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Evaluation of UCH-L1 and T-Tau as prognostic biomarkers of traumatic brain injury

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Abstract
Aim: The current study aimed to evaluate the ability of ubiquitin C-terminal hydrolase L1 (UCH-L1) and total Tau (T-Tau) to predict the need for neurosurgical intervention and neurological outcome in patients with acute mild to moderate traumatic brain injury (TBI).
Material and Methods: Eighty-five patients diagnosed with acute mild to moderate TBI were included in this study. Serum levels of UCH-L1 and T-Tau were measured using enzyme-linked immunosorbent assay (ELISA) technique. Outcome measures were the need for surgical intervention and Glasgow Outcome Scale (GOS), which was evaluated 3 months after the initial trauma. The outcomes were dichotomized into good outcomes (GOS=5) and poor outcomes (GOS<5).
Results: Serum levels of both UCH-L1 and T-Tau were significantly elevated in TBI patients who required neurosurgical intervention and those who had a poor outcome. Receiver operating characteristic (ROC) analysis revealed that UCH-L1 could predict the need for neurosurgical intervention and poor outcome with an accuracy of 82.4% (AUC= 0.872) and 83.5% (AUC= 0.878), respectively. Regarding T-Tau, it could predict the need for surgical intervention and poor outcome with an accuracy of 89.4% (AUC= 0.909) and 90.6% (AUC= 0.916), respectively.
Discussion: Both UCH-L1 and T-Tau can be used for outcome prediction in cases of mild to moderate TBI. However, t-tau could be a better prognostic biomarker of TBI as it was more accurate than UCH-L1.

Keywords
Biomarkers, UCH-L1, T-Tau, Traumatic Brain Injury, Outcome

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Introduction

Traumatic brain injury (TBI) is defined as a disruption in the normal function of the brain caused by a sudden trauma to the head. The annual incidence of TBI is estimated at 50 million cases worldwide [1]. Mild traumatic brain injury accounts for 85% of all TBI cases. Although the majority of patients with mild TBI recover completely, clinicians find it difficult to determine who will develop long-term complications [2].

The pathophysiology of TBI is still not fully understood. It is suggested that TBI occurs due to primary impact and secondary effects including neuronal inflammation, disruption of the blood-brain barrier, and metabolic disturbances. These secondary effects are thought to be risk factors for persistent symptoms and poor outcome in TBI patients [3].

The main tools used in the Emergency Department (ED) for TBI diagnosis and outcome prediction are Glasgow Coma Scale (GCS) and head computed tomography (CT). However, GCS is subjective and CT has limited sensitivity to diffuse injuries such as traumatic axonal injury that occur following TBI [4].

Surgical intervention is one of the main treatment options for TBI. It is the most effective treatment for large intracranial hematomas that TBI patients may develop. In addition, it is required if patients with TBI have brain edema and increased intracranial pressure, which is refractory to medical treatment [5].

A biomarker is an objective indicator of a patient's biological state that can be estimated precisely and consistently [6]. Several biomarkers such as S100 calcium-binding protein B (S100B), glial fibrillary acidic protein (GFAP), and neuron-specific enolase (NSE) have been studied in TBI patients, but there is still controversy between the results of these studies [7, 8]. Ubiquitin C-terminal hydrolase-L1 (UCH-L1) is a low molecular weight stable protein that is involved in axonal transport and removal of misfolded proteins [9]. UCH-L1 is a neuronal biomarker that is leaked from injured neurons and can be detected in the bloodstream [10]. Tau protein is an intracellular axonal protein linked with microtubules that regulates microtubule dynamic stability by phosphorylation. This leads to formation of phosphorylated tau (P-Tau). Following TBI, total Tau (T-Tau) is released and can be found as early as 6 hours [11].

As UCH-L1 and T-Tau are considered promising TBI biomarkers, the current study aimed to evaluate the ability of both biomarkers to predict the need for surgical intervention and neurological outcome in patients with acute mild to moderate TBI.

Material and Methods

1. Study design and patients:

The current study was conducted in the ED of Alexandria Main University Hospital (AMUH), Egypt. The study protocol was approved by the Research Ethics Committee of Alexandria Faculty of Medicine, Alexandria University, Egypt (Approval number: 0201383/08/20, IRB number: 00012098, FWA number: 00018699). Informed consent was obtained from each patient or his/her legally authorized representatives before participating in the study.

The study involved 85 patients, admitted with mild to moderate TBI.

1.1 Inclusion criteria:

(1) Age ≥18 years

(2) History of a blunt closed head trauma followed by loss of consciousness (LOC), amnesia, or vomiting

(3) Initial GCS of 9-15 on admission

(4) Presentation to the ED within 24 hours of the initial trauma

1.2 Exclusion criteria:

(1) History of a neurological disease

(2) Head trauma as a secondary event e.g., after syncope or seizure

(3) The time of injury was unknown

TBI was classified as mild if the patient had a LOC for up to 30 minutes, confusion, or disorientation lasting < 24 hours, an initial GCS of 13–15, or posttraumatic amnesia (PTA) of < 24 hours. On the other hand, TBI was classified as moderate if the patient had a LOC of > 30 minutes but < 24 hours, confusion or disorientation for > 24 hours, an initial GCS of 9–12, or PTA for > 24 hours but < 7 days.

2. Biomarkers measurement:

A venous blood sample (5 ml) was collected from each TBI patient (within 24 hours of the trauma). Sandwich enzyme-linked immunosorbent assay (ELISA) kits supplied by Innova Biotech, Beijing, China (catalog number: In-Hu4136) and Sunred Biotech, Shanghai, China (catalog number: 201-12-4295) were used to measure the levels of UCH-L1 and T-Tau, respectively. The lower limit of quantification was 0.1 ng/ml for UCH-L1 and 1.5 pg/ml for T-Tau according to the manufacturer's protocol.

3. TBI outcome:

Outcome measures included the need for surgical intervention and neurological outcome.

- Neurosurgical intervention was defined as the need for craniotomy or elevation of a skull fracture [5].
- Neurological outcome was assessed 3 months post-injury using Glasgow Outcome Scale (GOS) during the patient's follow-up visit to the hospital or by telephone survey with one of the patient's close relatives. The investigator who conducted the telephone survey was blinded to the laboratory results.

GOS categorizes the outcomes of patients after TBI, as follows [12]:

• Good recovery (GOS =5): resumption of daily life activities

• Moderate disability (GOS =4): disabled but independent from others

• Severe disability (GOS =3): disabled and dependent on others for daily support

• Vegetative state (GOS =2): minimal responsiveness

• Death (GOS =1)

For statistical analysis, the neurological outcome was dichotomized into good outcome (GOS =5) and poor outcome (GOS <5).

4. Statistical analysis:

The sample size required for this study was calculated with PASS software version 20 using independent t-test with an alpha error of 5% and a study power of 80%. This was done using data from a previous study [13].

Statistical analysis was done using IBM SPSS software version 25.0 (Armonk, NY: IBM Corp). The Kolmogorov-Smirnov test was used to determine the distribution of data. The Mann-

Whitney test was used to compare between the two groups. Receiver operating characteristic (ROC) curves were generated to assess the performance of UCH-L1 and T-Tau. Acceptable performance was defined as an area under the curve (AUC) of more than 50%, and the best performance was defined as an area of 100%. Cut-off values were obtained from the ROC curves using the Youden index to maximize both sensitivity and specificity.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

1. Characteristics of TBI patients (Table 1):

The study included 85 TBI patients. The majority of them were males (82.4%). The age ranged from 18 to 72 years with a mean of 35.8 years. Vehicle accident was the most common cause of TBI (55.3%).

According to GCS, 81.2% of the study patients had mild TBI (GCS 13-15) while 18.8% had moderate TBI (GCS 9-12). Regarding the clinical manifestations, 24.7% of the patients had vomiting, 21.2% had LOC and vomiting, and 18.8% had LOC and PTA. Intracranial CT lesions as extradural hemorrhage, subdural hemorrhage, cerebral contusion, and subarachnoid hemorrhage were found in 38.8% of all patients.

Surgical intervention was required in nearly 13 % of the study patients. GOS assessed 3 months after the injury showed that 85.9 % of the patients had good outcomes (GOS =5), while the remaining 14.1% had poor outcomes (GOS <5). No deaths (GOS=1) were reported in the study.

Table 1. Characteristics of TBI patients (n=85)

Characteristic	Number	Percentage
Cause of injury		
Vehicle accident	47	55.3%
Falling	16	18.8%
Alleged assault	15	17.6%
Direct trauma	7	8.2%
GCS		
Mild (13-15)	69	81.2%
Moderate (9-12)	16	18.8%
Clinical manifestations		
Vomiting	21	24.7%
LOC & vomiting	18	21.2%
LOC & PTA	16	18.8%
PTA	10	11.8%
LOC	10	11.8%
Vomiting & PTA	10	11.8%
Head CT scan		
Normal	52	61.2%
Abnormal	33	38.8%
Treatment		
Medical	74	87.1%
Surgical	11	12.9%
3-months GOS		
Complete recovery (GOS =5)	73	85.9%
Moderate disability (GOS =4)	7	8.2%
Severe disability (GOS =3)	4	4.7%
Vegetative (GOS =2)	1	1.2%
Death (GOS =1)	0	0%

SD: standard deviation, GCS: Glasgow coma scale, LOC: loss of consciousness, PTA: post-traumatic amnesia, GOS: Glasgow outcome scale

2. UCH-L1 and T-Tau results:

2.1 Neurosurgical intervention:

Table 2 compares the UCH-L1 and T-Tau levels in the studied TBI patients who required surgical intervention and those who did not. Regarding UCH-L1 levels, the medians in both groups of patients were 11 and 8 ng/ml, respectively while the medians of T-Tau levels were 140.1 and 57.2 pg/ml, respectively. There was a statistically significant difference between the medians of both biomarkers in the patients who required surgical intervention and those treated medically (p values <0.001).

ROC curves demonstrate that T-Tau (AUC =0.909) outperformed UCH-L1 (AUC =0.872) in distinguishing the patients who required surgical interference from those who did not. The need for neurosurgical intervention was predicted at a cut-off level of UCH-L1 of 9 ng/ml (accuracy 82.4 %, sensitivity 90.9%, specificity 81.1%, negative predictive value (NPV) 98.4%). Regarding T-Tau, the need for surgical intervention was predicted at a cut-off level of 125.7 pg/ml (accuracy 89.4%, sensitivity 81.8%, specificity 90.5%, NPV 97.1%) (Figure 1).

2.2 Neurological outcome:

Table 3 compares UCH-L1 and T-Tau serum levels in the studied TBI patients who had poor outcome (GOS <5) and those who had good one (GOS =5) 3 months post-injury. Regarding UCH-L1 levels, the medians in both groups of patients were 10.75 and 8 ng/ml, respectively while the medians of T-Tau levels were 137.95 and 57.2 pg/ml, respectively. There was a statistically significant difference between the medians of both biomarkers in the patients who had poor outcomes and those who completely recovered (p- values <0.001). ROC curves

Table 2. Distribution of serum levels of UCH-L1 and T-Tau in the studied TBI patients (n=85) according to the need for surgical intervention

Biomarker	Surgical intervention	Medical treatment	U	P value
UCH-L1 (ng/ml)				
Min. – Max.	5.5 - 12.5	4.05.2011		
Median (IQR)	11 (9.5 – 11.5)	8 (7.5 – 9)	709.5*	<0.001*
T-Tau (pg/ml)				
Min. – Max.	56.4 – 164.8	37.8 – 143.5		
Median (IQR)	140.1 (128.8 - 144.6)	57.2 (49.33 - 98.8)	704.0*	<0.001*

UCH-L1: ubiquitin C-terminal hydrolase L1, Min: minimum, Max: maximum, IQR: interquartile range, U: Mann-Whitney test, *: statistically significant at p ≤ 0.05

Table 3. Distribution of serum levels of UCH-L1 and T-Tau in the studied TBI patients (n=85) according to GOS

Biomarker	Poor outcome (GOS<5)	Good outcome (GOS=5)	U	P value
UCH-L1 (ng/ml)				
Min. – Max.	5.5 – 12.5	4.05.2011		
Median (IQR)	10.75 (9.63 - 11.5)	8 (7.5 – 9)	769.0*	<0.001*
T-Tau (pg/ml)				
Min. – Max.	56.4 – 164.8	37.8 – 143.5		
Median (IQR)	137.95 (130.15 - 144.28)	57.2 (49.15 - 98.3)	802.0*	<0.001*

UCH-L1: ubiquitin C-terminal hydrolase L1, Min: minimum, Max: maximum, IQR: interquartile range, U: Mann-Whitney test, *: statistically significant at p ≤ 0.05

demonstrate that T-Tau (AUC =0.916) outperformed UCH-L1 (AUC =0.878) in discriminating the patients who had poor outcome from those who completely recovered. A poor outcome was predicted at a cut-off level of UCH-L1 of 9 ng/ml (accuracy 83.5%, sensitivity 91.7%, specificity 82.2%, NPV 98.4%). Regarding T-Tau, poor outcome was predicted at a cut-off level of 125.7 pg/ml (accuracy 90.6%, sensitivity 83.3%, specificity 91.8%, NPV 97.1%) (Figure 2).

Discussion

TBI remains one of the major causes of mortality and disability all over the world. Accurate prediction of outcome in TBI cases is quite difficult because physicians depend on GCS and CT. Both of these tools have limitations; GCS is often inaccurate and may be under or over-estimated, while CT is not sensitive to minute neural and structural changes, which may occur after TBI [4]. Conversely, fluid biomarkers are more accurate and objective tools to assess the severity of TBIs and predict the risk of developing long-term sequelae [14]. However, no biomarker was approved for clinical use except for S-100B [15]. This study was conducted to evaluate the ability of UCH-L1 and T-Tau to predict the need for neurosurgical intervention and 3-months neurological outcome in patients with acute mild to moderate TBI. Those biomarkers were chosen as the pathophysiology of TBI is complex and each biomarker measures a different mechanism of injury; UCH-L1 measures neuronal injury, while T-Tau measures axonal injury [7]. The study was conducted on patients with mild to moderate head trauma due limited sensitivity of GCS and CT imaging as outcome predictors in those patients [16]. Pediatric TBI patients were not enrolled in the study as the pathophysiology of TBI in children is not similar to that in adults due to differences in brain anatomy and physiology [17]. Sandwich ELISA technique was used to measure the serum levels of UCH-L1 and T-Tau as it is reliable, available in many labs and provides highly sensitive and specific results [18]. In addition, it is easy and inexpensive compared to other protein measurement methods such as electrochemical biosensors and Raman spectroscopy [19]. Similarly, sandwich ELISA kits were used in previous studies to measure the concentrations of several biomarkers in TBI patients [20-21].

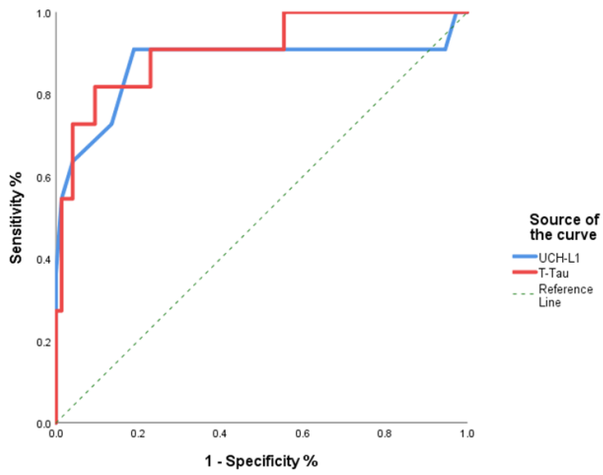

Figure 1. ROC curves for UCH-L1 and T-Tau to distinguish TBI patients who required surgical intervention (n = 11) from those treated medically (n = 74)

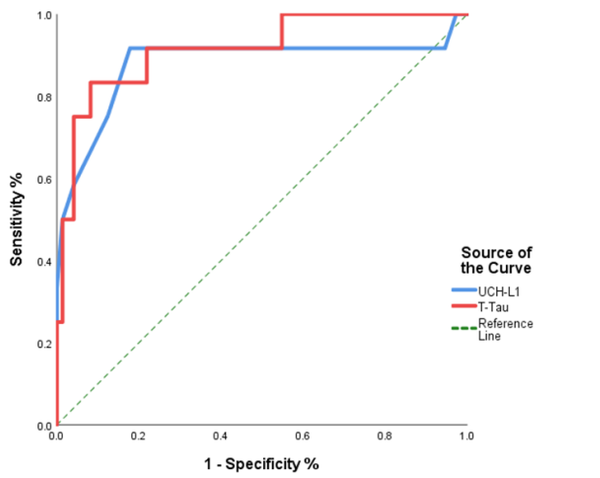

Figure 2. ROC curves for UCH-L1 and T-Tau to distinguish the patients who had poor outcome (n = 12) from those who had good outcome (n = 73)

In the current study, serum levels of UCH-L1 were significantly higher in the patients who required neurosurgical intervention than in those treated medically. In addition, the ability of UCH-L1 to discriminate between patients having and not having surgery was very good (AUC = 0.872). This is in agreement with a study conducted in 2012 by Papa et al who reported that the AUC for UCH-L1 was 0.860 in predicting the need of their study patients for neurosurgical intervention [13].

In the present study, serum levels of UCH-L1 were found to be significantly higher in patients who had poor outcome (GOS <5) than in those who completely recovered (GOS =5). This result is consistent with that of a study conducted in 2016 by Takala et al who measured the serum levels of UCH-L1 in 324 TBI patients and assessed their outcome using GOS or its extended version (GOS-E) [22]. In addition, Mondello et al in 2016 investigated the prognostic value of UCH-L1 in 45 pediatric TBI patients and reported that serum UCH-L1 levels were significantly elevated in patients who had unfavorable outcome [23]. The predictive performance of UCH-L1 for poor outcome in the current study (AUC= 0.878) is similar to that in Mondello et al study (AUC =0.86) and is better than that in Takala et al study (AUC =0.727). In 2022, Korley et al reported that the AUC of UCH-L1 for predicting incomplete recovery 6 months after TBI was 0.610, which is lower than that found in the current study [24]. This difference may be explained by including patients with severe TBI and assessment of neurological outcome 6 months post-TBI in that study.

Regarding T-Tau protein, the study herein revealed that its serum levels were significantly higher in patients who needed surgical interference than in those who did not. Compared to UCH-L1 (AUC= 0.872), the ability of T-Tau (AUC= 0.916) was better for the prediction of neurosurgical intervention in the current study. Concerning the 3-months outcome, T-Tau levels were found to be significantly higher in patients who had poor outcome than in those who had complete recovery. This finding is similar to that of a study performed in 2017 by Rubenstein

et al who correlated the plasma levels of T-Tau and P-Tau with the functional outcome in patients with acute and chronic TBI [25]. However, the ability of T-Tau (AUC =0.909) to predict poor outcome, in the present study, was found to be better than that in Rubenstein et al study (AUC =0.770). This variation could be attributed to the utility of a different measurement method by Rubenstein et al who estimated the levels of T-Tau by ultra-high sensitivity laser-based immunoassay multi-arrayed fiberoptics conjugated with rolling circle amplification.

An advantage of this study is the evaluation of the ability of T-Tau protein to predict the need for neurosurgical intervention and neurological outcome in TBI, which have not been adequately studied before. Another advantage is the comparison of the predictive performance for TBI outcome between two biomarkers that measure different mechanisms of injury. The current study points to that both UCH-L1 and T-Tau could be potential prognostic TBI biomarkers. Both biomarkers, especially T-Tau, could be used in clinical practice to help physicians for accurate prediction of TBI outcome. However, further studies with larger sample sizes are recommended to confirm the reliability of UCH-L1 and T-Tau as outcome predictors in patients with acute mild to moderate TBI.

Conclusion

This study revealed that serum levels of UCH-L1 and T-Tau were significantly high in TBI patients who required neurosurgical intervention and in patients who had poor outcome. Measuring the serum levels of UCH-L1 and T-Tau, on admission to the ED, could be used for precise prediction of outcome in patients with acute mild to moderate TBI. However, T-Tau could be a better prognostic TBI biomarker as it was more accurate than UCH-L1.

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Scientific Responsibility Statement
The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of interest
The authors declare no conflict of interest.

References

1. Khellaf A, Khan DZ, Helmy A. Recent advances in traumatic brain injury. J Neurol. 2019;266(11):2878-89.
2. McKee AC, Daneshvar DH. The neuropathology of traumatic brain injury. Handb Clin Neurol. 2015;127:45-66.
3. van der Horn HJ, Out ML, de Koning ME, Mayer AR, Spikman JM, Sommer IE, et al. An integrated perspective linking physiological and psychological consequences of mild traumatic brain injury. J Neurol. 2020;267(9):2497-506.
4. Visser K, Koggel M, Blaauw J, van der Horn HJ, Jacobs B, van der Naalt J. Blood-based biomarkers of inflammation in mild traumatic brain injury: A systematic review. Neurosci Biobehav Rev. 2022;132:154-68.
5. Pujari R, Hutchinson PJ, Kolias AG. Surgical management of traumatic brain injury. J Neurosurg Sci. 2018;62(5):584-92.
6. Strimbu K, Tavel JA. What are biomarkers? Curr Opin HIV AIDS. 2010;5(6):463-6.
7. Mehta T, Fayyaz M, Giler GE, Kaur H, Raikwar SP, Kempuraj D, et al. Current trends in biomarkers for traumatic brain injury. Open Access J Neurol Neurosurg. 2020;12(4):86-94.
8. Amoo M, Henry J, O'Halloran PJ, Brennan P, Husien MB, Campbell M, et al. S100B, GFAP, UCH-L1 and NSE as predictors of abnormalities on CT imaging following mild traumatic brain injury: a systematic review and meta-analysis of diagnostic test accuracy. Neurosurg Rev. 2022;45(2):1171-93.
9. Papa L, Brophy GM, Welch RD, Lewis LM, Braga CF, Tan CN, et al. Time course and diagnostic accuracy of glial and neuronal blood biomarkers GFAP and UCH-L1 in a 17 large cohort of trauma patients with and without mild traumatic brain injury. JAMA Neurol. 2016;73(5):551-60.
10. Shahjouei S, Sadeghi-Naini M, Yang Z, Kobeissy F, Rathore D, Shokraneh F, et al. The diagnostic values of UCH-L1 in traumatic brain injury: A meta-analysis. Brain Inj. 2018;32(1):1-17.
11. Edwards G, Zhao J, Dash PK, Soto C, Moreno-Gonzalez I. Traumatic brain injury induces tau aggregation and spreading. J Neurotrauma. 2020;37(1):80-92.
12. Rubin ML, Yamal JM, Chan W, Robertson CS. Prognosis of six-month Glasgow Outcome Scale in severe traumatic brain injury Using hospital admission characteristics, injury severity characteristics, and physiological monitoring during the first day post- injury. J Neurotrauma. 2019;36(16):2417-22.
13. Papa L, Lewis LM, Silvestri S, Falk JL, Giordano P, Brophy GM, et al. Serum levels of ubiquitin C-terminal hydrolase distinguish mild traumatic brain injury from trauma controls and are elevated in mild and moderate traumatic brain injury patients with intracranial lesions and neurosurgical intervention. J Trauma Acute Care Surg. 2012;72(5):1335-44.
14. Ghaith HS, Nawar AA, Gabra MD, Abdelrahman ME, Nafady MH, Bahbah EI, et al. A literature review of traumatic brain injury biomarkers. Mol Neurobiol. 2022;59(7):4141-58.
15. Unden J, Ingebrigtsen T, Romner B, Scandinavian Neurotrauma C. Scandinavian guidelines for initial management of minimal, mild and moderate head injuries in adults: an evidence and consensus-based update. BMC Med. 2013;11:50.
16. Connell GC, Alder ML, Smothers CG, Still CH, Webel AR, Moore SM. Use of high-sensitivity digital ELISA improves the diagnostic performance of circulating brain-specific proteins for detection of traumatic brain injury during triage. Neurol Res.2020;42(4):346-53.
17. Figaji AA. Anatomical and physiological differences between children and adults relevant to traumatic brain injury and the implications for clinical assessment and care. Front Neurol. 2017;8:685.
18. Hosseini S, Vázquez-Villegas P, Rito-Palomares M, Martinez-Chapa SO. Advantages, Disadvantages and modifications of conventional ELISA. In: Hosseini S, Vázquez-Villegas P, Rito-Palomares M, Martinez-Chapa SO, editors. Enzyme-linked immunosorbent assay (ELISA): From A to Z. Singapore: Springer Singapore; 2018. p. 67-115.
19. Krausz AD, Korley FK, Burns MA. The current state of traumatic brain injury biomarker measurement methods. Biosensors. 2021;11(9):319.
20. Raheja A, Sinha S, Samson N, Bhoi S, Subramanian A, Sharma P, et al. Serum biomarkers as predictors of long-term outcome in severe traumatic brain injury: analysis from a randomized placebo-controlled Phase II clinical trial. J Neurosurg. 2016;125(3):631-41.
21. Diaz-Arrastia R, Wang KK, Papa L, Sorani MD, Yue JK, Puccio AM, et al. Acute biomarkers of traumatic brain injury: Relationship between plasma levels of ubiquitin C- terminal hydrolase-L1 and glial fibrillary acidic protein. J Neurotrauma. 2014;31(1):19-25.
22. Takala RS, Posti JP, Runtti H, Newcombe VF, Outtrim J, Katila AJ, et al. Glial fibrillary acidic protein and ubiquitin C-terminal hdrolase-L1 as outcome predictors in traumatic brain injury. World Neurosurg. 2016;87:8-20.
23. Mondello S, Kobeissy F, Vestri A, Hayes RL, Kochanek PM, Berger RP. Serum concentrations of ubiquitin C-terminal hydrolase-L1 and glial fibrillary acidic protein after pediatric traumatic brain injury. Sci Rep. 2016;6:28203.
24. Korley FK, Jain S, Sun X, Puccio AM, Yue JK, Gardner RC, et al. Prognostic value of day-of-injury plasma GFAP and UCH-L1 concentrations for predicting functional recovery after traumatic brain injury in patients from the US TRACK-TBI cohort: an observational cohort study. Lancet Neurol. 2022;21(9):803-13.
25. Rubenstein R, Chang B, Yue JK, Chiu A, Winkler EA, Puccio AM, et al. Comparing plasma phospho tau, total tau, and phospho tau-total tau ratio as acute and chronic traumatic brain injury biomarkers. JAMA Neurol. 2017;74(9):1063-72.

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