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FREQUENCY OF ABNORMALITIES OF THYROID FUNCTION TESTS IN PATIENTS PRESENTING WITH ACUTE MEDICAL ILLNESS

Original Research

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ABSTRACT

Background: Euthyroid Sick Syndrome (ESS), also known as non-thyroidal illness syndrome, refers to transient alterations in thyroid hormone levels in patients with acute systemic illness, without intrinsic thyroid disease. It is commonly observed in critically ill individuals and is believed to be an adaptive physiological response to systemic stress. Accurate interpretation of thyroid function tests (TFTs) in such settings is crucial, as misinterpretation may lead to unnecessary interventions or misdiagnosis of true thyroid dysfunction.

Objective: To determine the frequency of abnormalities in thyroid function tests, specifically the occurrence of Euthyroid Sick Syndrome, in patients presenting with acute medical illness.

Methods: This comparative cross-sectional study was conducted at the Department of Medicine, Combined Military Hospital, Jhelum, from January to June 2024. A total of 220 patients admitted to the Medical Intensive Care Unit (ICU) for non-thyroidal illnesses were enrolled using non-probability consecutive sampling. Thyroid function was assessed by measuring serum T3, T4, and TSH levels. Patients with known thyroid disorders, pregnant or lactating women, and those with autoimmune diseases were excluded. Results were analyzed using SPSS version 24.0, with frequencies, percentages, medians, and interquartile ranges (IQRs) calculated for relevant variables.

Results: Of the 220 patients, 140 (63.6%) were male and 80 (36.4%) female. The overall median age was 60 years (IQR 18). The median serum levels were: T3 – 1.8 nmol/L (IQR 1.1), T4 – 15 pmol/L (IQR 9), and TSH – 3.6 mIU/L (IQR 1.3). Based on the diagnostic criterion of low T3 with normal T4 and TSH, 60 patients (27.3%) were found to have ESS.

Conclusion: Euthyroid Sick Syndrome is a frequent and clinically relevant cause of thyroid function test abnormalities in critically ill patients. Its recognition is essential for avoiding misdiagnosis and inappropriate treatment in ICU settings.

Keywords: Critical Illness, Euthyroid Sick Syndrome, Intensive Care Units, Non-thyroidal Illness Syndrome, Serum T3, Thyroid Function Tests, Thyrotropin.

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INTRODUCTION

Endocrine disorders, particularly those involving the thyroid gland, are a significant contributor to global morbidity and mortality. In Pakistan, the prevalence of thyroid-related illnesses is approximately 3%, reflecting a considerable public health burden (1). Among these, euthyroid sick syndrome—also known as non-thyroidal illness syndrome—emerges as a clinically relevant but often under-recognized condition. It is characterized by abnormal thyroid function test (TFT) results observed in patients who are severely ill, malnourished, or recovering from major surgeries, despite having no preexisting thyroid pathology (2). The syndrome is believed to reflect a disruption in the hypothalamic-pituitary-thyroid axis, resulting in a hormonal profile typically marked by decreased total and free triiodothyronine (T3), with normal or low thyroxine (T4) and thyroid-stimulating hormone (TSH) levels (3). Low serum T3 concentrations have been identified in as many as 40% to 100% of hospitalized individuals, while reduced TSH is observed in about 10% of cases (4). Importantly, serum total T4 has been shown to have prognostic significance, with mortality rates escalating from 50% to 80% as T4 levels decline below 4 mcg/dL and 2 mcg/dL, respectively (5,6). These findings underscore the clinical importance of accurately interpreting thyroid function in critically ill patients.

Misdiagnosis can lead to unnecessary and potentially harmful interventions, particularly since overt thyroid dysfunction may mimic or coexist with euthyroid sick syndrome. To minimize diagnostic confusion, it is recommended that TFTs in clinically euthyroid patients not be repeated until at least six weeks after hospital admission (7,8). Although the precise pathophysiology of euthyroid sick syndrome remains uncertain, several mechanisms have been proposed. These include the presence of thyroid hormone-binding inhibitors, increased circulating levels of proinflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-1 (IL-1), and interleukin-6 (IL-6), and the influence of certain medications like propranolol and amiodarone (9,10). Given the prevalence of thyroid dysfunction in hospitalized patients and the diagnostic challenges associated with distinguishing true thyroid disease from euthyroid sick syndrome, this study aims to evaluate the patterns of thyroid hormone alterations in acutely ill individuals and assess their potential clinical implications.

METHODS

This comparative cross-sectional study was conducted at the Department of Medicine, Combined Military Hospital (CMH), Jhelum, over a six-month period from January to June 2024. The sample size was estimated using the World Health Organization (WHO) Sample Size Calculator, employing a 95% confidence level, a 5% margin of error, and a 3% prevalence of thyroid-related illnesses in the Pakistani population (1). A non-probability consecutive sampling technique was employed to recruit participants. Ethical approval was obtained from the Institutional Ethical Review Board prior to the commencement of the study (IERB # A/13/02/24), and informed written consent was obtained from all participants before their enrollment. Patients aged between 18 and 65 years who were admitted to the Medical Intensive Care Unit (ICU) for non-thyroidal acute illnesses were included in the study. To ensure internal validity, individuals with a known history of thyroid disorders, pregnant or lactating women, and those diagnosed with immune-mediated illnesses were excluded. This stratification was aimed at eliminating potential confounding variables that might independently affect thyroid function tests. For each enrolled patient, thyroid function tests—including total triiodothyronine (T3), total thyroxine (T4), and thyroid-stimulating hormone (TSH)—were performed upon admission. Blood samples were analyzed in the hospital's diagnostic laboratory using standardized assay methods; however, the specific assay techniques or laboratory reference ranges were not reported, which may limit reproducibility and inter-laboratory comparability of findings. Data entry and analysis were conducted using Statistical Package for Social Sciences version 24.0 (SPSS-24.0). Descriptive statistics were applied, with frequencies and percentages calculated for categorical variables. Continuous variables such as age, T3, T4, and TSH levels were summarized using medians and interquartile ranges (IQR), owing to the expected non-parametric distribution of the biochemical data.

RESULTS

A total of 220 patients were included in the study, of whom 140 (63.6%) were male and 80 (36.4%) were female. The overall median age of participants was 60 years, with an interquartile range (IQR) of 18 years. Gender-specific analysis revealed that the median age

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for male participants was 57 years (IQR 19), whereas for females it was 67 years (IQR 23), indicating that female participants tended to be older. The median serum T3 level across the study population was 1.8 nmol/L (IQR 1.1), while the median T4 and TSH levels were 15 pmol/L (IQR 9) and 3.6 mIU/L (IQR 1.3), respectively. Based on the diagnostic criteria for euthyroid sick syndrome (ESS), defined as low T3 in the presence of normal T4 and TSH, 60 patients (27.3%) were identified to have ESS. Among these, 42 patients (70%) were male and 18 (30%) were female, suggesting a higher prevalence of ESS among male participants. Further analysis of the data was performed to explore age-related trends in euthyroid sick syndrome (ESS) prevalence. Among the 60 patients diagnosed with ESS, a higher proportion was observed in older age groups. Specifically, 70% (42/60) of ESS cases were found in patients aged 60 years and above, suggesting an age-associated increase in thyroid hormone alterations among critically ill individuals. In contrast, younger patients (<60 years) accounted for only 30% (18/60) of ESS cases. Although detailed stratification by illness category was not available, this age-based distribution underscores the vulnerability of older patients to develop non-thyroidal illness syndrome. Data on clinical outcomes such as length of ICU stay and mortality were not collected; thus, correlation of thyroid hormone levels with prognostic outcomes could not be assessed. Inclusion of such variables in future studies is recommended to better understand the clinical significance of ESS in hospitalized populations.

Table 1: Demographic Characteristics

Variable	Value
Total Patients	220
Male	140 (63.6%)
Female	80 (36.4%)
Median Age (Overall)	60 (IQR 18)
Median Age (Male)	57 (IQR 19)
Median Age (Female)	67 (IQR 23)

Table 2: Thyroid Function Test Results

Hormone	Median Value	IQR
T3	1.8 nmol/L	1.1
T4	15 pmol/L	9
TSH	3.6 mIU/L	1.3

Table 3: ESS Frequency by Gender

ESS Status	Total Patients	Male (%)	Female (%)
ESS Present	60	42 (70%)	18 (30%)
ESS Absent	160	98 (61.2%)	62 (38.8%)

Table 4: ESS Distribution by Age Group

Age Group	ESS Patients	Percentage of ESS Cases
<60 years	18	30%
≥60 years	42	70%

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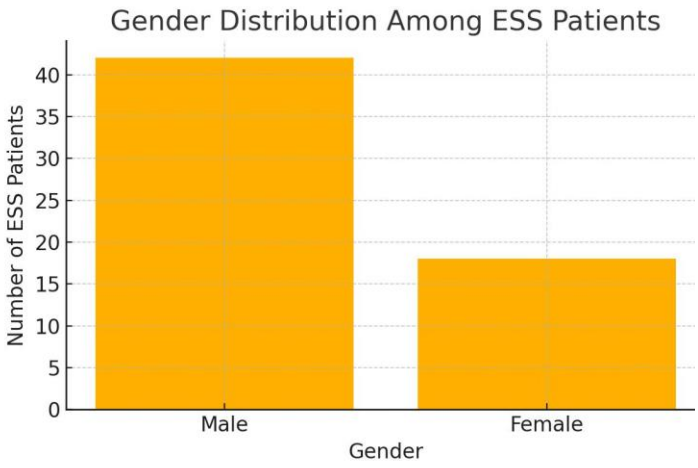


Figure 1 Gender Distribution Among ESS Patients

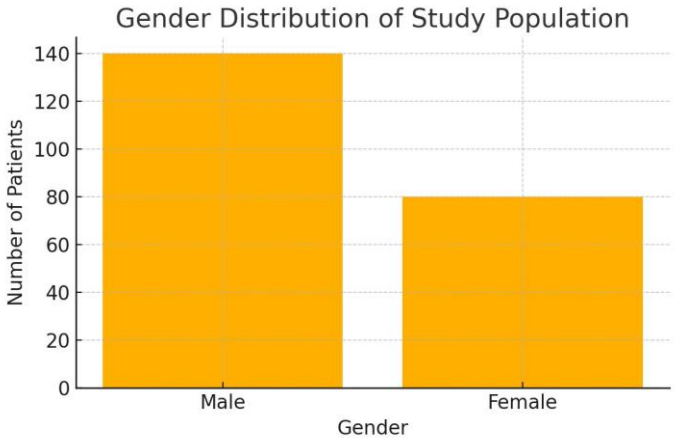


Figure 2 Gender Distribution of Study Population

DISCUSSION

The findings of this study, identifying a 27.3% prevalence of euthyroid sick syndrome (ESS) among critically ill patients, align with existing literature that demonstrates a wide range of ESS incidence in various clinical populations. The higher proportion of ESS among males and older individuals reinforces previously reported trends indicating increased vulnerability in these subgroups. This pattern is consistent with other studies that observed ESS in 24% to 58% of patients with critical illnesses, malignancies, and systemic infections, including those undergoing hemodialysis or diagnosed with COVID-19 (11-14). In particular, the presence of low T3 levels, often accompanied by normal or low T4 and TSH, has been reported in up to 100% of hospitalized patients, particularly those with severe systemic stress (15,16). These hormonal changes are thought to reflect an adaptive response to conserve energy in the setting of illness but may paradoxically worsen prognosis when sustained. The pathophysiology of ESS remains multifactorial and incompletely understood. The study's observations support current theories that implicate inflammatory cytokines—such as IL-1, IL-6, and TNF-alpha—in disrupting the hypothalamic-pituitary-thyroid axis, inhibiting deiodinase activity, and altering thyroid hormone transport and receptor binding (17,18). Additionally, factors such as reduced albumin, heparin, aspirin, corticosteroids, and beta-blockers may contribute to misleading thyroid function profiles in acutely ill patients, as reflected in the altered levels of T3, T4, and TSH seen in this cohort. These biochemical patterns can complicate diagnostic accuracy, especially in the absence of clinical hypothyroidism, and highlight the importance of careful interpretation of TFTs in ICU settings (19,20). It is notable that ESS has been associated with longer hospital stays, increased ventilatory support, and higher mortality, which underscores its clinical relevance and prognostic implications.

While the study provides valuable insight into the prevalence and distribution of ESS in a Pakistani tertiary care setting, it has several limitations. The absence of data on clinical outcomes such as duration of ICU stay, mortality rates, and long-term follow-up limits the assessment of ESS as a prognostic marker. Moreover, the exclusion of illness-specific categories prevents a deeper understanding of how different disease processes may differentially influence thyroid function. Additionally, the study relied solely on total hormone levels, without assessing reverse T3 or free hormone fractions, which are often more sensitive in diagnosing ESS. The use of a single-center design and non-probability sampling further limits generalizability. Despite these limitations, the study's strengths include a clearly defined patient population, adherence to standardized inclusion criteria, and consistent use of diagnostic thresholds for ESS. These elements lend credibility to the reported prevalence and demographic associations. The findings support existing evidence advocating against premature or unnecessary repeat TFTs in critically ill euthyroid patients, especially within the first six weeks of hospitalization, to avoid misdiagnosis and overtreatment (21,22). Future research should aim to include larger, multicentric cohorts with stratification by illness type, severity scores, and serial monitoring of thyroid hormones, including reverse T3 and free T3/T4. Incorporating clinical outcome data would allow for a more robust evaluation of the prognostic significance of ESS and the potential therapeutic value of thyroid hormone supplementation in select patient groups. As seen in studies involving patients undergoing cardiac

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surgery and COVID-19 infection, preemptive or corrective interventions targeting thyroid hormone abnormalities may offer measurable benefits and deserve further exploration.

CONCLUSION

Sick Euthyroid Syndrome should be carefully considered when interpreting thyroid function tests in critically ill patients, particularly those admitted to intensive care settings. The findings of this study emphasize the prevalence of ESS in such populations and highlight the risk of misdiagnosis if thyroid abnormalities are assessed without clinical correlation. Recognizing ESS as a physiological response to severe illness rather than true thyroid dysfunction is essential to avoid unnecessary treatment and to better predict patient outcomes. This reinforces the importance of a cautious, context-driven approach to thyroid function evaluation in acute care medicine.

AUTHOR CONTRIBUTION

Author	Contribution
Farah Rao*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Javed Ahmad Khan	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Asad Sufian Azeem	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Zaboor Ahmed	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Minahil Khaliq	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Syed Haider Tirmizi	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

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