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Original Research Article

ASSOCIATION OF THYROID DYSFUNCTION WITH DEVELOPMENT OF POLYCYSTIC OVARIAN SYNDROME AMONG REPRODUCTIVE AGE WOMEN OF SIALKOT, PAKISTAN

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Abstract: *Polycystic Ovary Syndrome (PCOS) is a prevalent hormonal disorder among women of reproductive age, often co-occurring with metabolic syndromes such as thyroid dysfunction. Understanding this association is crucial for addressing the broader reproductive and general health implications.* ***Objective:*** *This study aims to investigate the association between thyroid dysfunction and the development of PCOS in women of reproductive age in Sialkot, Pakistan.* ***Methods:*** *This prospective study was conducted from May 2023 to May 2024 at Civil Hospital, Sardar Begum Hospital, Cheema Family Hospital, and Waleed Hospital. A total of 100 females were included, divided into two groups: 50 in the control group (no disease) and 50 in the treatment group with both thyroid dysfunction and PCOS. Participants aged 23 to 45 were selected from medicine and gynecology wards. Blood samples were analyzed for thyroid function, and a comprehensive questionnaire was administered to assess the prevalence and characteristics of symptoms related to PCOS and thyroid dysfunction. Statistical analysis was performed using T-tests to compare mean values of Triiodothyronine (T3) and Thyroxine (T4) between groups.* ***Results:*** *The treatment group exhibited a significant prevalence of symptoms: 80% reported hirsutism, 92% had irregular menstrual cycles, 72% experienced weight gain, 60% suffered from hair loss, 76% had acne and high blood pressure, and 64% showed signs of Acanthosis nigricans. Significant differences in thyroid hormone levels were observed, with mean T3 levels at 9.4718 (SE = 1.7373, 95% CI [5.9783, 12.9653], T = 5.4525, $p < 0.05$) and mean T4 levels at 51.172 (SE = 6.7027, 95% CI [37.6952, 64.6508], T = 7.6333, $p < 0.05$) as compared to control group.* ***Conclusion:*** *The findings highlight a significant association between thyroid dysfunction and PCOS, with thyroid dysfunction impacting T3 and T4 levels in patients with PCOS. This underscores the need for targeted thyroid screening in PCOS patients to manage and mitigate the broader health implications effectively.*

Keywords: Acanthosis Nigricans, Hirsutism, Polycystic Ovary Syndrome, Thyroid Diseases, Thyroxine, Triiodothyronine

Introduction

Polycystic Ovarian Syndrome (PCOS) is one of the most common endocrine disorders affecting women of reproductive age, with significant implications for their metabolic, reproductive, and psychological health. (1). The syndrome is characterized by a range of symptoms, including oligo- or anovulation, hyperandrogenism, and polycystic ovaries, and is often associated with insulin resistance and obesity. (2, 3). Despite its prevalence, the etiology of PCOS remains multifactorial and incompletely understood, with a growing body of evidence suggesting a complex interplay between genetic, environmental, and hormonal factors. (4).

Thyroid dysfunction, particularly hypothyroidism, and subclinical hypothyroidism is another prevalent endocrine disorder among women of reproductive age and has been increasingly recognized as a potential contributor to the pathogenesis of PCOS. (5, 6). The thyroid gland plays a crucial role in regulating metabolism and reproductive function, and thyroid disorders can lead to menstrual irregularities, anovulation, and infertility, which are also hallmark features of PCOS. (7, 8). The overlap in symptomatology between thyroid dysfunction and PCOS suggests a possible association between the two conditions, which warrants further investigation. (9).

Recent studies have increasingly highlighted the association between thyroid dysfunction and the development of Polycystic Ovarian Syndrome (PCOS) (10). Thyroid disorders, particularly hypothyroidism and subclinical hypothyroidism, are common among women with PCOS, and these conditions may exacerbate the reproductive and metabolic disturbances seen in PCOS. (11). For example, elevated thyroid-stimulating hormone (TSH) levels have been linked to worsened cardiometabolic risk profiles and poorer reproductive outcomes in women with PCOS, particularly those undergoing fertility treatments. (10).

Furthermore, a 2023 bidirectional Mendelian randomization study has provided evidence suggesting a causal relationship between specific thyroid dysfunctions and the risk of developing PCOS. (12). This research emphasizes the importance of screening for thyroid abnormalities in women with PCOS, as thyroid function may significantly influence the severity and phenotype of PCOS.

This study aims to explore the association between thyroid dysfunction and the development of PCOS among reproductive-age women in Sialkot, Pakistan. Understanding this relationship is critical for improving the diagnosis and management of PCOS, particularly in regions where both conditions are prevalent. By examining the prevalence and impact of thyroid dysfunction in women

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with PCOS, this study seeks to contribute to the broader understanding of the pathophysiological mechanisms underlying PCOS and to inform clinical practice in managing this complex condition.

Methodology

This prospective, observational study was conducted at four healthcare facilities in the District of Sialkot, Pakistan: Civil Hospital, Sardar Begum Hospital, Cheema Family Hospital, and Waleed Hospital. The study was designed to assess the association between thyroid dysfunction and Polycystic Ovarian Syndrome (PCOS) in females of reproductive age. The study included a total sample size of 100 females aged 23 to 45, selected from the medicine and gynecology wards of the participating hospitals. The sample was divided into two groups: 50 females diagnosed with PCOS and concurrent thyroid dysfunction and 50 healthy females who served as the control group. All participants were non-smokers to eliminate confounding factors related to smoking.

Blood samples were randomly collected from the study participants over two months. The collection sites included Raheela Lab Sialkot, Allied Lab Lahore, and Al-Hameed Lab Lahore, selected for their cost-effective services in conducting thyroid function tests (T3, T4, and TSH).

Infertility due to PCOS was assessed based on the Rotterdam criteria (Rotterdam, 2003). A qualified gynecologist confirmed the diagnosis via ultrasound. Data collection was conducted using a structured questionnaire, which included demographic information (age, weight, marital status, occupation), menstrual cycle patterns, fertility issues, and a family history of thyroid disorders and PCOS. The questionnaire also inquired about specific symptoms related to thyroid dysfunction and PCOS.

Blood samples (5 mL) were collected from each participant's peripheral vein using a serum separator tube. The samples were allowed to clot at room temperature for 30 minutes before being centrifuged at 3000 rpm for 10 minutes to separate the serum. The serum samples were then stored at -20°C until analysis.

The thyroid hormone levels (T3, T4, and TSH) were measured using the Enzyme-Linked Immunosorbent Assay (ELISA) method. The assay employed a solid-phase sandwich technique to quantify TSH levels using antibodies specific to human TSH. Each sample's optical density (OD) was measured at 450 nm, and TSH concentrations were determined by comparing the OD values to a standard curve.

All collected data, including demographic information, medical history, physical examination findings, and laboratory results, were entered into SPSS version 26 for analysis. Descriptive statistics were used to summarize the data, and inferential statistics, such as t-tests and chi-square tests, were applied to assess the differences between the PCOS and control groups. Logistic regression was performed to evaluate the association between thyroid dysfunction and the presence of PCOS.

The ethical standards of the Declaration of Helsinki conducted the study. Informed consent was obtained from all participants before any data or blood samples were collected. The confidentiality of participant data was strictly maintained throughout the study.

Results

The prospective observational analysis included 100 female participants divided into two groups: 50 females in the control group (without disease) and 50 females in the treatment group with both thyroid dysfunction and PCOS. The participants were between 23 and 45 years old and were selected from the medicine and gynecology wards.

The prevalence of hirsutism was assessed among the study participants. In the control group, only 4.23% of women exhibited hirsutism. However, in the PCOS with thyroid dysfunction group, a significant 80% of the women reported hirsutism. This finding highlights a strong association between thyroid dysfunction and hirsutism in women with PCOS.

Another critical aspect studied was the occurrence of irregular menstrual cycles. The results revealed that 3.45% of women in the control group had irregular menstrual cycles, while 92% of women in the PCOS with thyroid dysfunction group reported irregular cycles. This substantial difference indicates a strong correlation between thyroid dysfunction and menstrual irregularities in PCOS patients.

Weight gain was reported by 72% of women in the PCOS with thyroid dysfunction group, compared to just 3.12% in the control group. This data underscores the link between thyroid dysfunction and weight gain among PCOS patients.

Hair loss was another prevalent symptom, with 60% of women in the PCOS with thyroid dysfunction group reporting it, compared to only 2.98% in the control group. This finding indicates a significant association between thyroid dysfunction and hair loss in PCOS patients.

The study also investigated the prevalence of acne and high blood pressure. Among the women with PCOS and thyroid dysfunction, 76% reported these symptoms, while only 5.23% in the control group experienced them. This highlights a strong relationship between thyroid dysfunction and the occurrence of acne and high blood pressure in women with PCOS.

Acanthosis nigricans was observed in 64% of the women with PCOS and thyroid dysfunction, compared to only 2.11% in the control group. This finding further emphasizes the connection between thyroid dysfunction and the development of acanthosis nigricans in PCOS patients.

Table 1: Symptoms in PCOS Patients with Thyroid Dysfunction

Symptom	Control Group (%)	PCOS with Thyroid Dysfunction (%)
Hirsutism	4.23	80
Irregular Menstrual Cycles	3.45	92
Weight Gain	3.12	72
Hair Loss	2.98	60
Acne and High Blood Pressure	5.23	76
Acanthosis Nigricans	2.11	64

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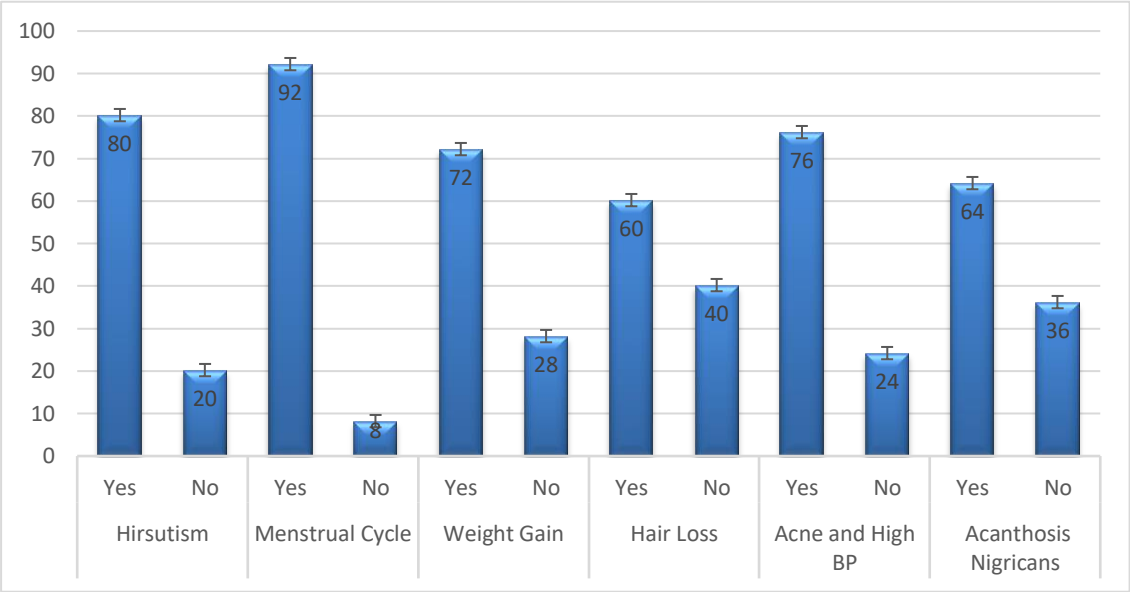

Figure 1: Prevalence of Symptoms Associated with PCOS in Women with Thyroid Dysfunction

Significant differences in thyroid hormone levels were observed, with mean T3 levels at 9.4718 (SE = 1.7373, 95% CI [5.9783, 12.9653], T = 5.4525, p < 0.05) and mean T4 levels at 51.172 (SE = 6.7027, 95% CI [37.6952, 64.6508], T = 7.6333, p < 0.05) as compared to control group.

Discussion

In women of reproductive age, PCOS (polycystic ovarian syndrome) is a common endocrine condition that is sometimes accompanied by metabolic problems such as thyroid dysfunction. (13). The purpose of this research was to investigate the relationship between PCOS development and thyroid dysfunction in women in Sialkot, Pakistan, who are of reproductive age. A thorough investigation was conducted at Civil Hospital, Sardar Begum Hospital, Cheema Family Hospital, and Waleed Hospital in May and June 2024. With 50 women in the control group (no disease) and 50 women in the treatment group (PCOS and thyroid dysfunction combined), the study's sample size was 100 women. The volunteers, aged 23 to 45, were chosen from the gynecology and medicine wards. Blood samples were taken to evaluate thyroid function, and a thorough questionnaire was given to determine the frequency and features of symptoms associated with PCOS and thyroid dysfunction. The research made sure that every participant did not smoke and that PCOS-related infertility was determined using the Rotterdam criteria. A gynecologist used ultrasonography to diagnose PCOS, and a questionnaire was used to gather demographic information. The results found that seventy-two percent of the individuals reported weight increase, sixty percent had hair loss, seventy-six percent had acne and high blood pressure, and sixty-four percent had Acanthosis nigricans. Of the participants, eighty percent had hirsutism. There were notable differences in triiodothyronine (T3) and thyroxine (T4) levels between the PCOS patients with thyroid dysfunction and the control group. The treatment group had significantly higher mean T3 and T4 levels (mean T3 = 9.4718, SE = 1.7373; mean T4 = 51.172, SE = 6.7027). Significant disparities in T3 and T4 levels were shown by the large t-values and p-values of 0.00, indicating that thyroid dysfunction has a major effect on these hormone levels in PCOS patients. Our results are similar to those of Pervin et al. (2020), who investigated thyroid disorders in women with polycystic ovary syndrome (PCOS) in a prospective cross-sectional study conducted from November 2018 to October 2019 at Bangabandhu Sheikh Mujib Medical University (BSMMU) in Dhaka, Bangladesh. (14). One hundred sixty women with PCOS who were between the ages of 16 and 45 were enrolled in the research, and information on their anthropometrics, sociodemographic, and clinical symptoms was noted. Serum FT3, FT4, and TSH assays were conducted at the hospital laboratory to assess thyroid function. Participants' average age was 25.53 ± 3.17 years, with 62% being between the ages of 16 and 25. Of the individuals, 22% were obese, 33% were overweight, and 40% were of an average weight. Of the individuals, 55% had hirsutism, 18% had acne, 32% had oligomenorrhea, and 36% had irregular periods. 9% of the 160 women with PCOS had hyperthyroidism, 20% had hypothyroidism, and 60% were euthyroid. According to this research, 32% of PCOS patients had thyroid abnormalities, with hypothyroidism being almost three times more frequent than hyperthyroidism.

Our findings are consistent with van der Ham et al. (2023), who conducted a retrospective cross-sectional investigation to look at the incidence of hyperprolactinemia and thyroid dysfunction in women with polycystic ovarian syndrome (PCOS) (15). The research included data from 299 control subjects and 1,329 PCOS-afflicted women. Thyroid-stimulating hormone (TSH), free thyroxine (FT4), and blood levels of anti-thyroid peroxidase antibodies (TPOab) were essential metrics. Between PCOS women and controls, the prevalence of thyroid illness was comparable (2.9% vs. 1.7%; P = 0.29 for hypothyroidism, 0.3% vs. 0%; P = 0.11 for hyperthyroidism). While FT4 levels were somewhat higher in the PCOS group but remained within the normal range (16.1 pmol/L vs. 16.7 pmol/L; P < 0.05), TSH levels were likewise similar (1.25 mIU/L vs. 1.18 mIU/L; P =

0.44). Both the frequency of hyperprolactinemia (1.4% vs. 2%; P = 0.05) and positive TPOab (4.7% vs. 9.7%; P = 0.11) were comparable. Thyroid dysfunction and hyperprolactinemia did not vary significantly between 235 age- and BMI-matched controls and 215 PCOS women in a subanalysis. In contrast to other phenotypes, PCOS phenotype B had a considerably greater frequency of subclinical hypothyroidism (6.3%).

Our findings are consistent with Cai et al. (2019) revealed that PCOS patients had higher levels of thyroid-stimulating hormone (TSH) than controls (3.29 ± 2.24 vs. 2.86 ± 1.90 mU/L, $p < 0.001$) (16). Higher TSH levels were associated with elevated levels of triglycerides (TG), total cholesterol (TC), LDL-c, and apolipoprotein B (apo B), as well as an increase in hyperandrogenism (HA), in individuals with euthyroid PCOS. TSH has a negative correlation with apolipoprotein A (apoA) and a positive correlation with TG, apoB, free testosterone (free T), and free androgen index (FAI). Regardless of age or waist circumference (WC), the proportion of HA increased with raised TSH. TSH and TG were shown to be essential factors in the HA phenotype by multivariate analysis.

Conclusion

The present study underscores the significant association between thyroid dysfunction and Polycystic Ovary Syndrome (PCOS) among reproductive-age women in Sialkot, Pakistan. The findings reveal that elevated levels of Triiodothyronine (T3) and Thyroxine (T4) are prevalent in PCOS patients with thyroid dysfunction, indicating a strong interplay between these conditions. This highlights the importance of regular thyroid screening and integrated healthcare strategies to manage both thyroid dysfunction and PCOS. Emphasis on lifestyle interventions, including diet and exercise, is crucial to reduce the risk of metabolic complications associated with PCOS, thereby improving patient outcomes.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate
Approved by the department concerned. (IRB-DZKD-088/22)

Consent for publication
Approved

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Conflict of interest

The authors declared the absence of a conflict of interest.

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