Original Article

Characteristics of Polycystic Ovarian Syndrome in Sub-fertile Woman Attending to GOPD in ShSMCH

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Abstract

Background: *Polycystic ovarian syndrome (PCOS) is a condition characterized by menstrual abnormalities (oligo/amenorrhea) and clinical or biochemical features of hyperandrogenism and may manifest at any age. It is a common cause of female subfertility. All the dimensions of PCOS have not been yet completely explored.*

Methods: *It was a cross sectional comparative study carried out at-GOPD of Shaheed Suhrawardy Medical College & Hospital from January, 2016 to December 2016 on 162 sub-fertile women. Among them 54 were PCOS group and 108 were non PCOS group. PCOS was diagnosed by (Rotterdam criteria 2003) (i) Oligo or anovulation (ii) hyperandrogenism (iii) Polycystic ovaries. Study was done to evaluate and compare the demographic characteristics, clinical, biochemical and ultrasoundgraphic features of sub-fertile women with and without PCOS.*

Results: *A total of 162 sub-fertile women aged 16-36 years. Mean age was 29.5±5.4. There were significant differences between the two groups in terms of (oligo/amenorrhea), hirsutism, WHR and ovarian ultrasound features. There were no significant differences between two groups in correlations between the level of obesity with the incidence of anovulation, hyperandrogenism or with hormonal features.*

Conclusion: *PCOS is one of the important factors causing Infertility. It is an ill-defined symptom complex needed due attention. There is a need to increase awareness regarding. The clinical features of PCOS are heterogenous thus can be investigated accordingly of selection of appropriate treatment modality.*

Key Words:
Polycystic Ovarian Syndrome, Infertility/Sub-fertility

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Operational definition:

Infertility/Sub-fertility: Inability of a couple to achieve conception after one year of unprotected coitus.

Amenorrhea: Defined as an absence of menstruation for more than 6 months.

Oligomenorrhea: Defined as delay of menstruation of more than 35 days to 6 months.

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Hyperandrogenemia: Defined as increased circulating level of androgen. The normal range of total testosterone for women is 15-70 ng/dl.

Waist-to-Hip ratio: This was calculated after measuring of waist circumference between pelvic brim & costal margin, while hip circumference was taken at the level of grater trochanter. AWHR0.85 was considered normal.

Introduction:

Polycystic ovarian syndrome (PCOS) is the most common gynecological endocrinopathy affecting 7-10% of women of reproductive age group.[1] It appears to be associated with an increased risk of metabolic aberration including insulin resistance and hyperinsulinism, type 2 diabetes mellitus, dyslipidemia, cardiovascular disease and endometrial carcinoma.[2] It is commonly diagnosed in young women with anovulatory infertility affecting 47% of women.[3] It is associated with oligomenorrhea,

hyperandrogenic problems such as hirsutism, acne and obesity. The syndrome is also frequently seen in women of normal body configouration.[4] Although the exact definition of PCOS has varied when described by various experts, following a consensus conference, held in Rotterdem in 2003; an internationally accepted definition has been adopted by European society for human reproduction and embryology and American society for reproductive Medicine, the ESHREZA SRM Rotterdam Consensus (Rotterdam Consensus).[5] According to this consensus, two of the following three diagnostic criteria must be met to achieve at a proper diagnosis.

(i) Oligo ovulation or anovulation (ii) Hyperandrogenemia/ Hyperandrognism (iii) Polycystic ovaries

Estimation of prevalence of PCOS depend on the population being assessed as there are ethnic difference in the clinical and biochemical features of PCOS.[6] The prevalence of PCOS ranges between 2.2 to 26% in various countries depending on the recruitment methods, the study population, the criteria used for its definition and the method used to define each criteria.[7] The prevalence of PCOS can be high as 30% in women with secondary amenorrhea, 40% in women with infertility, 75% in women with oligomenorrhea and 90% in women with hirsutism.[8] The pathophysiology of PCOS may have genetic component although it can be suggested that the main factors responsible for the increasing prevalence of PCOS are related to the influence of environment including dietary habits, behavior and other still undefined factors.[9] The clinical features of PCOS are heterogeneous and may change through the lifespan starting from adolescence to post-menopausal age.[10] This is largely dependent on the influence of obesity and metabolic syndrome, which consistently affect most women of PCOS.[11] This represents an important factor in the evaluation of the PCOS throughout life and implies that the PCOS by itself may not be hyper androgenic disorder exclusively restricted and relevant to young and fertile aged women but may also have some health implications later in life.

Whereas hyperandrogenism and menstrual irregularities represent the major complaints in young women with the PCOS, symptoms related to androgen excess, oligomenorrhoea or amenorrhoea and, particularly, infertility are the main complaints of adult women with PCOS during the reproductive age. Obesity has an important impact on the severity of these manifestations in proportion to its degree and particularly in the presence of the abdominal phenotype6. In addition, there is consistent evidence that it renders affected women more susceptible to develop type II diabetes, with some differences in the prevalence rates between countries and, potentially, in favouring the development of cardiovascular diseases.

The present study was carried out to evaluate the characteristics of PCOS among the sub-fertile women attending to tertiary level hospital in Dhaka city.

Methods and materials:

It was a cross sectional comparative study carried out on 162 sub-fertile women attending to the GOPD of ShSMCH from January, 2016 to December, 2016. Among 162 women 54 respondents were PCOS group and 108 were non PCOS group. PCOS was diagnosed by Rotterdam (2003) criteria having two of the following.

(i) Oligo and anovulation

(ii) Hyperandrognism (clinical and or two biochemical sign)

(iii) Polycystic ovaries on Ultrasound examination (Presence of follicle measuring 2-9 mm in diameter and or ovarian volume > 10 cm^3)

Women with other causes of endo-crinological abnormalities such as primary hyperprolactemia, thyroid dysfunction, (cushing's syndrome) and congenital adrenal hyperplasia were excluded from PCOS study group. Data was collected from face to face interview and also from registered book. A specially designed data collection sheet was prepared for recording detailed history, sociodemographic factors, medical & surgical history, examination findings, hormonal levels and ultrasonographic findings. Menstrual history including regularity, irregularity of cycle, history of cycle length, dysmenorrhea was recorded. Patients complain of amenorrhea pregnancy test was ruled out. BMI was calculated by divided weight in Kilogram by height in meters square. Clinical hyperendrogenism was diagnosed using modified Ferriman Gallery score for evaluating and quantifying hirsutism in women using nine body area (upper and lower back, upper arm, upper lip, chin, chest, upper and lower abdomen, thigh). Hair growth was rated from 0-4.

The presence of acne, greasy skin and thinning of hair of scalp were also recorded. Serum sample of hormone were analyzed in non-stimulated tracking cycle; Follicle stimulating hormone (FSH) luteinizing hormone (LH),

Prolactin, testosterone were done. D21 progesterone level was done. The normal cut off value for FSH and LH was takes as <10 mIu/ml. A prolactin level <35 ng/ml was taken as normal, a total testosterone level of <70 ng/dl was regarded as normal and progesterone level of > 20ng/ml at day 21 was regarded as confirming ovulation.

Transvaginal ultrasonography was performed twice for all 162 women. The first examination was done in early follicular phase for evaluating ovarian morphology. The 2nd TVS was done at mid cycle to evaluate mature follicle in cycle without prior use ovulating inducing drug. Follicles > 16 mm were regarded as mature.

Waist to hip ratio (WHR) after measuring the waist circumfeance was taken at the level of greater trochanter. A WHR .85 was considered normal while a WHR >.85 regarded abnormal.

This was a cross sectional comparative study conducted at Infertility clinical of Gynae outdoor of ShSMCH from January 2016 to December, 2016. Infertile women primary and 2ndary Infertility were enrolled of this study. Study was done after talking informed consent. 108 were non PCOS and 54 were PCOS diagnosed according to Rotterdam criteria.

Data was collected from face to face interview and also from registered book. Detailed menstrual history including regularity/irregularity of cycle, history of cycle length, dysmenorrhea was recorded. In patients complains of amenorrhea, pregnancy was ruled out whenever necessary. The data sheet also included age, sociodemographic features, obstetrical history, medical and surgical history, family H/O DM, HTN, BMI, acne, hisrsuitsm, thyroid status, BMI was measured by taking height and weight (weight machine), cut of BMI as standard consensus statement for India population was considered i.e. normal BMI 18-22.9 kg/m^2. Overweight 23.0 – 24.9 kg/m^2 obesity > 25 kg/m^2. Hirsuitsm was scored according to modified Ferreman Gall away score. Grading of severity based on the score was associated as < 4 – mild 4 – 7 moderate > 8 severe.

In the data sheet the findings of laboratory investigation included hormonal status like serum follicle stimulating hormone, Lutenizing hormone, 2hrs after 75gm glucose load, Serum Prolactin, Thyroid hormone, USG findings of lower abdomen including both ovaries were noted. Collecting data computed and analyzed using software SPSS v20.

Result:

162 sub-fertile women were recruited. Among them 54 were PCS group and 108 were non PCO group. The mean age in PCS and non PCOS groups were 29.5±5.45 years versus 30.9±6.95 years respectively (P = .00061). Most women in PCO group (33.7%) were aged 21 – 25 years. While in non PCOS group most (54.25%) were aged 26-30 years. There were no significant difference between the two groups regarding educational level, occupation or family history of infertility and obesity. (Table-1)

The mean age at marriage and the duration of infertility was not significantly less in the PCOS group than in non PCOS group. There was primary sub-fertility in (70.37%) of women in the PCOS group versus (68.57%) in the non PCOS group. (Table-1)

Oligomenorrhea and amenorrhea were significantly more among the PCOS women at 68.5% and 12.96% respectively, while in non PCOS group the rate were 20.37% and 7.40% respectively P =.000

Women in the PCOS group had more hirsutism than women in non PCOS group (P=.000)

Acne was not significantly more prevalent among women with PCOS than in women without PCOS: 33.5% versus 27.77%.

Women with PCOS had higher mean BMI than women in non PCOS group but the difference was not statistically significant (33.3%). WHR was significantly greater in PCOS group (81.48%) than non PCOS group (55.55%) P = .019.

Elevated LH level was significantly higher in PCOS group than non PCOS group (31.48% versus 12.03% P value .000)

There was no statistically significant difference between the two groups in terms of the LH/FHS ratio, total testosterone level, prolactin level. Progesterone was measured in the midluteal phase to confirm ovulation and there was statistically significance difference between the two groups 92.59% of PCOS versus 13.88% of non PCOS group showed anovulatory cycle (Table – II)

Table-III showed the ultrasonic appearance of polycystic ovaries of both groups. Correlation between BMI and oligomenorrhea, Hirsutism, LH/RSH ratio were shown in table I-IV. Oligomenorrhea increased with increasing BMI but statistically it was not significant (Table-IV).

Table I: *Characteristic of women with PCO and non PCO (n = 162)*

Characteristic (Age group)	PCO group (54)	%	Non PCO (108)	%	P. Value
16 – 20	5	9.26	20	18.52	
21 – 25	18	33.33	30	27.78	
26 – 30	15	27.78	37	34.26	.00061
31 – 35	10	18.52	13	12.04	
36 – 36	8	14.81	8	7.41	
Mean age					
PCOS	29.5±5.45				
Non PCOS	30.9±6.9				
Education					
Primary	19	35.19	57	52.78	
Secondary	25	46.30	36	33.33	.922
Illiterate	10	18.52	15	13.89	
Occupation					.797
Housewife	35	64.81	75	69.44	
Employed	19	35.19	33	30.56	
Socio economic					
Poor	3	5.56	28	25.93	
Middle	42	77.78	70	64.81	. 403
Rich	9	16.67	10	9.26	
Family History					
Infertility	12	22.22	6	5.56	
Obesity	9	16.67	10	9.26	
Both	7	12.96	3	2.78	.168
None	26	48.15	89	82.41	
Age of marriage					
< 30 years	44	81.48	78	72.22	.108
> 30 years	10	18.52	30	27.78	
Duration of Infertility					
< 2 years	17	31.48	44	40.74	.062
> 2 years	37	68.52	64	59.26	
Type of Infertility					
Primary	38	70.37	74	68.52	.617
2ndary	16	29.63	34	31.48	.000
Menstruation					
Amenorrhea	7	12.96	8	7.41	
Oligo menorrhea	37	68.52	22	23.37	
Regular	10	18.52	78	72.22	
Characteristic	PCO group (54)	%	Non PCO (108)	%	P. Value
Hirsutism					
Positive	15	27.78	25	23.15	.000
Negative	39	72.55	83	76.85	
AcnePositiveNegative	1836	33.3366.67	3078	27.7872.22	.403
BMI					.571
< 18	0	-	1	0.93	
18 – 24.9	28	51.85	75	69.44	
25 – 30	18	33.33	27	25.00	
> 30	8	14.81	5	4.63	
WHR					
< .85	10	18.52	48	44.44	.019
> .85	44	81.48	60	55.56	

Table II

Distribution of hormone level

Hormone	PCOS (54)	%	Non PCOS % (108)	%	P. Value
LH level					
High (> 14.7)	17	29.31	13	12.04	.000
Normal	37	63.79	95	87.96	
FSH level					.476
High	3	5.17	32	29.63	
Normal	43	74.14	69	63.89	
Low	8	13.79	7	6.48	
LH/FSH ratio					
< 2	42	72.41	105	97.22	.088
> 2	12	20.69	3	2.78	
Testosterone					.05
High	8	13.79	7	6.48	
Low	46	79.31	101	93.52	
S. Progesterone(midluteal)					
Low	50	86.21	15	13.89	.000
High	4	6.90	93	86.11	

Table III

Distribution of sample size according to USG findings

TVS findings	PCOS (54)		Non PCOS (108)	%	P. Value
PCOS feature					
Yes	39	72.22	10	9.26	.000
No	15	27.78	98	90.47	
Mature follicle					
Yes	8	14.81	35	32.41	.000
No	46	85.19	73	67.59	

Table IV

Correlation's between BMI and clinical and biochemical features of PCOS

PCOS features	18 – 24.9 kg/m^3	25 – 30 kg/m^3	> 30 kg/m^3	P. value
Menstruation				
Amenorrhea	3	4	5	
Oligo menorrhea	9	16	7	.553
Regular	2	7	1	
Hirsutism				
Positive	11	29	7	.403
Negative	3	8	6	
LH/FSH ratio				
< 2	11	34	7	.503
> 2	3	3	6	
Testosterone				
High	4	2	3	.320
Normal	10	25	10	

Discussion:

In this study we observed that there was heterogenicity in the presentation of patients with PCOS. The pathogenesis of PCOS is poorly understood, but the primary defect may be insulin resistance leading to hyperinsulinaemia. In the ovary, the cardinal feature is functional hyperandrogenism. Circulating concentrations of insulin and luteinizing hormone (LH) are generally raised. The theca cells, which envelop the follicle and produce androgens for conversion in the ovary to oestrogen, are overresponsive to this stimulation. They increase in size and overproduce androgens. The rise in LH levels is thought to be caused by the relatively high and unchanging concentrations of oestrogens that may alter the control of this hormone by the hypothalamicpituitary axis. This combination of raised levels of androgens, oestrogen, insulin and LH explains the classic PCOS presentation of hirsutism, anovulation or dysfunctional bleeding, and dysfunction of glucose metabolism. Paradoxically, although the insulin regulatory molecules on the theca cells are responsive to insulin, those in the muscle and liver are resistant.

Age is the single most important determining factor affecting female fertility, Monga[17] and Pedersen et al[13] found that delaying marriage until after the 30s will affect the fertility rate, because fertility declines rapidly after 35 years of age. PCOS is reported to be more pre- valent in younger (<35 years) than older women. This possibly arises from a physiological decline in the fol- licular cohort leading to a normalized ovarian ultrasonic appearance with advancing age. The results in our study were consistent with Alnakash and Al-Taee as they noted that 87.8% of the women with PCOS included in their study were less than 35 years of age.

The presence of a high frequency of oligomenorrhea and amenorrhea among the PCOS group in the current study was in consistent with the results in a large series of women diagnosed to have PCOS by Azziz *et al.*[14], as approximately 75% - 85% of women with PCOS had clinical evidence of menstrual dysfunction. Women with PCOS showed hirsutism more than women without PCOS. The prevalence and degree of hirsutism depend on the ethnicity of the patients. Compared with Asian women, Middle Eastern or Mediterranean women are more likely to complain of hirsutism.[15] Hirsutism is less prevalent in women with PCOS of East Asian ex- traction or Pacific Islanders[16] but is more prevalent in women of Indian origin.[17]

The high rate of obesity and central obesity among in- fertile women in the current study can be attributed to the dietary habits (high carbohydrate/low protein diet) and the lack of exercise among women. Elting et al[18] also found that 11.3% of women with PCOS were over- weight and 32.7% were obese. However, there are no controlled systematic studies to determine the exact pre- valence of obesity in women with PCOS. Most inves- tigators have found that 30% - 50% of women with PCOS are obese with a tendency to have an increased WHR, or abdominal obesity.[19] There is also evidence showing that even normal weight PCOS subjects have increased intraabdominal fat.[20]

In the current study, abnormally elevated LH levels and LH/FSH ratios were found only in small percentage of women with PCOS. The characteristic increase in LH relative to FSH release has long been appreciated as a feature of PCOS. Because of the pulsatile nature of their release, a single test fails to detect an increased LH/FSH ratio. This, as well as its lack of specificity, has led to the recommendation that LH/FSH ratios should not be in- cluded in the diagnostic criteria for PCOS. Thus, Cho *et al.*[21] found that the LH/FSH ratio had little use in diagnosing PCOS because the median LH/FSH ratio did not differ significantly between the PCOS and non- affected group.[21]

The total testosterone level was high in only 7.5% of these women with PCOS. This outcome was underesti- mated because we measured only total testosterone level, because of the lack of facilities for measuring free tes- tosterone and sex hormone binding globulin in our hos- pital although Alnakash and Al-Taee[20] found that not all women with PCOS possess hormonal and biochemi- cal changes suggestive of the disease.

This was consistent with the findings in the current study. A low progesterone level (confirming failure of ovula- tion) in PCOS group was consistent with the findings by Sheikhha *et al*[22], who found that the prevalence of infertility caused mainly by anovulation in women with PCOS varied between 35% and 94%.

The high prevalence of transvaginal ultrasound features of PCO in the PCOS group was in agreement with Najem *et al.* who reported that 74% of women with PCOS had ultrasound features of polycystic ovaries. PCO features were also found in the non-PCOS group, Balen and Michelmore found that PCO features can be detected in 19% - 33% of the general population. The low prevalence of midluteal ultrasound detection of mature follicles in the PCOS group was in agreement with Sheikhha *et al* [22] who reported anovulation in 35% - 94% of women with PCOS.[23]

The traditional belief that obesity plays a serious role in the pathophysiology of PCOS dates back to the years of Stein-Leventhal but the puzzling fact is that not all women with PCOS are obese. The diversity in the criteria for

diagnosing PCOS prompted us to estimate the correlations between disease manifestations and to determine whether higher BMI and WHR necessarily indicate a greater incidence of menstrual disturbance, hirsutism or higher LH/FSH ratio and elevated serum testosterone level. In the current study, the correlations be- tween BMI and WHR and menstrual disturbances, hirsutism, LH/FSH ratio and serum testosterone level were in agreement with the findings of Alnakash and Al-Taee. These findings may provide an answer to the question rose above, disproving the traditional concept of the disease that the heavier the patient, the worse is the dis- ease manifestation

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