



ORIGINAL ARTICLE

Transcranial Ultrasound Guided Assessment of Brain Midline Shift in Neuro Intensive Care Unit

Munta Kartik,¹ N. Sunil Kumar,^{2,*} Rajkumar Jupally³ and Suryaprakash Y¹

¹*Consultant Critical Care Physician, Yashoda Hospitals, Somajiguda, Hyderabad, Telangana, India*

²*Assistant Professor in Dept. of Anaesthesiology & Critical Care Medicine, Osmania Medical College / General Hospital Hyderabad, Telangana*

³*Consultant Critical Care Physician Apollo Hospitals Hyderabad, Telangana, India*

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Abstract

Background: Neuro Intensive Care Unit (Neuro-ICU) handles neurological emergencies that involve intracranial (IC) hemorrhages. It can be challenging to manage elevated intracranial pressure (ICP) and midline shift (MLS), as they require constant monitoring and frequent imaging. Trans-cranial Color Coded Sonography (TCCS), a bedside monitoring tool, may be helpful in monitoring MLS under such conditions. **Objectives:** To correlate MLS of the third ventricle in the brain measured by TCCS with CT midline shift. **Method:** A prospective observational study was conducted on patients with IC bleed who were mechanically ventilated and had a head CT done to rule out MLS. Within an hour of doing a CT brain, TCCS-MLS was identified. Data was collected and analyzed. **Results:** A total of fifty patients studied, the MLS (mean \pm SD) was 5.3mm \pm 3.1 mm using TCCS and 6.7 \pm 4.4 mm using CT brain. The calculated midline shift between TCCS and CT brain demonstrated a Pearson's correlation of 0.78 (P<0.001). With TCCS, the area under the ROC curve to identify a significant MLS was 0.91 (95%CI=0.8-1). TCCS-MLS of 3.9mm as a cut-off, predicted the occurrence of >5mm MLS on CT scan with a sensitivity of 95% and specificity of 90%. **Conclusions:** This study suggests that TCCS could serve as an alternative bedside monitoring tool in patients whose transportation is risky, in predicting the transcranial MLS >5mm with reasonable accuracy.

Keywords: Transcranial ultrasonography, Neuro-imaging techniques, Midline shift, Neuro critical care

*Corresponding Author: Sunil Kumar
Email: sunildockmc@gmail.com

Graphical Abstract

Transcranial Ultrasound Guided Assessment of Brain Midline Shift in Neuro Intensive Care Unit. Dr. MUNTA KARTIK,¹ Dr. N. Sunil Kumar,^{2*} Dr. RAJKUMAR JUPALLY,³ Dr. SURYAPRAKASH⁴ 1,3,4 Consultant Intensivist, Yashoda Hospital, Somajiguda, Hyderabad, India. 2: Assistant Professor Dept. of Anesthesiology & Critical Care Osmania Medical College/ General Hospital. *Corresponding Author.	
<p>Background: Neuro Intensive Care Unit (Neuro-ICU) handles neurological emergencies that involve intracranial (IC) hemorrhages. It can be challenging to manage elevated intracranial pressure (ICP) and midline shift (MLS), as they require constant monitoring and frequent imaging. Trans-cranial Color Coded Sonography (TCCS), a bedside monitoring tool, may be helpful in monitoring MLS under such conditions.</p> <p>Methods: A prospective observational study was conducted after ethical committee approval on 50 patients with IC bleed who were mechanically ventilated and had a head CT done to rule out MLS. Within an hour of doing a CT brain, TCCS-MLS was identified. Correlation between the TCCS and CT brain derived MLS were correlated with the help of Pearson's correlation coefficient and agreement between both methods was studied by using the Bland-Altman method. The receiver operating characteristic (ROC) curve was plotted to ascertain sensitivity and specificity for detecting the significant MLS.</p>	<p>Results: The mean age of the enrolled patients in the study was 56.3±16 years. Out of which 64% were men and 36% were women respectively. At the time of admission to emergency room, the mean admission GCS was 7.10±1.63. Of the fifty participants, 21 (42%) had spontaneous intracranial bleeding, while 13 (27%) suffered from a traumatic brain injury. MLS: Out of the fifty subjects, the mean CT-MLS estimated using Method-1 was 6.7 ± 4.4mm and for Method-2 it was 6.5 ± 3.8mm. All the patients who were involved in the trial had a TCCS-MLS measurement done and the mean TCCS-MLS was 5.3 ± 3.1mm. Measures of Correlation and Limits of Agreement: Pearson's correlation coefficient between USG-MLS and CT-MLS was 0.78 with method-1 (P <0.001) and 0.88 with method-2 (P<0.001). The boundaries of agreements for MLS measurements with TCCS and the two CT methods were plotted using Bland-Altman techniques. A Bland-Altman study comparing CT method-1 and TCCS revealed a 1.43mm bias with ranges of agreement ranging from 6.92 to -4.05mm. There were three measurements that fell outside the agreement range (~8%). A Bland-Altman study comparing TCS and CT technique 2 revealed limits of agreement ranging from 4.64 to -2.29 mm, with a bias of 1.17 mm. Two measures were outside the limits of the agreement (~5%). ROC curve analysis: The predictability of sonography in measuring 'significant' MLS (i.e. MLS >5 mm), was determined by the area under the ROC curve (AUC). AUC of 0.91 (95% confidence interval (CI) 0.80 to 1.0% with a cutoff of 3.9 mm. The sensitivity of TCCS in detecting a significant MLS (>5mm) was 95%, specificity was 90%, positive predictive value was 91.3%, negative predictive value was 93.3% and positive likelihood ratio was 9.5 respectively.</p>
 <p style="text-align: center;">National Board of Examinations Journal of Medical Sciences</p>	<p>Conclusions: This study suggests that TCCS could serve as an alternative bedside monitoring tool in patients whose transportation is risky, in predicting the transcranial MLS >5mm with reasonable accuracy.</p>

Introduction

Patients with traumatic brain injuries who are admitted to the Neuro-ICU need immediate attention to manage elevated intracranial pressure. Malignant MCA infarcts and spontaneous intracranial bleeding require vigilant observation and prompt decision-making to prevent the adverse effects of elevated ICP. The human head is approximately bilaterally symmetrical; therefore in neuro-radiology small anatomical alterations typically lack a significant clinical influence [1]. One of the most crucial elements in enabling neurosurgeons to take prompt, appropriate action when managing patients with MLS is the accurate assessment of the degree of midline shift on CT brain.

Over the past few decades, the diagnosis of serious neurological conditions has relied on the shift of midline structures. In earlier times, the initial step in

MLS detection was to observe a calcified pineal gland on an ordinary X-ray [2]. Since the invention of CT scan technology, it has become an essential aspect of head injury patients' treatment regimens. Currently, CT brain remains a highly reliable method of diagnosing MLS. A number of methods for estimating MLS on CT brain have been reported in the literature. This involves determining the distance between the septum Pellucidum and ideal midline [3,4], the deviation of the pineal body from the center of the brain [5], and the displacement of the third ventricle's center from either side of the skull bone [6]. The latter of which has been shown to correlate well with the outcome.

Marshall and coworkers established a CT scan classification utilizing information from the Traumatic Coma Data Bank. An MLS of greater than 5 mm was one of the elementary criteria for classifying

a degree of a traumatic brain injury according to this classification [7]. A number of CT indicators of injury severity, such as mass lesions, compressed basal cisterns, or traumatic SAH, have been demonstrated to have a strong correlation with the Glasgow Coma Score. [8, 9, 10] Within two weeks of traumatic brain injury, compression of the 3rd ventricle and an MLS exceeding five millimeters were significant predictors of death [11].

According to the Brain Trauma Foundation (BTF) statement, MLS on CT brain is measured at the level of the Foramen of Monro. They recommend for emergency surgical treatment for any traumatic disorder resulting in an MLS greater than 5mm. The risks associated with transferring critically ill patients to radiology units for performing serial CT scans is challenging always [12], for the same reason its value in acute care settings is questionable [13].

Ultrasound is a bedside, repeatable, non-invasive, and radiation-free modality. Its significance in the field of acute critical care settings continues to grow. As the age advances thickness of the temporal bone increases, limiting the application of sonography in this area, for that reason ultrasound is not the preferred diagnostic modality for adult brain imaging. With the advancements in tissue contrast and image resolution, the ability to visualize brain cross sectional images has become possible [14]. Intracranial blood vessels and parenchymal structures can be visualized using TCCS [14]. The display image of cranial ultrasound at the level of temporal bone can help in visualizing cerebrospinal

fluid containing the third ventricle along with brain parenchyma. This can be used as an accurate source of information regarding the lateral displacement of the third ventricle in space-occupying lesions of brain, and can be utilized as a diagnostic criterion for MLS [15,16].

The first approach for measuring MLS using TCCS was described by Seidel and colleagues in 1996. Several studies subsequently assessed the method's reliability in providing information about the third ventricle diameter and lateral displacement. Given that MLS measurement may be able to predict outcomes prior to clinical findings in critically ill patient; TCCS can be utilized for repeated monitoring at shorter intervals and even in these patients during the acute phases of their illness [17].

The purpose of our study was to evaluate the correlation between the measurements of the midline shift calculated by TCCS and CT scan among traumatic brain injury, spontaneous intracranial bleeding and acute infarct groups of patients on mechanical ventilator support being admitted to Neuro-ICU.

Methods

This prospective observational study was conducted in a Neuro-ICU of a tertiary care hospital from south India. After obtaining approval from the institutional ethical committee, all those patients who fulfilled the following inclusion criteria were enrolled into the study following the acquisition of a valid informed, written consent from the next of kin of the patients.

Inclusion criteria

- i. Patients aged ≥ 18 years admitted to Neuro-ICU with suspected raised ICP and requiring mechanical ventilator support.

Exclusion criteria:

- i. Post de-compressive craniotomy.
- ii. Maxillofacial trauma.
- iii. Poor image acquisition due to thick temporal bone.

A total of sixty-five mechanically ventilated Neuro-ICU admitted patients of both genders, who have suspected raised ICP were subjected to bedside TCCS. Two sonographers (consultants), who received training in comprehensive ultrasound workshops in ICU and had an experience of around five years performing USG in ICU, performed TCCS. Patients were subjected to CT brain within three hours of conducting a TCCS. Radiologist and investigators were

blinded of TCCS and CT brain findings respectively.

Procedure for determining MLS with TCCS

In patients when there is a suspicion of elevated ICP, the ultrasound MLS was conducted using a low frequency (2 to 4 MHz) probe (SonoSite) through the temporal acoustic bone window. Circle of Willis was identified, at the same level adjusting the depth and gain brain stem image was visualized as a butterfly like structure. Tilting the probe to 10° cephalic at this level third ventricle was visualized as double hyper echoic parallel running lines with hypo echoic centre. The distance between centre of third ventricle and the outer table of the skull bone was measured on either side. (Figure 1) The difference between both the measurements is divided by two to obtain the TCCS-MLS = $(B-A)/2$.

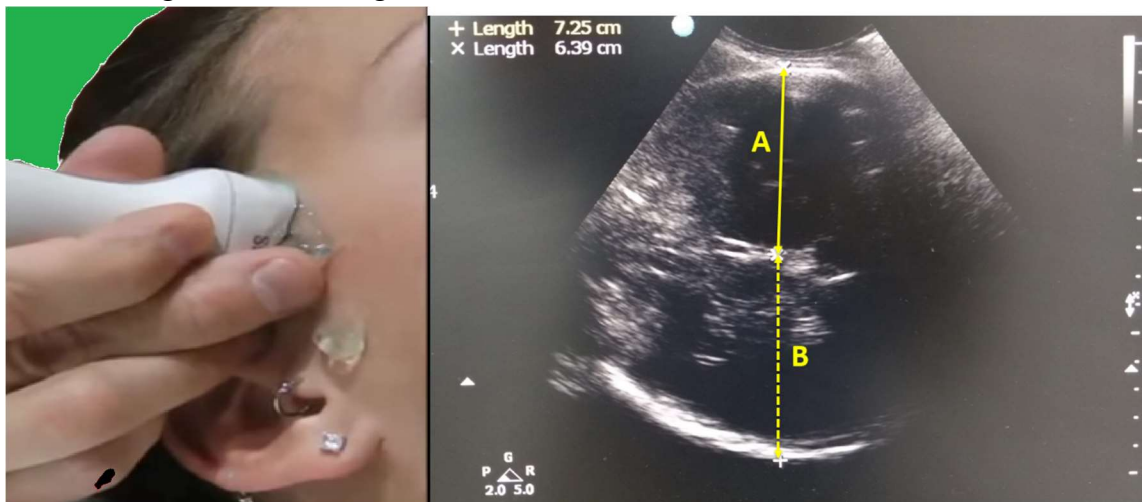


Figure 1. Figure showing placement of Ultrasound probe over Temporal bone (Left), Figure showing Ultrasound image with third ventricle in the center and measurement of MLS (Right). (A- Measurement on ipsilateral side third ventricle distance from skull bone, B- Measurement of distance from third ventricle to contralateral side of skull bone).

Procedure for determining MLS with CT brain

CT method 1

MLS in this method was defined as the distance between the midline determination and the septum pellucidum. It was used as a gold standard and any shift of $\geq 5\text{mm}$ was considered a significant MLS.

CT method-2

MLS in this method was defined as the distance between the external bone table and the center of the third ventricle at the orbito-meatal plane. [6] These CT methods were performed by the radiologist, who was blinded of TCCS findings. (Figure 2) Data was collected and analyzed for the association.

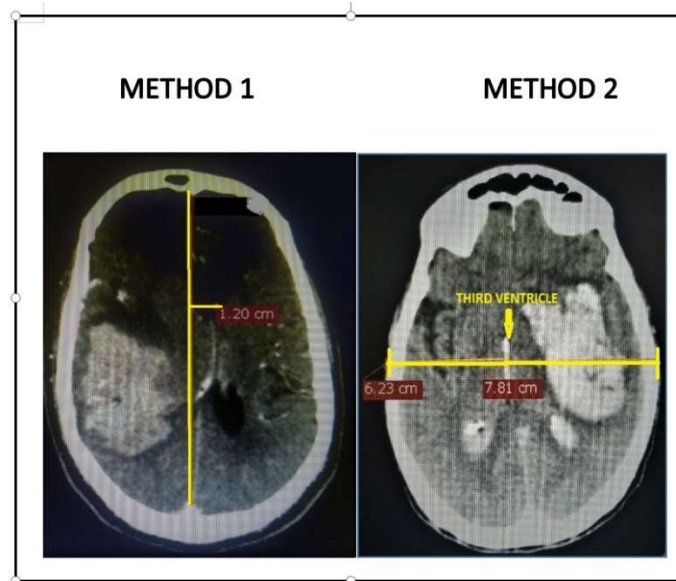


Figure 2. CT scan methods of measuring MLS. (Method-1: Distance between the midline and the septum pellucidum, Method-2: Determining midline from third ventricle).

Statistical analysis of data

Data was collected, tabulated using MS Excel and analysis was done using IBM-SPSS software. Qualitative data was analyzed by calculating percentages and quantitative data was analyzed as mean \pm SD. P-value <0.05 was considered significant. Correlation between the TCCS and CT brain derived MLS were correlated with the help of Pearson's correlation coefficient and agreement between both methods was studied by using the Bland-Altman method by measuring the limits of agreement and mean bias. The receiver

operating characteristic (ROC) curve was plotted to ascertain sensitivity and specificity for detecting the significant MLS.

Results

A total of sixty five participants were enrolled in the study over the study period. Fifteen individuals (23%) were deemed ineligible for the trial because of the non-visualization of the third ventricle through the skull bone. Remaining fifty patient's data has been collected and analyzed.

Demographic and Etiological data

The mean age of the enrolled patients in the study was 56.3 ± 16 years. Out of which 64% were men and 36% were women respectively. At the time of admission to emergency room, the mean admission GCS was 7.10 ± 1.63 . Of the fifty participants, 21 (42%) had spontaneous intracranial bleeding, while 13 (27%) suffered from a traumatic brain injury.

MLS

Out of the fifty subjects, the mean CT-MLS estimated using Method-1 was 6.7 ± 4.4 mm and for Method-2 it was 6.5 ± 3.8 mm. All the patients who were involved in the trial had a TCCS-MLS measurement done and the mean TCCS-MLS was 5.3 ± 3.1 mm.

Mean midline shift(mm)	Septum pellucidum shift	Third ventricle shift	USG midline shift
	6.75 ± 4.48 mm	6.50 ± 3.80 mm	5.32 ± 3.15 mm

Figure 3. Mean Midline Shift CT scan methods and Ultrasound Method.

Measures of Correlation and Limits of Agreement

Pearson’s correlation coefficient between USG-MLS and CT-MLS was 0.78 with method-1 ($P < 0.001$) and 0.88 with method-2 ($P < 0.001$). The boundaries of agreements for MLS measurements with

TCCS and the two CT methods were plotted using Bland-Altman techniques. A Bland-Altman study comparing CT method-1 and TCCS revealed a 1.43mm bias with ranges of agreement ranging from 6.92 to -4.05mm. There were three measurements that fell outside the agreement range ($\approx 8\%$).

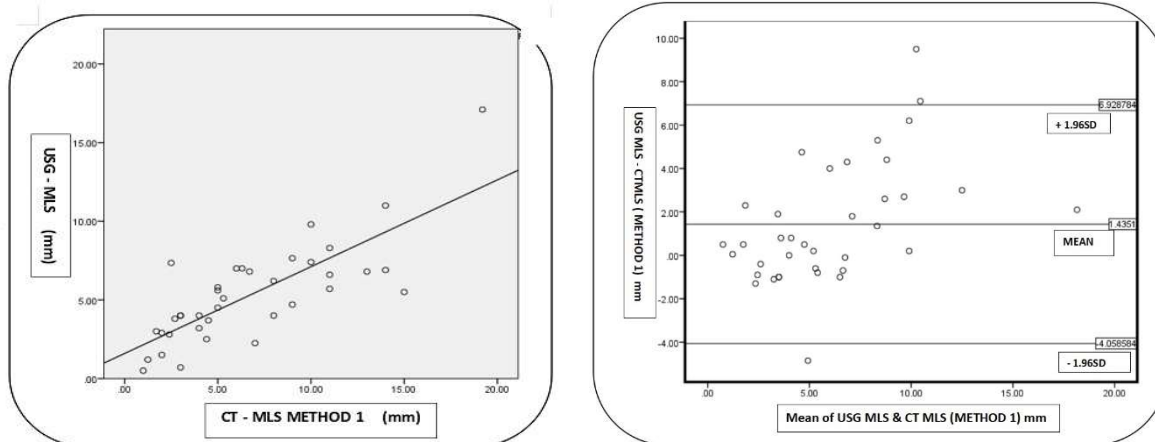


Figure 4. Comparison of CT method-1 and Ultrasound method.

A Bland-Altman study comparing TCS and CT technique 2 revealed limits of agreement ranging from 4.64 to -2.29 mm,

with a bias of 1.17 mm. Two measures were outside the limits of the agreement ($\approx 5\%$).

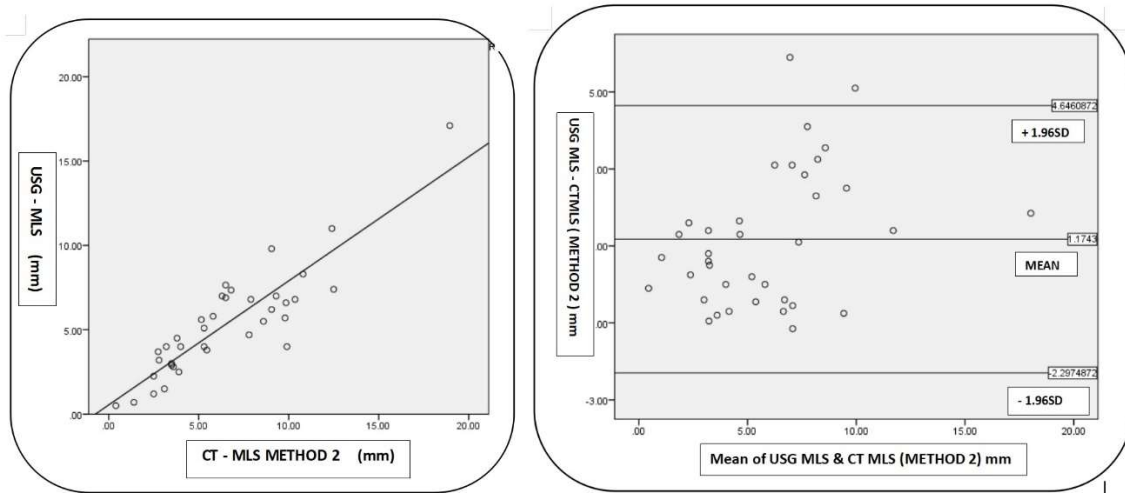


Figure 5. Comparison of CT method-2 and Ultrasound method.

ROC curve analysis

The predictability of sonography in measuring ‘significant’ MLS (i.e. MLS >5 mm), was determined by the area under the ROC curve (AUC). AUC of 0.91 (95% confidence interval (CI) 0.80 to 1.0% with a

cutoff of 3.9 mm. The sensitivity of TCCS in detecting a significant MLS (>5mm) was 95%, specificity was 90%, positive predictive value was 91.3%, negative predictive value was 93.3% and positive likelihood ratio was 9.5 respectively.

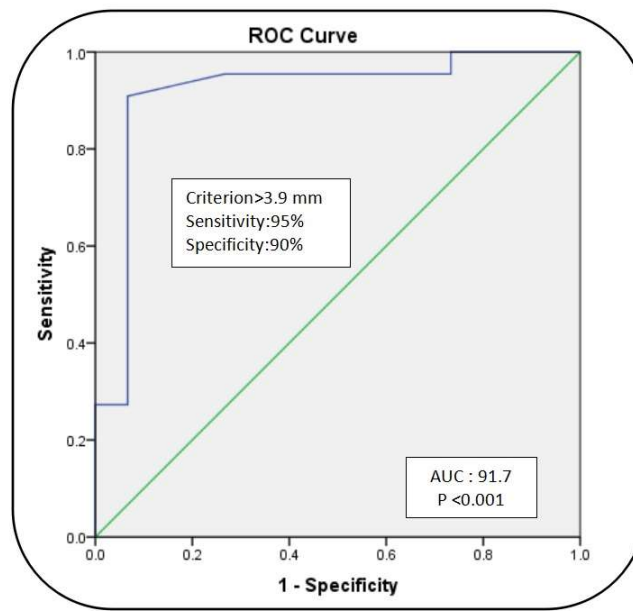


Figure 6. Receiver Operating Characteristic Curve showing Sensitivity and Specificity of Ultrasound.

DISCUSSION

A midline shift of brain parenchyma has been associated with a worsening in sensorium, like drowsiness, stupor and comatose condition. The management for patients with raised ICP has greatly benefited from the detection of horizontal displacement of brain parenchyma from the midline. It is essential to recognize major MLS in Neuro-ICU patients as early as possible for the execution of a suitable management plan. MLS on CT brain correlates well with GCS and magnitude of severity of brain injury [18]. In order to evaluate the precision of MLS determined by USG and assess if the values obtained were consistent with CT brain results, we carried out a prospective observational study.

Bogdhan et al. (1990) were the first to use sonography to identify the brain structures and were able to delineate third ventricle on USG [14]. Subsequently, in 1996, Seidel et al. proposed using sonography to quantify the MLS by using the third ventricle as an essential reference point [15]. They studied on sixty-one patients who presented with acute ischemic stroke (supratentorial infarction) leading to mass effect in brain. The correlation between sonographic measurements of MLS with CT brain in a span of 12-hour time duration was more than 0.9. They showed good reproducibility for the measurements even in the healthy subjects too [15].

Trans-cranial sonography has also been utilized to monitor ventricular width in patients with hydrocephalus. A study conducted by Tamer et al, over a period of one year, on thirty seven individuals

concluded that a ventricular width of ≥ 5.5 mm demonstrated a high sensitivity (100%) and specificity (83%) for raised ICP, and a decision was made on the basis of USG observations whether to clamp lumbar or extra-ventricular drainage system or not [19].

An ultrasound MLS of >4 mm within the first 32 hours of the event, was associated with nearly 100% mortality, according to a research by Gerriets et al in 1999, with the exception of patients who had undergone decompressive craniotomy [16]. In 2014, Motel et al. investigated 52 patients in a neurosurgical ICU utilizing sonographic MLS. The brain CT scan and sonography had a Pearson's correlation coefficient (r) of 0.65 ($P < 0.001$), with 84.2% sensitivity and 84.8% specificity [18]. Subsequently in 2019 Tamer et al. observed a Pearson's correlation of 0.986 and 0.984 with both the methods of determination of MLS on CT scan with respect to USG and an AUC of 0.98 with a 4mm cut off having 95% sensitivity and 96.6% specificity. These findings suggest that USG guided determination of MLS can serve as a handy bedside tool to facilitate early diagnosis and management of patients with a significant intracranial mass effect [19].

Present study included critically ill patients, with a mean APACHE II of 21 and SOFA score of 10, out of which 48% had a significant MLS on the CT brain. Values of correlation were 0.78 and 0.88 with both the methods of CT-MLS with respect to TCCS and ROC curve analysis showing AUC of 0.91 having a cut-off measure of 3.9mm with a sensitivity of 95% and specificity of 90% respectively, which are comparable to

those observed in earlier studies, even though our study included a versatile group of patients with neurological [20], and neurosurgical [6] issues, unlike prior studies which looked at specific group of patients. About 13(27%) of patients had traumatic brain injury with subcutaneous temporal haematoma, which influenced the measurement of sonography and could be a reason for a slight decrease in correlation values in our study. However, even though MLS may be underestimated by TCCS, the predictability to detect significant MLS (>5mm on CT brain) with TCCS was good in our study, with a sensitivity and specificity around 90%, when using a cut-off for a significant MLS set at 3.9mm. It is important to remember that a significant underestimation of MLS from TCCS in patients with large MLS has also been observed. The difference between sonography and CT brain seemed to increase with a higher value of MLS on CT brain; this was observed in around three patients in the present study [21].

In the literature search and to our knowledge, we could find very few of this kind studies which included versatile patients and second of its kind from an Indian subset of patients studying on bedside utilization of trans-cranial ultrasound in detecting intracranial MLS. Road traffic accidents are the major cause of mortality in developing countries like India, where medical facilities are constrained, and repeated CT imaging may add to morbidity, in such circumstances bedside assessment and monitoring of MLS with sonography adds an additive tool to the armamentarium of patient care in Neuro-ICUs.

There have been a few limitations in the study. First, a single operator performed the TCCS measurements at any given point of time. We could not study inter-observer variability, which could have been of interest to validate this method for clinical use. Second, we excluded nearly 23% of subjects from the study as TCCS could not be done due to poor temporal acoustic bone windows which could have caused selection bias. Thirdly, the location of bleed or infarct could not be captured in the study population which could have explained the variations of MLS. In the present study, the experience in performing brain sonography has been improving with the time duration of the study which might have affected the accuracy of earlier TCCS readings in determining MLS.

Ultrasound could be seen as a reliable bedside alternative modality in measuring midline shift in critically ill patients. It could play an important role in patients, in whom transportation on regular basis is not possible due to unstable clinical conditions and ventilatory support. Owing to its non-invasiveness, repeatability, accuracy, and reliability, it might be used as a prognostication and monitoring tool for raised intracranial pressure; nonetheless, a CT brain would be a more accurate diagnostic tool for MLS. Several more research trials of this kind are needed in the future to support the idea of bedside MLS monitoring for patients who are critically ill.

Conclusion

This study suggests, TCCS might be successful to predict raised intracranial mass effect in Neuro-ICU patients in the form of a

significant midline shift that is comparable to a CT midline shift of >5mm. It may also be an effective bedside tool that can replace CT brain in facilitating early diagnosis of worsening MLS as well as establishing early therapeutic interventions. With more and more literature being published and further development of the technology and experienced skilled operators, TCCS could serve as a potential tool in the armamentarium of critical care physicians in treating critically ill patients.

Statements and Declarations

Conflicts of interest

The authors declares that they do not have conflict of interest.

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