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The Pathophysiology of Traumatic Brain Injury (TBI): A Review

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Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

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Review Article

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ABSTRACT

Traumatic brain injury (TBI) is an insult to the brain from an external mechanical force. It may cause permanent or temporary impairment of cognitive, physical, and/or psychological functions. It may also be associated with an altered or diminished state of consciousness. It accounts for approximately 40% of all deaths from acute injuries. The economic burden due to loss of earning capacity is tremendous. It affects all age groups, but the main victims are the adults in the prime of their life. The major cause of TBI is road traffic accidents. The primary injury, sustained at the time of the accident, cannot be altered. The main aim of TBI management is to prevent or limit the secondary brain injury which develops after Primary injury. The proper recognition of trauma and secondary pathology goes a long way to limit mortality and morbidity. The skull fractures, intracranial bleeds can be surgically treated. Early recognition of cerebral edema, raised intracranial tension, hydrocephalus and brain herniation is the essential part of neurosurgical management.

Keywords: Traumatic Brain Injury (TBI); Glasgow Coma Scale (GCS); extradural hematoma; subdural hematoma; coup/contrecoup injury; brain herniation.

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1. INTRODUCTION

Traumatic brain injury (TBI) is an insult to the brain from an external mechanical force. It may cause permanent or temporary impairment of cognitive, physical, and/or psychological functions. It may also be associated with an altered or diminished state of consciousness. Many times, the word head injury is used as synonymous with TBI but it is not correct since all the head injuries may not have impaired neurological function, so the Traumatic Brain Injury is a more appropriate nomenclature [1]. In the United States, the TBI is responsible for approximately 40% of all deaths from acute injuries. Annually, 200,000 victims of TBI need hospitalization, and 1.7 million persons sustain mild TBI requiring an office visit or temporary disability for at least 1 day. The financial cost of TBI is estimated at approximately $4 billion per year. This estimate includes the loss of potential income of the patient and of relatives (who may need to become caregivers), the cost of acute care, and other medical expenses, such as continuous ambulatory and rehabilitation care. Approximately 52,000 deaths per year result from TBI in the US [2-3]. It affects all age groups. The majority of them are young adults of reproductive age group. As per the estimate by the Ministry of road transport, Government of India (2007), 40,612 people were killed and 1.5 lakhs injured in 2007 [4]. Hence, India is leading the world in fatalities due to road accidents. TBI is also associated with significant socioeconomic losses in India as well as in other developing countries [4-5]. Worldwide it is a major public health problem and is predicted to surpass many diseases as a major cause of death and disability by the year 2020 [5]. The majority (60%) cases are due to road traffic injuries (RTI), followed by falls (20-25%) and violence (10%) [6].

The severity of TBI can be judged and the outcome can be predicted by the Glasgow come scale (GCS). It was introduced in 1974 by *Sir Graham Michel Teasdale*. He is an English neurosurgeon and a co-developer of this neurological assessment tool. It is a simple and reliable method to measure the level of consciousness in a patient with TBI. The Glasgow coma scale assesses the response of three behavioral domains i.e., Eye-opening (E), Motor response (M), and Verbal activity (V) [7]. The person who is fully conscious, oriented, and an alert will have a score of E4 M6 V5 (15/15). Any reduction in the score is indicative of a deteriorated level of consciousness. [Table-1] So, the severity of the traumatic brain injury can be assessed and a prognosis can be made with the help of this table. Mild head injury is indicated by a GCS score of 13-15, and it makes up to 80% of cases. A score of 9-12 is considered a moderate head injury and the incidence of it is 10%. The score of 3-8 is severe head injury and its incidence is 10%, it also entails the worst prognosis [8].

Table 1. The Glasgow coma scale. [7-8]The essence of the GCS is the independent assessment of responses in three behavioral domains, and they are Eye opening (E), Motor Response (M) and Verbal Response (V)

Eye Opening (E)

Score	Parameter	Response
4	Spontaneous	Indicates arousal, not necessarily awareness
3	To Speech	When spoken to – not necessarily command to open eye
2	To Pain	Applied to limbs and not face where grimacing can causes closure of eye
1	None	

Motor Response (M)

6	Obeys command	Exclude grip reflex or postural adjustments
5	Localizes	Other limb moves to site of nail bed pressure
4	Withdraws	Normal flexion of Elbow or knee to local painful stimulus
3	Abnormal flexion	Slow withdrawal with pronation of wrist, adduction of shoulder
2	Extensor response	Extension of elbow with pronation and adduction
1	No Movement	

Verbal Response (V)

5	Oriented	Knows who, where, when; year, season, month
4	Confused	conversation Attends and responds but answers muddled/wrong
3	Inappropriate words	Intelligible words but mostly expletive or random
2	Incomprehensible speech	Moans and groans only-no words
1	None	

The new addition to the Glasgow Coma Scale is pupil reactivity score (PRS), the age of the patient and CT findings. If all these parameters are also taken into consideration the GCS becomes very useful tool to manage and prognosticate the Traumatic brain injury patients [9].

2. THE MECHANISMS OF INJURY [10]

- The leading cause of TBI is Motor Vehicle Accidents, and it constitutes almost 50% of all TBIs.
- The second leading cause of TBI falls. It accounts for 20-30% of all such injuries. It is the most common cause of TBI in individuals aged 75 years or older.
- The third leading cause of TBI is injury due to firearms. It constitutes 12% of all TBIs. It is more common among individuals aged 25-35 years. Gunshot-related, fatal TBIs are higher among men than women and are more prevalent among African Americans than they are in whites.
- Work-related TBIs constitute an estimated 45-50% of all TBIs. Incidence varies from 37 cases per 100,000 people for military employees (57% are related to transportation) to 15 cases per 100,000 people for civilians (50% are because of falls).
- Alcohol is a major factor in many TBIs and often is associated with the leading causes of TBI.

3. MATERIALS AND METHODS

Trauma is the leading cause of mortality and morbidity the world over. The Indian scenario is no exception. The present review is a descriptive study of important aspects of traumatic brain injury. It is important to understand the proper pathophysiology of TBI to manage the injury more efficiently, and to reduce mortality and morbidity. The data source is authentic, published literature and textbook. The search was done for the keywords like statistics, traumatic brain injury, pathophysiology, intracranial hemorrhage, etc. the data compiled and relevant material edited and presented as a review.

4. TRAUMATIC BRAIN INJURY AND ITS PATHOPHYSIOLOGY

Traumatic brain injury (TBI) is the result of an external mechanical force applied to the cranium and the intracranial contents, leading to temporary or permanent impairments, functional disability, or psychosocial maladjustments [11-12]. TBI can manifest clinically from concussion to coma and death. The type of Injuries is divided into 2 subcategories: Primary injury, which occurs at the moment of trauma, and Secondary injury, which occurs immediately after trauma and produces effects that may continue for a long time [13-14].

4.1 The Primary Injury

Primary injuries can manifest as focal injuries (e.g., skull fractures, intracranial hematomas, lacerations, contusions, penetrating wounds), or they can be diffuse (as in diffuse axonal injury) [15-16].

4.1.1 The Skull bone fractures [15-17]

Skull bone fractures can be vault fractures or fractures of the base of the skull. They may or may not be associated with hematoma, cranial nerve damage, or parenchymal injuries. The vault fractures are usually linear but may extend into the sinuses. Closed fractures are those that do not communicate with the outside environment, but open fractures communicate and thus have the potential for infection. Fractures may also be depressed or non-depressed. The depressed fractures are those which are displaced inwardly. Fractures of the base of the skull may be associated with injuries to the cranial nerves and discharges from the ear, nose, and throat [16].

4.1.2 Intracranial hemorrhages

The following types of intracranial hemorrhage can occur:

An extradural hematoma occurs from impact loading to the skull with associated laceration of the dural arteries or veins. Most commonly this type of hematoma occurs in the injury/ tears in the middle meningeal artery, due to side blow in the skull. The hematoma due to arterial bleeds may cause rapid collection and fast neurological deterioration. A subdural hematoma is more common in the older age group and is due to injured cortical veins. They are associated with high mortality rates (up to 60-80%). Intracerebral or parenchymal bleed is secondary to laceration or contusion of the brain. The neurological deficit depends upon the area and the severity of the damage. IN severe TBI, intraventricular hemorrhage can occur and they are associated with an unfavorable prognosis [18-19].

4.1.3 Coup and contrecoup contusions

A combination of vascular and tissue damage leads to cerebral contusion [21]. The direct impact to the skull distorts it at the site of impact and is called coup contusion. The contrecoup contusions are similar to coup contusion but are located opposite to the site of direct impact. The amount of energy dissipated at the site of direct impact determines whether the ensuing contusion is of the coup or contrecoup type. Most of the energy of impact from a small, hard object tends to dissipate at the impact site, leading to a coup contusion. In contrast, the impact from a larger object causes less injury at the impact site, because energy is dissipated at the beginning or end of the head motion, leading to a contrecoup contusion. A concussion is caused by the deformity of the deeper structures of the brain, causing widespread neurological dysfunction. This may result in impaired consciousness or coma [22-23].

4.2 The Secondary Injury

The consequence of cellular damage caused by primary injury is secondary injury. These may develop over hours or days following the initial traumatic assault [24]. The initial manifestations are due to direct tissue damage, disordered metabolism, and deranged autoregulation of cerebral blood flow (CBF). It leads to the accumulation of lactic acid, increased cell membrane permeability, and brain edema. This anaerobic metabolism cannot sustain the metabolic demands of the brain and it ultimately fails the ATP-dependent membrane ionic pump, which is essential for maintaining adequate homeostasis [25]. In the second stage of this cascade, there is sustained membrane depolarization, along with excitotoxicity (i.e., the excessive release of excitatory neurotransmitters such as glutamate and aspartate). This activates voltage-dependent Ca2+ and Na+ channels. It also causes calcium and sodium influx and activation of lipid peroxidase, proteases, and phospholipase. This triggers the apoptotic cascade and ultimately leads to membrane degradation and cell death [26].

4.2.1 TBI and neurochemical changes

For the normal transmission of signals, neurotransmitter mediated activation of the receptor is required. It is followed by the controlled ionic changes in the postsynaptic membrane. Within one hour after TBI, there is a massive release of glutamate from presynaptic terminals. It disrupts ionic equilibrium on the postsynaptic membrane. It also causes the accumulation of potassium [K^+] and calcium [Ca^{2+}] [24]. There is increased uptake of calcium by mitochondria due to the accumulation of intracellular Ca^{2+}. The overloading of mitochondria induces oxidative stress and impairs its functioning [27-28]. All these changes disrupt the normal functioning of the cell [29].

4.2.2 The deranged cerebral glucose metabolism

Glucose is the main energy source for the brain. The energy is stored in the form of ATP. TBI changes cerebral glucose metabolism (CMRglc). After the TBI there is increased cellular glucose metabolism. This is the period of hyperglycosis. It is because of increased cellular energy demand to restore the ionic balance and neuronal membrane potential [30].This acute increase in CMRglc is followed by a prolonged period of decreased CMRglc. This depressed glucose metabolism also affects the glucose uptake of the brain adversely and produces downstream negative effects [31].

4.2.3 Energy crisis in TBI

The exact mechanism of decreased glucose uptake after TBI is not well understood. There are three possible mechanisms: There is reduced cerebral blood flow CBF), the glucose

transport is hampered and metabolic demand for glucose is also decreased as a consequence of injury. As outlined above, immediately after injury there is increased glucose consumption and there is reduced cerebral blood flow [32-33]. The impaired glucose transport through the blood vessels to brain cell also contributes to decreased glucose uptake. It is well known that in TBI glucose transport is substantially affected both in animal models and the human brain. Not only this, but the glycolytic processing is also affected post-TBI. It ultimately decreases the oxidative metabolism of glucose and contributes to the post-TBI energy crisis and reduced ATP production. In the pathogenesis of energy crisis, the mitochondria play a crucial role. The impaired mitochondrial function is due to the accumulation of Ca^{2+} and ROS. There is the collapse of mitochondrial membrane-potential due to Ca^{2+} accumulation [34]. The result is reduced energy production and potential for apoptosis.

4.2.4 The increased intracranial pressure (ICP)

It is well known that in TBI there is an increase in intracranial pressure. The normal ICP is 7-15 mm of Hg, if the ICP increases beyond 40 mm of Hg it further complicates the outcome. The increased pressure leads to cerebral ischemia, cerebral edema, brain herniation, and hydrocephalus. Cerebral edema is caused by increased intracranial pressure and deranged neurochemical transmitters. TBI disturbs the vasomotor autoregulation and disrupts the blood-brain barrier. Hydrocephalus may be communicating or non-communicating type. The communicating type is more common. It is due to the presence of blood products that obstructs the flow of the cerebrospinal fluid (CSF) in the subarachnoid space and the absorption of CSF through the arachnoid villi. The non-communicating type of hydrocephalus is less common and is often caused by the blood clot which prevents the blood flow at the interventricular foramen, third ventricle, cerebral aqueduct, or fourth ventricle [15].

4.2.5 The coning/brain herniation

Anatomically brain is encased in a rigid cavity formed by the skull bones. There is very little space for any rise in volume due to any cause. In case of raised intracranial pressure as happens in TBI there is the compensatory displacement of cerebrospinal fluid (CSF) and changes in cerebral blood volume, as is governed by the Monro-Kellie doctrine [35]. When the increase in ICP overrides the compensatory mechanism there is herniation of brain tissue through specific foramina. These foramina are formed by the falx cerebri and tentorium.

This rise in intracranial pressure causes:

1. Herniation of contents of the supratentorial compartment through the tentorial hiatus.
2. Herniation of the contents of the infratentorial compartment through the foramen magnum.

The following types of supratentorial herniations are recognized:

- Sub-falcine herniation: It is said to occur when an expanding mass lesion causes a medial shift of the ipsilateral hemisphere. In this type of herniation, the cingulate gyrus of the frontal lobe is pushed beneath the falx cerebri. This is the most common type of herniation.
- Central transtentorial herniation: In this type of herniation, the basal nuclei and cerebral hemispheres are displaced downwards. The adjacent midbrain is pushed through the tentorial notch.
- Uncal Herniation: In this type of herniation, the medial edge of the uncus and hippocampal gyrus is displaced medially and over the ipsilateral edge of the tentorium cerebellar foramen. Such displacement causes compression of the midbrain. The third cranial nerve on the ipsilateral and contralateral side is also stretched/compressed [36].

The infratentorial herniation is said to occur when the tonsil of the cerebellum is pushed through the foramen magnum and compresses the medulla. It can cause bradycardia and respiratory arrest [37].

It is important to recognize coning in the time since the delay carries a grave prognosis. The coning leads to:

1. Decreased level of consciousness.
2. Ipsilateral dilatation of pupil (on the side of hematoma) and hemiparesis. This hemiparesis is due to the compression of the contralateral corticospinal tract.
3. This effect is called "Kernohan's notch".
4. Herniation of infratentorial contents through the foramen magnum obstructs the cerebral aqueduct which further damages the brain function [15,37].

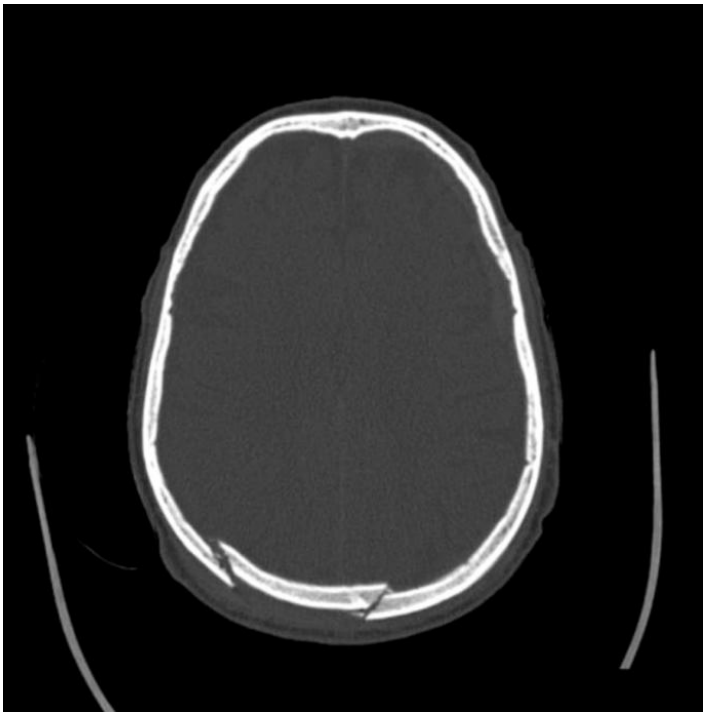

Fig. 1. The CT scan of the Skull (bone window) showing a depressed fracture of the occipital bone. It is an example of primary and focal injury [17]

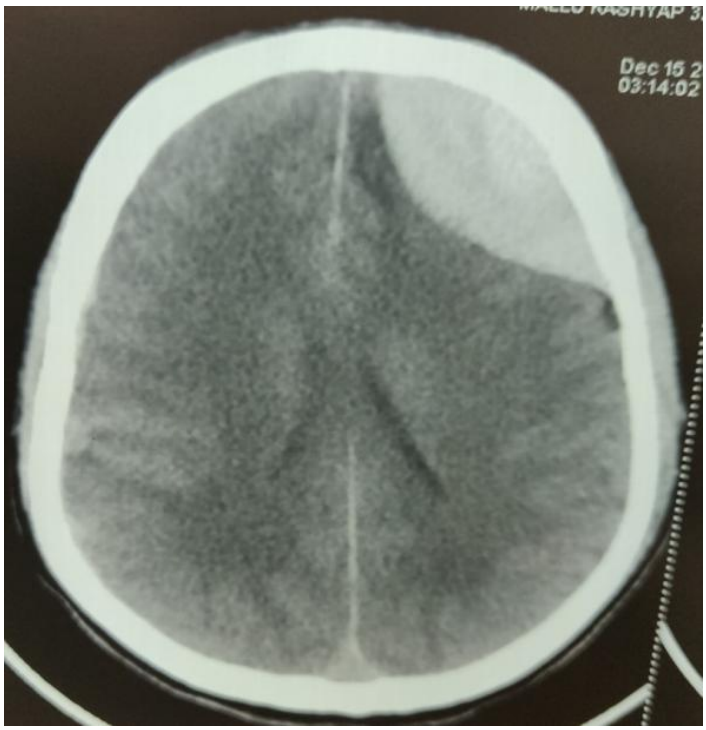

Fig. 2. CT Scan of skull showing extradural hematoma. The shape of the hematoma is typically biconvex

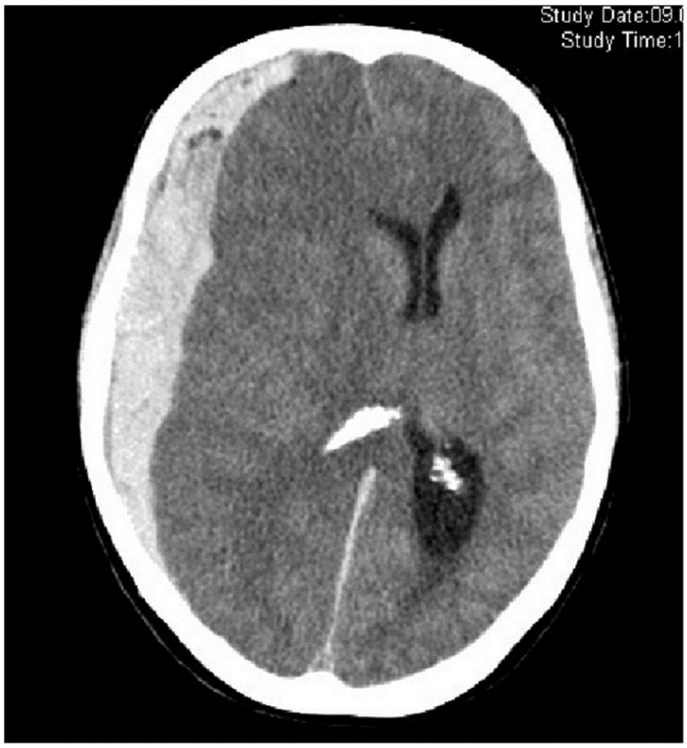

Fig. 3. Acute Sub-dural hematoma [20]. The CT scan of the brain showing subdural hematoma with the concavo-convex lesion. It is due to the rupture of veins between the dura and cerebral hemisphere, causing gradual collection of blood in the subdural space

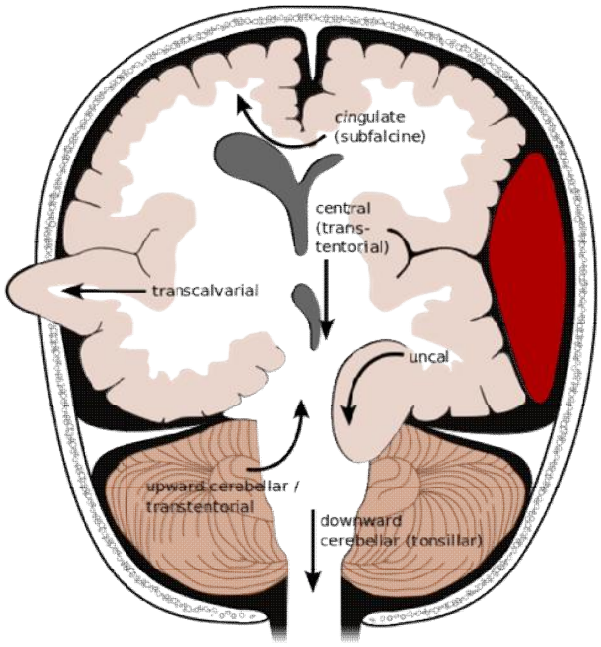

Fig. 4. Brain herniation [37]. Diagrammatic representation of various types of brain herniation. It occurs due to raised intracranial tension and failed compensatory mechanisms

5. CONCLUSION

The leading cause of mortality and morbidity in the 18-45-year age group is a traumatic brain injury.

Most of the patients survive, but many of them develop a significant disability. Their disability is a cause of major socio-economic burden to the family and the society. The financial burden of TBI is exorbitant. The leading cause of TBI is a road traffic accident followed by a fall. The knowledge and proper understanding of the pathophysiological mechanism in traumatic brain injury are essential for the proper recognition of the gravity of the injury and its appropriate management. The primary insult represents the direct mechanical damage incurred at the time of impact and it cannot be altered or therapeutically influenced. So, the main aim is to recognize and prevent secondary damages. This secondary damage consists of changes in cerebral blood flow, malfunctioning of the blood-brain barrier, disturbed cerebral metabolic function, and inadequate cerebral oxygenation. The excitotoxic cell damage and inflammation may lead to apoptosis and necrotic cell death. Fracture of skull bones, intracranial hemorrhages, brain herniation further adds to the complex pathophysiology of traumatic brain injury. So, the management of TBI is to recognize the secondary changes at an earliest and to understand the pathophysiological mechanism.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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