INTRODUCTION

Polycystic ovary syndrome (PCOS) is a common heterogeneous disorder of reproductive aged women with an estimated prevalence of 4-12\%\(^1\). Inappropriate gonadotropin secretion including elevated LH/FSH ratio is a typical finding among women with PCOS and also thought to play an important role in ovulatory dysfunction.\(^2\) However, when basal LH measurements were used as a diagnostic marker of PCOS, a significant number of patients failed to exhibit an elevated LH and hence, LH:FSH ratio.\(^3\)\(^,\)\(^4\) Both recent ovulation and progesterone exposure transiently reduce the LH/FSH ratio in women with PCOS.\(^5\)\(^,\)\(^6\) Furthermore, several studies have also shown that in PCOS women there is a negative influence of obesity on LH values.\(^7\)\(^,\)\(^8\)

Obese PCOS women have been observed to have decreased serum LH level as compared to lean PCOS patients. This study was, therefore, designed to evaluate the influence of adiposity in terms of anthropometric measurements on abnormal gonadotropin secretions (serum LH level and LH:FSH ratio) in women with PCOS.

METHODOLOGY

The study was carried out at IBMS, DUHS in collaboration with Gynae/infertility Clinics of two tertiary care hospitals (Civil Hospital and Lady Dufferin Hospital) in Karachi. The research proposal was approved from Ethical Review Board of Dow University of Health Sciences and all subjects were enrolled voluntarily in the study after being explained by concerned doctor and signing the consent form. One hundred and sixty three oligomenorrhic PCOS women of reproductive age (18 - 40 years) fulfilling revised Rotterdam 2003 criteria were studied during the period from October 2010 to February 2011.

PCOS women who were pregnant, or on any contraceptive pills or using oral hypoglycemic agents were excluded from the study. Amenorrhea PCOS women were also excluded from the study. A detailed history was taken on a pre-structured proforma that included current age, age at menarche, menstrual irregularities, presence of hirsuitism, acne, infertility, familial nature, blood pressure, BMI and waist-hip ratio. Blood samples for gonadotropin assay were taken randomly on day 6th to 30th of menstrual cycle, in a gel tube. Hormonal assay was performed using chemiluminescent immunoassay. Kruskul Wallis test was used to assess the influence of BMI levels on LH:FSH values.

Results: The mean weight was 66.14 ± 11.02 kg and mean BMI was 27.03 ± 4.42 kg/m\(^2\). There was no significant difference in mean LH/FSH ratio (p=.575) among BMI groups. However, there was a positive correlation between BMI and LH:FSH ratio (p=0.04, r=0.155).

Conclusion: There was high frequency of obesity (69\%) in women with PCOS. Although no significant difference was found between mean LH:FSH ratio among different BMI groups levels but significant correlation between BMI levels and LH: FSH suggested that there was positive relation between BMI and LH: FSH.

family. Complete physical examination was recorded including anthropometric measurements (body mass index [BMI] in kg/m², waist circumference in cm and waist-hip ratio).

For estimation of serum LH and FSH, blood samples (5 ml) were drawn in follicular phase of the menstrual cycle by venepuncture in random state. All these PCOS women had oligomenorrhea with average menstrual cycle of ≥ 45 days. Whole blood was collected in SST/gel clot activator tube and allowed to clot for 5 - 10 minutes.

Once the complete clot formation had taken place, the specimens were centrifuged at a rate of 3500 rotation/minutes for 5 - 7 minutes to get clear serum samples and subjected to chemiluminescent immunoassay. Serum LH and FSH were estimated using IMMULITE 1000 Analyzer from Siemens Medical Diagnostics.

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 16. At the beginning, normality test was performed on data and p-value of Kolmogorov-Smirnov test was 0.017, gave evidence that data was not normally distributed. Non-parametric Kruskal Wallis test was used to assess the influence of BMI levels on LH: FSH values. p-value < 0.05 was considered as significant. Spearman rank correlation was also used to see any correlation of LH: FSH with anthropometric measurements (BMI levels and waist to hip ratio) respectively. Correlation was considered as statistically significant with p-value < 0.05.

RESULTS

The mean age at presentation was 24.88 ± 5.35 years and the mean weight was 66.14 ± 11.02 kg. The mean BMI was 27.03 ± 4.42 kg/m² and mean waist to hip ratio was 0.89 ± 0.05. The hormonal profile of PCOS women showed mean serum LH of 9.39 ± 7.08 mlU/ml and mean serum FSH of 5.96 ± 2.84 mlU/ml with mean LH:FSH ratio 1.72 ± 1.15.

When means ± SD, LH: FSH was compared at different BMI levels (Table I), it was found that the LH:FSH on the average increased as the BMI level increased, but when BMI was at obese-II category, it decreased the mean LH:FSH. However, the effect was not statistically significant (p = 0.575).

Spearman Rank Correlation test was applied to assess any correlation between LH:FSH and anthropometric measurements and it showed a significant positive correlation of 0.155 between LH:FSH and BMI (p=0.048, Figure 1). When mean LH:FSH ratio was plotted at different BMI levels from normal to obese showed spread of values within mean ± 3 SD (Figure 2).

DISCUSSION

In the present study, the authors tried to explore the issue of inappropriate gonadotropin secretion and its heterogeneity among PCOS patients.

Serum LH level is an important parameter in PCOS; but is not included in Rotterdam 2003 criteria,9 as its level varies with days of menstrual cycle. Routinely, the measurement of serum LH and LH/FSH ratio are being done in early follicular phase of menstrual cycle i.e. day 1 - 3,10 when it is normally suppressed and therefore, prevalence of elevated LH/FSH ratio is underestimated and hence produce limited role in diagnosis of PCOS. In the present study, blood samples for gonadotropin were taken on specific days of menstrual cycle (from day 6th to day 30th) in oligomenorrhea PCOS and the study results showed a high frequency (71%) of elevated LH/FSH ratio > 1 among Pakistani population of PCOS. This high frequency of elevated LH/FSH ratio is quite significant as it points towards its potential role in diagnosis of PCOS. These results are

Table I: Comparison of LH:FSH in different BMI categories.

<table>
<thead>
<tr>
<th>BMI</th>
<th>N</th>
<th>Median</th>
<th>Mean rank</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (&lt;18.5)</td>
<td>18</td>
<td>0.94</td>
<td>67.72</td>
<td>0.575</td>
</tr>
<tr>
<td>Overweight (18.5-22.9)</td>
<td>33</td>
<td>1.42</td>
<td>82.39</td>
<td></td>
</tr>
<tr>
<td>Obese class I (23-24.9)</td>
<td>90</td>
<td>1.36</td>
<td>83.49</td>
<td></td>
</tr>
<tr>
<td>Obese class II (25-29.9)</td>
<td>22</td>
<td>1.59</td>
<td>87.0</td>
<td></td>
</tr>
</tbody>
</table>

*Using Kruskal Wallis test.
consistent with findings of Hsu et al. and Hendrick et al. which showed high prevalence of elevated LH/FSH ratio among PCOS women and recommended that gonadotropin assay should be done after 5th day of menstrual cycle.11,12

Obesity is a common clinical feature observed in approximately 50% of PCOS women.13

Recent studies have shown that surprisingly serum LH level tends to be normal, rather elevated in obese PCOS women. Lean PCOS women have the higher LH pulse amplitude in comparison with overweight PCOS women.14 The present study was an attempt to ascertain the influence of adiposity / anthropometric measurement on abnormal gonadotropin secretion in PCOS women among local population.

BMI, waist-hip ratio and waist circumference are the important parameters for assessing the level of obesity. It has been well established that Asian population has a higher fat deposition at a lower BMI as compared to Caucasians. WHO in collaboration with the International Association for study of obesity and the international obesity task force has, therefore, proposed a new BMI classification for Asian population.15 In the present study, the new BMI criteria for Asian population has been taken as a reference for assessing level of obesity. The study result shows a high frequency of obesity in our PCOS population (69%). This is consistent with study done by Alnakash et al. which also showed a frequency of 63.55% of obesity.16 This higher incidence of obesity may be attributed to rapidly increasing trends of sedentary life style among young Pakistani women.

As stated earlier; the new Asian BMI classification was used to divide the study population into 4 groups according to their BMI. No statistically significant (p = 0.575) difference was observed in the mean LH/FSH ratio among different BMI groups.

These results are in accordance with the findings of Iwasa et al. which showed decreased LH/FSH ratio with increase in BMI but this relationship was not statistically significant (p = 0.33).6 These results are also consistent with study conducted by Fulghesu et al. which also showed no significant relationship between LH/FSH ratio and BMI.17

It is well documented that PCOS women have a high prevalence of abdominal body fat distribution, even if they are normal-weight, making them more vulnerable to obesity related health problems like diabetes, hypertension and cardiovascular disorders.18

In the present study, the mean waist to hip ratio was 0.89 ± 0.05. This result is consistent with study done by Avrbikov et al. which also showed higher waist to hip ratio values in PCOS women, even among lean group, suggesting preferential abdominal fat deposition in these patients.19 Nowadays, waist circumference is considered to be more sensitive indicator for obesity. The present data did not show any significant relationship between the waist circumference and LH/FSH ratio, but it was found significant with BMI levels. One possibility is the relatively small sample size, (especially of fewer cases in obese-II category) as this difference might be significant if we had evaluated a large number of PCOS subjects. Racial differences in presentation of PCOS might be another possibility.

The frequency of different clinical features of PCOS was evaluated in local population. Majority (70 - 80%) of PCOS women have some form of menstrual irregularities including oligomenorrhea, amenorrhea and dysfunctional uterine bleeding. These are all the consequence of anovulation.20 In the present study, menstrual abnormalities were noted in almost all patients (99.4%). These results are comparable with the finding of Riaz et al. who also showed menstrual cycle disturbances among 98% of PCOS women.21

Hirsutism is considered the best clinical marker of hyperandrogenic; however, the severity of hirsutism varies with ethnicity. In the present study, hirsutism was observed in 71.9% patients. This finding is in accordance with the finding of Aziz et al. which also showed prevalence of hirsutism among PCOS women between 60 - 80%.22

Acne is a more variable marker of hyperandrogenism. In the present study, acne was observed in 88.8% of PCOS women. This finding is much higher than reported in literature which showed frequency of acne in only a third of PCOS women.23 However, this high frequency of acne among PCOS women was also observed in the study conducted by Zaidi et al. about 60%.24 Therefore, they recommended that PCOS should be ruled out in women of reproductive age who presented with acne along with menstrual abnormalities.

CONCLUSION

The present study concludes that although no significant difference is observed in mean LH:FSH among different BMI groups but significant correlation does exit between BMI levels and LH:FSH ratio, suggesting that there is a relation between BMI and LH:FSH.

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REFERENCES


