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Original Article

Analysis of Hormonal and Metabolic Parameters In Hypothyroidism, Subclinical Hypothyroidism and Pcos

Maleeha Iftikhar, Muhammad Naeem Qureshi, Fayyaz Hassan, Fuad Ahmad Siddiqi, Imran Khan, Laila Yaseen

Department of General Medicine, Combined Military Hospital Rawalpindi/National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To analyze the hormonal and metabolic parameters in subclinical hypothyroidism, hypothyroidism, and Polycystic Ovary Syndrome (PCOS) among women of reproductive age.

Study Design: Cross-sectional study.

Place and Duration of Study: Combined Military Hospital (CMH), Rawalpindi, Pakistan, from Jan 2024 to Dec 2024.

Methodology: Total 114 participants were enrolled and their blood samples analyzed by dividing into three groups: hypothyroidism without PCOS, subclinical hypothyroidism without PCOS, and PCOS. Blood samples were drawn into gel tubes and centrifuged at 3000 RPM for 5 minutes. The serum was then analyzed using chemiluminescence immunoassay to measure hormonal and metabolic parameters of women of reproductive age. A standardized proforma was used to collect data on demographics, clinical history, and biochemical evaluations.

Results: A total of 114 participants were included in this study. A significant difference was observed in serum follicle stimulating hormones (FSH) level across the group (p=0.007). However, all the other parameters showed no significant difference across the groups with p>0.05. For age and Body Mass Index (BMI), a weak negative correlation with thyroid stimulating hormone (TSH) and FSH, respectively was statistically significant while other hormones showed no significant correlation with age and BMI (p>0.05).

Conclusion: TSH level showed statistically significant difference among females with hypothyroidism, sub-clinical hypothyroidism and PCOS while other hormonal parameters showed no statistically significant difference among groups.

Keywords: Follicle stimulating hormone, Hypothyroidism, Thyroid stimulating hormone, Sub-clinical hypothyroidism.

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INTRODUCTION

Polycystic Ovarian Syndrome (PCOS) is a hormonal condition that affects women during their years of reproduction with high androgen levels, infertility and irregular menstrual cycles and lead to other health complications, like cardiovascular ailments and Type 2 Diabetes.[1] due to which early detection, lifestyle changes, and prompt treatment are crucial. Globally, PCOS is estimated to affect approximately 6–7% of the population.[2] while according to the World Health Organization (WHO), 8–13% of women of reproductive age suffer from PCOS, with over half of these cases remaining undiagnosed.[3] Subclinical hypothyroidism (SCH) is described by raised serum thyroid-stimulating hormone (TSH) levels, despite adequate free thyroxine (FT4) levels.[4] Often referred to as mild thyroid failure, SCH is relatively common, affecting 4–10% of the general population,[5] but its prevalence is around 2% in young women aged 12–39 years.[6] Common symptoms of PCOS and overt hypothyroidism include menstrual irregularities, miscarriage, oligo/anovulation, and infertility thus, overt hypothyroidism should be ruled out to accurately diagnose PCOS.[7] Insulin resistance is a crucial factor in the onset of PCOS and is also observed in individuals with overt hypothyroidism or SCH with both conditions associated with metabolic syndrome, obesity, dyslipidemia, abnormal glucose metabolism, and an increased risk of cardiovascular (CV) diseases. Recent investigations have demonstrated a greater prevalence of SCH in patients with PCOS than in healthy individuals of the same age.[6,8] Hypothyroidism, may influence hormonal and metabolic parameters in women with PCOS.[9] Previous research has examined the metabolic and hormonal disturbances associated with PCOS, clinical hypothyroidism, and hypothyroidism individually,[10] however, the combined occurrence of these conditions and their collective impact on metabolic and hormonal parameters have not been studied in our population. Thus, the objective of our study was to analyze the metabolic and hormonal parameters in

Correspondence: Dr Maleeha Iftikhar, Department of General Medicine, Combined Military Hospital Rawalpindi Pakistan

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hypothyroidism, subclinical hypothyroidism and PCOS.

METHODOLOGY

This cross-sectional study was conducted at the Combined Military Hospital (CMH), Rawalpindi, Pakistan, from January 2024 to December 2024. Approval from Institutional Review Board (IRB) was gained vide letter reference number 684. After a thorough literature search, we calculated a sample size of 114 via WHO calculator, keeping the margin of error at 5%, a confidence level of 95%, and the prevalence of PCOS during reproductive age at 7%.[1] For sampling, the non-probability consecutive sampling technique was employed.

Inclusion Criteria: All non-pregnant women of reproductive age between the ages of 18 to 45 years, who presented to the Endocrinology Department were included.

Exclusion Criteria: Patients with chronic illnesses, pregnancy, or lactation were excluded.

All participants' written consent was obtained before they were enrolled, and their privacy was maintained throughout the process. Data was collected using a structured proforma that included demographic information, clinical history, and biochemical measurements. The proforma captured data on age, and BMI. Clinical examinations included measurements of blood pressure, height and weight. After collecting preliminary and demographic data, blood samples of all participants were drawn into gel tubes and centrifuged at 3000 RPM for 5 minutes. Samples were divided into three groups: hypothyroidism without PCOS (based on elevated TSH levels and decreased T3 and T4 levels), subclinical hypothyroidism without PCOS (based on elevated TSH levels 4.5-10mlU/L with normal T3 and T4 levels), and PCOS (based on the presence of clinical symptoms such as hirsutism, menstrual irregularity, and elevated LH/FSH ratio upto 2:1 or ever 3:1, along with biochemical evidence of hyperandrogenism). The serum was then analyzed using chemiluminescence immunoassay methods on the ADVIA Centaur XP platform to measure TSH level (0.4-4.5mlU/L), Triiodothyronine (T3) level (80-120ng/dL in 16-20yr, 70-205ng/dL in 20-50yr), Thyroxine (T4) level (0.7-1.8ng/dL), FSH level (1.37-9.9IU/L in follicular phase, 6.17-17.2IU/L in ovulatory phase, and 1.09-9.21IU/L in luteal phase), Luteinizing Hormone (LH) level (1.68-15U/L in follicular phase, 21.9-56.6IU/L in ovulatory phase, and 0.61-16.3IU/L in luteal phase), prolactin (3-27ng/Ml in adult female), progesterone (<50ng/dL in follicular phase and 300-2500ng/dL in luteal phase), testosterone (15-70ng/dL in female), Sex Hormone Binding Globulin (SHBG) level (18-144nmol/L in non-pregnant women) and estrogen level (20-350pg/ml in follicular phase, 150-750pg/ml in mid cycle and 30-450pg/ml in luteal phase). Data analysis was conducted using version 25.0 of the Statistical Package for Social Sciences (SPSS). For both clinical and demographic data, descriptive statistics were computed where categorical variables were displayed as frequencies and percentages, while continuous variables were shown as mean ± standard deviation (SD). The Shapiro-Wilk test was employed to assess the normality of data distribution. Differences in hormonal levels among diagnostic groups were analyzed using one-way analysis of variance (ANOVA). To evaluate the relationship between age, BMI, and hormonal levels, correlation analysis was conducted, and Pearson correlation coefficients were computed to determine direction and strength of these associations with p-value ≤ 0.05 regarded as statistically significant.

RESULTS

A total of 114 participants were included in this study and blood samples taken. There were 32 patients with hypothyroidism, 44 patients with subclinical hypothyroidism and 38 patients with PCOS. Further baseline demographic characteristics of study population are presented in Table-I.

Table-I: Distribution of Demographic Characteristics of Patients (n=114)

Characteristic	Mean±SD
Age (years)	31.74±7.70
BMI (kg/mÂ²)	26.52±4.47
TSH (mIU/L)	5.32±2.77
T3 (nmol/L)	1.98±0.57
T4 (pmol/L)	8.33±2.19
FSH (mIU/L)	8.14±3.83
LH (mIU/L)	8.66±3.84
Prolactin (ng/mL)	16.51±6.94
Progesterone (nmol/L)	13.70±6.65
Testosterone (nmol/L)	1.33±0.68
SHBG (nmol/L)	87.13±41.34
Estrogen (pmol/L)	108.97±58.15

**BMI: Body Mass Index, TSH: Thyroid Stimulating Hormone, T3: Triiodothyronine, T4: Thyroxine, FSH: Follicle Stimulating Hormone, LH: Luteinizing Hormone, SHBG: Sex Hormone Binding Globulin*

Significant differences were observed in TSH levels, with hypothyroidism showing the highest mean value (6.26±2.60 mIU/L), followed by PCOS (5.66±2.72 mIU/L) and subclinical hypothyroidism

(4.36±2.67 mIU/L), yielding a statistically significant *p*-value of 0.007. However, no significant differences were found in T3 (*p*=0.902) and T4 (*p*=0.153) levels across groups. For gonadotropins, FSH levels were slightly higher in patients with PCOS (9.18±3.50 mIU/L) but this was not statistically significant (*p*=0.099). Similarly, LH levels showed minimal variation among the patients (*p*=0.723) while prolactin levels were comparable across all patients (*p*=0.869). Testosterone levels were highest in patients with PCOS (1.49±0.64 nmol/L), while SHBG and estrogen levels showed no significant variation, with *p*-values 0.206 and 0.648, respectively. Progesterone levels, although slightly elevated in patients with PCOS (15.35±7.25 nmol/L), did not show statistical significance (*p*=0.156). Table-II presents a comparative analysis of hormonal parameters among all enrolled patients.

Table-II: Comparison of Hormonal Levels across Groups (n=114)

Hormone	Hypothyroidism	Subclinical Hypothyroidism	PCOS	p-value (≤0.05)
TSH (mIU/L)	6.26±2.60	4.36±2.67	5.66±2.72	0.007
T3 (nmol/L)	1.96±0.62	1.97±0.48	2.01±0.63	0.902
T4 (pmol/L)	8.87±2.40	7.89±2.23	8.39±1.88	0.153
FSH (mIU/L)	7.29±4.14	7.86±3.75	9.18±3.50	0.099
LH (mIU/L)	8.19±3.23	8.85±3.85	8.84±4.33	0.723
Prolactin (ng/mL)	17.03±6.08	16.17±6.70	16.46±7.67	0.869
Progesterone (nmol/L)	13.28±5.88	12.57±6.49	15.35±7.25	0.156
Testosterone (nmol/L)	1.31±0.71	1.20±0.70	1.49±0.64	0.160
SHBG (nmol/L)	93.13±38.60	78.44±42.20	92.12±41.88	0.206
Estrogen (pmol/L)	106.52±60.39	115.27±57.74	103.74±57.57	0.648

**BMI: Body Mass Index, TSH: Thyroid Stimulating Hormone, T3: Triiodothyronine, T4: Thyroxine, FSH: Follicle Stimulating Hormone, LH: Luteinizing Hormone, SHBG: Sex Hormone Binding Globulin*

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FSH (mIU/L)	7.29±4.14	7.86±3.75	9.18±3.50	0.099
LH (mIU/L)	8.19±3.23	8.85±3.85	8.84±4.33	0.723

For age, a weak negative correlation with TSH (r = -0.187, *p*=0.046) was significant statistically, suggesting a slight decrease in TSH levels with increasing age. Other hormones, including T3, T4, FSH, LH, prolactin, progesterone, testosterone, SHBG, and estrogen, showed no significant correlation with age (p > 0.05). Regarding BMI, a weak negative correlation with FSH (r = -0.193, *p*=0.040) was significant statistically, indicating a marginal decrease in FSH levels with increasing BMI. However, no significant correlations were found between BMI and other hormonal markers, including TSH, T3, T4, LH, prolactin, progesterone, testosterone, SHBG, and estrogen (*p* > 0.05). Overall, the data suggest that age and BMI have limited but notable influences on specific hormonal parameters, such as TSH and FSH, in the studied population as shown in Table-III.

DISCUSSION

The current study provides a comprehensive examination of metabolic and hormonal markers in Pakistani women with SCH, hypothyroidism, and polycystic ovarian syndrome and our findings highlight several important aspects of these endocrine disorders and their interrelationships, offering valuable insights for clinical management and future research as this study is, to our knowledge, the first to explore the combined metabolic and hormonal markers in patients with subclinical hypothyroidism, hypothyroidism, and PCOS. While they are considered distinct clinical entities, they exhibit overlapping clinical and radiological features, such as menstrual irregularities, infertility, spontaneous miscarriages, obesity, lipid imbalances, and enlarged ovaries with a polycystic appearance.[11,12] Although the exact mechanisms linking the pathophysiology and clinical symptoms of thyroid disorders and PCOS remain unclear, certain shared factors may predispose individuals to both conditions, suggesting a possible pathophysiological relationship, as current evidence indicates that women with PCOS are at a higher risk of developing thyroid disorders compared to healthy women of the same age.[13,14] Hypothyroidism can lead to ovarian changes resembling PCOS, exacerbating

PCOS symptoms and insulin resistance.[15] Hypothyroidism patients also exhibited higher mean TSH levels in our findings compared to those with PCOS and SCH as the mean TSH level was 6.26±2.60mIU/L in hypothyroidism patients, 5.66±2.72mIU/L in PCOS patients and 4.36±2.67mIU/L in SCH patients while TSH levels differed statistically significantly between all three groups. According to one study16 performed on hypothyroidism and PCOS patients, TSH level was 4.55±1.79mIU/L in PCOS patients. Another study.[17] on hypothyroidism and sub-clinical hypothyroidism females, found elevated level of FSH and lower level of T3 and T4 hormones but in our study, no significant difference was observed, while the study also highlighted the complex interplay between thyroid hormones and reproductive hormones, where elevated TSH levels were associated with altered levels of estrogen and progesterone, indicating potential disruptions in reproductive function. These hormonal imbalances could contribute to the clinical manifestations of PCOS and hypothyroidism, such as menstrual irregularities, infertility, and Hirsutism.[18,19] The analysis of metabolic parameters revealed that women with PCOS and hypothyroidism had higher BMI, reflecting an increased risk of obesity, in line with the findings of another author.[20] who reported significant metabolic disturbances in PCOS patients.

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LIMITATION OF THE STUDY

This study has limitations despite the insights it provides as the findings may not be as widely relevant due to the cross-sectional study design and relatively small sample size, which makes it impossible to establish causality.

CONCLUSION

TSH level showed statistically significant difference among females with hypothyroidism, sub-clinical hypothyroidism and PCOS while other hormonal parameters showed no statistically significant difference. Age showed a weak negative correlation with TSH while BMI was negatively correlated with FSH.

Conflict of Interest: None.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MI & MNQ: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

FH & FAS: Conception, data analysis, drafting the manuscript, approval of the final version to be published.

IK & LY: Data acquisition, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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