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Original Research Article

PITUITARY DYSFUNCTION FOLLOWING MODERATE AND SEVERE TRAUMATIC BRAIN INJURY: A RETROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Traumatic brain injury (TBI) is a major cause of long-term disability worldwide. In addition to cognitive and motor deficits, moderate to severe TBI can disrupt the hypothalamic-pituitary axis, resulting in pituitary dysfunction that often goes undetected. These hormonal deficiencies can significantly impair rehabilitation, mood, and quality of life. This study aims to assess the prevalence and extent of pituitary dysfunction in patients recovering from moderate and severe TBI.

Materials and Methods: A retrospective observational study was conducted at Chandramma Dayanand Sagar Institute of Medical Education and Research, reviewing records of 100 patients (age 18–65 years) who sustained moderate (GCS 9–12) or severe (GCS ≤8) TBI between October 2023 and June 2025. Hormonal profiles were evaluated at the time of injury and again after 1 year. Functional outcomes were assessed using the Functional Independence Measure (FIM).

Results: At injury, 42% had at least one pituitary hormone deficiency, including 18% with multiple pituitary hormone deficiency (MPHD). At 1-year follow-up, 48% had at least one deficiency, and 22% had MPHD. Dysfunction was significantly more common in severe TBI patients (60%) than moderate TBI (24%, $p < 0.001$). Patients with dysfunction had lower mean FIM scores (78.4 ± 9.2 vs. 90.6 ± 8.7; $p = 0.002$) and longer rehabilitation stays (32.5 vs. 21.3 days; $p = 0.01$).

Conclusion: Pituitary dysfunction is a frequent and underrecognized complication of moderate and severe TBI, particularly in severe cases. It is associated with poorer functional outcomes and prolonged rehabilitation. Routine endocrine screening is essential for timely diagnosis and intervention.

Keywords: Traumatic Brain Injury, Pituitary Dysfunction, Hypothalamic-Pituitary Axis, Multiple Pituitary Hormone Deficiency, Functional Independence Measure, Rehabilitation Outcomes.

INTRODUCTION

Traumatic brain injury (TBI) remains a leading cause of disability, with an estimated 69 million people affected annually worldwide. Among the many long-term sequelae of moderate and severe TBI, dysfunction of the hypothalamic-pituitary axis is increasingly recognized as a significant yet often overlooked complication.[1-3] Damage to this axis can lead to partial or complete loss of pituitary hormone secretion, a condition known as post-traumatic hypopituitarism (PTHP).

The anterior and posterior pituitary glands are vulnerable to injury through mechanisms such as direct trauma, ischemia, oedema, or inflammatory responses.[4,5] This can result in a spectrum of hormonal deficits including growth hormone deficiency (GHD), hypogonadism, secondary adrenal insufficiency, central hypothyroidism, and diabetes

insipidus.[4,6,7] These deficiencies contribute to fatigue, depression, poor muscle mass, impaired cognition, and reduced quality of life—symptoms that can be mistakenly attributed solely to the primary brain injury. Studies have reported varying prevalence rates of PTHP, ranging from 15% to over 50%, influenced by injury severity, time since trauma, and testing methodology.[8-10] Despite its clinical importance, endocrine dysfunction remains underdiagnosed, partly due to nonspecific symptoms and lack of routine screening.

Given the potential for delayed or progressive hormone deficiencies, this study seeks to quantify the prevalence of pituitary dysfunction in patients with moderate and severe TBI and explore its correlation with functional outcomes using validated tools such as the Functional Independence Measure (FIM). By identifying at-risk individuals, timely hormone replacement can significantly improve rehabilitation and quality of life.

First described in 1918 by Cyran,[11] post-traumatic pituitary dysfunction has only recently gained clinical attention. Structural damage to the pituitary stalk, infarction of the pituitary, or autoimmune responses are common mechanisms implicated in hypopituitarism following head trauma.[4,7,12]

Patients may initially present with subtle symptoms—fatigue, poor concentration, or sexual dysfunction—but long-term consequences include reduced neurocognitive recovery, increased rehabilitation time, and psychosocial stress.[13,14] Growth hormone and cortisol deficiencies, in particular, have been linked with impaired healing, mood disorders, and higher dependency levels during rehabilitation.[15,16]

Despite increasing awareness, routine screening is still not universally practiced. The 2005 Consensus Guidelines by Ghigo et al,[17] and later recommendations by the Endocrine Society,[18] advocate for serial hormonal evaluation in moderate to severe TBI survivors. However, implementation remains limited in resource-constrained or non-specialist settings.

This study aims to address this gap by evaluating hormonal profiles and functional recovery trajectories in TBI patients, thereby providing evidence for integrating endocrinological evaluation in neurorehabilitation protocols.

Aims and Objectives

Aim

To assess the prevalence and impact of pituitary dysfunction in patients recovering from moderate and severe TBI.

Objectives

1. Determine the frequency of anterior and posterior pituitary hormone deficiencies.
2. Analyse the relationship between TBI severity and pituitary dysfunction.

MATERIALS AND METHODS

Study Design: Retrospective observational study conducted at Chandramma Dayanand Sagar Institute of Medical Education and Research.

Study Population

Inclusion:

100 patients aged 18–65 years with moderate (GCS 9–12) or severe (GCS ≤8) TBI.

Exclusion:

Patients with pre-existing endocrine disorders, cranial surgery, tumors or incomplete follow-up data.

Study Duration: The study was conducted between October 2023 and June 2025.

Hormonal Assessment: Performed at two time points: within 7 days of injury and again after 12 months. Hormones evaluated:

- Cortisol (8 AM)
- TSH, Free T4
- LH, FSH
- Testosterone (men), Estradiol (women)
- IGF-1
- Prolactin
- Serum/urine osmolarity and electrolytes

Deficiencies were diagnosed per laboratory reference ranges and Endocrine Society guidelines18.

Functional Outcome – FIM Score

Functional outcomes were assessed using the Functional Independence Measure (FIM) at 12 months post-injury. FIM evaluates independence in 18 activities across six domains including self-care, mobility, communication, and social cognition. Each item is scored from 1 (complete dependence) to 7 (complete independence), with total scores ranging from 18 to 12614,19. FIM is a validated and widely used tool in neurorehabilitation and correlates strongly with TBI recovery outcomes.

Statistical Analysis: Data analysed using SPSS software version 22. Chi-square test was used for categorical variables and t-tests for continuous variables. Significance was set at $p < 0.05$.

Sample size calculation: Based on an expected prevalence of pituitary dysfunction of 30%, with 95% confidence interval and 10% margin of error:

$$n = \frac{(1.96)^2 \cdot 0.3 \cdot 0.7}{(0.1)^2} \approx 81$$

Final sample size was rounded to 100 to account for potential dropouts.

RESULTS

Table 1: Frequency of Hormonal Deficiencies at Baseline (Time of Injury) and after 1-Year

Hormone Deficiency	No. of Patients (%) at Baseline	No. of Patients (%) at 1 yr Follow-Up
Multiple Pituitary Hormone Deficiency (MPHD)	18 (18%)	22 (22%)
At least one hormone deficiency	42 (42%)	48 (48%)
Growth Hormone Deficiency	20 (20%)	24 (24%)

Gonadotropin Deficiency	15 (15%)	19 (19%)
Secondary Adrenal Insufficiency	12 (12%)	15 (15%)
Central Hypothyroidism	8 (8%)	12 (12%)
Diabetes Insipidus	6 (6%)	5 (5%)

Growth Hormone Deficiency increased from 18% to 21%. Gonadotropin Deficiency rose from 16% to 19%, Secondary Adrenal Insufficiency increased from 14% to 17%, Central Hypothyroidism went up from 12% to 15%, Diabetes Insipidus slightly decreased from 6% to 5%. At least one pituitary hormone deficiency rose from 42% to 48% and MPHD increased from 18% to 22%.

Table 2: Pituitary Dysfunction by TBI Severity

TBI Severity	No. with Dysfunction	Prevalence (%)
Severe (n=50)	30	60%
Moderate (n=50)	12	24%
p-value		< 0.001

The results show that pituitary dysfunction was 60% in patients with severe TBI compared to 24% in patients with moderate TBI.

Table 3: Functional and Rehabilitation Outcomes

Outcome	With Dysfunction (n=48)	Without Dysfunction (n=52)	p-value
Mean FIM Score (±SD)	78.4 ± 9.2	90.6 ± 8.7	0.002
Mean Rehabilitation Duration	32.5 days	21.3 days	0.01

Patients with pituitary dysfunction had significantly lower FIM scores (78.4 vs. 90.6) and longer rehabilitation stays (32.5 vs. 21.3 days) which is statistically significant.

DISCUSSION

This study reinforces the growing body of evidence that pituitary dysfunction is a prevalent yet under-recognized complication of moderate and severe traumatic brain injury (TBI). With nearly half (48%) of the studied patients showing at least one hormonal deficiency one-year post-injury—and 22% having multiple pituitary hormone deficiencies (MPHD)—our findings are consistent with previously reported prevalence rates ranging from 30% to 50% in similar cohortS.[6,8,20,21]

Importantly, our study highlights that pituitary dysfunction is significantly more common in severe TBI (60%) compared to moderate TBI (24%), echoing findings from Schneider et al,[20] and Aimaretti et al.[3] The pathophysiology likely involves mechanical shearing of the pituitary stalk, vascular infarction, and secondary inflammatory responses, all of which are more pronounced in high-impact injuries.[4,5] Moreover, the posterior pituitary and hypothalamic regions are particularly vulnerable due to their anatomical location near the sella turcica and limited blood supply.

Our data also revealed that pituitary dysfunction evolves over time. While 42% of patients exhibited hormonal deficits at the time of injury, this number rose to 48% at the one-year follow-up. This progression emphasizes the dynamic nature of hypopituitarism, with both spontaneous recovery of function and delayed onset of new deficiencies being well-documented phenomena.[6,22,23] For example, growth hormone deficiency (GHD) and hypogonadism often manifest months after injury due to progressive hypothalamic-pituitary disconnection or evolving ischemic damage.[3,8,24]

A particularly striking finding in our study is the functional impact of these deficiencies. Patients with pituitary dysfunction had significantly lower Functional Independence Measure (FIM) scores at 1 year (mean 78.4 vs. 90.6; p = 0.002), and required longer rehabilitation stays (32.5 vs. 21.3 days; p = 0.01). This corroborates previous research by Bondanelli et al,[14] and Rosario et al,[25] which showed that anterior pituitary dysfunction is associated with poorer functional and cognitive recovery. Growth hormone, in particular, is known to play a critical role in neurogenesis, mood regulation, and neuromuscular rehabilitation, all of which contribute to FIM outcomes.[15,16]

The nonspecific nature of symptoms associated with hormonal deficiencies—fatigue, depression, cognitive slowing—often leads clinicians to attribute them to post-concussive syndrome or psychiatric conditions, resulting in underdiagnosis. Furthermore, routine hormonal screening is not yet a standard part of TBI management in many centers, despite consensus guidelines advocating otherwise.[17,18] Our findings support the need for routine endocrine evaluation in moderate and especially severe TBI survivors.

Interestingly, while anterior pituitary hormone deficiencies were more common, posterior pituitary involvement (e.g., diabetes insipidus) was seen in a small but clinically significant proportion (5–6%). These patients typically presented acutely and required electrolyte and fluid management. This aligns with prior studies by Dusick et al.4 and Maiya et al.5, who documented MRI evidence of posterior pituitary disruption in acute TBI.

There is also increasing evidence to suggest that autoimmunity may play a role in late-onset hypopituitarism, with studies detecting antipituitary

antibodies post-injury26. This could explain cases where dysfunction emerges months after trauma, even in the absence of structural abnormalities on imaging. Additionally, inflammation-driven oxidative damage and glial activation may contribute to hypothalamic injury, as described by Tanriverdi et al.[7,12]

From a clinical standpoint, the importance of early hormone replacement therapy cannot be overstated. Studies have shown that targeted hormone replacement—particularly with growth hormone, thyroxine, and hydrocortisone—can lead to marked improvements in mood, cognition, strength, and overall quality of life.[13,16,27] Our results strongly support the integration of endocrinological assessment and management into standard neurorehabilitation protocols, especially for patients with severe injuries or prolonged symptoms.

There are, however, several limitations to our study. Being a retrospective study, selection bias and incomplete data may have influenced results. Hormonal assays were not always uniformly repeated or dynamically tested, and subtle deficiencies may have been missed. Nonetheless, our findings provide a compelling case for prospective studies with standardized endocrine testing and long-term follow-up.

Moving forward, a multidisciplinary approach involving neurosurgeons, neurologists, rehabilitation specialists, and endocrinologists is essential. Clinicians should maintain a high index of suspicion for hypopituitarism in patients with TBI who present with unexplained fatigue, depression, sexual dysfunction, or poor functional recovery. Screening should ideally occur within 3–6 months post-injury and again at 12 months, as per guidelines.[17,18]

Finally, broader public and professional awareness is needed to improve early detection and treatment. As TBI survivors live longer and demand better quality of life, addressing the endocrine dimension of brain injury recovery becomes not just a clinical necessity but also a matter of holistic patient care.

CONCLUSION

Pituitary dysfunction is a common, clinically significant sequela of moderate to severe TBI. Routine screening—particularly in patients with severe injuries—should be integrated into follow-up protocols. Timely diagnosis and hormone replacement can improve rehabilitation outcomes and overall recovery trajectory.

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