Assessment of Serum Luteinizing hormone and Insulin Level of Polycystic Ovary Syndrome Women

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Abstract: Polycystic ovarian syndrome (PCOS) is the most common endocrinopathy that affects women. It 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. It is known that if patients with PCOS are screened for these diseases, many long-term complications can be prevented. Objective: The present study was designed to assess serum luteinizing hormone and insulin 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 luteinizing hormone and insulin levels were analyzed using ELISA technique. 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 luteinizing hormone and insulin were 11.06±6.21 µIU/ml, 14.60±9.80 ng/ml, respectively while that of control group, the (mean ± SD) of serum luteinizing hormone and insulin were 7.00±3.36 ng/ml, 4.52±1.60 µIU/ml respectively. There was statistically significant increased levels of serum luteinizing hormone and insulin in PCOS group when compared to the control group (P<0.05). Conclusion: It concluded that there was significantly higher fasting luteinizing hormone and serum insulin, there was significant correlation between serum luteinizing hormone, serum insulin and BMI in the study group.

Keywords: PCOS, Serum Luteinizing hormone, Insulin, Sudanese.

1. Introduction

Polycystic ovary syndrome (PCOS) is the most common female endocrine (hormonal) disorder, affecting 5-10% of women of reproductive age [1] It is characterized by chronic an ovulation with oligo-menorrhea which occurs in up to 80 per cent of patients. It is the commonest cause of anovulatory subfertility and recurrent miscarriage. PCOS is seen in around 50-60 per cent of women with more than three early pregnancy losses[2] infertility, typical sonographic appearance of the ovaries with multiple small follicles distributed around the ovarian periphery or throughout the echodense stroma[3] and clinical or biochemical hyper androgenism Insulin resistance is present in 40-50% of patients, especially in obese women [4]although this syndrome was first identified in 1935, physicians still do not know what causes it. Their research today, however, has been focused on the far-reaching effects of this syndrome on a woman’s health, as well as its role in infertility. Researchers most recently have achieved a new understanding of the role of insulin-resistance and high levels of insulin in PCOS patients.

Insulin resistance can be characterized as impaired action of insulin in the uptake and metabolism of glucose.[5] Impaired insulin action leads to elevated insulin levels, which causes a decrease in the synthesis of 2 important binding proteins: insulin-like growth factor binding protein (IGFBP-I) and sex hormone binding globulin (SHBG). IGFBP-I binds to IGFBP-II and SHBG binds to sex steroids, especially androgens. The triad of hyperandrogenism, insulin resistance, and acanthosis nigricans (HAIR-AN) syndrome appears in a subgroup of patients with PCOS.[5,6,7] Acanthosis nigricans, a dark and hyperpigmented hyperplasia of the skin typically found at the nape of the neck and axilla, is a marker for insulin resistance. Acanthosis nigricans is usually found in about 30% of hyperandrogenic women.

Increased luteinizing hormone (LH) relative to follicle-stimulating hormone, (FSH) was the first laboratory abnormality identified in classic PCOS. Elevated LH levels occur in about half of PCOS patients [7, 8]. Elevated LH is thought to play a role in the pathogenesis of PCOS by increasing androgen production and secretion by ovarian theca cells [9, 10]. Patients with PCOS have an increased LH pulse frequency and amplitude [11]. The increase in LH seems to be the result of abnormal sex steroid feedback rather than the cause of androgen excess [11]. Although frankly virilizing androgen levels will suppress LH in women, the modest rise in androgen levels in patients with PCOS paradoxically stimulates LH pulsatility. This is because patients with PCOS are less sensitive to suppression of LH by luteal phase hormones than are controls. Antiandrogen treatment normalizes the elevated LH pulse frequency of PCOS, suggesting that androgen excess interferes with the hypothalamic inhibitory feedback of female hormones, principally progesterone. Other lines of evidence also argue against the hypothesis that PCOS is primarily caused by abnormal pituitary function. About half of patients with PCOS, principally obese patients, do not have elevated LH levels or abnormal gonadotropin responses to gonadotropin-releasing hormone (GnRH) agonist testing [9, 11, 12]. Furthermore, about half of PCOS subjects with a documented ovarian source of
hyperandrogenism were demonstrated to have normal LH levels and LH responses to a GnRH agonist test, also suggesting that their ovarian dysfunction is independent of LH excess.

Luteinising hormone (LH)
This hormone is made in the pituitary gland (in the base of the brain.) It stimulates the ovaries to ovulate and works alongside insulin to promote testosterone production. A high level of LH is found in about 4 in 10 women with PCOS. A high LH level combined with a high insulin level means that the ovaries are likely to produce too much testosterone.

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 LH and serum insulin were measured by ELSIA technique. Body mass index (BMI) was calculated as the ratio of weight (Kg) to height squared (m2).

2.1 Statistics Analysis

Data were analyzed by computer program (SPSS) version IBM 20. Student T. test was used for the Calculation. P≤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 and higher mean LH were recorded in cases compared to controls and the difference between them were found to be statistically significant (P<0.05). No significant correlation could be found between BMI and serum Insulin in cases (r=0.06, p = 0.38)[Figure 1]. No significant correlation was found between LH and serum Insulin in cases (-0.08, p = 0.25)[Figure 2].In our study. There was a significant correlation between BMI and serum LH in cases (r=-0.15, p = 0.03)[Figure3].

### Serum Luteinizing Hormone

Table (2) shows a highly significant difference between the means of serum LH of the test group (n=200) and the control group (n=100). Mean±SD : (14.60±9.8) versus (7.00±5.26) µIU/ml, P=0.001. Figure (1) shows significant, very weak negative correlation between the body mass index (BMI) and the serum levels of Luteinizing hormone (r= -0.15, p = 0.03). Figure (3) shows significant, very weak negative correlation between the Insulin and the serum levels of Luteinizing hormone, (r = -0.08, p = 0.25). In this study 89 subjects with PCOS (44.5%) had abnormal high serum levels of Luteinizing hormone.

### Serum insulin:

Table (2) shows highly significant difference between the means of serum insulin of the test group and the control group. Mean±SD: (11.06±6.21) versus (4.52±1.60) µIU/ml, P=0.001. Figure (2) shows insignificant, very weak positive correlation between the body mass index (BMI) and the serum levels of Insulin, (r=0.06, p = 0.38). In this study, 70 subjects PCOS (35%) had abnormal high serum levels of Insulin.

### Table 1: Baseline characteristics of patients with PCOS and controls

<table>
<thead>
<tr>
<th>Variable</th>
<th>Case with PCOS</th>
<th>Control group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age/years</td>
<td>29.61±5.41*</td>
<td>31.23±4.93*</td>
<td>0.060</td>
</tr>
<tr>
<td>Weight/Kg</td>
<td>72.8±10.88*</td>
<td>68.03±11.31*</td>
<td>0.030</td>
</tr>
<tr>
<td>Height/Cm</td>
<td>160.00±6.00</td>
<td>162.60±5.52</td>
<td>0.210</td>
</tr>
<tr>
<td>BMI/Kg/m²</td>
<td>29.76±4.24*</td>
<td>24.14±3.76*</td>
<td>0.001</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Case with PCOS</th>
<th>Control group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SerumLuteinizing hormone(ng/ml)</td>
<td>14.62±9.80*</td>
<td>7.00±3.36*</td>
<td>0.001</td>
</tr>
<tr>
<td>Serum insulin (µIU/ml)</td>
<td>11.06±6.21*</td>
<td>4.52±1.60*</td>
<td>0.001</td>
</tr>
</tbody>
</table>

* The means is a significant difference between different values, (P<0.05)
Figure 1: Scatter plot shows a correlation between BMI and Luteinizing hormone ($r=-0.15, p=0.03$)

Figure 2: Scatter plot shows a correlation between BMI and insulin ($r=0.06, p=0.38$)

Figure 3: Scatter plot shows a correlation between Luteinizing hormone and insulin ($r=-0.08, p=0.025$)
4. Discussion

Polycystic ovary syndrome (PCOS) is one of the most female endocrine disorders affecting approximately 5%-10% of women of reproductive age (12-45 years old) and is one of the leading causes of infertility, metabolic abnormalities, obesity and cardiac disease [13, 14, 15].

In this study a test group of 200 patients with polycystic ovary syndrome were compared to 100 apparently healthy volunteers, both groups were matched for age and height. Weight and body mass index were significantly raised in patients with polycystic ovary syndrome compared to controls, according to interpretation of BMI, 51% were found to be overweight. (BMI between 25 and 29.9 Kg/m²), 36.6% were obese (BMI > 30 Kg/m²), whereas 11.5% were found to have normal reference weight (BMI between 19 and 25 Kg/m²), and only 1% were found to be under weight (BMI < 19 Kg/m²).

In the 1999 National Health and Nutrition Examination Survey in U.S on women with PCOS [16], it was reported that the prevalence of obesity, was found to be (42%) which was higher than in the present study (36.6%) whereas in Spanish patients with PCOS it was (30%) [17], while the prevalence of obesity in Greek women with PCOS was found to be (38%) [18]. The overweight women with PCOS in the present study constitute about (51%). These data suggest that the majority (more than 83%) of patients with polycystic ovary syndrome in the present study have BMI above the normal reference.

In this study, women with polycystic ovary syndrome had significant increases in the serum levels of Luteinizing hormone compared to controls subjects (p<0.001), this agrees with a study done by Wild et al [19] who reported that patients with polycystic ovary syndrome had higher serum (LH) to (FSH) ratios, also this agrees with a study done by Fauser et al., who reported that, Both the absolute level of circulating LH and its relationship to FSH levels are significantly elevated in PCOS women as compared with controls, thjis is due to increased amplitude and frequency of LH pulses. Elevated LH concentrations (above the 95th percentile of normal) can be observed in 60% of PCOS women [20], whereas the LH/FSH ratio may be elevated in up to 95% of subjects [21], if women who have ovulated recently are excluded. LH levels may be influenced by the temporal relationship to ovulation, which transiently normalizes LH, by the BMI (being higher in lean PCOS women) and by the assay system used. In the current study, there was a very weak negative correlation between the body Mass index (BMI) and the serum levels of LH, and there was a very weak negative correlation between the serum levels of luteinizing hormone and the serum levels of insulin, this result agrees with a study done by Yen et al [21], who reported that serum LH concentrations are commonly elevated in women with PCOS.

5. Conclusion

The current study demonstrated that the PCOS causes significant increases of serum insulin and LH levels in women and high body mass index. Weight reduction in obese women with the polycystic ovary syndrome should be encouraged [22] in an effort to limit the risk of hyperinsulinemia, type II diabetes and long-term cardiovascular disease. More investigations should be done to demonstrate the relationship between hyperinsulinemia, elevated LH level and insulin resistance obesity in PCOS patients. On the other hand the elevated BMI increases the risk for insulin resistance and Diabetes Mellitus.

References


