

Newly diagnosed patients of polycystic ovary syndrome: The status of thyroid function

Dr. JN Ambika Bai

Assistant Professor, Department of Physiology, Kamineni Institute of Medical Sciences,
Narketpally, Nalgonda, Telangana, India

Corresponding Author:

Dr. JN Ambika Bai

Abstract

Aim and objective: The purpose of this study is to evaluate patients with a new diagnosis of Polycystic Ovarian Syndrome for hypothyroidism by measuring their serum thyroid stimulating hormone levels. The goal of this study is to evaluate the difference in hormone levels and other parameters between euthyroid and hypothyroid polycystic ovary syndrome patients.

Materials and Methodology: This study was designed as an observational cross-section. Women over the age of puberty who presented with menstrual abnormalities for at least three months and/or infertility were recruited from the department of physiology, Kamineni Institute of Medical Sciences, Narketpally, Nalgonda clinic for our study. We started the trial before we had ultrasound proof of polycystic ovaries. The Institutional Ethic Committee all-clears this study.

Results: Student t-test and Chi-square test were used to compare Age, BMI, WHR, FBS, PPBS, Ovarian volume, Testosterone, and HOMA-IR between the two PCOS groups. TSH, Total Testosterone, and WHR were correlated using Pearson co-efficient.

Conclusion: This hormonal discord disrupts ovarian homeostasis, which ultimately causes anovulation. The results of this study suggest that screening for hypothyroidism, along with reproductive hormone profile, should be investigated in polycystic ovary syndrome (PCOS) / infertile women to allow for early detection and treatment of the condition.

Keywords: Polycystic ovarian syndrome, thyroid function

Introduction

Menstrual problems and infertility are the leading causes of emotional and physical distress in post-pubescent women. An article in a widely read Indian magazine from 2013 reported on the results of a survey done by the World Bank that found fertility rates in the country had been falling by 17% each year since 2000 ^[1]. Yet another well-known journal study found that 10% of urban Indian couples of childbearing age are sterile. Most women who experience menstrual irregularity try to suppress the complaint until they are stigmatized as infertile ^[2]. Polycystic ovary syndrome and hypothyroidism are the most common reasons for menstruation dysfunction. The most prevalent endocrine problem in women of reproductive age is polycystic ovary syndrome, which often coexists with other metabolic abnormalities and worsens in untreated cases ^[3]. In addition to numerous ovarian cysts, PCOS is

characterised by persistent anovulation, elevated androgen levels, and elevated insulin levels. In Western populations, PCOS affects around 4-8% of young women. According to the research, 5-10% of the population in India has this condition. Patients with polycystic ovary syndrome (PCOS) may experience a wide range of symptoms, from mild acne to severe infertility, depending on how their bodies react to the androgens that are currently in circulation. The majority of these women are overweight and so at increased risk for health problems such as diabetes, dyslipidemia, metabolic syndrome, cardiovascular disease, and endometrial and cervical cancer^[4].

Another difficult condition that affects young women of reproductive age is hypothyroidism. The symptoms of hypothyroidism range from general malaise to severe infertility. Hypothyroidism was unexpectedly discovered to occur at a higher rate among the young, healthy females included as controls in investigations. This suggests that despite appearances, many apparently healthy women actually suffer from hypothyroidism^[5]. They are discovered either after complications arise or during preventative medical exams. Polycystic ovaries and/or high serum TSH were found in a retrospective study of women seeking treatment at gynaecological clinics for menstrual dysfunction or infertility. Having polycystic ovary syndrome (PCOS) and hypothyroidism both increase the risk of infertility and menstrual abnormalities when present^[6]. Costs per birth for infertile PCOS women have skyrocketed, and infertility is becoming an increasingly significant problem in India. Joint research on these conditions has revealed a strong connection between them. Hyperandrogenism is PCOS's end result, and it's worsened by hypothyroidism. In our population, screening for hypothyroidism among PCOS patients helps us better understand the prevalence of the condition and the significance of assessing the patients' thyroid function. Treatment of hypothyroidism initially in patients with both illnesses has been shown to be effective, according to a study by Sridhar *et al.* As a result of these facts and findings from different literatures, we decided to perform a cross-sectional study on the state of thyroid function in newly diagnosed PCOS patients utilizing Thyroid Stimulating Hormone as the sole and best indication of thyroid function (TSH)^[7].

Materials and Methodology

This study was designed as an observational cross-section. Women over the age of puberty who presented with menstrual abnormalities for at least three months and/or infertility were recruited from the department of physiology, Kamineni institute of medical sciences, Narketpally, Nalgonda clinic for our study. We started the trial before we had ultrasound proof of polycystic ovaries. The Institutional Ethic Committee all-clears this study.

Inclusion criteria

1. Women between the ages of 18 and 40 who experience irregular menstruation or infertility
2. Rotterdam criteria-based validation of PCOS 2003
3. A history of protracted cycles or amenorrhea (cycle lasting more than 35 days) (no cycles in the past 6 months).
4. Hyper androgenism's clinical and/or biochemical characteristics.
5. Multiple cysts (more than 12 in number, 1-2 mm) in one or both ovaries were seen during an ultra-sonogram.

Exclusion criteria

1. Individuals taking metformin, oral contraceptives, anticonvulsants, and hypothyroidism

medication.

2. A thorough physical examination and detailed history allowed for the exclusion of other disorders that resemble PCOS.

Statistical analysis

SPSS version 17 is used for statistical analysis. Using the Student t-test and the Chi-square test, we compared the two sets of PCOS patients on the following metrics: age, body mass index, waist circumference, fasting blood sugar, postprandial blood sugar, ovarian volume, testosterone and HOMA-IR (with Euthyroid and Hypothyroidism). TSH, Testosterone, Total Testosterone and WHR were correlated using Pearson's coefficient.

Table 1: The mean of all participants' physical and biochemical measurements

Parameters	Mean and Std. Dev. for all participants	Reference interval
AGE	25.00(±3.99)	
BMI	27.99(±6.02)	18.5-24.9
WAIST/HIP Ratio	0.9(±0.05)	<0.85
FBS(mg/dL)	88.80(±20.10)	70-110 mg/dL
2 HRS Post Glucose (mg/dL)	125.29(±33.99)	<140 mg/dL
Fasting Insulin (mU/L)	29.02(±38.99)	2.6-37.6 mU/L
Homa-IR	5.99(±9.20)	<2.5
TSH(mU/L)	6.10(±11.2)	0.3-5.0 mU/L
Total Testosterone (ng/dL)	54.9(±26.8)	14-76 ng/dL

In Table 1, we can see how the study population's mean values for age, body mass index, waist-to-hip ratio, fasting blood sugar, two-hour post-glucose insulin, fasting insulin sensitivity, homeostasis model assessment of insulin resistance, thyroid-stimulating hormone, and total testosterone stack up against the reference interval.

Table 2: Presentational Criteria Presentational Percentage (rotterdam criteria)

PCOS patients as per rotterdam criteria (no. of. Criteria satisfied)	Percentage (%)	Number of patients
Patients With Menstrual Irregularities and Usg-Pco (2/3)	86%	55
Patients Having Clinical F/O Hyperandrogenism, Usg-Pco (2/3 Criteria)	77%	48
Patients With Bio-Chemical Evidence of Hyperandrogenism, Usg-Pco (2/3 Criteria)	27%	17
Patients Having Menstrual Irregularities, Clinical and/Biochemical F/O Hyperandrogenism, Usg-Pco (All 3 Criteria)	61%	38

77% (48) of women were hyperandrogenic and had polycystic ovaries detected by ultrasound, 27% (17) were biochemically hyperandrogenic and had polycystic ovaries detected by ultrasound, and 86% of women had period abnormalities and USG-PCO.

Table 3: Participant complaint distribution

Presenting complaints	No. of individuals	Percentage
Oligomenorrhoea/amenorrhoea	58	85%
Acne/hirsutism	48	73%
Weight gain	43	55%
Infertility	38	65%

65% of women who came in complaining of weight gain had hirsutism.

Table 4: The age distribution of patients with PCOS

Age	No. of Individuals	Percentage
<19yrs (Adolescence)	10	12%
≥20	50	88%

Table 5: Body mass index (BMI) readings for each of the sixty participants

Body mass index (BMI)	No. of Individuals	Percentage
Under-weight <18.4	5	6%
Normal 18.5-24.9	18	27%
Overweight 25-29.9	28	38%
Obese ≥30	22	31%

Table 6: The ratio of waist to hip circumference for each participant's distribution

W/H ratio	No. of Individual	Percentage
<0.8	22	30%
>0.8	48	70%

Table 7: The state of the sixty subjects' thyroid glands

Association of hypothyroidism	No. of Individuals	Percentage
Hypothyroid PCOS (>5µu/ml)	17	23%
Euthyroid PCOS (<5µu/ml)	43	77%

Table 8: The Serum Thyroid Hormone Distribution across Age Groups

Age in Yrs	TSH<5mU/L (No. of individuals)	TSH>5mU/L (No. of individuals)	Mean TSH
15-20	14	3	3.00
21-25	27	9	7.99
26-30	21	5	5.00
31-35	5	3	3.00

Table 9: All subjects' fasting glucose (mg/dl) distribution

Glucose Level	No. of Individuals	Percentage
70-110mg/dl	53	90%
110-126mg/dl	3	4%
>126mg/dl	4	6%

Table 10: 2 hour after glucose (mg/dl) percentage distribution for all 60 individuals

Glucose Level	No. of Individuals	Percentage
<140	57	78%
141-200	12	18%
>200	4	4%

Table 11: Testosterone levels in 60 participants

Serum Testosterone (ng/dL)	No. of Individuals	Percentage
<76ng/dL	52	73%
>76ng/Dl	21	27%

Table 12: WHR comparison between groups

Mean W/H Ratio For Euthyroid PCOS	0.90	Statistically Not Significant
Mean W/H Ratio For Hypothyroid PCOS	0.80	
P Value	0.30	

This table compares the mean waist/hip ratio of two PCOS groups.

Table 13: This table compares mean Fasting Insulin in two PCOS groups

Fasting Insulin		Not Statistically Significant
Euthyroid-PCOS	25.00	
Hypothyroid-PCOS	28.00	
P-Value	0.90	

Statistically significant p value <0.05.

Table 14: Mean homa Euthyroid and hypothyroid PCOS women's IR

Mean Homa-IR		Not Statistically Significant
Euthyroid-PCOS	6.00±8.99	
Hypothyroid-PCOS	6.20±4.00	
P Value	0.89	

Statistically significant p value= <0.05.

Mean age of participants in our study was 25.00 (3.99), 86% of 60 PCOS patients met 2/3 criteria (menstrual irregularity + USG discovery) and 77% met both criteria (clinical characteristics of Hyperandrogenism and USG-PCO finding). A total of 26% of women meeting all 3 criteria (Rotterdam) had biochemical signs of Hyperandrogenism and 60% of women meeting all 3 criteria had USG-PCO (Tables 1 and 2, respectively), whereas Table 3 illustrates the percentage distribution of different presenting complaints. Eighty-seven percent of female patients appeared with menstruation problems; seventy-five percent came for infertility; 55 percent presented with acne/hirsutism; 64 percent presented with unexpected weight gain. The incidence of polycystic ovary syndrome in young adults and adults (aged 20+) is detailed in Table 4. There were 8 females (19 years old) and 65 females (20 years old) in our study. The majority of those who took part in our study were overweight or obese. 5 % were classified as underweight, 26% as normal weight, 37% as overweight, and 32% as obese, as shown in Table 5. (Clinical and morbid). The Waist to hip ratio distribution for all participants is shown in Table 6. A total of 32% (23) had a W/H ratio below 0.8, while 68% (50) were above it. Thyroid-stimulating hormone (TSH) was measured, and a cutoff level of about 5 mU/mL was used to determine each participant's thyroid-function status (Table 7). Serum TSH levels by age group are shown in Table 7. Women between the ages of 30 and 35 had a mean TSH of 2.85, whereas men between the ages of 20 and 25 had a mean of 8.22, those between the ages of 25 and 30 had a mean of 4.52, and those between the ages of 15 and 20 had a mean of 2.93. TSH levels tend to peak in one's twenties and thirties. Figure 9 shows the range of fasting blood sugar levels in the sample population. A majority (67) of the subjects had normal blood sugar levels (70-110 mg/dL), whereas 4% had fasting blood sugars (FBS) above 126 mg/dL and 2% had impaired fasting glucose. The results of all 73 individuals' glucose levels 2 hours after the study's end are shown in Table 10. 59 persons had normal blood sugar levels, 13 had impaired glucose tolerance, and 1 was diagnosed with full-blown diabetes. Table 11 shows the frequency-based segregation (FBS) and 2-hour postprandial (PP) distributions for all individuals, and Table 12 provides the complete

information. Table 13 displays the serum testosterone levels of PCOS women. Differences in body mass index, waist-to-hip ratio, fasting blood sugar, 2-hour postprandial insulin, fasting insulin, testosterone, ovarian volume, and homeostatic model assessment of insulin resistance (HOMA-IR) were displayed in Table 20. There was statistically significant correlation between body mass index, testosterone, and ovarian volume. Fasting insulin, HOMA-IR, and the waist-to-hip ratio did not differ significantly between the two groups.

Discussion

With infertility on the rise and its related morbidity, it is crucial to identify the root cause and work to alleviate it. Menstrual dysfunction is the leading cause of infertility in women, even more so than structural or hereditary issues. Polycystic ovary syndrome and systemic hormone disorders such as hypothyroidism, hyperprolactinemia and hyperinsulinemia can also play a part in this type of monthly irregularity. The risk of having an anovulation is increased due to the aforementioned variables. There are occasions when numerous manifestations happen concurrently^[8]. The most common endocrine disorders in young women of childbearing age are polycystic ovary syndrome (PCOS) and hypothyroidism. After a few months of treatment for PCOS, it is common to see menstruation and ovulation restored in some patients while continuing to be wrong in others in the gynaecology outpatient department^[9]. Unresponsive patients with infertility or monthly irregularities were found to have hypothyroidism that had been misdiagnosed or neglected. The majority of these individuals were found to have subclinical hypothyroidism, although a few were found to have overt hypothyroidism. Through screening investigations, the prevalence of hypothyroidism may be determined, and the epidemiology of the disease can be better understood. However, research comparing the thyroid health of PCOS women across all of India is very lacking. In light of this, we set out to investigate whether or not thyroid function might be predicted for PCOS patients^[10, 11].

This cross-sectional study included 60 women who had just been diagnosed with PCOS and who had sought therapy at an out-patient gynaecology and endocrinology clinic for issues with monthly regularity and fertility^[12]. Maryam *et al.* showed that women with polycystic ovarian syndrome (PCOS) have an increased risk of developing autoimmune thyroiditis and goitre. Polycystic ovarian syndrome was shown to be present in 1.04% of hypothyroid patients (2/13) by Sridhar *et al.* In our research, 22% of the patients had hypothyroidism. These findings support the correlation between thyroid dysfunction and PCOS found by Maryam *et al.* and Sridhar *et al.* the significant frequency of hypothyroidism (20.6%) among PCOS women was also found by Onno E. Janssen *et al.* According to the age distribution table and the trend of TSH in PCOS, the highest values of serum TSH were seen between the ages of 20 and 30. A significant requirement for thyroxin at this age may explain for the observed peak, as physiological hypothyroidism can be extended to include the reproductive system. Failure to meet the body's thyroxin needs can lead to subfertility and, ultimately, infertility^[13-16].

Table 1 displays the mean and confidence interval for each parameter across the sample population. This suggests that Fasting Insulin, HOMA-IR, TSH, and Testosterone levels in PCOS patients are all above average. This implies that high androgen levels, inadequate thyroid function, excess body fat and elevated insulin levels are all major risk factors for polycystic ovarian syndrome^[17, 18].

Participants were divided into two categories based on their TSH levels, with a cutoff value of 5 mU/mL. Two groups of women with PCOS were studied; one had normal thyroid function (euthyroid) and the other did not (hypothyroid)^[19]. Of the women with PCOS, 78% had normal thyroid function, while 22% were hypothyroid. Testosterone levels were significantly greater in patients with hypothyroidism compared to those of euthyroid controls. Among the hypothyroid population, we found a somewhat positive correlation between testosterone and TSH levels ($r = 0.14$)^[20]. There was no correlation between testosterone and

thyroid stimulating hormone (TSH) in the healthy thyroid (euthyroid) group. Thus, it follows that hypothyroidism contributes to the emergence of hyperandrogenism, as elevated TSH levels are linked to increased Testosterone production (polycystic ovarian syndrome). Additionally, this suggests that the preexisting hyperandrogen condition is exacerbated by the presence of hypothyroidism. The symptoms of PCOS, such as irregular periods, infertility, and the discovery of cysts via ultrasound, persist in some women despite treatment. This emphasizes the value of determining a PCOS patient's serum TSH level. Table 14 shows that there is only a slight difference (0.026) between the mean BMIs of the two groups (Group 1=27.1(5.75), Group 2=30.71(5.06)). Since thyroid hormones are required for lipid and protein metabolism, their absence causes a slowing of this activity, leading to fat and extracellular matrix deposition and obesity in hypothyroidism^[21].

Ovarian volume increases and function decreases due to collagen/cellular matrix deposition in hypothyroidism, which affects most tissues of the body. The increased risk of developing cysts on the ovaries is likely further exacerbated by thyroid disease, which leads to the increase in ovarian volume. This again emphasizes the importance of screening for hypothyroidism in women with a new diagnosis of PCOS, as well as the recommendation from 2012 by the American Thyroid Association that serum TSH alone can be used to rule out thyroid problems.

Conclusion

Polycystic Ovarian Syndrome, a poorly understood condition, requires careful treatment. This disorder's traits vary by ethnicity, therefore knowing them is important. PCOS's hypothalamus-ovary cycle causes it. Hyperandrogenism concludes. Hypothyroidism, Hyperprolactinemia and Hyperinsuliemia reduce hepatic SHBG production, causing hyperandrogenism. These causes cause hormonal imbalance, ovarian homeostasis, and ovulation. The outcome may be simple acne or complex infertility. PCOS women typically have undetected hypothyroidism, which increases Hyperandrogenism. Early detection and therapy can stop this cycle. Hyperandrogenism is caused by hypothyroidism, hence PCOS/infertile women should be screened for it along with reproductive hormones.

Conflict of Interest: None.

Funding: None.

References

1. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia*. 1985;28(7):412-9.
2. Boyle J, Teede HJ. Polycystic ovary syndrome: an update. *Australian family physician*. 2012 Oct;41(10):752-6.
3. Zagrodzki P, Krzyczkowska-Sendrakowska M, Nicol F, Wietecha-Posłuszny R, Milewicz T, Kryczyk-Kozioł J, *et al.* Selenium status parameters in patients with polycystic ovary syndrome. *Journal of Trace Elements in Medicine and Biology*. 2017 Dec;44:241-6.
4. Setji TL, Brown AJ. Polycystic ovary syndrome: update on diagnosis and treatment. *The American journal of medicine*. 2014 Oct;127(10):912-9.
5. Chang RJ, Katz SE. Diagnosis of polycystic ovary syndrome. *Endocrinology and Metabolism Clinics of North America*. 1999 Jun;28(2):397-408.
6. Williams T, Mortada R, Porter S. Diagnosis and treatment of polycystic ovary syndrome.

American family physician. 2016 Jul;94(2):106-13.

7. Adams WC, Leatham JH. Influence of hypothyroidism & chronic Gonadotropin on ovarian collagen in rat; *Endocrinology*. 1964 July;75:138-9.
8. Marrinan Greg. (20 April 2011) Imaging in polycystic ovary Disease. In Lin Eugene C. E medicine, Retrived 19 November 2011. Richard scottlucidi (25 october 2011) polycystic ovarian syndrome.
9. Sridhar GR, Nagamani G. Hypothyroidism presenting with polycystic ovary syndrome. *J Assoc Physicians India* 1993;41:88-90.
10. Ghosh S, Kabir SN, Pakrashi A, Chatterjee S, Chakravarty B. Subclinical hypothyroidism: A determinant of polycystic ovarysyndrome. *Horm Res*. 1993;39:61-6.
11. Given JR. Familial ovarian hyperthecosis: A study of two families. *Am J Obstetrics Gynaecology*. 1971;11:959.
12. Wilroy RS, Givens JR, Weser WL, *et al.*: Hyperthecosis-an inheritable form of polycystic ovarian disease. *Birth defect*. 11(5): 81; 1975Givens JR: Familial polycystic ovarian disease. *Endocrinol Metab Clin North Am*. 1988;17:1.
13. Shaw's textbook of Gynecology-13th Edition. Chapter-3. William F. Ganong-Review of medical physiology-21st Edition-chapter-23.
14. Soules MR, MC Lachlan RI, EK M, *et al.* Luteal phase deficiency: Characterization of reproductive hormone over the menstrual cycle. *J Clinical Endocrinol Metab*. 1989;69:804-12.
15. Hull MG, Savage PE, Bromham DR. Anovulatory and ovulatory infertility: results with simplified management. *Br Med J (Clin Res Ed)*. 1982 June;284(6330):1681-5. Doi: 10.1136/bmj.284.6330.1681.
16. Balen AH, Dresner M, Scott EM, Drife JO. Should obese women with polycystic ovary syndrome receive treatment for infertility? *BMJ*. 2006;332(7539):434-435.
17. Sahin M, Demircioglu D, Oguz A, Tuzun D, Sarica MA, Inanc E, *et al.* Does insulin resistance increase thyroid volume in patients with polycystic ovary syndrome? *Archives of endocrinology and metabolism*. 2016 Nov;61:145-51.
18. Goyal D, Relia P, Sehra A, Khandelwal D, Dutta D, Jain D, *et al.* Prevalence of hypothyroidism and thyroid autoimmunity in polycystic ovarian syndrome patients: A North Indian study. *Thyroid Research and Practice*. 2019 May;16(2):55.
19. Jayasena CN, Franks S. The management of patients with polycystic ovary syndrome. *Nature Reviews Endocrinology*. 2014 Oct;10(10):624-36.
20. Dahiya K, Sachdeva A, Singh V, Dahiya P, Singh R, Dhankhar R, *et al.* Reproductive hormone and thyroid hormone profile in polycystic ovarian syndrome.
21. Sinha U, Sinharay K, Saha S, Longkumer TA, Baul SN, Pal SK. Thyroid disorders in polycystic ovarian syndrome subjects: A tertiary hospital based cross-sectional study from Eastern India. *Indian journal of endocrinology and metabolism*. 2013 Mar;17(2):304.