Prevalence of Clinical Manifestations of Polycystic Ovary Syndrome in Kashmiri Women

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Abstract

Aim: To study the prevalence of various primary clinical manifestations of polycystic ovary syndrome in Kashmiri women. Methods: Women attending endocrinology outpatient clinic with primary complaints of menstrual dysfunction, infertility and hirsutism were evaluated. The women were diagnosed according to Rotterdam criteria and two hundred forty-nine women with clinical diagnosis were recruited for the study. Age-matched healthy women were recruited in the study as controls. Different clinical and anthropometric parameters were recorded from each participant. Statistical analysis was done by Varstats computation software. Results: We found menstrual irregularities were present in 84.73% PCOS women. The prevalence of acne, alopecia and acanthosis was 56.62%, 38.55% and 32.93% respectively. The prevalence of obesity was significantly higher ($P<0.001$) in PCOS than controls. WHR >0.80 and >1.00 was present in 86.34% and 7.22% cases. The prevalence of hirsutism and polycystic ovaries was 76.30% and 80.72% respectively. Conclusion: The PCOS women had a significantly higher prevalence of obesity and central adiposity. The clinical symptoms in Kashmiri women were in accordance with previous data from other geographic and ethnic populations.

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is a widespread endocrine disorder in reproductive-aged women. It affects about 6-10% females worldwide [1,2]. Though the primary features of PCOS are hyperandrogenism, chronic anovulation and polycystic ovaries but it also presents with other clinical manifestations like acne, alopecia, obesity, acanthosis, menstrual dysfunction and hirsutism [1,3,4]. PCOS is a heterogeneous disorder and the presentation of clinical manifestations is variable from patient to patient depending on various factors. The etiology of PCOS is suggested to be multifactorial including a complex interplay of diverse factors like genetics, intrauterine factors, environment, race and ethnicity [5,6,7].

The exact prevalence of signs and symptoms is highly variable and depends on factors like selection of cases, age and ethnicity [8]. There is also a significant difference between unselected populations and

clinical cohorts. PCOS is associated with increased risk of infertility, insulin resistance, diabetes mellitus, Metabolic syndrome, cardiovascular disorders, anxiety, depression and obstetrical complications [1]. Since the major focus of clinicians is the management of clinical symptoms of PCOS, it becomes important to understand the prevalence and impact of these symptoms in different ethnic populations. There is little focus on understanding the prevalence of different clinical manifestations in Kashmiri women with PCOS. In this study, we report the clinical symptoms of women with PCOS attending endocrinology clinic in the SKIMS Srinagar India.

MATERIALS AND METHODS
Recruitment of subjects
In this case-control study, 349 women between the ages of 16-30 were recruited for the study. The women visiting endocrinology outpatient clinic of Sher e Kashmir Institute of Medical Sciences (SKIMS), Srinagar, India for PCOS-related symptoms such as hirsutism, acne, obesity, infertility or menstrual irregularities from June 2015 to March 2018 were evaluated for PCOS. The diagnosis of PCOS was done according to revised 2003 Rotterdam criteria [9]. The women were diagnosed with PCOS if at least two of the following three features were present: (1) oligo- and/or anovulation defined by menstrual cycles of <21 days, >35 days or less than 6–9 menstrual cycles in a year and amenorrhea as absence of at least 6 menstrual cycles), (2) clinical and/or biochemical signs of hyperandrogenism, (Ferriman Galleway score ≥8 or Total testosterone ≥ 50ng/dL, and (3) polycystic ovaries; ≥12 follicles measuring 2–9 mm in diameter or ovarian volume >10 mL by transabdominal ultrasonic examination[10]. All subjects were screened to exclude PCOS mimicking disorders. The control group consisted of 100 age-matched healthy women with regular menstrual cycles, no clinical or biochemical hyperandrogenism on physical examination. All subjects were ethnic Kashmiris living in Kashmir province. Subjects were recruited after written informed consent was obtained from them.
Anthropometric and clinical evaluation
Detailed clinical history was taken from the participants of the study and clinical symptoms like menstrual history, acne, alopecia, and acanthosis nigricans were recorded. The general anthropometric variables were collected: weight, height, waist-hip, and hirsutism. Height was measured in standing position without shoes. Weight was measured by weighing scale with least count of 500 g with light clothing and without shoes, using

Krupp's weighing scale. Waist circumference was determined in standing position as the minimum value between the iliac crest and the lateral costal margin at the end of a gentle expiration, and hip circumference was calculated as the maximum value over the buttocks.

Hirsutism was measured by Ferriman Gallway scoring system in which nine body parts were visually scored for hair growth from 0-4. A FG score ≥8 taken as significant.

Body mass index was measured as (BMI: weight [kg]/height^2 [m]), Waist-hip ratio was calculated by (WHR: waist circumference [cm]/hip circumference [cm].

Statistical analysis
All Continuous variables were presented as mean ± standard deviation and categorical variables as numbers and percentages. Parametric variables of clinical variables were compared between groups, PCOS and controls by chi-square test. The bar graphs were created using Sigma Plot 10 and pie chart by MS Excel software. The statistical analysis was performed using statistical computation software Vassar stats (http://vassarstats.net/). P-value of <0.05 was considered as statistically significant.

RESULTS
Table 1 shows that menstrual dysfunction was prevalent in 84.73% PCOS women in which 70.28% and 14.45% women presented with oligo menorrhea and amenorrhea respectively. 14.85% PCOS women in our study had regular menstrual cycles (Figure 1). Hirsutism was present in 76.30% PCOS women. No clinically significant hirsutism was recorded in 23.69% PCOS but 40.16% cases had mild (FG Score 8-16) and 36.14% presented with high (FG Score >16) hirsutism level (Figure 3). We found acne was present in a significantly higher proportion in cases than healthy controls (56.62% vs 12%, P<0.001). Androgenic alopecia was found in a significantly higher number of cases than controls (38.55% vs 1%, P<0.001). Acanthosis Nigricans was also found to be significantly higher (P<0.001) at 32.93% cases compared to 2% in controls (Figure 2)

We found significantly higher proportion of PCOS women were obese BMI>30kg/m^2 (12.44%, P <0.000) and overweight BMI-25.01-29.99 kg/m^2 (31.72% vs 9%, P<0.001). Significantly more women were of normal BMI in controls than cases (79% vs 42.15%, P<0.001) but more women were of lean BMI<18.5 kg/m^2 in PCOS women than in controls (13.65% vs 11%) but the difference was not statistically significant (P=0.503) (Figure 4).

We found 86.34% and 81.00% PCOS women and healthy controls had a waist to hip ratio greater than 0.80. On further analysis, we found 13.65% cases had WHR <0.80, 79.11% had WHR 0.81-0.99 and 7.22% cases were found to have WHR greater than 1.00 but in controls higher proportion of women had WHR <0.80 and only 1% women had WHR>1.00 (Figure 5). We also found 80.72% of women with PCOS had polycystic ovarian morphology on ultrasound examination.

**Table 1 Clinical features and cutaneous manifestations in study subjects**

Clinical Parameter	PCOS (n=249)	Control (n=100)	(X^2) P value
Cycles			
Regular	(37) 14.85%	(100) 100%	
Amenorrhea	(36) 14.45%	--	
Oligomenorrhea	(175) 70.28%	--	
Acne	(141) 56.62%	(12) 12%	(57.71) <0.001*
Alopecia	(96) 38.55%	(1) 1%	(50.13) <0.001*
Acanthosis	(82) 32.93%	(2) 2%	(37.35) <0.001*
Hirsutism	(190) 76.3	--	
WHR >0.80	(215) 86.34	(81) 81.00	
PCOM	(201) 80.72%	--	
BMI			
<18.5	(34) 13.65%	(11) 11%	(0.447) 0.503
18.6-25	(105) 42.15%	(79) 79%	(38.82) <0.001*
25.01-29.99	(79) 31.72%	(9) 9%	(19.54) <0.001*
>30.00	(31) 12.44%	---	

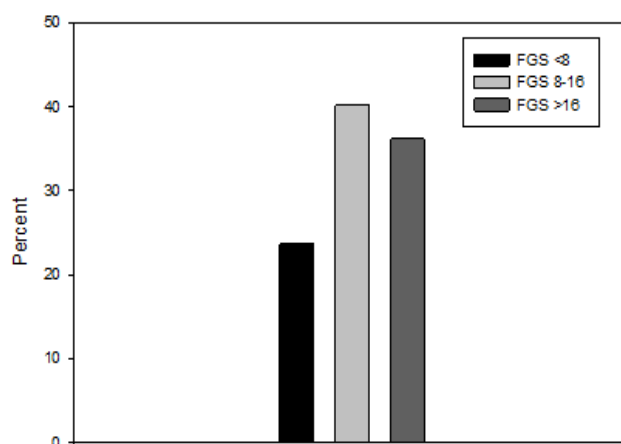**Data is presented as (number) percentage**
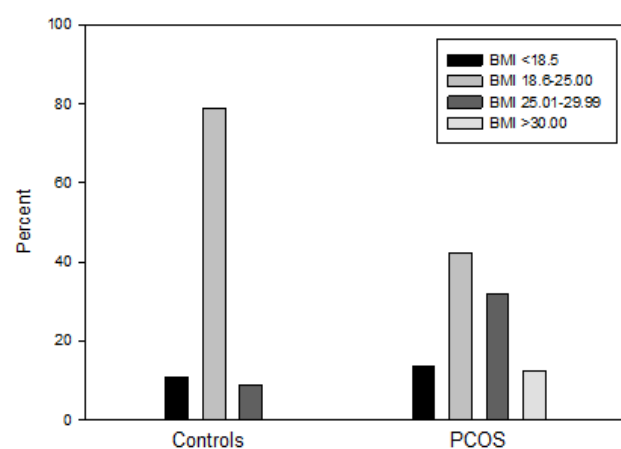**BMI body mass index, (χ^2) Chi square value, P value calculated by chi square test test**
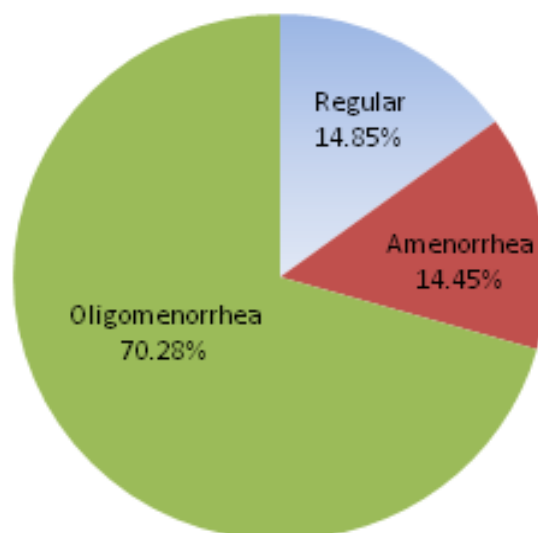
Figure 1 Percentage of various menstrual complications in PCOS women
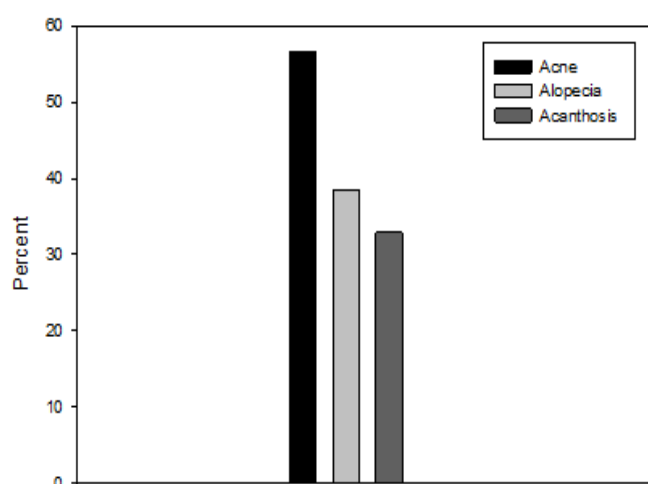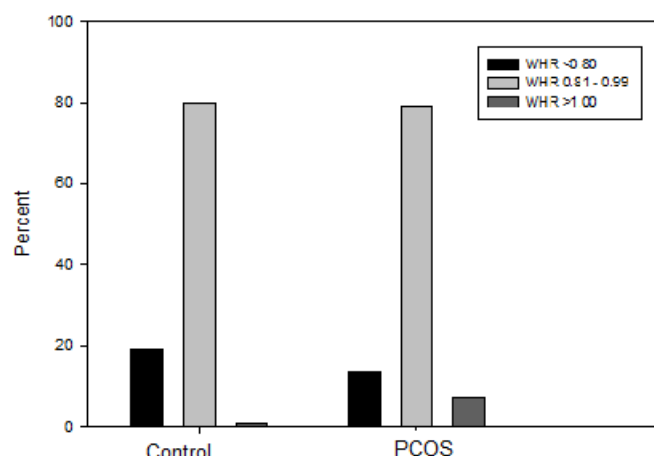
Figure 2 Prevalence of acne, alopecia, and acanthosis

Figure 1 Distribution and severity of hirsutism in PCOS women

Figure 4 Distribution of BMI in PCOS cases and controls

Figure 5 Distribution of Waist to Hip ratio in PCOS cases and controls

DISCUSSION

PCOS remains most common endocrinopathy in premenopausal women. It not only leads to increased risk of for infertility, endometrial carcinoma, obesity, type 2 diabetes mellitus, hypertension, and cardiovascular disease but its clinical manifestations bring along with it psychological problems like anxiety, low self-esteem, depression and decreased quality of life [11,12]. The clinical signs and cutaneous manifestations are the primary cause of discomfort and distress in such women. The extent of phenotypic expression in PCOS women varies greatly.

Hyperandrogenism, clinical and biochemical, is the hallmark of PCOS. [13] Clinically hyperandrogenism manifests itself as unwanted hair growth or hirsutism, acne, and androgenic alopecia. Hirsutism is defined as presence terminal hairs of male pattern of hair growth. In a study of 634 PCOS women, 69.55% of women had hirsutism [14]. Azziz et al [15] reported 72.20% prevalence of hirsutism in 873 women with PCOS and AE-PCOS taskforce reported an overall prevalence of 74.69% [13,15]. Our results are in confirmation with these studies as we found 76.30% PCOS women had clinically significant hirsutism with 40.16% and 36.14% had mild and severe hirsutism.

Acne is a consistent finding in PCOS. In one study 36% of women with treatment-resistant acne had PCOS [16]. The prevalence of acne in PCOS has considerably varied among different studies according to ethnicities. Studies have shown Asian Indians have a higher prevalence than Caucasian and Pacific Islanders [17, 18]. We found acne in 56% women, which are higher than many other studies. This can be attributed to the younger age of PCOS women in our study. Asuncion et al also reported 40% prevalence of acne in PCOS and Schmidt et al reported 61% prevalence of acne[2,19]. In a cross-sectional study on Kashmiri women with PCOS Hirsutism and acne was present in 78% and 48% women which are similar to our reports [20]. Loss of scalp hair in women is a distressing concern in PCOS with serious psychological impact. Androgenic alopecia or male pattern baldness is the effect of androgens of the pilosebaceous unit. Although the relation of alopecia with hyperandrogenism is unclear studies have reported 10-40% prevalence of alopecia. Keen et al [20] reported 31% prevalence of androgenic alopecia and Quinn et al reported a prevalence of 22% in 254 PCOS women. We found androgenic alopecia in 38% PCOS women. Acanthosis nigricans is velvety, hyperpigmentation of the neck and intertiginous area of skin generally considered as a marker of insulin resistance. PCOS is consistently associated with insulin resistance and hyperinsulinemia. In the present study, 32.93% of cases had acanthosis. Similar prevalence of AN (33% - 36%) was reported in Indian PCOS women by Ramanand et al. [21] and Schmidt et al [19] in Caucasian women.

Anovulation is a primary characteristic feature of PCOS and results in menstrual irregularities. Menstrual dysfunction is a chief complaint in PCOS women and is seen as a better marker of anovulation than its biochemical markers [21, 22]. Menstrual dysfunction is present as disruption in the pattern of menstruation which often results in abnormal uterine bleeding. It is present in the majority of PCOS women with 75%-85% have clinically evident menstrual dysfunction [13]. Our data shows 84.73% of cases had menstrual irregularities. Chang et al [23] reported 83.90% and Daimanti-Kandkaris and Danidis [14] reported 85.90% PCOS women with

oligo-amenorrhea which is similar to our findings. Previous studies have reported 14- 17% of PCOS women as eumenorrhic which is similar to our finding [14,22,24].

Polycystic ovaries were considered as one of the primary diagnostic feature of PCOS by Rotterdam criteria [9,25]. It defined PCO as the presence of 12 or more follicles measuring 2-9mm or increased ovarian volume>10ml in at least one ovary. PCO is relatively high in PCOS women with studies reporting >80% of PCOS women. [26, 27] We found 80.72% PCOS women had polycystic ovaries, our results are similar to previous studies.

Women with PCOS also present obesity and difficulty in losing weight as a chief clinical complaint. Studies have shown consistently that the majority of PCOS cases have insulin resistance, hyperinsulinemia, dyslipidemia, and obesity[28]. Our data is in line with previous studies which show the prevalence of obesity at 50%, we show >46% of cases were obese (>25kg/m^2). PCOS women also struggle with central adiposity and WHR is a key predictor of this condition. We found a higher proportion of cases had higher WHR than healthy controls. Obesity plays an important role in the severity of PCOS symptoms and it has been seen obese PCOS women have higher FG score, amenorrhea and hyperandrogenemia [29, 30]. Reduction of weight is seen to improve different clinical and biochemical symptoms associated with PCOS [31,32].

CONCLUSION

Clinical manifestations of PCOS are the most important concern in women affected. Besides primary reproductive and cosmetic concerns, the clinical symptoms are associated with various psychosocial conditions like anxiety, depression and reduced quality of life. The clinical presentation of signs and symptoms are variable between different ethnic populations. Our study reports the prevalence of various clinical and anthropometric parameters in Kashmiri women with PCOS. Our findings highlight that PCOS women have a significant proportion of women with central adiposity and obesity. Further studies are needed to understand the severity and impact of acne, alopecia and other related conditions in this population.

ACKNOWLEDGEMENT

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