Early Clinical, Biochemical and Radiological Features in Obese and Non-Obese Young Women with Polycystic Ovarian Syndrome: A Comparative Study

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ABSTRACT
Polycystic ovarian syndrome (PCOS) is a heterogenous condition accounting for serious health complications. The present study was conducted to assess the early clinical, biochemical, and radiological features in obese, non-obese young women with PCOS as compared to non-PCOS women. The study was conducted on 120 young women (18–22 years) with 80 having features of PCOS [40 obese (BMI ≥ 25 kg/m²) and 40 non-obese (BMI < 25 kg/m²)] PCOS as cases and 40 without PCOS as controls in a rural tertiary care center of Northern India over one year (2017–2018). After enrolment of cases and control, the anthropometric measurements, early clinical symptoms, and biochemical and ultrasonographic features were compared between the groups. Statistical analysis was done using SPSS software version 22.0 (p-value <0.05). A significant difference in anthropometric measurements were observed between obese and non-obese PCOS cases. Clinical features like acne, acanthosis nigricans, and hirsutism were more prevalent in obese PCOS as compared to non-obese and controls. On ultrasound, PCOS cases had a significantly increased number of peripherally arranged ovarian follicles, and ovarian volume. The LH: FSH ratio was significantly higher in cases as compared to controls. The levels of serum LH (10.04 ± 1.60 vs. 8.93 ± 2.40 mIU/ml) and total testosterone (2.71 ± 0.39 vs. 2.21 ± 0.39 pg/ml) were higher in obese PCOS as compared to non-obese PCOS cases. In conclusion, clinical, biochemical, and radiological features can be used in the early diagnosis of PCOS. Obesity is an independent risk factor for PCOS and is associated with an increased risk of complications.

Introduction
Polycystic ovarian syndrome (PCOS) is a heterogenous endocrinological disorder and one of the leading causes of infertility worldwide [1]. It is also associated with many serious long-term complications including metabolic disorders such as type 2 diabetes mellitus, hypertension, cardiovascular, cerebrovascular disorders, and endometrial carcinoma, if left untreated [2, 3]. The prevalence of PCOS in women all over the world shows wide variation due to the different diagnostic criteria used, that is, according to National Health Institute (NIH), 1990 it is 3.39 %, Rotterdam’s, 2003, 11.04 %, and Androgen excess society (AES), 2006 it is 8.03 % [4]. Despite its common prevalence in today’s era the exact pathophysiology of PCOS remains unclear due to complicated interwoven factors playing role in its development including genetic and epigenetic factors, ovarian abnormalities, neuroendocrine modifications, hyperinsulinemia, insulin resistance, endocrine and metabolic changes, adiposity, adrenal factors, etc. [5].

The classical clinical presentation of PCOS includes features of hyperandrogenism, chronic anovulation/oligomenorrhea, and ultrasonographic morphology of the ovary [6]. It was observed that the main pathology lies with ovarian steroidogenesis leading to increased androgen production and ovarian dysfunction [7]. Of many
criteria used for the diagnosis of PCOS, Rotterdam and AES criteria are most commonly used. According to the Rotterdam criteria, the women should fulfill two of the following: oligo-ovulation or anovulation, clinical or biochemical signs of hyperandrogenism, and/or polycystic ovarian morphology [8], whereas the AES has further broadened the criteria as a woman having clinical or biochemical hyperandrogenism, ovarian dysfunction (oligo-anovulation and/or polycystic ovaries), and exclusion of other androgen excess or related disorders [9]. Changing lifestyles, better diagnostic facilities, and increasing awareness, have led to a rise in cases of PCOS all over the world. Furthermore, early diagnosis and management of this chronic condition can help in preventing the various long-term complications associated with it. Hence, the present study was conducted to assess the early clinical, biochemical, and radiological features in obese, non-obese young women with PCOS as compared to non-PCOS women.

Subjects and Methods

Study design
This is a prospective comparative study involving healthy young women and women with suspected PCOS. Diagnosis of PCOS was made if the woman presents with two of three features of Rotterdam criteria [8]. Hirsutism was considered with a score of ≥ 8 by Ferriman-Gallwey scoring system [10]. For the Asian and South Asian populations, obesity is defined as BMI ≥ 25 kg/m² [11].

Study setting
The present study was conducted in the Department of Obstetrics and Gynaecology of a rural tertiary care center of Northern India over one year (January 2017 to January 2018).

Participants

Inclusion criteria
All young women between 18–22 years of age with or without features of oligo/amenorrhea, clinical signs of hyperandrogenism, and/or polycystic ovarian morphology on ultrasound were enrolled as study participants. A total of 80 participants fulfilling Rotterdam’s criteria for PCOS were included as cases. Based on the BMI, they were further divided into two groups: Group I as obese PCOS (BMI ≥ 25 kg/m²) and Group II as non-obese PCOS (BMI < 25 kg/m²) with 40 participants in each case group. There were 40 control participants (both obese and non-obese) not fulfilling Rotterdam’s criteria for PCOS.

Exclusion criteria
Women < 18 or > 22 years, those on oral contraceptive pills or any other drug that can affect gonadal function, adrenal or ovarian tumors, congenital adrenal hyperplasia, Cushing syndrome, acromegaly, hypergonadotropic hypogonadism, endocrine abnormalities like hyperprolactinemia, thyroid disorders, androgen-secreting tumors, women with Mullerian anomalies, Asherman’s syndrome, Turner’s syndrome, addicted to alcohol/smoking/drugs and those refusing to participate were excluded from the study.

Sampling procedure
Consecutive sampling of participants fulfilling the inclusion criteria was done for the entire duration of the study.

Data sources/measurements
After informed written consent from all the participants in their vernacular language various sociodemographic parameters like age, religion, education, and socio-economic status were recorded, followed by the anthropometric measurement and clinical examination including weight, height, BMI, waist and hip circumference, menstrual cycle details, acne, acanthosis nigricans (as identified by the presence of dark, velvety discoloration of skin folds and creases around armpits, neck or groin) and hirsutism were all recorded on a preformed data collection sheet by trained nursing staff. A detailed medical, surgical, and family history of all the participants was recorded, followed by a thorough physical examination and investigations of the participants.

Anthropometric measurements
The height was measured in an upright position using a stadiometer, closest to 0.5 cm. The participants were asked to remove their hair ornaments, ponytails, buns, braids, shoes and were made to stand on the floor with the heels of both feet together and the toes pointed slightly outward. Then they were asked to take a deep breath and stand as tall as possible with their eyes looking straight ahead and to hold this position for a while till the horizontal headboard is brought down firmly on top of the head. The reading in cm was recorded at the level where the headboard is aligned with the vertical scale.

The weight of the participants was measured in light clothing without shoes using a digital weighing machine in kilograms to the nearest 0.1 kg. BMI (kg/m²) was calculated by using the formula: weight in kg/height in meters².

Waist circumference (WC) was measured in the horizontal plane between the lower margin of the last rib to the iliac crest using an inch tape to the nearest 0.1 cm. Hip circumference (HC) was taken at the widest portion of the buttocks by wrapping the inch tape around it. This was followed by the calculation of waist to hip ratio (WHR) by dividing the two parameters (WC/HC).

Scoring of hirsutism
Hirsutism was assessed at a total of nine points: upper lip, chin, chest, upper and lower back, upper and lower abdomen, thigh, and upper arm using a modified Ferriman–Gallwey score. The minimum score was zero and the maximum 36 according to this scale. The scoring was done as 8 = no hirsutism; 8–16 = mild hirsutism; 17–30 = moderate hirsutism; ≥ 25 = severe hirsutism [12]. All the participants who had a score of ≥ 8 were considered clinically hirsute.

Following anthropometric measurements and clinical examination, baseline endocrinal investigations, and transabdominal pelvic ultrasonography for ovarian volume, the number, and arrangement of ovarian follicles were performed in the early follicular phase (day 2 or 3) of the spontaneous or induced menstrual cycle.

Biochemical test
The hormonal tests were performed after overnight fasting, with around 8–10 ml of blood drawn in a plain vial using a heparinized
syringe. The following biochemical and hormonal assays were done: Serum Thyroid-stimulating hormone (TSH), Prolactin, Follicle-stimulating hormone (FSH), Luteinizing hormone (LH), Total Testosterone, fasting, and postprandial sugar levels. The blood collected in test tubes was centrifuged to separate the serum, which was then stored at −20°C for hormonal assays. All the hormonal tests were carried out in duplicate in the same assay by Radioimmunoassay (RIA) in the laboratory of the Biochemistry department of the institute. Serum FSH, LH, and total Testosterone were determined by the sandwich ELISA technique.

Statistical analysis
Statistical analysis of data was performed using Statistical Package for Social Sciences (SPSS) software version 22.0. Comparison of the groups or continuous measures was done using a Student’s t-test and F-test was used to calculate the equity of two sample variations. Comparison between groups or nominal measures was done using Fisher’s exact test. Results were reported as mean ± SD wherever required. A p-value < 0.05 was considered statistically significant.

Ethical issues
The present research involving human subjects was conducted following the ethical standards of all applicable national and institutional committees and the World Medical Association’s Helsinki Declaration. It was conducted after informed written consent from the participants and ethical approval from the Institutional Ethical Committee (IEC number: 2016/841).

Results
The mean age and age of onset of menarche in obese PCOS was 20.43 ± 1.53 years and 13.05 ± 1.84 years, in non-obese PCOS 20.25 ± 1.45 years and 13.18 ± 0.93 years, and in controls 20.58 ± 1.47 years and 13.43 ± 0.90 years respectively. The mean height, weight, BMI, WHR in obese PCOS, non-obese PCOS, and controls were 20.25 ± 1.45 years and 13.18 ± 0.93 years, and 20.58 ± 1.47 years and 13.43 ± 0.90 years respectively. The mean height, weight, BMI, WHR in obese PCOS, non-obese PCOS, and controls were 1.52 ± 0.07 m, 65.88 ± 8.88 kg, 28.36 ± 2.47 kg/m², and 0.95 ± 0.08 m, 65.88 ± 8.88 kg, 28.36 ± 2.47 kg/m², and 0.91 ± 0.09 m, 61.45 ± 9.56 kg, 26.25 ± 3.63 kg/m² and 0.89 ± 0.09, respectively. A significant difference was observed between the anthropometric measurements of obese and non-obese PCOS cases (p < 0.05). The comparison of clinical features including acne, acanthosis nigricans, and hirsutism between obese, non-obese PCOS and controls is depicted in Table 1. Clinical features including acne, acanthosis nigricans, and hirsutism were more in obese PCOS cases as compared to non-obese PCOS and controls. On ultrasonography the mean ovarian volume and the number of follicles < 9 mm were significantly higher in both obese and non-obese PCOS cases as compared to controls. Furthermore, the peripheral arrangement of these follicles in the ovary on ultrasound was more commonly associated with cases as compared to controls (p = 0.000). The comparison of ultrasound findings in cases and controls is depicted in Table 2. Of all the biochemical tests performed a significant difference was observed in serum LH, FSH, and total Testosterone between cases and controls, with obese PCOS cases having significantly higher LH (10.04 ± 1.60 vs. 8.93 ± 2.40 mIU/ml) and total testosterone levels (2.71 ± 0.39 vs. 2.21 ± 0.39 pg/ml) as compared to non-obese PCOS cases. Furthermore, the LH: FSH ratio of 3:1 was significantly associated with cases as compared to controls. The comparison of biochemical parameters between cases and controls is depicted in Table 3.

Discussion
PCOS is one of the most common endocrinological diseases of multifactorial origin affecting women of all age groups. There is a strong correlation between obesity and PCOS [13, 14], though it can occur in non-obese women also. In the present study, the early clinical, biochemical, and radiological features in obese and non-obese PCOS cases were compared with the non-PCOS young women.

No significant difference in age at presentation and age of menarche was observed in our study between the cases and controls. This was similar to the results of a study that also reported insignificant differences between cases and controls regarding age at presentation and age of menarche [15]. Menstrual irregularity was the
most common presenting complaint in obese and non-obese PCOS cases as it was considered one of the criteria for diagnosis of PCOS. Similar results were reported by other studies also [16, 17]. In the present study, a significant difference was observed between the anthropometric measurements of obese and non-obese PCOS cases [height: 1.52 ± 0.07 m vs. 1.59 ± 0.07 m (p = 0.000); weight: 65.88 ± 8.88 kg vs. 57.23 ± 7.83 kg (p = 0.000); BMI: 28.36 ± 2.47 kg/m² vs. 22.58 ± 2.10 kg/m² (p = 0.000); WHR: 0.95 ± 0.08 vs. 0.91 ± 0.09 (p = 0.018)]. Furthermore, the mean BMI and WHR were significantly higher in cases as compared to controls. This was similar to a study that observed, women with PCOS had significantly higher central fat mass (waist, waist-hip ratio, and upper/lower fat ratio) and BMI as compared to controls [18]. Another study reported that lean PCOS cases despite low BMI have abdominal obesity [19].

In the present study, obese PCOS cases were significantly associated with acne, acanthosis nigricans, and hirsutism as compared to non-obese PCOS and controls. A recent study reported that PCOS women and higher BMI had increased hair growth as assessed by modified Ferriman–Gallwey scores that were found to be 2.96-fold higher as compared to healthy-normal BMI counterparts [20]. Another study compared hirsutism in normal weight and overweight PCOS cases as compared to non-obese PCOS cases. Furthermore, the LH:FSH ratio of 3:1 was significantly associated with cases as compared to controls. Similar results of significantly higher LH and LH:FSH ratio in obese PCOS as compared to non-obese PCOS cases were reported by a recent study [29]. Another study reported that obese PCOS cases had significantly higher levels of basal total testosterone and androstenedione levels in obese PCOS as compared to nonobese PCOS cases were reported by another study [23]. Other recent studies have observed no significant difference between obese and non-obese PCOS groups in terms of the LH/FSH ratio. Furthermore, they observed no significant correlation between BMI and LH/FSH ratio [23, 31]. Contrary to our results a study reported significantly higher serum levels of LH in lean PCOS women as compared to obese or overweight PCOS women [32].

### Conclusion

PCOS is a heterogeneous disorder of multifactorial origin with symptoms, ultrasonographic features, and biochemical parameters being more severely deranged in obese cases as compared to nonobese cases and controls. The cutaneous manifestation including acne, hirsutism, acanthosis nigricans, alopecia, and seborrhea is more commonly associated with increased BMI, and insulin resistance is more common in obese PCOS cases as it was considered one of the criteria for diagnosis of PCOS. Similar results were reported by other studies also [16, 17].

### Table 3

Comparison of biochemical parameters of cases (obese and nonobese PCOS) and controls.

<table>
<thead>
<tr>
<th>Biochemical parameters (mean ± SD)</th>
<th>Obese PCOS</th>
<th>Nonobese PCOS</th>
<th>Non-PCOS controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH (uIU/ml)</td>
<td>3.14 ± 0.84</td>
<td>3.20 ± 0.85</td>
<td>3.10 ± 0.91</td>
</tr>
<tr>
<td>Fasting blood sugar (mg/dl)</td>
<td>71.20 ± 6.98</td>
<td>69.35 ± 6.32</td>
<td>72.65 ± 6.78</td>
</tr>
<tr>
<td>Postprandial blood sugar (mg/dl)</td>
<td>135.33 ± 10.56</td>
<td>136.55 ±9.33</td>
<td>134.93 ±10.13</td>
</tr>
<tr>
<td>Serum prolactin (ng/ml)</td>
<td>10.02 ± 6.11</td>
<td>9.54 ± 5.95</td>
<td>11.03 ± 6.22</td>
</tr>
<tr>
<td>Serum FSH (IU/l)</td>
<td>3.71 ± 0.95</td>
<td>3.52 ± 0.99</td>
<td>5.16 ± 1.56</td>
</tr>
<tr>
<td>Serum LH (IU/l)</td>
<td>10.04 ± 1.60</td>
<td>8.93 ± 2.40</td>
<td>7.51 ± 2.85</td>
</tr>
<tr>
<td>Serum total testosterone (mmol/l)</td>
<td>2.71 ± 0.39</td>
<td>2.21 ± 0.39</td>
<td>1.79 ± 0.93</td>
</tr>
<tr>
<td>LH:FSH ratio [n (%)]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1:1</td>
<td>0 (0 %)</td>
<td>4 (10.0 %)</td>
<td>23 (57.5 %)</td>
</tr>
<tr>
<td>2:1</td>
<td>9 (22.5 %)</td>
<td>11 (27.5 %)</td>
<td>10 (25.0 %)</td>
</tr>
<tr>
<td>3:1</td>
<td>31 (77.5 %)</td>
<td>25 (62.5 %)</td>
<td>7 (17.5 %)</td>
</tr>
</tbody>
</table>

Kumar N, Agarwal H. Early Clinical, ... Horm Metab Res 2022; 54: 620–624 | © 2022. Thieme. All rights reserved.
sistance. Obese cases also have higher serum total testosterone, LH levels, and LH:FSH ratio of ≥ 3:1. Therefore, obese with PCOS are at a higher risk of having long-term complications and hence need early and vigorous management.

Conflict of Interest

The authors declare that they have no conflict of interest.

References