Assessment of Hematological and Hormonal levels of PCOS subjects: a case-control study

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Abstract
Polycystic ovarian syndrome (PCOS) is one of the most common endocrine disorders in reproductive-aged women. PCOS is considered to be a complex disease that affects childbearing age, adolescents and postmenopausal women. A significant number of cases were found in and around Tamil Nadu. The study recruited 65 (PCOS subjects) experimental and 65 age-matched controls (±5 years). Again, they were classified into three groups (Group I, II and III) based on age duration. The hematological and hormonal activities were analysed using laboratory technique. Epidemiological data were documented in clinical records including acne, hirsutism, irregular periods and obesity (BMI).

Obesity, irregular periods, hirsutism and oily skin type were observed. Among the findings, higher BMI level 30%, irregular periods 46%, hirsutism 10% and oily skin type 40% were found in PCOS. The mean level of hematological parameters appears to be insignificant compared to PCOS and controls. FSH and LH hormone levels were estimated. FSH and LH levels were significantly elevated in PCOS subjects. The findings of the study indicate that no associations were found in the hematological parameters but a larger sample size is required for future studies.

Keywords: PCOS, Hormone, FSH, LH, Haematological and Obesity.

Introduction

Polycystic ovary syndrome (PCOS) is well known to be a complex disease affecting childbearing age, adolescents and postmenopausal women[3]. PCOS is one of the most commonly reported endocrine and metabolic disorders among reproductive-aged women. Indian prevalence studies of PCOS were conducted in Tamil Nadu and assessed among young adolescent females with an occurrence of 18%[4]. It is regarded as a complex condition with complex genetic, metabolic, endocrine and environmental problems[12]. Urban women had a greater incidence of PCOS than rural women[20].

PCOS is a group of endocrine disorders that commonly affect reproductive-aged women[14]. PCOS influences women's fertility and reproductive health[30]. The common symptoms of PCOS are Hirsutism, enlarged ovaries with many small follicles[39], absence of menstrual cycle, excess hair in the body (amenorrhea) and infertility[8].

It is associated with infertility, metabolic conditions like obesity, insulin resistance, altered glucose tolerance and lipid spectrum disorder as well as long-term vulnerability to diabetes, cardiovascular disease and malignancies[10]. The ovarian malfunction and androgen excess are the most common characteristic features of PCOS. PCOS is a multi-gene disorder with significant environmental and epigenetic influences including lifestyle and nutrition factors[17]. Therefore, early diagnosis is essential since it allows for close monitoring to lower the risk of such problems[9]. The primary risk factor for IR expression and the metabolic phenotype in PCOS is obesity, particularly the accumulation of abdominal fat[33].

According to recent studies, there are erratic relationships between PCOS and the various hematological parameter components[34,36,45]. Hemoglobin, WBC count, mean platelet volume (MPV), red cell distribution width (RDW), basophil count[47], hemoglobin and PCOS have all had varying outcomes[18,32]. Hemoglobin (Hb) is an important oxygen transporter and its level can be influenced by genes and the environment factors[16]. PCOS is caused by a number of pathogenetic mechanisms such as follicular arrest, increased secretion of testosterone, estradiol and dehydroepiandrosterone (DHEA), decreased ovarian follicle response to FSH, increased anti-Mullerian hormone (AMH) and abnormal gonadotropin-releasing hormone (GnRH) regulation that results in increased luteinizing hormone (LH) and decreased FSH[33]. The analysis of clinical parameters is very good tool to maintain the disease and control the other complications, so the aim of the current study was conducted on the PCOS population and to describe the relationship between the obesity, hematological and hormonal levels of PCOS subjects.

Material and Methods

Study Participants and Grouping: The study recruited the 65 (PCOS subjects) experimental and age-matched controls (±5 years) in and around Erode district. Again, they were classified into three groups (Group I, II and III) based on age, group I included the age duration of up to 25 years of age, group II subjects included 26 to 35 years of aged persons and group III subjects included above the 36 years of aged persons. All experimental subjects were recruited successively, with controls being matched to the terms of age (±5 years relaxed). Healthy normal volunteer subjects served

as controls. Questionnaire data were collected with all participating subjects.

A written informed permission was obtained from all participating subjects. Information regarding habits, health status and occupation was recorded. The work was conceded by the ethical standards laid down in the 1964 Declaration of Helsinki. About 5 ml of peripheral blood sample was collected in heparin-coated vacutainers or blood collection tubes for analyzing the hematological and hormonal activity. Epidemiological studies for these cases were documented in clinical records including acne, hirsutism, irregular periods and obesity (BMI).

Selection of participants: Infertile women with PCOS (cases) identified according to the Rotterdam criteria between the ages of 19 and 42 met the inclusion criteria 2.

Assays: The research subjects height and body weight were measured. Analog scales were used to assess body weight while wearing light clothing and a stadiometer was used to measure height. The body mass index (BMI) was computed to determine the degree of obesity.

Hematological parameters: RBC, WBCs, Platelets, MCV, Hct, MCH, Hb, MCHC and ESR levels were measured by the standard in clinical laboratory method.

Serum hormonal assays: The level of serum Luteinizing hormone (LH) and Follicle-stimulating hormone (FSH) were determined using the commercially available ELISA kit (Life DNA Technology, Coimbatore).

Statistical analysis: Using the SPSS-16 version, all the data were subjected to Analysis of Variance (ANOVA) and then Bonferroni's and Duncan's multiple range tests were performed to assess the significant difference between groups at the probability threshold of $p<0.05$.

Results

The study recruited 65 subjects for the experimental and age-matched controls (±5 years). Again, they were classified into three groups (Group I, II and III) based on age. Group I included the age duration up to 25 years of age, group II subjects included 26 to 35 years of age persons and group III subjects included above the 36 years of aged persons. The study recorded the demographic details of PCOS patients and control subjects among the questionnaire data. A demographic detail of the PCOS patients and controls has been reported in table 1. The data documented based on the standard questionnaire indicates the classifications of study samples and other health risk factors like obesity (BMI), irregular periods, height, weight and family history. But no significant variant was found in control subjects.

Table 2 represents the data based on the standard questionnaire among the irregular periods, hirsutism, acne and oily skin symptomized cases were found in experiments. Among the data, 46 % of irregular periods symptoms were found. Hirsutism was found in 10% of samples and oily skin type was found in 40% of the samples, these are all symptoms of PCOS.

Hematological Parameters: In the present study, hematological parameters were examined in PCOS patients and controls and are represented in table 3. The blood parameters were compared with different age groups of controls and experimental subjects. However, the mean RBC levels of control and experimental were insignificantly varied. Among them group II experimental 4.66±0.21 and control 4.31±0.06 were observed. The experimental (Group II 12.30±1.25) Hb level was significantly increased when compared to the controls (11.41±1.63). However, MCV level was significantly decreased in the experimental (Group II 12.30±1.25) when compared to the controls (90.10±3.88). The platelet level was insignificantly varied when compared to the controls. However, the WBC, ESR, Hct and MCHC levels were no different.

FSH levels: The follicle-stimulating hormone levels were estimated in PCOS and controls. FSH level was significantly elevated in PCOS (7.2±3.50) when compared to controls (4.44±2.23) and reference range.

LH levels: In the present study the hormonal level of (LH) PCOS and control was analysed. There was a significant difference in LH levels (9.86±6.58) observed in all groups when compared to the controls (3.35±2.28). All the experimental groups' LH levels were statistically significant at $P>0.05$ level. The data is represented in table 4.

Table 1
The demographic detail of the PCOS patients and controls

Parameters	PCOS			Controls		
Age duration	16-25	26-35	36-45	16-25	26-35	36-45
Number of samples (65)	28 (43%)	23(35%)	14(22%)	28 (43%)	23(35%)	14(22%)
Mean Height (cm)	143.40±11.25	145.11±16.25	147.23±10.25	141.11±10.12	144.42±9.85	145.75±11.53
BMI	30.80±3.62	32.11±3.52	31.60±2.22	24.50±2.21	23.42±1.96	25.12±2.53
Weight (kg)	47.50±3.26	51.30±5.23	62.75±5.85	47.58±3.75	51.56±3.25	58.13±3.56
Family history	11 (39.28)	13 (56.52)	8 (57.14)	-	-	-
Irregular periods	13 (46.42)	12 (52.17)	6 (42.85)	-	-	-

SD = Standard Deviation
n = 65+65 (controls and experiments)

Table 2
Hematological analysis of PCOS patients and controls

Parameters	PCOS			Controls			*P* value
Age duration	16-25	26-35	36-45	16-25	26-35	36-45	
Number of samples (65)	28 (43%)	23 (35%)	14 (22%)	28 (43%)	23 (35%)	14 (22%)	
RBC (3.8-4.8mil/µL)	3.98±0.19	4.66±0.21*	4.45±0.05	3.74±0.64	4.31±0.06	4.45±0.7	0.12
WBC (4.0-10.0 thou/µl)	8.21±0.72	8.22±0.76	8.42±0.74	8.05±0.39	8.50±0.98	8.37±0.72	0.231
Hb (12.0-15.0 g/dL)	10.87±1.34	12.30±1.25*	11.55±0.93	9.98±2.23	11.41±1.63	12.04±1.48	0.01
Hct (36.0-46.0%)	38.17±1.82	40.08±3.13	40.85±3.77	38.42±1.93	38.95±3.00	43.00±2.77	0.01
MCV (83.0- 101 fl)	85.85±16.24**	88.43±2.99	89.57±1.98	90.10±3.88	90.78±1.83	94.57±1.94	0.001
MCH (27.0-32.0 pg)	28.21±1.66	28.08±1.53	28.64±1.73	28.35±1.90	27.91±1.27	28.57±1.55	0.435
MCHC (31.5-34.5 g/dL)	32.26±1.03	32.55±0.44	32.73±0.46	32.32±1.02	32.45±0.43	32.76±0.43	0.53
Platelet (150-410 thou/µl)	310.35±65.70[a]	347.95±32.73	319.42±44.30	311.89±58.07	335.47±47.57	336.00±41.31	0.23
ESR (<20 mm at 1 hrs)	14.57±2.02	16.04±1.55	15.14±1.29	14.71±2.19	15.13±1.25	16.07±1.32	0.13

* p <0.05; significantly different compared to controls and Experimental as estimated by ANOVA followed by DMRT test.
** p >0.001; insignificantly decreased when compared to the other experimental groups and controls as estimated by ANOVA followed by Bonferroni's correction but normal in reference range.
[a] p <0.05; insignificantly lower when compared to other control subjects.

Table 3
Showing the data of irregular periods, hirsutism, acne and oily skin of PCOS patients and controls

Parameters	PCOS			Controls		
Age duration	16-25	26-35	36-45	16-25	26-35	36-45
Number of samples (65)	28 (43%)	23 (35%)	14 (22%)	28 (43%)	23 (35%)	14 (22%)
Irregular periods	13 (46.42)	12 (52.17)	6 (42.85)	-	-	-
Hirsutism	3 (10.71)	2 (8.69)	2 (14.28)	-	-	-
Acne	3 (10.71)	2 (8.69)	1 (7.14)	-	-	-
Oily skin	12 (42.85)	7 (30.43)	4 (28.57)	-	-	-

SD = Standard Deviation
n = 65+65 (controls and experiments)

Table 4
Showing the data of hormonal assessments of PCOS patients and controls

Parameters	PCOS			Controls			*P* value
Age duration	16-25	26-35	36-45	16-25	26-35	36-45	
Number of samples (65)	28 (43%)	23 (35%)	14 (22%)	28 (43%)	23 (35%)	14 (22%)	
FSH values (*mIU/mL)*	6.30±2.13	6.64±1.53	7.2±3.50*	3.58±2.12	4.25±1.25	4.44±2.23	0.001
LH values	2.91±1.23	5.57±2.14	9.86±6.58**	2.56±1.03	3.12±1.12	3.35±2.28	0.001

* p <0.05; significantly elevated when compared to controls as estimated by ANOVA followed by DMRT test.
** p >0.001; significantly elevated when compared to the other experimental groups and controls as estimated by ANOVA followed by Bonferroni's correction.

Discussion

PCOS is an endocrine condition that affects women of reproductive age. There are several different clinical manifestations[15,38] between 70 to 80 percent of women with PCOS having infertility condition[48]. A sex hormone imbalance is the most common feature for PCOS[29]. It affects approximately 10% of this population[12,13,27]. In this present study, demographical details were documented in controls and experimental subjects based upon the questionnaire as follows: disease condition, disease duration, age, food habits, lifestyle factors, obesity, diabetes, hypertension and cardiovascular risk. In the present study, 65 PCOS samples and 65 control samples were collected. Koivunen et al[22]

reported that the occurrence of PCOS is more widespread among women younger than 36 years.

According to the current study, 75.61% of PCOS women were overweight or obese. This was consistent with the research carried out by Essah et al[11]. Menstrual irregularity was the most prevalent among all patients and the prevalence of the various menstrual cycle patterns did not differ between obese and lean women, the occurrence of menstrual irregularity was rarely defined by anthropometric results. Liou et al[24], Panidis et al[31] and Boumosleh et al[5] have already demonstrated it. The second most frequent presenting ailment in our study was infertility which affected 26 (86.67%) of the obese women and 27 (90%) of the slim women. Since women from lower socioeconomic strata sought treatment for infertility rather than PCOS symptoms, the prevalence of infertility was high in our study. PCOS increases serious complications in females' health. One in five to six women is dealing with severe issues related to irregular menstruation periods and infertility.

The main causes globally are hormone imbalance, stress and obesity[6]. Heterogeneity in erythrocyte size is measured by the red blood cell distribution width or RDW. Increased variance in red blood cell volumes is suggested by higher RDW readings. RDW has long been used in anemia differential diagnosis. Furthermore, metabolic syndrome and cardiovascular disease are linked to increased RDW[43,46]. In the present study, RBC level was estimated in controls and experimental subjects. The RBC level was significantly varied in experimental compared to controls. White blood cell count (WBC) level has been recognized as a predictive marker of cardiovascular events[40]. In contrast to normal, healthy women, WBC was consistently shown to be higher in PCOS-afflicted women.

Leucocytosis is an inherent feature of the disease or a byproduct of its metabolic features[19,37]. In the current study, WBC level was evaluated in controls and experimental subjects, the WBC was significantly elevated in higher-aged experimental subjects when compared to controls. Women with PCOS have been found to have elevated levels of chronic inflammatory markers like WBC and CRP[35]. Females aged 18 to 44 are affected by this endocrine condition[41]. Five to fifteen percent of women worldwide are affected[2]. There are many different clinical, biochemical and ovarian morphological characteristics of PCOS condition[42]. With a variety of genetic, endocrine, metabolic and environmental problems, PCOS is regarded as a multifactorial illness[12]. Although the exact cause of PCOS is unknown, nutritional and lifestyle variables like obesity and insulin resistance as well as hereditary components have been found[7].

By sonography, polycystic ovaries are significantly more prevalent in women aged 35 and under (21.6%) than in those over 36[22]. PCOS patients produced more LH[21]. PCOS was reported to have elevated LH levels[28]. Granulosa cells express LH and progesterone, which raises androgen levels and lowers estrogen levels[25]. PCOS patients may show LH elevated, LH/FSH ratio increased women with PCOS are at risk for weight gain[23,26].

The present study was undertaken with the associated significant hormonal analysis like LH and FSH in PCOS patients. All the age (<30) group of PCOS subjects had significantly elevated levels of LH and FSH compared to controls and reference range.

Recent studies indicated the importance of FSH and LH hormone values and it significantly high in PCOS subjects[44]. In the present study, FSH and LH level was quite elevated in PCOS as compared to healthy control individuals. Raised LH level leads to an increase in androgen levels that raise the progression of PCOS[1].

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