Association of Clinical Features with Obesity and Gonadotropin Levels in Women with Polycystic Ovarian Syndrome

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Abstract:

Objective: This study was conducted in order to evaluate the association of clinical features of polycystic ovarian syndrome (PCOS) with gonadotropin levels and weight gain.

Patients and Methods: Total 86 women of 19-38 years diagnosed by Rotterdam criteria of PCOS were included in study. Patients were labelled as normal weight and obese with BMI < 25 and ≥ 25kg/m² respectively. According to Ferriman-Gallwey (FG) hirsutism scoring system, score of ≥ 8 indicates the presence of hirsutism. Polycystic ovaries on ultrasound are diagnosed when 10 small antral follicles are seen in each ovary. Menstrual irregularity was described as presence of chronic amenorrhea, altered cycle length with less than 21 or more than 35 day and altered serum progesterone level at 21 day of 28 day cycle. Serum LH and FSH were measured on immunochemistry analyzer. Analysis was done on SPSS 19 software.

Results: Out of 86 patients 71% were obese, 91% women had positive polycystic finding on ultrasound. Regarding gonadotropin levels, LH/FSH ratio >2 was found in 31% women. Patients having LH ≥10 and FSH ≥ 7 were 23% and 29% respectively. Statistically significant association of obesity with hirsutism and presence of polycystic ovaries on sonography was found. Gonadotropin levels did not show any significant association with all clinical features of PCOS. Odd ratio of obesity for hirsutism and polycystic ovaries on ultrasound was statistically significant. Odd ratios of LH, FSH and LH/FSH for all clinical features of PCOS were statistically insignificant.

Conclusion: Obesity has significant association with presence of hyperandrogenism related clinical features such as hirsutism in PCOS. Thus prevention of obesity can decrease the incidence and progression of PCOS.

Key Words: Polycystic ovary syndrome, Signs and symptoms, Obesity, gonadotropins

Introduction

In women with reproductive age polycystic ovarian syndrome (PCOS) being the most common endocrine problem affects about 12-21% population. Its characteristic clinical features include hyperandrogenism, ovulatory dysfunctions and presence of polycystic ovaries on ultrasound examination. Clinical manifestations of hyperandrogenism consist of hirsutism, acne and alopecia. Biochemical parameters comprise of free testosterone and free androgen index. Ovulatory dysfunctions may include oligomenorrhea, amenorrhea and prolonged erratic menstrual bleeding. While 30% of women may have normal menses. These clinical and biochemical features can differ in different individuals, depending upon their age, BMI and ethnicity.

Different diagnostic criteria’s including National institutes of health (NIH) criteria, Rotterdam criteria and Androgen excess society diagnostic (AES) criteria are used now days for diagnosis of PCOS. Among all of them Rotterdam consensus is widely accepted in Asia. It confirms the diagnosis of PCOS by the presence of two of the following features: 1. Menstrual irregularities, 2. Hyperandrogenism (clinical or biochemical), 3. Polycystic ovaries on ultrasound examination. Other etiologies must be excluded such as congenital adrenal hyperplasia, androgen secreting tumours, Cushing syndrome, thyroid dysfunction and hyperprolactinaemia. These different PCOS diagnostic criteria’s may reveal different prevalence of disease even in same population. Many previously diagnosed women were not classified as having PCOS on second assessment. About 70% of women may remain undiagnosed. This may occur due to different reasons like presence of considerable variations among individuals on presentation, variability in application of diagnostic criteria’s and their cut offs or resolution of symptoms especially after weight loss. Obesity is a common finding in women presented with PCOS. There are
different views regarding its importance related to PCOS. Some studies describe the less role of obesity in PCOS. In a study conducted on women ranged from underweight to the severely obese and the risk of PCOS was minimally increased along with increasing obesity. Likewise Endocrine society of clinical practice guidelines describe the uncertain role of weight loss in improving PCOS status. While according to some other studies obesity has a key role in PCOS and its occurrence can significantly influence the development and expression of this disease.

In PCOS, obesity can be responsible for development of insulin resistance and associated hyperinsulinemia. Hyperinsulinemic condition, present in most women with PCOS plays an essential role in PCOS development and is thought to be the cause rather than the result of hyperandrogenism. Increased insulin concentration in blood via decreased levels of circulating sex hormone binding globulin leads to elevated free testosterone levels. Being having true gonadotropin function, increase in amount of insulin at the level of ovarian tissue increases the androgen synthesis. Obesity can be responsible to the development of different hyperandrogenemia related clinical features of syndrome like hirsutism and menstrual irregularities. It can increase the activity of cortisol metabolizing enzymes such as 5-α reductase. Increased cortisol metabolism decreases the negative feedback control of hypothalamus-pituitary adrenal axis. Thus associated increase of ACTH production leads to increased adrenal androgen levels in body and thus enhances their availability to peripheral tissues. That is why in many non-obese women polycystic ovaries may be found on sonography. But due to absence of other clinical features, these women become unable to meet diagnostic criteria for PCOS. Increased weight gain in such women may lead to appearance of PCOS specific clinical symptoms. High prevalence of PCOS has been studied in overweight and obese women. Increased tendency of weight gain of about 1-2 kg/ year and obesity associated increase in hirsutism and menstrual disturbances have also been observed in women having PCOS. Increased weight gain has an important role regarding metabolic syndrome. Study revealed that increased BMI along with increased age and presence of antracnosis nignars act as a significant predictor of metabolic syndrome in South Asian women having PCOS. The best first line treatment in PCOS includes a healthy life style together with balanced caloric restricted diet and regular exercises in order to lose weight and to prevent future weight gain.

Initially LH/FSH ratio greater than 2 was considered an important investigation in diagnosis of PCOS. The basic mechanism was thought to be the altered gonadotropin releasing hormone (GnRH) pulsatility due to abnormal hypothalamic-pituitary ovarian or adrenal axis in PCOS. This ultimately results in relative increase in LH to FSH release. In this condition abnormal feedback response by ovarian estrogen may be responsible for discriminated increase in LH release. This altered release of LH and FSH leads to reversal of LH/FSH ratio (≥2 to 1). But as the time passes diagnostic importance of LH, FSH and LH/FSH ratio in PCOS become controversial. A study conducted in 2012 revealed a significantly increased LH/FSH ratio and decreased FSH levels in PCOS patients. While some other studies showed no significant role of gonadotropin levels in diagnosing PCOS. Due to these contradictory effects of body weight and gonadotropin levels on diagnosis of PCOS, we planned this study in order to evaluate the association of clinical features present in PCOS with increase weight gain and with gonadotropin levels.

**Material and Methods**

This cross sectional study was conducted at Salma and kafeel Medical Centre, Islamabad from January 2014-october 2014. Total 86 women of age 19-38 years diagnosed by Rotterdam criteria were included in the study. Women having history of any major systemic illness, acromegaly, thyroid dysfunction, Cushing's syndrome, congenital adrenal hyperplasia, hyperprolactinemia, androgen secreting neoplasm, and other pituitary or adrenal disorders, and risk factors for endometrial cancer, mood disorders, obstructive sleep apnea, diabetes, and cardiovascular disease, functional hypothalamic amenorrhea based on clinical findings and laboratory investigations were excluded. The BMI was calculated as weight in kilogram (kg)/height in squared meter(m²). Patients were labelled as normal weight and obese with BMI < 25 and ≥ 25kg/m² respectively. According to Ferriman-Gallwey (FG) scoring system, score of ≥ 8 indicates the presence of hirsutism. Polycystic ovaries on ultrasound are diagnosed when ≥ 10 small antral follicles are seen in each ovary. Menstrual irregularity was described as presence of chronic amenorrhea, altered cycle length with less than 21 or more than 35 day and altered serum progesterone level at 21 day of 28 day cycle. Serum LH, FSH were measured on immunochemistry analyzer.

**Statistical analysis:** Statistical package for social sciences (SPSS 19) was used to analyze the data. Baseline characteristics of participants were measured as mean±SD and number (percentage). Occurrence of clinical symptoms with gonadotropins level and BMI were determined by chi-square test. Association of clinical features with gonadotropin levels and BMI was analyzed by multiple logistic regression. Odd ratio with 95% confidence interval was used to express results. P <0.05 was considered statistically significant.

**Results**

Baseline characteristics of women are shown in table 1. Out of total 86 patients of age range 19-38 years, LH/FSH ratio ≥2 was found in 31% women. Patients having LH≥10 and FSH ≥ 7 were 23% and 29% respectively. BMI ≥25 kg/m²
Table 1: Characteristics of women with PCOS (n=86)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean±SD</td>
<td>26.64±3.92</td>
</tr>
<tr>
<td>FSH (mIU/ml), mean±SD</td>
<td>5.29±2.79</td>
</tr>
<tr>
<td>LH (mIU/ml), mean±SD</td>
<td>8.15±5.41</td>
</tr>
<tr>
<td>LH/FSH ratio</td>
<td>1.68±1.04</td>
</tr>
<tr>
<td>BMI ≥25Kg/m², n (%)</td>
<td>61(71)</td>
</tr>
<tr>
<td>BMI &lt;25Kg/m², n (%)</td>
<td>25(29)</td>
</tr>
<tr>
<td>Hirsutism , n (%)</td>
<td>57(66)</td>
</tr>
<tr>
<td>Menstrual irregularity, n(%)</td>
<td>44(51)</td>
</tr>
<tr>
<td>Positive findings of Polycystic ovaries on sonography</td>
<td>66(77)</td>
</tr>
</tbody>
</table>

Table 2: Association of Clinical Features with LH, FSH levels and Body Mass Index (n-86)

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>FSH ≥7 OR (CI)</th>
<th>LH ≥ 10 OR (CI)</th>
<th>LH/FSH ratio ≥ 2 OR (CI)</th>
<th>BMI ≥ 25 OR (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Menstrual irregularity</td>
<td>0.50(0.19-1.26)</td>
<td>3.9(1.26-12.08)</td>
<td>1.07(0.43-2.68)</td>
<td>0.67 (0.26-1.70)</td>
</tr>
<tr>
<td>Hirsutism</td>
<td>1.31(0.49-3.51)</td>
<td>1.25(0.42-3.68)</td>
<td>2.59(0.86-7.84)</td>
<td>10.42(9.79-15.49)*</td>
</tr>
<tr>
<td>Polycystic ovaries on ultrasound</td>
<td>0.81(0.28-2.33)</td>
<td>3.37(0.71-16.03)</td>
<td>0.70(0.24-2.02)</td>
<td>4.0(1.41-11.38)</td>
</tr>
</tbody>
</table>

*p-value<0.05, obtained from chi square test. FSH= Follicle stimulating hormone, LH= Luteinizing hormone

Table 3: Odd Ratio of Clinical Features with LH, FSH Levels and Body Mass Index (n-86)

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>FSH ≥7 OR (CI)</th>
<th>LH ≥ 10 OR (CI)</th>
<th>LH/FSH ratio ≥ 2 OR (CI)</th>
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*p-value<0.05, obtained from multiple logistic regression. FSH= Follicle stimulating hormone, LH= Luteinizing hormone

Discussion

PCOS is one of the most common endocrine problems in females. Different diagnostic criteria’s have been used in order to evaluate this syndrome. Although obesity is not a part of any of the diagnostic criteria, but its importance regarding PCOS cannot be ignored.9,10 In our study among women diagnosed with PCOS 71% were obese. Results are similar to study conducted in Rawalpindi, Pakistan in which 65% girls were overweight.15 In our study among women having hirsutism 96% were found to be obese. In a study conducted by kiddy et al, 71% obese women with PCOS were found to have increased percentage (53%) of hirsutism as compared to non obese individuals.11 Increased percentage of obesity was present in women having positive polycystic ovarian finding on sonography in our study, but it was statistically insignificant. Odd ratio (CI) for sonographic view of polycystic ovaries in this study was 4(1.41-11.38). Results are in accordance with a study conducted by Esmaeilzadeh et al, who revealed that 69% over weight/obese women had positive polycystic morphology on ultrasound. Adjusted OR (CI) of obese women for sonographic finding of polycystic ovaries in the same study was 4.33 (1.42-13.15) in comparison with non obese patients.23

Regarding the importance of gonadotropins levels in PCOS different studies give variable results. Some studies reveal that LH/FSH ratio of > 2 is a characteristic finding of PCOS patients. Stimulation of granulosa theca cells due to the increased levels of LH was thought to be responsible for elevated androgen levels. While decreased FSH as compared to LH levels causes anovulation through decreased estrogen levels.24,25 In a study conducted by Alnakash about 2/3rd (64%) of the women with PCOS were found to have LH/FSH ratio >2.26 In 2012 another study conducted in Saudia demonstrated significantly high levels
of LH/FSH ratio in PCOS as compared to controls. According to some other studies LH/FSH ratio has no diagnostic value in PCOS. Cho et al studied this effect in PCOS and in control group. They did not find any significant difference in median ratio of LH/FSH between these two groups. Results of study conducted by Benaszewska et al reveal LH/FSH >2 in less than 50% of these two groups. Results of study conducted by PCOS and in control group. They did not find any diagnostic value in PCOS. Cho et al studied this effect in 10.

9.

2.

61

positive polycystic findings on sonography). These results manifests (menstrual irregularities, hirsutism and LH/FSH ratio > 2. We too did not find any significant association between LH, FSH, LH/FSH ratio and PCOS manifestations (menstrual irregularities, hirsutism and positive polycystic findings on sonography). These results are in accordance to the studies conducted by Esmaeilzadeh et al as they reported that adjusted odd ratio did not show any significant association of gonadotropin levels with clinical symptoms in PCOS women.

Conclusion

Results of our study show that obesity has significant association with presence of hyperandrogenism related clinical features of PCOS such as hirsutism. Thus it can be a major contributory factor for progression in clinical features of PCOS. It is vital to prevent the obesity in order to decrease the incidence and progression of PCOS.

References


