Thyroid Disorders in Polycystic Ovarian Syndrome and It's Association with Clinical and Biochemical Parameters

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Abstract

Background: Poly-Cystic Ovarian Syndrome (PCOS) is a common endocrine disorder which causes anovulatory female infertility. Thyroid dysfunction can lead to subtle change in ovulation and endometrial receptivity which may have profound effect on fertility. Objective of the study is to evaluate thyroid function in woman with PCOS to find out the frequency of thyroid disorders using TSH, FT_3, FT_4 in PCOS patients and to see association of altered thyroid function with clinical, hormonal and ultrasonogram features.

Materials and methods: This cross-sectional study was conducted in the Department of Obstetrics and Gynecology, Institute of Child and Mother Health (ICMH) Dhaka and Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka between May 2018 and February 2019. A total of 100 patients in reproductive age group (Aged between 20 and 40 years) attending theOutpatient Department (OPD) who were diagnosed as PCOS were included in this study. Among them 21 PCOS with normal thyroid function was considered as group I and 79 PCOS with abnormal thyroid function was considered as group II.All the cases of PCOS were subjected to investigations like FSH, LH, Serum Prolactin, TSH, Free T3, Free T4.

Results: A total of 100 patients were included in this study. It was found that 3/4 patients had euthyroid and 18% had subclinical hypothyroidism, 86% patients were Oligomenorrhea, 70% had primary sub fertility, 53% had hirsutism, 25% had secondary sub fertility.

Conclusion: Most of the Polycystic ovary syndrome patients belonged to age between 25 and 30 years. Oligomenorrhea, primary subfertility and hirsutism are the most common presenting complains. Hypothyroidism found in 20.0% of the women with PCOS.

Key words: PCOS; Female infertility; Thyroid disorder.

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Introduction

Poly-Cystic Ovarian Syndrome is a common endocrine disorder affecting 5-10% of reproductive age women. It is a common cause of anovulatory female infertility.[1] Globally its prevalence is increasing. PCOS was originally described by Stein IF and Leventhal ML in 1935.[2] Polycystic ovary syndrome (Also known as polycystic ovarian syndrome) was previously known as "Polycystic Ovary Disease" (PCOD) and even before that as "Stein-Leventhal syndrome.[3] Currently revised Rotterdam 2003 criteria is used for diagnosis of PCOS. According to this, PCOS is diagnosed by two of the following three features: i) oligomenorrhoea or anovulation ii) clinical and/or biochemical signs of hyperandrogenism iii) polycystic ovaries on ultrasound.[4]

The PCOS is a heterogenous collection of signs and symptoms that constitute a spectrum of disorder with mild presentation in some, but a severe disturbance of reproduction, endocrine and metabolic function in others. During adolescence she may present with menstrual irregularities, hirsutism, acne, alopecia, obesity, acanthosis nigricans. During reproductive years she may present with infertility. In later part of life, she may present with long term consequences like - gynecological cancer, diabetes or cardiovascular risk.[5] Etiology of PCOS is still inconclusive due to its complexity. The risk factors for PCOS including menstrual cycle disorder, family history of diabetes, family history of infertility and lack of physical exercise.[6] Thyroid gland is a butterfly – shaped gland at base of the neck weighing only about 20 grams, However the hormones it secrets are essential for the growth and metabolism. The gland is a regulator of all body functions.[7]

Dysfunction and anatomic abnormalities of the thyroid are among the most common diseases of the endocrine gland. Early stages of thyroid dysfunction can lead to subtle change in ovulation and endometrial receptivity, which may have profound effect on fertility.[8] Recently a publication has reported increased incidence of hypothyroidism especially subclinical hypothyroidism in female with PCOS.[9] Subclinical hypothyroidism poses increased risk of cardiovascular disorder in PCOS.[10]

This current study is done to evaluate thyroid function in woman with PCOS to assess the socio demographic features of study population, to evaluate clinical profile and hormonal profile and USG feature of PCOS patients, to find out the frequency of thyroid disorders using TSH, FT_3, FT_4in PCOS patients and to see association of altered thyroid function with clinical, hormonal & ultrasonogram features.

Materials and methods

This study was conducted in the Department of Obstetrics and Gynecology, Institute of Child and Mother Health (ICMH) Dhaka and Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka between May 2018 and February 2019. Ethical clearance for the study was taken from the Institutional Review Board, ICMH. A total of 100 patients in reproductive age attending OPD who were diagnosed as PCOS (2 of 3 revised Rotterdam's criteria) aged between 20 and 40 years were included in this study. Among them 21, PCOS with normal thyroid function considered as group I and 79, PCOS with abnormal thyroid function was considered as group II. Known case of hypothyroidism or hyperthyroidism, history of thyroidectomy operation, patients who suffered from chronic or acute disease such as renal, liver or cardiac disease were excluded from this study. Purposive sampling was done according to the availability of the participants, who had voluntarily joined this study. Weight, height, waist circumference, hip circumference, blood pressure measured. BMI and waist to hip ratio were calculated. BMI 25 kg/m or more considered as increased BMI. Waist: Hip ratio 0.88 or more considered as increased waist: hip ratio. From Ultrasonogram of pelvic organ (Preferably TVS), Ovarian volume in cc (0.523 x length x width x thickness) and polycystic appearance of ovary were noted. All the cases of PCOS were subjected to investigations like FSH, LH, Serum Prolactin, TSH, Free T_3, Free T_4. Blood sample was taken on day 2 of the menstrual cycle or on day 2 of the progesterone induced withdrawal bleeding (in amenorrheic women). LH: FSH ratio was calculated. TSH normal range was taken as 0.34-4.25 μIU/ml, Free T_3 normal range was 2.4-4.2 pg/ml, free T_4 normal range was 0.8-1.7 ng/dl. TSH above 4.25 μIU/ml, Free T_3 below 2.4 pg/ml and Free T_4 below 0.8 ng/dl was considered as overt hypothyroidism, high TSH with normal Free T_3 and Free T_4 are considered as subclinical hypothyroidism and TSH level below 0.34 μIU/ml considered as hyperthyroidism.[11] Serum prolactin level >25 ng/ml will be considered as raised prolactin level or Hyperprolactinemia.[4] Statistical analysis of the results was performed by using window-based computer software devised with statistical package for the social sciences (SPSS-22). Chi-square (χ^2) tests for qualitative variables and unpaired 't' test for quantitative variable was used. A p value <0.05 was considered as statistically significant.

Results

Table I Proportion of thyroid disorders in study populations (n=100)

Thyroid disorders	Frequency	Percentage
Abnormal thyroid function	21	21.0
Subclinical Hypothyroidism	18	18.0
Overt Hypothyroidism	2	2.0
Hyperthyroidism	1	1.0
Normal thyroid function	79	79.0

Table I shows more than three fourth patients had euthyroid and 18% had subclinical hypothyroidism.

Presenting complaints in majority (86%) patients were Oligomenorrhea, 70% had primary sub fertility, 53% had hirsutism, 25% had secondary subfertility, 11% developed amenorrhea and 6% had acne.

Table II Comparison of patientparameters between PCOS with normal and PCOS with abnormal thyroid function (n=100)

Patient parameters	Group I (n=19) Mean±SD/%	Group II (n=79) Mean±SD/%	p value
Age (In years)	25.71±3.8	26.04±3.82	a0.736ns
Weight (kg)	71.76±10.41	62.08±8.86	a0.001s
Height (cm)	153.14±5.01	152.26±4.72	a0.473ns
BMI (kg/m2)	30.28±3.9	26.68±4.41	a0.001s
Waist Circumference (cm)	99.5±8.2	90.46±5.98	a0.001s
Hip Circumference (cm)	103.52±6.79	100.18±5.95	a0.035s
Waist: Hip Ratio	0.96±0.05	0.89±0.1	a0.003s
Systolic BP (mm of Hg)	127.62±11.13	113.23±8.62	a0.001s
Diastolic BP (mm of Hg)	83.1±8.44	73.86±6.98	a0.001s
Hyperandrogenism (%)	80.9% (n=17)	53.2% (n=42)	b0.042s
Acanthosis Nigricans (%)	76.2% (n=16)	48.1% (n=38)	b0.021s
USG Features			
Morphology			
PCO morphology	19(90.5%)	54(68.4%)	a0.042s
Normal ovary	2(9.5%)	25(31.6%)	
Mean ovary volume (cc) (Mean±SD)	15.05±2.67	11.53±2.18	b0.001s

Table II shows the comparison of clinical parameter between PCOS with normal and PCOS with abnormal thyroid function. The difference of weight, BMI, waist circumference, hip circumference, waist: hip ratio, SBP, DBP, amenorrhea, hyperandrogenism, acanthosis nigricans, on USG PCO morphology and Mean ovary volume (cc) were statistically significant ($p<0.05$) between two groups.

Table III Distribution of the study patients according to BMI (n=100)

BMI (kg/m2)	Group I (n=21) n	%	Group II (n=79) n	%	p value
Normal range (18.5-24.9)	0	0.0	22	27.8	
Overweight (25-29.9)	6	28.6	40	50.6	0.001s
Obese I (30-34.9)	13	61.9	15	19.0	
Obese II (35-39.9)	2	9.5	2	2.5	

Table III shows that almost two third (61.9%) patients belonged to BMI obese I (30-34.9 kg/m²) in group I and 15(19.0%) in group II. The difference was statistically significant ($p<0.05$) higher in group I.

Table IV Comparison of hormonal parameter between PCOS with normal thyroid function and PCOS with abnormal thyroid function (n=100)

Hormonal parameter	Group I (n=21) Mean±SD/n%		Group II (n=79) Mean±SD/n%		p value
FSH (D2) mIU/mL	5.2±1.1		5.5±1.7		a0.464ns
LH (D2) mIU/mL	8.3±4.1		10.1±5.9		a0.198ns
LH: FSH Ratio	1.52±0.67		1.9±0.98		a0.097ns
<2:1	4	19.0%	13	16.5%	b0.778ns
ε2:1	17	81.0%	66	83.5%	
S. Prolactin (ng/ml)	20.18 ±23.48		13.85±8.08		a0.047s
2-25	16	76.2%	70	88.6%	b0.145ns
>25	5	23.8%	9	11.4%	

Table IV shows the comparison of hormonal parameter between PCOS with normal thyroid function and PCOS with abnormal thyroid function. The difference of S. Prolactin mean was significantly ($p<0.05$) higher in group I.

Discussion

In this study a total of 100 diagnosed case of PCOS aged between 20 and 40 years were included in this study. 79% patients were euthyroid,whereas18% had subclinical hypothyroidism, 2% had overt hypothyroidism and 1% had hyperthyroidism. A study done by Enzevaei and colleagues in Iran, have observed 25.5% of subjects having hypothyroidism, while in another study conducted by Sinha and colleague in Indian population revealed 22.5% subjects with PCOS were detected to be having subclinical hypothyroidism.[12,8] The pathogenesis of hypothyroidism and PCOS is completely different. But these two entities have many features in common.[13] This study reveals 86% patients had Oligomenorrhea, 70% had primary sub fertility, 53% had hirsutism, 25% had secondary subfertility, 11% developed amenorrhea and 6% had acne. The most commonly associated clinical abnormalities are hyperandrogenism, oligomenorrhea and polycystic ovaries.[12] Similar observations regarding the clinical presentations were also observed by studies conducted by Ramanand and colleagues, Khanam and colleagues and Nanda and colleagues.[14,15,11] In this study, the mean height difference was not statistically significant ($p<0.05$) between two groups, whereasweight was significantly ($p<0.05$) higher in hypothyroidism. Similarly, a study conducted by Ramanand and colleagues found the

mean weight was higher in hypothyroid PCOS women, where they found the mean weight of euthyroid and hypothyroid PCOS women was 63.74±16.67 kg and 70.61±16.58 kg respectively.[14] This study revealed the difference of the mean BMI was statistically significant ($p<0.05$) between two groups, which indicates that overweight significantly associated with hypothyroidism. A similar study conducted by Ramanand and colleagues showed that BMI of hypothyroid PCOS women was significantly more than euthyroid PCOS group.[14] In another study conducted by Zainab and colleagues mentioned that the increase of' BMI in PCOS is obvious in the majority of cases.[16] In this study, the mean waist circumference,the mean hip circumference and the mean waist: hip was statistically significant ($p<0.05$) between two groups. This is comparable with Genie and colleagues.[17] In this current study the mean systolic and diastolic blood pressure were significantly ($p<0.05$) higher in group I. In this current study, it was observed that hyperandrogenism was significantly ($p<0.05$) higher in group I. Acanthosis nigricans in PCOS is attributed to insulin resistance. Hypothyroidism can be added to the list of endocrine diseases associated with acanthosis nigricans. This is unlikely to be a direct effect of the hypothyroid state, but may instead be an indirect action mediated through obesity and subsequent insulin resistance.[14] In this present study, Acanthosis Nigricans was significantly ($p<0.05$) more common in group I. Similarly, a study conducted by Ramanand found acanthosis nigricans in 55.56% in hypothyroid PCOS and 42.16% patients in Euthyroid.[14] Similar observations also observed by Mustari and colleagues.[4] In this present study, it was observed that PCO morphology was significantly ($p<0.05$) higher in group I. Prolactin contributes toward polycystic ovarian morphology by inhibiting ovulation as a result of the change in the ratio of Follicle Stimulating hormone (FSH) and luteinizing hormone and increased dehydroepiandrosterone from the adrenal gland.[18] In this current study, the mean ovary volume was found significantly ($p<0.05$) enlarged in group I. Singla and colleagues conducted a study which found all women with primary hypothyroidism had significantly higher ovarian volumes and cystic changes in ovaries.[18] In this study it was observed that 76.2% patients had Oligomenorrhea in group I and 88.6% in group II, which showed no significant association between two groups. Polycystic Ovary Syndrome (PCOS) is a common cause of amenorrhea in women with evidence of androgen excess. In this present study, amenorrhea was significantly ($p<0.05$) higher in group I.Khanam conducted a study showed that majority (80.0%) of women had menstrual irregularities.[15] The clinical consequence of chronic anovulation is some form of menstrual irregularities like oligomenorrhoea, amenorrhea or dysfunctional uterine bleeding. Similar observations regarding menstrual irregularities were also observed by a study conducted by Mustari and colleagues.[4] In this current study, it was observed that 61.9% patients belonged to BMI obese I in group I and 19.0% in group II. The difference of Amenorrhea was statistically significant ($p<0.05$) higher in group I. The study conducted by Mustari and colleagues also showed hypothyroidism was significantly higher among the patients having BMI >25 kg/m^2 than those of have 25 kg/m^2.[4] Similar observations regarding the increased BMI (overweight and obese) were also observed by studies conducted by Zainab, Ramanand and Khanam.[16,14,15] The mean FSH was 5.2±1.1 (D2) in group I and 5.5±1.7 (D2) in group II. The difference was statistically not significant ($p>0.05$) between two groups. Ramanand and colleagues found the mean FSH was 5.70±1.80 Iu/L in euthyroid PCOS and 5.32±1.54 Iu/L in hypothyroid PCOS.[14] The difference was statistically not significant ($p>0.05$) between two groups which supports the present study. The difference of mean LH was statistically not significant ($p>0.05$) between two groups. The traditional belief is that obesity plays a serious role in the pathophysiology of PCOS, but not all PCOS women are obese. Moreover, not every woman with PCOS has an abnormal LH/FSH ratio and hormonal and biochemical changes suggestive of this disease. The mean LH: FSH ratio was 1.52±0.67 in group I and 1.9±0.98 in group II, that is almost alike between two group, no statistical significant ($p>0.05$) difference was observed between two groups, which is closely resembled with the study conducted by Ramanand and colleagues.[14] The difference was insignificantly

less in hypothyroid PCOS women and without hypothyroidism women. LH/FSH ratio is one of the characteristic attributes of PCOS women. In this current study, it was observed that 81% patients belonged to LH/FSH Ratio >2.1 in group I and 83.5% in group II and the difference was not statistically significant between two groups. The study conducted by Nath and colleagues found elevated LH/FSH ratio in 70.58% of the studied PCOS women and authors also mentioned that the high LH/FSH ratio with PCOS is still significant and may add more to the disease mystery.[19] Prolactin level was significantly ($p<0.05$) elevated in group I. In this present study, it was observed that 23.8% patients belonged to S. Prolactin >25 ng/ml in group I and 11.4% in group II. The difference was statistically not significant ($p>0.05$) between two groups.

Limitation

The present study was conducted within a short period of time with study population selected from two hospitals in Dhaka city. So, the results may not reflect the exact picture of the country. Small sample size with purposive sampling was also a limitation of the present study.

Conclusion

Most of the Polycystic Ovary Syndrome patients belonged to age 25-30 years. Oligomenorrhea, primary subfertility and hirsutism are the most common presenting complains. Hypothyroidism found in 20.0% of the women with PCOS. Increased weight, increased BMI, waist and hip circumference, waist/hip ratio, SBP, DBP, amenorrhea, hyperandrogenism, and acanthosis nigricans, elevated level of Serum Prolactin, TSH, decreased FT4, increased level of ovarian volume are significantly associated with in PCOS patients with hypothyroidism.

Recommendation

In future further studies with larger sample size in multiple centers with long duration may strengthen the outcome of this study results. PCOS should be offered lipid profile estimation along with all other necessary investigations to find associated metabolic syndrome and risk of CHD.

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Contribution of authors

RHS-Conception, acquisition of data, drafting & final approval.

NH-Data analysis, critical revision & final approval.

NH-Design, critical revision & final approval.

BHA-Acquisition of data, interpretation of data, drafting & final approval.

NP-Interpretation of data, drafting & final approval.

KD-Acquisition of data, data analysis, drafting & final approval.

RA-Interpretation of data, critical revision & final approval.

Disclosure

All the authors declared no conflict of interest.

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