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# Prediction of neurological outcome after moderate head trauma computed tomography versus a Serum biomarker fatty acid binding protein

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**ABSTRACT**
**Background**: Traumatic brain injury (TBI) is a major public health challenge, causing long-term disability and dependency. Computed tomography (CT) remains the diagnostic gold standard but poses risks such as radiation exposure and high costs. Heart-type fatty acid-binding protein (H-FABP) has emerged as a potential biomarker for brain and cardiac injuries. This study evaluates H-FABP's utility in predicting neurological outcomes following moderate TBI.
**Methods**: A prospective controlled trial was conducted at Minia University Hospital on 30 critically ill adult patients with moderate TBI (GCS 9–12). Patients were assessed using Advanced Trauma Life Support protocols, clinical scores (APACHE II, SOFA), and CT imaging classified by Marshall and Rotterdam scales. Serum H-FABP levels were measured at admission, 24, and 72 hours post-injury using electrochemoluminometric immunoassays. Data analysis included ROC curves, correlation studies, and statistical comparisons of CT findings and H-FABP levels.
**Results**: H-FABP levels significantly increased at 24 hours post-injury (mean: 2.85±0.89 ng/mL) compared to admission (1.86±0.58 ng/mL, $p<0.001$) and remained elevated at 72 hours. Positive correlations were observed between H-FABP levels and Marshall CT scores at 24 and 72 hours ($r=0.50, 0.53$; $p<0.05$). H-FABP showed a sensitivity of 100% and specificity of 87% at a cut-off value >2.45 ng/mL for predicting poor neurological outcomes.
**Conclusion**: H-FABP is a promising biomarker for predicting outcomes in moderate TBI, potentially reducing unnecessary CT scans, radiation exposure and costs. Further studies are needed to assess its utility across varying TBI severities and in biomarker panels for comprehensive diagnostics.

**Keywords:** Traumatic brain injury(TBI),HFABP,Biomarker, Neurological outcome

## INTRODUCTION

One of the leading killers in the world is traumatic brain injury (TBI). Traumatic brain injury (TBI) causes incapacity and dependency for the rest of one's life as well as emotional and cognitive consequences. A huge economic and social problem that impacts all countries, it is also a public health epidemic(1).
When it comes to diagnosing potentially fatal brain abnormalities, a head computed tomography (CT) scan is now the gold standard.It is expensive and not always accessible, but it provides more precise information about brain tissue. Although it only finds clinically significant lesions in under 10% of instances, it exposes patients to substantial radiation doses(2).
A family of 16 members, each encoded by its own gene, known as fatty acid-binding proteins (FABPs) was initially described in 1972. There are several subtypes of FABPs, and they are found in different organ systems(3). Members L-, I-, H-, A-, E-, Il-, B-, M-, and T-FABP are among the most well-known. The letters stand for many organs and tissues, including the liver, the intestines, the heart, the muscles, the testes, the brain, and myelin(4).
Most people are familiar with the Human heart-type FABP (H-FABP), which is another name for mammary-derived growth inhibitor. In the 1p33-p32 region of chromosome 1, you can find the FABP3 gene, which

encodes H-FABP. Its expression is detected in blastocysts, tissues with a high demand for fatty acids, the brain, adrenal glands, heart, skeletal muscle, kidneys, and mammary glands. One possible use for H-FABP as a biomarker for cardiac and brain damage is its dual distribution throughout the body(4).

**Patients and Methods**

At Minia University Hospital, researchers conducted this prospective controlled trial in the critical care unit (ICU). Following approval from the local ethical committee of the faculty of medicine (No. 505: 4/2022) and written informed consents from the patients' first degree relatives, the study was carried out on 30 critically ill adult patients with moderate traumatic brain injury who were admitted to the emergency department of Minia University Hospital between May 2022 and January 2024. Participants ranged in age from 18 to 60 years old and ASA physical status I or II, with a GCS score of 9 to 12, indicating a moderate traumatic brain injury.

**Exclusion criteria**

1-Patient suffered from polytrauma.
2-Refusal of first-degree patient's relatives.
3-Patient with positive history of alcohol intake.
4-Paient with previous history of CNS surgery or traumatic brain injury.
5-Patients with heart disease such as cardiac arrhythmia.

**Study Design**

After admission of patients to intensive care unit, patients were managed according to Advanced Trauma Life Support (ATLS) principles of management of airway, breathing, and circulation (5), the following parameters were recorded for all patients: demographics (age , gender), time, mechanism of injury. Also routine laboratory investigations were done to all patients.

Initial Computed Tomography (CT) of the brain without contrast was done on arrival to emergency department and Marshall CT classification and Rotterdam CT score were calculated by our radiology consultant then follow up was done at 24 and 72 hours from the trauma event, and the severity of trauma was evaluated by GCS, APACHE II, and SOFA scores.

Biochemical testing included drawing venous blood samples at admission, 24 hours, and 72 hours after the trauma incident to evaluate serum cardiac fatty acid binding protein. Within 30 minutes of sampling, a 3-centimeter blood sample was centrifuged to prevent clotting; the serum was frozen and stored at -80 C for subsequent analysis. To determine the levels of h-FABP, a fully-automated electrochemiluminescence immunoassay was used.

**Statistical Analysis**

The data was all gathered, organized, and analyzed statistically with the help of SPSS 26 for Windows (SPSS Inc., Chicago, IL, USA).

Using the Shapiro-Whitney U test. The qualitative data was shown using relative percentages and frequencies. To determine the difference between the qualitative variables, the chi-square test ($\chi 2$) and Fisher exact were employed. Measurement results were presented as the average plus or minus the standard deviation (SD), with parametric data shown as range and non-parametric data combined as median.

To forecast outcomes, we used ROC curve analysis and Pearson correlation to examine the relationship between HFABP and the other parameters.

We used two-tailed significance tests for all of our statistical comparisons. A p-value of less than or equal to 0.05 is considered significant, a p-value of less than 0.001 is considered very significant, and a p-value greater than or equal to 0.05 is considered non-significant.

**RESULTS**

This prospective, controlled study was carried out on atotal 30 patients of both sexes, aged between 18 and 60 years old with American Society of Anaesthesiologistsphysical status I and II with isolated moderate traumatic brain injury. All consecutive patients admitted to the emergency department with diagnosis of moderate TBI with GCS (9:12) were enrolled in the study.

**Admission data**

According to admission data; the median GCS was 11, ranged from 9 to 12 with (70%) of cases had no surgical intervention, (30%) underwent surgical intervention in the form of evacuation of hemorrhageand elevation of skull fracture.Alsoregarding brain CT finding; the majority of cases had SAH (60%), then skull fracture and intracranial hemorrhage was found in (33.3%) and (30%) respectively among studied cases as shown in table (1).

**Table 1:** admission data of the studied cases.

| Admission data | Descriptive statistics (N=30) |
|---|---|
| GCS | |
| Mean ± SD | 11±0.9 |
| (Range) | 9-12 |
| Brain CT finding | |
| Free | 2(6.7%) |
| SAH | 18(60%) |
| Fracture | 10(33.3%) |
| Contusion | 7(23.3%) |
| Intracranial hemorrhage | 9(30%) |
| EDH | 6(20%) |
| Pneumo-cephaly | 5(16.7%) |
| Midline shift | 2(6.7%) |
| Extra axial | 1(3.3%) |
| Ischemia | 1(3.3%) |
| DAI | 1(3.3%) |
| SDH | 5(16.7%) |
| Surgical intervention | |
| No | 20(66.7%) |
| Evacuation of Hemorrhage | 9(30%) |
| Elevation of fracture | 1(3.3%) |

 Data are expressed as mean±SD or numbers and percentage.

**GCS among studied cases:** Regarding GCS score among studied cases; it was found that the median GCS on admission was 11, there is insignificant difference between admission GCS score and subsequent GCS scores through the study period as shown in table (2).

**Table 2:** GCS score of studied cases at different times interval

| GCS score | | Median | Range |
|---|---|---|---|
| Admission | | 11 | 9-12 |
| Day 1 | 6h | 11 | 9-12 |
| | 12h | 12 | 9-14 |
| | 18h | 12 | 9-14 |
| | 24h | 12 | 9-14 |
| Day 2 | 12h | 12 | 7-14 |
| | 24h | 12 | 7-15 |
| Day 3 (n=25) | 12h | 12 | 4-15 |
| | 24h | 12 | 4-15 |
| Day 4 (n=20) | 12h | 12 | 8-15 |
| | 24h | 12 | 8-15 |
| Day 5 (n=18) | 12h | 12 | 6-15 |
| | 24h | 12.5 | 6-15 |
| Day 6 (n=17) | 12h | 13 | 5-15 |
| | 24h | 13 | 5-15 |
| Day 7 (n=13)) | 12h | 13 | 5-14 |
| | 24h | 13 | 4-15 |

 Data are expressed as mean±SD or numbers

**Heart Fatty Acid Binding Protein among studied cases**

Regarding HFABP among studied cases; there were significant differencesbetween admission value and subsequent values after 24,72h (p value <0.05) as shown in table (3).

**Table 3:** Heart Fatty Acid Binding Protein among studied cases at different times interval

| Heart fatty acid binding protein | Descriptive statistics (N=30) | P value |
|---|---|---|
| On admission<br>Mean ± SD(Range) | 1.86±0.58<br>1.17-3.9 | <0.001* |
| After 24 hours<br>Mean ± SD(Range) | 2.85±0.89#<br>1.9-6.8 | P1<0.001* |
| After 72 hours<br>Mean ± SD(Range) | 2.39±0.73#<br>1.3-5.1 | P2<0.001*<br>P3=0.004* |

_* significant at p value <0.05, _# significant with baseline
_P value was calculated by repeated measure ANOVA, paired sample t test for pairwise comparison
_P1 is p value between admission and after 24h _P2 is p value between admission and after 72h_P3 is p value between after 24h and 72h

**Follow up brain CT according to Marshall and Rotterdam classification among studied cases**

Regarding Marshall and Rotterdam classification of brain CT among all studied cases, there was significant decrease in total Marshall score after 72 h compared to admission day, while insignificant difference was noted regarding Rotterdam score after 24 and 72 h compared to admission day as shown in table (4).

**Table 4:** Follow up brain CT according to Marshall and Rotterdam classification.

| | Descriptive statistics (N=30) | P value |
|---|---|---|
| Marshal classification of brain CT on admission<br>Median (Range) | 4 (1-5) | 0.003* |
| Marshal classification of brain CT after 24h<br>Median (Range) | 3(1-6) | P1=0.03*<br>P2=0.05* |
| Marshal classification of brain CT after 72h<br>Median (Range) | 3 (1-6) | P3=0.29 |
| Rotterdam classification of brain CT on admission<br>Median (Range) | 2(0-4) | |
| Rotterdam classification of brain CT after 24h<br>Median (Range) | 2 (0-3) | 0.69 |
| Rotterdam classification of brain CT after 72 h<br>Median (Range) | 2 (0-4) | P1=0.19<br>P2=0.22<br>P3=0.73 |

_* significant at p value <0.05, _# significant with baseline
_P value was calculated by Freidman test for related variables.
_P1 is p value between admission and after 24h_P2 is p value between admission and after 72h_P3 is p value between after 24h and 72h

**DISCUSSION**

One of the leading causes of death and disability on a global scale, traumatic brain injury (TBI) is a pressing issue in public health around the world. The economic cost is considerable, and people's quality of life is disrupted. It causes incapacity and reliance for the rest of one's life as well as psychological, emotional, and cognitive consequences(6).

The capacity of computed tomography (CT) scans to detect intracerebral hemorrhages quickly and reliably makes them a valuable tool in the diagnosis of traumatic brain injury. More than 90% of CT scans fail to detect any clinically significant brain damage, even though they are used in approximately 80% of those patients (7). In order to reduce the hazards connected with CT scans, healthcare providers must weigh the advantages against their risks and only use them when absolutely necessary(8).

A new and potentially useful method that uses biomarkers to diagnose traumatic brain injury (TBI) has been proposed as a replacement for CT scans, point-of-care testing (POCT)(9).Steinmüller et al.,(2022)found that glial fibrillary acidic protein (GFAP) and S100 calcium binding protein B (S100B) are potential indicators of brain

damage and are among the most investigated biomarkers. Heart type Fatty Acid Binding Protein (H-FABP) is another promising biomarker that has been more popular in the past few years(10).
A protein called mammary-derived growth inhibitor, human heart-type FABP (H-FABP). The fact that H-FABP is mostly found in the brain and the heart makes it a promising candidate for use as a biomarker in the diagnosis of brain and cardiac ailments (4).
To further narrow down the pool of potential patients requiring imaging for intracerebral lesions, blood biomarkers can be used in this setting. In order to determine the best way to predict the neurological prognosis following moderate traumatic brain injury, this study compared the use of brain computed tomography (CT) with an innovative TBI biomarker, human heart fatty acid binding protein.
Participants in this randomized controlled trial ranged from 18 to 60 years old, with an ASA physical category I or II and isolated moderate traumatic brain injury.
In the current study, the median GCS was 11, ranged from 9 to 12 . As regard brain CT finding, the majority of cases had SAH, then skull fracture and intracranial hemorrhage.
The finding of the current study indicate that H-FABP is a promising TBI biomarker, where it exhibibits higher specificity and sensitivity as a prognostic tool in prediction of the neurological outcome after head trauma versus bain CT. Regarding correlation between follow up CT according to Marshall and Rotterdam classification and HFABP in prediction of outcomes, the results demonstrated that there was moderate positive correlation between HFABP and Marshall classification of brain CT at 24h and 72h (r=0.50 ,0.53) respectively with significant p value <0.05. Also there was mild positive correlation between HFABP and Rotterdam classification of brain CT at 72h (r=0.43) with significant p value <0.05.
To help decide whether mTBI patients can be discharged without a CT scan, Lagerstedt et al. (2017) evaluated the levels of cardiac fatty- acid binding protein and S100B, which is in agreement with the current study. A total of 261 patients who underwent CT scans within 24 hours of their trauma were included in the study. All patients had their levels of S100B and H-FABP tested, and those with positive CT scans had far greater quantities than those without. The panel improved specificity to 30% and sensitivity to 100% when compared to H-FABP alone. Patients who tested positive for CT among the mTBI population had considerably elevated levels of S100B and H-FABP. Based on their findings, H-FABP is a promising protein for identifying all patients with a CT-positive mTBI, a GCS score of 15, and at least one clinical symptom, as it outperformed S100B (11).
In contrast, a study conducted by Koivikko et al. (2022) examined 189 individuals who had traumatic brain injuries (TBI). The researchers looked at measures of S100 calcium-binding protein B (S100B), heart fatty acid binding protein (H-FABP), and interleukin-10 (IL-10). Within the first twenty-four hours of being admitted, serum samples were taken. We evaluated biomarkers' capacity to differentiate between CT-positive and CT-negative patients, as well as the severity of TBI. Although all biomarker levels varied significantly across severity classifications, no biomarker differentiated moTBI from sTBI patients. After leaving the emergency department, patients with mTBI exhibited reduced levels of IL-10, H-FABP, and NF-L. Using these biomarkers alone to identify mTBI in trauma patients is not feasible, according to their findings (12).
The research found that after 72 hours, the best H-FABP cut-off value is more than 2.45 ng/ml, with a significant p value less than 0.05 and a fantastic area under the ROC curve of 0.93. The sensitivity for outcome prediction is 100% and the specificity is 87% when using this cutoff value.
This study's findings are consistent with those of Lagerstedt et al. (2020), who assessed 88 patients with traumatic brain injury. Urine samples were collected no later than 24 hours following injury. The levels of GFAP, NF-L, S100β, H-FABP, and IL-10 proteins were assessed. Two distinct groups of patients were formed: (a) patients with traumatic brain injuries (TBIs) of varying severity (GCS 3–15) were assessed in the first, and (b) patients with mild traumatic brain injuries (mTBIs) (GCS 13–15) were included in the second. The following biomarkers and covariates were examined simultaneously: H-FABP, IL-10, S100β, NF-L, and GFAP. Other factors included age, Marshall grade, Injury Severity Score, Severity, and GCS. Even at sensitivity levels of 95% to 100%, the specificities of the individual proteins were low. In terms of sensitivity and specificity, H-FABP was the most effective in predicting full recovery in patients suffering from mTBI. In recognizing individuals with either a good result or complete recovery following TBI, they found that IL-10 and H-FABP in TBI diagnostics show potential (13).
Posti et al. (2022) investigated biomarkers in the blood and TBI, which is in line with the findings of the present investigation. When sensitivity was set at 95%-100%, a panel of biomarkers including glial fibrillary acidic protein (GFAP), heart fatty acid binding protein (H-FABP), and neurofilament light polypeptide (NF-L) could predict that patients with mild traumatic brain injury (TBI) would make a full recovery. This panel had a specificity of 40%. Combining injury severity score with H-FABP and NF-L improved specificity to 56% while keeping sensitivity at 95%-100%. The results were improved by include clinical variables. When IL-10, age, and TBI severity were added, the specificity reached 80% and the sensitivity ranged from 95% to 100% (14).
A research by Niiranen et al. (2023) on eighty-two individuals with moderate to severe TBI found results that contradict those of the present study. Within twenty-four hours of admission, the initial serum samples for IL-10 and H-FABP were collected. We gathered and evaluated C-reactive protein, leukocytes, troponin test, and

creatine kinase-MBm. The concentration of H-FABP differed significantly between TBI patients who had ECI and those who did not. Their findings imply that inflammatory reactions during the initial hospitalization following a traumatic brain injury (TBI) do not substantially cloud the utility of interleukin-10 (IL-10) or heat shock protein ABP (H-FABP) as prospective biomarkers for TBI. It is possible that cardiac sources and extracranial traumas impact the levels of H-FABP in TBI patients, as indicated by the correlations between the two and the link between H-FABP and ISS and CK/CK-MBm. The inclusion of extracranial injuries and cardiac causes was a limitation of this investigation (15).

## CONCLUSION

Traumatic brain injury (TBI) remains a significant public health concern, requiring accurate and efficient diagnostic tools to optimize patient outcomes and reduce unnecessary healthcare interventions. While CT brain scans continue to serve as the gold standard for identifying acute intracranial injuries, their overuse presents challenges, including increased healthcare costs, radiation exposure risks, and emergency department overcrowding.

The findings of this study highlight the promising role of heart-type fatty acid-binding protein (H-FABP) as a reliable biomarker for predicting neurological outcomes in patients with moderate TBI.

### Limitations

*The study involved only 30 patients, which is relatively small and may limit the generalizability of the findings.

*While H-FABP was extensively studied, the inclusion of additional biomarkers (e.g., GFAP, S100B) in a panel could have provided a more comprehensive assessment.

*Potential confounding factors like extracranial injuries, inflammatory responses, or pre-existing conditions were not fully accounted for, which could influence biomarker levels.

### Recommendations

*Evaluate the utility of H-FABP across the full spectrum of TBI severity for a more comprehensive understanding.

*Conduct studies with extended monitoring to assess the predictive value of biomarkers over weeks or months.

*Evaluate the economic impact of incorporating biomarker testing into standard TBI protocols, particularly in reducing unnecessary CT scans.

## REFERENCES

1. Weil ZM, Karelina K. Lifelong consequences of brain injuries during development: from risk to resilience. Frontiers in neuroendocrinology. 2019;55:100793.
2. Kabore AF, Ouedraogo A, Ki KB, Traore SSI, Traore IA, Bougouma CTH, et al. Head computed tomography scan in isolated traumatic brain injury in a low-income country. World neurosurgery. 2017;107:382-8.
3. Storch J, Corsico B. The Multifunctional Family of Mammalian Fatty Acid–Binding Proteins. Annual review of nutrition. 2023;43(1):25-54.
4. Rezar R, Jirak P, Gschwandtner M, Derler R, Felder TK, Haslinger M, et al. Heart-type fatty acid-binding protein (H-FABP) and its role as a biomarker in heart failure: what do we know so far? Journal of clinical medicine. 2020;9(1):164.
5. Galvagno SM, Nahmias JT, Young DA. Advanced trauma life support® update 2019: management and applications for adults and special populations. Anesthesiology clinics. 2019;37(1):13-32.
6. Capizzi A, Woo J, Verduzco-Gutierrez M. Traumatic brain injury: an overview of epidemiology, pathophysiology, and medical management. Medical Clinics. 2020;104(2):213-38.
7. Gudigar A, Raghavendra U, Hegde A, Menon GR, Molinari F, Ciaccio EJ, et al. Automated detection and screening of traumatic brain injury (TBI) using computed tomography images: a comprehensive review and future perspectives. International journal of environmental research and public health. 2021;18(12):6499.
8. Shobeirian F, Ghomi Z, Soleimani R, Mirshahi R, Sanei Taheri M. Overuse of brain CT scan for evaluating mild head trauma in adults. Emergency Radiology. 2021;28:251-7.
9. Jović M, Prim D, Saini E, Pfeifer ME. Towards a point-of-care (POC) diagnostic platform for the multiplex electrochemiluminescent (ECL) sensing of mild traumatic brain injury (mTBI) biomarkers. Biosensors. 2022;12(3):172.
10. Steinmüller JB, Lynnerup NM, Steinmetz J, Riis JJ, Doering P. Implementation of the S100 calcium-binding protein B biomarker in a clinical setting: a retrospective study of benefits, safety, and effectiveness. Neurotrauma reports. 2022;3(1):447-55.

11. Lagerstedt L, Egea-Guerrero JJ, Bustamante A, Montaner J, Rodríguez-Rodríguez A, El Rahal A, et al. H-FABP: A new biomarker to differentiate between CT-positive and CT-negative patients with mild traumatic brain injury. PloS one. 2017;12(4):e0175572.
12. Koivikko P, Posti JP, Mohammadian M, Lagerstedt L, Azurmendi L, Hossain I, et al. Potential of heart fatty-acid binding protein, neurofilament light, interleukin-10 and S100 calcium-binding protein B in the acute diagnostics and severity assessment of traumatic brain injury. Emergency Medicine Journal. 2022;39(3):206-12.
13. Lagerstedt L, Azurmendi L, Tenovuo O, Katila AJ, Takala RS, Blennow K, et al. Interleukin 10 and heart fatty acid-binding protein as early outcome predictors in patients with traumatic brain injury. Frontiers in neurology. 2020;11:376.
14. Posti JP, Tenovuo O. Blood-based biomarkers and traumatic brain injury—A clinical perspective. Acta Neurologica Scandinavica. 2022;146(4):389-99.
15. Niiranen TJ, Chiollaz A-C, Takala RS, Voutilainen M, Tenovuo O, Newcombe VF, et al. Trajectories of interleukin 10 and heart fatty acid-binding protein levels in traumatic brain injury patients with or without extracranial injuries. Frontiers in neurology. 2023;14:1133764.