Original Article

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Radiology Section

Utility of Optic Nerve Sheath Diameter as a Screening Tool in Detecting Raised Intracranial Pressure

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ABSTRACT

Introduction: Raised Intracranial Pressure (ICP) is one of the most important causes of morbidity and mortality in the setting of Intensive Care Unit (ICU). Identifying the raised ICP as early as possible correlates well with the positive outcome of patients, which as of now relies more on ocular fundoscopy/Computed Tomography (CT) of brain/invasive monitoring, which relies on professional expertise and/or radiation exposure which may not be available all the times at all the places. This study tries to rationalise the utilisation of the commonly available modality of ultrasound in the evaluation of raised ICP compared to CT of brain.

Aim: To measure optic nerve sheath diameter in cases of suspected raised ICP and to assess suspected raised ICP using the reference standard of radiologic diagnosis by CT of brain. Also, to assess diagnostic accuracy of sonography of the ONSD compared to CT brain for predicting raised ICP.

Materials and Methods: This is a hospital based prospective comparative study on 60 adults over a period from June to August 2016, divided into two groups A and B consisting of 30 each, Group A consisted of 30 healthy controls and Group B consisted of 30 test subjects with symptoms of possible elevated ICP.

The test subject's CT imaging result was considered to be positive if findings suggested radiologic diagnosis of raised ICP such as midline shift of >3 mm/effacement of ventricles/cisterns/significant cerebral oedema/sub arachnoid haemorrhage.

Ocular ultrasound and CT-scan of brain was done in both group of patients.

Results: Mean age was 31.9 years in the control group and 44.6 years in the test group. Median age was 30 years in the control group and 45 years in the test group. The upper limit of the normal ONSD in the control group was 4.9 mm and a mean of 4.7 mm, those patients in the test group had a mean ONSD of 5.5 mm and upper limit of 5.7 mm, which was significantly more than the control group. These results showed that patients with raised ICP have an ONSD in excess of the control data ($p<0.05$). The above results were confirmed with Levene's test for equality of means ($p< 0.005$).

Conclusion: Ocular ultrasonography for measuring ONSD can be used an early test for diagnosing raised ICP and can be repeated for re-evaluation. In addition, ONSD has the advantage of diagnosing raised ICP earlier than ocular fundoscopy. Utilising no radiation exposure and being portable, ultrasonography avoids dangers associated with transporting ill patients from ICU and enables repeated reassessment of ICP.

Keywords: Intracranial tension, Ocular sonography, Resource-limited conditions

INTRODUCTION

Identifying raised ICP in a quick, reliable and safe way is important in a setting like ICU, especially in a resource limited conditions, like the primary healthcare in rural India. Conditions such as metabolic encephalopathy, meningitis, stroke, meningoencephalitis and post resuscitation syndrome can result in raised ICP. Early detection with prompt treatment of raised ICP in such situations is essential. Invasive ICP monitoring is considered gold standard, but it is associated with various risks such as infection and bleeding, more over being expensive. Regular assessment and comparison by CT/Magnetic Resonance Imaging (MRI) in these critically ill patients is associated with dangers of transporting to radiology [1] and radiation dose in case of CT and most importantly may not be available at all centres.

The optic nerve sheath is contiguous with the dura mater,

and its contents are contiguous with the subarachnoid space. Thus, raised ICP leads to an increase in the Optic Nerve Sheath Diameter (ONSD) [2]. Eventually, the increase in ICP is transmitted to the optic nerve resulting in swelling of optic disc and papilloedema. In the setting of acutely elevated ICP, however papilloedema can take hours to develop and patients may show clinical signs of optic disc swelling [3]. While the mechanism of papilloedema and ONSD enlargement is similar, ONSD changes occur within seconds of ICP elevation.

CT-scan was chosen as reference standard for detection of raised ICP. Raised ICP was regularly diagnosed on CT and initiate various treatments such as hemicraniectomies, and intraventricular shunts. We acknowledge that CT is not as accurate as invasive monitoring.

However, using CT as our reference standard allows for assessment of sonography of the optic nerve diameter.

MATERIALS AND METHODS

A hospital based prospective comparative study was conducted from June 2016 to August 2016 in the Department of Radiodiagnosis at Bangalore Medical College and Research Institute, Bengaluru, India. A total of 60 adults (30 healthy controls and 30 test subjects) above the age group of 18 years who were referred to our department with clinical diagnosis of possible elevation of ICP were included in the test group and patients undergoing CT-scan of head for non specific indications like migraine, headache in refractory errors, sinusitis and screening CT for metastatic workup (whose results turned up negative) were included in our study in the control group using random sampling technique.

Patients above the age of 18 years presenting with the history of fever, headache, vomiting and/or altered sensorium and patients undergoing CT-scan of head for non specific indications were included in the study.

Patient with history of optic neuritis, arachnoid cyst of optic nerve, high myopic, optic nerve trauma and anterior orbital or cavernous sinus mass, patient with past history of epilepsy/ hydrocephalus and patients who were below 18 years of age were excluded from the study.

All patients with clinical suspicion of raised ICT, presenting to Victoria Hospital and Bowring and Lady Curzon Hospital attached to Bangalore Medical College and Research Institute, Bengaluru will be included in the study. Informed written Consent was taken from all the patients in case and control groups. Ethical Committee Clearance was obtained prior to the study.

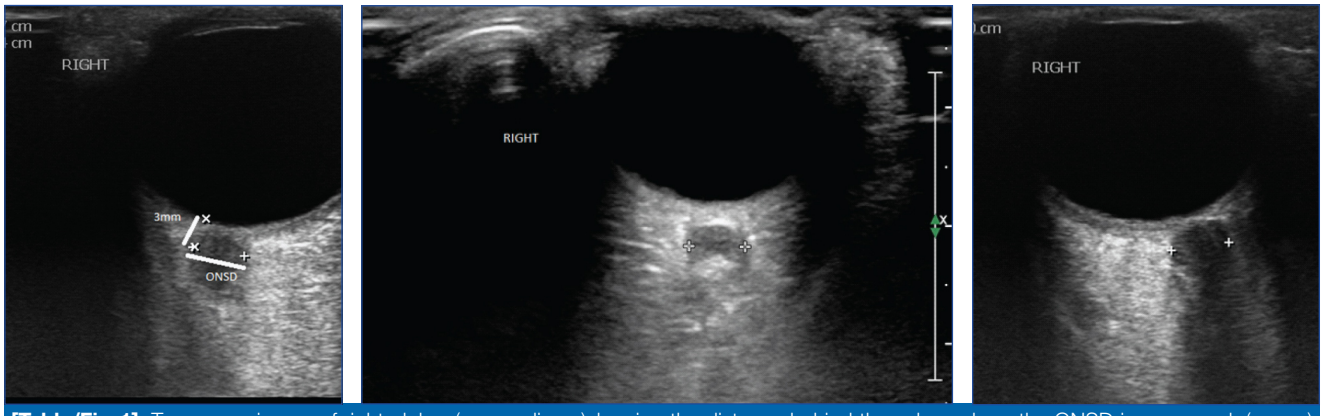
All the above patients satisfying the inclusion criteria underwent ultrasound examination.

After placing a barrier over the eyelid of the patient and coupling gel on top of the barrier, structures of the eyes were visualised to align the optic nerve directly opposite the probe, with the ONSD width perpendicular to the vertical axis of the scanning plane. The diameter of the optic nerve sheath 3 mm behind the posterior sclera was measured [Table/Fig-1] using a sector 7 MHZ phased array probe of either a Siemen's ACUSON SONOLINE and Philips AFFINITYG 50 system. The ONSD measurements were obtained using the digital cursor and measurement software of the ultrasound machine averaging three readings from each eye to create a binocular ONSD in both the control [Table/Fig-2] and test groups [Table/Fig-3].

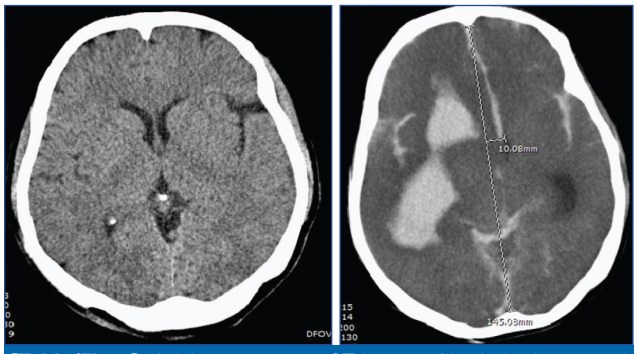
CT of the brain was done by Philips INGENUITY 128 slice CT and Siemens SOMATOM 6 slice CT.

The test subject's CT imaging result was considered to be positive if findings suggested radiologic diagnosis of raised ICP such as midline shift of >3 mm/effacement of ventricles/cisterns/significant cerebral oedema/sub arachnoid haemorrhage [Table/Fig-4,5].

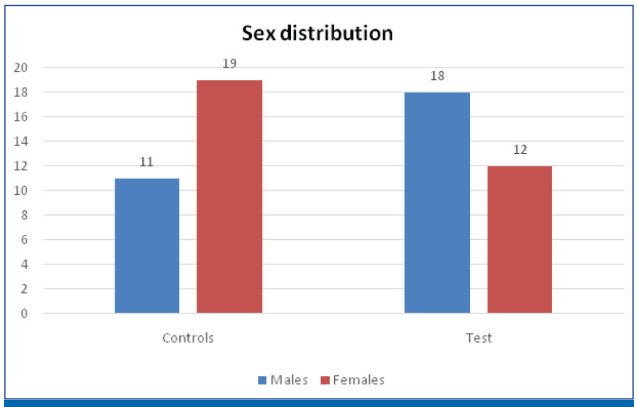
Ocular ultrasound and CT-scan of brain was done in both group of patients. Negative CT in the control group was used as a baseline to rule out causes of raised ICP and the same group was subjected to ocular ultrasound to obtain the values for



[Table/Fig-1]: Transverse image of right globe. (x---x calipers)showing the distance behind the sclera where the ONSD is measured. (+----+) Calipers denote the ONSD in the test group. **[Table/Fig-2]:** Transverse image of right globe.(+----+) Calipers denoting the ONSD in the control group. **[Table/Fig-3]:** Transverse image of right globe.(+----+) Calipers denoting the ONSD in the test group. (left to right)



[Table/Fig-4]: Axial non contrast CT image of brain in the control group for a migraine headache. (left) **[Table/Fig-5]:** Axial non-contrast CT image of brain. Traumatic brain injury showing significant mass effect in the form of midline shift of ~1 cm to left with intraparenchymal bleed with secondary intraventricular extension.



[Table/Fig-6]: Figure showing sex distribution in control and test group.

ONSD so as to compare it with the ONSD obtained with the test group with raised ICP. Statistical tests were used to determine if any significant differences were present between the groups.

Before doing CT-scan for definite diagnosis, ONSD of both eyes was determined by ultrasonography. Ultrasound evaluation of ONSD was done before CT examination of head to prevent diagnosis bias.

STATISTICAL ANALYSIS

ANOVA test to compare the intra and inter group variance and Levene's test for equality of variances.

Levene's test was done to determine the equality of variances between and within the groups. The significant value was $p<0.05$, hence the hypothesis of equal variances was not assumed.

RESULTS

Out of the 30 patients in the control group, 11 were males (36.7%), 19 were females (63.3%) and out of the 30 patients in the test group, 18 were males (60%), 12 were females (40%) [Table/Fig-6].

In our study, 19 years was the minimum age reported in the control group and 20 years was in the test group, whereas 70 years was the maximum age in both the groups.

Mean age was 31.9 years in the control group and 44.6 years in the test group. Median age was 30 years in the control group and 45 years in the test group. Overall the mean age was 38.8 years, median age was 35.5 years with a minimum age of 19 years and maximum of 70 years.

The data regarding the ONSD measurements of control and test group respectively [Table/Fig-7,8].

The mean value of ONSD with standard deviation and variance for control and test groups [Table/Fig-9].

The upper limit of the normal ONSD in the control group was 4.9 mm and a mean of 4.7 mm, those patients in the test group had a mean ONSD of 5.5 mm and upper limit of 5.7 mm.

The null hypothesis was established as no difference between the mean of two groups and the variances being the same in both groups.

Levene's test for the homogeneity of variance showed that we must reject the null hypothesis of the variances being the same in both the groups [Table/Fig-10].

ANOVA and Fisher's test were done between the two groups for intergroup and intra group variance. Hence, we reject the hypothesis of no difference between the mean of the two groups [Table/Fig-11].

These results showed that the patients in the test group with raised ICP have an ONSD in excess of the control data ($p<0.05$).

Ocular sonography shows good diagnostic test accuracy for detection of raised ICP compared to CT.

DISCUSSION

The optic nerve sheath is contiguous with the dura mater, and its contents are contiguous with the subarachnoid space. Thus, raised ICP leads to an increase in the ONSD, eventually resulting in papilloedema [2].

In the setting of acutely elevated ICP, however papilloedema can take hours to develop [3].

In 1996 Helmke H and Hansen HC went on to demonstrate, in cadaver studies, that the ONSD increased by up to 60% at a distance of 3 mm behind the globe compared with only 35% at 10 mm [4,5] .

Again in 1996 Helmke H and Hansen HC went on to prove that there was no significant difference in measurement by lateral, axial or transverse projection [4,5].

Ultrasonographic machines with a provision of high-frequency transducers (>7.5 MHz), now available in most of the intensive care unit systems, have high lateral and axial precision [6] .

Patient data			CT-findings						
S. No	Name	Age/Sex	Midline shift of >3 mm	Intra cranial haemorrhage	Effacement of ventricles/ cisterens	Effacement of cortical SULCI	Cerebral oedema	Hydrocephalus	Mean ONSD of both orbits
1	**	27/F	-	-	-	-	-	-	4.5
2	**	25/M	-	-	-	-	-	-	5.0
3	**	35/F	-	-	-	-	-	-	4.6
4	**	19/F	-	-	-	-	-	-	4.8
5	**	38/F	-	-	-	-	-	-	4.6
6	**	40/F	-	-	-	-	-	-	4.6
7	**	25/F	-	-	-	-	-	-	4.5
8	**	20/M	-	-	-	-	-	-	4.8
9	**	55/M	-	-	-	-	-	-	4.8
10	**	24/M	-	-	-	-	-	-	4.8
11	**	31/F	-	-	-	-	-	-	4.8
12	**	33/M	-	-	-	-	-	-	4.7
13	**	22/F	-	-	-	-	-	-	4.7
14	**	70/M	-	-	-	-	-	-	4.6
15	**	35/F	-	-	-	-	-	-	4.7
16	**	41/F	-	-	-	-	-	-	4.6
17	**	35/F	-	-	-	-	-	-	4.9
18	**	24/F	-	-	-	-	-	-	5.0
19	**	19/F	-	-	-	-	-	-	4.8
20	**	46/F	-	-	-	-	-	-	4.6
21	**	27/F	-	-	-	-	-	-	4.8
22	**	40/F	-	-	-	-	-	-	4.3
23	**	25/M	-	-	-	-	-	-	4.8
24	**	30/M	-	-	-	-	-	-	5.0
25	**	37/M	-	-	-	-	-	-	4.7
26	**	35/M	-	-	-	-	-	-	4.8
27	**	28/F	-	-	-	-	-	-	4.6
28	**	24/F	-	-	-	-	-	-	4.7
29	**	27/M	-	-	-	-	-	-	4.8
30	**	21/F	-	-	-	-	-	-	4.8

[Table/Fig-7]: ONSD measurements in control group.
**patient name not revealed to keep confidentiality

Patient data			CT-findings						
S. No	Name	Age/Sex	Midline shift of >3 mm	Intra cranial haemorrhage	Effacement of ventricles/ cisterens	Effacement of cortical SULCI	Cerebral oedema	Hydrocephalus	Mean ONSD of both orbits
1	**	69/M	-	+	+	+	+	-	5.6
2	**	68/M	-	+	-	-	-	-	5.5
3	**	20/M	+	+	+	+	+	-	5.4
4	**	54/F	+	+	+	+	+	-	5.0
5	**	48/M	-	+	-	-	+	-	5.6
6	**	35/F	-	-	+	+	+	-	5.5
7	**	40/M	+	+	+	+	+	-	5.6
8	**	50/F	-	-	-	+	+	-	5.5
9	**	23/M	+	-	+	+	+	-	5.4
10	**	35/F	-	+	+	+	-	-	5.1
11	**	45/M	+	-	+	-	-	-	5.5
12	**	23/M	-	+	+	+	+	-	5.3
13	**	70/F	-	-	+	+	+	-	4.9
14	**	60/M	-	+	+	+	+	-	5.3
15	**	30/M	-	+	+	+	+	-	5.2
16	**	65/M	-	+	+	+	+	-	5.1
17	**	39/F	+	+	+	+	+	-	5.6
18	**	40/M	+	+	+	+	+	-	5.7
19	**	45/M	-	+	-	+	+	-	5.4
20	**	55/M	-	+	+	+	+	-	5.4
21	**	36/M	-	+	-	+	+	-	5.6
22	**	45/M	-	+	-	+	+	+	5.5
23	**	24/F	+	-	+	+	+	-	5.1
24	**	65/F	-	-	+	+	+	-	5.0
25	**	55/M	+	-	+	+	-	-	5.2
26	**	38/F	+	+	+	+	+	-	5.4
27	**	45/F	-	-	-	+	+	-	5.7
28	**	38/M	-	+	-	+	+	-	5.6
29	**	51/F	-	+	-	+	+	-	5.5
30	**	27/F	-	-	-	+	+	-	5.6

[Table/Fig-8]: ONSD measurements in test group.
**patient name not revealed to keep confidentiality

There is a growing body of evidence stating a positive correlation between the increase in the sonographic ONSD and raised ICP. One such study demonstrating the relationship between the ONSD and CSF pressure was demonstrated by Hansen HC and Helmke K, by lumbar intrathecal infusion test in which maximal ONSD dilation was achieved at peak CSF pressure [7].

According to a recent meta-analysis conducted by Ohle R et al., conducted on a pool of 478 patients concluded that ONSD had a 95 % sensitivity and 92% specificity with negative and positive likelihood ratios of 0.05 and 12.5 respectively for diagnosing non-traumatic radiographic cerebral edema when compared to brain CT [8].

In a study conducted by Dubost C et al., in pre-eclampatic patients, to detect the incidence of raised ICP, concluded that in pre-eclampatic patients ONSD was 5.4 mm compared to 4.5 mm in healthy pregnant women [9].

	Control group	Test group
Number	30	30
Mean	5.3874	4.7078
Std. deviation	0.22692	0.15541
Std. error mean	0.04143	0.02837
Sum	3.8	7.321259
Average	0.126667	0.244042
Variance	0.0102529	0.029623

[Table/Fig-9]: Mean value of ONSD with standard deviation and variance for control and test groups.

		t-test for Equality of means		
		t	df*	Sig. (2-tailed)
ONSD Mean	Equal variances assumed	13.534	58	.000
	Equal variances not assumed	13.534	51.299	.000

[Table/Fig-10]: Levene's Independent Samples Test for equality of means.
*df – degree of freedom, Sig. – significance

Source of variation	Sum of squares	df	Mean square	F ratio	p-value	F critical
Between groups	0.206654	1	0.2066	10.36485	0.0021	4.0068728
Within groups	1.156404	58	0.0199			
Total	1.363059	59				

[Table/Fig-11]: Analysis of variance (ANOVA)and Fischer testfor determining significant intragroup and intergroup variations.
*F (dF between, dF within) = F_{ratio}, p value: dF - Degree of freedom.
F (1,58)=Mean square between/mean square within =10.364, p=0.002, Since F_{ratio} is >1 and F_{ratio} is >$F_{critical}$, the null hypothesis of no variance between the groups stands to be rejected.
Also, since the p-value is <0.05, the results are statistically significant between the groups.

Rajajee V et al., while studying ONSD in 65 patients with traumatic brain injury, intracranial haemorrhage and ischaemic stroke reported that for the detection of ICP >20 mmHg, the optimal ONSD for was ≥0.48 cm with a sensitivity of 96% (95% CI 91-99%) and specificity of 94% (92-96%) [10].

We chose CT as our reference standard for detection of raised ICP and we also acknowledge that CT is not as accurate as invasive monitoring, which is the gold standard [11]. However, using CT as our reference standard allows for assessment of sonography of the optic nerve diameter in its ability to identify cases with raised ICT. As showed by studies done by Rajajee V et al., and Dubourgh J et al., the patients with raised ICP are 51 times more likely to have a positive ONSD [10,12].

In adults with moderate traumatic brain injury, the ONSD correlates with signs of high ICP on CT-scan [13,14]. ONSD more than 5 mm correlates well with ICP more than 20 cm of water [15,16].

Ballantyne SA et al., reported ±0.01 intraobserver and ±0.2 interobserver variability in measuring ONSD [17]. This has corroborated by Hassen, in a retrospective study on 61 patients which said that there was a a high degree of agreement between ONSDs measured by trained radiologists and trained emergency room physicians with a correlation coefficient of 0.9 (0.88-0.93) [18].

The advantage lies in the fact that bedside ONSD takes only 1-2 min and diagnosis of raised ICP can be made rapidly. All these assumes further importance for the care of unstable patients who cannot be mobilized for a CT-scan or cannot have an intracranial probe implanted to measure ICP because of coagulation abnormalities [19,20].

LIMITATION

Detailed neurological exam or records of any specific localising neurologic signs while undertaking the measurements was not done and also individual GCS values and its relationship with the ONSD measurement was not recorded. Also, we restricted the present study in assessing only the effect of ICT on ONSD and did not measure the effect of treatment on the ONSD. However, all these could be addressed by future studies. Ocular trauma, optic nerve injury and neuritis are few of the conditions recognised as limits in the applicability of ocular sonography.

CONCLUSION

Ocular sonography has good negative predictive value for ruling out raised ICP. Ocular ultrasonography for measuring ONSD can be used an early test for diagnosing raised ICP as it is a non invasive, cost effective, devoid of ionising radiation and can be repeated for re-evaluation in cases where CT is not available at all times.

In addition, ONSD has the following advantages over CT and ophthalmoscopy of fundus. Increase in the ONSD, actually precedes development of papilloedema. In the setting of acutely elevated ICP, papilloedema can take hours to develop. To evaluate papilloedema bedside ophthalmoscopy requires expertise, whereas ONSD can be used with minimal training resulting in non dependence on an experienced ophthalmologist. It is also devoid of danger of transporting critically ill patients and repeated radiation exposures. This point of care method could be used for rapid interventions for raised ICP and can also be used to monitor patients during transport. Since, bedside ultrasound equipment is relatively easier to employ than a full fledged dedicated radiology setup, it is especially helpful in resource poor settings, like in the primary healthcare centres and we consider our results will help the bedside clinicians in dealing with patients in whom transferring to a farther up CT facility is hazardous or impractical.This point of care method of determining ONSD can also be used as part of a protocol to reduce CT usage.

Moreover, measurement of the ONSD is simple, easily learned and reproducible not only by trained radiologists, even by emergency room physicians.

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