Original Research Article Study on Adiponectin Levels in Polycystic Ovary Syndrome Cases Mehre Afshan Mehdi¹, Suhail Ahmad², Saleha Shaheen³, Farhan Usmani⁴

¹Senior Resident, Department of OBS/Gynae, Netaji Subhas Medical College & Hospital, Bihta, Patna, Bihar, India
²Associate Professor, Department of Pharmacology, R.D.J.M. Medical College and Hospital, Turki, Muzaffarpur, Bihar, India
³Associate Professor, Department of Biochemistry, Prashad Institute of Medical Sciences, Banthra, Lucknow, Uttar Pradesh, India
⁴Associate Professor, Department of Biochemistry, Patna Medical College, Patna, Bihar, India
Received: 08-10-2021 / Revised: 23-11-2021 / Accepted: 06-12-2021

Abstract

Introduction: Low adiponectin levels in polycystic ovarian syndrome (PCOS) have been largely attributed to obesity which is common among these patients. In addition, evidence also suggests that low adiponectin in PCOS may be related to insulin resistance (IR) in these women. However, studies on the role of adiponectin in younger and lean patients are limited. Therefore, the aim of the present study was to examine the association of adiponectin levels in young and lean women with PCOS.**Methodology:** This case control study included 75 participants for each.75 women for cases were included who had PCOS. This study was carried in Department of Biochemistry & Department of Obs/Gynae in Patna Medical College, Patna, Bihar. The duration of study was over a period of two years.**Results:** The result of this study revealed that adiponectin level <13.0 in 27 PCOS cases and in 45 healthy participants, rest were having >13.0 adiponectin level. **Conclusion:** This study **Keywords:** PCOS, Adiponectin Level, Endocrine-Metabolic Diseases.

This is an Open Access article that uses a fund-ing model which does not charge readers or their institutions for access and distributed under the t erms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0) and the Budapest Open Access Initiative (http:// www.budapestopenaccessinitiative.org/read), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Polycystic Ovary Syndrome (PCOS) has been reported to be one of the most common endocrine-metabolic diseases which affect up to 10% of females of reproductive age group.^{1,2} In approximately 44% of women with PCOS, obesity has been found to be an accompanying factor which is characterized by central distribution of fat. Hyperinsulinemia, dyslipidaemia, and/or hypertension are highly dependent on obesity, especially in women with PCOS and the presence of these worsens the clinical presentation of PCOS.^{1,3} It is now a known fact that the adipose tissue stores a large quantity of fat as an energy source[4]as well as expresses a variety of genes of secretory proteins[5-9]. The human apM1 gene, which is exclusively expressed in white adipose tissue, has been discovered just now.Adiponectin, the product of this gene is a 244-amino acid protein which has high structural homology to collagen VIII, X, complement C1q, and TNF. Peroxisome proliferator- activated receptor _ agonists increases the expression of this protein Adiponectin[10-14]. The physiological role of this protein adiponectin has not been established so far but some recent studies described it to be a kind of matrix protein and has role in antiatherogenic and anti-inflammatory properties[15-18]. As adiponectin is a fat cell product which is secreted into the circulating blood, therefore, it can be held responsible for the metabolic and neuroendocrine derangements attributes of obesity and obesityrelated disease, such as PCOS. It has been documented that

*Correspondence

Dr. Farhan Usmani

Associate Professor, Department of Biochemistry, Patna Medical College, Patna, Bihar, India. **E-mail:** <u>farhanusmani90@gmail.com</u> the plasma levels of adiponectin are lower in the obese subjects in comparison to non-obese subjects although it is secreted only from adipose tissue[19]. In recent studies, it has been shown that the plasma concentration of adiponectin increases with reduction in body weight[18], signifying that the expression of adiponectin is downregulated by adipose tissue. In few studies, the serum adiponectin concentrations have been found to be inversely correlated with the severity of insulin resistance as well as plasma levels of low-density lipoprotein cholesterol, and triglycerides. But no conclusive data is available at present on adiponectin plasma levels in women with PCOS. Keeping all these things in mind, the aim of the present study is to assess serum adiponectin levels in obese PCOS females and in normo-weight population.

Materials & Methods

Study Population: This case control study included 75 participants for each.75 women for cases were included who had PCOS.

Study Area: This study was carried in Department of Biochemistry & Department of Obs/Gynae in Patna Medical College, Patna, Bihar. **Study Duration**: Duration of study was over a period of two years.

Data Collection: We included 75 diagnosed cases of PCOS aged between16–35 years with desired BMI.PCOS was diagnosed using the Rotterdam Criteria which states that PCOS is diagnosed if patient have any two of the following three features, 1) oligo/amenorrhea and/or anovulation, 2) hyperandrogenism and/or hyperandrogenemia, and 3) polycystic ovaries on ultrasound after exclusion of other etiologies. While75 Controls were included healthy females with regular menstrual cycle from family and friends of the cases.

Controls participants also had BMI within desirable range. Sociodemographic information such as detailed menstrual and reproductive history, family history of menstrual or reproductive

International Journal of Health and Clinical Research, 2021; 4(22):61-64

problems, past medical history, and anthropometric profile were recorded. Fasting blood samples were drawn from all participants for assessment of blood glucose, lipid profile, adiponectin, insulin and androgen levels. Fasting serum adiponectin was estimated using the Bio-Rad PR 3100which uses Enzyme Linked ImmunoSorbent Assay (ELISA) technique of quantitative hormone estimation. Adiponectin was categorized using the median value of the sample, 13.0 μU/ml.

Data Analysis: Data were analysed by using Microsoft Excel.

Results

In this study we included 75 PCOs cases and 75 healthy participants as control. Out of 150 participants 24 cases and 23 control were aged group 31-35 followed by 21-25,16-20,26-30 age group. In this study, 37 cases and 43 control were married rest were unmarried. This study seen that 63 cases having family history of PCOS, while in control 54 having family history of PCOS. It was found total cholesterol in 69 control and in 68 cases having less than 6.2 and rest having more than 6.2. The present study also shows that high density of lipoprotein >1.29 in 35 cases and in 43 control. The result of this study revealed that adiponectin level <13.0 in 27 PCOS cases and in 45 healthy participants, rest were having >13.0 adiponectin level.



Fig 1: Distribution of cases-control according to age

Table 1: Characteristics & Adiponectin level in PCOS cases & control

Characteristics	Cases	Control
Marital status		
Unmarried	38	32
Married	37	43
Family history of PCOS		
Yes	63	54
No	12	21
Total cholesterol		
<6.2	68	69
>6.2	7	6
High density of lipoprotein		
<1.29	35	43
>1.29	40	32
BMI	19.3	18.3
Insulin resistance	3.1	2.9
Adiponectin level		
<13.0	27	45
>13.0	48	30

Discussion

The findings of the present study implied that the serum adiponectin levels of PCOS females with a desirable Body Mass Index (BMI) are significantly low. After adjustment for age, BMI, family history of PCOS, marital status, total cholesterol level, HDL and IR, the association of PCOS remained consistent and statistically significant with low adiponectin level. There was not much effect of age parameter as the relationship between PCOS and low adiponectin changed very little across different age groups. It has been also reported that the family histories of PCOS and IR were associated significantly with lower adiponectin levels. In the present study, the low levels of adiponectin were found in lean young women with PCOS. It has been well demonstrated by multiple studies that the decreased levels of serum adiponectin were commonly found in females with PCOS. Some studies have shown a correlation of low adiponectin levels with presence of PCOS irrespective of the weight and/or BMI of patients[20-24]. The relationship between PCOS and lower levels of adiponectin has been disclosed in systematic review and meta-analysis of Toulis et al. after controlling for the potential effects of obesity by BMI matching on a sub-analysis. This study established the fact that the serum adiponectin levels are not independently determined by the degree of female adiposity only, but underlying disease may also be attributed for the same. Increasing IR in PCOS females can be held responsible for the lower adiponectin levels in the previous study. The similar results have been observed in the present study. It has been observed in type 2 diabetes mellitus that the adiponectin possessed insulin-sensitizing and anti-diabetic properties as well as the levels of adiponectin were also reduced [25,26]. An increase in the plasma levels of the adiponectin were observed in randomized controlled trials with treatment of PCOS patients with anti-diabetic medication such as metformin [27,28], rosiglitazone[29], and pioglitazone[30].In the present study, an association of family history of PCOS and IR with lower adiponectin levels in PCOS females were observed. The genetic factors have been found to play an important role in the pathogenesis of PCOS. Familial clustering of PCOS has been reported in the first-degree relatives of the patients.³¹ It has been found that the pre-pubertal daughters with normal BMI, of PCOS females, present with disturbed metabolic profile including hypoadiponectenemia and hyperinsulinemia.³² In the present study, the cases and controls did not differ significantly regarding the history of PCOS. This finding pointed towards the hypothesis that the environmental factors e.g. diet, and exercise also play a role despite the fact that the family history is an important risk factor. PCOS is a syndrome and its polygenic causality cannot be ruled out and various dysfunctional changes in the metabolism of carbohydrates, insulin action, and steroid hormones have also been established. A similar family history of PCOS can therefore be found being a contributory factor along with others those cause PCOS. A similarity of family history in cases and controls is sometimes found. In the present study, significantly lower levels of adiponectin were found in PCOS patients of age younger than twenty-five years can be attributed to the involvement of a stronger genetic component in PCOS pathogenesis. It has been found that the serum adiponectin levels can be used as a potential independent biomarker for diagnosis of PCOS in lean females with fewer symptoms, or in females with a family history of PCOS. If we got the chances, we would like to enhance our research further using prospective design which may help us to establish role of adiponectin in early diagnosis or detection of PCOS among young lean females.

Conclusion

This study concludes that the serum adiponectin levels can be used as a potential independent biomarker for diagnosis of PCOS in lean females with fewer symptoms, or in females with a family history of PCOS.

References

1. Carmina E, Lobo RA. Polycystic ovary syndrome (PCOS): arguably the most common endocrinopathy is associated with

significant morbidity in women. J Clin Endocrinol Metab. 1999; 84:1897-9.

- Legro RS. Polycystic ovary syndrome: the new millennium. Mol Cell Endocrinol. 2001; 184:87–93
- Elting MW, Korsen TJM, Shoemaker J. Obesity, rather than menstrual cycle pattern or follicle cohort size, determines hyperinsulinemia, dyslipidemia and hypertension in ageing women with polycystic ovary syndrome. Clin Endocrinol. 2001; 55:767–76.
- Trayhurn P, Beattie JH. Physiological role of adipose tissue: white adipose tissue as an endocrine and secretory organ. Proc Nutr Soc. 2001; 60:329–39.
- Maeda K, Okubo K, Shimomura I, Mizuno K, Matsuzawa K. Analysis of an expression profile of genes in the human adipose tissue. Gene. 1997; 190:227–35.
- Koutnikowa H, Auwerx J. Regulation of adipocyte differentiation. Ann Med. 2001; 33:556–61.
- McTernan PG, McTernan CL, Chetty R, Jenner K, Fisher FM, Lauren MN, Crocker J, Barnett AH, Kumar S. Increased resistin gene and protein expression in human abdominal adipose tissue. J Clin Endocrinol Metab. 2002; 87:2407–10.
- Wasim A, Haque WA, Shimomura I, Matsuzawa Y, Garg A. Serum adiponectin and leptin levels in patients with lipodystrophies. J Clin Endocrinol Metab. 2002; 87:2395–98.
- Matsuzawa Y, Funahashi T, Nakamura T. Molecular mechanism of metabolic syndrome X: contribution of adipocytokines, adipocyte-derived bioactive substances. Ann N Y Acad Sci. 2002; 892:146-54.
- Saito K, Tobe T, Minoshima S, Asakawa S, Sumiya J, Yoda M, Nakano Y, Shimizu N, Tomita M. Organization of the gene for gelatin-binding protein (GBP28). Gene. 1999; 229:67–73.
- Halleux CM, Takahashi M, Delporte ML, Detry R, Funahashi T, Matsuzawa Y, Brichard SM. Secretion of adiponectin and regulation of apM1 gene expression in human visceral adipose tissue. BiochemBiophys Res Commun. 2001; 288:1102–7.
- Takahashi M, Arita Y, Yamagata K, Matsuzawa Y, Okutomi K, Horie M, Shimomura I, Hotta K, Kuriyama H, Kihara S, Nakamura T, Yamashita S, Funahashi T, Matsuzawa Y. Genomic structure and mutations in adipose specific gene, adiponectin. Int J Obes. 2000; 24:861–8.
- Maeda N, Takahashi M, Funahashi T, Kihara S, Nishizawa H, Kishida K, Nagaretani H, Matsuda M, Komuro R, Ouchi N, Kuriyama H, Hotta K, Nakamura T, Shimomura I, Matsuzawa Y. PPARy ligands increase expression and plasma concentrations of adiponectin, an adipose-derived protein. Diabetes. 2001; 50:2094–9.
- 14. Yang WS, Leng CY, Wu TJ, Tanaka S, Funahashi T, Matsuzawa Y, Wang JP, Chen CL, Tai TY, Chuang LM. Synthetic peroxisome proliferator-activated receptor agonist, rosiglitazone, increases plasma levels of adiponectin in type 2 diabetic patients. Diabetes Care. 2002; 25:376–80.
- Ouchi N, Kihara S, Arita Y, Maeda K, Kuriyama H, Okamoto Y, Hotta K, Nishida M, Takahashi M, Nakamura T, Yamashita S, Funahashi T, Matsuzawa Y. Novel modulator for endothelial adhesion molecules adipocyte derived plasma protein adiponectin. Circulation. 1999; 100:2473–76.
- Matsubara M, Maruoka S, Katayose S. Decreased plasma adiponectin concentrations in women with dyslipidemia. J Clin Endocrinol Metab. 2002; 87:2764-9.
- 17. Arita Y, Kihara S, Ouchi N, Maeda K, Kuriyama H, Okamoto Y, Kumada M, Hotta K, Nishida M, Takahashi M, Nakamura T, Shimomura I, Muraguchi M, Ohmoto Y, Funahashi T, Matsuzawa Y. Adipocyte-derived plasma protein adiponectin acts as a platelet-derived growth factor-BB-binding protein and regulates growth factor-induced common postreceptor signal in vascular smooth muscle cell. Circulation. 2002; 105:2893–98.

- Yang WS, Lee WJ, Funahashi T, Tanaka S, Matsazawa Y, Chao CL, Chen CL, Tai TY, Chuang LM. Weight reduction increases plasma levels of an adipose-derived antiinflammatory protein, adiponectin. J Clin Endocrinol Metab. 2001; 86:3815–9.
- Arita Y, Kihara S, Ouchi N, Takahashi M, Maeda K, Miyagawa JI, Hotta K, Shimomura I, Nakamura T, Miyaoka K, Kuriyama H, Nishida M, Yamashita S, Okubo K, Matsubara K, Muraguchi M, Ohmoto Y, Funahashi T, Matsuzawa Y. Paradoxical decrease of an adipose-specific protein, adiponectin, in obesity. BiochemBiophys Res Commun. 1999; 257:79–83.
- Ardawi MS, Rouzi AA. Plasma adiponectin and insulin resistance in women with polycystic ovary syndrome. FertilSteril. 2005; 83:1708–16.
- Barber TM, Hazell M, Christodoulides C, Golding SJ, Alvey C, Burling K et al. Serum levels of retinol-binding protein 4 and adiponectin in women with polycystic ovary syndrome: associations with visceral fat but no evidence for fat massindependent effects on pathogenesis in this condition. J Clin Endocrinol Metab. 2008; 93:2859–5.
- 22. Carmina E, Orio F, Palomba S, Cascella T, Longo RA, Colao AM et al. Evidence for altered adipocyte function in polycystic ovary syndrome. Eur J Endocrinol. 2005; 152:389–94.
- Escobar-Morreale HF, Villuendas G, Botella-Carretero JI, Alvarez-Blasco F, Sanchon R, Luque-Ramirez M et al. Adiponectin and resistin in PCOS: a clinical, biochemical and molecular genetic study. Hum Reprod. 2006; 21:2257-65.
- Sepilian V, Nagamani M. Adiponectin levels in women with polycystic ovary syndrome and severe insulin resistance. J Soc GynecolInvestig. 2005; 12:129–34.
- Wickham EP III, Cheang KI, Clore JN, Baillargeon JP, Nestler JE. Total and high-molecular weight adiponectin in women with the polycystic ovary syndrome. Metabolism. 2011; 60:366–72.
- 26. Weyer C, Tataranni PA, Bogardus C, Pratley RE. Insulin resistance and insulin secretory dysfunction are independent

Conflict of Interest: Nil Source of support:Nil

predictors of worsening of glucose tolerance during each stage of type 2 diabetes development. Diabetes Care. 2001; 24:89– 94.

- Agarwal N, Rice SP, Bolusani H, Luzio SD, Dunseath G, Ludgate M et al. Metformin reduces arterial stiffness and improves endothelial function in young women with polycystic ovary syndrome: a randomized, placebo-controlled, crossover trial. J Clin Endocrinol Metab. 2010; 95:722–30.
- Elkind-Hirsch K, Marrioneaux O, Bhushan M, Vernor D, Bhushan R. Comparison of single and combined treatment with exenatide and metformin on menstrual cyclicity in overweight women with polycystic ovary syndrome. J Clin Endocrinol Metab. 2008; 93:2670–78.
- 29. Majuri A, Santaniemi M, Rautio K, Kunnari A, Vartiainen J, Ruokonen A et al. Rosiglitazone treatment increases plasma levels of adiponectin and decreases levels of resistin in overweight women with PCOS: a randomized placebocontrolled study. Eur J Endocrinol. 2007; 156:263–9.
- 30. Glintborg D, Frystyk J, Hojlund K, Andersen KK, Henriksen JE, Hermann AP et al. Total and high molecular weight (HMW) adiponectin levels and measures of glucose and lipid metabolism following pioglitazone treatment in a randomized placebo-controlled study in polycystic ovary syndrome. Clin Endocrinol (Oxf). 2008; 68:165–74.
- Crosignani PG, Nicolosi AE. Polycystic ovarian disease: heritability and heterogeneity. Hum Reprod Update. 2001; 7:3– 7.
- Sir-Petermann T, Maliqueo M, Codner E, Echiburu B, Crisosto N, Perez V et al. Early metabolic derangements in daughters of women with polycystic ovary syndrome. J Clin Endocrinol Metab. 2007; 92:4637–42.