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Evaluation of Serum Prolactin and Insulin Resistance in Sudanese Women with Polycystic Ovarian Syndrome

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Abstract: **Polycystic ovarian syndrome (PCOS) has been one of a major public health problem in Sudan that leads to medical consequences. It causes multifactorial in etiology such as menstrual dysfunction, hyperandrogenism, hirsutism, insulin resistance (IR), dyslipidemia and obesity which increased risk of diabetes mellitus and cardiovascular disease.**

Objective*:* The present study was designed to assess serum prolactin and insulin resistance in PCOS Sudanese women and to compare them with healthy women as controls.

Materials and Methods: This study, was a descriptive, analytic, cross- sectional and hospital-based study, carried in Khartoum- State- Sudan; it was carried out in March 2013 to May 2014. 200 women with PCOS were enrolled in this study, they compared with 100 healthy women as control group, all of them were age-and weight-matched, Samples were taken after overnight fasting, then serum insulin and prolactin levels were analyzed using ELISA technique and enzymatic colorimetric method. Data management and analysis was done by using Microsoft excel and SPSS software, version 20.00.

Results: The patients with PCOS, having a mean age of 29.61± 5.4 years and mean age 31.23±4.93 years of control group, were included in the study, in PCOS group the (mean ± SD) of serum insulin, prolactin and blood glucose were11.06±6.21 µIU/ml,397.95±25.17 ng/ml, 95.75±22.53 mg/dl, respectively while that of control group, the (mean ± SD) of serum insulin, prolactin and blood glucose were 4.52±1.60 µIU/ml, 249.15±25.76 ng/ml and 80.35±11.76 mg/dl respectively. There was statistically significant increased levels insulin, prolactin and blood glucose in PCOS group when compared to the control group (P<0.05).

Conclusion: It concluded that there was significantly higher fasting insulin, glucose and HOMA in PCOS Patients, indicates presence of insulin resistance. IR may have a potential role in the prediction of dysglycemic disease in women with PCOS. Our study, observed that there was no any correlation between serum prolactin, serum insulin and BMI in the study group. .

Keywords: **PCOS, Insulin resistance and serum prolactin, Sudanese.**

1. INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common endocrine disease and metabolic disorder in adolescence and reproductive women, which is the first reason for female infertility, with the incidence of 5-10% of women of reproductive age [1]-[2]. It is characterized by chronic an ovulation, hyperandrogenism, and ovarian polycystic changes under ultrasound in clinic. The etiology of PCOS is still not very clear, but previous studies have shown that PCOS is closely related to lipid metabolism disorder and insulin resistance [3]-[4]. 50% of PCOS patients have obesity that to android obesity with an increased risk of diabetes mellitus and cardiovascular disease [5]. Insulin resistance is present in 40-50% of patients, especially in obese women [6].According to ESHRE/ASRM (European Society for Human Reproduction and Embryology/America Society for Reproductive Medicine) consensus conference on PCOS held in Rotterdam in 2003, PCOS was defined as at least 2 out of three following abnormalities (a) oligo and/or an ovulation, (b) clinical and/or biochemical signs of hyperandrogenism (hirsutism and/or acne or increased androgens levels) (c) detection of polycystic ovaries by ultrasound and presence of 10 or more cyst of 2-10mm in diameter in each ovary and

absence of other endocrine conditions such as thyroid disorder, cushing's syndrome, congenital virilizing adrenal-hyperplasia or hyperprolactinemia.

Prolactin (Prl) is a hormone of pituitary origin and a single-chain polypeptide involved in several actions, such as lactation, luteal function, reproduction, appetite, suppression of fertility, homeostasis, osmotic balance, immunity, and coagulation. Prolactin has been reported as a potent lipogenic and diabetogenic factor, that affecting energy balance and fuel metabolism [7]. Among the various physiological factors known to augment prolactin, insulin induced hypoglycemia which results in significant release of prolactin in normal subjects. In vitro lactogen treatment, in the form of oral prolactin alters insulin secretary behavior and β cell junctional communication. Hyperprolactinemia decreases glucose tolerance via an increase in insulin resistance [8]. Because there was few studies done in this area, the present study, was designed to assess serum prolactin and insulin resistance in women with PCOS and to compare them with healthy women as controls

2. MATERIALS AND METHODS

The present study is descriptive, analytic, cross- sectional and hospital-based study, it was carried out on 200 PCOS subjects in the age group of 17 to 40 years and 100 voluntary age and BMI matched healthy women with normal menstrual cycle as controls. The study was conducted at Khartoum educational teaching Hospital. The diagnosis of PCOS was fulfilled as per Rotterdam criteria. Presence of at least two criteria from clinical, hormonal and abdominal USG category was considered diagnostic of PCOS. Patients with diabetes mellitus, hypertension, dyslipidemia, renal and liver failure and other endocrine disorders and patients receiving hormonal / non-hormonal treatment for PCOS were excluded from the study. The institutional ethical committee approved the study protocol. Informed consent was obtained from all the participants. A pre-structured and pre-tested proforma was used to collect the data. Baseline data including age, BMI, detailed medical history, clinical examinations and relevant investigations were included as part of the methodology. Serum prolactin, serum insulin and blood sugar were measured in all participants from morning blood samples collected after 12 hours of fasting. Serum prolactin and serum insulin were measured by ELSIA technique. IR was estimated via the homeostasis model assessment insulin resistance index (HOMA-IR), as follows: HOMA-IR = fasting insulin (mU/L) × fasting glucose (mmol/L)/22.5. Body mass index (BMI) was calculated as the ratio of weight (Kg) to height squared (m2). Blood sugar was estimated by enzymatic colorimetric methods.

2.1 Statistics analysis:

Data were analyzed by computer program (SPSS) version IBM 20. Student T. test was used for the Calculation. $P \leq 0.05$ was considered significant.

All chemical reagents were purchased from Bio system company (Spine Company for Analytical material and chemical Reagents).

3. RESULTS

On continuous measurements are presented as Mean ± SD. The basic characteristics of all participants are shown in Table 1. And mean distribution of biochemical parameters in the cases and controls are depicted in Table 2. There was no significant difference in age between two groups. Slightly higher mean BMI was recorded in cases than in controls but the difference in mean BMI between the two groups was statistically significant ($P<0.05$). Higher mean fasting serum Insulin, Higher mean FBS and higher mean prolactin were recorded in cases compared to controls and the difference between them were found to be statistically significant ($P<0.05$). Correlation of prolactin with insulin is depicted in Table 2. No significant correlation could be found between BMI and serum Insulin in cases ($r=0.06$, $p = 0.38$) [Figure 1]. No significant correlation could be found between prolactin and serum Insulin in cases ($r = 0.13$, $p = 0.06$) [Figure 2].in our study. Similarly, no significant correlation could be found between BMI and serum prolactin in cases ($r= -0.12$, $p = 0.09$) [Figure3].

Table 1: Baseline characteristics of patients with PCOS and controls

Variable	Case with PCOS	Control group	P-value
Age/years	29.61±5.41*	31.23±4.93*	0.060
Weight/Kg	72.83±10.88*	68.03±11.31*	0.030
Hight/Cm	160.00±6.00	162.60±5.52	0.210
BMI/Kg/m²	29.76±4.24*	24.14±3.76*	0.001

** The means is a significant difference between different values, (P<0.05).*

Table 2. Mean distribution of biochemical parameters in PCOS cases and controls

Parameters	Case with PCOS	Control group	P-value
Serum prolactin (ng/ml)	397.95±25.17*	249.15±25.76*	0.002
Serum insulin (µIU/ml)	11.06±6.21*	4.52±1.60*	0.001
HOMA-IR	2.61± 1.56*	1.01±0.45*	<0.001
Fasting blood glucose (mg/dl)	95.75±22.53*	80.35±11.76*	0.025

** The means is a significant difference between different values, (P<0.05).*

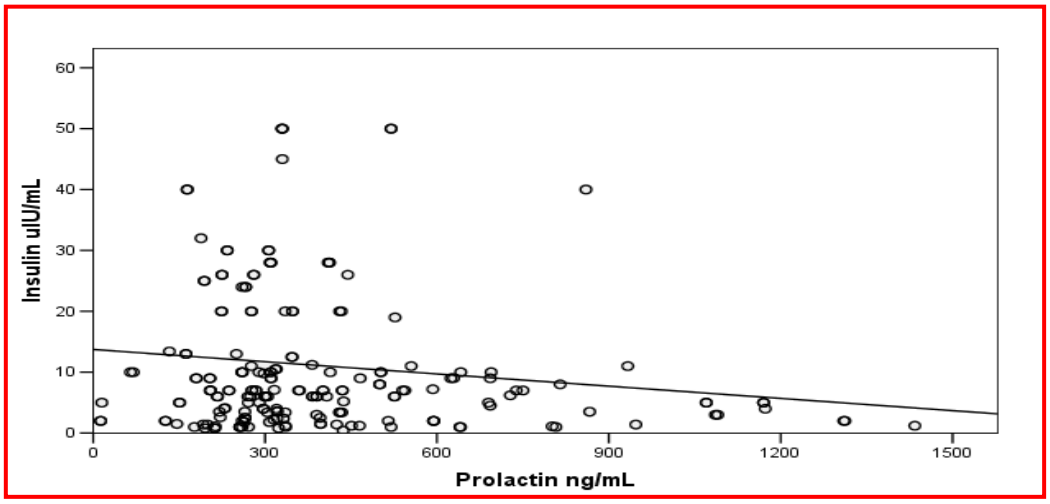

Figure 1: A scatter plot shows correlation between prolactin and insulin in the study group (r = 0.13, p= 0.06)

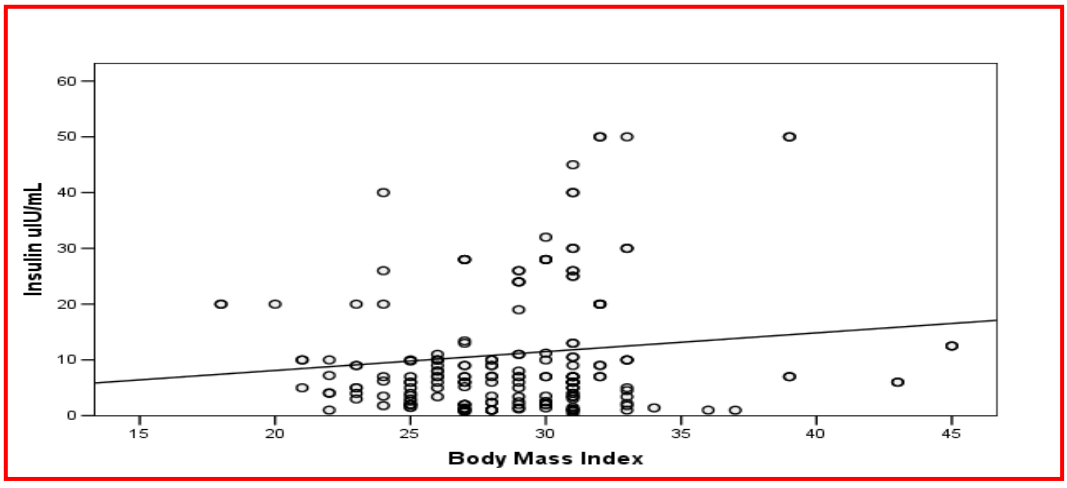

Figure 2: A scatter plot shows correlation between insulin and body max index in the study group (r = 0.06, p= 0. 38)

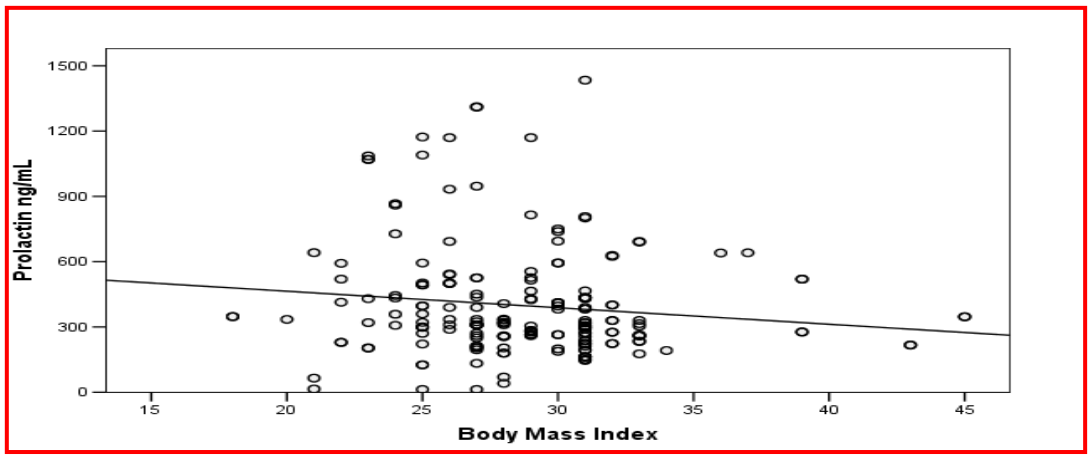

Figure 3: A scatter plot shows correlation between prolactin and body max index in the study group (r = - 0.12, p= 0.09)

4. DISCUSSION

The study was conducted to evaluate changes for lipids profile parameters in Sudanese polycystic ovarian syndrome (PCOS) patients and healthy women as control group. Polycystic ovarian syndrome is one of the important endocrine disorder causing reproductive abnormalities in women, which has heterogeneous clinical features and multifactorial in etiology [9].Obesity and insulin resistance occur frequently in association with this syndrome. Cardiovascular risk factors seem to cluster in women with PCOS compared with general population [10]. Insulin resistance is a metabolic disorder caused by the impairment of insulin function in inducing glucose uptake and utilization [11]. Seow et al. demonstrated that IR in PCOS involves both receptor and post receptor defects, including defects in phosphatidylinositol 3-kinase and the GLUT-4 glucose transporter. In addition, women with PCOS frequently exhibit impaired peripheral insulin-stimulated glucose utilization and higher basal insulin levels, probably caused by increased insulin secretion and/or decreased hepatic clearance of the hormone; such abnormalities were independent of obesity [12, 13]. Insulin resistance is defined clinically as the inability of a known quantity of exogenous or endogenous insulin to increase glucose uptake and utilization in an individual as much as it does in a normal population [14].

In present study, Higher mean fasting serum Insulin and higher mean HOMA-IR were recorded in PCOS subjects compared to controls and the difference between them were found to be statistically significant ($P<0.001$). This was consistent with Shou-Kul et al. They found in their study that the HOMA-IR of the PCOS women was significantly higher than that of the age-matched healthy women, which suggested that insulin resistance had a crucial role in pathogenesis of PCOS [14].

Higher mean FBS was recorded in PCOS women in our study compared to controls and differences between cases and controls was found to be statistically significant ($P= 0.025$). This result agrees with a study done by Burghen et al [15] who reported that the elevation of fasting plasma glucose was associated with hyperinsulinemia also Kierland et al [16] reported that there was insulin- resistant diabetes mellitus in patients with PCOS. The practical implication of these findings is that the polycystic ovary syndrome may be a marker of insulin resistance and dyslipidemia [17,18]Impaired glucose tolerance and frank type II diabetes mellitus are more prevalent in obese young women with the polycystic ovary syndrome than in weight-matched controls.[19]. In our present there was insignificant correlation between the body mass index and insulin level in PCOS Patients, this similar to that study done by Ravi et al [20], who reported that we could not find any significant correlation between BMI and serum insulin level in either of the groups mostly because of the limited number of subjects. Puder et al also showed in their study that women with PCOS were more insulin resistant compared to a group of age and BMI matched controls [21]. Sunita et al concluded in their study that Insulin resistance is common in Indian PCOS women and this is independent of obesity [22].

Studies showed mild hyperprolactinemia has been reported in 5% to 30% of patients with PCOS[23]. In present study, higher mean prolactin was recorded in PCOS women compared to controls and differences between cases and controls were statistically significant ($P=0.002$). This finding was consisted with Ansam[24], Soodabeh et al[25] and Sunita et al[22]. In contrast to this, Roy et al found in their study that serum insulin and prolactin both are significantly increased in PCOS women. This increased prolactin may augment adrenal androgen secretion by the inhibition of 3beta-hydroxysteroid dehydrogenase activity or, less often, through selective action on the sulfation of DHEA in adrenal or extra-adrenal sites. However, prolactin inhibits FSH-induced ovarian aromatase, leading to intraovarian hyperandrogenemia[26]. Cristianne et al also found prolactin is significantly higher in PCOS women [27].

In our study, there was significant, very weak negative correlation between insulin and serum levels of prolactin in PCOS patients, ($r = -0.13$, $p = 0.06$). Similarly, there was significant, very weak negative correlation between the body mass index (BMI) and the serum levels of Prolactin, ($r=-0.12$, $p = 0.09$).

The role of prolactin on glucose metabolism and insulin resistance depends on its circulating concentration. Prolactin knockout or prolactin receptor deficiency is accompanied by β-cell hypoplasia, a reduced pancreatic insulin mRNA level, a blunted insulin secretory response to glucose, and mild glucose intolerance. Physiologically elevated prolactin levels induce normal adaptive increases in glucose-stimulated insulin secretion through expanding β-cell mass and improving hepatic insulin sensitivity and have an indirect action by increasing hypothalamic dopamine synthesis to contribute to the improved energy and glucose homeostasis. Pathologically high levels of prolactin exacerbate whole-body and hepatic insulin resistance and impair the insulin secretory capacity in diabetic mice [28]. Differential effects on gene expression are associated with synergistic effects of glucose and PRL on islet DNA synthesis. PRL up-regulates β-cell glucose uptake and utilization, whereas glucose increases islet PRL receptor expression and potentates the effects of PRL on cell

cycle gene expression and DNA. Synthesis [29]. Available in-vitro studies suggest an influence of prolactin on ß-cell secretion via increased glucokinase activity, improved ß-cell specific survival, or inhibition of intrinsic ß-cell apoptosis [30].

5. CONCLUSION

Fasting Serum Insulin and HOMA-IR were found to be significantly higher in PCOS subjects compared to controls in our study. All the above derangements confirm that PCOS is associated with insulin resistance and this may be a feature of a higher risk of metabolic syndrome. We could not find any significant correlation between serum prolactin, serum insulin and BMI.

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