

## **Ultrasound-derived Optic Nerve Sheath Diameter to Eyeball Transverse Diameter Ratio in the Diagnosis of Acute Meningitis in Adults**

Dear Editor,

Ultrasound measurement of optic nerve sheath diameter (ONSD) is a rapid and easily obtained bedside surrogate measurement

for intracranial pressure (ICP). However, recent studies have shown that the ultrasound ONSD/eyeball transverse diameter (ETD) ratio (USG ONSD–ETD ratio) provides

more reliable data than ONSD itself as a marker of raised ICP. Data regarding the usefulness of USG ONSD–ETD ratio for the prediction of possible acute meningitis in an emergency department (ED) setting are lacking. We sought to determine whether a USG ONSD–ETD ratio  $>0.22$  (which is a surrogate marker of raised ICP) could predict acute meningitis in ED before imaging and lumbar punctures. A prospective study was conducted among all patients above the age of 18 years presenting to ED with a history of acute severe headache with or without fever and clinical features suggestive of a central nervous system (CNS) infection. The study was conducted over a period of 1 year from February 2020 to March 2021. An USG ONSD–ETD ratio was obtained in these patients before they underwent brain imaging (computed tomography [CT]/magnetic resonance imaging [MRI]) and diagnostic lumbar puncture. After a diagnostic lumbar puncture was obtained, cerebrospinal fluid (CSF) data were analyzed. A total of 102 patients who presented to ED were included in the study. Fifty-nine patients (57.85%) had an ONSD–ETD ratio  $>0.22$ . Among these patients, 53 (89.83%) had meningitis confirmed by CSF study. False negatives included six patients with USG ONSD/ETD  $>0.22$ , who showed a normal CSF study. There were two false positives (patients with an ONSD–ETD ratio  $<0.22$ , who had CSF-confirmed meningitis). The sensitivity of USG ONSD/ETD  $>0.22$ , as a marker of acute meningitis, was 87.23% (95% CI, 74.25–95.17) and specificity was 96.36% (95% CI, 87.47–99.56). The positive predictive value for ONSD/ETD  $>0.22$ , as a marker of raised ICP when a patient is clinically suspected to have meningitis, was 95.35% (95% CI, 83.95–98.77). The negative predictive value was 89.83% (95% CI, 80.68–94.92). Our study shows that ultrasound USG ONSD/ETD ratio  $>0.22$  has a high sensitivity and specificity (87.23% and 96.36%, respectively) for diagnosis of acute meningitis in adults presenting with acute headache to ED, in whom a CNS infection is suspected. This easy bedside tool can be rapidly used to triage and identify patients who require admission and further evaluation for CNS infections. As papilledema is often a late sign in raised ICP and may be absent at the initial presentation, the USG ONSD/ETD ratio provides the physician with a cost-effective, accessible, and simple way to exclude a CNS infection. A limitation of our study was that CSF opening pressure measurements were not obtained. Hence, the cut-off values of the ONSD–ETD ratio which corresponded to a specific ICP could not be determined. Further larger studies are needed to validate the utility of the USG ONSD/ETD ratio in the rapid diagnosis of acute meningitis among ED patients presenting with acute severe headaches.

Globally, CNS infections contribute to over 3 million cases annually.<sup>[1]</sup> Headache is a common presenting complaint to ED and also a prominent symptom in CNS infection. Hence, effective headache triaging in ED is both critical and cost-effective in identifying patients who require further evaluation. Noninvasive measurement of raised ICP in ED is ideal, but poses challenges in this setting. ONSD measurement

is a surrogate marker for ICP in conditions like meningitis.<sup>[2]</sup> It is safe, unaffected by patient factors, and can better predict prognosis when combined with ETD ratio.<sup>[3]</sup> We aimed to assess the utility of the USG-ONSD/ETD ratio in patients presenting with acute headaches in ED with a clinical suspicion of acute meningitis. Papilloedema may not be present at the outset in meningoencephalitis, and fundoscopy has limitations in the ED setting. Hence, ONSD changes that reflect raised ICP and can be easily measured with an ultrasound have clinical utility.<sup>[4]</sup>

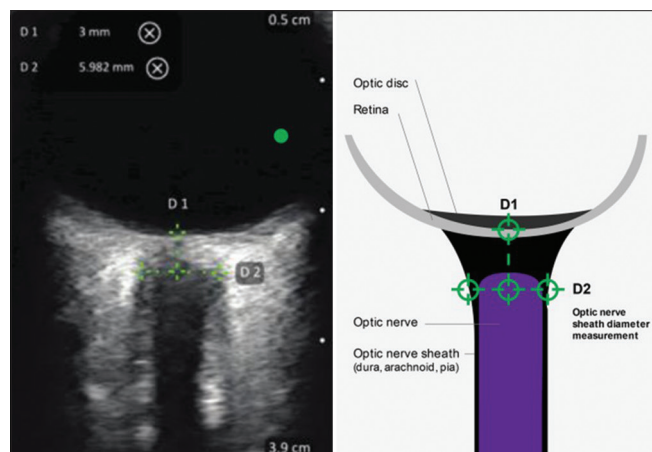
This prospective study was conducted in the ED of Aster Medcity, Kochi. Patients above the age of 18 years presenting to ED with an acute headache with fever or a recent history of fever were evaluated. The cut-off USG ONSD–ETD ratio was taken as 0.22, and those with a ratio  $>0.22$  underwent a diagnostic lumbar puncture. Patients were examined in the supine position with the head elevated to 20°–30° and eyes shut, and were asked to suppress any eye movement. A thick layer of conductive ultrasound gel was applied over the closed upper eyelid. B-mode ultrasound with a GE LOGIQ e portable ultrasound system and a GE 12L RS (5–13 MHz) linear probe was performed. The probe was placed gently on the gel in the upper eyelid to prevent undue pressure on the eye [Figures 1 and 2]. ONSD was defined as the distance between the external borders of the hyperechoic area, 3 mm posterior to the point where the optic nerve entered the globe, measured using an electronic caliper. ETD (retina to retina) was defined as the maximal transverse diameter of the eyeball that is obtained by scanning from the superior side to the inferior side [Figure 3]. Demographic details, ONSD/ETD ratio in each eye, and CSF analysis reports were collected. CSF was followed up further for characterization of the etiology of acute meningitis. The study was conducted after obtaining clearance from the Institutional Ethics Committee and informed consent from patients.

The study population included 102 patients, 59 males (57.8%) and 43 females (42.2%), between the ages of 18 and 82 years. The mean age of men in our study was 44.22 years and that of women was 44.07 years. Based on clinical assessment, all patients who underwent a CSF study also underwent neuroimaging (CT or MRI) before the lumbar puncture. The intervention was the measurement of USG ONSD–ETD ratio before brain imaging and CSF study. The USG ONSD–ETD ratio was  $>0.22$  in 59 of the 102 patients. This included 34 men and 25 women.

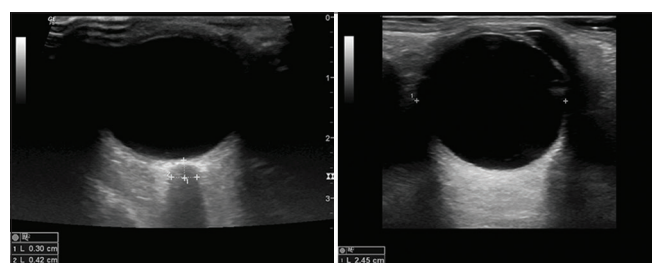
Out of the 102 patients included in the study, 55 patients were confirmed to have meningitis or encephalitis based on the CSF study (CSF Total count [TC] greater than 10 cells). This included 33 men (40%) and 22 women (60%). Thirty-five patients had fever (63%) and 20 (27%) were afebrile.

Out of the 59 patients who had ONSD/ETD  $>0.22$ , 53 patients had meningitis confirmed by the CSF study. Six patients with ONSD/ETD  $>0.22$  had a normal CSF study. Whereas of 43 patients with ONSD/ETD  $<0.22$ , only two ( $<3.6\%$ ) had

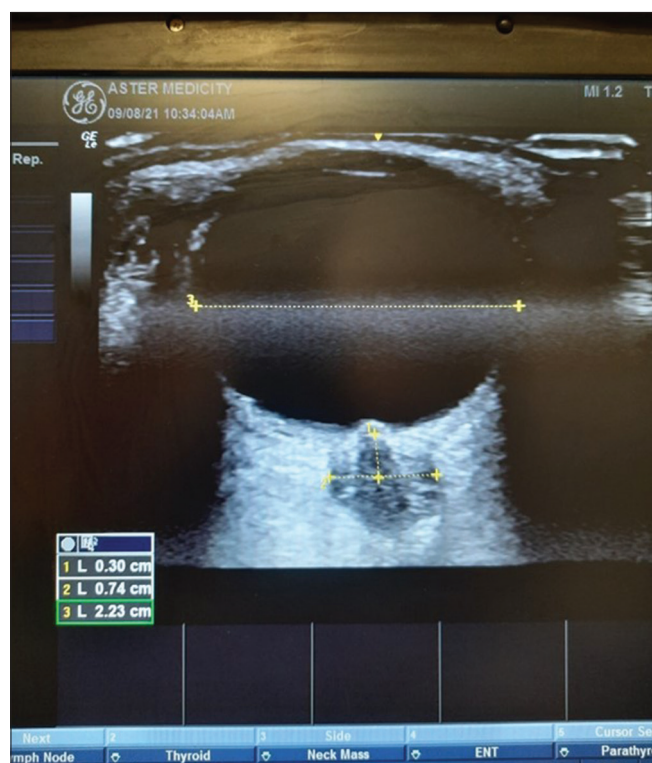
CSF-confirmed meningitis [Table 1]. The median ONSD in the study group with meningitis was 5.5 mm. The sensitivity



**Figure 1:** Electronic caliper adjustment for the measurement of optic nerve sheath diameter



**Figure 2:** Ultrasound measurement of ONSD and ETD. ETD = eyeball transverse diameter, ONSD = optic nerve sheath diameter



**Figure 3:** Measurement of ONSD/ETD. ETD = eyeball transverse diameter, ONSD = optic nerve sheath diameter

of ONSD/ETD >0.22 for the diagnosis of acute meningitis was 87.2% (95% CI, 74.25-95.17) and specificity was 96.4% (95% CI, 87.47-99.56). The positive predictive value for ONSD/ETD >0.22 for the diagnosis of acute meningoencephalitis was 95.35% (95% CI, 83.95-98.77). The negative predictive value was 89.8% (95% CI, 80.68- 94.92) [Table 2].

Among the 55 patients who had meningitis, nine patients with confirmed bacterial meningitis (*Klebsiella pneumoniae*, *Escherichia coli*, *Streptococcus suis*, methicillin-sensitive *Staphylococcus aureus*, *Serratia marcescens*, *Burkholderia pseudomallei* [from culture of biopsy specimen], and *Borrelia burgdorferi* [by detection of antibodies]), three patients with confirmed tuberculous meningitis, one patient with viral herpes simplex 2 (HSV2) meningitis, and two patients with confirmed fungal meningitis (*Nocardia farcinica* and *Aspergillus fumigatus*) had an USG ONSD–ETD ratio >0.22. In the remaining 40 meningitis patients, no definite etiology was determined. There were also two patients with aseptic meningitis in whom the USG ONSD–ETD ratio was <0.22.

Studies have shown the usefulness of ONSD in meningoencephalitis, with an ONSD of over 5 mm indicating elevated ICP.<sup>[4]</sup> However, demographic factors can affect ONSD values and this has led to the use of USG ONSD–ETD ratio as a better indicator of ICP.<sup>[5]</sup> This ratio has been validated in pathologies such as traumatic brain injury and idiopathic intracranial hypertension.<sup>[6]</sup> We evaluated the utility of USG ONSD–ETD ratios in patients presenting to ED with acute headaches. We found that a USG ONSD–ETD ratio >0.22 had a good sensitivity (96%) and specificity (87%) in identifying acute meningitis. This simple, noninvasive test can rapidly identify raised ICP as a surrogate for acute meningitis in patients presenting to ED with acute headache, even if they are afebrile. This potentially reduces the need for costly imaging or invasive procedures like lumbar punctures in low-resource settings. Our study’s limitation is the lack of CSF opening

**Table 1: ONSD/ETD measurements in our patients**

	No meningitis	Meningitis	Total
ONSD/ETD			
<0.22	41 (87.2%)	2 (3.6%)	43
>0.22	6 (12.8%)	53 (96.4%)	59
Total	47	55	102

ETD=Eyeball transverse diameter, ONSD=Optic nerve sheath diameter

**Table 2: Sensitivity and specificity of ONSD/ETD >0.22 for predicting raised ICP in acute meningitis**

Statistics	Value (%)	95% CI
Sensitivity	87.23	74.26–95.17
Specificity	96.36	87.47–99.56
Positive predictive value	95.35	83.96–98.77
Negative predictive value	89.83	80.68–94.92

CI=Confidence interval, ETD=Eyeball transverse diameter, ICP=Intracranial pressure, ONSD=Optic nerve sheath diameter

pressure measurement in all patients, which prevented us from determining whether the USG ONSD–ETD ratio corresponded to a specific CSF pressure. In conclusion, ultrasound evaluation of the orbital ONSD–ETD ratio is an easy and rapid technique with a good sensitivity and specificity for triaging patients with acute headaches in ED. It can identify patients who need further neurologic investigations, potentially reducing costs and invasive procedures.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

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**Submitted:** 03-Sep-2023 **Revised:** 18-Dec-2023 **Accepted:** 22-Dec-2023

**Published:** 07-Feb-2024

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**DOI:** 10.4103/aian.aian\_793\_23