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Research Article

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Clinical Manifestation of Polycystic Ovarian Syndrome and its Correlation with Thyroid Stimulating Hormone: A Preliminary Observational Study in Eastern India

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ABSTRACT

Background : Polycystic ovary syndrome (PCOS) affects 4 to 20% of women in their reproductive age. In younger life PCOS is asymptomatic; however, as the disease progresses, irregular menstruation, hyperandrogenism, and infertility are the eventual outcomes. The aim of this study was to detect PCOS in a relatively young population and find out its correlation with thyroid function.

Methods : A case-controlled observational study was conducted between PCOS (N=17) vs. normal control (N=17) in hospital set up. A through clinical examination, blood examinations (CBC, glucose, TSH, iron, estrogen) and imaging of lower abdomen by ultrasonography (USG) was conducted in all enrolled participants. The PCOS were confirmed according to Rotterdam Consensus Criteria.

Results : The mean age of control women was 23.64 yrs and PCOS was 23.23 yrs. The first menarche age was significantly lowered in PCOS group ($p<0.001$) and all PCOS participants had irregular periods. Only 29.41% PCOS participants crossed the borderline of normal BMI towards obesity. Hypertensions were not observed in any participants. Significant high difference in blood haemoglobin ($p<0.001$), TSH (<0.001) and estrogen (<0.001) was resulted in PCOS. Furthermore, inverse correlations between TSH, BMI and estrogen were reported.

Conclusion : The current investigation found a strong link between polycystic ovarian syndrome and subclinical hypothyroidism. Therefore, in order to limit or treat PCOS-related health issues, patients should undergo a thyroid profile screening.

Keywords: PCOS; menstrual cycle; TSH; estrogen; obesity

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most frequently reported hormonal and metabolic disorders in women during reproductive age. Although the etiopathology of PCOS is still unknown, accumulating evidence suggests that it is a multi-gene disorder with significant environmental and epigenetic influences, including lifestyle and diet factors. Menstrual irregularities and reproductive dysfunction leading to female infertility are the most commonly reported signs of PCOS.[1-2] According to the recent report, it affects 4%–20% of women of reproductive age worldwide.[3] Between 6% and 9% of females in the US, UK, Spain, Greece, and Australia have been reported to have PCOS.[4] There were 1.55 million PCOS incidents recorded worldwide in 2017 among women aged 15-49, which is a 4.47% rise from 2007. Conversely, from 2007-2017, there were 0.43 million DALYs globally among women of reproductive age as a result of PCOS, representing a 12.08% increase.2 In 2020, the prevalence of PCOS in China was 7.8% overall, resulting in an estimated 24 million women of their reproductive age suffering from this disorder.[5] In India, the pooled estimates of PCOS prevalence based on Rotterdam's criteria are 11.34%.[6] Rotterdam's criteria of PCOS define the presence of any two of the following conditions: (i) oligomenorrhea/anovulation, (ii) clinical/ biochemical hyperandrogenism and (iii) polycystic ovaries (≥12 follicles in each ovary measuring 2-9 mm).[7] Androgen Excess Society (AES) established the AES criteria, which included polycystic ovaries or oligo/anovulation in addition to clinical and biochemical hyperandrogenism.[8] Although, International Guidelines for PCOS accepted the Rotterdam's criteria for diagnosis purpose of PCOS.[9] In recent years, trans-vaginal and/or trans-abdominal ultrasonography (USG) has emerged as the most widely utilized diagnostic approach for PCOS detection. Although there isn't a consensus on the USG criteria for diagnosing polycystic ovaries, it is generally believed that the condition is characterized by an increase in ovarian size (volume) owing to a higher number of follicles and a larger stoma volume when compared to normal ovaries.[10-12]

The symptoms of PCOS-affected women vary greatly throughout their lives. So, there are several challenges in the execution of the diagnostic standardization approach. Hence, physical, biochemical, and radiological aspects as well as medical history provide corroborated evidence of PCOS. Moreover, geographical discrepancies in the prevalence rate of PCOS could be due to differences in diagnostic assessment criteria, socio-economic condition, risk factors, education and awareness.[1,13] Thus, it has become comprehensible that PCOS patients need better clinical and diagnostic care.

Recent research indicates that metabolic dysfunction, type 2 diabetes, insulin resistance, obesity, and hypertension have all been closely linked to PCOS.[14-15] Moreover, numerous studies have indicated that PCOS patients have a higher frequency of thyroid issues.[16-17]Although the pathophysiological grounds behind the thyroid function and obesity remain unknown, there is sufficient data to suggest that individuals with high body mass index (BMI) have higher thyroid stimulating hormonal (TSH) function.[18-19] But, the consequences of thyroid autoimmunity or subclinical hypothyroidism in PCOS remain unclear. Furthermore, the correlation between haemoglobin and white blood cells with PCOS has been emphasised.[20-21]

Despite PCOS being a common condition and carrying a high morbidity risk, the syndrome often remains underdiagnosed. But unfortunately, there is very little or no reliable information about the prevalence of also other correlations of PCOS in the eastern India.[22-23] (Chakraborty 2013; Mitra 2016). Hence, the goal of this hospital-based observational study was to detect PCOS in relatively young population in Kolkata, India, and find out any associations with subclinical hypothyroidism.

MATERIALS AND METHODS

The present case-controlled observational study was conducted to compare PCOS to normal control from August 2019 to February 2020 at the J.B. Roy State Ayurvedic Medical College & Hospital's Research Unit in Kolkata, India. The main goal of the study was to diagnose young Indian women with PCOS and determine whether there was any correlation between the hormonal and other factors. The target sample consisted of young, unmarried women who expressed concerns about their menstrual cycles or reproductive health in general. The Institutional ethics committee approved the study plan (JBR/ RU/CT-13/19 June 4, 2019). The age between 18 to 30 years, with the readiness to provide written informed consent and adhere to study-related protocols were the selection criteria for the freshly

diagnosed female volunteers. Diabetes, pregnancy, advanced or poorly managed thyroidisms and a history of PCOS were the exclusion criteria.

A comprehensive clinical examination, complete blood count, and biochemical estimations of fasting glucose, TSH, iron, and estrogen were performed on total 34 young participants. Additionally, they were screened for PCOS using digital ultrasonography (USG) of the lower abdomen and reproductive organs. The biochemical and hormonal parameters were estimated by chemiluminescence and blood cells were determined by automated cell counter equipment within 2 hours of blood collection and USG concluded the next morning. The blood samples (~5 ml) were collected between 2-4 days of menstrual cycle in 8-10 h fasting condition. The Rotterdam Consensus Criteria were followed in the clinical diagnosis of PCOS in the participants.[24]

The mean and standard deviation values were presented for all continuous variables, whereas number and percentage values were used for categorical variables. The comparison between the two groups was done using 95% confidence interval of the difference and t-test. Pearson's correlation was used to examine the associations between categorical variables. Data analyses were performed on SPSS version 20 (SPSS Inc., Chicago, USA) and the significance level was set at 0.05.

RESULTS

A total of 34 young women were enrolled in the study and were divided into two groups: normal control and PCOS, according to the Rotterdam Consensus Criteria for USG. Of these, 17 women (or 50%) had normal (non-PCOS), and the remaining participants had PCOS (Fig. I). The mean age of the two groups of participants was comparable. Compared to normal, the first menarche age was significantly lower ($p<0.001$) in PCOS. All PCOS patients, but only 4 (23.5%) in normal women, had irregular menstruation. USG showed significant changes in the uterine and endometrial length and thickness, along with a greater number of follicles in both ovaries in PCOS patients. Despite 29.41% of PCOS patients crossing the normal BMI boundary into obesity, it did not significantly differ from the control. The peripheral blood pressures were within the normal range, and no hypertension cases were reported for any of the participants (Table I).

There was a substantial difference in blood haemoglobin ($p<0.001$), TSH (<0.001), and estrogen (<0.001) levels between the two groups. Compared to normal participants, the haemoglobin (Hb g%) was lower in PCOS women, as 29.78% and 88.23% of them, respectively, had anaemia (Hb < 12 g/dl). Furthermore, PCOS had 1.5 times higher TSH and 65.69% lower estrogen in blood than control. Blood iron levels were 15.79% lower in PCOS than in the normal, however the difference was not significant (Table I).

Table 1. Clinical, biochemical and hormonal data of young female participants

Parameters	Control (N=17) Mean ± SD	PCOS (N=17) Mean ± SD	% difference	95% Confidence Interval of the difference		P value
				Lower	Upper	
Age (yrs)	23.64±2.89	23.23±2.53	-1.73	-1.4778	2.3014	0.650
Menarche age (yrs)	12.55±1.19	10.71±1.16	-14.66	0.9356	2.9421	<0.001
BMI (kg/m2)	21.08±3.67	21.41±3.25	1.57	-2.4809	1.8338	0.755
BP Systole (mmHg)	110.94±10.02	107.29±7.80	-3.29	-1.8694	9.1635	0.080
BP Diastole (mmHg)	71.88±6.46	68.47±5.22	-4.74	0.2472	6.5763	0.063
Fasting glucose (mg/dl)	87.82±7.23	90.68±6.67	3.26	-7.2752	1.5576	0.189
Iron (µg/dl)	78.52±36.02	66.12±10.31	-15.79	-19.7313	44.5290	0.452
Hb (g/dl)	15.58±0.52	10.94±1.44	-29.78	0.7900	2.4805	<0.001
TSH (µIU/dl)	1.86±0.72	4.97±1.80	167.20	-4.0835	-2.1293	<0.001
Estrogen (pg/ml)	193.12±79.60	66.25±31.84	-65.69	83.6113	170.1474	<0.001

Table 2. Pearson's correlations between variables of PCOS participants

Pearson Correlation	BMI	Hb	Iron	Glucose	TSH	Estrogen
BMI	1	0.343	0.556*	0.585*	-0.123	0.066
Hb		1	0.313	0.405	0.433	-0.132
Iron			1	-.009	0.496*	-0.234
Glucose				1	-0.135	-0.001
TSH					1	-0.238
Estrogen						1

Additionally, Pearson's correlations between variables (BMI, Hb, iron, glucose, TSH, and estrogen) of PCOS were identified (Table II). It was noted that BMI was significantly correlated with iron, glucose, and TSH. Moreover, there was an inverse relationship between glucose, TSH and estrogen; however, this relationship was not statistically significant. The relationships between TSH and other factors in PCOS are shown in Fig. 1 as dot curves. The substantial regression correlations between TSH, BMI, Hb, iron, and estrogen were demonstrated by the dot curves.

DISCUSSION

The hallmark features of polycystic ovaries are anovulation and hyperandrogenism, which are not always present in all PCOS patients. The

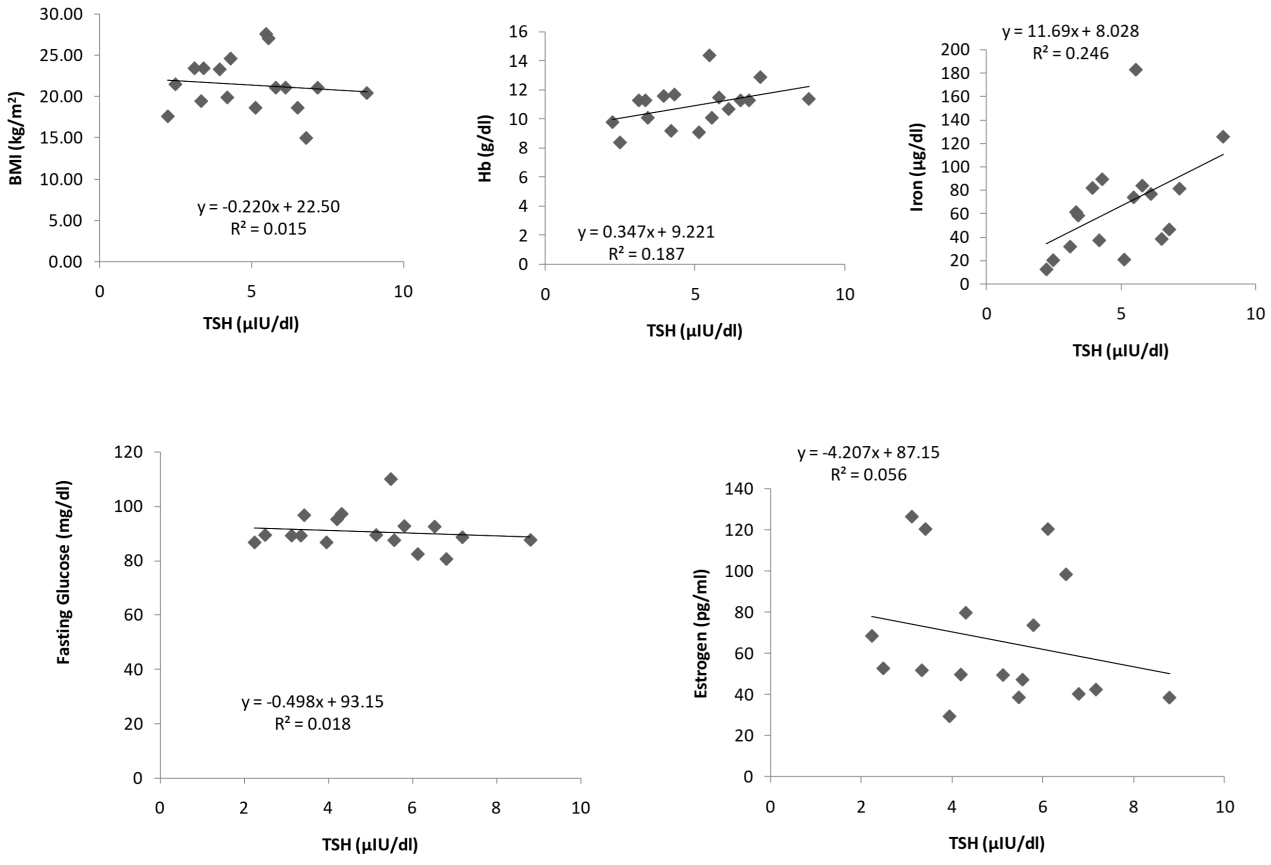

Figure 1: Correlations of TSH with other variables in PCOS participants

syndrome is characterized by multiple gynecologic, metabolic and psychological aberrations, including depression, anxiety, sexual dysfunction, and social problems that affect a woman's identity and health-related quality of life. It is one of the leading causes for infertility. The most common comorbidities are diabetes, hypertension and obesity. The outstanding complexity of its characteristics and the inadequate diagnostic criteria are the most difficult parts of this disease to deal with. By reducing comorbidities and enhancing quality of life, early deployment of specific therapeutic techniques will only improve overall PCOS management.[1,5,24]

The goal of the current study was to diagnose PCOS in relatively young women with their reproductive age, who showed symptoms but were unaware of the condition. Earlier studies in Kolkata reported that only 10% of the PCOS patients were found to be obese.[23] Another study reported approximately 28% of the college students were at high risk of developing PCOS and 55.6% were obese.25 A recent study in Nepal reported 78% of the PCOS patients had oligomenorrhoea and 22% were obese.[26] In the present study, only 29.4% of PCOS patients were crossing the normal BMI boundary into obesity. The notion of obesity and the manifestation of hyperandrogenism in PCOS are not compatible. Nonetheless, the similarities between type-2 diabetes and insulin resistance can be attributed to PCOS-related obesity.[15,18] The PCOS participants in this study were quite young, with a mean age of less than 25 years. It implies that co-morbid ailments such as obesity, diabetes, and hypertension might become more prominent in old age.

Several studies are ongoing on the relationship between haematological markers and PCOS. Neutrophilia may be one of the predictors of PCOS and provide insight into disease-specific inflammation.[20] Moreover, a recent study found a correlation between the haemoglobin level and markers of glucose metabolism and BMI in PCOS (Ha, 2023).[21] In the present study, haemoglobin level was significantly lower in PCOS women with iron deficiency anaemia. A further study reported there is doubtful to be any significant variation in hematological indices in PCOS.[27]

Clinical and experimental evidences exhibited estrogen is an endometrial marker in PCOS. Women with PCOS have a nearly 3 times higher risk for developing endometrial cancer. The association between PCOS and endometrial cancer involves prolonged endometrial exposure to unopposed estrogen by cyclic progesterone due to anovulation.[28-29] Changes in estrogen receptor signalling pathways affect cellular activities, like ovulation, proliferation, migration and invasion.30 In the endometrium, progesterone decreases estrogenic activity by promoting the local production of 17β-hydroxysteroid dehydrogenase, which converts estradiol to inactive estrone.[31-32] Our research supports the theory that progesterone converts more quickly to estrogen or androgen and shown a significant drop in blood estrogen levels in PCOS patients. However, other research found that PCOS patients had higher estradiol levels, which contradicted the current finding.[33-34]

PCOS and thyroid disorders are the most common endocrine disorders in the world. The prevalence of hypothyroidism in India is 11%, while PCOS is 11.3%.[6,35] In recent years, a number of publications have reported increased incidence of thyroid disorders in females with PCOS. Sinha and her co-workers reported a higher prevalence of goiter and subclinical hypothyroidism in PCOS.[16] However, there is still no clear report of how hypothyroidism can lead to polycystic morphology of the ovaries. The implications of subclinical hypothyroidism or thyroid autoimmunity in patients with PCOS are inconclusive.[19] On the other hand, thyroid hormone replacement therapy in PCOS also leads to a reduction in serum androgen as well as an improvement in the appearance of the polycystic ovaries.[36] Hypothyroidism and PCOS coexistence may exacerbate metabolic changes in comparison to disturbances present in the single disease. In fact, women suffering from both PCOS and hypothyroidism had higher values of BMI, fasting glucose and HOMA-IR index compared to women with hypothyroidism only or a control group.[37-38] In our study, TSH levels were considerably higher in PCOS and indicated the co-existence of subclinical hypothyroidism in comparatively young women in eastern India. Moreover, a significant inverse correlation was also observed in between TSH with hyperglycaemia and estrogen in PCOS. Thyroid profile is therefore thought to be one of the key diagnostic markers in PCOS treatment management and early identification. Although, to support the current observation, more research with larger samples and more variables are needed.

CONCLUSION

The current study unequivocally showed that thyroid and estrogen hormones are important factors in the majority of PCOS patients and these indications should be identified prior to contemplating PCOS treatment options.

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Nil

CONFLICT OF INTEREST

None.

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