



# **The Prevalence of Pituitary Dysfunction in Children Following Severe Traumatic Brain Injury in the Acute Phase**

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## **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors contributed to the writing of this work. All authors read and approved the final manuscript.*

## **Article Information**

DOI: 10.9734/JAMMR/2020/v32i130355

### Editor(s):

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(3) Geetanjali Rathore, University of Nebraska Medical Center, USA.  
Complete Peer review History: <http://www.sdiarticle4.com/review-history/53194>

**Original Research Article**

**Received 20 October 2019**  
**Accepted 24 December 2019**  
**Published 13 February 2020**

## **ABSTRACT**

Neuro-endocrine disorders are a frequent complication of head trauma. The exploration of these disturbances is important because it can contribute to the understanding of some symptoms presented by the patients for better management in the acute phase or during the evolution.

**Aim:** The objective of this study was to identify the anterior pituitary dysfunction of severe traumatic brain injury and to analyze the correlations between these disorders, brain lesions and clinical signs.

**Materials and Methods:** This is a prospective and descriptive study, conducted in collaboration between the pediatric intensive care unit and the clinical biochemistry laboratory of the Mohammed VI University Hospital of Marrakech. This study was spread over 9 months. It included children admitted for severe head trauma and with a clinical, hormonal and CT scan. And the interest was

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in 28 severely traumatized skulls in the acute phase. All patients received TSH, T3, T4, Prolactin and cortisol levels 8 hours after admission.

**Results:** There were twenty eight patients included in the study. Sex ratio m / f of 1.54, whose age varies between 9 months and 14 years, with an average age of 6.5 years. Half of the patients had an initial Glasgow score of 8/15. This was cerebral oedema in (46.42%) cases. In this study, the rate of endocrine disorders was 85.71%, the exploration of the thyrotropic axis proved normal in all of these patients. Low cortisol levels were observed in 11% of cases, 67.84% of children had hyperprolactinemia. One-third of the patient included in the study had 2-axis involvement, namely cortisol and prolactin. Half, on the other hand, showed only one axis.

**Conclusion:** In the aftermath of head trauma, pituitary disturbances are frequent and should be included in their management.

*Keywords: Anterior pituitary; axes; dysfunctions; trauma.*

## 1. INTRODUCTION

In children, head injuries are common, presenting the first cause of accidental death from the age of one year [1]. Their annual incidence in the United States is estimated at 1850/100 000 before 4 years, 1100/100 000 between 5 and 9 years, and 1170/100 000 between 10 and 14 years [1,2], with a predominance of boys all age [3,4]. About 80 to 90% of head injury are mild (Glasgow score 13-15) [2,5] 3 to 10% of them are graves [6].

Neuroendocrine disorders are a common complication of head trauma. Their pathophysiology revealed the sensitivity of portal vessels irrigating the pituitary gland [7]. Exploring these disturbances is important for understanding some of the symptoms of the disease.

The occurrence of pituitary deficits secondary to actual trauma (TC) is now well recognized in adults, but there are few studies in the pediatric population [5,6,7].

The objective of this study was to identify the anterior pituitary dysfunctions in children following severe traumatic brain injury in the acute phase.

## 2. MATERIALS AND METHODS

### 2.1 Study Design

This is a prospective and descriptive study, conducted in collaboration between the pediatric intensive care unit and the clinical biochemistry laboratory of the Mohammed VI University Hospital in Marrakech. This study was spread over 9 months. Included were children admitted for severe head trauma and with a clinical,

hormonal and CT scan. She was interested in 28 severely traumatized traumatic skulls in the acute phase.

The inclusion criteria were age less than 15 years at injury and severe TBI, defined as initial GCS score of 8 or less for accidental TBI.

Exclusion criteria were the presence of known pituitary deficiency before TBI and posttraumatic vegetative state for ethical reasons.

### 2.2 Hormonal Dosage

A dosage of TSH, T3, T4, Prolactin and cortisolemia was performed in all patients 8 hours after their admission.

Peripheral venous blood samples were taken within 3 hours of the trauma. In the laboratory, the tube was centrifuged for 15 minutes at 3500 rpm. After decantation, two aliquots were frozen at -20°C. The assay was performed using the Elecsys Roche Diagnostics test on the cobas 6000 analyzers.

For the serum cortisol (nmol/L), the assay has a calculated sensitivity of 10 nmol/L. For Prolactin in serum (mU/L) the assay has calculated sensitivity of 5 mU/L. For TSH (pmol/L), The assay has a calculated sensitivity of 1.3 pmol/L. The assay has a calculated sensitivity of 1.25 pmol/L for the Serum ft4 concentrations (pmol/l). And for T3 level of sera (nmol/L) The assay has a calculated sensitivity of 0.13 nmol/L.

### 2.3 Brain Scan

Patients underwent a brain CT scan without contrast injection, with double fenestration, one adapted to the central nervous system (parenchymal window) and the other to the

bones of the skull (bone window, with vault analysis and the base of the skull, the cervical-occipital hinge and the face).

Medical secrecy has been respected.

### 2.4 Statistical Analysis

All statistical analysis was performed with SPSS version 11.5.

### 3. RESULTS

This study involved 28 children, 11 girls (39.28%) and 17 boys (60.71%) with a sex ratio m / f of 1.54, ranging in age from 9 months to 14 years, with an average age of 6.5 years. 57.14% of the children were of rural origin against 42.85% of urban origin, none of the children was following for an endocrinopathy. For the circumstances of occurrence, we found a predominance of road accidents in 60.7% of cases, followed by falls in 38.28%. Half of the patients had an initial Glasgow score of 8/15, no child had GCS greater than 8/15 with secondary aggravation (Table 1). The presence of initial loss of consciousness (PCI) was reported in 79.1% of cases, vomiting in 58.33% of cases, and seizures in 29.16%. The clinical examination revealed in miosis in 32.14%, and anisocoria in 21.14%, mydriasis in 10.72% of cases, the rest of the patients had a normal pupil examination.

C-CT was applied in all patients, it showed the presence of brain lesions in all traumatized children (CT + in 100% of cases), the most frequently found lesion was cerebral oedema in 46.42% followed by cerebral contusion and embarrassment with rates of 39.28% and 35.71% respectively. The different brain lesions were often co-existing.

The rate of endocrine disorders in this series was 85.71%: 10 children had a lesion of 2 axes or 35.71%, namely cortisol and prolactin, against 13 who presented only the attack of a single axis for a proportion of 46.42%.

The exploration of the anterior pituitary axes in the 28 patients of this study gave the following results:

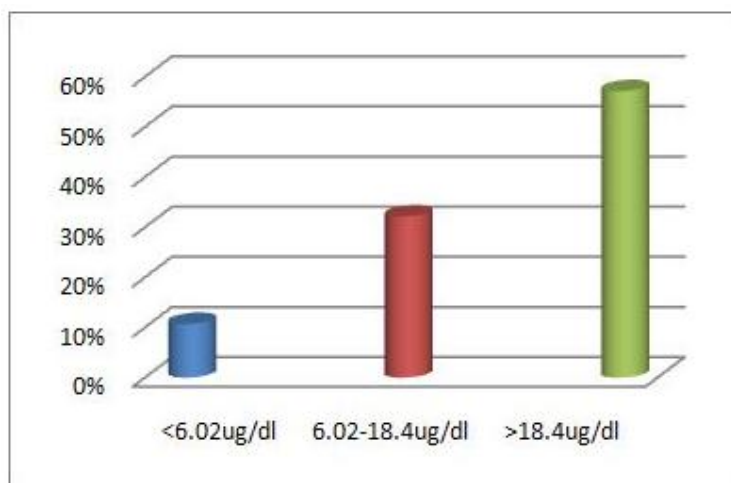
Thyrotropic axis: The values of TSH (thyroid stimulating hormone), T3, T4: these values were within the limits of normal to acute phase in all children.

Corticotropic axis: Values of morning serum cortisol (8 hours). A high level of cortisol was observed in 57.84% of cases, 32% of cases had a rate between 6.02 and 18.4 ug/dl and a rate lower than 6.02 ug/dl was observed in 11% of cases in the acute phase. (Fig. 1).

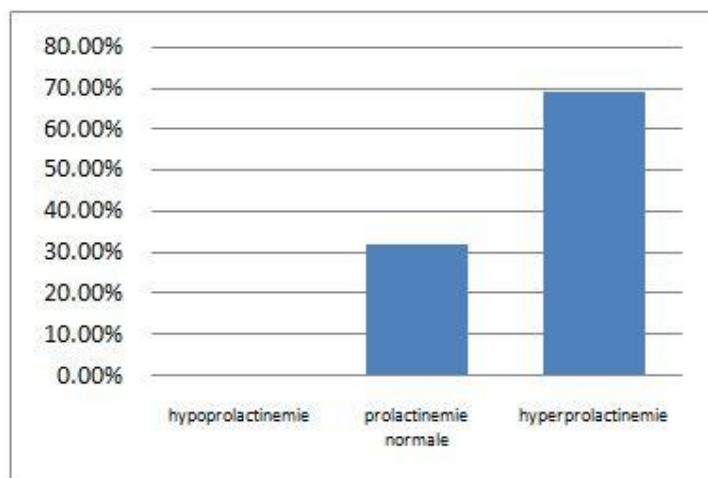
Prolactinoma: Hyperprolactinemia was found in 68.84% of cases, 32.14% of patients had a normal rate (Fig. 2).

**Table 1. Epidemiological and clinical data of the population studied**

Parameter	Nombre/ pourcentage
Number: n	28
sex ratio (M / F)	1.54
Average age: years	6.5
Mechanisms of trauma	- Public road accident: 17 cases (60.71%) - Fall: 11 cases (39.28%)
Associated clinical signs	--Possibility of initial consciousness: 24 cases (85.71%) -Vomiting: 16 cases (57.14%) -convulsion: 3 cases (10.71%)
Results of cerebral CT	-Brain edema: 13 cases (46.42%) -contusion: 11 cases (39.28%) -Fracture / embranch: 10cas (35.1%) -HSDA: 6 cases (21.14%) -Moningeal haemorrhage: 5 cases (17.85%) -Engagement: 3 cases (10.71%) Intraventricular haemorrhage: 1 case (3.57%) Intra-parenchymal haemorrhage: 1 case (3.57%)



**Fig. 1. Distribution of cortisolemia by population values**



**Fig. 2. Distribution of prolactinemia according to population values**

#### 4. DISCUSSION

For a long time, anterior pituitary hormonal alterations in children were considered marginal in head trauma [7,3]. Since the work Poomthavorm et al. [8], has been established that these disturbances are frequent in children. Edwige et al. [4] have demonstrated the need to analyze these endocrine disruptions and recommend systematic screening. These screenings would concern the basic hormones. Other studies have emphasized the need for screening in patients with mild trauma, but also in the acute phase with re-evaluation at 3 months and 1 year in prospective studies and at any time in retrospective situations [9,10].

In this study, the endocrine changes of 28 children after a serious head injury were evaluated prospectively and the sex ratio was 1.54. This male predominance in head trauma is reported in the literature [10].

In some studies [9,10] no association between anterior pituitary dysfunction and severity of the cerebral traumatic injury has been reported. Other studies report that lesions associated with hormonal disturbances are mainly severe trauma, fractures of the skull base, diffuse axonal lesions, and prolonged elevations of intracranial pressure [9,10]. In this study, the rate of endocrine disorders was 85.71%, the exploration of the thyrotropic axis proved normal in all of these patients. Low cortisol levels were observed

in 11% of cases, 67.84% of children had hyperprolactinemia. One-third of the patients studied had 2-axis involvement, namely cortisol and prolactin. Half, on the other hand, showed only one axis. In several studies with larger numbers, dysfunction of at least one pituitary axis is reported in a large number of patients (50 to 83%) [11,12,13].

The corticotrophic deficit, according to the studies (and therefore the evaluation methods) would be present in 3 to 20% of the patients if we consider the only dosage of cortisol [14,15,16].

Thyrotrophic deficiency is rarer: Between 1 and 35% of patients would have a thyrotrophic deficit [17,18,19]. It is generally appreciated by measuring plasma T4: if it is low without elevation of TSH, the diagnosis is made.

Hyperprolactinemia: It is found in 0 to 64% of patients in whom it has been sought [20,21]. It is sometimes a difficult interpretation in the case associated treatment by neuroleptics.

The prevalence of pituitary dysfunction varies by study. Different results may be due to differences in severity of the head injury, age of the child, the timing of pituitary function assessment and dynamic tests used to assess pituitary function, including criteria used to define hormonal deficiency.

## 5. CONCLUSION

Complete pituitary evaluation should be applied on in any child with severe brain injury and long-term endocrine, functional and neuropsychological monitoring is recommended, particularly for those with skull fractures.

## CONSENT

The informed consent of the guardians was sought and obtained in all cases.

## ETHICAL APPROVAL

As per international standard, written ethical approval has been collected and preserved by the author(s).

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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