

**COMPARISON AND CORRELATION OF ULTRASONOGRAPHIC ASSESSMENT OF OPTIC NERVE SHEATH DIAMETER (ONSD) WITH DIRECT MEASUREMENT OF INTRACRANIAL PRESSURE (ICP) IN TRAUMATIC BRAIN INJURY PATIENTS**

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**Abstract:**

**Background:** Traumatic brain injury (TBI) and spinal cord injury (SCI) are crucial worldwide health priorities. These injuries result in human dysfunction and health loss, as well as being a burden on health-care systems and economies due to high health-care cost and lost productivity. This study aimed to correlate the findings between the optic nerve sheath diameter (ONSD) with the intracranial pressure (ICP) value by the invasive ICP monitoring catheter along with evaluating the cut off value of ONSD measurement in predicting raised ICP, with its specificity and sensitivity value.

**Patients and Methods:** The prospective study included patients >18 years of age and with a suspected traumatic brain injury with an initial (Glasgow Coma Scale) GCS of  $\leq 12$ . Brief history, clinical examination findings and relevant investigation reports were recorded. Data was analyzed in R software version 4.1.0.  $P \leq 0.05$  was set as statistically significant.

**Result:** By using paired t test, we observed that there was significant difference in mean ICP from 0 hour to 12 hours. However, the variance in mean ICP from 0 hour to 24 hours was insignificant. ONSD and ICP was significantly correlated at 0 hour, 12 hours and 24 hours.

**Conclusion:** Increased value of optic nerve sheath diameter (ONSD) was helpful in predicting elevated intracranial pressure (ICP).

**Key Words:** Intracranial Pressure, Neurosurgery, Brain Injuries, Traumatic Brain Injuries, Spinal Cord Injuries, Optic Nerve.

**Highlight:**

TBI is one of the leading causes of mortality. We compared bedside ultrasonic measurement of ONSD to ICP monitoring, which required a Neurosurgical intervention. We could identify the optimum cut off ONSD, which predicted a rise in ICP and timely intervention to decrease ICP would decrease the Morbidity and mortality in TBI.

**INTRODUCTION**

Traumatic brain injury (TBI) can manifest itself in a variety of ways, from minor changes in consciousness to a permanent comatose state and death.<sup>1</sup> A diffuse type of swelling and injury affects the entire brain in severe TBI.<sup>1</sup> Because it is cost-effective and quick bedside procedure, ultrasonographic assessment of optic nerve sheath diameter (ONSD) is preferred, especially for cases requiring real-time intracranial pressure (ICP) monitoring and those not suitable for the intensive care unit (ICU).<sup>2</sup> The ICP is called as the pressure exerted between the calvarium and intracranial tissues, namely cerebrospinal fluid, brain parenchyma, and blood.<sup>3</sup> Direct measurements of ICP require neurosurgical intervention, which have risks associated with them.<sup>4</sup> Overview of traumatic brain injury between 1966 and 2014 revealed that the prevalence, mortality and case fatality of TBI in Bangalore, India, indicates that the rates were 150/1,00,000, 20/1,00,000 and 10%, respectively.<sup>5</sup> Nearly 1.5 to 2 million people every year injured in India, with 1 million death due to TBI. Road traffic injuries are the leading cause of TBI (60 %), followed by falls (20%-25%) and physical violence (10%).<sup>6</sup> Sudden slip and falls, while playing were the common modes for domestic falls (29% and 25%, respectively).<sup>6</sup> At the time of injury, 15 % to 20 % of TBIs have alcohol involvement.<sup>5,6</sup>

The ONSD and ICP correlation was used to detect increased intracranial pressure (IICP).<sup>7</sup> Increase in ICP results in a corresponding elevation of the ONSD.<sup>8</sup> Commonly used method for ICP measurement is direct and invasive measurement through lumbar puncture.<sup>9</sup> However, potential risks such as brainstem herniation, infection and hemorrhage with invasive assessment of ICP are of great concern.<sup>9</sup> ICP values were used for deriving correlations and to identify the optimum cut-off of ONSD (measured by ultrasonography) that could reliably predict intracranial hypertension at varying levels of increased ICP (at 20, 25, 30, and 35 mm Hg).<sup>10</sup>

Early evaluation of raised ICP is crucial for the treatment of TBI patients to allow timely ICP lowering measures and maintain adequate cerebral perfusion.<sup>11</sup> Ultrasonographic measurement of ONSD is an accurate monitoring method for elevated ICP.<sup>12</sup> In recent years, assessment of ONSD by ultrasonography has been developed and proposed as a potential indicator of intracranial hypertension.<sup>13</sup>

**MATERIAL AND METHODS**

This prospective study was performed between October 2017 to August 2019 at a tertiary care hospital. Approval from the Institutional Ethical Committee and a written informed consent from the patients were acquired prior to the study. Patients >18 years of age and with a suspected TBI with an initial (Glasgow Coma Scale) GCS of  $\leq 12$  were included. Patients with ocular trauma and acute head trauma, but without ICP monitoring i.e., those for whom ICP was not feasible for any reason were excluded. Brief history, clinical examination findings and relevant investigation reports were recorded. The ONSD was assessed in the emergency department and computed tomography (CT) brain was done. The subjects were followed up in the Neuro ICU. The ICP measured by invasive ICP measurement using an intra-ventricular catheter was documented. The ONSD was measured at 0, 12<sup>th</sup>, 24<sup>th</sup> hour after insertion of ICP monitor each eye 3 times and average of this calculated and real time ICP pressures were noted and correlation of ONSD and ICP was done.

Sample size was calculated by using following formula.<sup>14</sup>

$$n = \left( \frac{Z_{\alpha} + Z_{\beta}}{C} \right)^2 + 3$$

where n is the required sample size,  $\alpha$  is significance level and  $1-\beta$  is power and

$$C = \frac{1}{2} \log_e \left( \frac{1+r}{1-r} \right).$$

Considering Pearson Correlation Coefficient between ONSD (average of both eyes) and ICP is 0.499 (below reference), at 5% significance level and 90% power, the minimum sample size required was 38. As sample size increases, accuracy of result increases. Therefore, sample size of 44 was used in this study.

***ICP Monitoring Procedure***

The patient was placed (in) supine position headrest in the neutral position on ring under general anesthesia. Right Kocher’s point incision marked (3cm lateral to midline and 1cm anterior to coronal suture).Parts were painted. Draped incision taken over the markings and deepened in layers. Right frontal Kocher’s point burr hole was made. The durawas then coagulated and incised. External ventricular drains (EVD) inserted upto 5 cm. Tapping of clear CSF was done. EVD was tunneled out and anchored to skin using 1-0 suture with incision closed in layers.EVD tip placed at head level and connected to the monometer and ICP measured in millimeters of mercury.

***Statistical analysis***

The collected data was organized in MS-Excel (2016) and analyzed in R software version 4.1.0.Categorical variables are represented in frequency tables. Continuous variables are given in Mean  $\pm$  SD/ Median (Min, Max) form. Paired t test was employed to compare the mean of ONSD from baseline to subsequent time periods and mean ICP from 0 hour to subsequent time periods. The correlation between ICP and ONSD at various time points was evaluated using Pearson’s correlation test. ONSD was analyzed for diagnostic purposes in order to predict elevated ICP. Statistical significance was set at  $P \leq 0.05$ .

**RESULTS**

Of 44 participants, 37 (84.09%) were male and 7 (15.91%) were female, in the age range of 18-90 years, with a mean age of  $40.84 \pm 17.04$  years. The table 1 represents the demographic details of the patients.

**Table 1: Demographic details of the patients.**

Variables	Sub-Category	Number of patients (%)
	<30	14 (31.82%)
	30-40	9 (20.45%)

Age (years)	40-50	9 (20.45%)
	≥50	12 (27.27%)
	Mean ± SD Median (Min, Max)	40.84 ± 17.04 37.5 (18, 90)
Gender	Female	7 (15.91%)
	Male	37 (84.09%)

Table 2 represents the comparison of ONSD from baseline to subsequent time periods.

**Table 2: Comparison of ONSD from baseline to subsequent time periods.**

Time points	ONSD	P-value <sup>pt</sup>
Baseline	6.03 ± 0.6	-
0 hour	6.05 ± 0.61	0.5885
12 hours	6.01 ± 0.59	0.6587
24 hours	5.95 ± 0.68	0.312

*pt - Paired t test.*

The difference in mean ONSD from baseline to any subsequent time periods was found insignificant by using the paired t test.

Table 3 represents the comparison of ICP from 0 hour to subsequent time periods. **(Table 3 Insert Here).**

**Table 3: Comparison of ICP from 0 hour to subsequent time periods.**

Time points	ICP	p-value <sup>pt</sup>
0 hour	23.57 ± 5.22	-
12 hours	25.02 ± 5.6	<b>0.0291*</b>
24 hours	23.05 ± 6.56	0.6173

*pt - Paired t test, \*statistical significance*

With paired t test, a significant difference in mean ICP from 0 hour to 12 hours was noted but the difference in mean ICP from 0 hour to 24 hours was insignificant.

Table 4 represents the correlation of ICP and ONSD at different time points.

**Table 4: Correlation of ONSD and ICP at different time points.**

Time points	Correlation Coefficient	P-value <sup>P</sup>
0 hour	0.6661	< <b>0.001*</b>
12 hours	0.5745	< <b>0.001*</b>
24 hours	0.6822	< <b>0.001*</b>

*p-Pearson's correlation, \*statistical significance.*

By using Pearson’s correlation, a significant correlation was observed in ICP and ONSD at 0 hour, 12 hours and 24 hours.

Table 5 represents the cut-off values and accuracy indices of ONSD in predicting increased ICP at 24 hours.

**Table 5: Optimal cut-off and accuracy indices of ONSD in predicting raised ICP at 24 hours.**

Variable	ONSD		
Cut-off	(>) 5.25	(>) 5.3	(>) 5.35
Sensitivity (95% CI)	87.5% (47.35% - 99.68%)	87.5% (47.35% - 99.67%)	87.5% (47.35% - 99.68%)
Specificity (95% CI)	97.22% (85.47% - 99.93%)	94.44% (81.34% - 99.32%)	91.67% (77.53% - 98.25%)
PPV (95% CI)	87.5% (54.06% - 99.68%)	77.78% (47.29% - 99.37%)	70% (42.26% - 99.06%)
NPV (95% CI)	97.2% (81.81% - 99.93%)	97.14% (81.37% - 99.66%)	97.06% (80.91% - 99.41%)
AU-ROC (95% CI)	0.95 (0.872, 1)	0.95 (0.872, 1)	0.95 (0.872, 1)

There are three optimal cut-offs of ONSD in predicting increased ICP at 24 hours with area under the curve (AUC) to be 0.95 (0.872, 1).

**DISCUSSION**

Assessment of ONSD by ultrasonography is a non-invasive method to identify the presence of raised ICP, in patients with intracranial hemorrhage and TBI.<sup>15</sup> Intracranial pressure (ICP) is a fundamental parameter for monitoring the neurocritical patients since, when it overrides mean arterial blood pressure, cerebral perfusion stops and brain death (BD) occurs after cerebral circulatory arrest.<sup>16</sup> Now-a-days, lumbar puncture and intraventricular catheterization, are used as direct methods for ICP evaluation.<sup>17</sup> TBI is a critical public health and socioeconomic problem throughout the world.<sup>18</sup> Primary and secondary TBIs cause temporary and/or permanent dysfunction in the brain, which limits a patient's activities, affects participation in society, and lowers quality of life.<sup>18</sup>

In present study, mean age of the participants was found to be 40.84 ± 17.04 years. The difference in mean ONSD from baseline to any subsequent time periods was insignificant. The mean age of patients of this study was comparable (43.5±14.7) with the study by Chen et al.<sup>19</sup> Waheed et al reported lower mean ONSD than this study, in which the mean ONSD measured on CT scan was 3.8±1 and the Pearson's correlation between the brain injury severity as per ONSD was insignificant (P= -0.182).<sup>20</sup>

In the current study, mean ICP was  $23.57 \pm 5.22$  at 0 hours,  $25.02 \pm 5.6$  at 12 hours and  $23.05 \pm 6.56$  at 24 hours. There was significant difference in mean ICP from 0 hour to 12 hours ( $P=0.0291^*$ ). However, the variance in mean ICP from 0 hour to 24 hours was insignificant. Similarly, Stein DM et al. reported that ICP significantly higher in the 84–180-hour time period than the 0–84-hour time period in TBI patients.<sup>21</sup>

In present study there was significant correlation found in ICP and ONSD at 0 hour, 12 hours and 24 hours. Similarly, Wang J et al. reported ICP and ONSD measurements in TBI patients at 6 hours and 24 hours after decompressive craniotomy operation. In the control group, mean ONSD was  $4.09 \pm 0.38$  mm and in the normal, mildly elevated, and severely elevated ICP groups, it was  $4.92 \pm 0.37$ ,  $5.77 \pm 0.41$ , and  $6.52 \pm 0.44$  mm respectively ( $P < 0.001$ ).<sup>8</sup> A significant linear correlation was reported between ICP and ONSD ( $r = 0.771$ ,  $P < 0.0001$ ).<sup>8</sup>

In current study, there are three optimal cut-offs of ONSD in predicting elevated ICP at 24 hours with AUC to be 0.95 (0.872, 1). Similarly, Soliman I *et al* reported that measurements of ONSD were strongly correlated to ICP values ( $r=0.74$ ,  $P < 0.0001$ ).<sup>22</sup> When using the mean of both eyes, the ONSD cut-off value for predicting elevated ICP was 6.4 mm, according to receiver operator curve (ROC) analysis (AUC = 0.88, 95% CI = 0.80 to 0.95; sensitivity = 85.3%, specificity = 82.6%) at 48 hours.<sup>22</sup>

Evaluation of ONSD by ultrasonography is rapid and less time-consuming technique.<sup>7</sup> Researchers were able to predict ICP as measured by CT with a sensitivity of 70–100% and a specificity of 73–95% using this technique, which has a good correlation with ICP.<sup>7</sup> Ultrasonography of the ONSD could possibly replace conventional invasive methods of intracranial pressure management. ONSD measurement is a marker of prediction raised ICP.<sup>23</sup> The present data suggests a re-evaluation of previously defined thresholds for elevated ICP, either by re-measuring archived ONSD imaging utilizing the new criteria or through new large prospective studies. These findings are vital, as they indicate that cutoff values for elevated ONSD generated using the black stripe method would not be applicable to images obtained employing the new quality criteria.

Limitations of this study are small sample size, a cross-sectional single centered study and needs to be validated on a larger patient cohort in a multicenter setting. Ultrasound cannot be used to measure ONSD in intra orbital pathologies like neoplasms, inflammatory diseases affecting the orbit, pseudotumor cerebri and any extrinsic compression on the optic nerve caused by tumors.

## CONCLUSION

Increased value of optic nerve sheath diameter (ONSD) was helpful in predicting elevated intracranial pressure (ICP).

Conflict of Interest: No! Conflict of interest is found elsewhere considering this work.

Source of Funding: There was no financial support concerning this work.

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