stores of obese women withpolycystic ovary syndrome is a consequence of insulin resistance and hyperinsulinism and are not a result of reduced menstrual losses. Diabetes Care 2007; 30:2309-13.

[20] Ahmed HH, Fadl NN, Kotob SE. Impact of Long-Term Metformin Therapy on Hepcidin and Iron Status in Type II Diabetic Patients. International

Journal of Pharmaceutical and Clinical Research2015; 7:185-93.

[21] Lagaly DV, Aad PY, Grado-Ahuir JA, Hulsey LB, Spicer LJ. Role of adiponectin in regulating ovarian theca and granulosa cell function. Mol Cell Endocrinol. 2008;284(1-2):38-45.

[22] Comim FV, Gutierrez K, Bridi A, Bochi G, Chemeris R, Rigo ML, et al. Effects of Adiponectin Including Reduction of Androstenedione Secretion and Ovarian Oxidative Stress Parameters In Vivo. PLoS One. 2016;11(5): e0154453

[23] Azziz R, Carmina E, Chen Z, Dunaif A, Laven JSE, Legro RS, et al. Polycystic ovary syndrome. Nat Rev Dis Primers. 2016;2(1):16057.

[24] Amer H, Abo-Shady R, Elaziz D, Khattab Y. The role of serum adiponectin levels in women with polycystic ovarian syndrome. Egypt J Hosp Med. 2017; 68:837–44.

[25] Doh E, Mbanya A, Kemfang-Ngowa JD, Dohbit S, Tchana-Sinou M, Fou- mane P, et al. The relationship between adiposity and insulin sensitivity in african women living with the polycystic ovarian syndrome: a clamp study. Int J Endocrinol. 2016; 2016:1–6.

[26] Ehrmann DA, et al. Insulin secretory defects in polycystic ovary syndrome. Relationship to insulin sensitivity and family history of non-insulin- dependent diabetes mellitus. J Clin Invest. 1995; 96:520–7.

[27] Ziemke F, Mantzoros CS. Adiponectin in insulin resistance: lessons from translational research. Am J Clin Nutr. 2010;91(1):258S-261S.

[28] Orio F, Palomba S, Cascella T, Milan G, Mioni R, Pagano C, et al. Adiponectin levels in women with polycystic ovary syndrome. J Clin Endocrinol Metab. 2003;88(6):2619–23.

[29] Lecke SB, Mattei F, Morsch DM, Spritzer PM. Abdominal subcutaneous fat gene expression and circulating levels of leptin and adiponectin in polycystic ovary syndrome. Fertil Steril. 2011;95(6) :2044–9.

[30] Sam AH, Busbridge M, Amin A, Webber L, White D, Franks S, Martin NM, Sleeth M, Ism ail NA, Mat Daud N, Papamargaritis D, Le Roux CW, Chapm an RS, Frost G, Bloom SR, Murphy KG. Hepcidin levels in diabetes mellitus and polycystic ovary syndrome. diabetic Med 2013; 30: 1495-1499.

[31] Aroda V, Ciaraldi TP, Chang S-A, Dahan MH, Chang RJ, Henry RR. Circulating and cellular adiponectin in polycystic ovary syndrome: relationship to glucose tolerance and insulin action. Fertil Steril. 2008;89(5):1200–8

[32] Goldstein A, Jutel A, Drew K (2014): Social issues in diagnosis. Baltimore, MD: John Hopkins University Press.

[33] Pagotto U, Gambineri A, Vicennati V et al. (2002): Plasma ghrelin, obseity, and the polycystic ovary syndrome: Correlation with insulin resistance and androgen levels. J Clin Endocrinol Metab., 87: 5625-9.

[34] Khomami MB, Tehrani FR, Hashemi S et al. (2015): Of PCOS symptoms, hirsutism has the most significant impact on the quality of life of Iranian women. PLoS ONE, 10: e0123608.

[35] Jones GL, Hall JM, Lashen HL et al. (2011): Health related quality of life among adolescents with polycystic ovary syndrome. Journal of Obstetric, Gynecologic, and Neonatal Nursing, 40: 577–588.

[36] Jayasekara RS (2012): Focus groups in nursing research: Methodological perspectives. Nursing Outlook, 60: 411–6.

How to Cite

S. M. . Kadhim, F. S. . Al-Fartusie, and N. K. . Klichkhanov, “Evaluation of Adiponectin and Hepcidin with some Biochemical Parameters in Sera of Women with Polycystic Ovary Syndrome”, *Al-Mustansiriyah Journal of Science*, vol. 34, no. 1, pp. 52–57, Mar. 2023.