

Prospective observational study on assessment of mannitol and 3% hypertonic saline on intracranial pressure by ultrasonographic measurement of optic nerve sheath diameter

Authors:

Girish Chavan¹, Dr. Jeeva George², Dr. Balakeshwa Ramaiah³

¹Rajiv Gandhi University of Health Sciences, Bengaluru, Karnataka.

²Assistant Professor, Department of Pharmacy Practice, Rajiv Gandhi University of Health Sciences, Bengaluru, Karnataka.

³HOD, Department of Pharmacy Practice, Rajiv Gandhi University of Health Sciences, Bengaluru, Karnataka.

Corresponding Author:

Girish Chavan

<https://doi.org/10.5281/zenodo.18239592>

Revised: 06-December-2025, Accepted: 25-December-2025, Online First: 29-December-2025

ABSTRACT:

Background: Intracranial hemorrhage has been one of the leading causes of morbidity, disability, and mortality worldwide across all ages. Globally more than 50 million individuals suffer from intracranial hemorrhage each year. Intracranial pressure is a major predictor of neurological deterioration in patients with intracranial hemorrhage and post traumatic intracranial hypertension is being associated with poor neurological outcome. **Objective:** To Assess the reduction in the optic nerve sheath diameter after instituting the mannitol and 3% hypertonic saline. **Materials and method:** This observational study was conducted in a tertiary care hospital for a period of 6 months. Medical records of patients were reviewed for drug prescription including Scanning reports and laboratory reports. **Results:** The study was conducted on 30 patients, who had a intracranial hemorrhage, and most common type of intracranial hemorrhage were sub-archanoid hemorrhage (30%), followed by subdural hemorrhage (6.7%). In the study majority (43.3%) participants were between 16-35 years old, of these female represents 43% of the total sample and 56.7% represents male. majority of individual (56.7%) had a duration of 7-11 days of hospital stay. In the study 76.7% of patients underwent craniotomy, 90% of patients survived and mortality was found to be 10%. The mean ONSD value of left eye on day1 was 0.6425 ± 0.04889 , and decreased to 0.5568 ± 0.11633 on day2, and further declined to 0.5146 ± 0.11250 . The mean ONSD of right eye on day1 is 0.651 ± 0.046 , which decreased to 0.584 ± 0.050 on day2, and further declined to 0.533 ± 0.0049 on day3. **Conclusion:** Both mannitol and 3% hypertonic saline shown to be effective in reducing the raised intracranial pressure in patients with intracranial hemorrhage.

Keywords: Intracranial hemorrhage, neurological deterioration, mannitol and 3% hypertonic saline

INTRODUCTION:

ICP or intracranial pressure refers to the amount of pressure within the cranial vault, which is the space occupied by the brain. This pressure is regulated and maintained by a delicate balance between the production and absorption of cerebrospinal fluid. It is widely acknowledged in the medical community that proper brain function requires ICP values to be within a specific range. In adults, this ideal range is typically between 10 and 20 mmHg, while in infants and young children it may range from 3 to 7 mmHg. Any deviation from these normal ranges can have significant effects on brain functionality and overall health. Thus, monitoring ICP levels is crucial in diagnosing and managing various neurological conditions.¹ The intricate workings of the human body reveal that the brain, the epicenter of all cognitive and physiological processes, is allotted

between 15% and 25% of the cardiac output. This remarkable distribution ensures that an adequate amount of oxygenated blood, approximately 40 to 50 mL per 100 grams of brain tissue per minute, is constantly delivered to sustain its vital functions. These values are meticulously regulated by the interplay between cerebral metabolic rate of oxygen consumption (CMRO₂) and cerebral autoregulation through cerebral vascular resistance (CVR). Moreover, the crucial balance between mean arterial pressure (MAP) and intracranial pressure (ICP), known as cerebral perfusion pressure (CPP), also plays a critical role in determining CBF levels. Through such intricate mechanisms, the brain receives a sufficient blood supply to support its complex cognitive processes and maintain overall homeostasis.^{1,2} The skull, once the sutures and fontanelles have closed, becomes a rigid structure that

does not allow for any further expansion. This means that regardless of its content, the volume of the skull will remain constant. The contents of the skull can be divided into three main compartments according to the Monro-Kellie doctrine: cerebral parenchyma makes up 80% of the volume, cerebrospinal fluid (CSF) accounts for 10%, and blood comprises the remaining 10%. When the volume of any of these compartments increases, it creates pressure within the skull that exerts pressure on the other compartments. In normal conditions, the body has mechanisms in place to compensate for these variations. One such mechanism involves the displacement of CSF into the lumbar cistern to help maintain pressure equilibrium. Additionally, cerebral blood flow decreases to help regulate the pressure within the skull. In chronic situations, the brain parenchyma may undergo changes as it loses extracellular water, as well as neurons and glial cells. However, in cases where these compensatory mechanisms fail, an increase in intracranial pressure (ICP) can lead to a decrease in blood supply to the brain. This decrease in blood supply can then cause a decrease in cerebral perfusion pressure (CPP), which is essential for maintaining adequate blood flow to the brain. Therefore, it is crucial for healthcare providers to monitor intracranial pressure and cerebral perfusion pressure in patients with conditions that can lead to increased pressure within the skull. Failure to adequately manage intracranial pressure can result in serious complications and neurological damage.¹ In the context of this interaction, we can identify three distinct situations that occur in response to the increase in intracranial volume (IV). Initially, in the first stage, the augmented IV does not have an impact on intracranial pressure (ICP) since the cerebrospinal fluid (CSF) and cerebral blood are displaced to accommodate the change in volume. Essentially, the body's regulatory mechanisms are able to successfully adjust to the increased volume without causing a significant rise in pressure within the skull. However, as the intracranial volume continues to increase, the compensatory system becomes overwhelmed, leading to the second stage. During this phase, the regulatory system reaches its limit and is no longer able to effectively counteract the rise in pressure resulting from the increased volume. Consequently, the intracranial pressure starts to elevate due to the inability of the body to adequately compensate for the ongoing changes in intracranial volume. This ultimately leads to the third stage, where the self-regulatory system completely fails to function. Even small alterations in intracranial volume can now trigger a substantial and rapid increase in intracranial pressure, as the body is no longer able to regulate and adjust to the changes occurring within the skull. This loss of regulation can be extremely dangerous, as it can potentially result in severe complications and neurological deficits. In conclusion, the progression of intracranial volume increase and its effect on intracranial pressure follows a distinct pattern

characterized by the initial compensatory phase, followed by an overload of the regulatory system, and ultimately culminating in a complete failure of self-regulation. Understanding these stages is crucial in the management and treatment of conditions that lead to elevated intracranial pressure, as it allows for timely interventions to prevent potential complications and adverse outcomes.³ Cerebral autoregulation is a crucial mechanism that ensures the brain receives adequate blood flow to meet its metabolic oxygen requirements. This process involves the modification of vascular resistance through vasodilation or vasoconstriction to maintain cerebral blood flow (CBF) at an appropriate level. The regulation of CBF is primarily influenced by factors such as the partial pressure of arterial carbon dioxide (PaCO_2), mean arterial pressure (MAP), and to a lesser extent, the partial pressure of arterial oxygen, adenosine, and pH. When the brain's PaCO_2 levels are high due to increased metabolic activity, vascular resistance decreases, leading to vasodilation and an increase in CBF and oxygen supply to the brain (CDO_2). Conversely, when PaCO_2 levels decrease, indicating reduced metabolic activity, vasoconstriction occurs, decreasing CBF. Under normotensive conditions, CBF is estimated to fluctuate by approximately 4% for each mmHg change in CO_2 levels. MAP also plays a significant role in cerebral autoregulation, as CBF is regulated to protect the brain tissue from sudden spikes or drops in pressure that could compromise oxygen delivery. However, when the upper or lower limits of these autoregulatory mechanisms are exceeded, CBF becomes reliant on MAP to maintain adequate blood flow to the brain. In conclusion, cerebral autoregulation is a complex process that involves the dynamic adjustment of vascular resistance to maintain optimal blood flow to the brain. This mechanism ensures that the brain receives sufficient oxygen to meet its metabolic demands, thus safeguarding its function and integrity.⁴ Raised intracranial pressure (ICP) is frequently linked to higher mortality rates and unfavorable neurologic outcomes. It has been demonstrated that monitoring ICP in patients suffering from closed head injuries can significantly enhance their overall prognosis. This monitoring process serves as a vital tool in managing such cases, allowing medical professionals to intervene promptly and tailor treatment strategies to address the elevated ICP levels effectively, thus leading to improved patient outcomes in the long run.⁶

PATHOPHYSIOLOGY OF RAISED INTRACRANIAL PRESSURE:

The cerebral parenchyma, which makes up a significant portion of the intracranial content, plays a crucial role in maintaining this equilibrium. Comprising about 80% of the intracranial content, the cerebral parenchyma has a high-water content of 75% to 80%. The water is distributed between the intracellular space within the white and grey matter of the brain, as well as the

extracellular space known as the interstitial space. Additionally, CSF accounts for approximately 10% of the intracranial volume. Produced mainly by the choroid plexus, CSF is generated at a rate of 0.3 to 0.35 mL/min. The production of CSF can be influenced by various factors, including inflammation of the arachnoid villi and changes in ICP levels. Conditions such as diffuse cerebral edema or the presence of intracranial masses like hemorrhages or tumors can disrupt the normal production and circulation of CSF, leading to alterations in intracranial pressure. Understanding the intricate interplay between the brain, CSF, and cerebral blood flow is essential for managing conditions that affect intracranial pressure.⁵

When discussing ICP, it is common to focus on the average or static ICP measurement, overlooking the fact

that the ICP signal exhibits a pulsatile pattern that aligns with the heart's beating cycle. This dynamic nature of ICP manifests itself through three discernible peaks (P1, P2, P3) depicted in Figure 1, and comprehending these distinctive peaks is crucial for validating the precision of ICP signal capture. Further delving into the realm of ICP dynamics, the pressure fluctuations within each pulse, referred to as ICP pulse or wave pressure, are of notable importance, although they have been somewhat overshadowed by the emphasis on mean ICP pressure. Consequently, in the absence of specific indications to the contrary, discussions concerning ICP generally revolve around average ICP levels, underscoring the significance of acknowledging the multifaceted nature of intracranial pressure's behavior.⁶

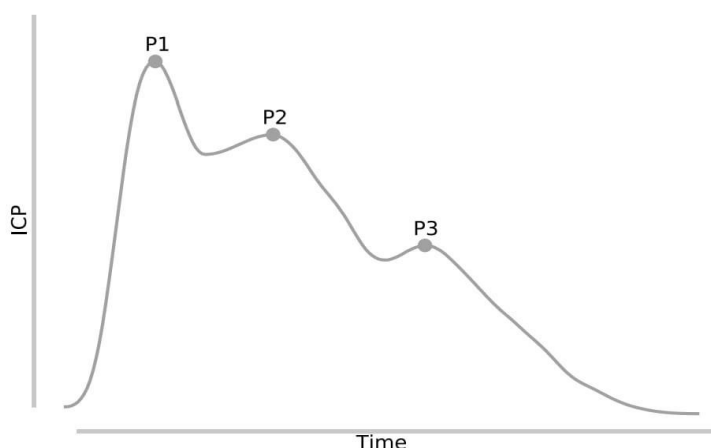


Fig. 1 An ICP pulse waveform, with three characteristic peaks: P1, P2, and P3

The blood supply, which is made up of the web of arteries and veins that carry blood to the brain, Parenchymal tissue, and cerebrospinal fluid (CSF) make up the intracranial space." Treating these parts as a closed system is possible since they are contained within an effectively stiff cranium. That being said, volume and pressure are correlated, therefore altering one of the two would alter the other's ICP proportionately. The hypothesis put forth by Monro and Kellie describes the connection between the intracranial component volumes and the ICP.⁷

A relationship known as the intracranial elastance curve [16–19] has been studied in several research involving ICP and volume. Within physiologically significant ranges, They discovered that an exponential function provides a good description of the elastance curve.

$$P = P_1 e^{(1) E_1 \cdot V}$$

where E_1 is the constant elastance coefficient V is the volume, P is the pressure, and P_1 is the pressure normalization coefficient. Fig. 2 illustrates this link. Volume expansions by one intracranial component can initially be complicated by variations in the volumes of the other components, especially when CSF or cerebral venous blood is displaced in TBI and stroke cases (area A in Fig. 2). The ICP, however, starts to rise quickly and

at an accelerated rate when this buffering capacity is depleted (area C in Fig. 2). The current capacity of the intracranial space to buffer is shown by the intracranial elastance $\Delta P / \Delta V$. As can be seen in region B of Fig., a normal ICP does not always imply that buffering has not previously been damaged, even if an elevated ICP often implies that the buffering capacity has been somewhat depleted.⁶

Since the brain's volume is usually fixed, the cerebral blood flow and the ratio of CSF generation to absorption or outflow are the two main factors influencing ICP. If one of these two components experiences an increase in volume without a corresponding drop in another, such as in the case of cerebral hemorrhage or an incapacity to effectively absorb or drain CSF, the net volume expansion that results will eventually raise ICP. cerebral hypertension⁶

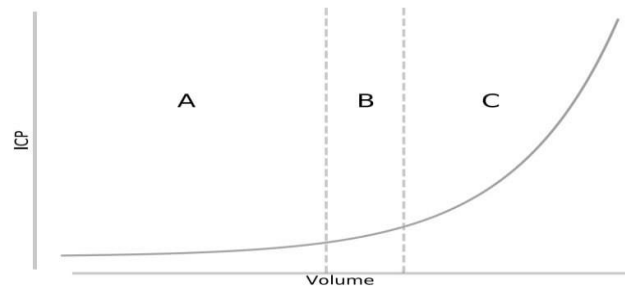


Fig. 2 The relationship between pressure and volume within the intracranial compartment. In region A, changes in the volume of one intracranial component can be buffered by changes in the volume of other components, resulting in minimal change in ICP. In region B, this buffering capacity is becoming exhausted, and ICP, though still within a normal range, begins to rise. Finally, in region C, the buffering capacity has been completely exhausted, and ICP rises rapidly at an accelerating rate in response to an increase in one or more intracranial components

There are compensatory mechanisms that allow for small volume expansions caused by the extrusion of venous blood or CSF, but when these buffering mechanisms are depleted, intracranial pressure (ICP) will rise quickly until it is equivalent to the pressure inside cerebral arterioles. The arterioles will start to collapse at this pressure, which is known as the critical closure pressure (CrCP), and blood flow to the brain will stop. According to the following relationship, the input pressure in the form of the mean arterial blood pressure (MAP), the intracranial pressure (ICP), and the cerebrovascular resistance (CVR) determines the cerebral blood flow (CBF) itself:⁶

$$CBF = \frac{MAP - ICP}{CVR}$$

A cascade of mechanisms usually operates for you to try and hold CBF in instances of elevated ICP; however, those mechanisms can in a few instances bring about a run away remarks loop that effects in intracranial hypertension and eventual cerebral ischemia. First, withinside the presence of raised ICP, distal cerebral arterioles go through vasodilation for you to decrease CVR in a try and of set the effects of growing ICP on CBF. If this isn't always sufficient to hold CBF, then arterial blood strain additionally increases. Both of those mechanisms have the effect of growing cerebral blood quantity and, consequently, in addition growing ICP, till a whole cessation of cerebral blood flow occurs. ICP monitoring is crucial in neuro-intensive care settings, as this scenario represents one of the main ways that subsequent ischemic brain injury can develop in the hours or days after a primary lesion.⁸

Causes of Raised intracranial pressure⁹:

Increased brain volume:

- A. Increased volume eg. Extradural haematoma
Eg. Subdural haematoma Eg. Brain tumor
Eg. Cerebral abscesses
Eg. Vascular malformation
- B. Brain oedema eg. Head injury
eg. Cerebral infection eg. Reyes syndrome eg.meningitis
Eg.Eclampsia

Eg. hypertensive encephalopathy Eg.lead encephalopathy

1. Increased CSF volume eg.Obstructive Hydrocephallus

Eg.non obstructive hydrocephalus Eg.choroid plexus papilloma

2. Increased blood volume eg. Increased haemmorage

Eg.sub-Archanoid haemmorage(SAH)

Invasive ICP monitoring methods:

There are two primary methods of invasive ICP monitoring that are considered gold standards: external ventricular drain (EVD) or intraparenchymal probe¹²

Intraventricular: this is the gold standard since it enables treatment of ICH in addition to being the simplest and most cost-efficient method. Following precoronal trepanation, the intraventricular device is placed ideally on the hemisphere with the most lesions visible in imaging studies, since an interhemispheric pressure gradient may exist. The main complication is infection, especially for catheters that remain inserted for more than 5 days (2%-22%). Tunnelling the catheter as far as possible from the incision site is recommended to minimise this risk¹³

Intraparenchymal: Unlike all other catheter systems, this one allows the catheter to be inserted bedside in the critical care unit. In addition to ICP, several of these sensors may provide clinicians with other types of data, like brain temperature. It has less difficulties and an insertion method very similar to that of an intraventricular catheter, however it cannot be used to drain CSF. To prevent harming the fiber optic transducer, experts advise recalibrating it as little as possible once it has been installed.¹

With an invasive ICP monitoring technique called external ventricular drainage (EVD), cerebrospinal fluid can be drained using a catheter inserted through a burr hole into one of the lateral ventricles. The EVD is coupled with a using a pressure transducer to detect pressure and furthermore to a drainage system that permits the elimination of CSF as required. At the

moment, EVD is thought to be the gold standard for ICP monitoring because, in part, that after insertion, they can be continuously recalibrated to prevent measurement drift and because the added benefit to clinical efficacy of doing Drainage of CSF.¹⁵

EVD is viewed as a relatively minor surgical procedure that poses minimal risk; however, there are a number of complications that can occur, namely hemorrhagic and infectious complications. A meta-analysis that included studies which were published after 1970 and which included greater than 25 ventriculostomy procedures found that out of a total of 1,790 procedures, 5.7% of cases resulted in hemorrhagic complications with 0.61% of the total resulting in clinically significant hemorrhages¹⁶

According to another study, of 188 patients with EVDs, 41% had postoperative hemorrhages. However, of these, 40 patients, the majority had trace, punctate, or insignificant hemorrhages, and of the bigger hemorrhages that remained, only one needed surgery.¹⁷

Pneumatic, strain gauge, and fiber optic sensors are the three types of microtransducer ICP monitors. These intraparenchymal probes have been shown to be just as precise as EVDs; however, in contrast to EVDs, they cannot be recalibrated after implantation, which may present a challenge because zero drift occurs.¹⁸

Nevertheless, some research has found significant differences in the mean ICP scores that are concurrently measured by two ICP sensors that are positioned close to one another to prevent intracranial pressure gradients from affecting them.¹⁹

NON-INVASIVE METHODS OF MONITORING INTRACRANIAL PRESSURE:

The advantages of noninvasive ICP monitoring techniques stem from the avoidable nature of consequences that may develop from invasive approaches, despite their rarity. Furthermore, a suitable method could eliminate the necessity for some of the more difficult features of the invasive measurement methods used today, namely their high cost and requirement for neurosurgery training to carry out the operation. An accurate, dependable, pathology-based noninvasive ICP measurement method would be ideal independent and able to work with a variety of patient populations, make use of easily accessible tools, and withstand systematic variations like operator experience⁶

According to the AAMI, noninvasive ICP measurement differences from invasive measurements of ± 2 mm Hg for ICP between 0 and 20 mm Hg and $\pm 10\%$ for ICP > 20 mm Hg are acceptable.²⁰

Different types of Non-Invasive ICP Monitoring methods

1. Transcranial doppler ultrasonography (TCD)
2. Two-depth ophthalmic artery Doppler ultrasonography (TDTD)
3. Dynamic MRI

4. Near-infrared spectroscopy (NIRS)
5. Tympanic membrane displacement (TMD)
6. Optic nerve sheath diameter (ONSD)
7. Optical coherence tomography (OCT)
8. Electroencephalography (EEG)
9. Electrophysiologic Visual evoked potentials (VEP)

Transcranial Doppler (TCD) ultrasonography was first described by Aaslid et al. in a groundbreaking study and has since evolved into a vital tool for measuring cerebral blood flow velocity (CBFV), predominantly in the middle cerebral artery, which is crucial for assessing cerebral hemodynamics. This non-invasive technique employs ultrasound waves to evaluate the speed of blood flow within the cerebral vessels, providing real-time data that is invaluable in both clinical and research settings. By analyzing the frequency shifts of the reflected ultrasound waves, clinicians can glean insights into various neurological conditions, such as stroke, vasospasm, and other disorders that affect cerebral perfusion. Furthermore, TCD ultrasonography has gained prominence due to its ability to monitor patients in critical care settings, enabling timely interventions that can significantly improve patient outcomes. As advancements in technology continue to enhance the precision and reliability of TCD measurements, its application is expanding, thereby solidifying its role as an indispensable tool in modern neurological assessment and management.²¹

In order to measure flow velocities in both the intracranial and extracranial segments of the ophthalmic artery (OA) simultaneously and apply external pressure to the surrounding tissues in a series of steps, the two-depth transorbital Doppler (TDTD) technique was developed by Ragauskas et al.²²

In their comprehensive study, Glick et al. meticulously examined the usefulness of this innovative MR imaging-derived technique for estimating intracranial pressure (ICP), focusing on a specific cohort of 26 symptomatic hydrocephalus patients. Their research aimed to assess the effectiveness of this non-invasive imaging method in predicting the resolution of elevated ICP, which is crucial in managing hydrocephalus without resorting to surgical interventions. The noteworthy findings of the study revealed that MR-derived ICP measurements were a strong predictor of whether patients would experience significant alleviation of elevated ICP levels, eliminating the need for more invasive procedures like shunt placement or ventricular drains. This breakthrough discovery has the potential to revolutionize the clinical approach to managing hydrocephalus by providing a safer, less invasive option for monitoring and treating this condition, thereby reducing the risks associated with surgery and improving patient outcomes. The implications of this research extend beyond immediate clinical applications, underscoring the increasing significance of advanced imaging techniques in

neurology and the continuous pursuit of innovative strategies to enhance patient care and treatment outcomes.²³

Reid A, Marchbanks R, Burge D, Martin A, Bateman D, Pickard J, et al. investigated the fascinating association between intracranial pressure and tympanic membrane displacement in their notable study published in the British Journal of Audiology in 1990. Their research shed light on the correlation between these factors, contributing valuable insights to the field.²⁴

Otoacoustic emissions (OAEs) are sounds generated by the inner ear in response to a loud sound, which can be evoked using a number of techniques.²⁵ The magnitude of these OAEs has been shown to be sensitive to changes in ICP.²⁶

Near-infrared spectroscopy (NIRS) is a non-invasive optical technique that holds the capability to estimate dynamic changes in cerebral blood volume by detecting alterations in the local levels of oxygenated hemoglobin within the blood, providing valuable insights into cerebral perfusion and metabolic activity.²⁷

Optical coherence tomography (OCT) is an imaging technique that acts effectively as an “optical ultrasound” and can be used to measure retinal nerve fiber layer (RNFL) thickness in papilledema. Intracranial hypertension can result in swelling of the RNFL. A patented method exists that uses OCT to measure RNFL thickness and thereby infer ICP values.²⁸

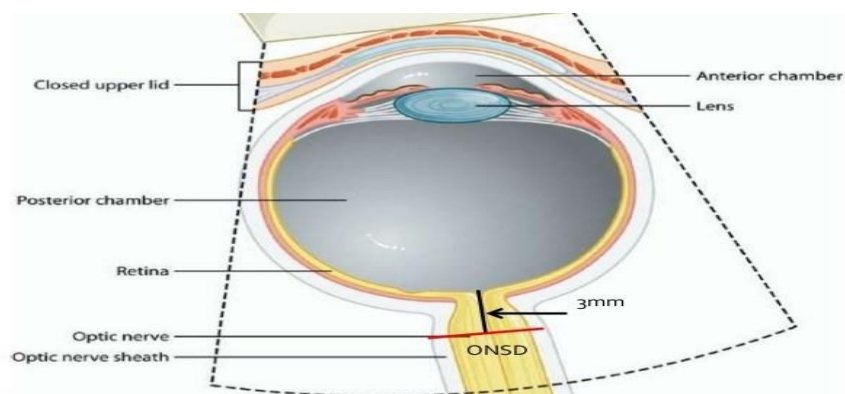
OPTIC NERVE SHEATH DIAMETER:

The eye is considered an optimal configuration for ultrasound imaging due to its superficial location and the clear delineation of its fluid-filled structures, making it an excellent medium for the transduction of ultrasound beams. To proficiently conduct optic nerve sheath ultrasound (ONSUS), it is necessary to possess a fundamental comprehension of ocular anatomy. Being able to identify and distinguish anterior structures within the eye not only enhances the accuracy of measurements but also significantly improves the chances of

successfully capturing the optic nerve sheath in the appropriate plane, thus aiding in diagnostic evaluations and clinical assessments.

Within the intricate network of the ocular anatomy, the eyeball finds its place nestled tenderly in the protective embrace of the Tenon capsule, a membranous sac. This holding structure, reinforced by a combination of periocular fat, soft tissues, and the robust walls of the orbit, secures the eyeball seamlessly. Its anchorage is established through the corneoscleral junction and the connection to the optic nerve, while the dynamic interplay of extraocular muscle tendons, which penetrate the Tenon sac to affix themselves onto the sclera, enables versatile movements of the eyeball along numerous axes. Immersed within this complex framework are notable fluid-filled compartments essential for examination – the anterior chamber (AC) and posterior chamber (PC). These chambers, demarcated by the lens, feature an uncanny resemblance in both hosting anechoic fluid. Beyond the confines of the PC lies the retina, characterized by the presence of a notable hyperechoic nervous membrane that encapsulates the essence of visual perception.²⁹ Posterior to the retina and optic disc, within the eye anatomy, lies the optic nerve, distinguishable by its characteristic features in ultrasound imaging. This nerve is characterized by an anechoic core surrounded by hyperechoic sheath on its medial and lateral aspects in the transverse view. Functionally, the optic nerve can be visualized as an extension of the brain tissue, enclosed by protective layers of dura, arachnoid, and pia mater in its intraorbital course. This unique encapsulation allows the optic nerve sheath to accommodate cerebral spinal fluid and respond dynamically to changes in intracranial pressure. The meningeal covering of the optic nerve maintains continuity with the dural and subarachnoid spaces, contributing to its structural integrity. Notably, the bulbar segment of the optic nerve, located about 3 mm behind the eye, exhibits great distensibility and is particularly sensitive to alterations in intracranial pressure, as evidenced by studies using in-vivo and cadaveric models of elevated ICP.³⁰

Figure3=Optic Nerve Sheath Diameter



The upper limit of the normal ONSD includes

- 4 mm in infants.
- 5 mm in children.
- 5 mm in adults.

ONSD shows linear increment till 7.5 mm, after which it plateaus off.³¹:

ONSUS is usually performed in the setting of suspected or confirmed traumatic brain injury (TBI), intracranial hypertension, or optic neuritis.³² The ONSUS procedure stands out for its non-invasive nature, effectively sidestepping the potential risks associated with invasive methods such as infection, hemorrhage, and exposure to ionizing radiation, which are commonly encountered with intracranial monitors and computed tomography (CT) scans.³³

In addition to its use in helping to “rule out” elevated intracranial pressure (ICP) in non-acute trauma settings, ONSUS can also prove beneficial in scenarios like troubleshooting anomalies in intraventricular devices, both pre and post lumbar punctures, and in assessing the appropriateness of neuraxial anesthesia in patients with prior elevated ICP episodes. Importantly, it is crucial to bear in mind that these readings must always be assessed within the broader clinical framework due to the lack of extensive research and validation in these specific applications.⁴³

The intracranial pressure (ICP) can be computed by applying the formula for optic nerve sheath diameter (ONSD), where the calculated value nICPONSD equals 5.00 multiplied by the ONSD measurement, subtracting 13.92 mmHg from the result.³⁵ After carefully applying a sterile dressing to cover the closed eye and generously applying ultrasound gel, the next step involves gently placing the high-frequency ultrasound transducer over the eye. It is crucial to ensure minimal contact between the transducer and the sterile dressing in a transverse orientation. Additionally, the sonographer must position their hand on a non-compressible surface, such as the patient's nose, midface, or forehead, to prevent direct pressure on the globe, avoid causing discomfort, and maintain the anatomical structure's integrity. Delicate movements in different directions nasally, temporally,

caudally, and cephalad are essential to accurately capture the optic nerve sheath in alignment with the anterior chamber (AC), posterior chamber (PC), and lens, thus preventing any obliquity in the imaging. As soon as the anechoic streak posterior to the optic disc becomes visible, it is essential to capture the image promptly and proceed with taking measurements from the saved image. Notably, due to the optic nerve's relatively cylindrical and symmetric nature, obtaining a clear view from a single angle is typically adequate for precise measurements.³⁶

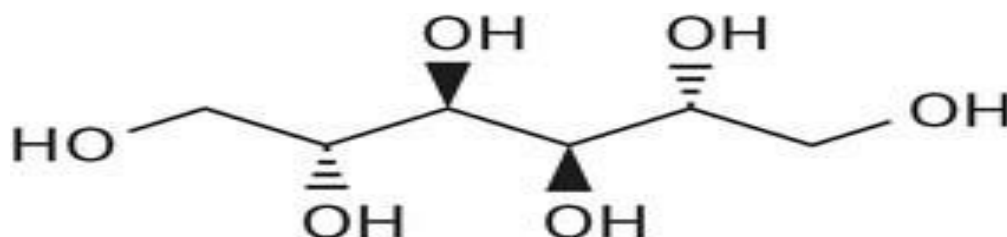
Once the optic nerve sheath diameter is determined in a clinical setting, it is essential to consider it within the broader clinical picture. Previous studies have often utilized a cutoff of 5.0 mm, which has shown excellent sensitivity and predictive values. However, the specific cutoffs indicating elevations in intracranial pressure (ICP) above 20 mm Hg have varied among studies, ranging from less than 5 mm to greater than 6 mm. In a comprehensive meta-analysis of 12 studies comparing optic nerve sheath measurements to computed tomography (CT) findings of increased ICP, the specificity was determined to be 92.3% and the sensitivity was 95.6%, using a 5 mm cutoff for adult patients.³⁷

Utilizing A-mode scan is strongly recommended due to the presence of the 'blooming' artifact in B-mode scan imaging. Despite this, it is simple to determine a specific distance on the optic nerve located behind the eyeball using B-mode scan. Moreover, the B-mode scan proves to be convenient for evaluating non-compliant patients efficiently and effectively.³⁸

MANNITOL:

Mannitol, a sugar alcohol derived from mannose sugar, plays a vital role in the management of patients suffering from elevated intracranial pressure (ICP). By effectively reducing brain swelling, mannitol helps alleviate the dangerous pressure within the skull. Its mechanism involves drawing excess fluids out from cells and tissues through osmotic processes, thus increasing plasma osmotic pressure and potentially decreasing ICP levels via induced diuresis.³⁹

Fig no.4 chemical structure of Mannitol



Mannitol, by creating an osmotic pressure differential across the blood-brain barrier (BBB), induces the flow of water from the cerebral tissue into the circulatory system. Consequently, this process triggers brain desiccation and subsequently lowers intracranial pressure (ICP). Normally, the osmolality within brain tissues is marginally higher compared to that in the serum, resulting in an approximate blood-brain osmotic gradient of 3 mOsm/kg. Nonetheless, the administration of mannitol markedly elevates serum osmolality, effectively reversing the osmotic gradient and prompting the migration of moisture from the brain parenchyma into the blood vessels. This action ultimately mitigates cerebral edema by facilitating the reduction of water content within the brain region.³⁹

Mannitol serves as a valuable contributor to the regulation of intracranial pressure (ICP) by targeting blood viscosity reduction among its effects. This critical function intertwines with the regulation of four key factors driving blood viscosity levels: plasma viscosity, hematocrit, red blood cell aggregation, and red blood cell deformability. The multifaceted approach of mannitol in lowering ICP involves several mechanisms, of which the reduction in blood viscosity plays a significant role. Research has evidenced mannitol's efficacy in decreasing blood viscosity by specifically impacting hematocrit levels, mean corpuscular volume (MCV), and enhancing the deformability of red blood cells.⁴⁰

Mannitol has the capability to cause vasoconstriction in the cerebral blood vessels, resulting in a decrease in blood volume within the brain. This reduction in blood volume subsequently leads to a further decrease in intracranial pressure (ICP).⁴¹

The most concerning complications of mannitol administration are acute kidney injury (AKI) and electrolyte disturbances. Specifically, the risk of AKI is closely associated with the upper limit of the mannitol dosage administered. Although there was a prior belief that mannitol could prevent postoperative AKI by increasing renal blood flow, subsequent studies have contradicted this notion. Instead, AKI tends to occur when the rate of mannitol administration surpasses the urinary excretion rate. Animal experiments and histological examinations have revealed that the renal complications observed, such as acute tubular necrosis and swelling in proximal renal tubules, are more likely to manifest when high doses of mannitol (ranging from 1.8 to 2.1 g/kg) are consistently used over time.³⁹

High-quality evidence demonstrating the optimal mannitol dose is regrettably lacking in the medical field. It is important to note that low doses of mannitol, specifically amounts less than 0.5 g/kg, pose challenges related to limited efficacy and persistent effects. Conversely, administering high doses exceeding 1.5 g/kg may result in complications such as nephrotoxicity, underscoring the necessity for caution. Thus, the recommended dose falls within the range of 0.5–1.5

g/kg, aligning with the established best practices. Nevertheless, during critical scenarios necessitating immediate neuro-resuscitation in response to intracranial pressure crises, the temporary implementation of a higher dosage of at least ≥ 1.5 g/kg is advisable. It is essential to maintain vigilance in suspected cases of escalating ICP by carefully adjusting the dosage through iterative administrations ranging from 0.25–1.5 g/kg while consistently monitoring ICP levels, ensuring a prompt response evaluation following mannitol administration.³⁹

In their study, Dorman and colleagues observed 8 patients who developed mannitol-induced acute kidney injury (AKI) and established a clear association between AKI and the osmolar gap (OG), a parameter that indirectly reflects blood mannitol concentration. They noted that when the blood concentration of mannitol falls below 1,000 mg/dL, there is a notable reduction in renal microvascular resistance accompanied by an increase in renal blood flow. However, once the blood concentration of mannitol reaches or surpasses 1,000 mg/dL, it triggers renal microvessel constriction, contributing to ischemic renal injury. Remarkably, the researchers found that in all AKI cases, except for one patient, the OG exceeded 55, which correlated with the critical 1,000 mg/dL threshold. This data underscores the importance of monitoring OG levels in patients exposed to mannitol as a preventive measure against the development of AKI associated with hypermannitolism.⁴²

3% HYPERTONIC SALINE:

Hypertonic saline should be discontinued once the patient's symptoms improve or they have an adequate increase in serum sodium level. It is crucial to consider the management of cerebral edema and elevated intracranial pressure (ICP) as significant factors contributing to morbidity and mortality in a variety of neurological conditions, such as intracranial tumors, cerebral hematomas, traumatic brain injuries, cerebral infarcts, and intracranial hemorrhages. The mechanism of action of hypertonic saline involves an increase in the blood osmolality, which facilitates the movement of fluid from the extravascular space into the intravascular space. This process results in a reduction of brain edema, enhancement of cerebral blood flow, and a decrease in cerebrospinal fluid (CSF) production. Noteworthy research findings indicate that the administration of 3% hypertonic saline exhibits comparable efficacy in reducing ICP to that of 20% mannitol.⁴³

Hypertonic fluids are characterized by their elevated solute concentration in comparison to plasma and interstitial fluid. This disparity sets up an osmotic gradient, compelling fluid movement from the interstitial compartment to the intravascular space. As this shift occurs, there is a notable escalation in intravascular volume, contributing to heightened mean

arterial pressure (MAP), increased stroke volume (SV), and augmented cardiac output (CO) when juxtaposed with equivalent quantities of standard saline or other isotonic solutions.⁴⁴ Hypertonic saline, when introduced into the body, triggers a physiological response by stimulating the release of vasopressin (VP) from the pituitary gland. This hormone acts on the kidneys to reduce water loss through a process known as antidiuresis. By increasing the concentration of solutes in the blood, hypertonic saline effectively alters the osmotic gradient, prompting the kidneys to reabsorb more water and concentrate the urine. Ultimately, this mechanism helps to maintain fluid balance in the body and prevent excessive dehydration.⁴⁵ Hypertonic saline is generally well-tolerated with few adverse effects, primarily linked to prolonged infusion rather than bolus administration. One potential side effect stems from hyperchloremic metabolic acidosis resulting from sodium chloride addition, while prolonged use may lead to hyponatremia. Additionally, rapid correction of severe hyponatremia can trigger osmotic demyelination syndrome. Thus, healthcare providers must carefully monitor patients receiving hypertonic saline to preemptively address these potential complications and ensure safe administration of the treatment.⁴⁴

Mannitol and HTS combination:

In certain clinical scenarios, healthcare providers may find it necessary to administer both mannitol and HTS, which could be a course of action taken when facing challenges such as refractory increased intracranial pressure that fails to respond to mannitol treatment alone or situations where adjusting the mannitol dosage is warranted based on specific blood test findings. However, the collective effectiveness and safety profile of concomitant mannitol and HTS administration are not definitively established. Notably, the development of acute kidney injury (AKI) poses a significant concern in these contexts, as both mannitol and HTS have the potential to trigger AKI through distinct pathological mechanisms.³⁹

Narayan et al. conducted a study affirming that the concurrent administration of mannitol and HTS showed no escalated incidence of renal injury when compared to sole HTS treatment in traumatic brain injury patients. It is essential to acknowledge that despite these findings, there remains inadequate substantiation regarding the overall effectiveness and safety associated with the simultaneous utilization of these pharmacological agents. Consequently, a prudent approach is recommended in situations where both substances are used concurrently until further comprehensive investigations are conducted to elucidate the potential benefits and risks associated with their combined application.⁴⁶

DECOMPRESSIVE CRANIOTOMY(DC):

Decompressive Craniotomy (DC) is a surgical procedure commonly employed to alleviate elevated intracranial pressure refractory to standard treatments. The etiology of intracranial hypertension varies widely, leading to a diverse literature base on the applicability of this intervention. Historically, DC has predominantly been used in cases of Traumatic Brain Injury (TBI), middle cerebral artery (MCA) infarction, and aneurysmal subarachnoid hemorrhage (SAH). However, while recent reports increasingly favor DC, debates persist regarding its appropriateness and the criteria for patient selection. Although the bulk of existing studies are retrospective in nature, the emergence of several randomized prospective trials necessitates a fresh evaluation of DC's utility.⁴⁷

Our examination of the literature concerning DC in TBI, MCA infarction, and SAH centres on addressing prevalent queries related to the timing and laterality of the procedure. Presently, the data remains inconclusive to unequivocally advocate for the routine use of DC in TBI, stroke, or SAH. Current evidence suggests that prompt and bold implementation of DC in well-functioning patients could potentially enhance outcomes. Nevertheless, the assertion that DC should be routinely performed in such cases is disputed.⁴⁷

It is recommended that the decision to proceed with DC be made on a case-by-case basis, with an in-depth discussion around its potential long-term impact on outcomes involving the patient's healthcare provider. Ultimately, a personalized approach to the indication for DC is deemed most appropriate, considering the complexities and uncertainties that persist in the existing body of knowledge related to this intervention.⁴⁷

In the absence of supporting evidence for the routine use of secondary decompressive craniectomy (DC) in adults with severe traumatic brain injury (TBI) and refractory high intracranial pressure (ICP), the pediatric population stands out where DC has shown to reduce mortality and unfavorable outcomes. Despite the limitations of wide confidence intervals and small sample size in the sole identified study, the consideration of this intervention can be warranted for patients under 18 years of age when traditional medical management fails to manage ICP effectively. While there is a current lack of randomized trial results to validate or challenge the efficacy of DC in adult patients, findings from non-randomized trials and controlled studies with historical controls in adults indicate that DC could be a viable alternative after exhausting maximal medical interventions to control ICP. Presently, ongoing randomized controlled trials such as Rescue ICP and DECRAN offer the potential for additional insights into the effectiveness of decompressive craniectomy in adults, paving the way for clearer conclusions regarding the utility of this procedure in clinical practice.⁴⁸

OBJECTIVE:

Primary objective:

1. To assess reduction in optic nerve sheath diameter (ONSD) with mannitol and 3% hypertonic Saline.

Secondary objective:

1. To calculate the length of hospital days.
2. To calculate mortality rate.
3. To calculate no. of people undergoing decompressive craniotomy surgery

REVIEW OF LITERATURE:

In-jung jun et al(2018), Analyses were performed on a total of 36 patients to investigate changes in optic nerve sheath diameters (ONSDs). The findings revealed a notable decrease in ONSDs at T2, T3, and T4 as compared to baseline measurements at T1. The difference was statistically significant ($p < 0.001$), with measurements showing a reduction from 4.81 ± 0.3 mm at T1 to 4.46 ± 0.2 mm at subsequent time points. Additionally, intriguing observations were made during pneumoperitoneum and in the Trendelenburg position, where there were discernible variations in mean arterial blood pressure and heart rate. However, no significant differences were observed in regional cerebral oxygen saturation, cardiac output, corrected flow time, peak velocity, body temperature, arterial CO₂ partial pressure, peak airway pressure, plateau airway pressure, dynamic compliance, or static compliance in this patient cohort.⁴⁹

Yoan, Launey, et al. (2014) conducted analyses on a cohort comprising 36 patients. The investigation revealed a significant decline in optic nerve sheath diameters (ONSDs) at time points T2, T3, and T4 compared to baseline (T1), with measurements showing a marked difference (4.46 ± 0.2 mm vs. 4.81 ± 0.3 mm, $p < 0.001$). Of particular note, alterations in mean arterial blood pressure and heart rate were observed during pneumoperitoneum and while in the Trendelenburg position. However, no substantial variations were noted in regional cerebral oxygen saturation, cardiac output, corrected flow time, peak velocity, body temperature, arterial CO₂ partial pressure, peak airway pressure, plateau airway pressure, dynamic compliance, or static compliance in the study's parameters.⁵⁰

Huda fahmy et al, In this prospective, double-blind, randomised, observational, and comparative study, a total of 30 patients who were hospitalised in the surgical intensive care unit at Aswan University Hospital with severe traumatic brain injury were included. To assess intracranial pressure (ICP), all patients underwent ultrasound examination to measure the optic nerve sheath diameter (ONSD), with a defined cut-off value of 5.5 mm indicating an ICP elevation of more than 20 mm Hg. Subsequently, patients exhibiting signs of increased ICP were allocated into two distinct groups: Group A was treated with Mannitol 20% at a dosage of

0.5 gm/kg (2.5 ml/kg) every 6 hours intravenously for 48 hours, while Group B received hypertonic saline 3% at a dosage of 3 ml/kg every 6 hours, administered intravenously over a 48-hour period. The analysis of the ONSD values in the hypertonic saline and Mannitol groups revealed statistically significant findings, indicating the efficacy of the treatment approaches in managing raised ICP.⁵¹

Shiva p paudyal et al (2013) This study presents prospective cohort-based observational research involving 40 patients who were admitted to our adult ICU with traumatic brain injury (TBI), acute stroke, or cerebral hemorrhages. The patients included in the study had a mean screening optic nerve sheath diameter (ONSD) greater than 5mm and were undergoing mannitol osmotherapy. The measurement of the ONSD was conducted during screening using a high-frequency linear array probe with a frequency of over 10 Hz. Following the ONSD measurement, mannitol was administered intravenously over a period of 20-30 minutes through a dedicated line, with the specific dosages determined by the attending physician. Subsequent ONSD evaluations were performed at intervals of 30, 60, and 120 minutes post-mannitol administration. Data collected at each time point included demographic information, baseline ventilator parameters for mechanically ventilated patients, Glasgow Coma Scale (GCS) scores, and mean arterial pressure. Throughout the study, comparisons were made regarding these parameters at the specified time points to evaluate the effects of mannitol osmotherapy on patients with TBI, acute stroke, or cerebral hemorrhages.⁵²

Dina hassan Zidan et al,(2019),; In this prospective study, a total of 50 adult patients who had suffered from brain edema due to ischemic infarction along the middle cerebral artery territory participated. These patients were divided into two groups for treatment comparison. Group A consisted of twenty-five patients who were administered intravenous mannitol 20%, while Group B comprised twenty-five patients who received intravenous hypertonic saline 3%. Throughout the study, intracranial pressure was monitored using non-invasive methods, such as CT scans of the brain conducted at the initiation of hyperosmolar therapy and after 48 hours. Additionally, the Glasgow Coma Score (GCS) was regularly assessed every 6 hours over a 48-hour period, and optic nerve sheath diameter (ONSD) was measured twice: initially upon the diagnosis of brain edema and again after 48 hours of receiving hyperosmolar therapy. The results revealed that patients treated with hypertonic saline exhibited higher GCS scores, while those who underwent this treatment showed a significant decrease in ONSD.⁵³

AL hassani et al,(2020),This prospective study, involving 50 adult patients suffering from brain edema caused by ischemic infarction in the middle cerebral artery territory, aimed to compare the effectiveness of

two treatment methods. Patients were divided into two groups: Group A, comprising twenty-five patients who received intravenous mannitol 20%, and Group B, consisting of another twenty-five patients treated with intravenous hypertonic saline 3%. To monitor intracranial pressure non-invasively, brain CT scans were conducted at the beginning of hyperosmolar therapy and 48 hours later. Additionally, the Glasgow Coma Score (GCS) was regularly assessed every 6 hours over the next 48 hours. Optic nerve sheath diameter assessment (ONSD) was also performed twice: initially at the time of brain edema diagnosis and then again after 48 hours of continued hyperosmolar therapy. The results indicated a higher GCS among patients treated with hypertonic saline, while ONSD measurements were significantly lower in this group compared to patients receiving mannitol infusion.⁵⁴

Sima patel et al,(2020); In this prospective study, a total of 50 adult patients who experienced brain edema due to ischemic infarction along the middle cerebral artery territory were enrolled. These patients were then divided into two groups for treatment comparison. Group A, comprising twenty-five patients, received intravenous mannitol 20%, while Group B, also consisting of twenty-five patients, was administered intravenous hypertonic saline 3%. The study monitored intracranial pressure through non-invasive methods, including CT scans of the brain at the onset of hyperosmolar therapy and after 48 hours. Additionally, the Glasgow Coma Score (GCS) was regularly evaluated every 6 hours for a duration of 48 hours. Furthermore, the optic nerve sheath diameter assessment (ONSD) was conducted twice: initially at the time of brain edema diagnosis and then again after 48 hours of continuous hyperosmolar therapy. The results of the study indicated that patients treated with hypertonic saline exhibited higher GCS levels, while those undergoing this treatment showed a significant decrease in ONSD.⁵⁵

Amr Samir wahdan et al,; In this prospective study, a total of 50 adult patients who had brain edema due to ischemic infarction along the territory of the middle cerebral artery were included. These patients were split into two groups for treatment. Group A consisted of twenty-five patients who received intravenous mannitol 20%, while Group B comprised twenty-five patients who were administered intravenous hypertonic saline 3%. Monitoring of intracranial pressure was conducted non-invasively through various methods: CT scans of the brain were performed at the initiation of hyperosmolar therapy and after 48 hours, Glasgow Coma Scores (GCS) were regularly checked every 6 hours for 48 hours, and optic nerve sheath diameter assessments (ONSD) were conducted twice - initially at the time of brain edema diagnosis and then 48 hours later after receiving continuous hyperosmolar therapy. The study results indicated that patients who received hypertonic saline had higher GCS scores and significantly lower ONSD measurements compared to

those treated with intravenous mannitol.⁵⁶

Mirski et al(2000),; This prospective study involved a cohort of 50 adult patients who had developed brain edema due to ischemic infarction along the territory of the middle cerebral artery. These patients were split into two groups for treatment: Group A consisted of twenty-five individuals who received intravenous mannitol 20%, while Group B included twenty-five patients treated with intravenous hypertonic saline 3%. To monitor intracranial pressure, non-invasive methods were utilized. This included performing a CT scan of the brain at the initiation of hyperosmolar therapy and again after 48 hours. Additionally, the Glasgow Coma Score (GCS) was regularly evaluated every six hours over a 48-hour period. Optic nerve sheath diameter assessment (ONSD) was conducted twice: first at the time of brain edema diagnosis and then 48 hours later following the continuation of hyperosmolar therapy. The study results indicated that patients treated with hypertonic saline showed higher GCS scores and had significantly lower ONSD measurements compared to those receiving other treatments.

METHODOLOGY:

Study design:

This was a prospective observational study.

Study site:

This study was conducted in general medicine, intensive care unit Bangalore Baptist hospital.

Study period:

This study was conducted during a period of 6 months

Study Population:

Study criteria:

Inclusion criteria:

- Patients with increased intracranial pressure
- Patients who had treated with mannitol
- Patients treated with 3% Hypertonic saline
- Patients treated with combination of mannitol and 3% Hypertonic saline.

Exclusion criteria:

- Pediatric patients were not included in the study.
- Patient on chemotherapy were not included in the study.
- Pregnant patients were not included in the study.

Patient and diagnosis criteria:

A total of 30 patients with increased intracranial pressure diagnosed with subarachnoid, hemorrhage, epidural hemorrhage, Hypertensive intracranial bleeding, Traumatic Brain injury, Capsulo-ganglionic Bleed, Obstructive Hydrocephalus Ischemic Infarct, Sub-dural hemorrhage.

Sources of data and materials:

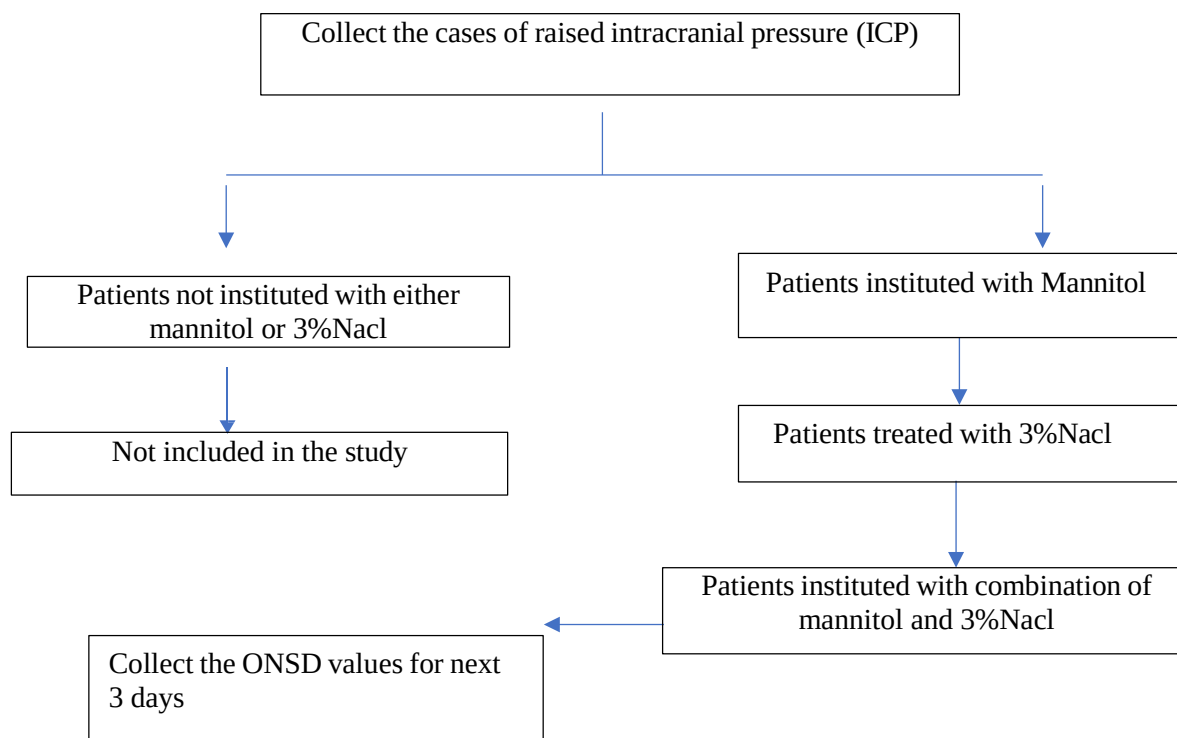
- Patient profile form
- Medication chart
- Scanning Reports
- Lab reports
- MRD

Method of collection of data:

A total of 30 Patients with increased intracranial pressure was included in the study. Data are collected from patient profiles forms, medication charts, scanning reports and laboratory reports. For the next 3 days medication charts will be evaluated and ONSD values from the chart will be collected.

Study Procedure:

- This prospective observational study is conducted in the ICU, in patients who had a increased intracranial pressure.
- This study involves measurement of intracranial pressure (ICP) by ultrasonographic measurement of optic nerve sheath diameter (ONSD) of both eye as a surrogate measure, of ICP.
- Different cases with raised intracranial pressure were included in the study.
- Only patients with who are treated with mannitol or 3%NaCl or combination of both are included in the study.
- ONSD values are collected are for next three days after instituting with either mannitol or 3%NaCl, or combination of both.



Study Outcome:

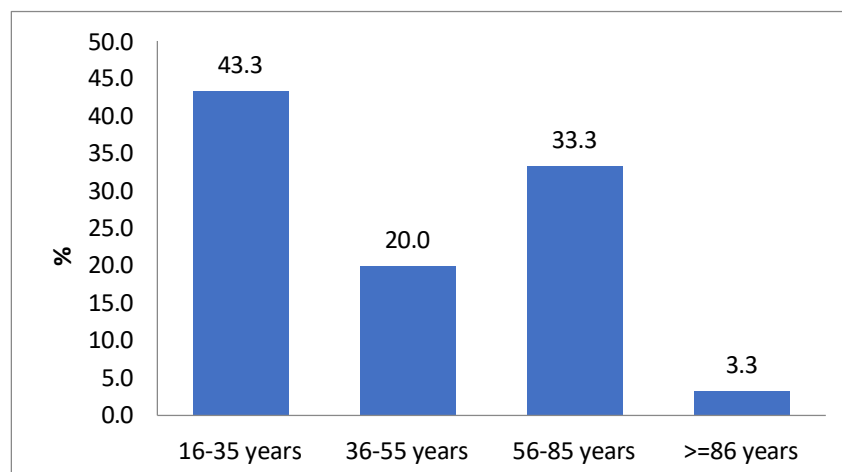
Reduction of ONSD of both eye as measure of ICP after instituting the mannitol and/or 3%NaCl or combination of both will be assessed. Demographics of the study population will be estimated. Along with it, number days patient was admitted will be calculated and number of patients undergoing decompressive craniectomy and mortality rate will be calculated.

RESULTS:

Table 1: Distribution based on age

		Frequency	Percent
Age	16-35 years	13	43.3
	36-55 years	6	20.0
	56-85 years	10	33.3
	>=86 years	1	3.3
	Total	30	100.0

Figure 5: Distribution based on age

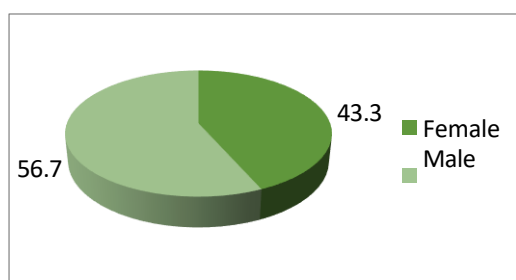


The age distribution of the participants shows that 43.3% were between 16-35 years, 20.0% were between 36-55 years, and 33.3% were between 56-85 years. A smaller proportion, 3.3%, were aged 86 years or older. The total sample size was 30 participants, accounting for 100.0%.

Table 2: Distribution based on gender

		Frequency	Percent
Gender	Female	13	43.3
	Male	17	56.7
	Total	30	100.0

Figure 6: Representation of gender



Based on the table, there are 30 individuals in the sample. Of these, 13 are female, representing 43.3% of the total sample, while 17 are male, representing 56.7% of the total sample.

Table 3: Distribution based on Diagnosis

	Frequency	Percent
ACUTE ON CHRONIC SUB-DURAL HEMORRHAGE	1	3.3
ACUTE SAH RIGHT CEREBRAL HEMISPHERE	1	3.3
ACUTE SUB-ARACHNOID HEMORRHAGE	2	6.7
ACUTE SUBARACHNOID HEMORRHAGE IN CEREBRAL SULCAL SPACES OF BILATERAL HIGH FRONTAL AND PARIETAL REGION	1	3.3
ANEURYSMAL BLEED	1	3.3
BILATERAL SUB-ARACHNOID HAEMMORAGE	2	6.7
CAPSULO-GANGLIONIC BLEED	2	6.7
CEREBELLITIS	1	3.3
CEREBRAL INFRACT WITH HEMORRHAGE	1	3.3
CHRONIC SUBDURAL HEMORRHAGE POST SURGERY	1	3.3
CONTUSION	1	3.3
DIFFUSE AXONAL INJURY	2	6.7
DIFFUSE CEREBRAL OEDEMA	1	3.3
DURAL VENOUS SINUS THROMBOSIS	1	3.3
FRONTO-PARIETAL SUB-ARACHNOID HAEMMORAGE	1	3.3
HERNIATION	1	3.3
HYDROCEPHALUS	1	3.3
HYPERTENSIVE BLEEDING	1	3.3
HYPERTENSIVE INTRA-CRANIAL BLEED IN RIGHT MID BRAIN	1	3.3
HYPERTENSIVE INTRACRANIAL BLEEDING	1	3.3
INTRACRANIAL BLEED-LEFT GANGLIO CAPSULAR BLEED	1	3.3
INTRAVENTRICULAR HEMORRHAGE	1	3.3
LEFT SUB-DURAL HEMORRHAGE	2	6.7
LEFT TEMPORAL SUBDURAL HEMATOMA	1	3.3
LRTI	1	3.3
MIDDLE CRANIAL ARTERY INFRACT	1	3.3
MID-LINE SHIFT	1	3.3
MILD HYDROCEPHALUS	2	6.7
MULTIPLE HEMORRHAGIC CONTUSIONS IN BILATERAL FRONTOTEMPORAL LOBES	1	3.3
MULTIPLE HEMORRHAGIC CONTUSIONS IN BILATERAL FRONTOTEMPORAL LOBES	1	3.3
OBSTRUCTIVE HYDROCEPHALUS	1	3.3
RIGHT FRONT PARIETAL BURR HOLE	1	3.3
RIGHT INTRACRANIAL HEMORRHAGE	1	3.3
RIGHT SIDE EPIDURAL HEMORRHAGE	1	3.3
SEVERE TRAUMATIC BRAIN INJURY-	1	3.3

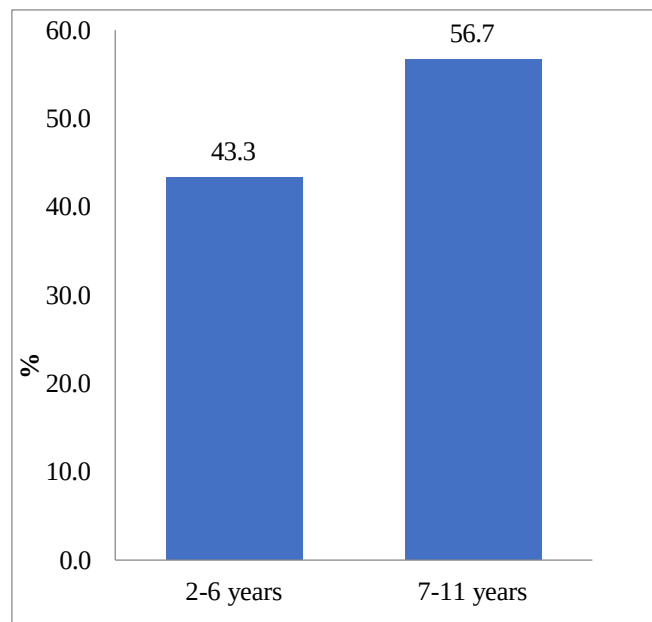
SMALL ISCHEMIC INFRACT	1	3.3
SUB ARACHNOID HEMORRHAGE	5	16.7
SUB FALCINE HERNIATION	1	3.3
SUBARACHNOID HEMORRHAGE	4	13.3
SUB-DURAL HEMORRHAGE	2	6.7
TRAUMATIC BRAIN INJURY	1	3.3
TRAUMATIC BRAIN INJURY - RIGHT TEMPORAL CONTUSION	1	3.3
SUBACUTE INFRACT	1	3.3

The most common intracranial hemorrhage types in this sample were subarachnoid hemorrhage (16.7%), followed by subarachnoid hemorrhage in the cerebral sulcal spaces of bilateral high frontal and parietal regions (13.3%), and subdural hemorrhage (6.7%).

Table 4: Distribution based on length of hospital stay.

Duration	Frequency	Percent
2-6 days	13	43.3
7-11 days	17	56.7
Total	30	100.0

Figure 7: Representation based on duration of hospital stay

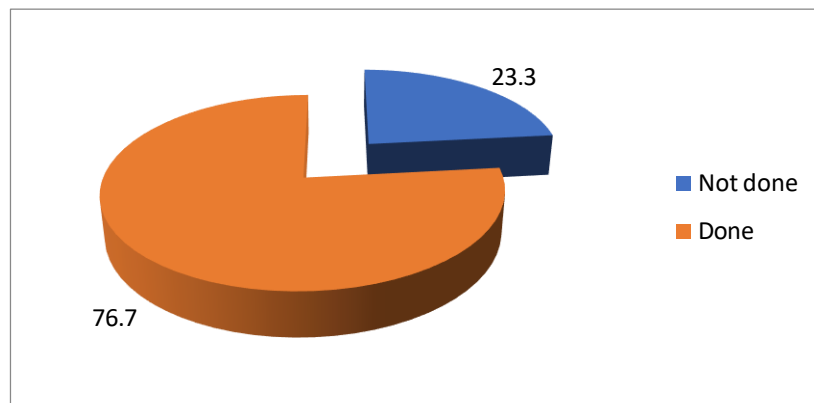


The table shows the distribution of duration of hospital stay, the majority of individuals (56.7%) had a duration of 7-11 days, while 43.3% had a duration of 2-6 days.

Table 5: Distribution based on CRANIOTOMY.

		Frequency	Percent
CRANIOECTOMY	Not done	7	23.3
	Done	23	76.7
	Total	30	100.0

Figure 8: Representation based on CRANIOTOMY

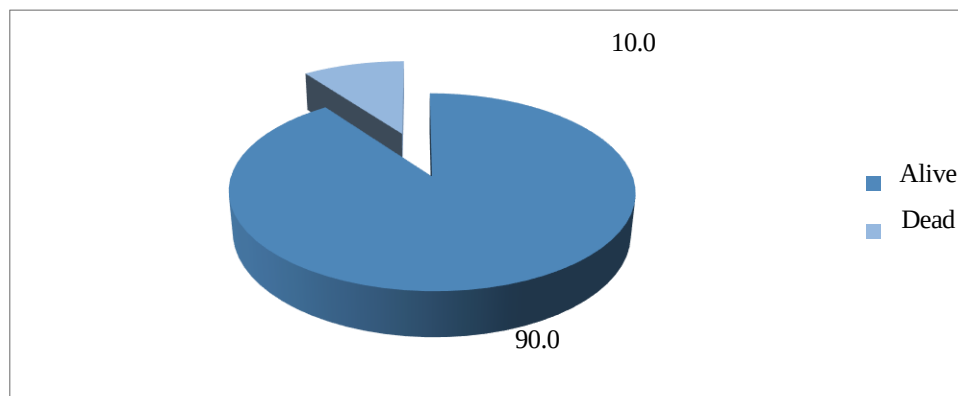


The table shows the distribution of craniotomy performance for a sample of 30 individuals. The majority of individuals (76.7%) underwent craniotomy, while 23.3% did not.

Table 6: Distribution based on mortality

		Frequency	Percent
Mortality	Alive	27	90.0
	Dead	3	10.0
	Total	30	100.0

Figure 9: Distribution based on mortality

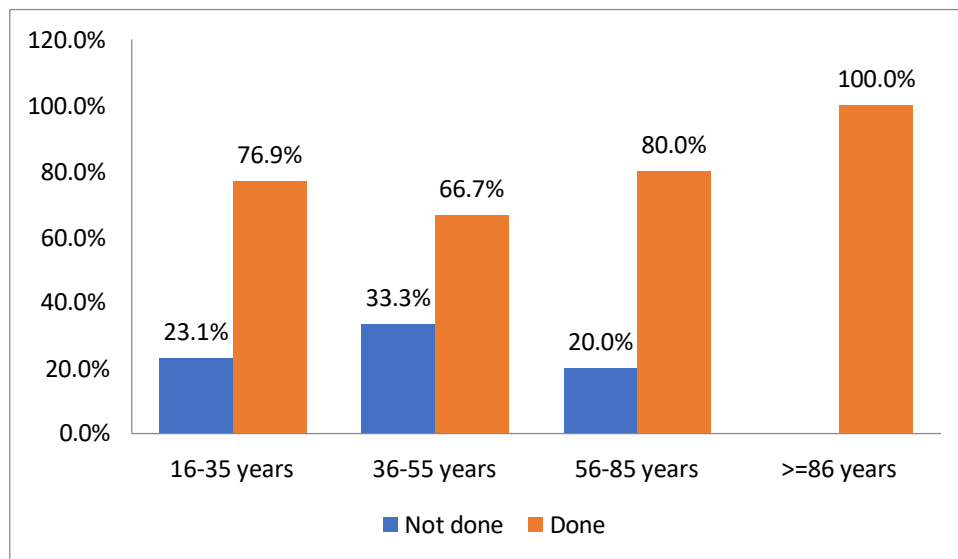


The table shows the mortality rate for a sample of 30 individuals. Of these, 27 individuals survived (90%), while 3 died (10%).

Table 7: Age and craniotomy

	CRANIOTOMY		Total
	Not done	Done	
16-35 years	3	10	13
	23.1%	76.9%	100.0%
36-55 years	2	4	6
	33.3%	66.7%	100.0%
56-85 years	2	8	10
	20.0%	80.0%	100.0%
>=86 years	0	1	1
	0.0%	100.0%	100.0%
Total	7	23	30
	23.3%	76.7%	100.0%

Figure 10: Representation of age and Craniotomy

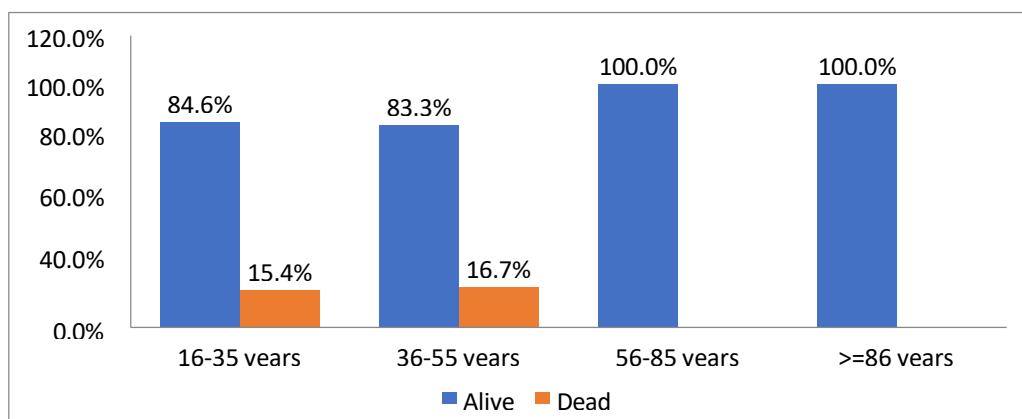


The table shows the distribution of craniotomy performance based on age groups. In the 16-35 age group, 23.1% did not undergo craniotomy, while 76.9% did. In the 36-55 age group, 33.3% did not undergo craniotomy, while 66.7% did. In the 56-85 age group, 20.0% did not undergo craniotomy, while 80.0% did. In the >=86 age group, all individuals underwent craniotomy.

Table 8: Age and mortality

Age	Mortality		Total
	Alive	Dead	
16-35 years	11	2	13
	84.6%	15.4%	100.0%
36-55 years	5	1	6
	83.3%	16.7%	100.0%
56-85 years	10	0	10
	100.0%	0.0%	100.0%
>=86 years	1	0	1
	100.0%	0.0%	100.0%
Total	27	3	30
	90.0%	10.0%	100.0%

Figure 11: Representation of age and mortality

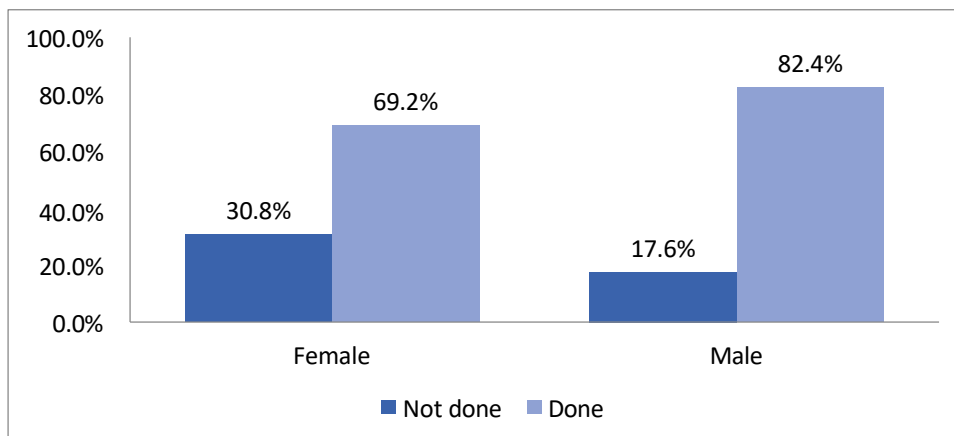


The table shows the mortality rates by age group. In the 16-35 age group, 84.6% survived, while 15.4% died. In the 36-55 age group, 83.3% survived, while 16.7% died. Notably, all individuals in the 56-85 and ≥ 86 age groups survived.

Table 9: Gender and CRANIOTOMY

	CRANIOTOMY		Total
	Not done	Done	
Female	4 30.8%	9 69.2%	13 100.0%
Male	3 17.6%	14 82.4%	17 100.0%
Total	7 23.3%	23 76.7%	30 100.0%

Figure 12: Representation of gender and CRANIOTOMY

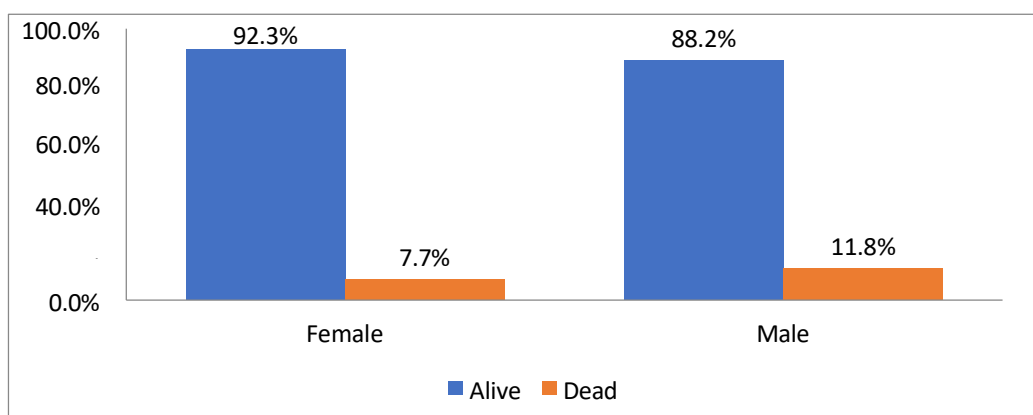


The table shows the distribution of craniotomy performance by gender. Among females, 30.8% did not undergo craniotomy, while 69.2% did. Among males, 17.6% did not undergo craniotomy, while 82.4% did.

Table 10: Gender and mortality

	Mortality		Total
	Alive	Dead	
Female	12 92.3%	1 7.7%	13 100.0%
Male	15 88.2%	2 11.8%	17 100.0%
Total	27 90.0%	3 10.0%	30 100.0%

Figure 13: Representation of Gender and mortality



The table shows the mortality rates by gender. Among females, 92.3% survived, while 7.7% died. Among males, 88.2% survived, while 11.8% died.

Table 11: Comparison of ONSD across the time points

	Mean	Std. Deviation	F value	p value
Day1	.651	.046	79.489	p<0.001
Day2	.584	.050		
Day3	.533	.049		

The mean value of ONSD on right side on Day 1 was 0.651 ± 0.046 , which showed a decrease to 0.584 ± 0.050 on Day 2, and further declined to 0.533 ± 0.049 on Day 3. Statistical analysis revealed a significant difference between the measurements across the days, with an F value of 79.489 and a p-value of less than 0.001.

Table 12: Pairwise Comparisons

Measure : ONSD Right						
Factor1		Mean Difference (I-J)	Std. Error	p value	95% Confidence Interval for Difference ^b	
					Lower Bound	Upper Bound
Day1	Day1	.086	0.26	.009	.018	.153
	Day2	0.124	0.22	.000	.071	.185
Day2	Day3	.042	0.35	.703	.046	.131

There is significant difference in all the pair wise comparison ($p < 0.001$) Figure 14: ONSD right

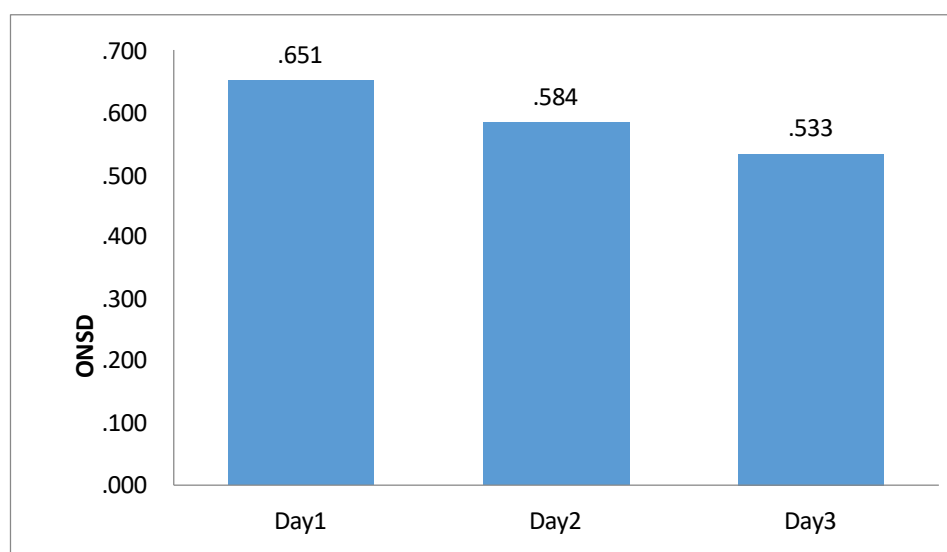


Table 13: ONSD comparison across the time points

	Mean	Std. Deviation	F value	p value
Day1	.6425	.04889	10.672	p<0.001
Day2	.5568	.11633		
Day3	.5146	.11250		

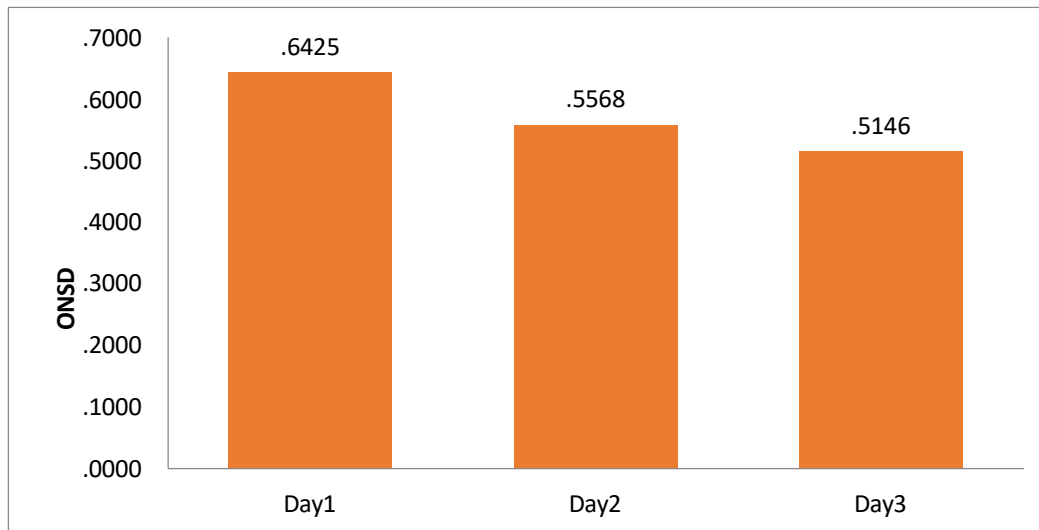
The mean value of ONSD on left side on Day 1 was 0.6425 ± 0.04889 , which decreased to 0.5568 ± 0.11633 on Day 2, and further declined to 0.5146 ± 0.11250 on Day 3. The statistical analysis yielded an F-value of 10.672, with a p-value of less than 0.001 ($p < 0.001$), indicating that the differences in means across the three days are statistically significant.

Table 14: Pairwise Comparisons

Measure: ONSD Left

(I) factor1		Mean Difference (I-J)	Std. Error	p value	95% Confidence Interval for Difference ^b	
					Lower Bound	Upper Bound
Day1	Day2	.086*	.026	.009	.018	.153
	Day3	.128*	.022	.000	.071	.184
Day2	Day3	.042	.035	.703	-.046	.131

There is significant difference in all the pair wise comparison ($p < 0.00$ Figure 15: ONSD left)



DISCUSSION:

This study encompasses a total of 30 patients, focusing on the analysis of changes in the ONSD (Optic Nerve Sheath Diameter) values following the administration of mannitol and 3% NaCl. The investigation will also examine the length of hospital stay, the number of patients requiring craniotomy, and mortality rates.

The age distribution of the participants reveals a varied demographic: 43.3% were aged between 16-35 years, 20.0% were aged 36-55 years, and 33.3% fell within the 56-85 years range. A smaller segment of the population, 3.3%, was aged 86 years or older. The overall sample comprises 30 individuals, accounting for 100.0% of the participants. Among these, 13 individuals were female (43.3%), while 17 were male (56.7%), indicating a greater predisposition among males. This finding aligns with previous research by Gupta et al., which indicates that males are 40% more likely to experience traumatic brain injury (TBI).⁵⁸ Intracranial hemorrhage types were analyzed, revealing that the most prevalent was subarachnoid hemorrhage (16.7%), followed by bilateral high frontal and parietal region subarachnoid hemorrhage (13.3%), and subdural hemorrhage (6.7%). The study showed that 56.7% of participants experienced a hospital stay of 7-11 days, while 43.3% stayed for 2-6 days, consistent with findings from Rubin et al. that report an average hospital stay of 6.8 days for TBI patients.⁵⁷

Mortality in this was documented at 10%, which contrasts with findings from Ferando et al., who reported a mortality rate of 32%. In the 16-35 age group, 84.6% survived, while 15.4% succumbed. Likewise, in the 36-55 age group, 83.3% survived, and 16.7% died. Notably, all individuals aged 56-85 and over 86 years survived. Within the age group of 16-35 years, 23.1% did not undergo craniotomy, compared to 76.9% who did. In the 36-55 age group, 33.3% did not have the procedure, while 66.7% did. In the 56-85 age group, 20.0% did not undergo craniotomy, and 80.0% did. All individuals aged 86 or older underwent craniotomy.

The mean ONSD value for the right eye side on Day 1 was recorded at 0.651 ± 0.046 , decreasing to 0.584 ± 0.050 on Day 2, and further to 0.533 ± 0.049 on Day 3. Statistical analysis indicated a significant difference in the measurements across the three days, with an F-value of 79.489 and a p-value of less than 0.001. These findings are consistent with the results of a study conducted by Amin et al., which reported R.ONS values in the range of 5.6 – 7.2 mm (SD 6.51 ± 0.45).⁶⁰ In terms of the left side ONSD, the mean value on Day 1 was 0.6425 ± 0.04889 , which decreased to 0.5568 ± 0.11633 on Day 2, and further to 0.5146 ± 0.11250 on Day 3. The statistical analysis for the left side yielded an F-value of 10.672, with a p-value of less than 0.001, underscoring the statistical significance of the differences observed across the three days. These results align with findings from Amin et al., indicating

L. ONSD values in the range of 5.8 – 7.4 mm (SD 6.75 ± 0.45).⁶⁰

In summary, this comprehensive analysis of ONSD, hospital stay duration, and patient outcomes provides valuable insights into the management and prognosis of patients experiencing traumatic brain injury. The findings underscore the importance of ongoing research in this domain to enhance understanding and improve clinical practices.

CONCLUSION:

The current study population had 43% of 16-30 years age patients, 20.0% were between 36-55 years, and 33.3% were between 56-85 years. A smaller proportion, 3.3%, were aged 86 years or older. Majority of patients were male and the most common type of intracranial haemorrhage was found to be Sub-arachnoid haemorrhage, followed by sub-dural haemorrhage. In the study it was found that mean value of ONSD on right side on Day 1 was 0.651 ± 0.046 , which showed a decrease to 0.584 ± 0.050 on Day 2, and further declined to 0.533 ± 0.049 on Day 3. And the mean value of ONSD on left side on Day 1 was 0.6425 ± 0.04889 , which decreased to 0.5568 ± 0.11633 on Day 2, and further declined to 0.5146 ± 0.11250 on Day 3. In the 16-35 age group, 23.1% did not undergo craniotomy, while 76.9% did. In the 36-55 age group, 33.3% did not undergo craniotomy, while 66.7% did. In the 56-85 age group, 20.0% did not undergo craniotomy, while 80.0% did. The majority of individuals (56.7%) had a duration of 7-11 days, while 43.3% had a duration of 2-6 days. In the 16-35 age group, 84.6% survived, while 15.4% died. In the 36-55 age group, 83.3% survived, while 16.7% died. Notably, all individuals in the 56-85 groups survived.

Future directions:

- The study needs to be further carried out on a larger population and follow up with patients.
- Mannitol can be used to manage the intracranial pressure (ICP) by monitoring the onsite performed optic nerve sheath ultrasound.
- 3% hypertonic saline can be used to manage the intracranial pressure (ICP) by monitoring the onsite performed optic nerve sheath ultrasound.
- Combination of 3% hypertonic saline and mannitol can be used to manage the intracranial pressure (ICP) by performing the onsite performed optic nerve sheath ultrasound.

LIMITATIONS:

- This is a single center study and we do not have long term follow up data of patients.
- ONSD values have only sensitivity around 85% and specificity of 86.5% -92.3%.
- ONSD measurement was taken only for first 3

days.

- ONSD Values are collected after craniotomy is performed.
- Small sample size
- Study conducted only for 7 months.
- Variation in response to dose change was not calculated.

REFERENCES:

1. Youmans JR, editor. Neurological surgery, vol. 3, 4th ed. Philadelphia: WB Saunders; 1996.
2. Anonymous. Guidelines for the management of severe traumatic brain injury. VIII. Intracranial pressure thresholds. *J Neurotrauma*. 2007;24:S55—8.
3. Briones-Galang M, Robertson C. Cerebral metabolism: implications for neurocritically ill patients. In: Suárez JI, editor. Critical care neurology and neurosurgery. New Jersey: Human Press; 2004. p. 37—47.
4. Martin NA, Patwardhan RV, Alexander MJ, Africk CZ, Lee JH, Shalmon E, et al. Characterization of cerebral hemodynamic phases following severe head trauma: hypoperfusion, hyperemia, and vasospasm. *J Neurosurg*. 1997;87:9—19.
5. G. Rodríguez-Botó*, M. Rivero-García b, R. Gutiérrez-González c, J. Márquez-Rivas. Basic concepts about brain pathophysiology and intracranial pressure monitoring. *J Neurologia*. 2015;30(1):16-22.
6. Nicolas Canac*, Kian Jalaieiddini, Samuel G. Thorpe, Corey M. Thibeault and Robert B. Hamilton. Review: pathophysiology of intracranial hypertension and noninvasive intracranial pressure monitoring. *Fluids and Barriers of the CNS*. (2020);17(40):1-21.
7. Kellie G. An account of the appearances observed in the dissection of two of three individuals presumed to have perished in the storm of the 3D, and whose bodies were discovered in the vicinity of Leith on the morning of the 4th, November 1821; with some reflections on the pathology of the brain: part I. *Trans Medico-Chirurg Soc Edinb*. 1824;1:84.
8. Smith M. Monitoring intracranial pressure in traumatic brain injury. *Anesth Analg*. 2008;106(1):240—8.
9. Ashwani Kumar Chaudhary, Anurag Tewari. Increased Intracranial Pressure. *J Anaesth Clin Pharmacol*. 2005; 21(3) : 247-256.
10. Cushing H. Concerning a definite regulatory mechanism of the vasomotor center which controls blood pressure during cerebral compression. *Johns*

- Hopkins Hosp Bull 1901; 12: 290-299.
11. Schrader H, Hall C, Zwetnow NN. Effects of prolonged supratentorial mass expansion and regional blood flow and cardiovascular parameters during the Cushing response. *Acta Neurol Scand* 1985; 72: 283-294
 12. Le Roux P, Menon DK, Citerio G, Vespa P, Bader MK, Brophy GM, et al. Consensus summary statement of the international multidisciplinary consensus conference on multimodality monitoring in neurocritical care. *Neurocrit Care*. 2014;21(2):1–26.
 13. Gutiérrez-González R, Boto GR, Pérez-Zamarrón A. Cerebrospinal fluid diversion devices and infection. A comprehensive review. *Eur J Clin Microbiol Infect Dis*. 2012;31:889— 97.
 14. Poca MA, Sahuquillo J, Arribas M, Báguena M, Amorós S, Rubio E. Fiberoptic intraparenchymal brain pressure monitoring with the Camino V420 monitor: reflections on our experience in 163 severely head-injured patients? *J Neurotrauma*. 2002;19:439— 48.
 15. Zhong J, Dujovny M, Park HK, Perez E, Perlin AR, Diaz FG. Advances in ICP monitoring techniques. *Neurol Res*. 2003;25(4):339–50.
 16. Binz DD, Toussaint LG, Friedman JA. Hemorrhagic complications of ventriculostomy placement: a meta-analysis. *Neurocrit Care*. 2009;10(2):253.
 17. Gardner PA, Engh J, Atteberry D, Moossy JJ. Hemorrhage rates after external ventricular drain placement. *J Neurosurg*. 2009;110(5):1021–5.
 18. Bratton S, Chestnut R, Ghajar J, McConnell FH, Harris O, Hartl R, et al. Guidelines for the management of severe traumatic brain injury. VI. Indications for intracranial pressure monitoring. *J Neurotrauma*. 2007;24:S37–44.
 19. Fernandes HM, Bingham K, Chambers I, Mendelow A. Clinical evaluation of the codman microsensor intracranial pressure monitoring system. In: *Intracranial pressure and neuromonitoring in brain injury*. Springer; 1998. p. 44–46.
 20. Evensen KB, Eide PK. Measuring intracranial pressure by invasive, less invasive or non- invasive means: limitations and avenues for improvement. *Fluids Barriers CNS*. 2020;17:1–33.
 21. Aaslid R, Markwalder TM, Nornes H. Noninvasive transcranial Doppler ultrasound recording of flow velocity in basal cerebral arteries. *J Neurosurg*. 1982;57(6):769–74.
 22. Ragauskas A, Matijosaitis V, Zakelis R, Petrikonis K, Rastenyte D, Piper I, et al. Clinical assessment of noninvasive intracranial pressure absolute value measurement method. *Neurology*. 2012;78(21):1684–91.
 23. Glick RP, Niebruegge J, Lee SH, Egibor O, Lichtor T, Alperin N. Early experience from the application of a noninvasive magnetic resonance imaging-based measurement of intracranial pressure in hydrocephalus. *Neurosurgery*. 2006;59(5):1052–61.
 24. Reid A, Marchbanks R, Burge D, Martin A, Bateman D, Pickard J, et al. The relationship between intracranial pressure and tympanic membrane displacement. *Br J Audiol*. 1990;24(2):123–9.
 25. Bruce BB. State-of-the-Art Review: Non-invasive assessment of cerebrospinal fluid pressure. *J Neuro-ophthalmol*. 2014;34(3):288.
 26. Olzowy B, von Gleichenstein G, Canis M, Mees K. Distortion product otoacoustic emissions for assessment of intracranial hypertension at extreme altitude? *Eur J Appl Physiol*. 2008;103(1):19–23.
 27. Zweifel C, Castellani G, Czosnyka M, Helmy A, Manktelow A, Carrera E, et al. Noninvasive monitoring of cerebrovascular reactivity with near infrared spectroscopy in head-injured patients. *J Neurotrauma*. 2010;27(11):1951–8.
 28. Borchert M, Lambert J. Non-invasive measurement of intracranial pressure. WO Patent. 1998;980:34536
 29. Roque PJ, Hatch N, Barr L, Wu TS. Bedside ocular ultrasound. *Crit Care Clin*. 2014 Apr;30(2):227–41.
 30. Helmke K, Hansen HC. Fundamentals of transorbital sonographic evaluation of optic nerve sheath expansion under intracranial hypertension II. Patient study. *Pediatr Radiol*. 1996 Oct;26(10):706–10.
 31. Hylkema C. Optic Nerve Sheath Diameter Ultrasound and the Diagnosis of Increased Intracranial Pressure. *Crit Care Nurs Clin North Am*. 2016 Mar;28(1):95–9.
 32. Tayal VS, Neulander M, Norton HJ, Foster T, Saunders T, Blaivas M. Emergency department sonographic measurement of optic nerve sheath diameter to detect findings of increased intracranial pressure in adult head injury patients. *Ann Emerg Med*. 2007 Apr;49(4):508–1.
 33. Betcher J, Becker TK, Stoyanoff P, Cranford J, Theyyunni N. Military trainees can accurately measure optic nerve sheath diameter after a brief training session. *Mil Med Res*. 2018 Dec 20;5(1):42.
 34. Karmanioliou I, Petropoulos G, Theodoraki K. Management of idiopathic intracranial

- hypertension in parturients: anesthetic considerations. *Can J Anaesth*. 2011 Jul;58(7):650.
35. Hanafi MG, Verki MM, Parei SN. Ultrasonic Assessment of Optic Nerve Sheath to Detect Increased Intracranial Pressure. *J Med Ultrasound*. 2019 Apr-Jun;27(2):69-74.
 36. Tayal VS, Neulander M, Norton HJ, Foster T, Saunders T, Blaivas M. Emergency department sonographic measurement of optic nerve sheath diameter to detect findings of increased intracranial pressure in adult head injury patients. *Ann Emerg Med*. 2007 Apr;49(4):508-14.
 37. Ohle R, McIsaac SM, Woo MY, Perry JJ. Sonography of the Optic Nerve Sheath Diameter for Detection of Raised Intracranial Pressure Compared to Computed Tomography: A Systematic Review and Meta-analysis. *J Ultrasound Med*. 2015 Jul;34(7):1285-9.
 38. Kim DH, Jun JS, Kim R. Ultrasonographic measurement of the optic nerve sheath diameter and its association with eyeball transverse diameter in 585 healthy volunteers. *Sci Rep*. 2017 Nov 21;7(1):15906.
 39. J H Kim, H jeong, Y H Choo, M kim, E J ha. Korean J neurotrauma;2023 jun;19(2):162- 76.
 40. Burke AM, Quest DO, Chien S, Cerri C. The effects of mannitol on blood viscosity.1981;*J Neurosurg* 55:550- 53.
 41. Muizelaar JP, Wei EP, Kontos HA, Becker DP. Mannitol causes compensatory cerebral vasoconstriction and vasodilation in response to blood viscosity changes. *J Neurosurg*.1983;59:822-28.
 42. Dorman HR, Sondheimer JH, Cadnapaphornchai P. Mannitol-induced acute renal failure. *Medicine (Baltimore)* 69:153-159, 1990.
 43. Sokhal N, Rath GP, Chaturvedi A, Singh M, Dash HH. Comparison of 20% mannitol and 3% hypertonic saline on intracranial pressure and systemic hemodynamics. *J Clin Neurosci*. 2017;42:148-54.
 44. Pfortmueller CA, Schefold JC. Hypertonic saline in critical illness - A systematic review. *J Crit Care*. 2017;;42:168-77.
 45. Adrogue HJ, Madias NE. Hyponatremia. *N Engl J Med*. 2000;25;342(21):1581-9
 46. Narayan SW, Castelino R, Hammond N, Patanwala AE. Effect of mannitol plus hypertonic saline combination versus hypertonic saline monotherapy on acute kidney injury after traumatic brain injury. *J Crit Care*. 2020;57:220-24.
 47. Schirmer CM, Ackil AA Jr, Malek AM. Decompressive Craniectomy. *Neurocrit Care*. 2008;8(3):456-70. doi: 10.1007/s12028-008-9082-y. PMID: 18392785.
 48. Sahuquillo J, Arikan F. Decompressive craniectomy for the treatment of refractory high intracranial pressure in traumatic brain injury. *Cochrane Database Syst Rev*. 2006 Jan 25;(1):CD003983. doi: 10.1002/14651858.CD003983.
 49. I J Jun, M kim, J lee,S U Park, J H Hyuk, Y K kim, .Effect of Mannitol on Ultrasonographically measured Optic nerve sheath diameter as a Surrogate for intracranial pressure During Robot Assisted Laproscopic Prostatectomy with Pneumoperitoneum and Trendelenburg Position..*J. of Endourology*. 2018;32(7);608-13.
 50. Y Launey, N Nessler, P L Maguet,P seguin, .Effect of osmotherapy on optic nerve sheath diameter in patient with increased intracranial pressure. *J. Neurotrauma* 2014;31(10);984- 88.
 51. H Fahmy, A Mohhamad, Optic nerve sheath diameter;An Ultrasonoigrapicaly window for comparing between Hypertonic solution and Mannitol in traumatic Brain injury. *of Anaesthesia and clinical research*. 2019;10(4):888-94.
 52. S P Paudyal, .;Effect of intravenous administration of Mannitol on Optic netve sheath diameter in patients with raised intracranial pressure, j. of neoalese society of critical care,2023;1(1);7-13
 53. D H Zidan, H shakr, .Mannitol vs Hypertonic solution in treatment of cerebral oedema post (MCA) Middle cranial arety Infraction.International, *J. of Advanced research on medicine*.2019;6(4):107-112
 54. A-hassani, Amarr, Gustav, E menya, .Relationship Of Optic nerve sheath diameter and intracranial hypertension in patients with Traumatic brain injury. *J.of emergency Trauma and Shock* 2020;13(3):183-189.
 55. S patel J M-Rios, A Parik, Diagnosis Aand management of elevated intracranial hypertension in Emergency department.International.International *j. of emergency medicine*.2023;16(72);1-9
 56. A S wahadan, A A Al madawi. K A El-shafey, Comparispon of Internittent vs continuousinfusion of 3% hypertonic solution on Intracranial pressure using uktrasound assessment with optic nerve sheath diameter..*Egyptian j. of Anaesthesia*. 2020;38(1):291- 99
 57. Rubin R. Traumatic Brain Injury Hospital Stays Are Longer, More Costly. *JAMA*. 2020;323(20):1998. doi:10.1001/jama.2020.8130
 58. Gupte R, Brooks W, Vukas R, Pierce J, Harris J.

Sex Differences in Traumatic Brain Injury: What We Know and What We Should Know. *J Neurotrauma*. 2019 Nov 15;36(22):3063-3091. doi: 10.1089/neu.2018.6171.

59. Fernando SM, Qureshi D, Talarico R, Tanuseputro P, Dowlatshahi D, Sood MM, Smith EE, Hill MD, McCredie VA, Scales DC, English SW, Rochweg B, Kyeremanteng K. Intracerebral Hemorrhage Incidence, Mortality, and Association With Oral
60. Anticoagulation Use: A Population Study. *Stroke*. 2021 May;52(5):1673-1681. doi: 10.1161/STROKEAHA.120.032550. Epub 2021 Mar 9. PMID: 33685222.
61. Amin, S., Adel Alkady, G., Elmorshedy, H., Ibrahim, W. MONITORING OSMOTHERAPY IN TRAUMATIC BRAIN INJURY PATIENTS: CORRELATION BETWEEN ULTRASOUND ASSESSMENT OF OPTIC NERVE SHEATH
62. DIAMETER AND COMPUTED TOMOGRAPHY SCAN. *Ain Shams Medical Journal*, 2021; 72(3): 657-670. doi: 10.21608/asmj.2021.205386