Evaluating the predictive factors affecting outcome in patients with severe traumatic brain injury: a prospective observational study

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ABSTRACT

Background: Severe traumatic brain injury (TBI) is a neurosurgical emergency and timely intervention is critical for favorable outcome. We aimed to evaluate certain demographic, clinical and radiological factors for outcome prediction in TBI patients in terms of morbidity and mortality.

Methods: A prospective observational study was conducted in 100 patients of severe TBI admitted to our hospital from September 2016 to June 2018. Those with penetrating head injury, associated severe chest, abdominal or orthopedic trauma and pregnant or lactating women were excluded. Clinical outcome was assessed at the time of discharge and after three months according to Glasgow outcome score (GOS).

Results: Majority of patients were adults in the age group 20 to 39 years. Road-side accident (75%) was the commonest mode of injury followed by fall (23%) and assault (2%). Out of 100 patients, 51 had in-hospital mortality. Of 49 patients who survived for GOS assessment at 3 months, three (6.1%) patients had unfavourable GOS I to III. Presence of hypoxemia, pupil non-reactivity, computerised tomography (CT) head findings of hemorrhagic contusion, subarachnoid hemorrhage (SAH), midline shift and effacement of basal cisterne were associated with significantly increased risk of unfavorable early and late outcome after severe TBI (p<0.05). Poor GCS score and fracture skull were associated with adverse early and late outcome respectively (p<0.001).

Conclusions: Low GCS score at admission, pupil non reactivity, presence of hypoxemia, abnormal CT head findings (hemorrhagic contusion, SAH, midline shift and effacement of basal cisterne) were strong predictors of adverse outcome after severe TBI.

Keywords: Outcome prediction, Traumatic brain injury, Glasgow outcome score

INTRODUCTION

Traumatic brain injury (TBI) is a major burden with approximately 10 million annual victims reported on the health care system throughout the world.1 TBI is defined as ‘an alteration in brain function, or other evidence of brain pathology, caused by an external force’.2 A severe TBI is defined by a Glasgow coma score (GCS) score of 8 or less during the first post traumatic day.3 It is a neurosurgical emergency and timely intervention is critical for favorable outcome. In addition to the impact of TBI on the individual, it can negatively impact families, communities, and the economy. Its outcome prediction is paramount in clinical decision making, counselling relatives and targeted use of limited healthcare resources in developing countries like India. Although several prognostic models have been developed, the accurate assessment of short term and long-term prognosis of severe TBI needs further evaluation. A number of factors are believed to influence the outcome of TBI patients including age, gender, GCS, intracranial pressure (ICP), pupillary size and...
responsiveness, hypoxia, computerised tomography (CT) findings and type of treatment (operative or non-operative). The present study aimed to evaluate certain demographic variables, clinical factors and radiological findings for outcome prediction in severe TBI patients in terms of morbidity and mortality.

**METHODS**

This was a prospective observational study conducted in patients of severe TBI admitted to our hospital from September 2016 to June 2018 A total of 100 patients of TBI with GCS Score 8 or less at presentation within age group 15-70 years who presented in emergency department within 24 hours of trauma were included in the study. Exclusion criteria included those with penetrating head injury, associated severe chest, abdominal or orthopedic trauma, pregnant and lactating women and patients already on ventilator. The study was conducted after ethical approval from institutional ethics committee. Written explicit consent was taken from the attendant accompanying the patient. A complete history (from attendant) was taken and a neurological assessment was performed on each patient. The following factors were taken into consideration for prediction of prognosis: age, gender distribution, GCS on admission, hypoxemia (defined as peripheral oxygen saturation levels on pulse oximetry below 90%), hypotension (defined as systolic blood pressure (SBP) < 90 mm Hg), pupillary assessment and CT head findings.

Depending on the type of injury, patients were treated either conservatively (close observation, antibiotics, anti-edema measures, antiepileptics, ventilatory support) or by surgery (surgical debridement of scalp lacerations, craniotomy, evacuation of hematoma and treatment of associated extra-cranial injuries). Patients were followed up till discharge or death (whichever occurred first) for early outcome and up to three months for late outcome. Early clinical outcome was considered unfavourable if there was in-hospital mortality and favourable if patient survived. Late outcome at three months was assessed by Glasgow outcome score (GOS) Grade I to V as follows: Grade I: death, Grade II: vegetative, Grade III: mostly dependent, Grade IV: minimally dependent and Grade V: Good recovery. A score of I-III was considered as unfavourable outcome and IV, V was considered as favourable outcome.

**Statistical analysis**

Descriptive statistics such as mean, standard deviation (SD) and range values were calculated. Qualitative data were expressed as frequency and percent values. Frequency data across categories were compared using Chi-square or Fishers’ exact test as appropriate. For all statistical tests a two-sided probability of p<0.05 was considered as statistical significance.

**RESULTS**

During the study period, the mean age of the patients was 36.9±14.5 years (16-70 years) with 83% males and 17% females. Majority of patients were adults in the age group 20 to 39 years. Road side accident (75%) was the commonest mode of injury followed by fall (23%) and assault (2%). Majority of the patients (74%) reached hospital within 6 hours after injury.

| Variables | Number of patients n(%) (N=100) | % age of unfavorable early outcome | P value | Number of patients n(%) (N=49) | % age of unfavorable GOS at 3 months | P value |
|-----------|---------------------------------|----------------------------------|---------|---------------------------------|----------------------------------|---------|
| Age (years) | | | | | | |
| <20 | 8 (8%) | 1 (12.5 %) | 0.93 | 7 (14.2%) | 0 (0 %) | 0.40 |
| 20-39 | 52 (52%) | 28 (53.8 %) | | 24 (48.9%) | 2 (8.3 %) | |
| 40-59 | 28 (28%) | 16 (57.1%) | | 12 (24.4%) | 1 (8.3 %) | |
| 60-70 | 12 (12%) | 6 (50 %) | | 6 (12.2%) | 0 (0 %) | |
| Gender | | | | | | |
| Male | 83 (83%) | 40 (48.1 %) | 0.37 | 43 (87.7%) | 3 (6.9 %) | 0.37 |
| Female | 17 (17%) | 11 (64.7 %) | | 6 (12.2%) | 0 (0 %) | |

The most common presenting symptom was loss of consciousness (97%) followed by vomiting (64%) and bleeding from ear, nose or throat in 34% patients. The mean GCS score at presentation was 5.8±1.8. Most of the patients (81%) had conservative management of head injury whereas surgical intervention in the form of craniotomy was required in only 19% patients. Out of 100 patients, 51(51%) had in-hospital mortality. Of 49 patients who survived for GOS assessment at three months, 28 patients (67.1%) had good recovery, 18 (36.7%) were minimally dependent, 1 (2%) patient was mostly dependent, no patient (0%) was in vegetative state and 2 patients (4%) died.

The results were as shown in tables 1-3. Among the demographic factors, age and gender were not found to be significant predictors of outcome after severe TBI (Table 1).
Table 2: Correlation of clinical parameters with unfavorable outcome after severe TBI.

| Variables          | Number of patients n(%) (N=100) | %age of unfavorable early outcome | P value | Number of patients n(%) (N=49) | %age of unfavorable GOS at 3 months | P value |
|--------------------|---------------------------------|-----------------------------------|---------|---------------------------------|-------------------------------------|---------|
| **GCS Score**      |                                  |                                   |         |                                 |                                     |         |
| 3                  | 21 (21%)                        | 21 (100 %)                        | <0.001  | 0 (0%)                          | 0 (0 %)                             |         |
| 4                  | 5 (5%)                          | 4 (80 %)                          |         | 1 (2.0%)                        | 0 (0 %)                             |         |
| 5                  | 17 (17%)                        | 12 (70.5 %)                       |         | 5 (10.2%)                       | 1 (20.0 %)                          | 0.44    |
| 6                  | 5 (5%)                          | 2 (40.0%)                         |         | 3 (6.1%)                        | 0 (0 %)                             |         |
| 7                  | 27 (27%)                        | 7 (25.9%)                         |         | 20 (40.8%)                      | 2 (10 %)                            |         |
| 8                  | 25 (25%)                        | 5 (20.0 %)                        |         | 20 (40.8%)                      | 0 (0 %)                             |         |
| **Hypoxemia**      |                                  |                                   |         |                                 |                                     |         |
| Present            | 31 (31%)                        | 26 (83.8 %)                       | <0.001  | 5 (10.2%)                       | 0 (0 %)                             | <0.001  |
| Absent             | 69 (69%)                        | 25 (36.2 %)                       |         | 44 (89.7%)                      | 3 (6.8 %)                           |         |
| **Hypotension**    |                                  |                                   |         |                                 |                                     |         |
| Present            | 6 (6%)                          | 5 (83.3 %)                        | 0.96    | 1 (2.0%)                        | 0 (0 %)                             | 0.24    |
| Absent             | 94 (94%)                        | 46 (48.9 %)                       |         | 48 (97.9%)                      | 3 (6.2 %)                           |         |
| **Pupil reactivity** |                               |                                   |         |                                 |                                     |         |
| Both reactive      | 57 (57%)                        | 14 (24.5 %)                       |         | 43 (87.7%)                      | 3 (23 %)                            |         |
| One reactive       | 12 (12%)                        | 7 (58.3 %)                        | <0.001  | 5 (10.2%)                       | 0 (0 %)                             | <0.001  |
| None reactive      | 31 (31%)                        | 30 (96.7 %)                       |         | 1 (2.0%)                        | 0 (0 %)                             |         |

The assessment of clinical parameters suggested that presence of hypoxemia and pupil non-reactivity were associated with significantly increased percentage of unfavorable early and late outcome (p<0.001) whereas poor GCS score showed a significant association with adverse early outcome alone (p<0.001) (Table 2).

A linear relationship was observed between falling GCS score and % age unfavorable early outcome after severe TBI. Among the CT scan findings, presence of hemorrhagic contusion, subarachnoid hemorrhage (SAH), midline shift and effacement of basal cisterne were strong predictors of unfavorable early outcome after severe TBI whereas fracture skull bone was associated significantly with adverse late outcome (Table 3).

Table 3: Correlation of CT findings with unfavorable outcome after severe TBI.

| CT findings                 | Number of patients n(%) (N=100) | %age of unfavorable early outcome | P value | Number of patients n(%) (N=49) | %age of unfavorable GOS at 3 months | P value |
|-----------------------------|---------------------------------|-----------------------------------|---------|---------------------------------|-------------------------------------|---------|
| Normal                      | 2 (2%)                          | 0 (0 %)                           | 0.14    | 2 (4.0%)                        | 0 (0 %)                             | 0.45    |
| Hemorrhagic contusion       | 59 (59%)                        | 40 (67.7 %)                       | <0.001  | 19 (38.7%)                      | 0 (0 %)                             | 0.15    |
| SDH                         | 50 (50%)                        | 29 (58.0 %)                       | 0.25    | 21 (42.8%)                      | 3 (14.3 %)                          | 0.38    |
| EDH                         | 18 (18%)                        | 10 (55.5 %)                       | 0.67    | 8 (16.3%)                       | 0 (0 %)                             | 0.43    |
| SAH                         | 24 (24%)                        | 19 (79.1 %)                       | 0.002   | 5 (10.2%)                       | 0 (0 %)                             | 0.54    |
| IVH                         | 16 (16%)                        | 8 (50.0 %)                        | 0.93    | 8 (16.3%)                       | 0 (0 %)                             | 0.43    |
| Midline shift              | 24 (24%)                        | 22 (91.6 %)                       | <0.001  | 2 (4.0%)                        | 0 (0 %)                             | 0.71    |
| Effacement of basal cisterne | 14 (14%)                        | 13 (92.8 %)                       | 0.001   | 1 (2.0%)                        | (0 %)                               | 0.78    |
| Fracture skull bone         | 50 (50%)                        | 27 (54.0 %)                       | 0.83    | 23 (46.9%)                      | 2 (8.0 %)                           | <0.001  |
| Pneumocranium              | 15 (15%)                        | 7 (46.6 %)                        | 0.71    | 8 (16.3%)                       | 2 (25.0 %)                           | 0.015   |

*SDH-Subdural hemorrhage, EDH-Extradural hemorrhage, SAH-Subarachnoid hemorrhage, IVH-Intraventricular hemorrhage.
DISCUSSION

Evaluating prognostic factors affecting head trauma patients is crucial to reduce the complication rate and ameliorate after effects. The findings from the present study suggests factors such as presence of hypoxemia, GCS score, pupil reactivity and some CT findings strongly influence outcome after severe TBI.

Age and gender are important prognostic predictors of TBI outcome. The present study has shown worse outcome in 40-59 years age group with an unfavorable early and late outcome in 57.1% and 8.3% patients respectively. Contrary to previous reported literature, the study did not demonstrate any significant relationship between age and unfavourable outcome after severe TBI.5,7 The findings from the medical research council (MRC) Corticosteroid Randomisation After Significant Head Injury (CRASH) trial revealed an association between increasing age and worse outcome that was apparent only after the age of 40.8 The published literature on effect of gender on outcomes after TBI shows conflicting results.5-7 Contrary to some previous reports, we were unable to demonstrate any influence of gender on outcomes after TBI.7 Our results were in accordance with the study by Saini et al in which gender was not found to be a significant predictor of outcome after sTBI.6 The study by Leitgeb et al in 2013 reported higher mortality in females which was due to their significantly higher mean age (52±24 versus 43±20 years; p=0.027).7

The reported literature demonstrates that secondary insults occur frequently and exert a powerful adverse influence on outcomes of severe TBI, hypoxemia and hypotension being the most important among them.6,7,9 Hypoxemia was found to be a significant predictor of outcome (p<0.001) in present study. The results of our study were in agreement with Saini et al who found an unfavorable GOS at 6 months in 82.6% patients of severe TBI with concomitant hypoxia as compared to 41.4% patients without hypoxia (p<0.005). Contrary to the published series, hypotension was not a significant predictor of outcome after severe TBI in present study.7,9 It may be due to a small number of patients having hypotension on admission (6%).

In present study, GCS was found to be a strong predictor of prognostic outcome after severe TBI. There was a trend towards increase in mortality rate with falling levels of GCS score. The findings were consistent with observations made by Husson et al who found GCS at admission and GCS motor score as a reliable predictor of final outcome after moderate and severe TBI.10 A large cohort study including 10008 international patients with TBI in 2008 also observed poor prognosis in patients with low GCS and demonstrated a clear linear relation with mortality which was in accordance with our results.8

Two mechanisms for pupillary dilatation in TBI has been proposed: firstly, as a result of uncal herniation leading to compression of third cranial nerve. Secondly, it may be a consequence of reduced blood flow to the brain stem and resulting brain stem ischemia.3,11 In the present study, it was found that pupil reactivity was a significant predictor of both early and late TBI outcome (p<0.001). This finding was in agreement with other published series by Leitgeb et al and Saini et al.6,7 Leitgeb et al observed a significantly higher mortality rate among patients of severe TBI with both non-reactive pupils as compared to both reactive pupils (88.9% versus 25.7%; p<0.001).7 Saini et al reported an unfavorable GOS at 6 months in 75% patients of TBI with anisocoria versus in 46.8% with normal pupillary assessment (p<0.001).6

A range of CT findings have been shown individually to relate to prognosis in head injury. Our study has demonstrated that presence of hemorrhagic contusion, subarachnoid hemorrhage (SAH), midline shift and effacement of basal cisterns to be strong predictors of early outcome. The CT finding of fracture skull bone was found to be significantly associated with unfavourable GOS at 3 months (p<0.001). In a multivariable prognostic analysis study by Murray et al, Marshall CT classification and traumatic SAH were among the most powerful independent prognostic factors for TBI.12 Husson et al has found strong evidence for predicting outcome at 6 months for midline shift on CT scan, subdural haematoma and pulsatility index. Strong evidence of no association was found for gender and IVH.10 The analysis of CT findings from the large MRC CRASH trial revealed that the presence of “obliteration of third ventricle or basal cisterns” was associated with the worst prognosis at 14 days.8 Saini et al described midline shift as the most important factor among all the CT findings that influences the outcome.8 In a study by Tasaki et al, 104 patients with severe TBI were evaluated for 14 predictive factors, absent cisterns, midline shift, and extensive SAH were significantly associated with outcome (p<0.05).13

CONCLUSION

Prognosis after severe TBI is critical and is influenced by many factors. The study concludes that low GCS score at admission, pupil non reactivity, presence of hypoxemia, abnormal CT head findings (hemorrhagic contusion, SAH, midline shift and effacement of basal cisterne) are significant predictors of outcome after severe TBI.

ACKNOWLEDGEMENTS

The author acknowledges the patients who participated in the study and colleagues who supported us while conducting the study.
Funding: No funding sources  
Conflict of interest: None declared  
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Singh V, Nath A, Beniwal M, Singh P, Dahiya R. Evaluating the predictive factors affecting outcome in patients with severe traumatic brain injury: a prospective observational study Int Surg J 2021;8:1762-6.