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Insulin status in polycystic ovaries syndrome in relation with inflammation

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ABSTRACT

Polycystic ovarian disease is poly cysts present in the state of enlarged ovaries. It is a hormonal imbalance disease which alters the insulin status and these poly cysts can cause local inflammation which in-turn results in increase of CRP to infertility and other problems in female age group of 20-35 years. 30 PCOS patients and 30 healthy individuals from the OPD of Saveetha Dental College and hospital were collected and the serum samples were analyzed for their hormonal status by using kit method in Robonik Elisa reader. There is a significant increase in Insulin ($p<0.005$) and CRP ($p<0.001$) as well as there is an increase in fasting blood sugar (FBS) and insulin resistance (IR) by the influence of PCOS on other metabolisms. Our findings suggest that prolonged or highly hormonal imbalance in PCOS can cause problems like diabetes mellitus (DM) by increasing the levels of IR and by triggering the inflammation pathway.

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INTRODUCTION

Polycystic ovarian syndrome is the most common hormonal abnormality in reproductive aged women of 5-10% population. This is characterised by elevated androgens levels, menstrual irregularities and small cysts on one or both ovaries. This disorder can be morphological or predominantly biochemical. PCOS is the cause of up to 30% of infertility. There is no cure for PCOS. Hyperandrogenism, polycystic ovaries and ovulatory dysfunction are the main phenotypic abnormalities occur in it (Erin K Barthelmess and Rajesh K Naz., 2014). It generally manifests with oligo/anovulatory cycles, hirsutism and polycystic ovaries, together with a considerable prevalence of insulin resistance. PCOS is considered affected with various genetic, endocrine and environmental problems. PCOS patients have a higher chance of metabolic and cardiovascular diseases in their life style (V. De Leo *et al.,* 2016). It is a hormonal disorder sometimes a common cause of infertility among women (Uche Anadu Ndefo *et al.,* 2013)

It also refers to the association of chronic anovulation with hyperandrogenism in women without specific underlying disease of adrenal of pituitary glands (Stephen Franks., 2017). The symptoms of PCOS usually start from the first occurrence of menstruation (David A *et al.,* 2005). The symptoms include irregular menstruation, irregular ovulation, excess hair growth on face and body, thinning of hair and accumulation of unruptured follicles (Ruksana Sheik *et al.,* 2015). Polycystic ovaries are characterised by a cell hyperplasia an ovarian cortical thickening (Michael T. Sheehan *et al.,* 2004). The management of PCOS is regulation of menses, fertility problems, control of Hirsutism and the management of insulin resistance syndrome and its association with type 2 diabetes mellitus, dyslipidemia and cardiovascular risk disease (Evanthia Diamanti *et al.,* 2012). PCOS exhibit insulin resistance, which may enhance the risk of heart disease and diabetes (Thomas Tang *et al.,* 2009). Treatment is directed at the present complaint and

for infertility women includes weight loss, exercise, food control and skin care (Marlon E. Cerf., 2013).

In the presence of peripheral insulin resistance, pancreaticβ -cell insulin secretion increases in a compensatory fashion. Under normal circumstances, this relationship is constant. β-Cell dysfunction is felt to be present for values falling below this hyperbolic curve (Priyanka Shenoy.B *et al.,* 2016). This relationship can be quantitated as the product of insulin sensitivity and first-phase insulin release known as the disposition index. Fasting hyperinsulinemia is present in obese PCOS women. Significant increase in insulin secretion and decrease in insulin clearance are may be due to the hyperinsulinemia. Even though insulin clearance is receptor mediated there is a decrease in insulin clearance can occurs often in insulin resistant states (Dunaif A., 1997).

Streptococcus pneumonia was the first acute phase protein to be described and is exquisitely sensitive systemic marker of inflammation and tissue damage by denoting C reactive protein (Pepys MB *et al.,* 2003). CRP is a pentameter of 23 kDa subunits, CRP level is usually low in normal individuals but can rise 100 to 200 fold or higher with acute systemic inflammation (Yeh ET *et al.,* 2004).

The inflammatory response is essential in the response of pathogens. The mediators of the response initiate metabolic changes to provide nutrients for immune system, from host tissues. These changes include increased gluconeogenesis. Insulin resistance occurs in diabetes mellitus. This examines that inflammation links to insulin insensitivity (Grimble RF., 2002). This study aims to study the information about the relation between insulin and inflammation in PCOS patients.

METHODS AND MATERIALS

Patients were selected from those attending the outpatient department of Saveetha Dental College and hospitals and divided into two groups as follows

Group I – Normal healthy individuals with normal BMI (19-24.9) – 30 individuals
Group II – PCOS Patients – 30 individuals

Inclusion Criteria

Individuals with the age group of twenty to thirty years
PCOS Patients

Exclusion Criteria

Individuals with other systemic illness like diabetes mellitus, cardio vascular disease, renal failure, Stroke, endocrine illness.
Individuals with acute illness like fever.
Immunocompromised individuals

Sample collection and Procedure

Informed consent was obtained from the patient before sample collection. 5ml of venous blood was collected and distributed in plain collection tubes and centrifuged in 3000 rpm for 10 mins. Then serum was separated and used to estimate the FBS by GOD-POD Method, CRP by Turbilatex Method using ERBA CHEM 5 plus analyser. Insulin level by ELISA method using ROBONIK ELISA READER.

Insulin resistance was calculated by using HOMA-IR calculation.

<1 indicates Optimal / No insulin resistance
>1.9 indicates Early Insulin Resistance
>2.9 indicates Significant Insulin Resistance

RESULTS AND DISCUSSION

The FBS levels of PCOS 102 ± 14.15 were significantly high when compared with health individuals 84.8 ± 6.48 the significant value is $p<0.05$. The insulin levels of PCOS 8.4 ± 2.12 were significantly high when compared with health individuals 3.18 ± 1.3, the significant value is $p<0.05$. The Insulin Resistance of PCOS 2.12 ± 0.63 were significantly high when compared with health individuals 0.66 ± 0.3, the significant value is $p<0.05$. The CRP level of PCOS 7.63 ± 1.97 were significantly high when compared with health individual 2.78 ± 0.97, the significant value is $p<0.05$.

Table 1: Mean, SD and Significance value of LH, FSH and LH, FSH ratio in two groups

Parameters	Controls	PCOS patients	p-Value
FBS	84.8 ± 6.48	102 ± 14.15	<0.05
Insulin	3.18 ± 1.3	8.4 ± 2.12	<0.005
IR	0.66 ± 0.3	2.12 ± 0.63	<0.05
CRP	2.78 ± 0.97	7.63 ± 1.97	<0.005

Hyperinsulinemia plays an important role in hyperandrogenism causing an elevation of ovarian androgen production and reduction of serum sex hormone binding globulin concentration (Nestler JE *et al.,* 1994, Barbieri RL *et al.,* 1986). The insulin secretion is reduced by metformin, diazoxide thereby the concentration of serum free testosterone decrease in women with PCOS (Kiddy DS *et al.,* 1989, Kiddy DS *et al.,* 1992). The hyperandrogenism women have insulin resistance which plays a significant role in PCOS (John E. Nestler *et al.,* 1996).

The Increased level of plasma insulin concentration and the decrease of insulin like growth factor-1 binding protein-1 which takes place in insulin resistance results in the enhancement of pituitary LH

response to LH releasing hormone and potentiation of its action in ovarian theca and strong, with inhibition of androgen aromatization to estrogen in the granulose. These changes and the development of polycystic ovaries lead to ovarian hyperandrogenism, oligo anovulation, stromal growth, and accumulation of dysfunctional, cystic follicles in the ovaries (Alexandros N *et al.,* 2018).

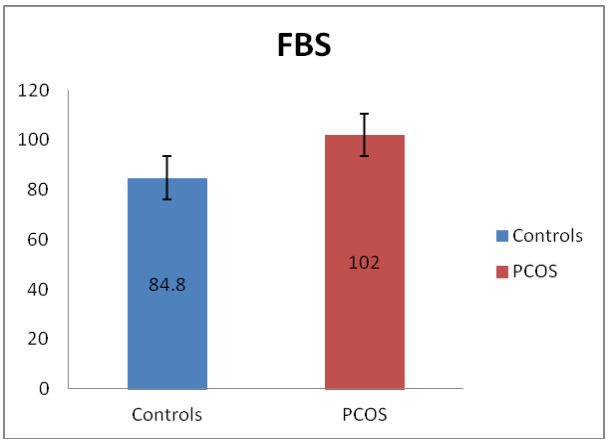

Figure 1: FBS levels comparison between controls and PCOS patients

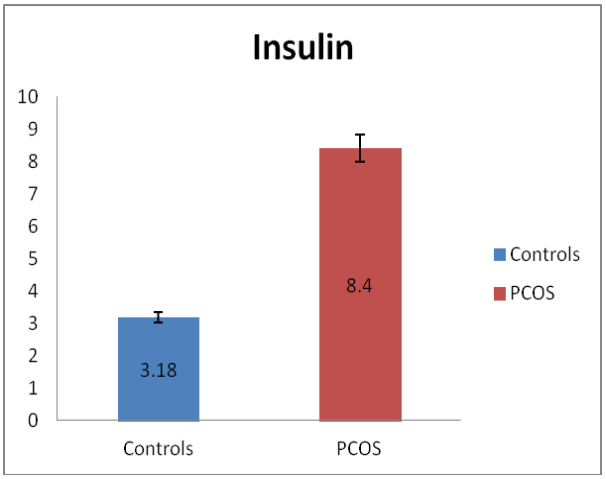

Figure 2: Insulin levels comparison between controls and PCOS patients

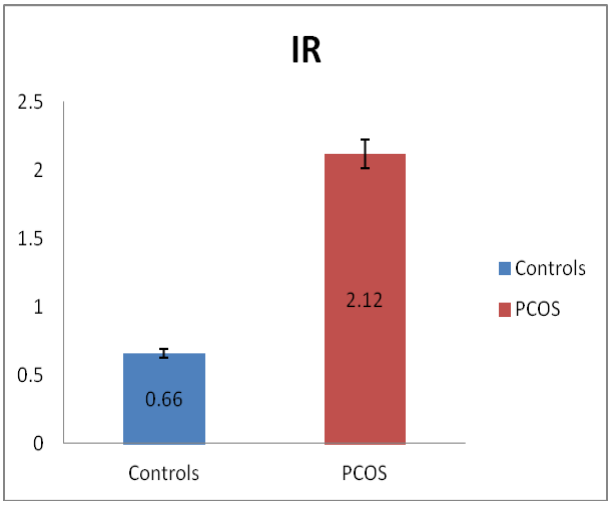

Figure 3: Insulin resistance levels comparison between controls and PCOS patients

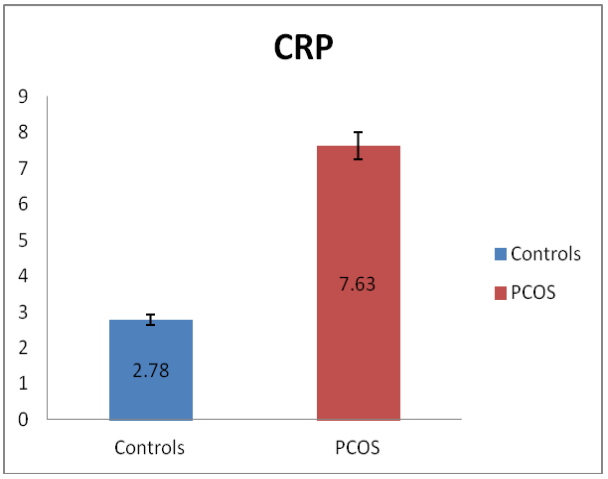

Figure 4: CRP levels comparison between controls and PCOS patients

Women with both PCOS and obese were shown significant increase in their blood glucose levels during their oral glucose tolerance test (OGTT) when they were compared with controls and as well as ovulatory hyperandrogenic women. And it shows there is a significantly higher glucose intolerance prevalence in PCOS women that the controlled women. In PCOS hyperinsulinemia is probably the result of a combination of increased basal insulin secretion and decreased hepatic insulin clearance.

Highly sensitive assay are significantly increased in women with PCOS relative to those in healthy women with normal menstrual rhythm and normal androgen levels after correction for BMI. Women with PCOS have significantly increased CRP concentrations relative to those in healthy women with normal menstrual rhythm and normal androgens (Evanthia Diamanti-Kandarakis Andrea Dunaif., 2012).

CONCLUSION

Our study states that prolonged or highly hormonal imbalance in PCOS can cause problems like diabetes mellitus (DM) by increasing the levels of IR and by triggering the inflammation pathway by increasing CRP levels, monitoring of these inflammatory markers may be beneficial for earlier diabetes of complications like diabetes.

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