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Original Research Article

Association of Subclinical Hypothyroidism with Neurological and Functional Recovery Following Traumatic Brain Injury

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Conflict of interest: Nil

Abstract

Background: Neuroendocrine dysfunction is increasingly recognised as a significant consequence of traumatic brain injury (TBI). Alterations in thyroid hormone regulation may influence neuronal repair, cerebral metabolism, and functional recovery. Subclinical hypothyroidism (SCH), defined as elevated thyroid-stimulating hormone (TSH) with normal free thyroxine (fT4), may adversely affect recovery courses following TBI.

Objective: To evaluate the association between subclinical hypothyroidism and neurological as well as functional recovery in patients with traumatic brain injury.

Methods: This prospective observational study included 100 adult patients with mild-to-severe TBI admitted to a tertiary neurosurgical centre. Thyroid function tests (TSH and fT4) were performed within 72 hours of admission. Patients were categorised into SCH and euthyroid groups. Neurological recovery was assessed using Glasgow Coma Scale (GCS) improvement, and functional outcome was measured using the Glasgow Outcome Scale (GOS) at 28 days. Hospital stay duration and mortality were also analysed.

Results: Subclinical hypothyroidism was identified in 18% of patients. Baseline injury severity was comparable between groups. SCH patients demonstrated significantly lower discharge GCS scores (11.3 ± 3.8 vs 13.9 ± 2.9; p=0.01), reduced GCS improvement (2.3 ± 1.9 vs 4.5 ± 2.1; p=0.003), lower rates of favorable GOS outcome (44% vs 74%; p=0.02), and longer hospital stay (14.8 ± 4.9 vs 9.6 ± 3.4 days; p<0.001). TSH levels correlated negatively with neurological improvement and positively with the duration of hospital stay.

Conclusion: Subclinical hypothyroidism is associated with delayed neurological recovery and poorer functional outcomes following TBI. Early thyroid axis screening may aid prognosis and risk stratification.

Keywords: Traumatic Brain Injury, Subclinical Hypothyroidism, Thyroid Dysfunction, Neurological Recovery, Prognosis.

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Introduction

Traumatic brain injury (TBI) remains a major global health burden and is a leading cause of death and long-term disability across all age groups [1,2]. Despite improvements in neurocritical care and surgical management, variability in recovery outcomes persists. Secondary injury mechanisms—including neuroinflammation, excitotoxicity, oxidative stress, and metabolic dysregulation—significantly influence neurological outcomes [3].

Increasing evidence highlights neuroendocrine dysfunction as an under recognized yet clinically significant consequence of TBI [4,5]. The hypothalamic–pituitary axis is particularly vulnerable due to its subtle vascular supply and anatomical location. Pituitary dysfunction following TBI may result from ischemia, haemorrhage, inflammation, or direct mechanical injury [6].

Thyroid hormones play a central role in neuronal differentiation, synaptogenesis, mitochondrial function, and cerebral metabolism [7]. Experimental models suggest thyroid hormones exert neuroprotective effects, reducing apoptosis and enhancing neuroplasticity after brain injury [8].

Alterations in thyroid function have been documented in critically ill patients, including those with severe TBI [9,10]. While non-thyroidal illness syndrome has been extensively studied, subclinical hypothyroidism (SCH) has received comparatively less attention in neurotrauma research. SCH is defined biochemically as elevated TSH with normal circulating free T4 levels [11]. Although often asymptomatic, SCH has been associated with cognitive impairment, mood disturbances, and slowed information processing [12]. Recent studies suggest that thyroid hormone levels may correlate with injury severity and clinical outcomes in TBI patients [13,14]. However, data specifically examining SCH and its impact on neurological and functional recovery remain limited. The present study aimed to evaluate the association between subclinical hypothyroidism and recovery outcomes following traumatic brain injury.

Materials and Methods

Study Design and Setting: This prospective observational study was conducted in the Department of Neurosurgery at a tertiary care teaching hospital over 12 months.

Study Population: Adult patients (≥18 years) admitted within 24 hours of traumatic brain injury were included. Exclusion criteria comprised known thyroid disease, pregnancy, pituitary disorders, prior thyroid hormone therapy, and severe systemic illness affecting thyroid function.

Data Collection: Baseline demographic data, mechanism of injury, and admission neurological status were recorded. Injury severity was classified based on the Glasgow Coma Scale (GCS):

- Mild: 13–15
- Moderate: 9–12
- Severe: ≤8

Thyroid Function Assessment: Serum TSH and free T4 were measured within 72 hours of admission using standardised immunoassay techniques. SCH was defined as elevated TSH (>4.5 mIU/L) with normal free T4.

Outcome Measures: Neurological recovery was assessed by comparing admission and discharge GCS. Functional outcome at 28 days was evaluated using the Glasgow Outcome Scale (GOS). Outcomes were categorised as favourable (good recovery + moderate disability) or unfavourable.

Statistical Analysis: Data were analysed using SPSS. Continuous variables were expressed as mean ± SD and compared using Student's t-test. Categorical variables were compared using Chi-square test. Correlations were assessed using Pearson's coefficient. A p-value <0.05 was considered statistically significant.

Results

Baseline Characteristics: Among 100 enrolled patients, 18 (18%) were diagnosed with subclinical hypothyroidism. Baseline characteristics were comparable between groups.

Table 1: Baseline Characteristics and Clinical Outcomes

Variable	Euthyroid (n=82)	SCH (n=18)	p-value
Age (years)	35.9 ± 13.8	39.7 ± 15.4	0.31
Male (%)	73%	67%	0.58
Admission GCS	9.4 ± 3.2	9.0 ± 3.5	0.61
Discharge GCS	13.9 ± 2.9	11.3 ± 3.8	0.01
GCS Improvement	4.5 ± 2.1	2.3 ± 1.9	0.003
Favourable GOS (%)	74%	44%	0.02
Hospital Stay (days)	9.6 ± 3.4	14.8 ± 4.9	<0.001

Patients with SCH demonstrated significantly reduced neurological improvement and poorer functional outcomes.

Favourable GOS outcomes were observed in 74% of euthyroid patients compared to 44% of SCH patients (p = 0.02).

The mean hospital stay was significantly longer in the SCH group.

Correlation analysis revealed:

- TSH vs GCS improvement: r = –0.34, p=0.002
- TSH vs hospital stay: r = 0.41, p<0.001

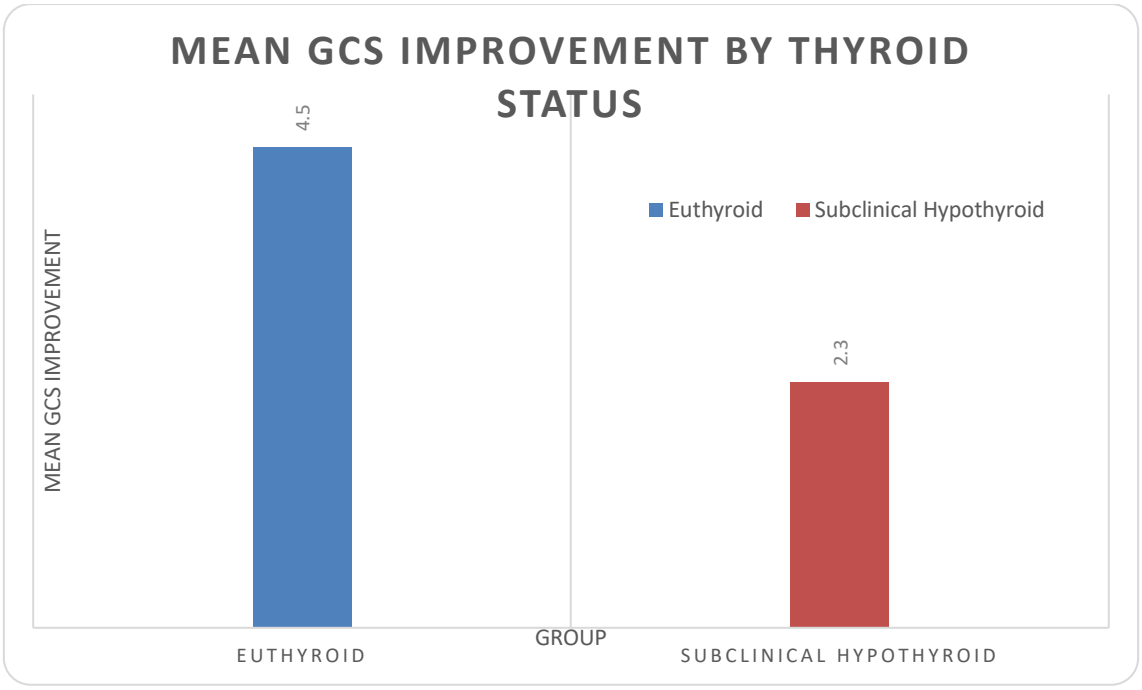

Figure 1: Mean GCS Improvement by Thyroid Status

Patients with subclinical hypothyroidism demonstrated significantly lower mean GCS improvement compared to euthyroid patients, indicating delayed neurological recovery.

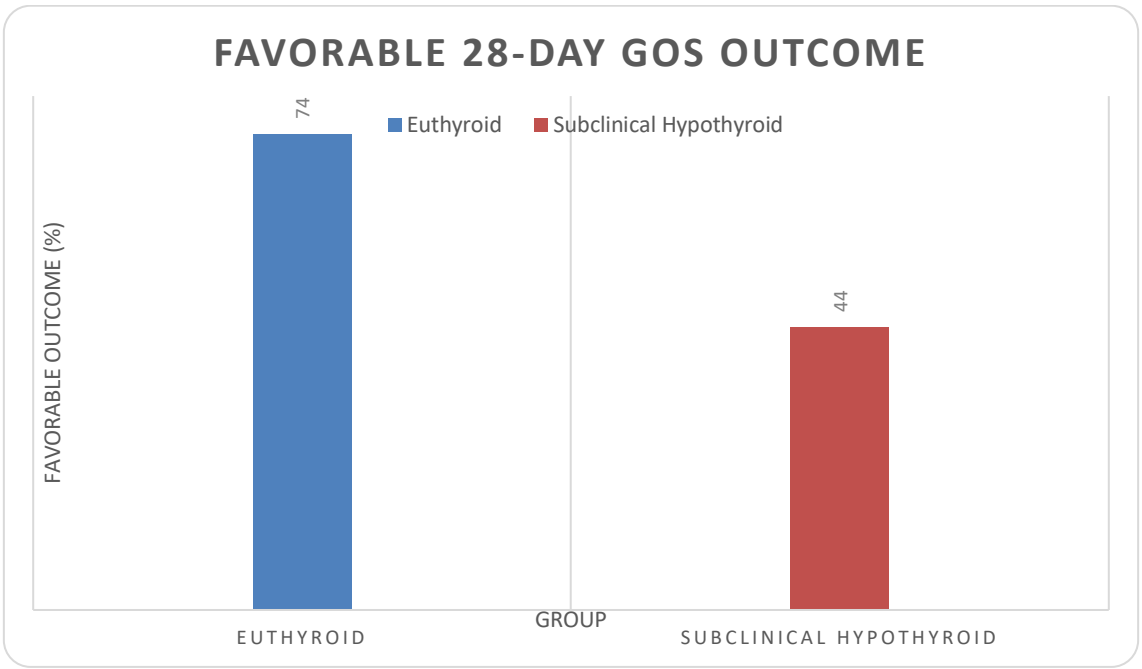

Figure 2: Favourable 28-Day GOS Outcome

The proportion of favourable 28-day functional outcomes was substantially lower in the subclinical hypothyroid group compared to euthyroid patients.

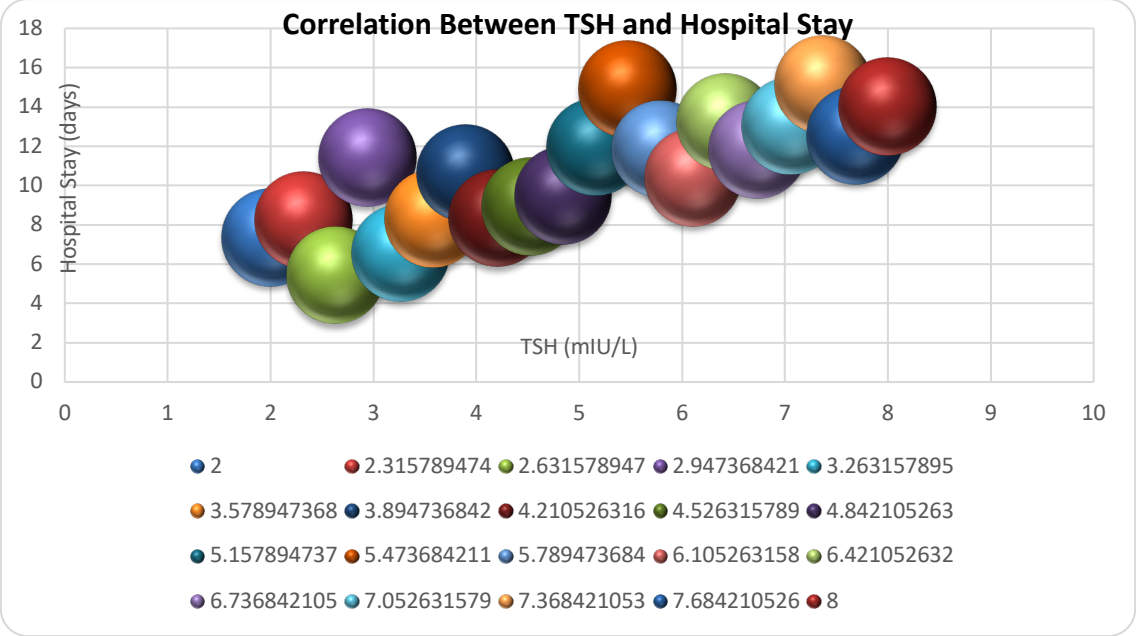

Figure 3: Correlation between TSH and Hospital Stay (Scatter plot demonstrating positive correlation)

A positive correlation is observed between serum TSH levels and the duration of hospital stay, indicating that longer hospitalisation is associated with higher TSH values.

Discussion

This study demonstrates that subclinical hypothyroidism is present in nearly one-fifth of patients with acute traumatic brain injury and is associated with delayed neurological recovery and poorer functional outcomes. Patients with SCH exhibited significantly lower GCS improvement, reduced rates of favourable Glasgow Outcome Scale, and prolonged hospitalisation compared to euthyroid individuals. These findings suggest that even subtle thyroid axis disturbances may have clinically meaningful implications in the acute phase of neurotrauma.

Our findings are consistent with previous literature documenting neuroendocrine dysfunction following TBI [4,5]. The hypothalamic–pituitary axis is particularly susceptible to traumatic and ischemic insults, potentially leading to transient or persistent hormonal alterations [6]. Thyroid hormones play a central role in regulating cerebral metabolism, mitochondrial activity, synaptic plasticity, and neurogenesis [7,8]. Therefore, impaired thyroid axis responsiveness, reflected by elevated TSH levels in SCH, may compromise neuronal repair mechanisms during the critical recovery period. While prior clinical studies have demonstrated associations between thyroid dysfunction and adverse neurological outcomes [13,14], most investigations have focused on low T3 syndrome or overt hypothyroidism. The present study adds to the literature by specifically evaluating subclinical hypothyroidism and demonstrating its association with early functional recovery.

The significant negative correlation between serum TSH levels and GCS improvement indicates that even mild biochemical alterations may influence neurological restitution. Additionally, the observed association between elevated TSH and prolonged hospital stay suggests broader implications for healthcare resource utilisation. Although mortality differences were not statistically significant, the numerical trend toward worse outcomes in the SCH group underscores the need for larger multicenter studies to better define this relationship.

Several limitations must be acknowledged. First, this was a single-centre study with a relatively modest sample size, which may limit generalizability. Second, thyroid function was assessed only during the acute phase; dynamic hormonal changes during subacute and chronic recovery were not evaluated. Third, we did not perform a comprehensive pituitary axis assessment, and therefore cannot exclude concomitant hormonal deficiencies. Fourth, pre-injury thyroid status was not available, raising the possibility that some cases of SCH may have predated trauma. Finally, long-term functional and neurocognitive outcomes beyond 28 days were not assessed.

Despite these limitations, the prospective design and early endocrine evaluation strengthen the clinical relevance of our findings. Future research should include larger multicenter cohorts with serial thyroid function monitoring to determine whether SCH is transient or persistent following TBI. Randomised studies evaluating the potential role of thyroid hormone modulation in selected patients may further clarify causality and

therapeutic implications. Additionally, integrating endocrine screening into standardised TBI management protocols could improve early risk stratification and individualised rehabilitation planning.

Conclusion

Subclinical hypothyroidism is relatively common in the acute phase of traumatic brain injury and is associated with slower neurological recovery, reduced rates of favourable functional outcome, and prolonged hospitalisation.

Elevated TSH levels correlate with poorer recovery parameters, suggesting that SCH may serve as a potential prognostic biomarker in TBI. Early thyroid function screening may enhance prognostic assessment and guide tailored management strategies.

Larger longitudinal studies are required to determine the long-term impact of SCH and to evaluate whether targeted endocrine interventions can improve recovery outcomes following traumatic brain injury.

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