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INFLAMMATION IS ASSOCIATED WITH INSULIN RESISTANCE IN PCOS WOMEN

Medical Biochemistry

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ABSTRACT

Background: Polycystic Ovarian Syndrome has been regarded as a state of chronic low grade inflammation and these women have marked insulin resistance. This low grade inflammation is thought to play a key role in induction of insulin resistance in these women but its role is not clear. The present study was designed to study the association of inflammation with insulin resistance in PCOS women. **Design:** Cross Sectional Study. **Materials & Methods:** The study included 60 PCOS women of age group 18-30 years and 50 age matched healthy females. The Anthropometric measurements, Fasting Plasma Glucose, serum insulin and hs-CRP were measured in all these subjects. HOMA- IR formula was used to calculate insulin resistance. **Results:** The Mean BMI & Waist Hip Ratio were significantly higher in PCOS women than in Controls (P<0.001). While no significant difference in fasting plasma glucose was observed between PCOS women and controls (p<0.24), levels of hs-CRP, fasting insulin and HOMA-IR were found to be significantly elevated in PCOS women than controls (p<0.001). A significant positive correlation between hsCRP with fasting insulin (r=0.5, p<0.05) and insulin resistance (r=0.59, p<0.049) was also observed. **Conclusion:** Our study indicates the presence of both inflammation and insulin resistance in PCOS women. Inflammation appears to be strongly associated with insulin resistance in women with PCOS.

KEYWORDS

hsCRP, Insulin, HOMA- IR, PCOS.

INTRODUCTION

Polycystic Ovarian Syndrome is the most common endocrinopathy affecting women of reproductive age [1]. It is characterized by clinical or biochemical hyperandrogenism, chronic ovulatory dysfunction, and polycystic ovaries on ultrasound [2]. Though the etiology of PCOS is not known, evidences support the presence of chronic low grade inflammation, as indicated by raised serum hs-CRP levels, a sensitive ideal marker of low grade inflammation in PCOS women [3]. This chronic low grade inflammation promotes the development of metabolic aberrations and ovarian dysfunction in PCOS [4].

Another important key feature of PCOS is insulin resistance, which is observed in both normal weight and overweight PCOS women [5]. The compensatory hyperinsulinemia in turn stimulates the ovarian androgen production and increases the likelihood to develop Type 2 diabetes, metabolic syndrome, and cardiovascular disease [6]. Though the exact cause of insulin resistance in PCOS is not clear, chronic low grade inflammation is thought to play a key role in the development of insulin resistance [7]. Studies evaluating the association of inflammation on insulin resistance in PCOS have yielded mixed results. In the present study we assessed the relationship of inflammation with insulin resistance in PCOS women.

METHODS:

This cross sectional study was conducted in department of Biochemistry in collaboration with department of Obstetrics and Gynecology at Rajah Muthiah Medical College & Hospital. The study was approved by Institutional ethical committee. An informed written consent was obtained from Subjects and controls who participated in this study.

Inclusion criteria:

Sixty subjects of age group 18-30 years who were diagnosed as PCOS according to Rotterdam criteria and fifty age matched healthy females were chosen as controls.

Exclusion criteria:

Subjects with the history of diabetes, hypertension, systemic inflammatory conditions and clinical evidence of acute infections, renal and hepatic diseases and Oral contraceptive pill usage were all excluded from the study.

Complete physical examination was recorded including anthropometric measurements (Height and weight, BMI, Blood pressure, waist circumference, Hip circumference and Waist hip ratio). 5 ml of venous blood was collected from all the subjects after 12 hours of fasting. Fasting Plasma Glucose, serum hs-CRP and serum insulin were all measured. Blood glucose was estimated by GOD-POD method. Insulin and hs-CRP were measured by ELISA method. Insulin resistance was calculated via Homeostasis Model Assessment insulin resistance index: HOMA IR = [fasting plasma glucose (mg/dL)× fasting insulin (IU/mL)]/405.

Statistical Analysis:

Statistical analysis was carried out using SPSS 20.0 and values were expressed in mean ± standard deviation, Statistical difference between the control and PCOS groups were carried out using Student "t" test and p value of < 0.05 was considered to be statistically significant. Pearsons Correlation analysis was performed for correlation of hsCRP with Insulin and HOMA-IR.

RESULTS:

Table I shows the mean Clinical and Biochemical characteristics of PCOS women and control subjects. Table II shows the correlation statistics of serum hs-CRP with Insulin and insulin resistant indice HOMA-IR values in PCOS women

There was no significant difference in age, blood pressure and fasting plasma glucose between PCOS women and control subjects. The BMI and Waist Hip Ratio were significantly higher (p<0.01) in PCOS women than the control subjects.

Fasting insulin, HOMA-IR and hsCRP were all significantly higher in women with PCOS than control group (p<0.001). In PCOS women Serum hs-CRP was significantly positively correlated with insulin [r=0.5 & p<0.05] and HOMA-IR value [r=0.59 & p<0.05]

Table 1: Clinical and Biochemical parameters in PCOS women and Control subjects.

VARIABLES	GROUP-I (CONTROLS) (N=50)	GROUP-II (PCOS) (N=60)	p Value
AGE	24.06±4.01	23.8±4.18	NS
SYSTOLIC BLOOD PRESSURE (mmHg)	119±3.75	118±4.3	NS
DIASTOLIC BLOOD PRESSURE (mmHg)	78.2±2.8	77.5±1.9	NS
BMI	23.2±1.6	25.64±2.65	P<0.001
WHR	0.84 ± 0.04	0.87 ± 0.04	P<0.005

FASTING PLASMA GLUCOSE (mg/dl)	87.94±6.24	90.33±5.59	NS
FASTING INSULIN (µU/ml)	8.62±1.27	19.02±2.53	P<0.001
HOMA-IR	1.8±0.3	4.52±0.64	P<0.001
hs-CRP (mg/L)	3.2±0.97	4.88±0.54	P<0.001

Values are expressed as Mean ± standard deviation.

Table 2: Correlation of hsCRP with insulin and HOMA-IR in PCOS women.

Variables	PCOS subjects (r value)	p Value
hs-CRP and Insulin	0.5	p<0.05
hs-CRP and HOMA-IR	0.59	p<0.05

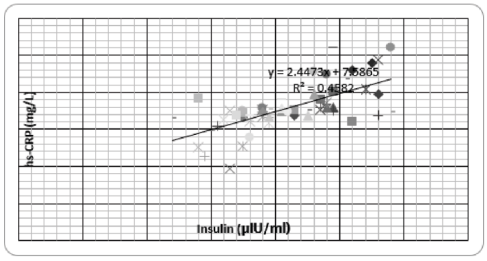

Fig 1. Correlation between hs-CRP and insulin in PCOS women

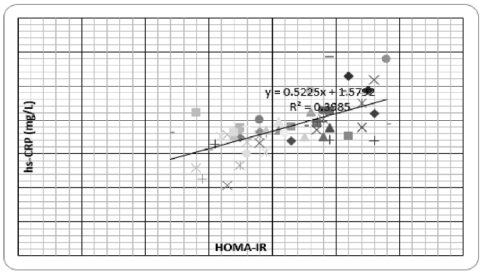

Fig 2.Correlation between hs-CRP and HOMA-IR in PCOS women.

DISCUSSION:

The objective of the present study was to assess the relationship between serum highly sensitive C reactive protein (hs-CRP) and insulin resistance in PCOS women. The participants in both study groups were of same age group (24.06 ± 4.01 and 23.8 ± 4.18) and no significant difference was observed between the groups (p>0.05). In our study fasting plasma glucose in PCOS women was not significantly different from the control group. This might be due to the late onset of glucose intolerance in PCOS women which usually occurs at typically in 3rd - 4th decade of life [8].

In this study we also found significantly higher levels of BMI and Waist Hip Ratio in PCOS women compared to controls (p<0.001). This indicates the presence of central obesity in PCOS women [9]. The serum hs-CRP level was significantly higher in PCOS women than controls (p<0.001). This indicates the presence of chronic low grade inflammation in PCOS. This was in consistent with the findings of Boulman et al., who had also reported significantly high hs-CRP levels in PCOS women [10]. However, Matthias et al., in their study had observed no significant difference in hs-CRP levels between PCOS subjects and Controls [11]. The discrepancies might be due to small sample sizes or due to difference in phenotypes in PCOS population. The low grade inflammation may be due to the presence of excess adiposity in PCOS women, which promotes systemic inflammation by producing inflammatory cytokines [12].

Also in this study Insulin concentration and insulin resistance were significantly higher in PCOS women compared to controls suggesting it to be an insulin resistant state. Similar observations were also seen by Thathapudi et al., [13]. A significantly positive correlation of hs-CRP with both insulin as well as HOMA-I.R in PCOS women was also observed in this study. Thus chronic low grade inflammation is associated with insulin resistance in PCOS women. This was inconsistent with the findings of sunita et al., [14]. In contrast Sapna Jangir et al., observed a insignificant positive correlation of hs-CRP with insulin and HOMA-IR [15]. The possible mechanism for the association of inflammation with insulin resistance might be due to increased expression of inflammatory cytokines due to increased visceral adiposity [16]. These inflammatory cytokines in turn may induce insulin resistance by directly acting on insulin signaling post receptor molecule or by inducing central obesity through activation of hypothalamic-pituitary adrenal axis [17]. Thus both inflammation and insulin resistance play a significant role in the pathogenesis of PCOS. Chronic low grade inflammation is strongly associated with insulin resistance in PCOS women. Assessment of insulin resistance and inflammation in PCOS women can also help to identify those who are at risk of developing metabolic syndrome.

REFERENCES:

1. Goodarzi MO, Dumesic DA, Chazenbalk G, Azziz R. Polycystic ovary syndrome: etiology, pathogenesis and diagnosis. Nat Rev Endocrinol. 2011; 7(4):219–31.
2. The Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod 2004; 19: 41–47.
3. Ramanand SJ et al. High sensitivity C - reactive protein (hs-CRP) and clinical characteristics, endocrine, metabolic profile in Indian women with PCOS: a correlation. Int J Reprod Contracept Obstet Gynecol. 2014 Mar; 3(1):118-126
4. González F, Rote NS, Minium J, Kirwan JP. Increased activation of nuclear factor jB triggers inflammation and insulin resistance in polycystic ovary syndrome. J Clin Endocrinol Metabolism 2006; 91:1508–12.
5. Jayashree S. Insulin resistance in obese and lean women with polycystic ovarian syndrome. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. VOL. 8 NO. 1 (2019): January 2019 .
6. Z.T. Bloomgarden, "Second world congress on the insulin resistance syndrome," Diabetes Care, vol. 28, no. 7, pp. 1821–1830, 2005.
7. Rehman, K., Akash, M.S.H. Mechanisms of inflammatory responses and development of insulin resistance: how are they interlinked? *J Biomed Sci* 23, 87 (2016).
8. Dunaif A. Insulin resistance and polycystic ovary syndrome: mechanism and implication for pathogenesis. Endocrinology Rev 1997; 18:774-800.
9. Lim SS, Davies MJ, Norman RJ, Moran LJ. Overweight, obesity and central obesity in women with polycystic ovary syndrome: a systematic review and meta-analysis .Hum Reprod update. 2012; 18(6):618-637.
10. Boulman N, Levy Y, Leiba R, Shachar S. Increased C-reactive protein levels in the polycystic ovary syndrome: a marker of cardiovascular disease. J Clin Endocrinology Metabolism. 2004; 89(5):2160–2165.
11. Matthias Mohlig, Joachim Spranger, et al., The polycystic ovary syndrome per se is not associated with increased chronic inflammation. European Journal of Endocrinology (2004) 150 525–532.
12. Gregor, M.F.; Hotamisligil, G.S. Inflammatory Mechanisms in Obesity. *Annu. Rev. Immunol.* 2011, *29*, 415–445.
13. Thathapudi S, Kodati V. Anthropometric and biochemical characteristics of polycystic ovarian syndrome in South Indian women using AES-2006 criteria. Int J Endocrinol Metab 2014; 12: e12470.
14. Ramanand Sunita, Jaiprakash Ramanand, et al., "High sensitivity C reactive protein (hs-CRP) and clinical characteristics, endocrine, metabolic profile in Indian women with PCOS: a correlation", International Journal of Reproduction Contraception Obstetrics and Gynecology, 2014.
15. Sapna Jangir, Jairam Rawtani. Evaluation of hs-CRP, Insulin and Insulin resistance in Polycystic Ovarian Syndrome. International Journal of Clinical biochemistry and Research, April-June 2017: 4(2):195-197.
16. Shoelson SE, Lee J, Goldfine AB. Inflammation and insulin resistance. J Clin Invest. 2006 Jul;116(7):1793-801. doi: 10.1172/JCI29069. Erratum in: J Clin Invest. 2006 Aug; 116(8):2308.
17. Chen, Li & Chen, Rui & Wang, Hua & Liang, Fengxia. (2015). Mechanisms Linking Inflammation to Insulin Resistance. International Journal of Endocrinology. 2015. 1-9.