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● *Original Contribution*

EVALUATING AFFORDABLE CRANIAL ULTRASONOGRAPHY IN EAST AFRICAN NEONATAL INTENSIVE CARE UNITS

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Abstract—Neuroimaging is a valuable diagnostic tool for the early detection of neonatal brain injury, but equipment and radiologic staff are expensive and unavailable to most hospitals in developing countries. We evaluated an affordable, portable ultrasound machine as a quantitative and qualitative diagnostic tool and to establish whether a novice sonographer could effectively operate the equipment and obtain clinically important information. Cranial ultrasonography was performed on term healthy, pre-term and term asphyxiated neonates in Rwandan and Kenyan hospitals. To evaluate the detection of ventriculomegaly and compression injuries, we measured the size of the lateral ventricles and corpus callosum. The images were also assessed for the presence of other cerebral abnormalities. Measurements were reliable across images, and cases of clinically relevant ventriculomegaly were detected. A novice sonographer had good-to-excellent agreement with an expert. This study demonstrates that affordable equipment and cranial ultrasound protocols can be used in low-resource settings to assess the newborn brain. (E-mail: annikalinke@gmail.com)

Key Words: **Cranial ultrasound, Neonatology, Perinatal brain injury, Prematurity, Birth asphyxia, Ventriculomegaly.**

INTRODUCTION

Approximately half of all neonatal deaths in sub-Saharan Africa are due to perinatal asphyxia and complications of prematurity (Lawn and Kerber 2006). Early detection and treatment of brain injuries associated with these conditions is crucial to reduce mortality and long-term cognitive, behavioral, sensory, language and motor sequelae in survivors.

Cranial ultrasonography (cUS) is the preferred initial modality for imaging the neonatal brain (Van Wezel-Meijler 2007). cUS is non-invasive and can be performed at the bedside in neonatal intensive care units (NICUs). The development of ultrasound technology into affordable, lightweight, portable devices (Hwang et al. 1998) confers a great advantage over other imaging modalities. These portable ultrasound models include simple, user-friendly software interfaces, which reduce the traditional requirement for an operator with advanced technical expertise. Together, these characteristics have made implementing ultrasonography in developing world hospitals increasingly more feasible. Studies in Cameroon (Steinmetz and Berger 1999), Tanzania (Adler et al. 2008), Rwanda (Shah et al. 2009) and Ghana (Spencer and Adler 2008) provide evidence that portable ultrasound machines can be effective as a diagnostic tool in multiple clinical contexts by adding to diagnoses and influencing outcome or decisions regarding treatment. However, there is a lack of evidence demonstrating the utility of these devices as a neurodiagnostic tool in neonates.

Fluid-filled lateral ventricles are relatively easy to visualize with cUS because they are anechoic and situated below the anterior fontanelle, the most commonly used acoustic window. Qualitative and quantitative assessment of the lateral ventricles and periventricular

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areas from ultrasound scans can facilitate early diagnosis of the most common brain anomalies found in neonates, such as ventriculomegaly, intraventricular hemorrhage (IVH), periventricular leukomalacia and edema (indicated by slit-like ventricles combined with hyper-echogenic parenchyma and the loss of normal tissue differentiation [Van Wezel-Meijler et al. 2010]).

In neonates with perinatal asphyxia, edema is a strong indicator of severe, global hypoxic-ischemic insult and is prognostic of poor outcome (Roland et al. 1998; Van Wezel-Meijler et al. 2010). IVH is particularly common in pre-term neonates, usually originating from the immature germinal matrix and subsequently spreading throughout the ventricular system (Volpe 2008). After a severe bleed (grade III and IV IVH) the risk of developing post-hemorrhagic ventricular dilation (PHVD) is substantial. Hemorrhage can prevent drainage of cerebrospinal fluid, leading to hydrocephalus.

In low-income countries, where ultrasound equipment is mostly unavailable, basic clinical observations are used to diagnose PHVD and other causes of ventriculomegaly. For example, the rate of head growth and signs of increased intra-cranial pressure, such as persistent bulging and a tense fontanelle, can be used to help diagnose post-hemorrhagic hydrocephalus. Unfortunately, the onset of rapid head growth and intra-cranial hypertension are often late indicators, manifesting days to weeks after the onset of ventricular distention, distortion of the parenchyma and possibly mechanisms leading to secondary brain injury (Volpe et al. 1977). Early detection is crucial as ventriculomegaly in pre-term infants is a strong predictor of cortical and white matter injury (Kuban et al. 1999), and PHVD is associated with a high risk of serious cognitive disability, cerebral palsy and visual and hearing impairments (Brouwer et al. 2008). cUS can facilitate early detection as it provides a means to directly assess ventricular dilation and parenchymal distortion, such as thinning of the corpus callosum (Barkovich 2005).

To detect ventricular enlargement early and to monitor its subsequent changes, it is most effective to perform quantitative measurements and compare them to established norms (Sondhi et al. 2008). A few studies in the developing world have quantitatively assessed ventricle size, but they utilized complex cUS equipment (Ebruke et al. 2010; Hagmann et al. 2011) that is too expensive to be feasibly implemented in low-resource settings. The objective of the present study was to evaluate the efficacy of an affordable ultrasound unit as both a quantitative and qualitative neurodiagnostic tool in Rwandan and Kenyan NICUs. Specifically, the aims of this study were (i) to evaluate the machine's sensitivity to ventriculomegaly by measuring lateral ventricle size in patient and control neonate populations; (ii) to explore the broader diagnostic capacity of the ultrasound machine by identifying other cerebral abnormalities from the patients' images; and (iii) to assess the reliability of the measurements and qualitative findings made by novice sonographers with respect to an expert observer.

MATERIALS AND METHODS

Patients

This study was carried out at Centre Hospitalier et Universitaire de Kigali (CHUK) in Kigali, Rwanda, and Kenyatta National Hospital (KNH) in Nairobi, Kenya. The study was approved by local ethics committees (Rwanda, KUTH EC/CHUK/061/13; Kenya, KNH-ERC/R&R/389), and parents gave written consent before participating. Neonates admitted to the NICU and healthy term-born neonates from the postnatal wards were recruited to the study. Convenience samples were recruited that reflected the patient profile of the NICUs (Table 1). At CHUK, a higher number of pre-term infants were recruited than term infants with perinatal asphyxia, while at KNH, a larger referral hospital, the proportion of term neonates with perinatal asphyxia was higher. Therefore, in Kenya NICU patients were targeted for recruitment if they were diagnosed with perinatal asphyxia, had a gestational age greater than 38 wk and could be tested within 48 h of birth. For each subject, the resident physicians assisting with the study confirmed the diagnosis and assigned a hypoxic-ischemic encephalopathy

Table 1. Comparison of clinical parameters between subject groups

Clinical parameter	Healthy, N = 14	Asphyxia, N = 17	Pre-term, N = 7
Mean birth weight, g (SD)	3023 (368), n = 13	3045 (468)	1736 (424)*
Mean GA, wk (SD)	39.8 (0.73)	39.8 (1.5)	32.8 (2.1)*
Males, %	35.7	64.7	71.4
Mean Apgar Score (SD)			
1 min	8.0 (1.4), n = 7	4.1 (2.0), n = 14*	7.7 (1.5), n = 6
5 min	9.1 (1.2), n = 7	5.7 (1.9), n = 14*	8.6 (1.3)
10 min	9.7 (0.82), n = 6	6.6 (2.1), n = 13*	9 (0.82)
Mean HC at first test (cm)	342 (1.5), n = 9	35.7 (1.7), n = 13	31.7 (2.3)*
Median Age at testing (d)	2.5	1*	3

GA = Gestational age; HC = Head circumference; SD = standard deviation.
* $p < 0.05$.

(HIE) score of I–III (based on the Sarnat and Sarnat Scoring System [Sarnat and Sarnat 1976]). Head circumference was also measured for each subject.

Cranial ultrasonography

The portable ultrasound unit (EMP-N5, Emperor Medical, Shenzhen, China) used in this study was designed by Emperor Medical and was purchased with two transducers. The EMP-N5 unit (Fig. 1) is easily portable, weighing 6.5 kg, and has a high-resolution 12-inch liquid crystal display screen. The device can be powered by AC current from a wall outlet or by rechargeable (DC) battery. A multi-frequency micro-convex transducer (EMP-N5, Emperor Medical) was utilized for this study; although 6.5 MHz was the most commonly used frequency, in some cases 8 MHz or 5 MHz were used.

The cUS examinations were performed by D.E.C., with A.C.L. completing some of the initial scans. cUS was performed using the anterior fontanelle as the acoustic window. A continuum of images was acquired from anterior to posterior and from right to left. This procedure was repeated to allow for analysis of the reliability of image acquisition and subsequent measurement accuracy. The mid-anterior coronal plane showing the foramen of Monro was of particular interest, as this view has been established as the standard plane for various measurements of the lateral ventricles, including the ventriculo-hemispheric ratio and anterior horn width (AHW). All images were stored digitally and evaluated at a later time. Patients were examined at the cots, resuscitaires or incubators in the case of the NICU patients and at the mothers' bedside in the case of the healthy infants. The cUS examinations lasted between 15 and 25 min, during which time the nurses and physicians were urged to continue with their standard care.

Fig. 1. EMP-N5 ultrasound unit (Shenzhen Emperor Electronic Technology Co., Ltd.).

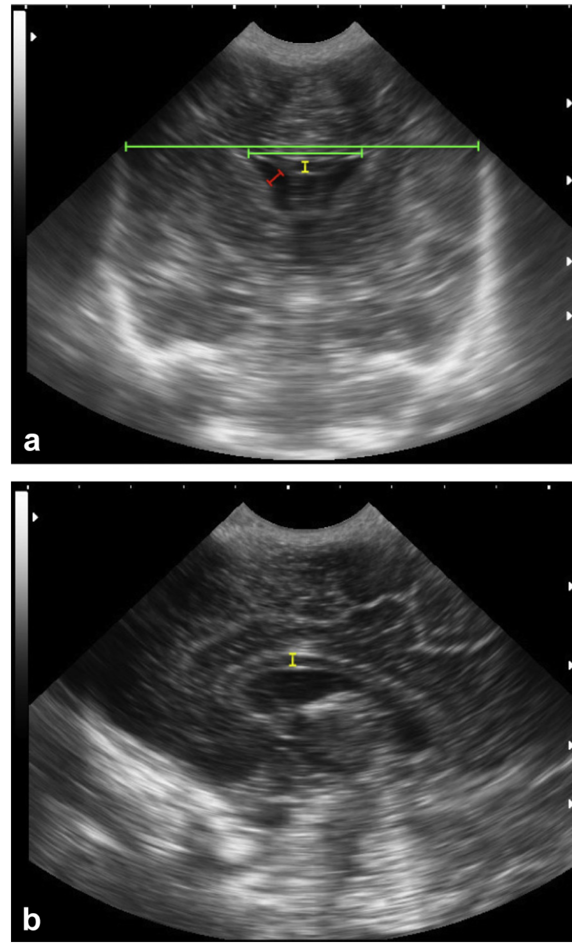


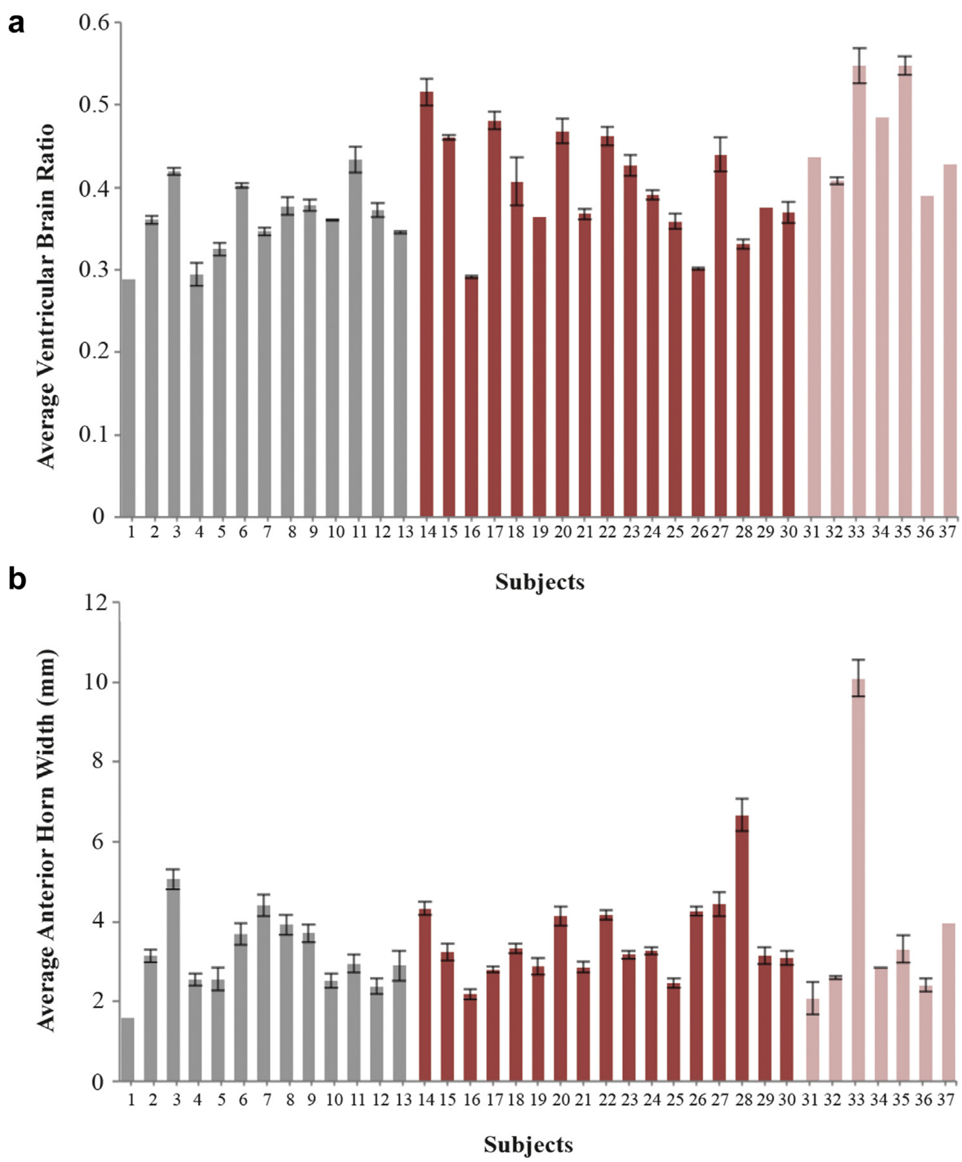
Fig. 2. Illustration of key imaging planes and measurements. (a) Mid-anterior coronal plane passing through the foramina Monro and third ventricle. The ventriculohemispheric ratio (VHR; *green*) is defined as the width of both ventricles at the border of the frontal horns and mid-bodies as a ratio to the bi-parietal lobe diameter. The anterior horn width (AHW; *red*) is the maximal diagonal width between the two walls of the anterior horn. The corpus callosum (CC) thickness (*yellow*) is measured as the distance between the upper and lower echogenic margins of the CC. The CC appears as a linear hypoechogenic structure that crosses the midline and is situated above the cavum septum pellucidum. (b) Mid-sagittal plane. The CC thickness (*yellow*) measurement was repeated in this plane (at the anterior body of the corpus callosum).

Qualitative image assessment

Each subject's images were assessed for the presence of abnormalities, including ventriculomegaly, edema, germinal matrix hemorrhage (GMH), IVH, parenchymal lesions, periventricular cysts and cava septum pellucidum by D.E.C. An expert pediatric neurosurgeon, S.dR., assessed validity in a subset (64%) of the examinations.

Measurements and statistical analysis

Quantitative measurements were made using Ginkgo CADx (version 3.3.0; MetaEmotion S.L., Valladolid, Spain), an open-source medical image viewer (Fig. 2). To assess for the presence of ventriculomegaly, the ventriculo-hemispheric ratio and the AHW were measured in the mid-anterior coronal plane. To assess potential secondary compressive effects on the corpus callosum, its thickness was measured in both the mid-anterior coronal and mid-sagittal planes. As the set of images was acquired twice during each cUS session and a continuum of images was obtained in each set, several images in similar planes were available. This allowed calculation of the mean and standard error for each of the subject's measurements. All statistical analyses were performed with SPSS 21 (IBM, Armonk,



c

Ventricle Measurement	Healthy, n=13† (SD)	Asphyxia, n=17 (SD)	Preterm, n=7 (SD)
Ventricular Brain Ratio	0.36 (0.043)	0.40 (0.065)	0.46* (0.065)
Anterior Horn Width (mm)	3.18 (0.94)	3.55 (1.0)	3.90 (2.8)

†The lateral ventricles could not be visualized in one healthy infant

*Statistical significance, $p<0.002$

Fig. 3. Average ventriculohemispheric ratio (a) and anterior horn width (b) measurements with standard error bars for each subject clustered by study group (*gray* = healthy, *red* = HIE, *pink* = pre-term). Group averages and standard deviations are also presented (c).

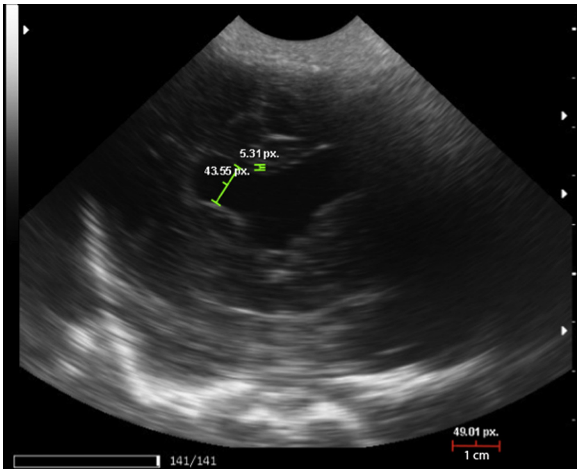


Fig. 4. Coronal image from subject 33 showing measurement of the AHW.

NY, USA) using Pearson's correlation or intra-class correlation as appropriate. Significance was always taken at $p \leq 0.05$. To evaluate inter-observer reliability amongst novices, in addition to the primary sonographer (D.E.C.), another novice observer repeated measurements in a sample of randomly selected images from 16 of the patients. To evaluate the validity of the measurements from novice observers, a pediatric neurosurgeon (S.dR.) with substantial expertise as a sonographer also performed measurements on the same images.

RESULTS

A total of 41 newborns were recruited and tested by cUS at CHUK (n = 21) in Kigali, Rwanda, and KNH (n = 20) in Nairobi, Kenya. Twenty-seven were patients admitted to the NICU, while 14 comprised the healthy control cohort. From the NICU recruits, two study populations were obtained: "perinatal asphyxia" or "HIE" (n = 17) and "pre-term" (n = 7). Two NICU infants had an unreported diagnosis, while one term baby had suspected sepsis. The data for these three infants are not included in any group analyses. Additionally, the ventricles of one healthy infant could not be visualized. The majority of newborns with perinatal asphyxia were diagnosed with moderate or severe HIE, with only two (14%) infants being scored with mild HIE.

Quantitative measurements

Figure 3 displays two lateral ventricle measurements, the ventriculohemispheric ratio (VHR) and AHW, showing individual averages (a and b) and group averages (c). There was a main effect of group (F [2,34] = 6.990, $p < 0.03$). Group-level analysis revealed that the VHR was significantly higher in the pre-term group (t[18] = 4.211, $p < 0.001$), compared with

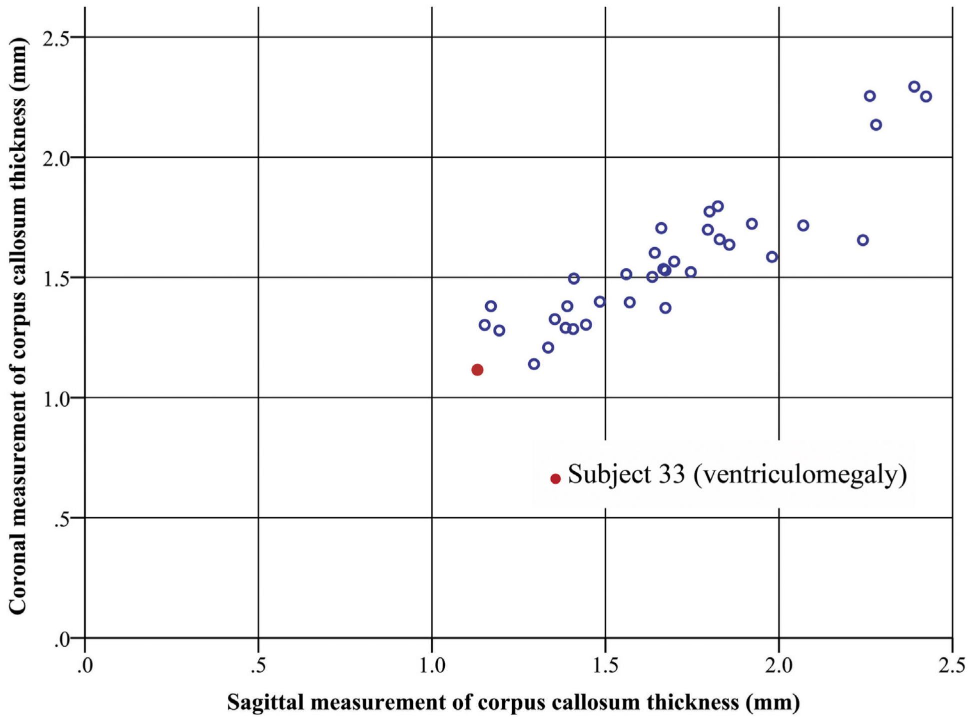


Fig. 5. Average corpus callosum thickness measured in coronal and sagittal planes. The correlation between the coronal and sagittal planes was high (r[34] = 0.91, $p < 0.01$), illustrating that this measurement was highly reliable.

the healthy controls, while there were no significant differences in the AHWs among the three groups (F [1,18] = 0.731, not significant). That group comparisons are reliable (and in the expected direction) illustrates the sensitivity of cUS in quantifying differences in clinically important brain structures.

In clinical practice, it is important that measurements from individuals are reliable and that deviations from the healthy distribution can be detected. To address this, first note that the intra-subject variability, as assessed by the standard errors about each subject's mean, was small relative to the differences between individuals (Fig. 3). Second, in both the pre-term and HIE groups, some infants had significantly larger VHRs and AHWs compared with the measurements in the healthy cohort. Most notably, patients 28 and 33 cause a positive skew within their respective study groups, demonstrating dramatically larger AHWs compared to the other patients in Figure 3b. Subject 33, the most severe case of ventriculomegaly, is discussed below.

Case study

Subject 33 is a pre-term infant born at 34 wk of gestation at Centre Hospitalier et Universitaire de Kigali. The baby weighed 2.14 kg and measured 31 cm in head circumference. Measurements (Fig. 4) acquired from images obtained on the 8th post-natal d revealed an average AHW of 10.1 mm, which differed significantly from the mean of the healthy group (t[12] = 26.4, $p < 0.001$). Specifically, the AHW of 10.1 mm was seven standard deviations above the healthy AHW mean. An AHW of this magnitude suggests the need for treatment before progressive hydrocephalus develops. As illustrated in Figure 5, this patient also presented with the thinnest corpus callosum (1.12 mm and 1.13 mm in coronal and sagittal planes, respectively), presumably marking a secondary injury. This potential white matter injury emphasizes the severity of the ventriculomegaly.

Inter-observer reliability

To evaluate the reliability of quantitative measurements across three observers (Table 2), intra-class correlation coefficients (ICCs) were calculated (Table 3). The ICCs were interpreted according to the strength of agreement scale by Brennan and Silman (1992): agreement is good when the ICC is between 0.6 and 0.8 and excellent when ICC >0.8. The VHR was the most variably measured across observers. Although observer 2 is educated in human anatomy, she has no experience performing cUS or interpreting ultrasound images, which likely explains the lower agreement with observer 3, the expert. This suggests that acquisition of cUS may be a useful part of training to read images.

Qualitative assessment

In addition to ventriculomegaly, further neonatal cerebral abnormalities could be imaged and identified (Fig. 6). To assess validity, the expert analyzed the images from approximately two-thirds of the cUS sessions. Ninety-eight percent (50/51) of the abnormalities identified by the primary observer (observer 1) were confirmed by the expert. Additionally, the expert observer added only four additional abnormalities, giving a miss rate of 8% for the novice observer.

The distribution of abnormalities across the diagnostic groups (Fig. 7) was mostly as expected, with the pre-term group having higher prevalence of GMH and IVH, while infants with perinatal asphyxia were the only patients to present with edema. Unexpectedly, the highest prevalence of parenchymal lesions was found in the healthy infants (although the difference was not statistically significant across groups, χ^2 [2, N = 38] = 0.7379, not significant). It is possible that some of these are merely transient echogenicities that would subside on serial scans.

DISCUSSION

Using a portable and affordable ultrasound unit, a novice sonographer obtained reliable, valid measurements of clinically important neonatal brain anatomy. The measurements showed differences between groups in the expected direction. Furthermore, all four measurements were consistent across images within an individual, and cases of clinically relevant ventriculomegaly could be detected. The novice sonographer had good-to-excellent agreement with an expert observer on three of the four measurements. Additionally, there was high agreement between qualitative findings made by the novice sonographer and those made by the pediatric neurosurgeon.

Table 2. Education and cUS experience of observers

Observer	Y of post-secondary education	Anatomy education	Experience with cUS
Observer 1 (sonographer)	6 (BSc, MSc)	MSc in Clinical Anatomy	Novice (mo)
Observer 2	7 (BSc, MSc)	MSc in Clinical Anatomy	None
Observer 3 (Expert)	12 (MSc, MD, FRCSC)	MD, 8 y of clinical practice	Expert (y)

Table 3. Interobserver reliability between three observers of varying experience

Measurement	Intraclass correlation coefficient*			
	Observers 1 and 2	Observers 2 and 3	Observers 1 and 3	All 3 observers
VHR	0.747	0.136	0.317	0.478
AHW	0.642	0.484	0.854	0.741
CC thickness (coronal)	0.802	0.466	0.662	0.736
CC thickness (sagittal)	0.813	0.288	0.690	0.702

AHW = anterior horn width; CC = corpus callosum; VHR = ventriculohemispheric ratio.
Observer 1: novice sonographer; Observer 2: naïve observer; Observer 3: expert.
* Average measures, two-way random model for absolute agreement.

Clinical significance of ventricle measurements

The average VHR in the healthy group (0.36 ± 0.043) was larger than previously reported for infants in developed countries (0.28 measured slightly differently [Brouwer et al. 2010]), and it was found to be significantly smaller than in the pre-term group. This is not surprising as pre-term infants have a higher incidence of IVH, which can cause ventricular enlargement (Maunu et al. 2009). However, clinically, it is important to detect individual patients who diverge from the healthy norm. Significant differences were found in two ventricle measurements in specific patients compared to the distribution in the control group. Although many of the VHRs in the pre-term group are significantly larger than in the healthy group, it is the AHW measurement that shows the most dramatic differences and thus appears to be the more sensitive marker of ventriculomegaly. The sensitivity of AHW to early enlargement is consistent with other reports (Grasby et al. 2003). Values exceeding 6 mm indicate the need for treatment before secondary brain injuries occur (Du Plessis 1998). Therefore, despite the AHW measurements like the VHRs in this study being larger (3.18 mm average for healthy infants) than reported reference values for developed countries (Brouwer et al. 2010), they only warrant close monitoring and possible treatment in a few patients.

Without access to neuroimaging, diagnosis and treatment of ventriculomegaly is delayed until hydrocephalus is evident from pathologic head growth rate or other signs of increased intracranial pressure. However, defining pathologic head growth is contentious. A rate of head growth up to 1 cm/wk is considered normal (Gross and Eckerman 1983), and an increase of 2 cm/wk is used as a cut-off for the diagnosis of hydrocephalus (Allan et al. 1982). For subject 33, head circumference grew approximately 1.5 cm over the first eight d of life. From this clinical presentation, ventriculomegaly might be suspected, but with the use of cUS and the subsequent finding of an AHW of 10.1 mm, this diagnosis can be confidently confirmed. Although no further scans were obtained, 10 mm is an ominous AHW size associated with a high risk of progressive hydrocephalus. Therefore, AHW measurements from images obtained with an affordable ultrasound unit can offer an earlier and more sensitive indicator of clinically relevant ventriculomegaly compared to the current observational methods used in low-resource hospitals.

Qualitative findings: Evidence for a broad utility of budget cUS

As expected, pre-term neonates had the highest incidence of GMH and IVH. The latter is comparable to the 30% incidence reported by Leijser et al. (2009) in a pre-term population, while GMH and IVH incidence in the healthy infants is higher than previously reported (Hsu et al. 2012). As postulated by the authors of a Ugandan study (Hagmann et al. 2010), the high incidence of congenital infections in this population may contribute to the high frequency of cysts (29%–41%) and parenchymal lesions (29%–43%). Small sample sizes and the inclusion of small cysts that are likely transient and inconsequential also play a role in bolstering these figures.

The success of this affordable ultrasound machine in identifying a variety of the most common cerebral abnormalities demonstrates its extensive utility as a neonatal diagnostic tool. Early diagnosis and subsequent monitoring of abnormalities, such as edema, cystic lesions and hemorrhage play an essential role in prognostic and management decisions. For example, in term newborns who suffered perinatal asphyxia, edema is a strong indicator of severe hypoxic-ischemic insult and is predicative of poor outcome (Roland et al. 1998; Van Wezel-Meijler et al. 2010).

Assessing the effectiveness of a novice sonographer

In addition to illustrating the utility of an affordable, portable ultrasound unit, this study offers insight into the expertise required to operate the machine and interpret the images (Nguyen et al. 2011). There was in general high agreement between the novice sonographer and the expert in both quantitative measurements of anatomy and qualitative identification of common abnormalities in the neonatal brain. However, a novice observer with

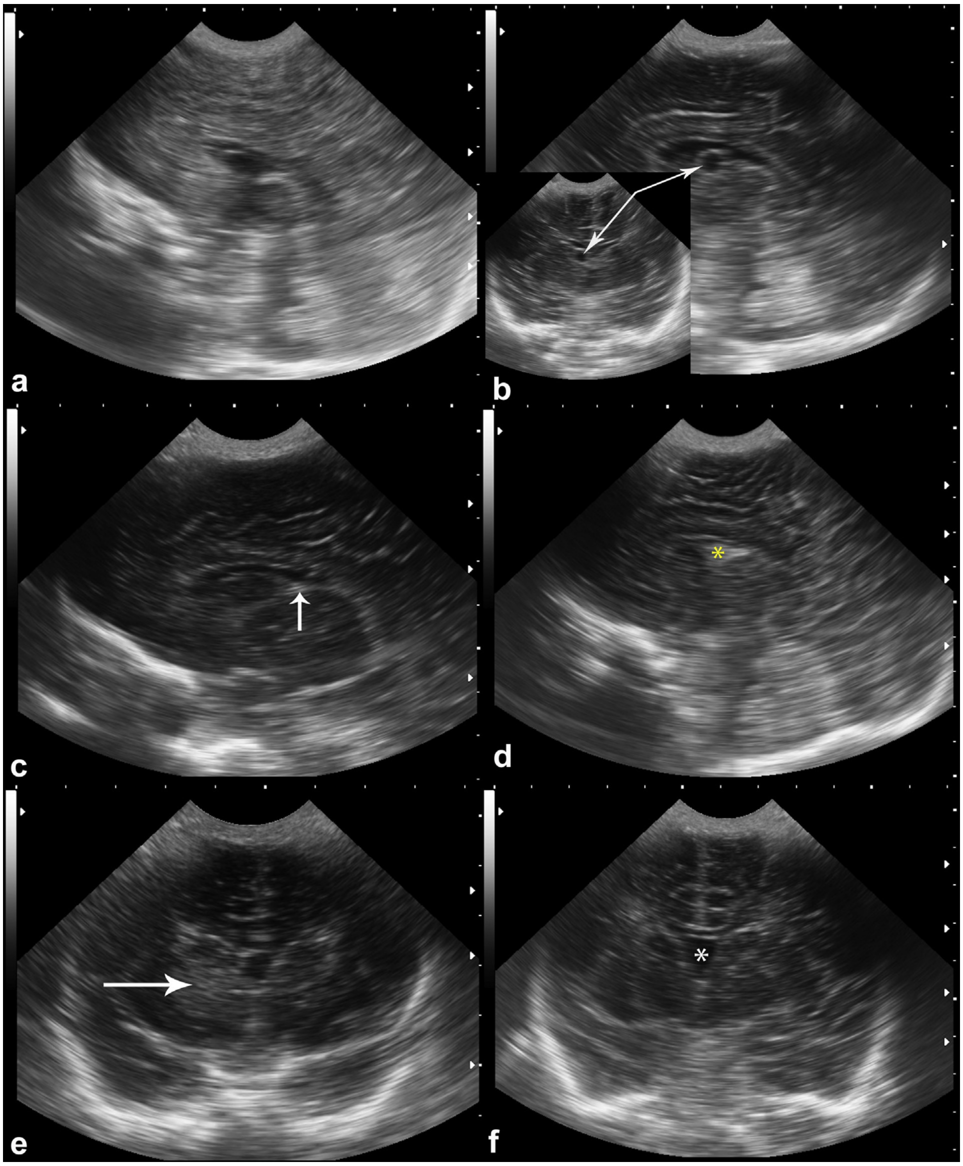


Fig. 6. Examples of the abnormalities identified in this study. (a) Edema is evidenced by diffusely increased echogenicitiy and loss of normal tissue architecture. (b) A round periventricular cyst (*double-headed arrow*) can be easily visualized in both the sagittal and coronal (inset) plane. (c) The echodense lesion (*short arrow*) at the caudo-thalamic groove indicates germinal matrix hemorrhage. (d) The echogenic mass (*yellow asterisk*) within the lateral ventricle signifies intraventricular hemorrhage (grade I). (e) The unilateral hyperechogenic area (*long arrow*) near the lateral ventricle is indicative of a parenchymal lesion. (f) A cavum septum pellucidum is evident by the presence of a fluid-filled (anechoic) space (*white asterisk*) between the frontal horns.

experience performing ultrasonography had higher agreement in measurement with an expert than an observer of similar training who had not performed ultrasonography. This suggests acquisition of ultrasonography may form a valuable part of training for its interpretation.

The skill sets of observers 1 and 2 in this study may appropriately estimate East African physicians in public hospitals who have expertise in anatomy, but a lack of specialized experience with sonography. A Ugandan study (Hagmann et al. 2010) illustrates that short training sessions and posters outlining cUS protocols can prepare physicians to successfully detect abnormalities. Additionally, a variety of hospital personnel can be trained to operate ultrasound machines like the EMP-N5, due to their user-friendly interface and easily adjustable settings (Shah et al. 2008).

Our results in combination with these reports demonstrate the feasibility of including ultrasound as

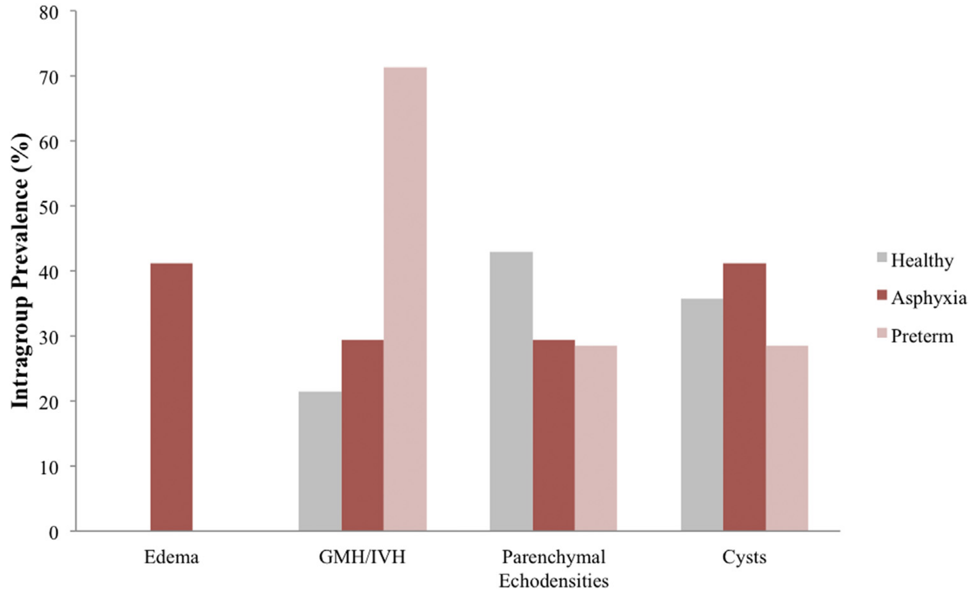


Fig. 7. Prevalence of common abnormalities in each diagnostic group. GMH = germinal matrix hemorrhage; IVH = intraventricular hemorrhage.

part of the standard diagnostic protocol in NICUs of low-income countries. The small size and portability of the EMP-N5 ultrasound unit facilitated easy navigation of crowded rooms, minimizing interference with hospital personnel and equipment. An ultrasound unit that can be easily operated at the bedside to assess newborn brain health can play an extremely valuable role in low-income countries.

The scans performed in this study permitted detection of ventriculomegaly, edema, IVH and cysts, all of which would otherwise go unnoticed and untreated. The effective implementation of this form of neuroimaging will depend on basic training of hospital personnel to operate and maintain the equipment and interpret the images. This study indicates that a novice can successfully operate the equipment but that experience with cUS is necessary for accurate image interpretation. A practical solution would involve training nurses to acquire cUS images to be viewed by the expert on site or by a physician at a collaborating institution, thus allowing cranial ultrasonography to be incorporated into the standard assessment of at-risk newborns in low-resource settings.

Limitations of the present study

The present study shows that with training it is possible for a novice ultrasonographer to use portable, affordable ultrasound technology in low-resource settings to assess the newborn brain for common brain injuries following pre-term birth or asphyxia. For this evaluation only one ultrasonographer performed the scans. Future studies should focus on scaling this training and technology to include local staff, assess consistency in performance and determine the most efficient approach to train novices. This study was also limited to one model of portable ultrasound device. The market for affordable ultrasonography is expanding rapidly, but no systematic evaluation of image quality for diagnostic purposes has been conducted. It would be valuable to assess in future studies whether even cheaper ultrasound machines offer the same diagnostic value as the model used here. Lastly, establishing cranial ultrasonography as a standard of care for infants at risk of perinatal brain injury in low-resource settings would benefit from the same measurement methods (*e.g.,* for the VHR) used universally, and for norms to be established in local populations.

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