Original Article

Role of ultrasonographic optic nerve sheath diameter in the diagnosis and follow-up of papilledema and its correlation with Frisén's severity grading

Nithya Raghunandan, Mary Joseph, Suneetha Nithyanandam, Shubhashree Karat

Purpose: The aim of this study was to compare the ultrasonographic optic nerve sheath diameter (ONSD) in different grades of papilledema and in controls and to evaluate ONSD in atrophic papilledema/optic atrophy when raised ICP was suspected. **Methods:** Prospective cross-sectional case–control study. Following an ocular examination, papilledema was graded clinically using modified Frisén's grading. An ultrasonographic cross section of the retrobulbar optic nerve was obtained with a posterior transverse scan. Independent *t*-test and analysis of variance were the statistical tools used in the study. **Results:** The study included 55 cases and 55 age- and gender-matched controls; mean (± standard deviation) age was 37.17 (±11.25) years and male: female ratio was 49:61. There was a statistically significant difference in the mean ultrasonographic ONSD between cases [4.89 (±0.65) mm] and controls [3.12 (±0.22) mm] ($P < 0.001$). There was a significant difference in the mean ONSD across Frisén's grades of papilledema ($P < 0.001$). The mean ONSD in atrophic papilledema was 6.2 (±0.75) mm. **Conclusion:** In the presence of symptoms, ultrasonographic ONSD >4 mm is diagnostic of papilledema. Ultrasonographic ONSD correlates well with the severity of papilledema and can be used to follow-up patients with chronically elevated ICP. It is useful in detecting raised ICP in the presence of optic atrophy and to distinguish true papilledema from pseudopapilledema.

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Papilledema is a passive swelling of the optic disc secondary to elevated intracranial pressure (ICP).[1-3] Treatment and prognosis of patients with increased ICP depends to a great degree on early and prompt diagnosis. Intracranial hypertension can only be established with certainty by direct measurement of intraventricular or subdural pressure, which is however not feasible in a clinical setting.[4] The most common and credible sign of raised ICP is papilledema.

A complete history and detailed funduscopic examination of the optic nerve head and adjacent retina and blood vessels will suffice to not only establish a diagnosis of papilledema but also differentiate papilledema from optic disc swelling due to other conditions.[5] On the contrary, the diagnosis may be difficult in patients with very early papilledema and in patients with optic atrophy where papilledema may not manifest. Differentiation from pseudopapilledema is also important as the patients with pseudopapilledema may only need reassurance, monitoring, and follow-up.[6] In such patients, fundus fluorescein angiography (FFA) has been used to establish the diagnosis; then again FFA is an invasive technique associated with potential serious systemic side effects.[7,8] Various other techniques have been considered to detect increased ICP including lumbar puncture, magnetic resonance imaging, and optical coherence tomography.[9]

An indirect, noninvasive method of detecting raised ICP is using ocular ultrasound to detect dilation of the optic nerve sheath 3 mm behind the eye.[10-13] In patients with increased ICP, optic nerve sheath diameter (ONSD) increases due to its continuity with meninges and subarachnoid space, detected on B-scan ultrasonography (USG). It has also been shown that ONSD is increased before manifestation of papilledema. While papilledema may take time to develop, dilatation of the optic nerve sheath occurs much earlier and may be a near-instantaneous manifestation of raised ICP.[14]

There are studies describing the use of B-scan USG in the diagnosis of papilledema.[15-19] The correlation between the measured B-scan ONSD and the severity of papilledema has not been assessed, neither its role in atrophic papilledema. This method of indirectly detecting papilledema is still not used extensively in clinical practice.

The aim of our study is to compare the ONSD measured using B-scan USG in different grades of papilledema and in controls. The study also evaluated the ONSD in patients with optic atrophy with suspected raised ICP.

Methods

This prospective cross-sectional case–control study was conducted from August 2014 to August 2016 in our hospital. The study was approved by the institutional ethical committee. The

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study included 55 cases with a clinical diagnosis of papilledema and 55 age- and gender-matched controls who were patients who came for routine examination and for refractive error corrections to our outpatient department. The study also evaluated six eyes of three patients with atrophic papilledema.

After obtaining informed consent from the patient and controls, a detailed history regarding demographics, symptomatology of raised ICP and ocular diseases, medical history, and significant drug history was taken. A detailed ocular examination including slit-lamp examination of anterior segment and fundus examination using indirect ophthalmoscope and slit-lamp biomicroscopy using +90D lens was done.

Papilledema was graded clinically using modified Frisén's grading.[18] Patients with preexisting optic nerve head changes such as glaucoma, ocular diseases such as cataract, chorioretinitis, retinal scars, posterior uveitis, macular disorders, retinal artery/vein occlusions, and high ametropia (refractive error of >5D sphere, 3D astigmatism) were excluded from the study.

Ocular B-scan USG was performed with a 10-MHz probe. A cross section of the retrobulbar optic nerve (Salami cut) was obtained by placing the USG probe temporally on the eye to obtain a posterior transverse scan. The scan was performed with the patient fixing in primary gaze. A cross section of the optic nerve indicated by a circular echolucent defect displayed just behind the globe was obtained. The diameter of this echolucent disc was measured using callipers to obtain the retrobulbar ONSD [Fig. 1a and b].

Inferential statistics was done using *t*-test and analysis of variance to compare means and Chi-square test for two categorical variables. All statistical analysis was done using SPSS version 17, and $P < 0.05$ was considered statistically significant.

Results

The study population included 55 cases and 55 age- and gender-matched controls [Table 1]. The mean [± standard deviation (SD)] age of the study population was 37.17 (±11.25) years with a range of 16–68 years and male:female ratio of 49:61. The cause for raised ICT among the cases included idiopathic intracranial hypertension (IIH) [24/55 (43.6%)], cerebral venous thrombosis (CVT) [14/55 (25.45%)], space-occupying lesion [8/55 (14.54%)], and infection [9/55 (16.36%)]. According to the Frisén's grading of papilledema, more than 50% belonged to Frisén's grade 1 and 2 papilledema.

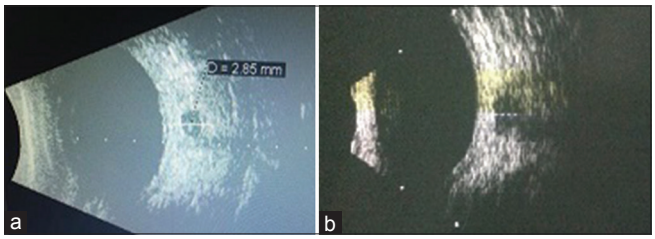

Figure 1: (a) Normal, ONSD. (b) B-scan ultrasound picture showing a circular echolucent defect displayed just behind the globe indicating the cross section of the optic nerve. The diameter measured using callipers to obtain the retrobulbar optic nerve sheath diameter

On comparing the mean ONSD (±SD) between cases [4.89 (±0.65) mm] and controls [3.12 (±0.22) mm], a statistically significant difference was noted ($P < 0.001$) [Table 2]. There was a statistically significant difference in the mean B-scan ONSD across the Frisén's grades ($P < 0.001$) [Table 3]. On *post hoc* analysis between the Frisén's grade's mean differences, there was a statistically significant difference between each of the groups ($P < 0.05$) [Figs. 2 and 3].

During the study period, six eyes of three patients presented with decreased vision and either atrophic papilledema or secondary optic atrophy. Bilateral involvement was seen in all the three patients. The mean (±SD) ONSD in these patients was 6.2 (±0.75) mm and this was statistically significantly higher than the mean (±SD) of patients [4.89 (±0.65) mm] ($P < 0.001$). In addition, seven patients with symptoms suggestive of raised ICT and suspected papilledema were evaluated. Clinically, there was pseudopapilledema, which was confirmed using B-scan ONSD [3.12 (±0.34) mm], with optic disc drusen in five of seven patients and hypermetropic tilted discs in two of seven patients.

Discussion

Measurement of ONSD using USG is based on the fact that the subarachnoid space around the optic nerve is in continuity with the intracranial subarachnoid space.[20] Hence, any raised ICP will be transmitted to the optic nerve subarachnoid space. This

Table 1: Demographic details of cases and controls

	Groups (*n*=110)	Mean (±SD)	Statistic	*P*
Age	Case (55)	35.66 (±1.45)	0.29	0.17
	Controls (55)	38.66 (±1.66)		
Gender	Case (55)	Males 22		0.07
		Females 33		
	Control (55)	Males 27		
		Females 28		

SD=Standard deviation

Table 2: Comparison of mean B-scan ONSD of cases and controls (and also comparison of mean ONSD of cases with atrophic papilledema/optic atrophy)

Groups (*n*=110)	Mean (±SD)	*t*	*P*
Cases (55)	4.89 (±0.65)	22.34	<0.001
Controls (55)	3.12 (±0.22)		
Cases (55)	4.89 (±0.65)	17.27	<0.001
Atrophic papilledema (6)	6.2 (±0.75)		

ONSD=Optic nerve sheath diameter; SD=Standard deviation

Table 3: Comparison of B-scan ONSDs between Frisén's grades in the cases

Frisén's grading	*n*=55	Mean (±SD) ONSD	*F*	*P*
1	19	4.31 (0.31)	28.5	<0.001
2	11	4.36 (0.23)		
3	10	4.8 (0.55)		
4	7	4.9 (0.50)		
5	8	6.1 (0.81)		

ONSD=Optic nerve sheath diameter; SD=Standard deviation

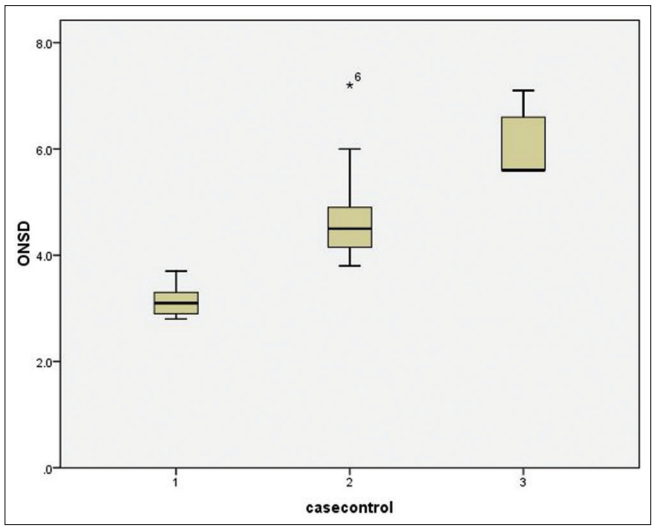

Figure 2: Boxplot graph of OSND of controls - 1, papilledema - 2, and atrophic papilledema - 3.This shows the median with the upper and lower quartiles and the minimum and maximum values. This plot clearly depicts that 4 mm ONSD was the cut-off value of normals. In our data, there were no controls with a value above 4 mm

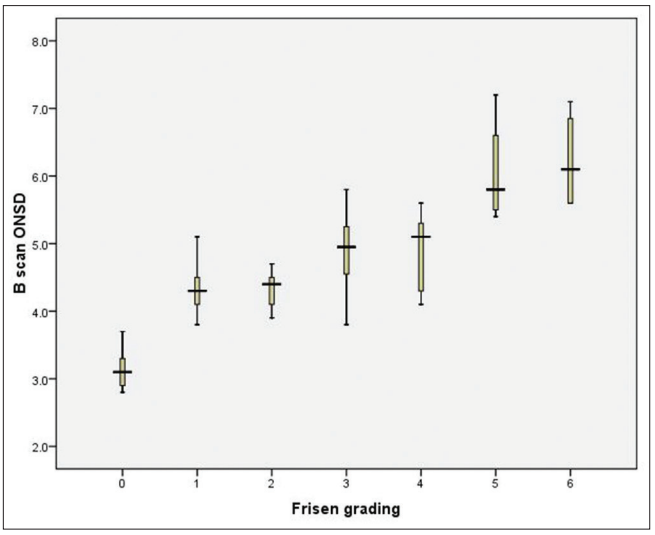

Figure 3: Boxplot graph of ONSD of Frisen grades 0 to 5.Atrophic papilloedema -6

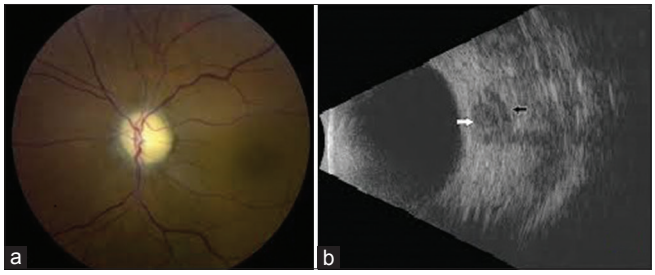

Figure 4: (a) Fundus photograph of a patient with optic atrophy. (b) B-scan image with increased optic nerve sheath diameter in atrophic disc (white and black arrows)

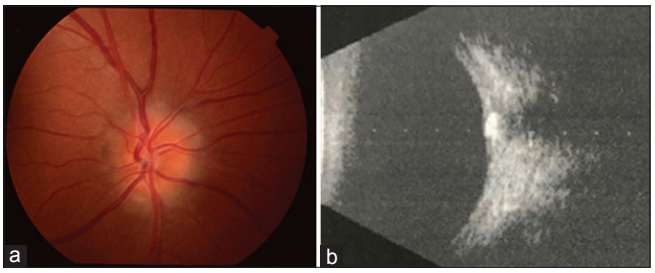

Figure 5: (a) Fundus photograph simulating papilledema. (b) B-scan image of the same patient with optic disc drusen showing a high spike

will lead to the inflation of retrobulbar portion of optic nerve sheath which can be measured using B-scan USG. Numerous small studies suggest its validity. In a study conducted by Goeres *et al*.,[21] the measured ONSD in healthy adult volunteers and the mean ONSD measurements for men were 3.78 mm [95% confidence interval (CI), 3.23–4.48) compared with 3.60 mm (95% CI, 2.83–4.11) for women. In our study, the mean ONSD in normal controls was much less at 3.12 (±0.22).

Standardized A-scan orbital USG allows for precise measurement of the ONSD. If this diameter is noted to be increased in primary gaze and diminishes by 25% in eccentric gaze (30° test), then increased subarachnoid fluid surrounding the optic nerve is presumed to be present and this finding is consistent with papilledema.[22] Presence of fluid around the optic nerve as a "crescent" or "doughnut" sign has been shown to be useful in confirming papilledema.[22]

This study has shown that in patients with papilledema, ONSD was increased compared with controls and similar results were found in other studies. However, the mean ONSD measurements in patients with raised ICP described in these studies (6.3 ± 0.66, 6.4 ± 0.6, 6.6 ± 0.58)[11,18,19] were much higher than that found in our study.

In our study, this increased ONSD was found even in very early papilledema, when clinical diagnosis of papilledema was equivocal. Thus, this noninvasive, objective imaging technique can be used in the diagnosis of early papilledema when the clinical diagnosis is ambivalent.

This study has also shown that with increasing severity of papilledema as graded by Frisén's grading, there was an associated progressive increase in ONSD which was statistically significant. The Frisén's grading is a staging scheme based on ophthalmoscopic signs of disturbed axoplasmic transport, which is widely used to clinically grade papilledema.[23] However, there are studies which have shown correlation of cerebrospinal fluid (CSF) opening pressures by lumbar puncture with ONSDs.[24-26] The study by Wang *et al*. repeated lumbar puncture after treatment to show decreasing CSF opening pressures were associated with decreasing ultrasonographic ONSD.[25] Hence, the measurement of ONSD in patients with raised ICP can also be used to monitor response to treatment especially in patients with conditions characterized by long-standing raised ICPs such as IIH and CVT and also in children.

Papilledema does not clinically manifest in patients with optic atrophy. However, raised ICPs can coexist in patients with optic atrophy [Fig. 4a and b]. In this study, we found increased ONSD in patients with optic atrophy and clinically absent papilledema with suspected raised ICP in six patients. Raised ICP was established with lumbar puncture. These patients

benefitted from medical reduction of ICP and optic nerve sheath fenestration. B-scan USG is a very useful noninvasive tool to confirm and monitor raised ICP in the presence of optic atrophy.

Our study has shown that B-scan is a useful tool to differentiate papilledema from pseudopapilledema [Fig. 5a and b]. Other studies have reported similar findings,[27] wherein the role of orbital USG in distinguishing papilledema from pseudopapilledema was evaluated. It is important to diagnose pseudopapilledema as it will save the patient unnecessary expensive investigations and the worry of a potentially ominous diagnosis.

The drawback of the study is the likelihood of investigator bias, as often the diagnosis of raised ICP or normal controls was known to the physician performing the B-scan USG.

Conclusion

In conclusion, in the presence of symptoms of raised ICP, an ultrasonographic ONSD >4 mm is diagnostic of papilledema. As ultrasonographic ONSD correlates well with the severity of papilledema, it is useful not only in the diagnosis of papilledema but also in the follow-up of patients with disorders with long-standing papilledema. It is also very useful in detecting raised ICP even in the presence of optic atrophy and to distinguish a true papilledema from pseudopapilledema. It is a safe and noninvasive technique easily available in most ophthalmology setups.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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