

# Can sonographic measurement of optic nerve sheath diameter be used to detect raised intracranial pressure in patients with tuberculous meningitis? A prospective observational study

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## Abstract

CNS Tuberculosis can manifest as meningitis, arachnoiditis and a tuberculoma. The rupture of a tubercle into the subarachnoid space leads to Tuberculosis Meningitis (TBME); the resulting hypersensitivity reaction can lead to an elevation of the intracranial pressure and hydrocephalus. While bedside optic nerve sheath diameter (ONSD) ultrasonography (USG) can be a sensitive screening test for elevated intracranial pressure in adult head injury, little is known regarding ONSD measurements in Tuberculosis Meningitis. **Objectives:** The aim of this study was to determine whether patients with TBME had dilation of the optic nerve sheath, as detected by ocular USG performed in the emergency department (ED). **Materials and Methods:** We conducted a prospective, observational study on adult ED patients with suspected TBME. Patients underwent USG measurements of the optic nerve followed by MRI. The ONSD was measured 3 mm behind the globe in each eye. MRI evidence of basilar meningeal enhancement and any degree of hydrocephalus was suggestive of TBME. Those patients without evidence of hydrocephalus subsequently underwent a lumbar puncture to confirm the diagnosis. Exclusion criteria were age less than 18 and obvious ocular pathology. In total, the optic nerve sheath diameters of 25 adults with confirmed TBME were measured. These measurements were compared with 120 control patients. **Results:** The upper limit of normal ONSD was 4.37 mm in control group. Those patients with TBME had a mean ONSD of 5.81 mm (SD 0.42). These results confirm that patients with tuberculosis meningitis have an ONSD in excess of the control data ( $P < 0.001$ ). **Conclusion:** The evaluation of the ONSD is a simple non-invasive and potentially useful tool in the assessment of adults suspected of having TBME.

**Key words:** Ophthalmic Ultrasound; optic nerve sheath diameter; tuberculous meningitis

## Introduction

More than four decades ago, it was shown by Hayreh that the optic nerve is surrounded by an extension of

the subarachnoid space covering the brain, and hence the cerebrospinal fluid (CSF) pressure changes can be transmitted along the optic nerve sheath.<sup>[1]</sup> It has also been observed that fundus changes begin to manifest several days after the rise in intracranial pressure (ICP), hence fundoscopy can be normal in the early stages in spite of raised ICP.

While bedside optic nerve sheath diameter (ONSD) on USG is known to be a sensitive screening test for elevated ICP in adult head injury, the potential of this tool in tuberculous meningitis (TBME) has not been explored. As the clinical outcome in meningitis depends on the stage at which

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therapy is initiated, early detection and treatment is of great importance. Early recognition would allow rapid treatment and improved resource utilization.

We conducted a prospective study using USG to measure ONSD in patients with TBME and compared the same with a control group.

## Materials and Methods

### Subjects

Patients with clinically suspected TBME were studied. Patients with history of ocular pathology like glaucoma/ocular trauma and past history of head injury/surgery/epilepsy/hydrocephalus were excluded. Subjects were of either gender of age 18-60 years.

### Scanning protocol

Bedside USG was done by emergency physician SS with 4 years of experience in the emergency department (ED). The examiner scanned both the eyes through closed eyelids in supine position using a high-resolution 10 MHz linear array transducer [Figure 1] with USG machine of Sonosite micromaxx (Sonosite, Inc., Bothwell, WA, USA). Ample amount of USG gel was used so as to prevent direct physical contact of the transducer with the eyelid. The power output and gain were turned down to minimum possible settings to achieve acceptable imaging. Each eye was scanned in both sagittal and transverse planes.

### Image analysis

The ONSD was measured 3 mm posterior to the globe for both eyes in each patient [Figure 2]. The two measurements were averaged. An average ONSD of 5 mm or greater was considered abnormal [Figure 3].

Patient was then sent to the radiology department for head magnetic resonance imaging (MRI). Other investigations like fundus examination, CSF findings, and biochemical and hematological profile were collected.

Data were analyzed using Student's paired/unpaired "t" test.

## Results

Twenty-five patients with suspected TBME were studied. Of these, 5 patients were female and 20 were male. The duration of presentation to ED varied from 1 to 15 days. All patients had basal meningeal enhancement on MRI study and all patients had undergone CSF examination for confirmation of the diagnosis of TBME. ONSD of more than 5 mm was considered abnormal.<sup>[2]</sup> All the patients in our study group had increased ONSD bilaterally. In the study group, average ONSD in the right eye was 5.83 mm (SD 0.42) and in the left eye was 5.78 mm (SD 0.43) ( $P = 1$ ). Overall, mean

ONSD in the study group was 5.81 mm (SD 0.42). None of the patients had papilledema on USG or fundoscopy. The highest ONSD recorded in the study group was 6.8 mm. The control group consisted of 120 healthy adults aged between 16 and 60 years. Control data suggested that the upper limit of normal for ONSD was 4.37 mm. These results confirmed that patients with TBME had ONSDs in excess of the control data ( $P < 0.001$ ). There were no complications from ocular USG examination. No patients complained of discomfort or pain. Time between USG examination and head MRI was not controlled, and hence it varied from patient to patient.

## Discussion

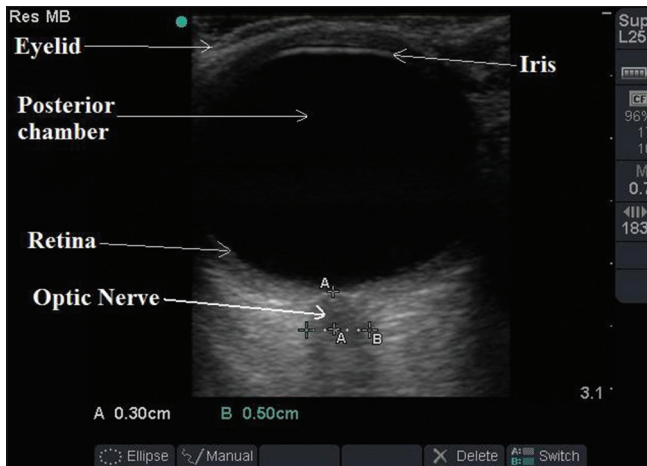
Tuberculosis constitutes a large global burden of disease. Central nervous system (CNS) tuberculosis can manifest as meningitis, arachnoiditis, and a tuberculoma. TBME, being the most common form of CNS tuberculosis, remains a common serious neurological emergency, especially in the developing world. The rupture of a tubercle into the subarachnoid space leads to TBME; the resulting hypersensitivity reaction can lead to an elevation of the ICP and hydrocephalus.

TBME is typically a subacute disease with symptoms that may persist for weeks before diagnosis. In our study also, the time of presentation of the patient to ED varied from a single day to 15 days after the onset of symptoms.

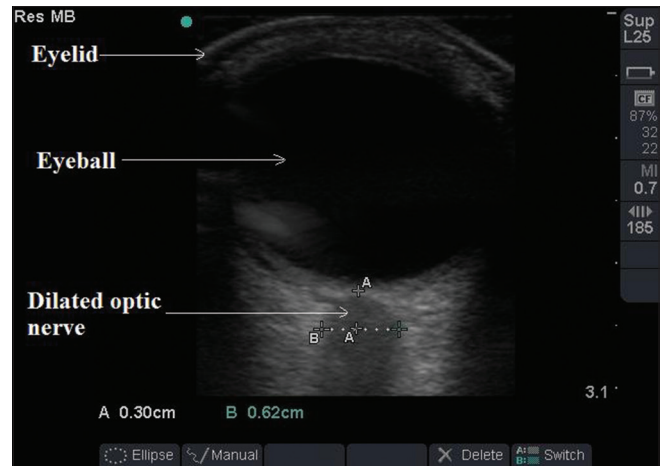
CSF examination and neuroimaging can aid in the diagnosis of TBME. Characteristic CSF findings of TBME include lymphocyte predominant leukocytosis, increased protein



**Figure 1:** High resolution 10MHz linear array transducer used in the study to measure optic nerve sheath diameter



**Figure 2:** Showing optic nerve sheath diameter (distance B) being measured 3mm (distance A) behind the eyeball



**Figure 3:** Showing abnormally increased optic nerve sheath diameter of 6.2 mm (distance B)

levels, and low glucose levels. However, presence of papilledema is a relative contraindication for performing CSF examination. Classic neuroradiologic features of TBME are basal meningeal enhancement, hydrocephalus, parenchymal granulomata and infarcts.<sup>[3]</sup> Hypodensities due to cerebral infarcts, cerebral edema, and nodular enhancing lesions may also be seen. MRI is the imaging test of choice for visualizing the abnormalities associated with TBME, as it is superior to computed tomography (CT) for evaluating the brainstem and spine. The T2W MRI imaging has been shown to be particularly good at demonstrating brainstem pathology; diffusion-weighted imaging (DWI) is considered to be the best for detection of acute cerebral infarcts due to TBME.<sup>[4]</sup>

Elevated ICP is often a feature of severe TBME and is associated with high morbidity and mortality. The pathological conditions associated with TBME, such as cerebral edema, hydrocephalus, tuberculomas, and infarcts related to arteritis, contribute to increase in intracranial volume and, therefore, elevated ICP. Rapid diagnosis of TBME and raised ICP is fundamental to clinical outcome.

There is no means of detecting elevated ICP in a rapid, noninvasive, bedside manner, with the exception of physical examination. But unfortunately, it would be difficult and inaccurate to detect raised ICP by physical examination alone, particularly when the patient is unconscious, sedated, or paralyzed. Increasing ICP can give rise to variable patterns of respiration. Papilledema and pupillary changes are the late findings that can take hours to appear.

The optic nerve (also known as cranial nerve II) is a continuation of the axons of the ganglion cells in the retina. The optic nerve, as a part of the CNS, is surrounded by a dural sheath that is distensible in its retrobulbar segment. Therefore, in the case of raised pressure in the CSF, the retrobulbar optic nerve sheath can inflate.

Ocular USG is extensively and safely used for ophthalmic evaluation after more than 20 years without specific contraindication, except for wounds of the ocular globe.<sup>[5]</sup> Multipurpose USG units with high-frequency transducers (>7.5 MHz), now available in most intensive care unit systems, have high lateral and axial precision.<sup>[6]</sup> There is increasing evidence suggesting that increase in the sonographic ONSD is related to and suggests raised ICP. It was shown during a lumbar intrathecal infusion test that maximal ONSD dilation was achieved at peak CSF pressure.<sup>[7]</sup> High ONSD values have been observed in children with clinical signs of high ICP during hydrocephalus or hepatic failure.<sup>[8,9]</sup> In adults with moderate traumatic brain injury, the ONSD correlates with signs of high ICP on CT scan.<sup>[10,11]</sup> Before Soldatos and colleagues' paper, however, only one clinical study had compared sonographic ONSD with invasive ICP, which remains the gold standard.<sup>[12]</sup>

Bedside ED ONSD USG has the potential to act as a sensitive screening test for elevated ICP in adult TBME. ONSD more than 5 mm correlates well with ICP more than 20 cm of H<sub>2</sub>O.<sup>[13]</sup> In our study, mean ONSD in patients with TBME was 5.81 mm which was significantly more than our control group mean ONSD (4.37 mm). Bedside ONSD takes only 1-2 min and diagnosis of raised ICP can be made rapidly.

As with fetal USG, it is important to limit the duration of the examination as much as possible, especially when using spectral and color Doppler, which are thought to produce increased levels of mechanical energy. Although there is still no evidence of harm to human tissues with properly set diagnostic medical USG, the most conservative approach is justified. Original recommendations about power output levels for ocular USG date back to 1976 and it is unclear whether they have any relevance to modern USG equipment.<sup>[14]</sup>

The major limitation to this study is its small sample size. However, to the best of our knowledge, this is the first study of its kind. The validation of this technology, although on a limited scale, should prompt its use by emergency ultrasonographers, and it will soon become possible to conduct larger studies.

To conclude, USG evaluation of the ONSD is a simple noninvasive procedure, which is a potentially useful tool in the assessment of raised ICP in adults suspected of having TBME.

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