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Department of Neurosurgery, Narayana Medical College Hospital, Chinthareddypalem, Nellore, Andhra Pradesh. <sup>1</sup>Department of Neurosurgery, NIMHANS, Bengaluru, Karnataka, 2Department of Community Medicine, ESIC Medical College and Hospital, Faridabad, Harvana, <sup>4</sup>Department of Neurosurgery, S.M.S. Medical College, <sup>9</sup>Department of Neurosurgery, CK Birla Hospitals - Rukmani Birla Hospital, Jaipur, Rajasthan, <sup>5</sup>Department of Health Research, National Institute of Medical Statistics, Indian Council of Medical Research, Ansari Nagar, New Delhi, 7Department of Statistics. Bhabha Atomic Research Centre, Mumbai, Maharashtra, <sup>8</sup>Virus Research and Diagnostic Laboratory, National Institute of Epidemiology (ICMR), Chennai, Tamil Nadu, India, <sup>3</sup>El Bosque University, Red Latino. Meditech Foundation, Bogota, Colombia, <sup>6</sup>Department of Emergency Medicine, University of Florida, Jacksonville, Florida, USA

## Address for

correspondence: Dr. Amit Agrawal, Department of Neurosurgery, Narayana Medical College Hospital, Chinthareddypalem, Nellore - 524 003, Andhra Pradesh, India. E-mail: dramitagrawal@ gmail.com

# Pattern of reporting and practices for the management of traumatic brain injury: An overview of published literature from India

Amit Agrawal, Amey Savardekar<sup>1</sup>, Mitasha Singh<sup>2</sup>, Ranabir Pal<sup>2</sup>, Dhaval P Shukla<sup>1</sup>, Andres M Rubiano<sup>3</sup>, Virendra D Sinha<sup>4</sup>, Geetha R Menon<sup>5</sup>, Sagar Galwankar<sup>6</sup>, Luis Rafael Moscote-Salazar<sup>3</sup>, Prashant Bhandarkar<sup>7</sup>, Ashok Munivenkatappa<sup>8</sup>, Ugan Meena<sup>4</sup>, Amit Chakrabarty<sup>9</sup>

#### Abstract:

**Background:** Published literature regarding the demographics and mechanism of injury for traumatic brain injury (TBI) in India has not been analyzed in an organized sample.

**Objectives:** The objective of this systematic review was to organize the published literature from India related to TBI and analyze it in a very specific sample to identify the specific patterns of injury and associated mortality.

**Materials and Methods:** A search strategy with specific inclusion criteria was performed in PubMed, Cochrane, Web of Science, and the World Health Organisation (WHO) Global Health Library. The process included an additional search within the indexed literature and the website-based population survey reports.

**Results:** Our review identified 72 studies from 300 potentially relevant articles based on the broad criteria that defined the demographics of the patients suffering from TBI and the details of trauma sustained, including the mechanism of injury as well as its diagnosis, management, and outcome. Changes in demographic patterns, the patterns of the body regions involved, the associated injuries, the clinical presentation, the follow-up status of patients suffering from TBI, who may or may not have shown clinical improvement, the overall outcome, as well as the mortality and disability status reported in the literature were analyzed. A high incidence of TBI in the productive population is of serious concern. Extremes of ages are more vulnerable to severe injury and a poor outcome.

**Conclusion:** Quantitative analysis of injuries and outcomes of TBI victims shows a bigger health impact in the economically active population and in patients in the extremes of age groups.

#### Key Words:

Guidelines, India, management, outcome, traumatic brain injury

#### Key Message:

The present study was designed to identify reporting patterns of traumatic brain injury (TBI), including the additional descriptions of clinical aspects, diagnosis, management, and reported outcomes from the published literature on TBI from India.

The review showed that the collection of follow-up data after discharge of a patient with severe TBI was difficult in India and majority of the studies reported the condition at discharge as the follow up status of the patient, which is not appropriate.

The literature related to TBI from India is growing; however, the quality of reporting of quantitative studies on TBI in India is low and there is a need for systematic data collection and its timely publication from India.

Traumatic brain injury (TBI) is globally, a major issue of public health importance. India accounts for one-fourth of global deaths due to TBI.<sup>(1)</sup> A reliable quantification of the burden is an intricate issue owing to insufficient

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standardization and incomplete documentation on the incidence and outcome of TBI, with variability in case definition.<sup>[2]</sup> As research on TBI forms a very low priority amongst the healthcare fraternity, the fundamental patterns

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of TBI in India are still nebulous and not clearly defined.<sup>[3]</sup> Over a quarter of the world's trauma-related deaths occur in India, with TBI forming the leading cause of death and disability associated with trauma. To address this emergent TBI pandemic, we need high-quality research to guide policy decisions on holistic national trauma prevention and treatment guidelines. High-quality research on TBI in India is lacking but is essential for a systematic nationwide study. The implementation of certain checklists, such as the CONSORT (Consolidated Standards of Reporting Trials) statement for randomized-controlled trials, has led to significant improvements in the reporting quality.<sup>[4]</sup> We have attempted to conduct a systematic analysis from the Indian literature<sup>[3,5-75]</sup> on TBI for demographic estimates; and, explored the mechanism of TBI as a step towards quality intervention to reduce the magnitude of preventable morbidity, mortality, and disability by identifying opportunities for improvement.

#### **Material and Methods**

We attempted a comprehensive, annotated assembly of survey results by exploring various resources: published surveys, field studies, meeting presentations, and personal communications on recent surveys. Some of these sources were not included in the previously published analyses on TBI. Through an extensive search of the indexed literature and website-based population survey reports, we identified 73 research publications from 250 potentially relevant articles. All published articles in indexed journals available from various institutional libraries of India and the websites based upon the epidemiologic and analytical studies on TBI were included. The search terms included combinations of MeSH terms and empirical taxonomies related to the nomenclature used for describing various conditions related to TBI. The body regions involved, patterns of injuries, clinical presentation, demographic distribution, investigations, management, follow-up, guidelines, prediction models, randomized controlled trials (RCT), and outcomes including deaths were studied. PubMed (from January 1st, 1946 to October 31st, 2017), Cochrane Library (from January 1st, 1898 to October 31st, 2017), Web of Science (from January 1st, 1864 to October 31st, 2017), and the World Health Organisation (WHO) Global Health Library (from January 1st, 1947 to October 31st, 2017) were searched along with abstracts from scientific meetings (2000-2017). A review of citations and reference lists was performed to identify additional eligible studies. Wherever possible, sources were contacted for further information on the survey data not readily available in the public domain. Manual searches were conducted from review articles, previous meta-analyses, and from hard copy publications not sourced in repeated internet searches. Whenever necessary, we contacted authors for further details or for translations from languages other than English.

Few criteria were developed to select studies from peer-reviewed articles. First, a broad criterion of TBI was developed based on the information provided in the WHO publication by global experts prior to the performance of the study for ensuring the feasibility, acceptability, and reliability of the study included in the analysis. Second, TBI with the body regions involved and patterns of injuries, their clinical presentations, demographic distributions, investigations, management, follow-up, guidelines, prediction models, randomized control trials (RCTs), and outcomes including deaths were included. Studies that did not meet these criteria were excluded. Finally, in the absence of nationally representative database on TBI and the monolithic pattern of reporting by researchers in India, all reports on TBI were considered in this review, irrespective of the criteria of diagnosis.

The research questions included –What are the body regions involved and the patterns of injuries? How did the patients present clinically? How the patients were demographically distributed? How were the patients demographically distributed? What were the guidelines and the prediction models? How many RCTs were reported? How many of the reported studies mentioned outcomes? The main outcome variables were the specific patterns of injury and the associated mortality among patients who sustained TBI, as ascertained from the published reports [Tables 1 and 2].

#### **Statistical analysis**

We managed data using Microsoft Office Excel 2016 (Microsoft, Redmond, WA), and analysed the data using Statistical Package for the Social Sciences [SPSS; version 24.0; IBM, USA] for Windows to calculate the median value and the interquartile range.

#### **Results and Discussion**

The literature reports changes in the epidemiological patterns of TBI; the median age of individuals who experience TBI is increasing, and 'falls' have now surpassed 'road traffic incidents' as the leading cause of TBI. Despite claims to the contrary, no clear decrease in TBI-related mortality, or an improvement in the overall outcome has been observed over the past two decades.<sup>[2]</sup>

#### Body regions involved in associated injuries

Ahmed *et al.*, analysed the incidence, predictive factors, and outcome of acute kidney injury (AKI) in operated cases of TBI. The study was conducted over a period of one year on 395 patients who underwent neurosurgical intervention. This study did not strictly deal with the associated kidney injury in TBI, but analysed the incidence of AKI in operated patients of TBI. This association of kidney injury in patients with TBI may be attributable to the stress that the patients underwent, as well

# Table 1: Distribution and relative frequencies of the areas of focus of the studies included in this article

Area of interest	Frequency
Body regions involved <sup>[5-14]</sup>	10
Clinical presentation <sup>[3,15-28]</sup>	17
Demographics <sup>[8,16,21,22,24,27,29-36]</sup>	14
Follow-up <sup>[28,31,36-41]</sup>	8
Guidelines <sup>[35,42]</sup>	2
Injury pattern <sup>[6,9,17,32,33]</sup>	5
Investigations <sup>[5,6,10,11,14,15,23,25,26,29,34,42-58]</sup>	31
Management <sup>[6,12,16,19,23,37,40,44,57,59-64]</sup>	15
$Outcome^{[3,6\text{-}8,11,12,14,15,19,20,23,26,27,31,32,36\text{-}41,43,45,47,48,51,52,56,57,62,64\text{-}71]}$	38
Prediction model <sup>[41,70,72-74]</sup>	5
Randomized controlled trials <sup>[19,59,60]</sup>	3

Table 2. Unaracteristics and report	ווות					IUIA							
Title	Year N	Jumber F	3ody regions involved	Clinical D presentation	emographics	<sup>=</sup> ollow Gu up	idelines	Injury Ir attern	ivestigations M	lanagement C	Dutcome P	rediction R( model	сŢ
Genetic variation of ApoE gene in ethnic/ Kashmiri population and its association with outcome after traumatic brain injury <sup>[38]</sup>	2015	150				Yes					Yes		
Decompressive craniectomy in traumatic 2 brain injury: A single-center, multivariate analysis of 1,236 patients at a tertiary care hospital in India <sup>[37]</sup>	2015	1236				Yes				Yes	Yes		
Symptomatic contralateral subdural hygromas after decompressive craniectomy: Plausible causes and management protocols <sup>[64]</sup>	2015	266								Yes	Yes		
Prognostic value of FOUR and GCS scores in determining mortality in patients with traumatic brain injury <sup>770</sup>	2015	138									Yes	Yes	
Neuroendocrine dysfunction in acute bhase of moderate-to-severe traumatic brain injury: A prospective study <sup>iss</sup>	2015	100							Yes				
Surgical results of decompressive craniectomy in very young children: A level one trauma centre experience from India <sup>[63]</sup>	2015	71								Yes			
Lifetime prevalence and factors associated with head injury among older people in low and middle-income countries: A 10/66 study <sup>[30]</sup>	2015	150			Yes								
Characterization of traumatic brain injury 2 in human brains reveals distinct cellular and molecular changes in contusion and pericontusion <sup>(46)</sup>	2015	56	No						Yes				
Characteristics of traumatic intracerebral 2 haemorrhage: An assessment of screening logs from the STITCH (trauma) trial <sup>[29]</sup>	2015	713			Yes				Yes				
Validation of a new clinico-radiological 2 grading for compound head injury: Implications on the prognosis and the need for surgical intervention <sup>[41]</sup>	2015	244				Yes					Yes	Yes	
Acute kidney injury in survivors of surgery for severe traumatic brain injury: Incidence, risk factors, and outcome from a tertiary neuroscience center in India <sup>[5]</sup>	2015	95	Yes						Yes				
Profile of patients with head injury among 2 vehicular accidents: An experience from a tertiary care centre of India <sup>[35]</sup>	2014	1545			Yes		Yes						

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Table 2: Contd													
Title	Year I	Number	Body regions involved	Clinical	Demographics I	-ollow C	Guidelines	Injury I pattern	nvestigations	Management	Outcome	<b>Prediction</b> model	RCT
A prospective randomized study of use of drain versus no drain after burr-hole evacuation of chronic subdural hematoma <sup>[60]</sup>	2014	60								Yes			Yes
Ocular manifestations of head injury and incidence of post-traumatic ocular motor nerve involvement in cases of head injury: A clinical review <sup>[8]</sup>	2014	594	Yes					Yes					
Silent epidemic: The effects of neurofeedback on quality-of-life	2014	60								Yes	Yes		
Study of insomnia and associated factors in traumatic brain injury <sup>fe2</sup>	2014	102		Yes		Yes							
Comparative evaluation of MRS and SPECT in prognostication of patients with mild to moderate head injury <sup>48</sup>	2014	344							Yes		Yes		
Pressure ulcer in patients with severe traumatic brain injury: Significant factors and association with neurological outcome <sup>(11)</sup>	2014	88	Yes						Yes		Yes		
Perioperative glycernic status of adult traumatic brain injury patients undergoing craniotomy: A prospective observational study <sup>[34]</sup>	2014	200			Yes				Yes				
Impact of rehabilitation on functional outcome during the first year of moderate and severe traumatic brain injury <sup>(40)</sup>	2014	20				Yes				Yes	Yes		
Phenytoin toxicity in patients with traumatic brain injury <sup>(25]</sup>	2014	100		Yes					Yes				
Cognitive, functional, and psychosocial outcome after severe traumatic brain injury: A cross-sectional study at a tertiary care trauma center <sup>[65]</sup>	2013	22									Yes		
Repeated measure analysis in raga therapy: A case study on head injury patients. <sup>[61]</sup>	2013	330								Yes			
Does isolated traumatic subarachnoid hemorrhage affect outcome in patients with mild traumatic brain injury? <sup>[38]</sup>	2013	1149				Yes					Yes		
Magnitude of pedestrian head injuries and fatalities in Bangalore, South India: A retrospective study from an apex neurotrauma center <sup>i221</sup>	2012	73		Yes	Yes								

Contd...

RCT	Yes												
Prediction model													
Outcome		Yes		Yes		Yes	Yes	Yes		Yes	Yes		
Management	Yes								Yes				
Investigations					Yes		Yes	Yes	Yes	Yes		Yes	Yes
Injury   pattern			Yes	Yes									
Guidelines													
Follow up		Yes											
Demographics		Yes		Yes									
Clinical I presentation			Yes			Yes		Yes					
Body regions involved													
Number	270	53	414	51	1292	520	529	290	66	51	355	50	50
Year <b>N</b>	2012	2012	2012	2011	2011	2010	2010	2010	2009	2009	2008	2008	2008
Title	CRASH-2 (Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage) intracranial bleeding study: The effect of tranexamic acid in traumatic brain injury-a nested, randomised, placebo-controlled trial <sup>[59]</sup>	Prognostic significance of age in traumatic brain injury <sup>[36]</sup>	Developing traumatic brain injury data bank: Prospective study to understand the pattern of documentation and presentation <sup>(17)</sup>	Missile injury to the pediatric brain in conflict zones <sup>(32)</sup>	Initial experience with mobile computed tomogram in neurosurgery intensive care unit in a level 1 trauma center in India <sup>[53]</sup>	Post-traumatic seizures-A prospective study from a tertiary level trauma center in a developing country <sup>[3]</sup>	Apolipoprotein E polymorphism and outcome after mild to moderate traumatic brain injury: A study of patient population in India <sup>[43]</sup>	Audiological deficits after closed head injury <sup>(15)</sup>	Assessment of endocrine abnormalities in severe traumatic brain injury: A prospective study <sup>(44]</sup>	Comparative evaluation of corpus callosur. DTI metrics in acute mild and moderate traumatic brain injury: Its correlation with neuropsychometric tests <sup>[47]</sup>	A new scale for prognostication in head injury <sup>(68)</sup>	Erythrocyte indicators of oxidative changes in patients with graded traumatic head injury <sup>[50]</sup>	Relationship between markers of lipid peroxidation, thiol oxidation and Glasgow coma scale scores of moderate head injury patients in the 7-day post-traumatic period <sup>[75]</sup>

Table 2: Contd													
Title	Year N	umber	Body regions involved	Clinical	Demographics	Follow Gu	lidelines	Injury In pattern	nvestigations	Management (	Outcome F	Prediction I model	RCT
Pattern of fatal head injuries due to vehicular accidents in Mangalore <sup>[33]</sup>	2008	682			Yes			Yes					
Early prediction of outcome in very severe closed head injury <sup>(18]</sup>	2008	204		Yes									
Utility of optic nerve ultrasonography in head injury <sup>[13]</sup>	2008	100	Yes						Yes				
Intensive care management of head injury patients without routine intracranial pressure monitoring <sup>(67)</sup>	2007	208							Yes		Yes		
Relationship between neurological outcome and early oxidative changes in erythrocytes in head injury patients <sup>[56]</sup>	2007	55							Yes		Yes		
Demographic profile, clinical presentation, management options in cranio- cerebral trauma: An experience of a rural hospital in Central India <sup>[16]</sup>	2007	200		Yes	Yes					Yes			
Expanding traumatic intracerebral contusion/hematoma <sup>[51]</sup>	2006	262							Yes		Yes		
The incidence and severity of injury in children hospitalised for traumatic brain injury in Kashmirt <sup>211</sup>	2006	1500		Yes	Yes								
A mathematical model for predicting the outcome in moderate head injury <sup>72</sup>	2006	85										Yes	
Economics of head injuries[66]	2006	60									Yes		
Correlating facial fractures and cranial injuries <sup>[7]</sup>	2006	108	Yes								Yes		
Technetium Tc-99m ethyl cysteinate dimer brain single-photon emission CT in mild traumatic brain injury: A prospective study <sup>[56]</sup>	2006	92							Yes				
Outcome of "unknown" head injury patients at a tertiary care neurosurgical centre <sup>[24]</sup>	2006	298		Yes	Yes								
Fatal head injury in homicidal victims <sup>[8]</sup>	2005	77	Yes		Yes						Yes		
Repeat CT scan in closed head injury <sup>[42]</sup>	2005	175					Yes		Yes				
Mild head injury: revisited <sup>[23]</sup>	2004	381		Yes					Yes	Yes	Yes		
Prognosis in children with head injury: An analysis of 340 patients <sup>[27]</sup>	2003	340		Yes	Yes						Yes		
Missile injuries of the brain: Results of less aggressive surgery <sup>[31]</sup>	2003	200			Yes	Yes					Yes		
Serial pattern learning after mild head injury <sup>r71</sup>	2003	80									Yes		

Contd...

Table 2: Contd													
Title	Year !	Number I	Body regions involved	Clinical	Demographics	Follow up	Guidelines Inj	ury Invesitern	tigations <b>N</b>	lanagement	Outcome F	rediction	RCT
Outcome prediction model for severe diffuse brain injuries: Development and evaluation <sup>174</sup>	2003	97										Yes	
Evaluation of nimodipine in the treatment of severe diffuse head injury: A double-blind placebo-controlled trial <sup>[19]</sup>	2003	289								Yes	Yes		Yes
Predictors of gastrointestinal bleeding in acute intracerebral haemorrhage <sup>(10]</sup>	2003	51	Yes	Yes				-	ŕes				
Magnetization transfer and T2 quantitation in normal appearing cortical gray matter and white matter adjacent to focal abnormality in patients with traumatic brain injury <sup>[64]</sup>	2003	83							Yes				
Association among duration of unconsciousness, Glasgow Coma Scale, and cranial computed tomography abnormalities in head-injured children <sup>[45]</sup>	2001	400		Yes					Yes		Yes		
Prognostic factors in children with severe diffuse brain injuries: A study of 74 patients <sup>(69)</sup>	2001	74		Yes							Yes		
A mathematical outcome prediction model in severe head injury: A pilot study <sup>[73]</sup>	2000	103										Yes	
A comparative study of the effects of famotidine and sucralfate in prevention of upper gastrointestinal bleeding in patients of head injury <sup>(40)</sup>	2000	75							ŕes				
Improvement in the information content of the Glasgow Coma Scale for the prediction of full cognitive recovery after head injury using fuzzy logic <sup>[52]</sup>	2000	253						-	ŕes		Yes		
Predictors of posttraumatic convulsions in head-injured children <sup>[28]</sup>	1999	400		Yes				-	Yes		Yes		
Severe head injury patients in a multidisciplinary ICU: Are they a burden? <sup>[57]</sup>	1999	171						-	ŕes	Yes	Yes		
Visual outcome in optic nerve injury patients without initial light perception <sup>[14]</sup>	1999	100	Yes					-	Yes		Yes		
Trans-ethmoidal optic nerve decompression <sup>[12]</sup>	1994	111	Yes							Yes	Yes		

Injury Investigations Management Outcome Prediction RCT model Yes Yes Yes Yes pattern Yes **Demographics Follow Guidelines** dn presentation Clinical Yes fear Number Body regions involved Yes Dbs = Observational study; RCT = Randomized controlled trial 551 61 1989 1993 different emergency medical services and communal riot victims--the KEM Hospital Head injury mortality in two centers with Analvtical data of January 1993 **Fable 2: Contd..** intensive care<sup>[20]</sup> experience<sup>[6]</sup> Title

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as to the iatrogenic injury sustained during the management of TBI. Based upon these stringent inclusion criteria, 95 patients were recruited. The incidence of AKI was 11 (11.6%) [As per the Acute Kidney Injury Network (AKIN) staging criteria – stage I (7%), stage II (3%), and stage III (1%)];use of an aminoglycoside during the management of TBI was a significant factor in the development of AKI.<sup>[5]</sup>

Dhandapani *et al.*, studied the factors associated with the development of pressure ulcers in patients of TBI. The study included 89 cases (with the age of the patients ranging from 20–60 years). The Glasgow Coma Scale (GCS) score of these patients ranged from 4–8; out of them, >6 (7%) developed pressure ulcers at 2 weeks and 14 (16%) developed pressure ulcers at three weeks post-injury.<sup>[11]</sup>

Goel *et al.*, evaluated the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of optic nerve ultrasonography (ONUS) in detecting raised intracranial pressure (ICP) in TBI; the study revealed evidence of raised ICP in 74 patients. However, this study did not deal with the associated ocular or other injury in these patients who had sustained TBI.<sup>[13]</sup>

Mohanty *et al.*, studied the incidence of fatal TBI in 77 homicidal victims; the incidence of associated fatal injuries in other body regions was noted in 18 (23.4%) cases. The incidence of fatal injuries in different body parts in a decreasing order of frequency (related to the regions involved) were: neck (6%), chest (6%), limbs (5%), and abdomen (3%).<sup>[13]</sup> Pappachan *et al.*, studied the relationship between various isolated or combined fractures of the facial skeleton and cranial injuries over a period of five years among 12,329 patients who had sustained trauma; 772 patients among them had facial fractures; central mid-facial bony involvement was more commonly associated with TBI.<sup>[7]</sup>

Sharma *et al.*, studied the ocular manifestations in 1184 patients with TBI; 594 (50.17%) of them had ocular manifestations. These manifestations included ecchymosis (51.9%), sub-conjunctival hemorrhage (44.4%), lid edema (41.5%), lacerated wound (22.6%), pupillary involvement (21.04%), ptosis (6.73%), cranial nerve palsy (11.62%), orbital fractures (10.5%), optic nerve trauma (4.04%), and exposure keratitis (4.25%).<sup>[9]</sup>

Tandon et al., over a five-year period (1987-1991), studied 111 patients with indirect optic nerve injury in patients who had sustained a closed head trauma ; in Group A, among the 66 patients included, 27 (40.91%) patients had visual improvement with a high dose steroid treatment alone. The 39 patients who did not improve with steroid treatment were subjected to a transethmoidal optic nerve decompression. Following this procedure, 22 (56.41%) patients revealed a visual improvement, resulting in an overall improvement of 74.2% in group A. In Group B (the control group), 45 patients were included and treated with steroids alone, of which 23 (51.11%) improved. The study revealed that nearly half of such patients improved on steroids alone; optic nerve decompression led to significantly improved recovery rates in patients where conservative treatment was unsatisfactory (P < 0.05). This study focused on the treatment of indirect optic nerve injury associated with mild TBI and did not comment on the incidence of this entity in those patients with TBI who sustain a direct trauma to the optic nerve.<sup>[6,12]</sup> Agrawal *et al.*, studied visual outcome among 100 patients with optic nerve injury who initially did not have light perception. These patients had sustained a mild TBI and unilateral/bilateral blindness; visual improvement was reported in 23 patients. Bilateral optic nerve injury was recorded in two cases. The most common finding was that of an orbital wall fracture, which was found in 22 patients. Optic nerve laceration was seen in one patient.<sup>[14]</sup>

#### **Clinical presentation**

In their study, Colohan et al., mentioned that pupillary reaction to light was normal in 89.8% of the patients; as per the motor component of the Glasgow Coma Scale (GCS-M), 92.4% patients had a score of 5 or 6 and only 7.6% of them were having a score of between 1 to 4 (representative of severe head injury); skull fracture was noted in 40.4% patients with an overall mortality of 6.9%.<sup>[20]</sup> Thirupathy et al., in "Mild head injury (HI): Revisited," analysed 381 patients, aged 3 months to 78 years. It was reported that majority of the patients were adult males (63%) and the modes of injury included RTA (52%), assault (25%), fall (20%), and others (3%). The relative incidence of their GCS scores was: 15 (75%), 14 (14%) and 13 (11%); 148 (38.9%) patients had positive findings on their CT scans; the most common intracranial injury was hemorrhagic contusion; and, the significant predictors of positive CT scan findings in mild TBI included: a GCS score of 13 and 14; fracture on skull X-rays; and, focal neurological deficits.<sup>[23]</sup>

Tabish *et al.*, studied the incidence and severity of TBI among 1500 hospitalized children in Kashmir. The most common age group was 4–6 years, the predominant gender of the afflicted patients was male (60.2%), the causes of injury included a fall (68.1%) followed by RTA (28%), assault (2%), flying objects like a cricket ball (2%), and others (1%).<sup>[21]</sup>

Ratan *et al.*, studied the predictors of posttraumatic convulsions among 400 children with TBI;84 cases (21%) had a posttraumatic seizure. Eighty patients had an early seizure (within one week), whereas four had a late-onset seizure. The mean age of the patients who had post-traumatic seizures was  $4.5 \pm 2.9$  years, and their mean GCS score was  $10.96 \pm 3.75$  years. In those patients without post-traumatic seizures, the mean age was  $5.5 \pm 2.9$  years and the mean GCS scale score was  $12.88 \pm 2.91$  years; radiographic abnormalities were observed in 39.29% and CT abnormalities in 60.71% patients. In the subgroup analysis, a higher likelihood of post-TBI related convulsions were observed among children with an age less than 2 years, in those who had sustained severe TBI (GCS score of  $\leq 5$ ); and, in those with loss of consciousness (LOC) >12 hours.<sup>[26]</sup>

Pruthi *et al.*, studied 2555 patients with TBI. In the first part of the study, (in the time frame from June to September 2009), 529 (20.7%) consecutive pedestrians with RTA were studied. Majority [221 (41.8%)] of injuries occurred during the peak hours, of which 461 (87.1%) patients received primary care. The incidence of TBI while using various modes of transport was as follows: two-wheeler accidents 49%; heavy vehicular accidents 10.8%; unknown 10.5%. Two hundred and ninety-two (55.2%) patients sustained a moderate or severe TBI, and associated injuries were seen in 478 (90.4%) patients.

Major thoracoabdominal trauma was seen in 4%, whereas spinal injury occurred in 2.3% of the patients. On the CT scan, the most common injury was cerebral contusion (47.2%); surgery was done on 5.67% patients, and the mortality rate was 6.62%. In the second part of the study (representing the mortality data) conducted on 326 patients who died as pedestrians after suffering RTA during the duration from 2007-2009, pedestrian deaths constituted 26.23% among the post-mortems conducted; the age group of these patients was 18-50 years ; majority (73.6%) of the cases were male subjects ; the cause of TBI leading to death included two-wheeler (39.9%) and four-wheeler (27.9%) accidents. The most common autopsy finding was diffuse brain edema; associated injuries were seen in 95% of the patients; TBI alone was the cause of death in 84.9% patients; while, significant associated injury was the cause of death in the remaining 15.1% patients.[22]

Agrawal *et al.*, studied 414 patients who had sustained a TBI from January to June 2010;10.23% of them required resuscitation at admission with a mean hospital stay of 5.42 days and the incidence of fatality was 7.75%; one-third (33.6%) of the patients presented in the month of June. RTA (mainly representing highway trauma) was the main cause of TBI accounting for 56.76% of the cases ; the major associated injuries were ear, nose, and throat (ENT) bleed (2.17%) and limb fractures (5.07%); 291 cases had positive CT findings that included a subdural hemorrhage (SDH; n = 45), cerebral contusion (n = 29); extradural hemorrhage ([EDH]; n = 22), and traumatic subarachnoid hemorrhage ([SAH] n = 11).<sup>[17]</sup>

Suresh *et al.*, discussed the prognosis of TBI in children in a retrospective study involving 340 patients (conducted from January 1993 to December 1998). At admission, the GCS scores were 3–5 in 40 children, 6–8 in 55 children, 9–12 in 96 children, and 13–15 in 152 children; and, according to the stratification of age groups, the incidence was: less than 2 years: n = 11, 3–5 years: n = 53, 6–10 years: n = 140, and 11–15 years: n = 156. The relationship of a poor outcome among patients associated with various intracranial pathologies was as follows: EDH: 95 (8.4%) patients, cerebral contusion (CC): 85 (18.2%) patients, diffuse cerebral edema: 100 (25%) patients, and SDH: 34 (35.3%) patients. The clinical features associated with a poor prognosis included absence of ocular movements, an abnormal pupillary size and reaction, and age less than 2 years.<sup>[27]</sup>

Ahmad *et al.*, studied the outcome of 325 "unknown" TBI patients in a retrospective analysis from January 2002 to March 2005. Surgery was conducted on 18% patients with a mild, 34% patient with a moderate, and 50% patients with a severe TBI. Mortality was naturally higher in patients suffering from severe TBI, with the relative incidence of patients suffering from a mild TBI being 1%, moderate TBI being 6%, and severe TBI being 40%. The details of clinical presentation were not discussed in this study. The details of GCS scores at admission were not discussed.<sup>[24]</sup>

Pillai *et al.*, studied the role of nimodipine in the treatment of severe diffuse brain injury among 50 patients in the treatment group, and in 47 in the placebo arm. Their mean age was  $30 \pm 12$  years in the treatment arm (the mean age in the placebo arm being  $29 \pm 10$  years); there was a male dominance in both the arms (>90%). RTA was the cause of injury in the nimodipine

group in 66% cases, and in 76.6% in the control group; a fall was the main cause of TBI in 30% patients in the treatment group and in 12.77% patients in the placebo group; the GCS score at presentation was 3–5 in 18% in the treatment group and 17.02% in the placebo group, and was 6–8 in 82% in the treatment group and 82.98% in those in the placebo group; pupillary reaction was absent in both the groups of patients along with the absence of extraocular movements in 3 patients in the nimodipine group and in 1 patient in the placebo group, respectively.<sup>[19]</sup>

Abraham *et al.*, studied phenytoin toxicity among 100 TBI patients with mild and moderate injury (all having a GCS score >8 with the mean GCS score being 12.6  $\pm$  2.2). Their clinical profile, percent of patients associated with mild versus moderate TBI, and the causes of TBI were not adequately stated.<sup>[25]</sup>

Thapa et al., studied posttraumatic seizures (PTS) in patients with a TBI in a prospective study that included 520 patients with TBI from July 2007 through July 2008. At a median follow-up of 386 days, 59 (11.4%) patients developed PTS with the relative incidence of immediate, early and late seizures being 6.5%, 2.1%, and 2.7%, respectively. The modes of injury included RTA (250 patients), fall from height [FFH; 195 patients], physical assault (46 patients), gunshot injuries (2 patients) and others (27 patients). The duration of loss of consciousness [LOC] was as follows: transient LOC <5 min was seen in 53 (10.2%) patients; a LOC  $\geq$  5 min was seen in 391 (75.2%) patients; a delayed LOC was seen in 6 (1.2%) patients; and, post-traumatic amnesia was seen in 24.7% patients. The incidence of associated injuries in the included patients included: ENT bleed (40.6%), fractures involving long bones, scapulae, and nasal bones (11.5%), chest injuries (3.8%), and spinal injuries (10%). The GCS score at presentation was severe (≤8) in 129 (24.8%), moderate (9–13) in 116 (22.3%), and mild (>13) in 275 (53%) patients. This article gives a good overview of the clinical profile of the patients.<sup>[3]</sup>

Dalvie *et al.*, reported on 440 TBI patients of the 1993 Mumbai communal riot victims. The vital parameters at admission were as follows: 32 (16.5%) patients had a mild- to- moderate shock (the pulse ranging between 100 and 120 per min and the BP ranging between 80 and 100mm/Hg); 15 (7.7%) patients were critical (with the pulse > 120 per min and the BP <80 mm/Hg); and, 14 (7.2%) were gasping (pulse not palpable and the BP not recordable with an abnormal breathing pattern).<sup>[6]</sup>

Of all the articles analysed, it was noted that only a few of the studies discussed the basic and vital clinical profiles of the included cases including their age, gender, cause of head injury, a history of loss of consciousness , vomiting, seizures, ENT bleed, GCS at presentation, pupillary status, presence of functional neurological disorders (FNDs), and associated injuries.

#### **Demographics**

In the prospective observational study by Bhattacharjee *et al.*, on the perioperative glycemic status of adult TBI patients undergoing a craniotomy, the demographic and baseline characteristics were adequately described; the mean age

of the included patients was  $33.9 \pm 8.6$  years (n = 200) with the male: female ratio being 9:2. The ratio of severity of TBI, classified as mild: moderate: severe was 1:3:6; an extradural hemorrhage had the highest (44%) incidence followed by an equal incidence of intracerebral hemorrhage and acute subdural haemorrhage (28% each). The preoperative value of capillary blood glucose was 136.8  $\pm$  11.9 mg/dL, and the one-hour postoperative value was 166.7  $\pm$  11.4 mg/; whereas the median duration of anesthesia was 130 (range 90–215) minutes.<sup>[34]</sup>

During screening for the Surgical Trial In Traumatic intra Cerebral. Haemorrhage (STITCH) described by Francis *et al.*, the demographics of the traumatic intracerebral hemorrhage (ICH) was mentioned without defining the age groups. During the 60- month study duration, the profile of 713 patients from seven centres in India were as follows: the median age (with interquartile range) was 37 (25, 50) years, with a male dominance (76%); the median (with interquartile range) time from injury was 16 (10, 20) hours; the median ICH volume (with interquartile range) was 8 (6,16) ml; both pupils were reactive in 76% of the patients.<sup>[29]</sup>

Menon et al., conducted a retrospective analysis of 682 fatal TBI cases due to vehicular accidents who underwent an autopsy in Mangalore. The study duration was for 5 years (from January 1997 to December 2003). Male subjects comprised the majority (84.6%) of the cases; the youngest victim was aged 1 year, and the oldest was 90 years old; both were of male gender. The highest (24.21%) incidence of deaths occurred in the 21-30 year age group, and the least incidence (0.7%) in the 81-90-year group; accidents mainly occurred between 2 and10 pm (in 45.3% of the cases) followed by 6 am to 2 pm (in 33.43% of the cases), and the least number of accidents occurred during 10 pm to 6 am (21.26%). The accidents mainly involved two- wheeler riders (37.4%), followed by pedestrians (36.8%), and four- wheeler riders (25.8%); occupants of light motor vehicles and heavy motor vehicles were almost equally involved, constituting nearly one-fourth of the victims. Of the victims, 62.75% died on the spot, whereas 26% were treated surgically; the mean survival period was 6-24 (16.12%) hours. Majority of the victims had an external injury on the face and scalp (82%) as well as skull fractures (88.88%); fissured fracture was the most common (23.1%) type of fracture, followed by depressed fracture (21.28%), with the least common (14.6%) being the sutural fracture. The cranial vault was involved in a large number (88.88%) of patients. This was followed by fractures involving base of the skull (35.97%) as well as both vault and base fractures (35%); the anterior cranial fossa, parietal bone, and temporal bone were mostly involved in the fracture (with their incidence being 36.23%, 34.48%, 34.46%, respectively); the least involved area was the occipital bone (seen in 23.1% victims). Contusions and brain lacerations were noted in equal numbers (35%). Intracranial hemorrhage was mainly subdural (52.63%) followed by subarachnoid (27.27%), whereas it was extradural in a comparatively less number of cases (17.15%); a combination of all types of hemorrhages were seen only in 5% of the victims.[33]

Colohan *et al.*, conducted a prospective study over a 20-month period from 1977 to 1979 among 551 TBI cases from New Delhi; the mean age was  $25 \pm 1.4$  (only 2.7% patients

were over 60 years of age); 81% subjects were males; the cause of TBI included RTA (60.6%), FFH (18.5%), assault (8.6%), unknown cause (5.9%), and others (6.4%).<sup>[20]</sup> Mohanty et al., prospectively studied fatal head injury in homicidal victims from the whole of Berhampur city and adjacent rural areas of south Orissa by conducting a post-mortem study on the victims from January 1998 through December 2001. Out of 162 homicidal deaths, 77 died from head injuries; 88% were males; and most were in the age group of 21-40 years. A blunt weapon was used for killing in a majority (54%) of cases, followed by a sharp weapon (in 22% of cases); whereas, both a blunt and a sharp weapon were used in 20% of the patients; the least incidence of TBI occurred following the use of firearms (4%). Defence wounds were present in nearly half of the patients; the majority (46.7%) of the incidents took place in the streets or outdoors, and in 48 cases, more than one offender was involved. Multiple transactions were common and present in 70.1% of the victims. In the remaining 29.9%, a single transaction was present over the head resulting in the death of the victim. In two cases, fatal injuries were sustained on both chest and abdomen. Majority of the victims died either instantly (45.4%) or within 24 hours (29.2%).[8]

In a prospective observational hospital-based study conducted for 1 year (from January to December 2003), Tabish et al., analysed the age groups, sex ratio, incidence, and severity of TBI among 1500 children admitted to the accident and emergency department of a hospital in Kashmir. TBI constituted one-fifth of the total admissions to the department. Males were major attendees (60.2%) to the emergency with TBI. The most common cause of head injury was a fall (68.1%) followed by RTA (28%), whereas assault and injuries due to flying objects (like a cricket ball) constituted 2% each, respectively. Most of the falls were from unprotected roofs, windows and stair cases. About half of all falls occurred in the age group of 4—6 years. Most of the children (50.3%) involved in RTA were pedestrians. Only 2% were passengers and the remainder had bicycle injuries. Nearly all (99%) of the patients with TBI who recovered were discharged within 16-24 hours after admission.[21]

Wani et al., analysed age, gender, and the mechanism of TBI occurring due to a missile injury in the conflict zones among 51 children aged 2-18 years (mean age: 12.17 years, median age: 11.0 years) with a high male preponderance (male:female = 6.1:1). Children younger than 13 years had a better outcome than other teenagers; nearly all were victims of roadside grenade attacks on security forces, crossfire between security forces and militants, or firing on processions; only two were injured while playing with unidentified objects found in grazing fields (which turned out to be grenade explosives; there was no instances of suicide or murder). Bullet injury accounted for 15.7% of the cases, whereas the rest were caused by fragments from grenade blast injuries; there was a significant difference in the outcome between the two groups. Among the clinical factors, the GCS score was the strongest predictor of outcome; with a score of 3–7, there was a 66.7% mortality rate, and none of the patients had a good outcome; patients with a GCS score of 8-13 were associated with a 15.0% mortality, 71% of the patients had minimal or no deficits and no deaths were encountered; whereas, patients with a GCS score of  $\geq 13$ had a normal outcome or minimal deficits. The mortality rate in the anisocoria group was 55.5%, with no patients having a GCS score of 5 or less. On studying the hemodynamic status of the patients include in the study, it was noted that after resuscitation, 6 (13.3%) patients remained in shock because of the brain injury itself and not due to any other injuries; all of them died, indicating that the hemodynamic status of the patients is a very strong negative prognostic factor. A CT scan could not be done in 7 (13.7%) patients— 6 were in a state of shock and could not be resuscitated, and another patient had an open wound with active hemorrhage and brain matter emerging from the open scalp wound; this patient had to be immediately taken for surgery.<sup>[32]</sup>

Pruthi et al., highlighted the demographic profile of 2555 patients who had sustained a TBI. 529 (20.7%) patients were injured as pedestrians of them; majority of them (n = 277, 52.4%) were between 18 and 50 years of age, while extremes of ages contributed the other half (n = 252, 47.6%); males were predominantly affected (n = 372, 70.3%). Commonly pedestrian injuries (221/529, 41.8%) occurred during the peak traffic hours in the evening (16:00 to 21:00 h). The casualty attended to 4.17 injuries per day during the weekdays and 4.8 injuries per day on weekends. Bangalore city (urban and rural) accounted for 57.5% (n = 304) of all injuries. Nearly all (461/529, 87.1%) received a prehospital primary care and nearly two-thirds reached casualty services (71.6%) in less than 24 hours after the injury. The mean GCS score in this group was significantly (P < 0.05) low and the mortality rate was relatively high compared to patients who had presented more than 24 hours after the injury. Two-wheeler accidents were a major risk factor for pedestrian injury (260/529, 49.1%); heavy vehicles (bus or truck) were also a risk factor for injury (10.8%). The maximum number (27/53, 50.9%) of three-wheeler (auto) and pedestrian crashes occurred between 16:00 and 21:00 hours; offending vehicles were unknown in 10.5% of pedestrian injuries. Interestingly, 41% (23/56) of TBI occurred during late night (21:00 to 07:00 h).[22]

Bhole et al., studied 200 patients who had sustained craniocerebral trauma with their mean age being 32.64 years (range, 4-76 years); majority of the patients were young adults; The male: female ratio was 6.4:1; the most common cause of injury was motor vehicular accidents (82%) followed by FFH (9.5%) and assault (7.5%). Headache and vomiting were the most common clinical features followed by loss of consciousness. Closed head injury was the most common neurological injury followed by skull fractures. The pattern of head injuries was as follows: 92 had mild head injuries, 76 had moderate head injuries, and 32 had severe head injuries. Associated clinical findings were nasal bleed and/or ear bleed, ecchymosis over the mastoid (Battle's sign), and CSF otorrhoea/rhinorrhoea. Post traumatic seizures were observed in 8.5% of the patients. Cerebral contusions were the most common findings on CT scan followed by skull fracture, SDH, EDH, and ICH, whereas the CT scan was normal in 26 cases. No mortality was reported in the cohort that had sustained minor head injuries. The majority (81.8%) of the patients were treated conservatively while 18.2% required surgical intervention. The majority (86.7%) improved despite having associated injuries; 9 left against medical advice either due to financial constraints or because they had a poor prognosis. Mortality was mainly seen in patients with severe TBI.<sup>[16]</sup>

Dhandapani *et al.*, studied 244 patients who had sustained a TBI. They were in the age range of 1–80 years (median, 30 years) with the male: female ratio being 7:1. The primary mode of injury was motor vehicle accidents (67%), followed by FFH (28%); rest 5% patients had sustained an assault, a fall of an object on the head, etc. Falls were significantly more frequent in children and the elderly patients, possibly due to the ignorance of risk factors in children, and due to a poor coordination of their motor movements present in the elderly. Among 244 patients, 25% had a mild, 16% had a moderate, and 59% had a severe TBI, with their mean age being 26, 33, and 35 years, respectively. An advancing age was significantly associated with the severity of injury as well as the severity of the clinical grade ( the latter was more frequently associated with an increasing age).<sup>[36]</sup>

Khan et al., conducted a survey using a telephonic interview among residents aged >65 years to determine the prevalence of TBI in developing countries. The study was not conducted on a scientifically calculated sample of patients. Interviews were completed among 17,009 individuals in 8 countries (Cuba, Dominican Republic, Venezuela, Mexico, Peru, India, China, and Puerto Rico) with a good overall response rate (>80%) in all but two centres: urban China (74%) and urban India (72%). Missing data with respect to the variables of interest chosen were observed in less than 1% of the sample. The results for 16,925 participants were reported in this study. Across all 10/66 study sites, there were more women than men (60.7% of the patients were female); most were either married or widowed, and this trend was consistent across all centres. 50% to 70% of the participants at all the sites included in the study were aged between 65 and 74 years, though there was a higher proportion of people aged 80 years or more in Latin America and the Caribbean (especially in Cuba, the Dominican Republic, Peru, and Puerto Rico) compared to Asia, indicating a demographic shift to a more advanced age in these countries. Urban Peru and Puerto Rico had the highest proportion of tertiary educated participants (>20%), whereas rural India and rural China had the lowest (<1%) proportion of this group of participants. In rural China and rural India, 57.8% and 66.1% respectively, of the population did not have any education. In general, these numbers were lower in Latin America, with 2.6-32.7% of the subjects included having no education.<sup>[30]</sup>

Ahmad et al., studied 325 patients with TBI of whom 9 were in the pediatric age group and 16 were in the geriatric age group (>60 years). The proportion of patients with various types of head injury, and included: 18% with minor head injury, one third with moderate injury, and half with severe head injury. The indications of surgery were major cerebral contusion and/or subdural hematoma. The mortality in mild, moderate, and severe head injury groups was 1, 6, and 46%, respectively. In the final outcome at discharge between January 2002 and December 2004, it was noted that, out of the 298 patients admitted during this period, 193 could be identified during the hospital stay. An additional 40 patients were sent home after they regained memory of their addresses, while 47 expired as unknown patients; 17 remained unknown and were sent to rehabilitation/poor peoples' homes with the help of a medical social worker; all pediatric patients were identified.<sup>[24]</sup>

Singh et al., studied 60 patients with missile injuries of the head who were admitted to the Command Hospital (NC) C/O56 APO; their age ranged from 19-40 years (mean age: 25 years) with a single female. 49 injuries were caused by shrapnel of shells, 12 by gunshot wounds, and 5 by indigenous explosive devices (IEDs). Regarding their, regional distribution, parietal injury was the most common one followed by orbitocranial/faciocranial penetration. Punctate wounds were found in 10 cases. The remaining 50 patients had significant scalp lacerations, and brain matter was herniating out in 40 cases. The GCS score was 3-5 in 8, 5-8 in 14, 8-12 in 30, and 13-15 in 8. Associated eye injuries were found in 7, facial injuries in 8, limb injuries in 10, chest injuries in 3 patients, and tracheal injuries in a single patient. The radiograph of the skull was carried out in all the cases and revealed skull penetrance without significant comminution in 35, and extensive comminution of bone in 10 cases,. Missile fragments were seen in 48 cases. CT scan of the head was done in 54 cases and was helpful in assessing the extent of brain damage and the location of bone and missile fragments.<sup>[31]</sup>

Tripathi et al., reported a study carried out on 1545 admitted patients of RTAs during the 9-month period; 1346 were two-wheeler riders where drivers significantly outnumbered pillion riders (5.76:1) and the median age of the drivers and pillion riders was 30 and 36 years, respectively. Of the 199 four-wheeler vehicles riders, the maximum were co-passengers (1.34:1). Overall, the most commonly affected age group was 18-29 years comprising 45.43% and 46.43 of the patients on two-wheelers and four-wheelers, respectively; overall, the male: female ratio was 10.8:1. Despite the institution of various legislation and public awareness programs, only 13.4% of all the two-wheeler drivers (16.5% drivers and 3.7% pillion riders) were wearing a helmet at the time of the accident; there was no statistically significant difference in the helmet usage among patients of different age groups. Only 14.7% male and 5.6% female patients were wearing a helmet; 72.7% were wearing a full coverage helmet and only 44.4% helmets were certified by the Indian Standards Institute (ISI). Similarly, only 7.5% of all the four-wheeler riders (12.9% drivers and 3.5% co-passengers) were wearing a seat belt. Only 2% of the rear seat co-passengers were wearing seat belt; no statistically significant difference in the seat belt usage was noted in different age groups amongst both drivers, and co-passengers, which suggests a generalized lackadaisical attitude.<sup>[35]</sup>

Thapa *et al.*, conducted a prospective study that included 520 TBI patients in a period from July 2007 until July 2008. At a median follow-up of 386 days, 59 (11.4%) patients developed PTS with the incidence of immediate seizures occurring in 6.5% patients, early seizures occurring in 2.1% patients, and late seizures occurring in 2.7% patients. The demographic characteristics of the cohort was: gender: 420 (81%) males; mean age: 28 years with 16.7% subject below the age of 10 years, and 10% over 60 years.<sup>[3]</sup>

Colohan *et al.*, conducted a prospective study for 20 months from 1977 to 1979 among 551 TBI cases from New Delhi; the mean age of the patients was  $25 \pm 1.4$  years (only 2.7% patients were over 60 years) and 81% were males. A much higher proportion of patients were injured in bus-related accidents (11.1%) and as pedestrians.<sup>[20]</sup>

#### **Injury pattern**

In a clinical review of head injury by Sharma et al., the pattern of ocular injury and nerve involvement was presented for 594 patients: ecchymosis (51.8%), subconjunctival hemorrhage (44.4%), lid edema (41.4%), lacerated wound (22.5%), pupillary involvement (21%), cranial nerve palsy (11.6%), orbital fractures (10.4%), ptosis (6.7%), exposure keratitis (4.2%), and optic nerve trauma (4%) were the main types of injuries; third and fourth cranial nerves were the most commonly involved cranial nerves.<sup>[9]</sup> In a descriptive observational prospective study in a tertiary care rural teaching hospital by Agrawal et al., it was noted that, among 414 cases with TBI, the majority of injuries comprised acute subdural hematoma (10.87%), followed by cerebral contusion (7.01%), extradural hematoma (5.31%), and traumatic subarachnoid hemorrhage (2.66%). Minor injuries were mainly due to the associated trauma, which included bruises (40.10%), abrasions (50.97%) and cuts (44.69%), while a few had major associated injuries that included ENT bleed (n = 2.17%) and limb fractures (5.07%).<sup>[17]</sup>

Wani *et al.*, presented the pattern of missile injury to the pediatric brain from conflict areas of Kashmir, India. They retrospectively included data before 2006, and prospectively collected data from 2006 onwards, for 51 children. The patterns of injury sustained were mainly for ocular manifestations with pupillary abnormalities in 11 cases –anisocoria in 9 (17.6%) and dilated nonreactive pupils in 2 (3.9%).<sup>[32]</sup>

In a retrospective analysis of 682 fatal head injury cases due to RTA from Mangalore, Menon *et al.*, reported the patterns of craniocerebral trauma. External injury to the face and scalp were noted in 82% and skull fractures were found in 88.8% patients. Fissured fractures were the most common fractures (23.1%) followed by depressed fractures in 21.28% patients. Anterior cranial fossa, parietal bone, and temporal bone were the most commonly involved areas where fracture occurred, which corresponds to 36.23%, 34.48%, and 34.46% of the patient population, respectively. Subdural hemorrhage (52.63%) was commonly observed, followed by subarachnoid hemorrhage (27.27%).<sup>[33]</sup>

Dalvie *et al.*, in their analysis involving 1993 communal riot victims of Mumbai, presented injury patterns for 440 patients. Among patients with head injuries (61), only 8 (13.1%) presented with altered consciousness; 10 (l6.4%) were unstable on admission and 8 eventually died. A major surgical intervention was eventually required in only 2 cases; the majority had wounds, which required suturing; or, they were kept for observation only.<sup>[6]</sup>

In the above discussed literature, the pattern of injury was reported in the context of ocular injuries in a majority of studies whereas the fracture pattern of the skull and the location of hemorrhage were discussed in only a few studies.

#### Follow-up

Munjal *et al.*, studied audiological deficits in 290 patients after closed TBI – these included mild (150), moderate (100), and severe (40) injuries. The cases were assessed at two weeks post-injury. The mode of injury was as follows –RTA (219), FFH (35), assault (26), and others (10). The study included only

patients of TBI who presented to the outpatient department for follow-up 2 weeks after the injury and did not actually deal with the presentations of TBI in the casualty.<sup>[25]</sup>

Yousuf *et al.*, conducted a cohort study on ethnic Kashmiris who were followed up at 6 months using Glasgow outcome scale (GOS) and categorized the outcome as favorable and unfavorable. The patients with TBI were categorized as those being an Apoe4 allele carrier (117) and those not being a noncarrier (33); the effect of e4 allele on the outcome showed that, of the 33 TBI patients with the presence of the e4 allele, 63% had a good recovery while 36% suffered from an unfavorable outcome, which was comparable to that of noncarriers of APOE e4 group, where 33% had an unfavorable outcome compared to 67% with a good recovery. This difference was statistically insignificant.<sup>[39]</sup>

Sinha *et al.*, evaluated outcomes of 1236 patients undergoing decompressive craniectomy (DC) following their TBI in a single centre. They collected retrospective data on the DC surgical procedure conducted during the period from 2008 to 2013. Seven hundred and twenty patients were alive on discharge, and the follow-up GOS was assessed in 324 patients (45%) for a mean duration of 25.3 ( $\pm$ 12.2) months; 19 (7.5%) were in a persistent vegetative state, 37 (14.6%) suffered from severe functional disability, and 197 (77.8%) had a favorable outcome (GOS 4 and 5) in the severe head injury group at the last known follow-up among the surviving patients; and, 71 patients (21.9%) expired. The infection rate in patients undergoing a cranioplasty was 10.5%.<sup>[37]</sup>

Dhandapani et al., validated a new clinicoradiological grading for patients with compound head injury and followed them up at regular intervals to assess the various outcome parameters. Out of the 386 patients recruited, only 319 could be assessed for GOS at 3 months; 103 patients (32%) had an unfavorable GOS (1e3) whereas 76 (24%) died; among the fatal cases, 13 had infective complications and some patients died due to various other causes. The comparison of outcome between nonsurgical and surgical management in different grades of compound injury showed that surgical management had a significant association with infective complications in Grade 1 and Grade 2 compound injury. The admission GCS of the patients had a significant independent impact on the infective complications, unfavorable GOS, mortality, and hospital stay, whereas the delay in admission had a significant independent association with infective complications, mortality, and hospital stay.<sup>[41]</sup>

In single-centre study on new cases who had sustained TBI, evaluation was done initially after 2 weeks and at 4 weeks of injury, and then at monthly intervals for a year. Insomnia was assessed on Insomnia Severity Index, and depression using the patient health questionnaire (PHQ-9); more than half (63.41%) of those with insomnia developed it within the first 3 months of injury compared to those who developed insomnia subsequently between 3 months and 1 year (36.57%), which was statistically significant.<sup>[28]</sup>

All patients with mild TBI (1149), defined as a GOS score of 13 or more over a period of 3 months, were retrospectively reviewed by Deepika *et al*. The outcome was assessed prospectively for 1 year after injury through telephonic

interview using the Glasgow Outcome Scale–Extended (GOSE) questionnaire, Rivermead Post-Concussion Symptoms Questionnaire (RPCSQ), and Rivermead Head Injury Follow-up Questionnaire (RHFUQ); 18 with isolated SAH underwent an outcome assessment. The group of patients with or without subarachnoid haemorrhage had an upper level of good recovery on GOSE with a significant difference in the RPCSQ and RHFUQ scores between the two groups.<sup>[38]</sup>

Cases who had sustained a missile TBI (n = 60) were studied for one year at a single centre, and the 55 surviving patients were followed up until 6 months post injury. The outcome as per the Glasgow scale was good in 42, with moderate disability occurring in 7, severe disability occurring in 6, and death occurring in 5 cases. More than one-third of the cases (36.3%) revealed retained bone fragments, and 18 (32.7%) revealed missile fragments on follow-up CT scans.<sup>[31]</sup>

Agrawal et al., studied the impact of comprehensive rehabilitation on functional levels achieved by moderate and severe TBI survivors during the first-year post-injury with evaluation on the functional independence measures (FIM) and disability rating scale (DRS) for functional outcome, whereas the global outcome was assessed on Glasgow outcome scale-extended (GOSE). The mean change in the FIM scores was significant at all times in both moderate and severe TBI groups; no disability was noted at 12 months in 24 individuals in the moderate group and 19 in the severe group. The outcome was good recovery in 89% of the moderate injury group, and in 52% of the severe injury group patients; a moderate level of disability occurred in 11% of patients in the moderate injury group and in 45% of the patients in the severe injury group; and, severe disability did not occur in any of the patients who had sustained a moderate degree of injury but occurred in 3% patients who had sustained a severe TBI.[40]

Dhandapani *et al.*, evaluated the age thresholds based on clinical and radiological parameters, mortality, and neurological outcome at 6 months following TBI. The GOS at 6 months showed a significant correlation with age; greater scores were more frequent in younger patients, with a significantly better outcome noted in the second decade compared to the first decade; an unfavourable outcome showed significant association with an increasing age, a phenomenon that was seen in every decade.<sup>[36]</sup>

The follow-up period in the reported literature discussed above ranged from 1 month to 1 year among the TBI patients. All the studies assessed the outcome using GOS at follow-up.

#### Investigations

Agarwal *et al.*, reported the outcome in 100 consecutive patients presenting with unilateral or bilateral blindness resulting from a minor head injury over a 4-year period (January 1992 to December 1995). The CT scan of the head and orbit was performed for all these patients, an MRI was performed for four patients; and, the visual evoked potentials (VEPs) were assessed using light-emitting diodes (LEDs). The CT scan findings were abnormal in 26 patients; the most common finding was orbital wall fracture (n = 22). The initial VEPs were abnormal in 71 and absent in 29 patients; of the 29 patients with an negative initial VEP, the VEP in 15 patients remained persistently negative, and none of these patients showed an improvement in their visual status, indicating that VEP was the single most important factor determining the outcome after TBI.<sup>[14]</sup>

Kannan et al., undertook a study to compare several parameters related to severe closed head injury in patients who had sustained TBI with all other patients in the intensive care unit. They studied the age groups involved, the duration of stay in the intensive care unit, the complications seen, and the outcome. The patients were classified into two groups: group A comprising patients with severe closed head injury; and, group B consisting of all other patients. Hypotension (need for inotropes to maintain the mean blood pressure above 60 mmHg), renal failure (creatinine value of more than 1.6 mg/dl), septicemia (blood culture was positive in the presence of fever and leucocytosis), and hypoxia (PaO<sub>2</sub> of 60 mmHg or less at FIO<sub>2</sub> of 0.6 or more) were the most common complications in both the groups; however, there was no significant difference (P > 0.05) in the relative incidence of the parameters studied in the two groups.[57]

Children aged 12 years or less, who suffered from even a single episode of seizure after sustaining head injury, were studied by Ratan *et al*. Out of the 400 recruited patients who had a posttraumatic convulsion, two-thirds had CT scan abnormalities. Intracranial calcification was the only finding that was determined to be associated with post-traumatic seizures (P < 0.05).<sup>[26]</sup>

Of the 1084 pediatric patients admitted in the pediatric surgery ward, in 400 children, the duration of loss of consciousness was also noted by Ratan *et al.* Of the 260 cranial CT scans performed, a positive scan was observed in 68% (174) of the patients who had sustained a head injury, and out of these 25% had isolated findings of skull fracture. A positive scan was observed in 74% children with a severe head injury, and in 70% each, with a moderate and mild head injury y, respectively. The association between loss of consciousness and the CT scan findings was not statistically significant (P = 0.89) even after excluding skull fractures (P = 0.60).<sup>[45]</sup>

Kumar *et al.*, subjected 51 patients with severe head trauma to an MRI to study the extent of parenchymal injury. Out of the 16 patients with T1-weighted, magnetization transfer (MT) visible abnormality, there were 4 patients only with a T1-weighted MT visible abnormality, and 17 patients with gray matter atrophic changes. The calculated T2 and MT ratio values in the adjacent normal appearing gray matter of T2 and T1-weighted MT abnormal visible white regions were 72.03  $\pm$  3.45 and 24.92  $\pm$  1.2, respectively; however, the calculated T2 and MT ratio value in the atrophic gray matter regions were 70.01  $\pm$  1.77 and 25.87  $\pm$  1.55, respectively. These values were significantly different from the contralateral normal gray matter (*P* < 0.05).<sup>[54]</sup>

Misra *et al.*, recruited 51 patients with CT-proven intracerebral hemorrhage within 10 days of ictus. They evaluated the frequency, severity, and factors responsible for gastrointestinal (GI) hemorrhage in patients with primary intracerebral hemorrhage (ICH). The best set of predictors for the occurrence of GI hemorrhage included the size of the hematoma (using the CT scan image), as well as the presence of septicemia (when at least two of the following features were present: (1) temperature >38°C or below 36°C, (2) heart rate >90/min, (3) respiratory rate >20/min or paCO<sub>2</sub> <32 Torr, and (4) leucocyte counts >12000/mm<sup>3</sup> or <4000/mm<sup>3</sup> or more than 10% band forms) and the GCS score].<sup>[10]</sup>

Thiruppathy *et al.*, in their prospective study, included all consecutive patients admitted to the head injury unit with an admission GCS score of 13–15 during a 4-month period. One hundred and forty-eight (38.85%) out of the 381 patients had a total of 220 positive findings on the CT scan image. Sixty-four percent of patients with focal neurological deficits at admission had a positive CT scan. There was a statistically significant difference in the duration of hospital stay among patients with a positive CT scan and those with a negative CT scan (P < 0.001). They concluded that the definition of "positive CT image" is appropriate because even lesions that do not require surgical intervention such as contusions, basal fractures with CSF leaks, and pneumocephalus can contribute to a significant long-term morbidity suffered by the patient.<sup>[23]</sup>

Dharap *et al.*, in their prospective observational study, analyzed the effect of repeating a CT scan with the aim of formulating a guideline for their use. A total of 175 cases were included. The CT scan was repeated in 53 patients. In 11 (20%) patients, the lesion was found to be resolving, in 13 (25%) it was unchanged, in 13 (25%) it worsened, and in 16 (30%) a new lesion was found. The common new lesions found on a repeat CT were hydrocephalus, intraventricular hemorrhage, subarachnoid hemorrhage, and contusion, which were not obvious on the initial CT scan images.<sup>[42]</sup>

Gowda et al., correlated single photon emission computed tomographic (SPECT) findings with the common clinical symptoms such as postconcussion syndrome (PCS), posttraumatic amnesia (PTA), and loss of consciousness (LOC), which were present in 120 patients with mild TBI. The SPECT showed perfusion abnormalities characterized by decreased uptake of the radiotracer technetium-99m ethyl cysteinate dimer (Tc99m-ECD) in 58 (63%) patients. The CT scan findings were abnormal in just 31 (34%) patients. The CT scan showed an epidural hematoma in 7 patients, a hemorrhagic contusion in 25, and a subarachnoid hemorrhage in 3 patients. In all patients with an epidural hematoma and hemorrhagic contusion, the SPECT scan showed an area of hypoperfusion corresponding to a lesion seen on the CT scan. A significantly higher number of perfusion abnormalities were seen in patients with PTA (*P* < 0.03), LOC (*P* < 0.02), and PCS (*P* < 0.01) compared with patients without these symptoms.<sup>[58]</sup>

Yadav *et al.*, analyzed 262 prospective cases of posttraumatic intracerebral hematomas/contusions. There were 21 (8.0%) patients with a single ICH/contusion compared to 241 (92.0%) with multiple lesions such as an acute subdural hematoma (SDH) in 134 (55.6%), other ICH in 51 (21.2%), an extradural hematoma in 9 (3.7%), a SDH, and other ICH in 47 (19.5%) patients. Coagulation tests such as prothrombin time (PT), activated partial thromboplastin time (APTT), bleeding time, clotting time, and platelet count were assessed in all the patients. Coagulopathy was seen in 39 patients with an ICH. Of these, 41% developed an expanding hematoma in comparison to 12.1% where coagulopathy was absent.<sup>[51]</sup>

Nayak *et al.*, compared the early changes in oxidative stress status of head injured patients with different neurological outcomes using erythrocyte parameters. Washed erythrocytes were used for estimating thiobarbituric acid-reactive substances (TBARS) and glutathione (GSH) levels. Erythrocyte TBARS levels were significantly higher in the groups with extended Glasgow Coma Outcome Scale score of 1 (death [D]), 2–4 (severe disability [SD]), and 5–8 (moderate disability [MD]) compared to normal controls (normal controls [NC]) [P = 0.001]. The erythrocyte GSH levels were significantly lower in the D and SD groups compared to the MD group (P = 0.01). Erythrocyte superoxide dimuate (SOD) activity was significantly higher in the D (P = 0.01) and the SD (P = 0.001) groups compared to the NC, with no change observed in the MD group.<sup>[56]</sup>

A retrospective study involving all patients admitted following head injury to the intensive care unit (ICU) of a neurosurgical center in India over a 2-year period was conducted by Santhanam *et al.* The records of 208 patients were analyzed. The CT findings were abnormal among 31.5% (63) of the patients. Of these, the majority of patients had a subdural hematoma (44.8%). The presence of hyponatremia, diabetes insipidus, hyperglycemia, anemia, and septicemia were positively associated with mortality.<sup>[67]</sup>

Acute head injured patients (100) were subjected to optic nerve ultrasonography (ONUS) and brain CT by Goel *et al.* The CT scan in 73 cases showed at least one feature suggestive of intracranial hypertension, as mentioned earlier, whereas no such feature was noted in 27 cases. The binocular mean optic nerve sheath diameter (ONSD) in 73 cases with the CT evidence of elevated ICP was  $5.8 \pm 0.57$  mm, and in the other 27 cases, it was  $3.5 \pm 0.75$  mm (P < 0.0001). There were 74 participants showing evidence of intracranial hypertension on ONUS, as defined earlier (the mean ONSD being 5 mm or more). The sensitivity of ONUS for predicting the need for surgery was found to be 98.3%, with a negative predictive value (NPV) of 96.2%, a specificity of 62.5%, and positive predictive value (PPV) of 79.8%.<sup>[13]</sup>

Twenty-five patients with a moderate head injury (MHI) with an admission GCS score of greater than 8 were included in this clinical study by Nayak *et al.* The erythrocyte thiobarbituric acid reactive substances (TBARS) levels that reflected lipid peroxidation, remained significantly elevated in these patients with MHI on day 1 and 7 post-injury (P = 0.001) compared to normal controls. The total thiol oxidation in erythrocytes was estimated by their total reduced GSH levels. Erythrocyte glutathione (GSH) levels were significantly decreased on day 1 and 7 compared to normal controls (P = 0.01). They concluded that erythrocyte oxidative damage remained significantly increased in the posttraumatic period in patients with MHI as compared to NC.<sup>[75]</sup>

Nayak *et al.*, also attempted to evaluate and compare the oxidative stress status in head injured patients with a graded traumatic head injury using erythrocyte indicators. The patients were divided into severe head injury group (SHI: GCS score 8 or less) and mild HI group (MHI: GCS score more than 8) groups. The erythrocyte thiobarbituric acid-reactive substance (TBARS) levels were significantly increased in both patients with SHI and MHI (P < 0.001) compared to controls, with the magnitude of increase being

significantly higher in the SHI patients (P < 0.043) compared to the MHI patients. The erythrocyte GSH levels were significantly decreased in the SHI (P < 0.001) and the MHI patients (P < 0.01) compared to controls with a more pronounced decrease in the SHI patients compared to the MHI patients (P < 0.031).<sup>[50]</sup>

Kumar et al., recruited 83 patients with TBI to ascertain if diffusion tensor imaging (DTI) abnormalities in the corpus callosum (CC) would be any different in moderate TBI compared to mild TBI and if these abnormalities correlated with differences in the neuropsychometric tests (NPTs) performed later in these patients. Out of 57 patients, 26 had diffuse axonal injury (DAI) (hemorrhagic DAI = 15; nonhemorrhagic DAI = 11) whereas 31 patients had no apparent DAI. Number connection test (NCT) A, NCT B, figure connection test (FCT) A, and FCT B scores were significantly higher, while the picture completion test, object assembly test, picture arrangement test, block design test, and digit symbol test scores were significantly lower in patients with mild TBI and moderate TBI compared to healthy controls. It was concluded that DTI abnormalities in the regions of CC were more in patients with moderate TBI compared to mild TBI, predicting a trend towards a worse outcome at 6 months, as suggested by the neuropsychological scores.<sup>[47]</sup>

Endocrinal abnormalities in severe TBI were assessed by Tandon *et al.* A noncontrast computed tomography (NCCT) scan was performed in all patients at admission. A complete anterior pituitary hormone analysis was performed within 24 h of injury, which included T3, T4, thyrotropin (TSH), prolactin (PRL), growth hormone (GH), cortisol, luteinizing hormone (LH), and follicle-stimulating hormone (FSH). Abnormality was detected in all hormones that were studied at various stages of follow-up. Although TSH abnormalities were the most common among the thyroid hormonal abnormalities, hypercortisolemia and hyperprolactinemia were the most common hormonal abnormalities that occurred just after head injury.<sup>[44]</sup>

Audiological deficits after closed head injury (CHI) were assessed by Munjal et al. The audiological assessments included were pure tone audiometry (PTA), speech audiometry, tympanometry, auditory brainstem response (ABR) audiometry, and middle latency response (MLR) audiometry. High-frequency sensorineural (HFSN) hearing loss was observed in 26.0%, 32.88%, and 33.3%, of the participants in the right ear of the three CHI groups- mild, moderate, and severe, respectively. In the right ear, in all the three groups, >30% patients had an abnormal tympanogram, whereas in the left ear, approximately 27.5% in the mild and moderate groups and 15% in the severe CHI group had abnormalities. There was a high incidence of audiological deficits in patients with a head injury. Peripheral and central auditory areas were affected, as revealed by the subjective as well as electrophysiological auditory investigations.[15]

The level of apolipoprotein E (APOE) polymorphism and its effect on the outcome after the patient had sustained a mild- to- moderate traumatic brain injury was studied by Pruthi *et al.* Of the 98 patients tested for APOE polymorphism, 20 (20.3%) patients out of them had one or more APOE  $\varepsilon$ 4 allele. None of the patients with  $\varepsilon$ 4 as one of the alleles had

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a poor outcome. The digit symbol substitution test (DSST) was completed by 44 patients; the digit vigilance test (DVT) was completed by 45 patients; the complex figure test (CFT) was carried out by 45 patients; and the token test was performed by 51 patients. On comparing the results of APOE genotype between the two groups, patient with APOE  $\epsilon$ 4 alleles had slightly lower DSST scores; however, this difference was not statistically significant. To conclude, the study suggested that in the study region, patients with mild- to- moderate TBI with the  $\epsilon$ 4 allele have a better outcome when compared to the patients without it.<sup>[43]</sup>

Agrawal *et al.*, reported the usefulness of a mobile CT scanner in a neurosurgical ICU (NICU) at a Level 1Trauma Center in India. A total of 1292 head CT scans were done during the study period. Five patients had an isolated head injury and hypotension at admission, and the CT head showed brainstem hemorrhage in 3 patients. The most important aspects which influenced the widespread usage of the mobile CT scanner were the image quality and ease of use.<sup>[53]</sup>

Abraham et al., studied the prevalence of phenytoin toxicity in patients with TBI (n = 100) and demonstrated the suitability of using the ideal body weight (IBW) to guide the phenytoin dosing. Thirty-six patients had an adjusted serum phenytoin level that was in the toxic range. The diagnostic test that characterized clinical suspicion of phenytoin toxicity had a sensitivity of 36%, a specificity of 97%, a PPV of 87%, and a NPV of 73%. In this study, there were 11 patients with an impaired renal function (with a glomerular filtration rate [GFR] in the range of 40-60 ml/min/1.73 m<sup>2</sup>); among them, only 2 patients had phenytoin toxicity. Five patients had mildly deranged liver function tests, in which none had hyperbilirubinemia, but all 5 patients had toxic serum phenytoin levels. On a multivariate analysis, a lower abdominal girth, a lower neck circumference, and a larger proportion of maintenance dose given intravenously (>80%) were independent risk factors responsible for toxicity.[25]

The perioperative glycemic status of adult patients with TBI who had undergone a craniotomy was studied by Bhattacharjee et al. Out of the 200 patients recruited, 87 had an extradural hemorrhage, 56 had an intracerebral hemorrhage, and 57 had an acute subdural hemorrhage. There was a significant difference in the baseline capillary blood glucose (mild head injury:  $127.3 \pm 12.8 \text{ mg/dL}$ , moderate head injury:  $133.8 \pm 11.6 \text{ mg/dL}$ , and severe head injury:  $140.1 \pm 10.7 \text{ mg/dL}$ ; P = 0.000) across the severity of head injury (P = 0.000) and the type of injury (P = 0.005). Twenty percent (40/200) of the total number of patients recruited had at least one episode of intraoperative hyperglycemia (capillary blood glucose [CBG]  $\geq 180 \text{ mg/dL}$ ). Twenty-one of the 200 patients (10.50% of the total) had at least one episode of severe hyperglycemia (CBG  $\geq 200 \text{ mg/dL}$ ). Generalized estimating equation identifies intracerebral hemorrhage (adjusted odds ratio [AOR]: 2.95; 95% confidence interval [CI]: 1.21-7.18) as an independent risk factor for postoperative hyperglycemia.[34]

Dhandapani *et al.*, recruited adult patients admitted within 24 hours of severe TBI. Sixty-seven patients were prospectively assessed at weekly intervals till 21 days, for assessing changes in the hemoglobin and serum albumin levels during their

hospital stay. The mean fall in haemoglobin among those who developed pressure ulcer was significantly greater than the fall among those who did not develop pressure ulcer (3  $\pm$  93 vs. 1  $\pm$  85 g/dl; mean difference 2  $\pm$  07 g/dl; *P* = 0.005), whereas the fall in serum albumin was not found to be significant.<sup>[11]</sup>

In another study Dhandapani et al., recruited 53 patients with closed head injury with a Glasgow Coma Scale (GCS) score of 9-14, where no episode of hypotension was detectable and the patients had a normal renal function. These patients were subjected to an magnetic resonance spectroscopy (MRS) and single-photon emission computed tomography (SPECT) scan, whenever feasible, following appropriate ethical approval. The MRS and SPECT were performed within 24 hours of each other. There was a non-significant association between SPECT and MRS findings. After adjusting for various confounding factors using binary logistic regression, only the GCS score and severe hypoperfusion seen on SPECT were noted to have a significant association with neurological outcome that was independent of the age of the patients, the traumatic coma data bank (TCDB) CT scan category, the MRS abnormalities, and of each other (P = 0.02 and 0.04, respectively). MRS and SPECT appear to be promising prognostic tools in filling the current gaps.<sup>[48]</sup>

Ahmed *et al.*, recruited all patients with severe TBI [Glasgow coma scale (GCS  $\leq$  8)] caused by RTA who underwent surgery. Among 95 patients, 11 (11.6%) had an acute kidney injury (AKI) as per the acute kidney injury network [AKIN] definition. Out of the 11 patients, 7 (63.6%) belonged to stage-I, 3 (27.3%) belonged to stage-II, and one (9.09%) belonged to stage-III kidney injury category. Nine patients (81.8%) developed AKI within the first 5 days of their admission to the hospital. This study discussed the burden of occurrence of AKI in TBI on the healthcare resources and highlighted the need for its early detection and prompt management, possibly with more sensitive predictors of AKI than the AKIN criteria.<sup>[5]</sup>

Harish *et al.*, investigated the anatomical, cellular, and molecular changes attributable to contusion (Ct) and pericontusional (PC) injuries in human TBI. There was a distinct and scorable change in Ct and PC in TBI. The study provided the characteristic findings in two anatomically adjacent yet distinct regions. These finding have the potential for an improved mechanistic understanding of the primary injury and the development of therapeutic strategies.<sup>[46]</sup>

Prasanna *et al.*, recruited 100 consecutive patients suffering from moderate-to-severe TBI and evaluated them for their basal hormonal levels. The free thyroxine 3 [fT3], free T4 (fT4), thyroid stimulating hormone (TSH), growth hormone (GH), prolactin (PRL), and cortisol were measured and repeated on the 7<sup>th</sup> day among the patients who survived. The most common hormone to decrease was GH, which revealed a maximum decrease on day 7 compared to day 1, and the most common hormone to increase was cortisol, which was maximum on day 1 compared to day 7, which was statistically significant (P < 0.005). The study reported a high frequency of pituitary hormone deficiency in the acute phase after moderate-to-severe TBI and there is a correlation with severity of injury, GOS,

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and radiological findings. This study raises the importance of pituitary function assessment after traumatic brain injury.<sup>[55]</sup>

Majority of the studies available in literature report the CT scan as the most preferred investigation. However, a few studies have also reported on the significance of biochemical parameters in TBI. Relevant blood investigations have also been reported by many studies. Ophthalmological and audiometric investigations focusing on particular regions have also been reported by two studies.

#### Intervention/treatment

Sinha et al., conducted a retrospective study of TBI patients who underwent decompressive craniectomy (DC) at a tertiary care center. The first line medical management included intubation (depending upon the GCS), fluid resuscitation, intracranial pressure monitoring using an intraparenchymal (Codman) catheter, elective ventilation targeting a pCO<sub>2</sub> of 32–35 mmHg, head end elevation (by 30°), heavy sedation (0.05-0.1 mg/kg/h midazolam), analgesia (1 mcg/kg/h fentanyl), hyperosmolar therapy (0.25-1g/kg mannitol every 6-8 h), diuretic therapy (0.5-1 mg/kg furosemide every 8-12 h), and maintenance of normothermia (36.5-37°C), and normoglycemia (80-120 mg/dl). The extent of the craniectomy included an approximate anteroposterior length of 15 cm, that was medially extending until 3 cm lateral to the superior sagittal sinus, and inferiorly reaching till the floor of the middle cranial fossa at the origin of the zygomatic arch. The evacuation of the hematoma was done, if required, followed by a lax duraplasty using an autologous pericranial graft. Postoperative ICP monitoring was done in all the recently operated cases. The bone flap, after its removal, was placed either in a subcutaneous pocket in the abdomen or in a bone bank facility (at <70°C). The patients in the severe TBI group had a higher incidence of intraoperative brain bulge (P = 0.01), and consequently, a higher proportion of slit durotomy (P = 0.001). On the contrary, a lax duraplasty (P = 0.01) was performed more commonly in patients with minor/moderate TBI. 5.5% of patients were re-operated and a contralateral DC was also performed.<sup>[37]</sup>

Salunke et al., in 10-month period, recruited 306 patients who underwent a wide DCs at their center for intractable ICP after a head injury, for infarctions with edema due to the concomitant presence of subarachnoid haemorrhage (SAH), or for malignant arterial infarction (i.e., thrombotic stroke) with a mass effect. The authors studied the plausible causes for the formation of contralateral subdural collections (CLSDCs). Out of the 17 patients who developed a CLSDC, the first 5 patients underwent a burr-hole drainage for the symptomatic CLSDCs, which led only to transient improvement. A burr- hole tap was repeated in 2 patients without much improvement. The last 2 patients underwent a cranioplasty directly, without a burr- hole drainage. All the 7 patients showed resolution of the CLSDC after the cranioplasty. The authors concluded that a cranioplasty performed as soon as the brain swelling diminishes after a DC may avert the CLSDCs. However, if a patient shows symptoms of a CLSDC earlier, an urgent cranioplasty seems to be the definitive treatment choice. A burr-hole drainage appears to be only a temporary measure, leading to the recurrence of a CLSDC.<sup>[64]</sup>

Prasad et al., conducted a retrospective analysis to identify very young children, all aged  $\leq 3$  years, with TBI undergoing a DC for intracranial hypertension. Primary DC was performed in 38 cases and secondary DC (after measuring the ICP) was performed in 33 cases. A unilateral, bilateral, bifrontal, and posterior fossa DC were performed in 58, 4,5 and 4 cases, respectively. A lax duraplasty was performed in 61 patients, while only a slit durotomy could be performed in the remaining 10 patients due to a massive intraoperative brain bulge. An autologous bone flap was used in 22 patients and a polymethylmethacrylate (PMMA) bone cement cranioplasty was performed in five cases (two cases had a redo-cranioplasty with bone cement due to resorption of the autologous bone flap). This study strongly agrees with the fact that an early surgery is beneficial and the outcome was better in cases in whom an early surgical decompression has been performed. With this therapeutic strategy, with the exception of one patient, all the survivors had a good-to-excellent outcome, as assessed by the Glasgow outcome scale-extended (GOS-E). The decompressive craniectomy offered a survival advantage in almost 50% of the young children with severe TBI.[63]

Singh et al., allocated 100 patients each of symptomatic chronic subdural hematoma (CSDH), proven by a CT scan, and admitted to the Department of Neurosurgery, into two groups -"with a drain" group included patients who were treated by a burr-hole craniostomy with institution of a closed-system drainage system; and "without a drain" group that included those patients who were treated with a burr-hole craniostomy without a closed-system drainage. The closed-system drain was placed in the subdural space in patients belonging to the "with drain group" and was not placed in the "without drain" group patients. The mean midline shift on the NCCT scan was  $11.2 \pm 4.8$  mm in the "with drain" group and  $10.6 \pm 5.0$  mm in "without drain" group (P = 0.384). The volume of CSDH was  $103 \pm 35.0$  ml in the "with drain" group and  $100.4 \pm 32.7$  ml in the "without drain" group (P = 0.467). In this study, the recurrence rate of CSDH was significantly lower if the subdural drain was inserted after the burr-hole drainage of CSDH in comparison to those patients in whom the usage of the subdural drain was not carried out.[60]

Agrawal *et al.*, recruited 70 patients, 27 with moderate, and 43 with severe injury to determine the impact of comprehensive rehabilitation on the functional levels attained during the first year post-injury. No disability was seen at 12 months in 24 individuals in the moderate head injury group and in 19 among the severe head injury group. Thirty patients with severe head injury could achieve independence at 12 months. The authors concluded that rehabilitation should no longer be considered as the final stage of the recovery process, but rather rehabilitative assessment and intervention should be implemented during the acute recovery period and continued through the subacute and chronic stages for a comprehensive rehabilitation program that maximizes functional outcome.<sup>[40]</sup>

Singh *et al.*, studied the impact of Hindustani ragas on the cognitive function of cerebrovascular accidents (CVA) and head injured patients. The case group consisted of 30 patients to whom both medicine and pre-recorded north Indian ragas were administered, whereas the control group of 30 patients received medicine only. Ten Hindustani ragas were selected

for the case group patients at different times of the day. One slot of 20 minutes was recommended to the patients for listening to music, with the corresponding ragas given a specific time interval, for a duration of 1 up to 6 months. Univariate repeated-measures analysis using a split plot design revealed that the mini-mental status examination (MMSE) score was significantly higher among cases at different follow-ups. The authors concluded that the ragas, when as a therapeutic tool, act as a catalyst in improving the cognitive function of patients who have sustained a CVA or diffuse head injury. These ragas also help in reducing the time of recovery of the patients.<sup>[61]</sup>

Perel *et al.*, in the Clinical Randomization of an Antifibrinolytic in Significant Hemorrhage Intracranial Bleeding Study (CRASH-2 IBS), quantified the effect of an early short course of tranexamic acid (TXA) on intracranial hemorrhage and the development of new-onset focal cerebral ischemic lesions in patients with TBI. A beneficial effect of TXA was highly probable (range, 89–94%) for all binary CT scan outcomes. The sensitivity analysis for significant growth of hemorrhage gave an adjusted odds ratio (OR) of 0.53 (95% CI, 0.41–0.68) with a very high probability (99%) of a clinically significant beneficial effect. The sensitivity analysis for new focal cerebral ischemic lesions gave an adjusted OR of 1.18 (95% CI 0.87–1.60). There was a reduction in the new-onet focal cerebral ischemic lesions in the TXA allocated patients.<sup>[59]</sup>

Thiruppathy *et al.*, evaluated the frequency and nature of surgical intervention in patients who had sustained a TBI. Out of the 380 patients recruited in the study, 27 underwent surgery. Fifteen patients were operated upon for a compound depressed fracture, 5 for an acute epidural hematoma, 4 for a subdural hematoma, and 3 for an elevated fracture.<sup>[23]</sup>

Pillai *et al.*, conducted a prospective, randomized, double-blind, placebo-controlled trial with the aim of establishing whether or not nimodipine given orally for three weeks improved outcome in patients with a traumatic SDH. It was observed that there was no significant difference in the outcome between the patients who were treated with nimodipine and those who were not. Nimodipine did not significantly influence outcome even in patients with a traumatic subarachnoid hemorrhage (tSAH).<sup>[19]</sup>

Kannan *et al.*, conducted a retrospective study and classified the patients into two groups: group A comprising of patients with a severe closed head injury (n = 171), and group B consisting of all other patients (n = 545). Considering the management of all the patients in group A and group B, 474 patients (87%) needed a mechanical ventilation. Ninety-one of the 171 patients in group A were tracheostomized (53.2%), and in comparison, 158 of the 474 patients in group B were tracheostomized (33.3%).<sup>[57]</sup>

Tandon *et al.*, compared the efficacy of transethmoidal optic nerve decompression in patients who failed to improve on steroids alone (group A), with the results of steroid therapy alone (group B) on 111 patients who were treated for vision loss following blunt head injury. In group A, 66 patients agreed to undergo surgery. In group B, 45 patients declined the surgical option at the outset and were treated with steroids alone for 3 weeks. In group A, seven patients recovered with normal vision on steroids alone. Thirty patients who did not respond to steroids had transethmoidal decompression. Twenty-two of the 39 patients operated upon improved, thus giving an overall improvement rate of 74.2%. Recovery was complete in six patients, partial in 17, and did not occur in 22; therefore, an overall improvement was noted in 51%.<sup>[12]</sup>

Majority of interventions reported in the literature were on decompressive craniectomy. However, two studies also evaluated nonsurgical interventions. Only one study observed the effect of optic nerve decompression.

#### **Prediction model**

Mukherjee *et al.*, developed a prediction model with the following variables; motor response (M) as the motor score as assessed on GCS, the brain stem reflexes (BSR), and the reaction level scale (RLS) at admission, at the end of 24 and 48 hours, as well as the 1st and 2nd week on 159 patients with severe TBI admitted to emergency services during a 3- month duration. The combination of BSR and GCS was the most accurate predictor of outcome with a corrected predictability of 84%. The expected value of the outcome score was  $K+(G \times C1)$  $+(M \times C2) + (B \times C3) + (R \times C4)$  that revealed a value between 0 and 2 (K: constant; G: GCS score, M: Motor score; B: BSR score; R: RLS score; and C1, C2, C3 and C4: coefficients of the respective scores). The net sum of mathematical probabilities of outcome, for any calculated outcome score, for a given patient had to be 1; the predicted mathematical outcome based on GCS of 7 + BSR of 3 (i.e. Glasgow Leige Scale [GLS] score of 10) at admission was calculated as - 0.2980 (constant of GLS) +  $10 \times 0.131$ (coefficient of GLS)=1.012; the probability of severe disability and persistent vegetative state (PVS-SD) was the greatest in this situation and the actual outcome was PVS-SD. It was a simple linear relationship, relatively easier for a doctor to apply, as it utilized simple addition and multiplication and did not require even a calculator to derive the outcome value.<sup>[73]</sup>

Pillai et al., aimed at developing a simple and effective model to predict a poor outcome with severe diffuse brain injury (SDBI-GCS, 3-8) to help in guiding the initial therapy where prognostic factors and outcomes of 289 patients were analyzed retrospectively. The factors analyzed were age of the patient, the mode of injury, the pupillary reaction, the horizontal oculocephalic reflex, and the GCS score. The developed equation (NIMHANS model) was subsequently applied prospectively in a similar group of 26 patients who were managed using the cerebral perfusion pressure (CPP) management protocol between January 1999 and February 2000. The following prediction score was developed based on the relative importance of the predictors. The prediction score was calculated by the formula  $(3 \times OCR) + (0.5 \times MGCS) - (MS) - 6.6$ . To develop an outcome scoring system, each of these factors was coded as follows: OCR -Oculocephalic reflex -Absent: 1, Present: 2. MGCS - Motor score of GCS: 1 to 5. MS - Midline shift score–Absent: 1, <5 mm: 2, >5 mm: 3. If the prediction score was found to be less than zero, then the outcome was likely to be unfavorable. The sensitivity of NIMHANS model was 74% and specificity 67%, which was second in rank after Narayan's model.<sup>[74]</sup>

Srinivasan developed a mathematical model for predicting death, neurological deterioration, or the development of neurobehavioral sequel lasting for more than 3 months, following the occurrence of moderate TBI. The following eight clinico-radiological parameters were analyzed at admission in the first 64 patients - (a) the mode of injury, (2) the duration of loss of consciousness (LOC), (3) the duration of posttraumatic amnesia (PTA), (4) the motor response (MR), (5) the verbal response (VR), (6) the eye opening (EO), (7) the neurological signs (NS), and (8) the computed tomography scan data. Regression model equation that was developed was  $P = 1 + e^{[0.472 + 0.227 \times 1 + 0.175 \times 2 + 0.148 \times 3] - 1}$  where 0.472 was the coefficient of determination (r<sup>2</sup>), X1 was CT, X2 was VR, and X3 was NS. It was found that the CT scan (0.472/0.449), neurological signs [NS] (0.433/0.417), and verbal response [VR] (0.384/0.340) were the three most important statistically significant variables. Overall, the accuracy of the equation in the first 64 patients in group A was 79.7% compared to 85.7% in group B when it was used prospectively in the next 21 cases. It was considered that the mathematical model,  $CT \times (VR + NS)$  at the admission stage in cases of moderate TBI, was a useful tool for a reliable prediction of outcome.<sup>[72]</sup>

Dandhapani et al., validated a new clinicoradiological grading scheme with implications on the outcome and the need for surgical debridement. All patients with external compound TBI (open calvarial fractures) enrolled for 1 year were included. The proposed grading was partly based on the previous literature and partly on the intuitive experience on external compound TBI. Simple compound injuries were considered as grade 1, whereas the next tier of dural violation was categorized as grade 2. The exposed brain was assumed to be to the result of a more severe dural violation and was grouped as grade 3. The most decisive factor, the midline shift that required a surgical intervention, was naturally classified as grade 4. Those patients with both exposed brain and midline shift were classified under grade 5. There were 182 (53%) patients in Grade 1, 56 (16%) in Grade 2, 34 (10%) in Grade 3, 47 (14%) in Grade 4, and 25 (7%) in Grade 5. Patients in Grades 3-5 had a significantly lower GCS at admission compared with rest of the patients. All patients in Grade 4–5 (n = 72) underwent surgical management. The proposed grade of compound injury had a significant association with infective complications, an unfavorable GOS, delayed seizures, and hospital stay, and was independent of age, sex, admission delay, mechanism of injury, GCS, and internal compounding. Each successive grade had an incremental impact on both infective complications and an unfavorable GOS, independent of age, sex, admission delay, mechanism of injury, GCS, and internal compounding.[41]

Saika *et al.*, aimed to compare the predictability of full outline of unresponsiveness (FOUR) score and GCS for the occurrence of early mortality after moderate and severe TBI through an observational study. To overcome the disadvantages of GCS, the FOUR score was developed that provides additional information about brainstem function and respiratory drive; the FOUR score is useful even in intubated patients as the verbal response is not a component of the score. The four components of FOUR score are eye tracking, motor response, brainstem function, and respiratory drive. Out of 138 patients, the mean GCS and FOUR scores for the entire patient cohort were 9.5 (standard deviation [SD] 2.4) and 11 (SD 3), respectively. The total FOUR and GCS scores were higher in those who survived than those who did not. When using a cut-off score of 7 for the FOUR score, the area under the curve (AUC) was 0.97 with a sensitivity of 97.5% and a specificity of 88.2%; with a cut-off score of 6 for GCS, the AUC was 0.95 with a sensitivity of 98.3% and a specificity of 82.4%, which were both significant. The Spearman's correlation showed a significant correlation coefficient of 0.758 between the GCS and the FOUR score. The predictive value of the FOUR score at admission with TBI was found to be no better than the GCS score.<sup>[70]</sup>

#### Randomized controlled trial

Singh *et al.*, reported a randomized study on the use of drain versus no drain after burr-hole evacuation of a chronic subdural hematoma on 100 allocated CT scan patients of symptomatic CSDH. The results of this study have already been mentioned in this article.<sup>[60]</sup>

Perel *et al.*, in Clinical Randomization of Antifibrinolytic in Significant Hemorrhage-- Intracranial Bleeding Study (CRASH-2 IBS) quantified the effect of an early short course of TXA on intracranial hemorrhage and new focal cerebral ischemic lesions in TBI. A favorable effect of TXA was highly probable (range, 89–94%) for all binary CT scan outcomes.<sup>[59]</sup>

Pillai *et al.* conducted a randomized double-blind placebo-controlled trial to establish whether nimodipine given orally for 3 weeks improved outcome in patients with a SDH. It was observed that there was no significant difference in outcome between the patients who were treated with nimodipine and those who were not. Nimodipine did not significantly influence outcome even in patients with traumatic subarachnoid hemorrhage (tSAH).<sup>[19]</sup>

#### Outcome

Yousuf *et al.*, in their study on ethnic Kashmiris, followed up the patients at 6 months. They applied GOS and categorized the outcome as 'favorable' and 'unfavorable'. The effect of e4 allele on the outcome of patients was studied, and it was found that, out of the 33 TBI patients with e4 allele, 63% had a good recovery while 36% patients had an unfavorable outcome. This was comparable to that of noncarriers of APOE e4 group where 33% of patients had an unfavorable outcome compared to 67% of patients with a good recovery. Hence, the genotype containing the e4 allele (e4/e3 and e4/e4) was not found to be associated with a poor outcome after TBI.<sup>[39]</sup>

Suresh *et al.*, studied 340 children aged  $\leq 15$  years suffering from TBI; 11 were aged<2 years. Poor outcome was observed in 27.2% children <2 years, in 16.9% children in the age range of 3-5 years, in 15% children in the age range of 11-15 years; children <2 years of age had a worse outcome, although it was not statistically significant. The best GCS response after resuscitation was considered, and the GCS was found to be a good indicator of outcome; 41 patients were in the GCS range of 3–5, of which 24 (58.5%) had a poor outcome; whereas out of 51 patients in the GCS range of 6-8, 18 (35.2%) had a poor outcome In the GCS range of 9-12, out of the 96 patients, 11 had a poor outcome. The maximum score achieved by children aged <2 year was 11, and these patients had a good outcome as expected. Two children with their GCS between 13-15 had a poor outcome; of them, one had an EDH and had deteriorated before surgery, while the other had multiple associated injuries such as fracture femur, and hypotension. Pupillary size and reaction were good indicators of outcome. 69 patients had an abnormality of pupillary size and reaction. Of them, a poor outcome was seen in 49.3% patients in contrast to only 7.4% patients who had a poor outcome with a normal pupillary response, which was statistically significant. Ocular movement was a good predictor of outcome; 77 children had abnormal ocular movements and a poor outcome was seen in half of them; and, in patients with normal ocular movements, a poor outcome was seen in 6% of the patients.<sup>[27]</sup>

Sinhala et al., evaluated the outcome of 1236 patients undergoing a decompressive craniotomy (DC) following TBI at a single centre. It was observed that patients in the severe TBI group had a higher incidence of intraoperative brain bulge (P =0.01), and consequently, a higher proportion of slit durotomy (P = 0.001). In a multivariate analysis, the factors predicting a favorable GOS were a younger age, no pupillary abnormalities at admission, absence of preoperative hypotension, an isolated TBI, absence of a preoperative infarct, presence of a minor head injury, performance of a duraplasty when compared to a slit durotomy, and avoidance of a contralateral DC. On the long-term follow-up, 19 (7.5%) patients were in a persistent vegetative state (PVS), 37 (14.6%) patients had a severe functional disability, and 197 (77.8%) patients had a favorable outcome (GOS 4 and 5) in the severe head injury group among the surviving patients. It was concluded that patients with TBI who have undergone a DC have an overall favorable outcome with an acceptable morbidity and mortality.<sup>[37]</sup>

In a 10-month duration, Salunke *et al.*, recruited 306 patients who underwent a wide DC at their center for intractable, raised intracranial pressure (ICP) after a head injury; infarction with edema due to the presence of subarachnoid hemorrhage (SAH), or malignant arterial infarction (i.e., thrombotic stroke) with mass effect. All patients improved after their cranioplasty, irrespective of the CSF diversion performed. The authors have suggested a management algorithm for patients with subdural CSF collections after a DC.<sup>[64]</sup>

Saika et al., aimed to compare the value of the FOUR score and GCS in predicting an early mortality after moderate and severe TBI through an observational study. Of the138 patients recruited, the mean GCS and FOUR scores for the entire patient cohort were 9.5 (standard deviation [SD] 2.4) and 11 (SD 3); respectively. The total FOUR and GCS scores were higher in patients who survived than those who did not. When using a cut-off score of 7 for the FOUR score, the AUC was 0.97 with a sensitivity of 97.5% and specificity of 88.2% (P<0.0001). With a cut-off score of 6 for the GCS score, the AUC was 0.95 with a sensitivity of 98.3% and a specificity of 82.4 % (P<0.0001). Spearman's correlation showed a correlation coefficient of 0.758 between the GCS and FOUR score with a P-value of<0.001. It was concluded that the predictive value of the FOUR score at admission of patients with TBI was no better than the GCS score.<sup>[70]</sup>

Dhandapani *et al.*, who validated a new clinico-radiological grading for compound head injury also followed up patients at regular intervals to assess the various outcome parameters. The GOS was used to assess neurological outcome at least 3 months after injury. Good or moderate disability (representing a GOS of 4–5) was considered as a favorable GOS, and severe as well as persistent disability, or death (representing a GOS of

1-3) was considered an unfavorable GOS. Simple compound injuries were considered as grade 1, whereas the next tier of dural violations was categorized as grade 2. Exposed brain could be assumed to be due to the result of a more severe dural violation and was grouped as grade 3. The most decisive factor related to the presence of a midline shift mandating a surgical intervention was classified as grade 4. Those patients with both an exposed part of the brain as well as the presence of a midline shift were kept under the grade 5 category. Of the 386 recruited patients, only 319 could be assessed for GOS at 3 months. Of these, 103 patients (32%) had an unfavorable GOS (1-3), whereas 76 (24%) patients died. The grade of compound injury had a significant association with infective complications (P < 0.001), an unfavorable GOS (P = 0.01), as well as delayed onset of seizures (P= 0.001), and a delayed hospital stay (P< 0.001). The factors were independent of age, sex, admission delay, mechanism of injury, GCS, and internal compounding. The admission GCS had a significant independent impact on infective complications, an unfavorable GOS, mortality, and hospital stay, whereas an admission delay had a significant independent association with infective complications, mortality, and hospital stay.<sup>[41]</sup>

Reddy *et al.*, examined the effects of neurofeedback training (NFT) on the quality of life (QOL) in patients with TBI. Sixty patients were recruited and divided into two groups, the 'intervention' (IG) and the 'wait-list' (WG) groups. The physical domain of QOL in the WG was greater than in the IG. Education was positively correlated with the environmental domain of QOL in both the IG and the WG. The results indicate that there existed a statistical significant difference between the pre- and post-intervention scores across all domains of QOL in the IG group. The results indicated that neuro feedback as a training mechanism can be useful in enhancing the QOL in patients with TBI.<sup>[62]</sup>

Dhandapani et al., recruited 53 patients with closed head injury with a GCS score of between 9-14, with no episode of hypotension, and a normal renal function, and subjected them to magnetic resonance spectroscopy (MRS) and single photon emission computed tomography (SPECT) scan, whenever feasible. The data related to the neurological outcome at 3 months was available for only 34 patients. After adjusting for various confounding factors using binary logistic regression, only the GCS score and severe hypoperfusion seen on the SPECT scan were noted to have a significant association with neurological outcome independent of age, traumatic coma data bank (TCDB), the CT scan category, the MRS abnormalities, and of each other (P= 0.02 and 0.04, respectively). Hence, severe hypoperfusion on the SPECT scan was associated with an unfavorable outcome independent of other factors. A lower N acetyl aspartate (NAA)/creatinine (Cr) ratio showed a predisposition in predicting an unfavorable outcome, which, however, was not statistically significant.<sup>[48]</sup>

Dhandapani *et al.*, recruited adult patients admitted within 24 hours of having sustained a severe TBI. Eighty-nine patients were prospectively assessed weekly until 21 days to assess for the factors associated with the development of a pressure ulcer in patients with severe TBI. On univariate analysis, the development of a pressure ulcer was significantly associated with a poorer GCS (P= 0.05), delayed enteral feeding

(*P*= 0.005), and a fall in hemoglobin levels at 2 weeks (*P*= 0.005). Only the latter two were found to be significant on a multivariate analysis. The presence of a pressure ulcer was significantly associated with mortality at 21 days (*P*= 0.006) and an unfavorable neurological outcome at 3 months (*P*= 0.01). The development of the pressure ulcer had a significant association with mortality at 21 days and the recovery status at 3 months.<sup>[11]</sup>

Agrawal et al., recruited 70 patients, 27 with moderate and 43 with severe injury, to determine the impact of comprehensive rehabilitation on the functional levels during the first year postinjury. They were evaluated on the functional independent measure (FIM) and the disability rating scale (DRS) for the functional outcome attained. The global outcome was assessed on the Glasgow outcome scale extended (GOSE). No disability was seen at 12 months in 24 individuals in the moderate injury group and 19 patients in the severe injury group. Thirty individuals with severe injury could achieve independence at 12 months. The outcome was a good recovery in 89% patients with a moderate, and in 52% of the patients with a severe injury. A moderate disability was seen in 11% patients of the moderate injury group and in 45% of the patients in the severe injury group; and, a severe disability was seen in none of the patients in the moderate injury group but in 3% patients of the severe TBI group.[40]

Sinha et al., assessed a total of 77 survivors of severe TBI treated prospectively in the outpatient department 1 year after the injury. These patients were assessed for cognitive, functional, and psychosocial outcome using cognitive outcome tests, dysfunctional analysis questionnaire, and personality trait inventory, respectively. The cognitive and functional outcomes were graded as 'average' and 'above average' recovery (representing a good recovery); or, 'below average' recovery (representing a poor recovery). The psychosocial outcome was assessed as an 'average recovery' (representing a good recovery), 'mild impairment' and 'severe impairment' (representing a poor to very poor recovery). Approximately 56-99% patients had a poor outcome in various domains of cognition. The ability to learn new things was the most affected aspect of cognitive function and only 1% of patients had a good recovery in this domain. However, 44% patients had a good outcome in retaining their simple memory. A total of 61% patients showed a good recovery in several aspects of functional status. Forty-seven (61%) patients had a good recovery in all domains of dysfunctional analysis questionnaire (DAQ), whereas 30 (39%) patients showed a poor recovery.<sup>[65]</sup>

Data of all patients with a mild TBI (n=1149), defined as a GCS score of 13 or more, collected over a period of 3 months, were retrospectively reviewed by Deepak *et al.* The outcome was assessed prospectively 1 year after injury through a telephonic GOSE assessment, and by asking the patient to fill the Rivermead Post-Concussion Symptoms Questionnaire (RPCSQ), and the Rivermead Head Injury Follow-up Questionnaire (RHFUQ). This protocol was conducted specifically among those patients with an isolated subarachnoid hemorrhage. There was no significant difference in the outcome scores between the SAH and the normal CT scan groups (RHFUQ, P = 0.45; RPCSQ, P = 0.25).<sup>[38]</sup>

Dhandapani *et al.*, evaluated the influence of different age thresholds on various clinical and radiological parameters, mortality, and neurological outcome at 6 months following TBI. The GOS at 6 months showed a significant correlation with age, with greater scores being more frequent in younger patients (P < 0.001). There was a significantly better outcome in the second decade compared to the first decade. The unfavorable outcome showed a significant association with increasing age, with a poorer outcome occurring in every decade (P < 0.001).In patients with TBI, age demonstrated an independent association with an unfavorable outcome at 6 months in a stepwise manner with the threshold age being 40 years.<sup>[36]</sup>

Wani *et al.*, presented the pattern of missile injury to the pediatric brain from conflict areas of Kashmir, India. Data were retrospectively collected before 2006 and prospectively collected from 2006 onwards for 51 patients. In patients with a score of 3–7, there was a 66.7% mortality and none of the patients had a good outcome. In patients with a GCS score of 8–12, there was a 15.0% mortality and 71% of the patients had minimal or no deficits. There were no deaths in the group with GCS scores of 13–15, with all patients having a normal outcome or minimal deficits (P<0.0001). Normal pupils indicated a less severe injury, as supported by their better outcome (P<0.0001) and hemodynamic status was also a very strong negative prognostic factor (P<0.0001). Pediatric missile injuries did not differ significantly from other types of head injury as far as the prognostic factors were concerned.<sup>[32]</sup>

A prospective observational study of 520 patients with traumatic brain injury (TBI) was conducted by Thapa *et al.* At a median follow-up of 386 days, 59 (11.4%) patients developed posttraumatic seizures. The incidence of immediate, early and late onset seizures were 6.5%, 2.1%, and 2.7%, respectively. The incidence of PTS was 18.3% among children. On multivariate analysis, the risk of post-traumatic seizures (PTS) was 3.7 times higher in those patients who had fallen from height, 4.4 times higher in those patients with associated medical problems, and 3.7 times higher in those patients who had suffered from severe head injury (with a GCS < 9) at presentation. PTS was associated with a poor GOS and a higher incidence of behavioral abnormality at follow up visit. Thirty-two percent of the patients with PTS developed recurrent delayed seizures. The seizure recurrence was significantly higher in late onset PTS.<sup>[3]</sup>

The association between apolipoprotein E polymorphism and outcome after mild to moderate traumatic brain injury was studied by Pruthi et al. Of the 98 patients tested for APOE polymorphism, 20 (20.3%) had one or more APOE ε4 allele. None of the patients with ɛ4 as one of the alleles had a poor outcome. Digit symbol substitution test (DSST) was completed by 44 patients; digit vigilance test (DVT) by 45 patients; complex figure test (CFT) by 45 patients, and token test was performed by 51 patients. On comparing the results of APOE genotype between the two groups, patient with APOE £4 alleles had slightly lower Dantes subject standardized test (DSST) scores; however, this difference was not statistically significant. Hence, on the neuropsychological tests, performance of patients with APOE e4 allele did not differ significantly from those without these alleles. To conclude, the study suggested that in the study region, patients with mild-to-moderate TBI with ɛ4 allele have a better outcome as compared to patients without it.<sup>[43]</sup>

Audiological deficits after closed head injury were assessed by Manjul et al. The sample population consisted of 290 patients with closed head injury (study group) and 50 with ontologically normal individuals (control group). The patients in the study group were further divided into mild (150), moderate (100), and severe (40) category based on the Glasgow Coma Scale score. The audiological assessment consisted of pure tone audiometry, speech audiometry, tympanometry, acoustic reflex testing, auditory brain stem response (ABR) audiometry, and middle latency response (MLR) audiometry. There was a higher prevalence of hearing impairment in the study group compared with the control group. Majority of the patients who incurred hearing loss after closed head injury had a mild degree of hearing impairment. The higher prevalence of MLR abnormalities than ABR suggested a greater chance of primary auditory cortical area being affected than the brain stem. The recognition of this deficit at the earliest is of important in the rehabilitation of patients who have sustained a closed head injury.<sup>[15]</sup>

Kumar et al., recruited 83 TBI patients to ascertain if abnormalities in the corpus callosum would be any different in moderate TBI compared to mild TBI, and if it would correlate with the differences in NPT performed later in these patients. Significantly, decreased fractional anisotropy (FA) in the genu and splenium significantly increased radial diffusivity (RD) values in the genu, mid body, and splenium. A significant increase in the mean diffusivity (MD) and a decrease in the axial diffusivity (AD) only in the genu, respectively, in patients with moderate TBI compared to healthy controls were observed. However, in patients with moderate TBI, a significantly decreased FA was found only in the genu compared to those with a mild TBI. Patients with a moderate TBI showed poor NPT scores compared to those with a mild TBI, but this did not reach statistical significance. It was concluded that diffusion tensor imaging (DTI) abnormalities in the regions of corpus callosum were more in patients with a moderate TBI compared to those with a mild TBI, and this was associated with a relatively poor neuropsychological outcome 6 months post-injury.<sup>[47]</sup>

Ramesh et al., devised a new prognostic scale, the Madras Head Injury Prognostic Scale (MHIPS), for prediction of outcome after head injury. There are six major prognostic factors incorporated in the MHIPS: age, best motor response (measured using the Glasgow Coma Scale, GCS17), pupillary response to light, oculocephalic response, CT scan findings, and other associated systemic injuries. Two studies were undertaken to test the validity of the MHIPS, one being a retrospective and the other being a prospective study. The retrospective study involved 355 patients admitted to the head injury ward. The outcome in each of the patients at the time of discharge was noted based upon the GOS of the patients. The sensitivity (the true positive rate) of the MHIPS was 98.9% and the specificity was 97.4%. A prospective study was undertaken to further test the validity of MHIPS. Patients (n = 104) admitted with moderate and severe head injury were studied prospectively. Ninety-one patients (87.5%) had the expected outcome. Of the 13 patients who did not have the expected outcome, the authors found that factors such as postsurgical complications, status epilepticus, and infection affected the predicted outcome. MHIPS is a simple, easy to apply, and accurate bedside prognostication scale for head injury, which can be used in any centre.<sup>[68]</sup>

A retrospective study of all patients admitted following a head injury to the intensive care unit (ICU) of a neurosurgical center in India over a 2-year period was conducted by Santhanam *et al.* The records of 208 patients were analysed. The initial GCS at admission, diastolic blood pressure (DBP) at admission, the presence or absence of hemodynamic instability during the ICU stay of the patients, and the status of basal cisterns on repeat CT scans was found to influence the outcome significantly. It was recommended by the authors that if every caregiver encountering the patient during the transportation from the site of injury to the ICU maintains hemodynamic stability (a DBP>70mmHg and systolic blood pressure [SBP]>90 mmHg) at all times, the mortality can be reduced.<sup>[67]</sup>

Nayak et al., compared the early changes in the status of oxidative stress of patients who have sustained a head injury with different neurological outcomes using erythrocyte parameters. In the D (patients who died) group, the erythrocyte thiobarbituric acid reactive substance (TBARS) levels were significantly higher compared to the normal controls (NC), as well as in the severe deficit (SD) and mild/moderate (MD) groups (P = 0.001); the glutathione (GSH) levels were significantly lower in the D group when compared to the NC (P = 0.001) and MD (P = 0.01) groups; and, the superoxidase dismutase (SOD) activity was significantly higher than in the NC (P = 0.01) and MD (P = 0.01) groups. In the SD group, the TBARS levels were significantly higher than in the NC (P = 0.001) and MD (P = 0.05) groups; the GSH levels were significantly lower than in the NC (P = 0.001) and MD (P =0.01) groups; and, the SOD activity was higher compared to the NC ( $\vec{P} = 0.01$ ) group. In the MD group, the TBARS levels were significantly higher and the GSH levels significantly lower compared to the NC group (P = 0.001).<sup>[75]</sup>

Yadav *et al.*, analyzed 262 prospective cases of post-traumatic intracerebral hematomas/contusions. The incidence of an expanding hematoma in cases with a lower GCS was significantly higher. A linear trend was observed in GCS and the expanding hematoma, i.e., the cases with a lower GCS had higher chances of developing an expanding hematoma (P<0.001). The impact of GCS showed its direct correlation with the development of hematomas. A coagulopathy was seen in 39 patients having an ICH. Of these, 41% developed an expanding hematoma in comparison to 12.1% where coagulopathy was absent. The prognosis was poor with a 50–60% mortality with an increased morbidity among the patients with a hematoma.<sup>[51]</sup>

Pappachan *et al.*, conducted a retrospective analysis among 12,329 patients reporting to the trauma center of the study hospital during a 5-year period with various injuries. A total of 772 (6%) patients had facial fractures. A total of 108 (14%)patients with a combination of cranial injuries and facial fractures were identified within the latter group. It was found that isolated maxillary and isolated mandibular fractures correlated with a more severe head injury. Moreover, whenever an isolated zygomatic fracture or the combinations of maxillary/zygomatic fractures occurred, the head injury was less severe. There was no relationship between the cranial bone fracture and the severity of head injury.<sup>[7]</sup>

Of the 162 total homicidal deaths studied during a 4-year period, 77 (45.7%) cases died from head injuries in a study

conducted by Mohanty *et al.* All three head structures, i.e., the scalp, the skull and meninges, and/or the brain were injured in 55(71.4%) of the victims. Forty-seven (61%) victims had an intracranial hemorrhage; most of them had a subdural hemorrhage. The authors concluded that the head is the target of choice in the great majority of fatal and nonfatal assaults.<sup>[8]</sup>

Three hundred and forty consecutive children with head injury, aged 15 years or less, were evaluated neurologically by assessing their best GCS (following their resuscitation, where ever necessary) and its modification for children below 2 years of age. A poor outcome was noticed in 5.4% of the patients with a fracture, 8.4% with an extradural hematoma, 18.2% with a contusion, 25% with a diffuse head injury, and 35.3% with an acute subdural hematoma. Ocular movement was found to be a good predictor of outcome. Seventy-seven children had abnormal ocular movements, and a poor outcome was seen in 38 (50%) of them.Among the children with normal ocular movements, a poor outcome was seen in 6% of the cases. Overall, a poor outcome was seen in 15.8% of 340 children with a head injury.<sup>[27]</sup>

In a single-centre study on 60 cases of missile injuries of the brain assessed in one year, the role of less aggressive debridement of the missile tract was studied. The outcome based upon the Glasgow scale was good in 42 patients; and, there was moderate disability in 7, severe disability in 6, and death in 5 cases. More than one-third (36.3%) of the cases revealed retained bone fragments and 18 (32.7%) of them revealed missile fragments on follow-up CT scans. The GCS score had been found to be the main determinant of outcome in this study. Other factors that were associated with a poor outcome included multilobar injuries, intraventricular hemorrhage, and dominant hemispheric injuries.<sup>[31]</sup>

Shanmukhi *et al.*, recruited 80 patients using a purposive sampling. Among them, 40 had a mild head injury and 40 were uninjured. Nonverbal serial pattern learning in patients with mild brain injury was examined using a serial pattern, a learning task introduced by Nissen *et al.* It was observed that the head injured patients had a marked disruption in their ability to learn and remember in a serial pattern learning (which included both simple and complex patterns of learning).<sup>[71]</sup>

Pillai *et al.*, conducted a prospective, randomized double-blind placebo-controlled trial with the aim of establishing whether or not nimodipine given orally for 3 weeks improved the outcome in patients with severe diffuse head injury (SDHI). Out of the 97 patients recruited, 41 patients expired in the hospital and 3 patients were discharged in a vegetative state. At 6 months, 61.9% patients in the nimodipine group had an unfavourable outcome compared to 57.5% in the placebo group. Nimodipine did not significantly influence outcome even in patients with traumatic subarachnoid hemorrhage (tSAH).<sup>[19]</sup>

Of the 1084 pediatric patients admitted in the pediatric surgery ward, in 400 children, the duration of loss of consciousness was also noted by Ratan *et al.* In this analysis, the association between loss of consciousness and the CT scan findings was not significant. A positive scan was observed in 74% head injured children with a severe injury, and in 70% children with a moderate and mild head injury, respectively.<sup>[45]</sup>

Pillai *et al.*, conducted a retrospective study to analyze the factors that influenced outcome in children with severe diffuse injuries. Severe motor or cognitive disability was suffered by 9.5% of the participants, while 5.4% had a moderate disability, and a good recovery was observed among 20.3% cases. The following factors were found to be independent predictors of a poor outcome: a GCS 3–5 (*P*<0.003), absent verbal response (*P*<0.001), a motor response score of 1–3 (*P*<0.001), absent pupillary reaction (*P*< 0.001), absent oculocephalic reflex (*P*< 0.001), and presence of traumatic subarachnoid hemorrhage on the CT scan (*P*<0.002).<sup>[69]</sup>

Amin *et al.*, aimed to modify the existing GCS into a fuzzy GCS using fuzzy information representation and fuzzy inferencing. The study compared the information content of the existing GCS with the new fuzzy GCS for prediction of full cognitive recovery in patients with head injury. It included 253 patients with a head injury. Full cognitive recovery (code 0) was observed in134 (52.96%) of the 253 patients. Recovery with a mild deficit was observed in 33 (13.04%) patients. Recovery with a moderate deficit was observed in 9 (3.56%) patients. Recovery with a severe deficit was observed in 11 (4.35%) patients.<sup>[52]</sup>

Children aged 12 years or less who had developed even a single seizure after sustaining cranial trauma were studied by Ratan *et al.* The occurrence of the first convulsion after head injury was taken as the outcome variable in the study. Out of the 400 patients studied, 84 (21%) had post-traumatic seizures. The study revealed that children younger than 2 years of age (OR 2.96; 95% CI 1.42–6.21), those suffering from severe head injuries, i.e., with a low GOS (OR 3.07; 95% CI 1.40–6.77) and those with a longer period of unconsciousness after head trauma [especially those with unconsciousness longer than 12 h (OR 1.71; 95% CI 0.69–4.19)] had a higher likelihood of suffering from convulsions after head injury.<sup>[26]</sup>

Kannan *et al.*, conducted a retrospective study and classified the patients into two groups –group A, comprising patients with severe closed head injury (n=171); and, group B consisting of all other patients (n=545). The average stay of patients in the unit was 12.71±11.9 days in group A, compared to 9.9 ±14.4 days in group B (P< 0.05). The duration on the ventilator or on an endotracheal airway was not different between the groups (P> 0.05). The mortality in group A was 46.8% and that in group B was 38.5% (P> 0.05).<sup>[57]</sup>

One hundred consecutive patients presenting with unilateral or bilateral blindness due to minor head injury over a 4-year period were studied by Agarwal *et al.*, to assess the prognosis related to vision recovery in patients who had become blind due to head injury. Visual improvement was recorded in 23 patients. The initial visual evoked potential (VEP) failed to reveal any wave in 29 patients and was abnormal in 71 patients. All 14 patients in whom the VEPs were repeatedly normal, irrespective of their initial VEP status, showed varying degrees of visual improvement, and none of the 15 patients with persistently negative VEPs showed visual improvement.<sup>[14]</sup>

Tandon *et al.*, compared the efficacy of transethmoidal optic nerve decompression in patients who failed to improve on steroids alone, with the results of steroid therapy alone in 111 patients who were treated for vision loss following blunt head injury. In group A, 66 patients agreed for surgery. In group B, 45 patients declined the surgical option at the outset and were treated with steroids alone for 3 weeks. In group A, 7 patients recovered normal vision on steroids alone. Thirty patients who did not respond to steroids had transethmoidal decompression. Twenty-two of the 39 patients operated upon improved, thus giving an overall improvement rate of 74.2%. Recovery was complete in six patients, partial in 17 patients , and did not occur in 22 patients; therefore, an overall improvement was noted in 51% patients in the control group (B).<sup>[12]</sup>

Dalvie *et al.*, in their analysis on 1993 communal riot victims of Mumbai, presented the analysis of injury in 440 patients. Among patients with head injuries, only 8 (13.1%) presented with altered consciousness. Ten (16.4%) patients were unstable on admission and 8 eventually died. Major surgical intervention was eventually required in only 2 patients. Majority of the patients either had wounds that required suturing or they were kept for observation only.<sup>[6]</sup>

Colohan *et al.*, presented the mortality related to head injury reporting on the data retrieved from two centers (Virginia and Delhi) with different emergency medical services and intensive care. It was observed that in Virginia, in patients with a GCS M of between 1 to 4, the factors that increased mortality were the presence of an abnormal pupillary response to light or being over 40 years of age. None of the five factors (skull fracture, abnormal pupillary reaction to light, presence of other injuries, systolic blood pressure < 90 mmHg, or age of the patient) influenced mortality in the patients from New Delhi with a GCS M of 4 or less. However, when one examines the group with GCS M = 5 (which included the only group with a significant difference in mortality rates between the two centers), the presence of a skull fracture significantly increased the mortality rate in New Delhi compared to Virginia.<sup>[20]</sup>

The GCS score at admission and at follow-up has been reported to be an important predictor of outcome in patients with TBI. A few studies also analysed the pupillary reflexes, neuropsychological outcomes, VEPs, and mechanical ventilation. The types of injury have also been reported as a predictor of outcome.

#### Conclusion

The pattern of reporting of TBI in the literature is analyzed in this review. In the majority of studies, the outcome of TBI at the time of discharge as well as the investigations performed for TBI have been reported. A moderate number of studies have also reported on the clinical presentation, demographics and management of TBI. The clinical presentation in the majority of studies has been presented in form of the incidence of fractures of skull and associated fractures of other parts of the body. A few studies have also demonstrated the data on posttraumatic seizures, focal neurological deficits and also the assessment of vital parameters after TBI. The findings on CT scan of the head done immediately after the occurrence of TBI has been reported by almost all the studies, with a few reporting on the CT findings related to orbital injuries also. A CT scan with positive findings has been stated to be as an important predictor of morbidity following the occurrence of TBI. MRI has been conducted after TBI. Its findings have been reported by a few studies that focus on the extent of parenchyma injuries. In rare cases, the coagulation profile, the endocrinal abnormalities, the audiological deficits and the glycemic status have also been studied to test the hypothesis that these are predictors of long term morbidity. The erythrocytic glutathione study and the apo E study have also been conducted by two researchers.

Craniotomy, craniectomy and craniostomy were the common interventions performed, wherever they were indicated. The effect of antifibrinolytic agents on the occurrence of intracerebral haemorrhage has been studied in one study. In other rare interventional studies, the effect of nimodipine, tracheostomy and transethmoidal optic nerve depression have also been studied. To study the outcome, the GOS has been the most commonly used tool. The duration of follow up ranged from 2 weeks to one year. The most common duration of follow up in the reported studies has been for 3 and 6 months. Apart from the GOS, the ocular movements of patients have also been studied as an outcome predictor.

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#### **Conflicts of interest**

There are no conflicts of interest.

#### References

- Global Burden of Disease Study C. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: A systematic analysis for the Global Burden of Disease Study 2013. Lancet 2015;386:743-800.
- Roozenbeek B, Maas AI, Menon DK. Changing patterns in the epidemiology of traumatic brain injury. Nature Rev Neurol 2013;9:231-6.
- Thapa A, Chandra SP, Sinha S, Sreenivas V, Sharma BS, Tripathi M. Post-traumatic seizures—A prospective study from a tertiary level trauma center in a developing country. Seizure 2010;19:211-6.
- 4. Massenburg BB, Veetil DK, Raykar NP, Agrawal A, Roy N, Gerdin M. A systematic review of quantitative research on traumatic brain injury in India. Neurol India 2017;65:305-14.
- Ahmed M, Sriganesh K, Vinay B, Umamaheswara Rao GS. Acute kidney injury in survivors of surgery for severe traumatic brain injury: Incidence, risk factors, and outcome from a tertiary neuroscience center in India. Br J Neurosurg 2015;29:544-8.
- Dalvie SS, Pai PR, Shenoy SG, Bapat RD. Analytical data of January 1993 communal riot victims-the KEM Hospital experience. J Postgrad Med 1993;39:5.
- 7. Pappachan B, Alexander M. Correlating facial fractures and cranial injuries. JOral MaxillofacSurg 2006;64:1023-9.
- 8. Mohanty S, Mohanty MK, Panigrahi MK, Kumar S. Fatal head injury in homicidal victims. Med Sci Law 2005;45:244-8.
- Sharma B, Gupta R, Anand R, Ingle R. Ocular manifestations of head injury and incidence of post-traumatic ocular motor nerve involvement in cases of head injury: A clinical review. Int Ophthalmol 2014;34:893-900.
- Misra UK, Kalita J, Pandey S, Mandal SK. Predictors of gastrointestinal bleeding in acute intracerebral haemorrhage. J Neurol Sci 2003;208:25-9.
- 11. Dhandapani M, Dhandapani S, Agarwal M, Mahapatra AK. Pressure ulcer in patients with severe traumatic brain injury: Significant

factors and association with neurological outcome. J Clin Nurs 2014;23:1114-9.

- Tandon DA, Thakar A, Mahapatra AK, Ghosh P. Trans-ethmoidal optic nerve decompression. Clin Otolaryngol Allied Sci 1994;19:98-104.
- Goel RS, Goyal NK, Dharap SB, Kumar M, Gore MA. Utility of optic nerve ultrasonography in head injury. Injury 2008;39:519-24.
- Agarwal A, Mahapatra AK. Visual outcome in optic nerve injury patients without initial light perception. Indian J Ophthalmol 1999;47:233.
- 15. Munjal SK, Panda NK, Pathak A. Audiological deficits after closed head injury. Trauma Acute Care Surg 2010;68:13-18.
- Bhole AM, Potode R, Agrawal A, Joharapurkar SR. Demographic profile, clinical presentation, management options in cranio cerebral trauma: An experience of a rural hospital in Central India. Pak J Med Sci 2007;23:724.
- Agrawal A, Kakani A, Baisakhiya N, Galwankar S, Dwivedi S, Pal R. Developing traumatic brain injury data bank: Prospective study to understand the pattern of documentation and presentation. Indian J Neurotrauma 2012;9:87-92.
- Jain S, Dharap SB, Gore MA. Early prediction of outcome in very severe closed head injury. Injury 2008;39:598-603.
- Pillai SV, Kolluri VR, Mohanty A, Chandramouli BA. Evaluation of nimodipine in the treatment of severe diffuse head injury: A double-blind placebo-controlled trial. Neurol India 2003;51:361.
- Colohan ART, Alves WM, Gross CR, Torner JC, Mehta VS, Tandon PN, *et al.* Head injury mortality in two centers with different emergency medical services and intensive care. J Neurosurg 1989;71:202-7.
- 21. Tabish A, Lone NA, Afzal WM, Salam A. The incidence and severity of injury in children hospitalised for traumatic brain injury in Kashmir. Injury 2006;37:410-5.
- Pruthi N, Ashok M, Shiva KV, Jhavar K, Sampath S, Devi BI. Magnitude of pedestrian head injuries and fatalities in Bangalore, South India: A retrospective study from an apex neurotrauma center. Indian J Med Res 2012;136:1039.
- 23. Thiruppathy SP, Muthukumar N. Mild head injury: Revisited. Acta Neurochir (Wien) 2004;146:1075-83.
- Ahmad FU, Mahapatra AK, Mehta VS. Outcome of "unknown" head injury patients at a tertiary care neurosurgical centre. Neurol India 2006;54:73.
- Abraham AP, Vidyasagar A, Lakshmanan J, Nair S, Joseph M. Phenytoin toxicity in patients with traumatic brain injury. Neurol India 2014;62:285.
- Ratan SK, Kulshreshtha R, Pandey RM. Predictors of posttraumatic convulsions in head-injured children. Pediatr Neurosurg 1999;30:127-31.
- Suresh HS, Praharaj SS, Indira Devi B, Shukla D, Sastry Kolluri VR. Prognosis in children with head injury: An analysis of 340 patients. Neurol India 2003;51:16.
- Jain A, Mittal RS, Sharma A, Sharma A, Gupta ID. Study of insomnia and associated factors in traumatic brain injury. Asian J Psychiatry 2014;8:99-103.
- 29. Francis R, Gregson BA, Mendelow AD, Rowan E. Characteristics of traumatic intracerebral haemorrhage: An assessment of screening logs from the STITCH (Trauma) Trial. Br J Neurosurg 2015;29:655-60.
- 30. Khan A, Prince M, Brayne C, Prina AM. Lifetime prevalence and factors associated with head injury among older people in low and middle income countries: A10/66 study. PloS One 2015;10:e0132229.
- 31. Singh P. Missile injuries of the brain: Results of less aggressive surgery. Neurol India 2003;51:215.

- Wani AA, Ramzan AU, Malik NK, Qayoom A, Nizami FA, Kirmani AR, *et al.* Missile injury to the pediatric brain in conflict zones. J Neurosurg Pediatr 2011;7:276-81.
- Menon A, Pai VK, Rajeev A. Pattern of fatal head injuries due to vehicular accidents in Mangalore. J Forensic Legal Med 2008;15:75-7.
- Bhattacharjee S, Layek A, Maitra S, Sen S, Pal S, Gozi NK. Perioperative glycemic status of adult traumatic brain injury patients undergoing craniotomy: A prospective observational study. J Neurosurg Anesthesiol 2014;26:313-9.
- Tripathi M, Tewari MK, Mukherjee KK, Mathuriya SN. Profile of patients with head injury among vehicular accidents: An experience from a tertiary care centre of India. Neurol India 2014;62:610-7.
- Dhandapani SS, Manju D, Sharma BS, Mahapatra AK. Prognostic significance of age in traumatic brain injury. J Neurosci Rural Pract 2012;3:131.
- 37. Sinha S, Raheja A, Garg M, Moorthy S, Agrawal D, Gupta DK, et al. Decompressive craniectomy in traumatic brain injury: A single-center, multivariate analysis of 1,236 patients at a tertiary care hospital in India. Neurol India 2015;63:175.
- Deepika A, Munivenkatappa A, Devi BI, Shukla D. Does isolated traumatic subarachnoid hemorrhage affect outcome in patients with mild traumatic brain injury? J Head Trauma Rehabil 2013;28:442-5.
- Yousuf A, Khursheed N, Rasool I, Kundal V, Jeelani H, Afroze D. Genetic variation of ApoE gene in ethnic Kashmiri population and its association with outcome after traumatic brain injury. J Mol Neurosci 2015;56:597-601.
- Agrawal M, Joshi M. Impact of rehabilitation on functional outcome during the first year of moderate and severe traumatic brain injury. Brain Injury 2014;28:292-7.
- 41. Dhandapani S, Sarda AC, Kapoor A, Salunke P, Mathuriya SN, Mukherjee KK. Validation of a new clinico-radiological grading for compound head injury: Implications on the prognosis and the need for surgical intervention. World Neurosurg 2015;84:1244-50.
- Dharap SB, Khandkar AA, Pandey A, Sharma AK. Repeat CT scan in closed head injury. Injury 2005;36:412-6.
- 43. Pruthi N, Chandramouli BA, Kuttappa TB, Rao SL, Subbakrishna DK, Abraham MP, *et al.* Apolipoprotein E polymorphism and outcome after mild to moderate traumatic brain injury: A study of patient population in India. Neurol India 2010;58:264.
- 44. Tandon A, Suri A, Kasliwal MK, Mahapatra AK, Mehta VS, Garg A, *et al.* Assessment of endocrine abnormalities in severe traumatic brain injury: A prospective study. Acta Neurochir (Wien) 2009;151:1411-7.
- Ratan SK, Pandey RM, Ratan J. Association among duration of unconsciousness, Glasgow Coma Scale, and cranial computed tomography abnormalities in head-injured children. Clin Pediatr 2001;40:375-8.
- 46. Harish G, Mahadevan A, Pruthi N, Sreenivasamurthy SK, Puttamallesh VN, Keshava Prasad TS, *et al.* Characterization of traumatic brain injury in human brains reveals distinct cellular and molecular changes in contusion and pericontusion. J Neurochem 2015;134:156-72.
- 47. Kumar R, Gupta RK, Husain M, Chaudhry C, Srivastava A, Saksena S, *et al.* Comparative evaluation of corpus callosum DTI metrics in acute mild and moderate traumatic brain injury: Its correlation with neuropsychometric tests. Brain Injury 2009;23:675-85.
- Dhandapani S, Sharma A, Sharma K, Das L. Comparative evaluation of MRS and SPECT in prognostication of patients with mild to moderate head injury. J Clin Neurosci 2014;21:745-50.
- Kaushal S, Midha V, Sood A, Chopra SC, Gupta C. A comparative study of the effects of famotidine and sucralfate in prevention of

upper gastrointestinal bleeding in patients of head injury. Indian J Pharmacol 2000;32:246-9.

- Nayak CD, Nayak DM, Raja A, Rao A. Erythrocyte indicators of oxidative changes in patients with graded traumatic head injury. Neurol India 2008;56:31.
- 51. Yadav YR, Basoor A, Jain G, Nelson A. Expanding traumatic intracerebral contusion/hematoma. Neurol India 2006;54:377-81.
- Amin AP, Kulkarni HR. Improvement in the information content of the Glasgow Coma Scale for the prediction of full cognitive recovery after head injury using fuzzy logic. Surgery 2000;127:245-53.
- 53. Agrawal D, Sahoo S, Satyarthee GD, Gupta D, Sinha S, Misra MC. Initial experience with mobile computed tomogram in neurosurgery intensive care unit in a level 1 trauma center in India. Neurol India 2011;59:739.
- 54. Kumar R, Gupta RK, Rao SB, Chawla S, Husain M, Rathore RKS. Magnetization transfer and T2 quantitation in normal appearing cortical gray matter and white matter adjacent to focal abnormality in patients with traumatic brain injury. Magn Reson Imaging 2003;21:893-9.
- 55. Prasanna KL, Mittal RS, Gandhi A. Neuroendocrine dysfunction in acute phase of moderate-to-severe traumatic brain injury: A prospective study. Brain Injury 2015;29:336-42.
- Nayak C, Nayak D, Bhat S, Raja A, Rao A. Relationship between neurological outcome and early oxidative changes in erythrocytes in head injury patients. Clin Chem Lab Med 2007;45:629-33.
- Kannan S, Marudachalam KS, Puri GD, Chari P. Severe head injury patients in a multidisciplinary ICU: Are they a burden? Intensive Care Med 1999;25:855-8.
- Gowda NK, Agrawal D, Bal C, Chandrashekar N, Tripati M, Bandopadhyaya GP, *et al.* Technetium Tc-99m ethyl cysteinate dimer brain single-photon emission CT in mild traumatic brain injury: A prospective study. Am J Neuroradiol 2006;27:447-51.
- 59. Perel P, Salman RA-S, Kawahara T, Morris Z, Prieto-Merino D, Roberts I, *et al.* CRASH-2 (Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage) intracranial bleeding study: The effect of tranexamic acid in traumatic brain injury-a nested, randomised, placebo-controlled trial. Health Technol Assess 2012;16:iii-xii, 1-54.
- 60. Singh AK, Suryanarayanan B, Choudhary A, Prasad A, Singh S, Gupta LN. A prospective randomized study of use of drain versus no drain after burr-hole evacuation of chronic subdural hematoma. Neurol India 2014;62:169.
- 61. Singh SB, Chakraborty S, Jha KM, Haider S, Chandra S. Repeated measure analysis in raga therapy: A case study on head injury patients. Res J Pharm Biol Chem Sci 2013;4:420-8.
- 62. Reddy RP, Rajeswaran J, Bhagavatula ID, Kandavel T. Silent epidemic: The effects of neurofeedback on quality-of-life. Indian J Psychol Med 2014;36:40.
- Prasad GL, Gupta DK, Mahapatra AK, Sharma BS. Surgical results of decompressive craniectomy in very young children: A level one trauma centre experience from India. Brain Injury 2015;29:1717-24.
- Salunke P, Garg R, Kapoor A, Chhabra R, Mukherjee KK. Symptomatic contralateral subdural hygromas after decompressive craniectomy: Plausible causes and management protocols. J Neurosurg 2015;122:602-9.
- 65. Sinha S, Gunawat P, Nehra A, Sharma BS. Cognitive, functional, and psychosocial outcome after severe traumatic brain injury: A cross-sectional study at a tertiary care trauma center. Neurol India 2013;61:501.
- 66. Singh M, Vaishya S, Gupta S, Mehta VS. Economics of head injuries. Neurol India 2006;54:78.
- 67. Santhanam R, Pillai SV, Kolluri SVR, Rao UM. Intensive care management of head injury patients without routine intracranial

pressure monitoring. Neurol India 2007;55:349.

- 68. Ramesh VG, Thirumaran KP, Raja MC. A new scale for prognostication in head injury. J Clin Neurosci 2008;15:1110-3.
- Pillai S, Praharaj SS, Mohanty A, Kolluri VRS. Prognostic factors in children with severe diffuse brain injuries: A study of 74 patients. Pediatr Neurosurg 2001;34:98-103.
- Saika A, Bansal S, Philip M, Devi BI, Shukla DP. Prognostic value of FOUR and GCS scores in determining mortality in patients with traumatic brain injury. Acta Neurochir (Wien) 2015;157:1323-8.
- 71. Shanmukhi S, Panigrahi M. Serial pattern learning after mild head injury. Neurol India 2003;51:518.

- 72. Srinivasan US. A mathematical model for predicting the outcome in moderate head injury. Neurol India 2006;54:28.
- Mukherjee KK, Sharma BS, Ramanathan SM, Khandelwal N, Kak VK. A mathematical outcome prediction model in severe head injury: A pilot study. Neurol India 2000;48:43.
- Pillai SV, Kolluri VR, Praharaj SS. Outcome prediction model for severe diffuse brain injuries: Development and evaluation. Neurol India 2003;51:345.
- 75. Nayak C, Nayak D, Raja A, Rao A. Relationship between markers of lipid peroxidation, thiol oxidation and Glasgow coma scale scores of moderate head injury patients in the 7 day post-traumatic period. NeurolRes 2008;30:461-4.

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