Journal Of Medical Science And Clinical Research
IGM Publication   An Official Publication Of IGM Publication

Original Research Article

Polycystic ovarian syndrome: Clinical correlation with biochemical status among Indian females

Authors
Dr Dipankar Bhattacharyya[1], Dr Paramita Pal[2*], Dr Sukanta Sen[3]
[1]Professor, Department of Physiology, ICARE Institute of Medical Sciences & Research, Banbishnupur, P.O. Balughata, Haldia, Dist-Purba Medinipur, West Bengal 721645
[2]Assistant Professor, Department of Pharmacology, Jagannath Gupta Institute of Medical Sciences And Hospital, KP Mondal Road, Buita, Nishchintapur, Budge Budge, Kolkata, West Bengal 700137
[3]Professor, Department of Pharmacology, ICARE Institute of Medical Sciences & Research, Banbishnupur, P.O. Balughata, Haldia, Dist-Purba Medinipur, West Bengal 721645
*Corresponding Author
Dr Paramita Pal
Email: *paulparamita14@yahoo.com*, Contact No.:8240037958

Abstract

Background: *Polycystic ovary syndrome is a common and heterogeneous endocrine disorder characterized by hirsutism, amenorrhea, infertility, and obesity. Our primary aim to conduct this study was to find out the correlation between various biochemical and clinical features of polycystic ovarian syndrome and to determine the best hormonal marker for the same among Indian women at an early age.*

Materials & Methods: *The study was done on outdoor patients over seventy women with PCOS diagnosed by history and hormonal levels (LH: FSH ratio>2, total testosterone>0.76 ng/mL) and ultrasonogrpahy (USG) (cortical cysts each 5 mm in diameter, >5 in number in a single ovary) were compared with 10 normal women who served as control at a tertiary care teaching hospital, Kolkata. Obesity was measured by body mass index (BMI) (>25 kg/m^2 taken as overweight). Waist: hip ratio (WHR) was used as a marker of abdominal obesity (measured at ASIS). Ferriman-Gallway (FG) scoring was done and a score of > 8 was taken as significant hirsutism.*

Results: *Hormonal status and BMI in PCOS individuals, who were overweight (BMI > 25 kg/m^2). They had a mean BMI 28.98 kg/m^2, mean basal insulin (BI) 33.49 μ IU/ ml, mean LH: FSH ratio 2.01, mean testosterone level 1.38 ng/ml. Mean body mass index (BMI) was 21.6 kg/m^2 in normal women, 27.44 kg/m^2 in overweight subjects(n=44) and 31.86 kg/m^2 in obese subjects (n=21). When FG score>8 was considered, it was found that overweight subjects were 35.4% and obese 40%. Increased value of basal insulin was found in 14 subjects (40%). Family history of hirsutism was positive in 7 subjects (22.5%). In this group, mean BMI 29.24 kg/m^2, mean basal insulin 32.94 m-IU/ml, mean LH/FSH Ratio 1.96 and mean testosterone 1.96 ng/ml.*

Conclusion: *Most of the PCOS patients of this city are overweight rather than obese. In PCOS there was increased LH and there by increased LH-FSH ratio, which is usually used as a single hormonal estimation for diagnosis. In accordance to previous studies it may be suggestable that the free or total testosterone level can be a singular and vital hormonal marker for diagnosis. Both LH-FSH ratio and testosterone can be taken for accuracy of diagnosis.*

Keywords: *Polycystic ovarian syndrome, clinical, biochemical, ultrasonography, acanthosis nigricans, hirsutism.*

Introduction

Polycystic ovary syndrome is a common and heterogeneous endocrine disorder characterized by hirsutism, amenorrhea, infertility, and obesity. Women with polycystic ovarian syndrome (PCOS) have abnormalities in the metabolism of androgens and estrogen and in the control of androgen production. PCOS can result from abnormal function of the hypothalamic-pituitary-ovarian (HPO) axis.[1] PCOS was defined as the presence of any two of the three features: (1) Oligo/amenorrhea: absence of menstruation for 45 days or more and/or ≤8 menses per year. (2) Clinical hyperandrogenism: Modified Ferriman and Gallway (mFG) score of 6 or higher. (3) Polycystic ovaries: presence of >10 cysts, 2-8 mm in diameter, usually combined with increased ovarian volume of >10 cm, and an echo-dense stroma in pelvic ultrasound scan. PCOS is a common female endocrine disorder with prevalence ranging from 2.2% to 26%. Most reports have studied adult women with age ranged from 18 to 45 years. [2-5]

The major features of PCOS include menstrual dysfunction, anovulation, and signs of hyperandrogenism. Other signs and symptoms of PCOS may include the following: hirsutism, infertility, obesity and metabolic syndrome, diabetes, and obstructive sleep apnea.[6] PCOS is associated with various endocrine abnormalities such as increased serum LH levels, increased ratio of LH:FSH, increased serum testosterone. Estimation of these hormones aids in the diagnosis. In PCOS ovary is enlarged >9 ml in volume, is smooth, sclerotic, has thickened capsular & subcapsular follicular cysts with atresia and hyperplastic theca and stroma.[7] Our primary aim to conduct this study was to find out the correlation between various biochemical and clinical features of polycystic ovarian syndrome and to determine the best hormonal marker for the same among Indian women at an early age.

Materials & Methods

The study was done on outdoor patients over seventy women with PCOS diagnosed by history and hormonal levels (LH: FSH ratio>2, total testosterone>0.76ng/mL) and ultrasonogrpahy (USG) (cortical cysts each 5 mm in diameter, >5 in number in a single ovary) were compared with 10 normal women who served as control at a tertiary care teaching hospital, Kolkata. Detailed history of menstruation and hyperandrogenic problems was recorded and clinical examination done. A detailed history of presenting complaints, age of presentation, past illness and demographic information were noted. Obesity was measured by body mass index (BMI) (>25 kg/m^2 taken as overweight). Waist: hip ratio (WHR) was used as a marker of abdominal obesity (measured at ASIS). Ferriman-Gallway (FG) scoring was done and a score of > 8 was taken as significant hirsutism.[8]

Acanthosis nigricans was observed on the nape of the neck which is standard and accessible site for examination. Ovarian ultrasonography, preferably accomplished by using a transvaginal approach, can be performed to assess ovarian morphology was done with 3.5 MHz trans-abdominal probe. The diagnostic characteristics are bilateral enlarged ovaries, multiple small follicles and increased stromal ecogenecity.[9]

LH was measured by ELISA (Herrickson Diagnostics, Texas, USA), and FSH by ELISA (Genzyme Diagnostic Medix, Biotech, CA, USA). Total testosterone (TT) was measured by chemiluminiscence (CLIA) kit supplied by Ciba Corning Diagnostic Corporation. Statistical analysis was done with Student's t test using Microsoft Excel.
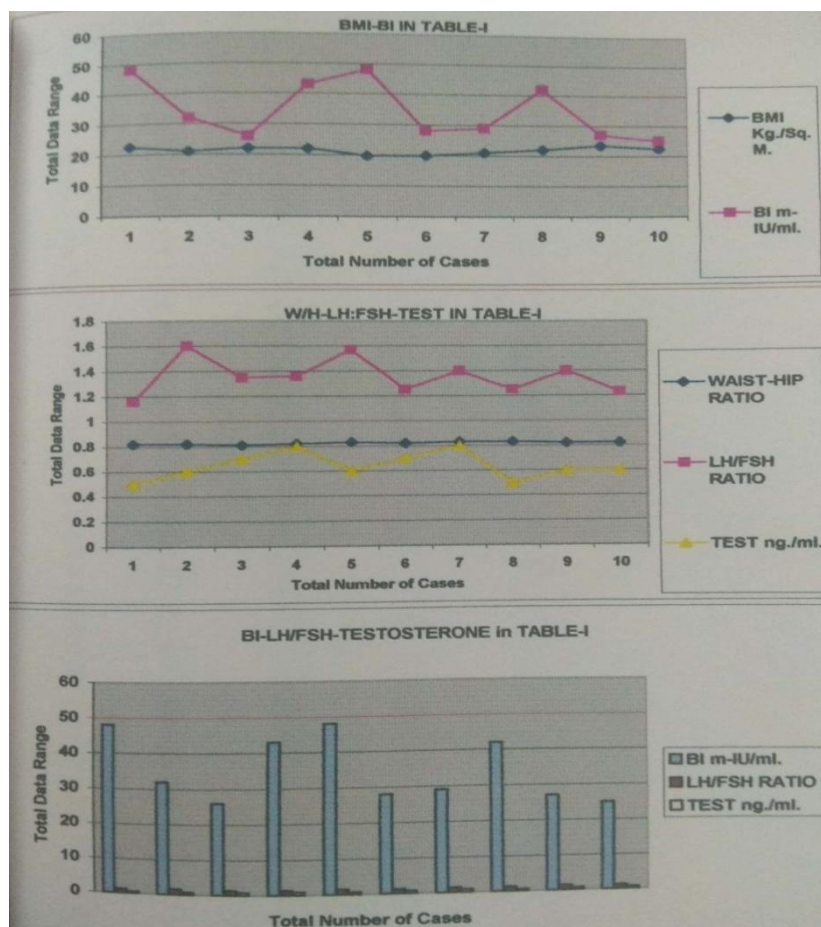
Results

Table 1: Demographic characteristics, clinical and biochemical parameters in normal female individuals (n=10)

Characteristics	Age (Yrs)	Height (CMs)	Weight (Kg)	BMI (Kg/m^2)	Waist-Hip ratio	BI (Basal insulin) m-IU/ml	LH m-IU/ml	FSH m-IU/ml	LH/FSH Ratio	Testo. ng/ml
Means ± SD	21.9± 3.07	158.5± 6.52	53.9± 2.13	21.63± 1.16	0.82± 0.06	34.8± 9.37	5.04± 0.6	3.78± 0.37	1.34± 0.15	0.64± 0.1

Table 1/Fig. 1 shows that the controls (n=10) had a mean age of 21.9 years, mean height 158.5 cm, mean weight 53.9 kg, mean BMI 21.63 kg/m^2, mean WHR 0.82, mean basal insulin (BI)/34.8μIU/mL, mean LH 5.04mIU/mL, mean FSH 3.78mIU/mL, mean LH:FSH ratio 1.34 and mean testosterone 0.54 ng/ml.

Figure 1: Demographic characteristics, clinical and biochemical parameters in normal female individuals (n=10)

Table 2: Clinical and biochemical parameters in overweight individuals (BMI > 25 kg/m^2) with PCOS (n=49)

Characteristics	BMI > 25 kg/m^2	Basal Insulin (m-IU/ml)	LH/FSH Ratio	Testo. (ng/ml)
Means ± SD	28.98±3.11	33.49±13.32	2.01±1.46	1.38±1.34

Table 2/Fig. 2 shows hormonal status and BMI in PCOS individuals, who were overweight (BMI > 25 kg/m^2). They had a mean BMI 28.98 kg/m^2, mean basal insulin (BI) 33.49 μ IU/ ml, mean LH: FSH ratio 2.01, mean testosterone level 1.38 ng/ml.

Table 3: Clinical and biochemical parameters in obese individuals (BMI ≥ kg/m^2) with PCOS (n=21)

Characteristics	BMI ≥ 30 kg/m^2	Basal Insulin (m-IU/ml)	LH/FSH Ratio	Testo. (ng/ml)
Means ± SD	31.86±2.51	34.63±13.67	1.56±1.18	1.25±1.04

Mean body mass index (BMI) was 21.6 kg/m^2 in normal women, 27.44 kg/m^2 in overweight subjects (n=44) and 31.86 kg/m^2 in obese subjects (n=21) [Table 3/Fig.3a,3b].

Table 4: Clinical and biochemical parameters in overweight individuals (BMI 25-30 kg/m^2) with PCOS (n=23)

Characteristics	BMI ≥ 30 kg/m^2	Basal Insulin (m-IU/ml)	LH/FSH Ratio	Testo. (ng/ml)
Means ± SD	26.86±1.04	32.64±13.24	2.35±1.57	1.47±1.53

In this group, mean BMI 26.86 kg/m^2, mean basal insulin 32.64 m-IU/ml, mean LH-FSH ratio 2.35 and mean testosterone 1.47 ng/ml [Table 4].

Table 5: Hormonal status and BMI in hirsute individuals (F-G score>8) with PCOS (n=31) and presence of family history of hirsutism

Characteristics	BMI ≥ 30 kg/m^2	Basal Insulin (m-IU/ml)	LH/FSH Ratio	Testo. (ng/ml)	Family hist. of Hirsutism
Means ± SD	29.24±4.78	32.94±14.11	1.96±1.08	1.96±1.51	Post. 7 (22.58%) Neg. 24 (77.42%)

When FG score>8 was considered, it was found that overweight subjects were 35.4% and obese 40%. Increased value of basal insulin was found in 14 subjects (40%). Family history of hirsutism was positive in 7 subjects (22.5%). In this group, mean BMI 29.24 kg/m^2, mean basal insulin 32.94 m-IU/ml, mean LH/FSH Ratio 1.96 and mean testosterone 1.96 ng/ml (Table 5/Fig. 5).

Table 6: Hormonal status and BMI in insignificant or no hirsute individuals (F-G score<8) with PCOS (n=39) and presence of family history of hirsutism

Characteristics	BMI ≥ 30 kg/m^2	Basal Insulin (m-IU/ml)	LH/FSH Ratio	Testo. (ng/ml)	Family hist. of Hirsutism
Means ± SD	26.24±2.83	29.02±14.25	2.11±1.5	1.28±1.34	Pos. 6 (15.38%) Neg. 33 (84.62%)

When FG score<8 (insignificant hirsutism) was considered along absence of hirsutism in the study subjects, it was found that overweight subjects are 66.66%. Family history was positive in 6 subjects (15.38%). In this group, mean BMI 26.24 kg/m^2, mean basal insulin 29.02 m-IU/ml, mean LH/FSH Ratio 2.11 and mean testosterone 1.28 ng/ml (Table 6).

Table 7: Hormonal status and BMI in sonographically determined PCOS individuals (n=45)

USG +Ve findings	BMI (kg/m^2)	Testo. (ng/ml)	LH/FSH Ratio	Basal Insulin (m-IU/ml)
Both sides 32 (71.11%) Right side 3 (6.67%) Left side 10 (22.22%)	26.9±3.37	1.34±1.31	2.09±1.44	31.64±14.16

On USG, bilateral affect was found in 71.11%, only right side 3 (6.67%) and only left side 10 (22.22%) [Table 7]. In this group, mean BMI 26.9 kg/m^2, mean basal insulin 31.64 m-IU/ml, mean LH/FSH Ratio 2.09 and mean testosterone 1.34 ng/ml. From this table it was evident that within the USG determined subjects, positive predictive value of high total testosterone was 64.44% in comparison to the same of LH-FSH ratio 55.55%.

Table 8: Relationship of basal insulin with acanthosis nigricans in PCOS individuals (n=40)

Basal Insulin (m-IU/ml)	Acanthosis Nigricans (observed over neck)
38.94±12.39	Pos. 36 (90%), Neg. 04 (10%)

Acanthosis nigricans was found in 36 subjects (90%), out of which increased basal insulin was found in 24 subjects (66.66%) [Table 8]. In this group, mean basal insulin was 38.94 m-IU/ml.

Table 9: Relation of increased LH-FSH ratio (≥2) with USG in PCOS individuals (n=37)

LH:FSH	USG findings
2.81±0.74	Normal 11 (29.73%)
	Left + Right 19 (51.35%)
	Right 01 (2.7%)
	Left 6 (16.22%)

When USG criteria was taken for diagnosis, it was seen that for increased LH:FSH (ratio ≥2), both right as well as left sided cysts had been found in total 37 cases. In this group, mean LH:FSH ratio was 2.81 [Table 9].

Table 10: Relation of high testosterone (>0.76 ng/ml) and other hormones and USG findings in PCOS individuals (n=42)

| Testosterone (ng/ml)	LH:FSH	Basal Insulin (m-IU/ml)	USG findings
1.91±2.1	2.5±1.4	30.18±13.43	Right 2 (4.76%)
			Left 7 (16.67%)
			Right +Left 20 (47.62%)
			Normal 13 (30.95%)

Table 10 shows relationship between high testosterone ((>0.76 ng/ml) with other hormones and USG findings in PCOS individuals (total 42 subjects). In this group, mean basal insulin was 30.18 m-IU/ml, mean LH:FSH ratio was 2.5 and mean testosterone was 1.91.
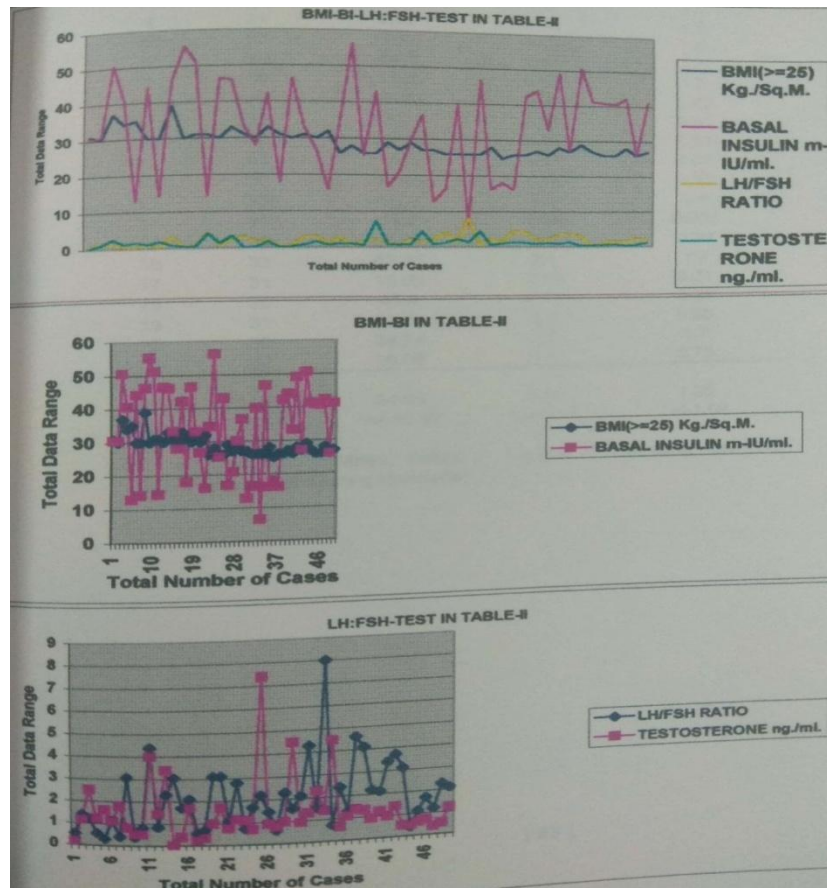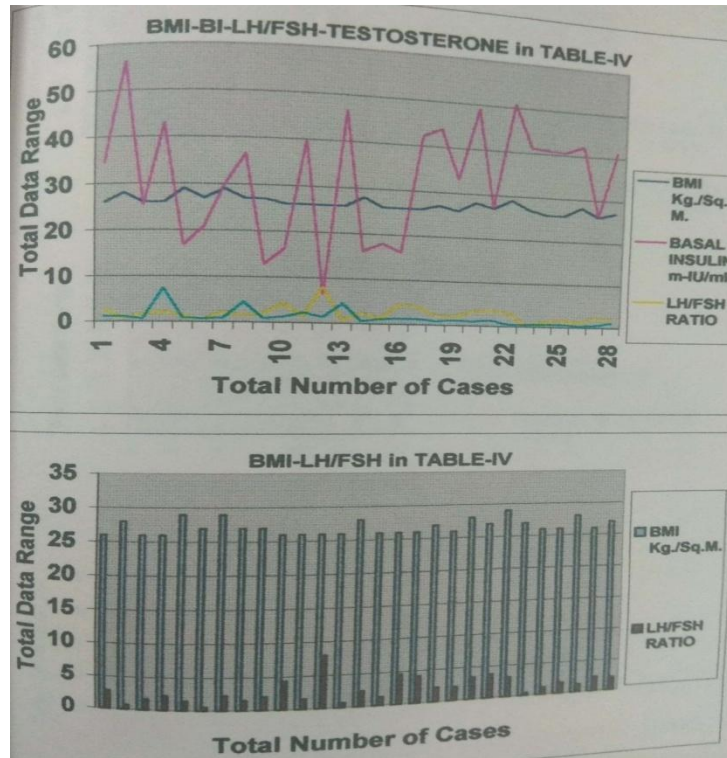

Figure 2: Clinical and biochemical parameters in overweight individuals (BMI > 25 kg/m^2) with PCOS (n=49)
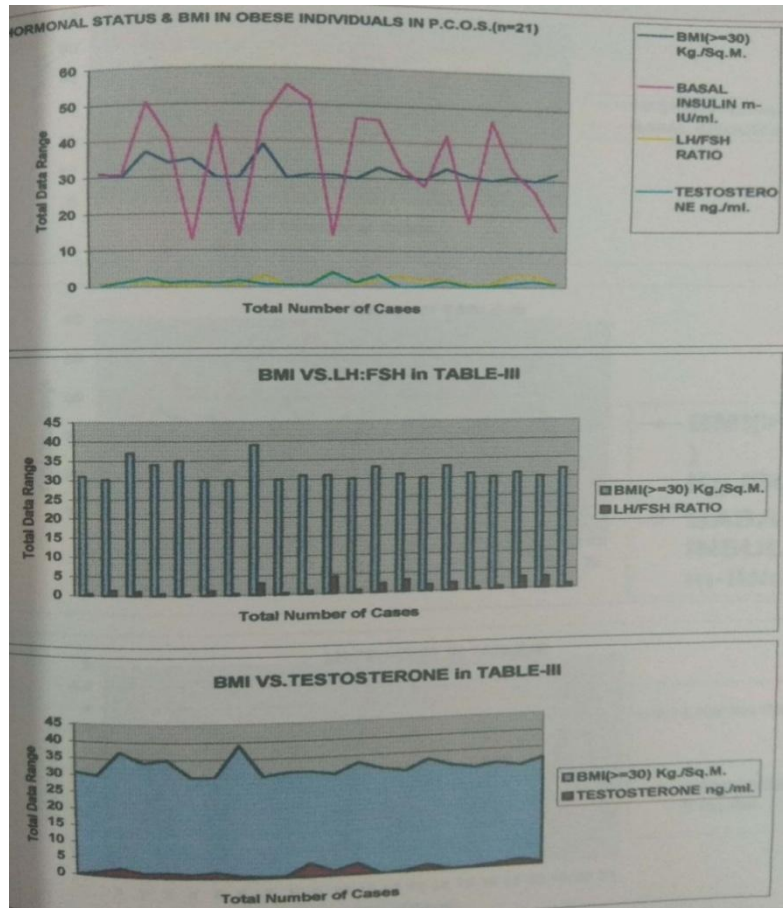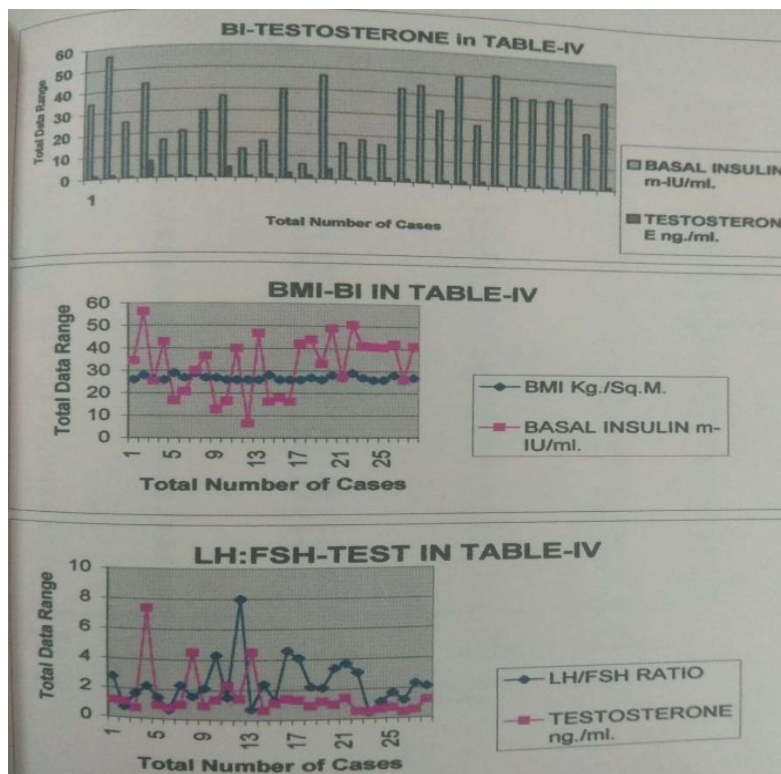
Figure 3a: Clinical and biochemical parameters in obese individuals (BMI $\geq$ kg/m^2) with PCOS (n=21)
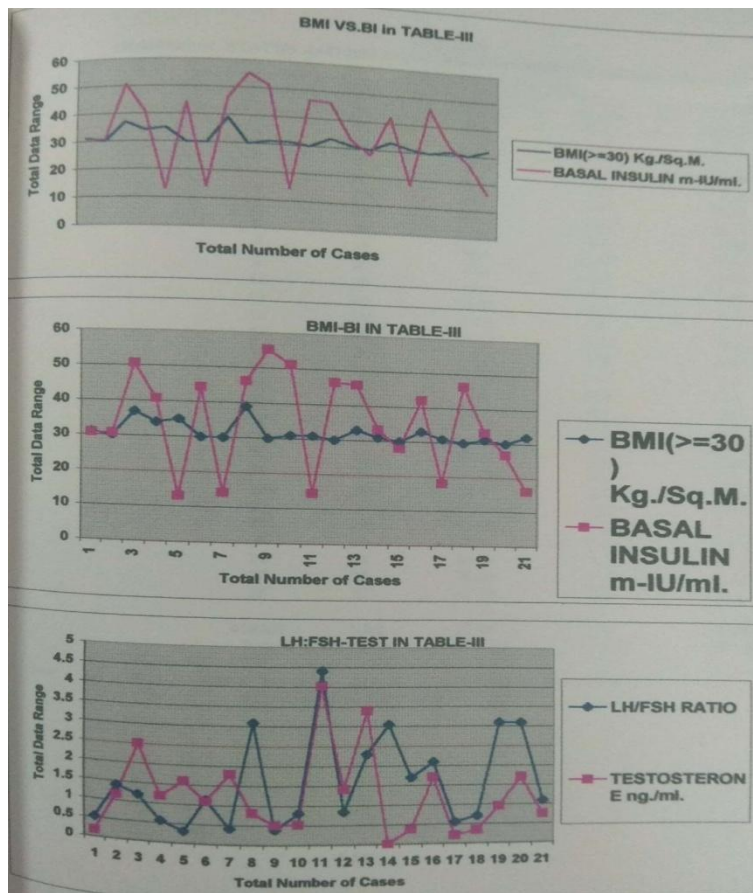
Figure 3b: Clinical and biochemical parameters in obese individuals (BMI $\geq$ kg/m^2) with PCOS (n=21)
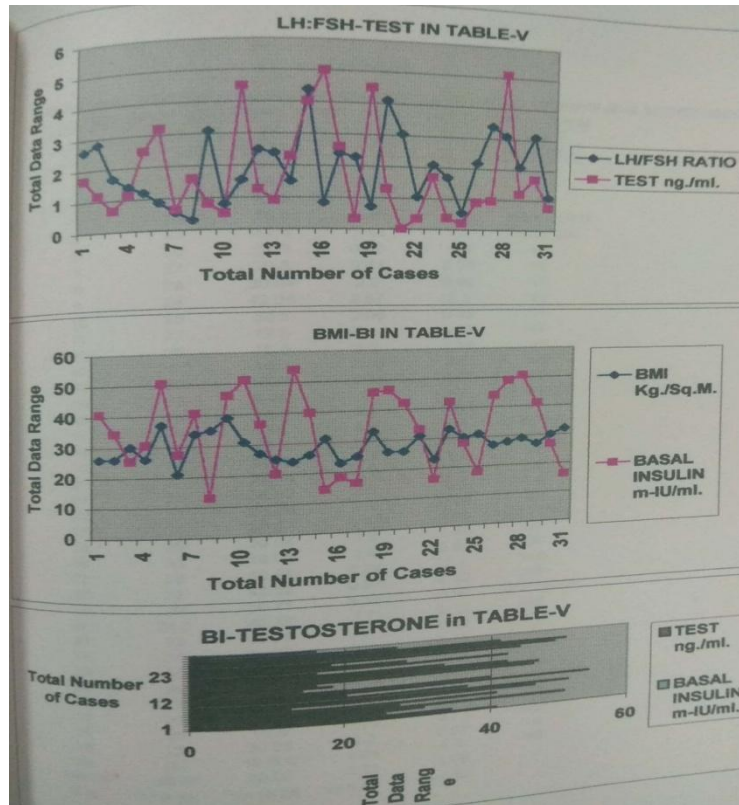
Figure 4a: Clinical and biochemical parameters in overweight individuals (BMI 25-30 kg/m^2) with PCOS (n=23)

Figure 4b: Clinical and biochemical parameters in overweight individuals (BMI 25-30 kg/m^2) with PCOS (n=23)

Figure 5: Hormonal status and BMI in hirsute individuals (F-G score>8) with PCOS (n=31) and presence of family history of hirsutism

Discussion

In the present study, the normal population showed the mean height of 158.5 cm, mean weight of 53.9 kg and mean BMI of 21.6kg/m^2. Earlier studies done upon the population of western countries[7] showed a mean BMI of 25.9kg/m^2. In our study the mean waist:hip ratio was found to be 0.82, in comparison to the western group having the mean ratio of 0.77[7]; the mean LH level was 5.04 m-IU/ml in comparison to the western data showing 4.1 m-IU/ml. Similarly, the mean FSH level was 3.78 m-IU/ml, while in western findings it was 4.9 m-IU/ml.[7] The mean LH:FSH ratio was 1.34 in the present study, whereas it was 0.9 in the western group.[7] The mean total testosterone level was 0.64 ng/ml, whereas the western group showed the same as 1.2 ng/ml.[8]. The above data suggested that the Indian population (Bengali women) has a lower body weight but with increased abdominal fat in comparison to western group and both LH:FSH and hyperandrogenism are less in our population.

Prevalence of PCOS in our study was 19.7%. Fouzia Nazir *et al.* (1999) conducted a retrospective study on 52 women having polycystic ovary syndrome with fertility deprivation.[10] The prevalence of PCOS in their study was found 20.7% which is almost similar to our study. Ahemad Aboul Nasr *et al.* (2004) conducted a prospective study on 50 patients to assess the morphological findings of the ovary based on trans- vaginal ultrasound in infertile oligomenorrheic women and their productivity for endocrine sign of polycystic ovary syndrome.[11] They found prevalence of PCOS in their study was 22%. R. Hart *et al.* (2004) concluded that PCOS perplexing endocrine disorder of women in their reproductive years with prevalence up to 10%.[12]

About 42.22% (19/45) USG diagnosed PCOS subjects had significant hirsutism (FG >8). In this hirsute PCOS subset, high BMI was found in 35.4%, high BI in 40%, high LH:FSH ratio in 51.6% and high testosterone in 64.5%. By Student's t-Test, it was derived that BMI was very

significantly high (P<0.0002; 29.24 ± 4.78 vs 21.67 ± 1.18) and testosterone value significantly high (P < 0.01; 1.76±1.51 vs 0.54 ± 0.1) than that in the control. It supports the idea that LH produced increased androgen by thecal stimulation, which in turn, caused hirsutism.[13] It also supports the result of an earlier study done in the Kashmir valley of India that PCOS was a cause of hirsutism in 37.3% of the Indian population.[14] Western study also showed high testosterone level in hirsute subgroup (>95th percentile of normal) . Greater body mass in hirsute group was also the result of high testosterone causing obesity.[13]

H. Hassa *et al.* (2006) conducted a retrospective study to determine the hormonal and clinical profiles of polycystic ovarian syn- drome. 46% patients in their study had oligomenorrhea.[15] On correlating oligomenorrhea with hormone levels we found that it significantly correlated with raised LH:FSH ratio and raised total testosterone levels. There was statistical significance of raised LH with oligomenorrhea. Abdul Razak *et al.* (2007)[18] concluded that oligomenorrhea correlated with raised LH:FSH ratio.[16]

According to NIH-NICHHD criteria for diagnosis of PCOS (set in 1990), USG was not mandatory.[17] Western data showed that around 50% of biochemically diagnosed PCOS had fulfilled USG criteria.[18] It was done for comparison of hormonal levels in the present study. 62.8% or 45 of 70 subjects demonstrated the USG proof of diagnosis and of them, 70.45% had bilateral involvement. Only left side was involved in 22.72% and only right side in 6.81% of the USG detected PCOS subjects. This implied that if only a single ovary is involved, there is a propensity for left-sided involvement.

About 31% patients were hirsute. Pache TD *et al.* (1991) conducted a study on 95 patients and found hirsutism in 63% patients.[19] Fouzia Nazir (1999)[20] conducted a study on diagnosis and management in fertility deprivation in patients of PCOS found the hirsutism in 84.6% of patients. Abdul Razzak *et al.* (2007)[21] found 64.49% patients hirsute.

Analysis of their biochemical data showed that women with polycystic ova- ries had higher total testosterone levels than in women with normal ovaries (P = 0.03 Sharquie et al. (2007) found that total Testosterone levels were seen elevated in 60% of patients in the study the results are in agreement with results obtained in Rahila Yousouf et al study.[22]

Conclusion

PCOS is fairly a common entity in West Bengal female population. Many of the young women present with irregular period and oligomenorrhea at their post menrachal life (15-20 yrs). A significant number present with hirsutism as cosmetic problems and a small number of individuals come with obesity. There is a significant abdominal obesity in this city, which can be measured by waist-hip ratio. Most of the PCOS patients of this city are overweight rather than obese. In PCOS there was increased LH and there by increased LH-FSH ratio, which is usually used as a single hormonal estimation for diagnosis. In accordance to previous studies it may be suggestable that the free or total testosterone level can be a singular and vital hormonal marker for diagnosis. Both LH-FSH ratio and testosterone can be taken for accuracy of diagnosis.

USG imaging of ovaries is also a very sensitive modality for diagnosis, although the syndrome cannot be established without laboratory data. A significant proportion of patients in this study presented with acathosis nigricans with a strong correlation with hyperinsulinemia in PCOS subjects. Hirsutism subset is directly related to high testosterone level and also body weight is more in the hirsute subset of the present study compared to the western data.

References

1. Franks S. Polycystic ovary syndrome. N Engl J Med. 1995;333(13):853- 861.
2. Copp T, Jansen J, Doust J, Mol BW, Dokras A, McCaffery K. Are expanding

disease definitions unnecessarily labelling women with polycystic ovary syndrome? *BMJ.* 2017 Aug 16. 358:j3694.

3. Hackethal V. PCOS Diagnosis: One Size Does Not Fit All. Medscape News & Perspective. Available at http://www.medscape.com/viewarticle/884712#vp_1. Accessed: August 28, 2018.

4. Nidhi R, Padmalatha V, Nagarathna R, Amritanshu R. Prevalence of polycystic ovarian syndrome in Indian adolescents. J Pediatr Adolesc Gynecol. 2011 Aug;24(4):223-7.

5. Hart R, Hickey M, Franks S. Definitions, prevalence and symptoms of polycystic ovaries and polycystic ovary syndrome. Best Pract Res Clin Obstet Gynaecol. 2004 Oct;18(5):671-83.

6. Azziz R, Carmina E, Dewailly D, et al. Task Force on the Phenotype of the Polycystic Ovary Syndrome of The Androgen Excess and PCOS Society. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report. Fertil Steril. 2009 Feb. 91(2):456-88.

7. Lobo RA, Carmina E. Importance of Diagnosing PCOS. Annuals of Internal Medicine 2000; 32:989-993.

8. Ferriman D, Gallwey JD. Clinical assessment of body hair in women. J Clin Endocrinol Meta. 1961; 21:1440–7.

9. Buckett WM1, Bouzayen R, Watkin KL, Tulandi T, Tan SL. Ovarian stromal echogenicity in women with normal and polycystic ovaries. Hum Reprod. 1999 Mar;14(3):618-21.

10. F. Nazir, S. Sayeed, M. Malik, H. Aziz and S. A. S. Rana, "Polycystic Ovarian Syndrome—Diagnosis and Management in Fertility Deprivation," Pakistan Journal of Obstetrics & Gynecology, Vol. 12, No. 1-2, 1999, pp. 59-71.

11. Nasr AA, Hamzah H, El Maaty ZA, Gaber H, Azzam O. Transvaginal Appearances of Ovary in Infertile Women with Oligomenorrhae: Association with Clinical & Endocrine Profile. Middle East Fertility Society Journal 2004; 9(2):140-149.

12. Hart R, Hickey M, Franks S. Definitions, prevalence and symptoms of polycystic ovaries and polycystic ovary syndrome. Best Pract Res Clin Obstet Gynaecol. 2004 Oct;18(5):671-83.

13. Duignan NM, Shaw RW, Rudd BT, et al. Sex hormone levels and gonadotrophin release in the PCOS. Clin Endocrinol (Oxf) 1975; 4:287-95.

14. Zargar AH, Wani AI, Masoodi SR, et al. Epidemiologic and etiologic aspects of hirsutism in Kashmiri women in Indian subcontinent. Fertil Steril 2002; 77: 674-78.

15. Hassa H, Tanvir HM, Yildiz Z. Comparison of Clinical and Laboratory Characteristic of Cases with Polycystic Ovarian Syndrome Based on Rotterdam Criteria and Women with Only Clinical Signs Are Oligo/Anovolution or Hirsutism. Archives of Gynecology and Obstetrics 2006; 274(4):227-232.

16. Razak A, Nadak A, Tace A. Polycystic Ovarian Syndrome: The Correlation between the LH: FSH and Disease Manifestations. Middle East Fertility Society Journal 2007; 12(1):35-40.

17. Asuncion M, Calvo RM, San Milan JL, et al. A prospective study of the prevalence of the PCOS in unselected caucasian women from Spain. J Clin Endocrinol Metabol 2000; 85: 2434-8.

18. Khan MI, Klachko DM. Polycystic ovarian syndrome. e-Medicine Journal online, updated in 2002.

19. Pache TD, Fauser BCJM. Arrest of follicular maturation in the polycystic ovary syndrome: endocrine and sonographic aspects. Exp Clin Endocrinol (Life Sci Adv) 1991;10:1-6.

20. Nazir F, Sayeed S, Malik M, Aziz H, Rana SAS. Polycystic Ovarian Syndrome—Diagnosis and Management in Fertility Deprivation. Pakistan Journal of Obstetrics & Gynecology 1999; 12(1-2):59-71.

21. Razak A, Nadak A, Tace A. Polycystic Ovarian Syndrome: The Correlation between the LH:FSH and Disease Manifestations. Middle East Fertility Society Journal 2007; 12(1):35-40.

22. Yousouf R, Khan M, Kounsar Z, Ahangar S, Lone WA. Polycystic Ovarian Syndrome: Clinical Correlation with Biochemical Status. Surgical Science 2012; 3: 245-248.