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SICK EUTHYROIDISM IN CRITICALLY ILL PATIENTS: A CROSS-SECTIONAL STUDY IN A TERTIARY CARE FACILITY

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Abstract

OBJECTIVE

To determine the frequency of sick euthyroidism in critically ill patients admitted to a tertiary care hospital.

METHODOLOGY

This research was carried out in the ICU of SMBBMU, Civil Hospital Larkana, focusing on critically ill individuals aged 18 to 70 years, each requiring at least a 24-hour ICU stay. To prevent potential biases, participants with a history of thyroid disorders, endocrine-related tumors, or pregnancy were omitted. Blood samples were collected and examined to assess thyroid function, diagnosing sick euthyroidism based on variations in T3, rT3, and TSH levels. Statistical computations were performed using SPSS 26.0, applying descriptive metrics and Chi-square assessments to analyze findings ($p \leq 0.05$).

RESULTS

Among the 186 patients in intensive care, the average age was 56.70 ± 11.70 years, with 78.0% being older than 50 years and 22.0% falling within the 20–50 age range. Women (68.3%) were more frequently affected than men (31.7%). Sick euthyroidism was observed in 39.24% of cases. Those diagnosed with the condition exhibited notably reduced FT3 ($p=0.026$) and TSH levels ($p=0.032$) and had longer ICU stays compared to others ($p=0.003$).

CONCLUSION

Sick euthyroidism is commonly prevalent in tertiary care ICU's among critically ill patients and is associated with prolonged ICU stay but relatively older age and female predominance. The observed thyroid dysfunction, especially low FT3 and TSH levels, may indicate disease severity by affecting immune function,

metabolism, and morbidity. The long-term prognostic value and potential benefits of thyroid hormone therapy in critically ill patients need further study.

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INTRODUCTION

Sick euthyroidism (also called NTIS or low triiodothyronine syndrome) is the most common thyroid dysfunction observed in critically ill patients [1]. Thyroid function tests changes or where treatment has been begun without a primary thyroid disease is the key feature of this condition, and it is often considered an adaptive reaction to acute or critical illness. Due to its considerable effect on patient outcomes—especially being linked to increased morbidity and mortality—it has become an important area of interest in critical care medicine [2].

There are completely different populations of patients who are transferred to tertiary care hospitals, specifically those with sepsis, organ failure, trauma, and acute cardiovascular events [3]; these patients have different disease processes specifically associated with complications in the care of the critically ill patients themselves.Many of these diseases are physiologic and systemic stressors, placing them at risk for the disruption of normal thyroid physiology.

Most common features of sick euthyroidism are low serum triiodothyronine (T3) concentrations, high reverse triiodothyronine (rT3) concentrations and thyrotropin (TSH) concentrations which are variable [4,5]. These hormonal changes are associated with impaired metabolic function and may lead to adverse clinical consequences. The metabolic effects of NTIS include reduced energy expend-iture associated with alterations in substrate metabolism that may underlie muscle loss, and vulnerability to infection [6]. Well-known studies have demonstrated a wide variability in the rate of sick euthyroidism in the critically ill patient. As such, depending on the population characteristics, the frequency of underlying pathologies and the criteria used for diagnosis, its prevalence can vary between 10% and 40% [7,8]. One study found this conditional NTIS in 38.7% of critically ill patients upon hospital admission [9].

Besides the above, sick euthyroidism has also been implicated in underlying critical illness. Disruption of thyroid hormone homeostasis contributes to multi-system organ dysfunction and may impair the immune response, tissue repair, and propensity to develop muscle wasting. These metabolic derangements can prolong length of stay and are associated with increased infection rates, translating to increased morbidity burden of the critically ill [10,11].

Sick euthyroidism may also be present and aggravate the critical illness. Dysregulated thyroid hormone may lead to multi-organ dysfunction, decrease in immune function, delayed wound healing, and increased muscle atrophy. These metabolic alterations can lead to extended hospital stays and increased risk for the development of infections thereby enhancing the overall morbidity burden in critically ill patients [10,11]. In addition, sick euthyroidism has been associated with higher mortality risk in this patient group largely due to the impact of thyroid hormone changes on cardiovascular, immune and metabolic function [12].

The existence of sick euthyroidism in critically ill patients has important clinical implications, hence it should be studied in a tertiary care hospital environment. This condition, characterized by subclinical hyper- or hypothyroidism in the absence of intrinsic thyroid disease, has profound effects on cardiovascular, immunological and metabolic health and can impact morbidity and mortality [5]. Identifying NTIS as a biomarker may allow stratification of risk, and guide the personalized approach to patient management. Given substantial variability in reported prevalence, further investigation of NTIS in a tertiary care setting is needed to improve clinical awareness and management of such patients.

METHODOLOGY

A descriptive cross-sectional study was conducted to determine the prevalence of sick euthyroidism in critically ill patients admitted in the Intensive Care Unit (ICU) of SMBBMU Medical Unit 2, Civil Hospital Larkana, for a period of 6 months. A total of 186 patients, aged between 18 and 70 years, irrespective of gender, were selected through non-probability consecutive sampling, provided they met

the predefined criteria for critical illness and had an ICU stay of at least 24 hours. Critically ill patients were identified as those requiring ICU admission due to severe, acute medical conditions or injuries, necessitating intensive medical intervention, continuous monitoring, and in some cases, advanced life support measures such as mechanical ventilation or hemodynamic support. To eliminate potential confounding variables, individuals with a pre-existing history of thyroid disease, those on thyroid hormone replacement therapy or medications affecting thyroid function, patients with ICU stays shorter than 24 hours, organ donors, individuals diagnosed with endocrine-related tumors, and pregnant or lactating women were excluded from the study. Upon obtaining informed consent from the patient's next of kin, key clinical parameters, including body temperature, respiratory rate, heart rate, and blood pressure, were recorded. Body temperature was measured using a mercury thermometer, while other vital signs were monitored with a Philips MP series monitor. Blood samples were collected and analyzed in the hospital laboratory for thyroid function testing, and sick euthyroidism was diagnosed based on the presence of at least one of the following criteria: serum triiodothyronine (T3) levels below 70 ng/dL, reverse triiodothyronine (rT3) levels exceeding 30 ng/dL, or abnormal thyroid-stimulating hormone (TSH) levels, specifically below 0.3 mIU/L or above 5 mIU/L. Data entry and analysis were conducted using SPSS version 26.0, with descriptive statistics applied to summarize demographic and clinical characteristics, using mean and standard deviation for continuous variables and frequencies with percentages for categorical variables. The Chi-square test was employed to assess statistical significance, considering a p-value ≤ 0.05 as indicative of statistical significance.

RESULTS

In this study involving 186 participants, the mean age was 56.70 ± 11.70 years, with 78.0% of the individuals aged over 50 years and 22.0% between 20 and 50 years. Females constituted the majority of the study population at 68.3%, while males accounted for 31.7%. The average duration of ICU stay was 2.39 ± 1.29 days, with 83.9% of patients remaining in the ICU for 1 to 3 days, whereas 16.1% had an extended stay of more than 3 days. Thyroid function analysis revealed a mean TSH level of 4.44 ± 0.90 mIU/L, an FT3 level of 2.74 ± 0.26 pmol/L, an FT4 level of 1.50 ± 0.50 ng/dL, and an rT3 level of 233.43 ± 47.89 pmol/L (TABLE I).

A comparative analysis of thyroid hormone levels between Sick Euthyroid (n=73) and Non-Sick Euthyroid (n=113) groups highlighted significant variations. The FT3 levels in the Sick Euthyroid group were significantly lower (2.69 ± 0.25 pmol/L) than those in the Non-Sick Euthyroid group (2.78 ± 0.26 pmol/L; p=0.026). Similarly, TSH levels were notably lower in the Sick Euthyroid group (4.27 ± 0.96 mIU/L) compared to the Non-Sick Euthyroid group (4.56 ± 0.85 mIU/L; p=0.032). Although FT4 levels tended to be lower in the Sick Euthyroid group (1.41 ± 0.49 ng/dL) than in the Non-Sick Euthyroid group (1.56 ± 0.49 ng/dL), the difference was marginally non-significant (p=0.051). Conversely, rT3 levels were similar between both groups (232.21 ± 50.54 pmol/L vs. 234.22 ± 46.31 pmol/L), showing no statistical significance (p=0.780) (TABLE II).

A further comparison of demographic and clinical characteristics between the Sick Euthyroid (n=73) and Non-Sick Euthyroid (n=113) groups revealed significant differences in gender distribution, age, and ICU stay duration. The proportion of males was considerably higher in the Non-Sick Euthyroid group (38.9%) compared to the Sick Euthyroid group (20.5%), a difference that was statistically significant (p=0.008). Regarding age distribution, a significantly larger proportion of Sick Euthyroid patients were above 50 years (87.7%) compared to 71.7% in the Non-Sick Euthyroid group, while the latter had a greater percentage of patients aged 20–50 years (28.3%) than the Sick Euthyroid group (12.3%; p=0.010). ICU stay duration also varied significantly, with 26.0% of Sick Euthyroid patients requiring an ICU stay of more than 3 days, compared to only 9.7% in the Non-Sick Euthyroid group (p=0.003). Conversely, 90.3% of the Non-Sick Euthyroid patients had ICU stays between 1 and 3 days, compared to 74.0% in the Sick Euthyroid group (TABLE III).

DISCUSSION

Sick euthyroid syndrome (SES), also referred to as non-thyroidal illness syndrome, is frequently observed in critically ill patients and is characterized by abnormal thyroid function tests without intrinsic

thyroid disease. In our study, SES was present in 39.24% of critically ill patients, which aligns closely with the 38.7% prevalence reported by Guo J et al [9]. However, Amorim FF et al. found a considerably lower prevalence of 11.8%, suggesting variability in SES occurrence among different populations, possibly due to differences in study design, patient selection, or severity of illness [3]. This indicates the need for a more standardized method of assessing thyroid function in these patients.

Thyroid dysfunction seen in critical illness is commonly associated with low triiodothyronine (T3) levels with or without changes in thyroxine (T4) and thyroid-stimulating hormone (TSH). This adaptive response is thought to conserve energy during severe stress, yet it remains unclear whether SES is simply a marker of disease severity or if it actively contributes to worsened outcomes. Schwarz Y et al. found that SES on presentation in COVID-19 patients was linked to greater disease severity, reinforcing the hypothesis that altered thyroid function may correlate with critical illness prognosis [13]. Similarly, El-Mekkawy MS et al. reported that SES was predictive of illness severity in pediatric sepsis, emphasizing the potential utility of thyroid function tests as prognostic markers [14].

In sepsis-related studies, SES prevalence and its impact on outcomes have been extensively investigated. A study by Krishna A et al. in an ICU setting in South Korea found a significant proportion of septic patients exhibiting SES, mirroring our findings [15]. Furthermore, Yanni GN et al. demonstrated that SES is prevalent among children with sepsis, reinforcing the notion that critical illness universally affects thyroid function across age groups [16]. The underlying mechanism is believed to be related to reduced peripheral conversion of T4 to T3, inflammatory cytokine-mediated suppression of deiodinase activity, and altered binding protein levels, all of which contribute to the observed biochemical pattern.

Given the high prevalence of SES in critical illness, several studies have explored whether thyroid hormone supplementation could improve outcomes. Kovacevic M et al. conducted two randomized, placebo-controlled trials evaluating triiodothyronine (T3) supplementation in septic shock patients with SES [17]. These trials provided insights into potential therapeutic strategies, but the findings remain inconclusive regarding mortality benefits. While some evidence suggests that correcting low T3 levels may improve hemodynamic stability, concerns regarding adverse effects, particularly increased myocardial oxygen demand, necessitate further large-scale trials before routine supplementation can be recommended.

Our study findings suggest that SES is common among critically ill patients and may serve as a marker for disease severity. This is supported by Ahmed MA et al., who assessed thyroid dysfunction in ICU patients at Aswan University Hospital, demonstrating a significant association between SES and clinical outcomes [18]. Bhat K et al. further reinforced the need for routine thyroid function assessments in critically ill patients to better understand the clinical implications of SES [19]. However, despite the strong association, causation remains unclear, and whether SES directly affects morbidity and mortality is yet to be definitively established.

One of the strengths of our study is its robust sample size and the inclusion of critically ill patients across various conditions, allowing for a broad assessment of SES prevalence. Additionally, comparison with multiple studies strengthens the validity of our findings. However, limitations include the lack of long-term follow-up to determine the impact of SES on patient outcomes and the absence of interventional analysis to assess the benefits of thyroid hormone replacement therapy.

Future research should focus on standardized diagnostic criteria for SES in critically ill patients and evaluate the potential benefits and risks of thyroid hormone supplementation in well-designed clinical trials. Additionally, studies should explore whether SES correction can lead to improved patient outcomes or if it remains merely an epiphenomenon of critical illness. Given the high prevalence and potential prognostic significance of SES, routine thyroid function screening in ICU patients may be beneficial for risk stratification, though therapeutic interventions should be approached with caution until more definitive evidence emerges.

CONCLUSION

Sick euthyroidism is commonly prevalent in tertiary care ICU's among critically ill patients and is

associated with prolonged ICU stay but relatively older age and female predominance. The observed thyroid dysfunction, especially low FT3 and TSH levels, may indicate disease severity by affecting immune function, metabolism, and morbidity. The long-term prognostic value and potential benefits of thyroid hormone therapy in critically ill patients need further study.

Table I: Characteristics of Study Participants (n=186)	
Variable	**n** (%)
Age (Mean ± SD) = 56.70 ± 11.70 years	
20 – 50 years	41 (22.0)
>50 years	145 (78.0)
Gender	
Male	59 (31.7)
Female	127 (68.3)
Duration of ICU Stays (Mean ± SD) = 2.39 ± 1.29 days	
1 – 3 days	156 (83.9)
>3 days	30 (16.1)
TSH (Mean ± SD) = 4.44 ± 0.90 mIU/L	
FT3 (Mean ± SD) = 2.74 ± 0.26 pmol/L	
FT4 (Mean ± SD) = 1.50 ± 0.50 ng/dL	
rT3 (Mean ± SD) = 233.43 ± 47.89 pmol/L	

Table II: Comparison of thyroid hormone levels between Sick Euthyroid and Non-Sick Euthyroid (n=186)			
Groups	**Sick Euthyroid** (n=73)	**Non-Sick Euthyroid** (n=113)	**P-value**
FT3(pmol/L)	2.69 ± 0.25	2.78 ± 0.26	0.026
FT4 (ng/dL)	1.41 ± 0.49	1.56 ±0.49	0.051
TSH (mIU/L)	4.27 ± 0.96	4.56 ±0.85	0.032
rT3(pmol/L)	232.21 ± 50.54	234.22 ± 46.31	0.780

Table III: Characteristics of the study population between Sick Euthyroid and Non-Sick Euthyroid (n=186)

Characteristics		**Sick Euthyroid** (n=73)	**Non-Sick Euthyroid** (n=113)	**P-Value**
Gender	Male	15 (20.5%)	44 (38.9%)	0.008
	Female	58 (79.5%)	69 (61.1%)	
Age	20 – 50 years	9 (12.3%)	32 (28.3%)	0.010
	>50 years	64 (87.7%)	81 (71.7%)	
Duration of ICU Stays	1 – 3 days	54 (74.0%)	102 (90.3%)	0.003
	>3 days	19 (26.0%)	11 (9.7%)	

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