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Original Research Article

To Determine the Association between Poly Cystic Ovary Syndrome and Thyroid Function Status in a Tertiary Care Hospital in Western Rajasthan

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Abstract

Background: Polycystic ovary syndrome (PCOS), a major and complex endocrine disorder among 5-20% women of reproductive age, is an important health issue which has not yet perceived as a serious concern of public health. Prevalence, aetiology, diagnosis, management, psychological issues, clinical practices and prevention are some most confusing aspects associated with PCOS. PCOS and thyroid dysfunction are commonly found to occur together and both disorders share some common and overlapping features. The exact nature of this link is yet to be elucidated. Both these disorders cause various metabolic, reproductive and psychological syndromes. So, the present study was aimed to determine the association of thyroid function tests in PCOS patients and also to correlate them to body mass index (BMI) and waist -hip ratio (WHR).

Methodology: In this cross-sectional study which was performed in Sardar Patel Medical College and Associated group of Hospitals, total 50 subjects were included, out of which 30 were cases (women with polycystic ovary syndrome) and 20 were controls (healthy women). Thyroid function tests which included T3, T4 and TSH were performed for both cases and controls and anthropometric measurements were done for estimating BMI, and waist hip ratio WHR in both the groups.

Results: Observations of our study show significant higher levels of TSH (3.83 ± 1.73µIU/ml ; p = 0.0005), BMI (25.11±0.57 kg/m^2 ; p = 0.0001) and WHR (0.88 ± 0.01 ; p = 0.0001) in PCOS patients than controls (TSH = 2.48 ± 0.72 µIU/ml, BMI = 23.31 ± 1.06 kg/m^2, WHR = 0.85 ± 0.02) while level of T3 and T4 was significantly lower T3 (0.88 ± 0.21ng/ml ; p = 0.03), T4 (6.58 ± 1.62 µg/dl ; p = 0.0061) in PCOS patients than Controls(T3 = 1.01 ± 0.18 ng/ml, T4 = 7.63 ± 0.93 µg/dl).

Conclusion: Based on our findings, this study demonstrates strong association of hypothyroidism in women with PCOS. It also indicates high fat distribution in PCOS patients. Females with high BMI and WHR should be educated about the complications and made aware to loose wait to improve quality of life. PCR and FISH techniques could be helpful in molecular and cell biology researches. Epigenetic studies would also be helpful for finding the nature of this syndrome. Exposure to sunlight is also essential for women with polycystic ovarian syndrome.

Keywords: Polycystic Ovary Syndrome, Thyroid Dysfunction, Body Mass Index, Waist Hip Ratio.

Introduction

Polycystic ovary syndrome (PCOS) is a heterogenous endocrinopathy among females of reproductive age involving wide spectrum of manifestations, affecting 5-20% of population worldwide. Similarly, thyroid dysfunction is frequently observed among young women. [1] Both PCOS and thyroid dysfunction share some common and overlapped characteristics, risk factors, and pathophysiological abnormalities but their etiopathogenesis is dissimilar and yet to be elucidated. [2,3] [Figure. 1]

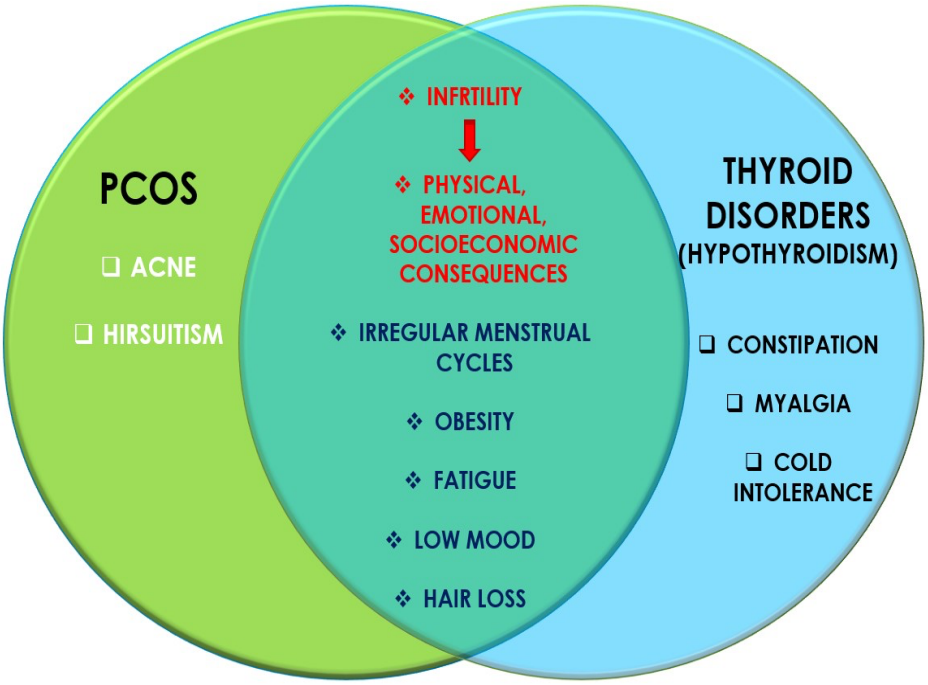
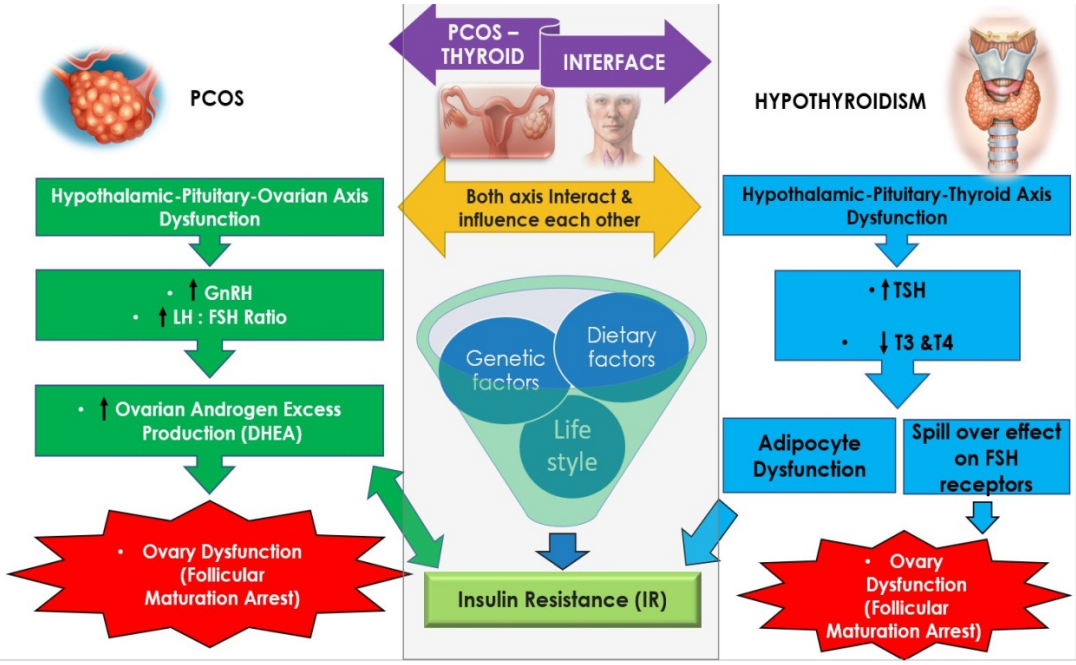


Figure 1: Overlapping clinical findings between polycystic ovary syndrome(PCOS) and subclinical hypothyroidism

However hormonal interplay in both disorders is reported in literature, the exact nature of this link is still unclear and to be unfolded yet. [1-5] [Figure.2]



(GnRH - Gonadotropin Releasing Hormone, FSH – Follicle Stimulating Hormone, LH- Luteinizing Hormone, DHEA – Dehydroepiandrosterone , TSH–Thyroid Stimulating Hormone, T3 – Triiodothyronine, T4 - Thyroxine)

Figure 2: Hormonal interplay between polycystic ovary syndrome (PCOS) and hypothyroidism

Though strong genetic influence on the development of these two diseases is well documented, both disorders are multifactorial resulting in a wide range of metabolic disorders causing weight gain, glucose tolerance impairment, insulin resistance (IR), and dyslipidaemia resulting in obesity, diabetes and cardiovascular disease over life time. Moreover, both disorders are major causes of infertility as these affect the reproductive system adversely. [1] This influence is growing as a reason behind emotional and psychological consequences in women threatening their womanhood as a "Silent Killer".

It is increasingly realized that thyroid disorders are more common in women with PCOS as compared to normal population but its significance is still to be explored. [5] Co-occurrence of two disorders in infertile women is associated with poor response to the treatment and hence pregnancy outcomes with live birth, than either of these disorders alone. [1] . So PCOS and thyroid disorder association can be designated as an affair of active research to comprehend and corroborate the substantial etiology and pathogenesis in order to develop novel therapeutic approach. It also becomes important for clinicians to rule out thyroid dysfunction in PCOS patients.

The intent of the present study was to determine the association of thyroid function tests in PCOS patients and also to correlate them to body mass index (BMI) and waist -hip ratio (WHR).

Methodology

Present study was an analytical cross-sectional study, conducted in Department of Anatomy in collaboration with Department of Obstetrics and Gynaecology, S.P Medical College and Associated group of Hospitals, Bikaner, Rajasthan. The study incorporated total of 50 females between the age group of 15-45 years of age, out of which 30 women were with polycystic ovary syndrome (cases) and 20 apparently healthy women (controls).

Prior approval of Institutional ethics committee and consent of the subjects in the form of Informed Consent Form was taken.

- Transabdominal/Transvaginal ultrasound (US) was done for all the subjects to evaluate the reproductive system.

Cases:

Rotterdam's criteria were followed for diagnosis of PCOS. Women with irregular menstruation, hyperandrogenism and enlarged ovaries with ≥ 12 follicles of 2-9 mm diameter, increased ovarian volume >10ml in each ovary on US examination were included as cases. Women taking contraceptive pills and pregnant women were not included in case group.

Controls:

Women without any gynaecological and endocrine pathology were included in control group and women with positive medical history for hypertension, cardiovascular diseases etc. were excluded from control group.

- Thyroid function tests were performed which included serum triiodothyronine (T3), serum thyroxine (T4) and serum thyroid stimulating hormone (TSH). The normal range of T3, T4 and TSH was 0.87-1.78 ng/ml, 6.09-12.23µg/dl and 0.50-5.60 µIU/ml respectively for local population as per our laboratory.
- Anthropometric measurements were performed for the estimation of body mass index (BMI) and waist hip ratio (WHR). BMI (kg/m^2) was calculated using following formula:

BMI= Weight

BMI<18 were underweight, BMI between 18.1 to 22.9 were healthy, BMI between 23 to 24.9 were overweight and BMI ≥ to 25 were obese.

- For WHR, waist circumference was divided by hip circumference. The waist circumference was measured at the mid-point between 12th rib and the outer border of iliac crest and the hip circumference was measured with the subjects standing erect, feet together and on a horizontal plane at the level of the greater trochanters.

Statistical analysis: The data was entered into Microsoft Excel and then analysed with the help of SPSS software. Mean and standard deviation were calculated for each of the parameters by applying Student's T test. p-value of less than 0.05 was taken to be statistically significant.

Results

Table 1: Comparison of various parameters between cases and controls

Parameters	PCOS patients (n=30)	Controls (n=20)	p- Value
Age(Years)	23.6 ±3.95	26.35±4.99	0.0463*
Weight (in kg)	62.27±3.37	61.15±2.96	0.2233
Height (in cm)	157 ±3.31	161 ±3.42	0.0001**
BMI# (kg/m2)	25.11±0.57	23.31±1.06	0.0001**
WHR#	0.88±0.01	0.85±0.02	0.0001**
Serum TSH(µIU/ml)	3.83±1.73	2.48±0.72	0.0005**
Serum T3 (ng/ml)	0.88±0.21	1.01±0.18	0.03*
Serum T4 (µg/dl)	6.58±1.62	7.63±0.93	0.0061**

BMI – Body Mass Index WHR – Waist Hip Ratio
*- Significant, **-Highly significant

Total 30 cases and 20 controls were incorporated, Table no.1 shows the results of thyroid function tests and anthropometric measurement. Mean Age of PCOS patients and controls was 23.6 ±3.95 & 26.35±4.99 years respectively. Mean Weight of cases was 62.27±3.37 kg & of controls was 61.15±2.96 kg and mean height of cases and controls was 157 ±3.31& 161 ±3.42 cm respectively. It was found that the mean TSH level of cases was significantly higher than controls (p=0.0005). The mean TSH of cases was 3.83±1.73 µIU/ml and for controls it was 2.48±0.72 µIU/ml. The mean T3 level of cases (0.88±0.21 ng/ml) was significantly lower than controls (1.01±0.18 ng/ml; p= 0.03). The mean T4 level of cases was also significantly lower (6.58±1.62 µg/dl) than controls (7.63±0.93 µg/dl; p= 0.0061). The BMI of cases was significantly higher than controls (p-0.0001) with mean value of cases (25.11±0.57 kg/m^2) and controls (23.31±1.06 kg/m^2). The mean WHR of cases (0.88±0.01) was significantly higher (p-0.0001) than controls (0.85±0.02).

Discussion

PCOS is a serious endocrine disorder of growing concern in reproductive years of females as this has not received the attention it deserved in the past decade. The clinical picture gets more complex when thyroid disorders are co-occurring with PCOS. These comorbidities serve as the host for inviting various other metabolic complications, accompanied with social, economic and psychological issues in due course, if not handled properly and well in time. [1,6] The exact data on the joint occurrence of Polycystic Ovary Syndrome and thyroid dysfunction is not well established. Which of the two disorders is a forerunner of the other is also still speculative and a matter of research. [7] Although the endocrinal axis of PCOS and thyroid dysfunction interplay and influence each other, probably involving epigenetic and heritable components as the underlying key, but the exact mechanism is yet to be explored and established separately for the two so that the clinical influences are better handled and new therapeutic approaches can be developed. [8,9]

The current study was to assess the status of thyroid disorder occurrence in females with polycystic ovary syndrome in local population in western Rajasthan.

In our cohort, serum TSH level was significantly higher in PCOS population than their age matched counterparties having normal thyroid function (p=0.0005). The mean value of TSH in cases, was found to be 3.83 ± 1.73 µIU/ml , while in controls, which was non-PCOS group, it's mean value was found to be 2.48 ± 0.72 µIU/ml. Our findings are in agreement with a study in 2019 by *Kshama V. Kedar et al* [10] who compared thyroid function status in PCOS vs Control group. Their results were similar to our current study in stating that the PCOS patients show higher mean TSH level (4.024±1.09 mIU/ml) compared to controls (2.84±0.83 mIU/ml) with p < 0.007. Another case- control study conducted by *Deepak Raj et al* [11] in a tertiary care hospital in Pakistan in 2021 clearly depicted higher prevalence of subclinical hypothyroidism (SCH) in women with PCOS as compared to the non-PCOS females (43.5% vs. 20.5%; p < 0.00001). The TSH levels in this study was significantly higher (p < 0.0001) in participants with PCOS (5.01±1.02 mIU/L) than those without PCOS (3.42±0.76 mIU/L). Our findings were consistent with the findings of *Cai j et al* [12] in 2019 on Chinese women with PCOS, which stated that the TSH level was significantly higher (p<0.001) in PCOS than in controls (2.29±1.24 vs 1.86±0.90 mIU/L respectively). Our findings also accorded with the observations of *M shareefa et al* [5] in reporting an association between PCOS and thyroid dysfunction. In their work the mean TSH levels in controls, PCOS euthyroid group and PCOS hypothyroid group were 1.76±0.81 µIU/ml, 1.86±0.65 µIU/ml and 7.09±2.68 µIU/ml,

respectively. The TSH levels in PCOS euthyroid group was significantly higher than control group (p=0.001) and very high in the PCOS hypothyroid group. A research on correlation of PCOS with SCH was undertaken by *Fatima et al* [4] in which they found considerably higher prevalence of SCH among women with PCOS (34.4%). Significantly high TSH levels ($p < 0.001$) were found in PCOS patients with SCH (3.9±1.09 mIU/L) when compared to euthyroid PCOS group (1.8±0.38 mIU/L). Another findings from a study report by *Pervin,H. et.al* [13] in 2020 are consistent with previous reports which state that thyroid disorders were prevalent in 30% of PCOS patients, among them most common thyroid disorder was hypothyroidism which was almost three fold more prevalent than hyperthyroidism. Women with PCOS are more likely to develop SCH and greater awareness is needed for their treatment says a meta-analysis report in 2018. [14] A recent study in 2022 [15] on *in vitro* fertilization embryo transfer (IVF-ET) PCOS vs non- PCOS group clearly reports significantly higher TSH levels in former group than the later (2.42±0.86 vs 2.00±0.89 uIU/ml respectively, $p < 0.001$).

In our study T3 and T4 levels were also estimated along with TSH and compared among the PCOS and control cohorts. It showed significantly lower mean values of T3 in PCOS patients than in controls (0.88±0.21 vs 1.01±0.18 ng/ml respectively; $p = 0.03$). Our results are in accordance with the previous study by *M Shareefa et al* [5] who reported marked decrease in T3 levels in PCOS hypothyroid patients (1.10±0.23 ng/dl) compared to controls (1.17±0.83 ng/dl). *Kedar KV et.al* [10] in their study on thyroid dysfunction in PCOS women documented lower values of T3 in PCOS group (0.91±0.35 ng/ml) than controls (1.18±0.61 ng/ml) but the difference was not significant ($p <1$). A case- control study by *Deepak Raj et al* [11] on frequency of SCH in PCOS women showed decreased values of free triiodothyronine (FT3) in PCOS than controls (301.21±87.65 vs. 312.18 ± 85.23 pg/dl respectively ; $p = 0.20$).

In our study the mean T4 levels in PCOS patients was significantly lower (6.58±1.62 µg/dl) than in controls (7.63±0.93 µg/dl) ; $p = 0.0061$. *Kedar KV et al* [10] in their study also reported decreased T4 levels in PCOS patients than controls but the difference was not significant ($p < 0.43$). The study by *M Shareefa et al* [5] in 2020 reported almost similar levels of T4 in PCOS hypothyroid group (8.35±1.22 µg/dl) and controls (8.5 ±0.72 µg/dl). *Deepak Raj et al* [11] in their research in 2021 documented almost similar levels of FT4 (free thyroxine) in PCOS and non - PCOS participants i.e. 1.42 ±0.34 ng/dl, 1.47 ±0.39 ng/dl respectively; $p = 0.17$.

Women with BMI ≥ 25 were considered obese and our results showed that women with polycystic ovary syndrome were obese as compared to the control group. The mean BMI ($kg/m^{2)}$ of PCOS cohort in our study was found to be significantly higher ($p = 0.0001$) i.e. 25.11±0.57 than in controls i.e 23.31±1.06. Our results accorded with a previous study in Bhopal, Central India [16] which documented strong association of risk factors like BMI ($p < 0.0001$) with presence of PCOS and lack of awareness there were in girls (78.4%). Xu et al, 2022 [15] also recorded similar findings of significant difference in mean BMI (kg/m^2) values in PCOS and non- PCOS group (24.30 ± 3.93 and 23.18 ± 3.77 respectively; $p < 0.001$). *Fatima et al* [4] also found significant difference in BMI of SCH group (32.5 ± 3.75) as compared to euthyroid group (25.7 ± 3.27) in PCOS women. A review report presented by *Zeber-Lubecka and Hennig*[1] also support the findings of our study by stating the fact that patients with PCOS and autoimmune thyroid disease (AITD) were obese by an average of $2kg/m^2$. Our results were also supported by previous study by *Shah A et al* [17], which revealed that 47.05% of women with polycystic ovarian syndrome were obese or

overweight. In a study conducted by *Chacko A et al* [18] the results were similar in which the mean BMI was higher for PCOS i.e. 24.42±1.9 than controls (22.53±2.53). *Raj D et al*, [11] also agrees to our current findings that the BMI was significantly higher in PCOS than non PCOS participants (25.12 ± 2.51 vs. 22.51 ± 2.01 kg/m^2 respectively ; $p < 0.0001$).

On evaluation of WHR, it was found in our study that the mean WHR of cases was highly significant than controls (0.88±0.01 vs. 0.85±0.02 respectively; $p = 0.0001$). *Gupta M et al* [16] stated strong association of risk factors like WHR ≥ 0.85 ($p < 0.0001$) with the presence of PCOS. *Yadav S et al* [19] also found that WHR > 0.8 is significantly associated with the PCOS ($p = 0.0001$). Similar results were obtained by *Deepa Anurekha A* [20] in which the mean WHR of women with PCOS was significantly higher than controls and also suggested lifestyle modification and exercise for women with polycystic ovarian syndrome. [21]

Having discussed above, the results of present and previous studies, it can be observed that women with PCOS have higher chances of hypothyroidism than control group and also PCOS women have higher BMI and WHR. However mutual inter relationships appears to exist but the situation is still speculative. The question whether PCOS predisposes to the development of hypothyroidism or whether hypothyroidism is a fore runner of PCOS, remains open.

Conclusion

a) The data of the present study suggests that the women with polycystic ovary syndrome have higher chances of thyroid disorder, expressed as hypothyroidism. However, the question whether PCOS predisposes to development of thyroid dysfunction or thyroid disorders are forerunners of PCOS still remains open and is yet to be established.

b) The study also revealed that women with polycystic ovary syndrome have higher distribution of fat than controls. Equally important is that obesity in these patients could be a key factor that influences thyroid hormone levels. So it can be said that overweight and obese patients with PCOS show a higher tendency toward thyroid dysfunction.

These results imply that patients with PCOS should be evaluated for thyroid functions at the early stage. The results of the present study would help clinicians in early detection and better management of PCOS. Females with high BMI and WHR should be educated about the complications and made aware to loose wait to improve quality of life

c) Also, in this context, as indicated in literature that genetic and epigenetic environmental factors probably contribute to the dysregulations of varied systems causing various comorbidities in PCOS, opens new avenues of molecular and cell biology research in the rapidly growing field of PCOS using tools like PCR and Fluorescence in situ hybridization (FISH) techniques which might be more helpful.

d) Formulation of epigenetic studies would unveil the nature and nurture of the syndrome.

e) Role of Vitamin D in the development of PCOS is also important to be established as lack of sunlight exposure and outdoor physical activities have taken a back seat in today's life style.

Limitations and Recommendations

1. Since the present study was a cross sectional study, long term studies are required to establish the significance of thyroid function disorders in PCOS, especially in infertility, so as to rule out the classic dilemma of, "Which comes first, the chicken or the egg?"

2. The present study does not provide any information regarding the epigenetic influences and genetic predisposition of both disorders in the subjects under study. So more studies are required to establish the exact mechanism and genetic susceptibility of PCOS and thyroid dysfunction and also understanding the role of other contributing factors.

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Data Availability statement: The datasets generated during and analysed during the current study are available from the corresponding author on reasonable request.

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