

Ultrasound Assessment of Severe Dehydration in Children With Diarrhea and Vomiting

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Abstract

Objectives: The objective of this study was to determine the test characteristics for two different ultrasound (US) measures of severe dehydration in children (aorta to inferior vena cava [IVC] ratio and IVC inspiratory collapse) and one clinical measure of severe dehydration (the World Health Organization [WHO] dehydration scale).

Methods: The authors enrolled a prospective cohort of children presenting with diarrhea and/or vomiting to three rural Rwandan hospitals. Children were assessed clinically using the WHO scale and then underwent US of the IVC by a second clinician. All children were weighed on admission and then fluid-resuscitated according to standard hospital protocols. A percent weight change between admission and discharge of greater than 10% was considered the criterion standard for severe dehydration. Receiver operating characteristic (ROC) curves were created for each of the three tests of severe dehydration compared to the criterion standard.

Results: Children ranged in age from 1 month to 10 years; 29% of the children had severe dehydration according to the criterion standard. Of the three different measures of dehydration tested, only US assessment of the aorta/IVC ratio had an area under the ROC curve statistically different from the reference line. At its best cut-point, the aorta/IVC ratio had a sensitivity of 93% and specificity of 59%, compared with 93% and 35% for IVC inspiratory collapse and 73% and 43% for the WHO scale.

Conclusions: Ultrasound of the aorta/IVC ratio can be used to identify severe dehydration in children presenting with acute diarrhea and may be helpful in guiding clinical management.

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Acute diarrhea accounts for 1.8 million deaths annually in children under 5 years of age, or roughly 17% of all pediatric deaths worldwide.¹ Even in developed countries such as the United States, diarrhea remains a major cause of morbidity in children, accounting for more than 1.5 million outpatient visits, 200,000 hospital admissions, and 300 deaths each year.² As the severity of the disease can vary widely, accurately assessing dehydration status remains a crucial step in

preventing mortality from this disease. While children with severe dehydration require immediate treatment with intravenous (IV) fluids to prevent hemodynamic compromise and metabolic acidosis, children with mild to moderate dehydration have a significant reduction in hospital length of stay and fewer adverse events when treated with oral rehydration solution.³

Unfortunately, the diagnostic tools available to both emergency physicians in the developed world and

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practitioners in the developing world to assess the degree of dehydration in children are limited. The World Health Organization (WHO) recommends using a system of four clinical signs to classify children as having no dehydration, some dehydration, or severe dehydration, which remains the current standard of care for assessing dehydration in most developing countries, including Rwanda.⁴ However, most signs and symptoms of dehydration, including general appearance of the child, have not been found to have adequate sensitivity, specificity, or reliability.⁵ While ultrasound (US) of the inferior vena cava (IVC) has been suggested as a means for assessing dehydration status in children, it has never been tested against an accepted criterion standard.⁶

Bedside IVC US has the potential to reduce unnecessary interventions, admissions, and hospital costs by helping clinicians identify those patients who can be safely treated with oral rehydration and brief observation. This is especially true in the developing world, where resources such as IV fluids and hospital beds are scarce. Even more importantly, US could aid providers in identifying those children who may not appear overtly ill but are actually severely dehydrated and require immediate life-saving therapy.

The primary goal of this study was to determine the test characteristics of two different US methods and one clinical method for the detection of severe dehydration in children compared to an accepted criterion standard. Based on the available adult literature, we hypothesize that IVC US would be an accurate predictor of severe dehydration in children. Given the poor test characteristics of its component parts in the literature, we hypothesized that the WHO scale would not be an accurate predictor of severe dehydration in children.

METHODS

Study Design

In this diagnostic test assessment, we prospectively enrolled a nonconsecutive cohort of children presenting with symptoms of diarrhea and/or vomiting. The study was approved by both the Partners Healthcare (Massachusetts General Hospital) Institutional Review Board and the Rwanda National Ethics Committee. The child's parent or guardian provided either written or verbal consent in the local language, Kinyarwanda.

Study Setting and Population

Enrollment for this study took place at Kirehe, Rwinkwavu, and Butaro district hospitals in Rwanda from March 2009 to July 2009. The hospitals all serve rural and relatively impoverished populations and are supported by Partners in Health, a US-based nonprofit organization. Each hospital sees an average of 15 to 20 pediatric outpatients per day, with an average of 25 to 40 patients on their inpatient pediatric wards.

We enrolled children less than 15 years of age, the limit for admission to the pediatric ward at each hospital. All children presenting with diarrhea and/or vomiting who were admitted to the pediatric ward were eligible for inclusion, regardless of their final discharge

diagnoses. We enrolled a convenience sample of patients presenting on weekdays from 7:00am. to 5:00p.m. and on occasional nights and weekends based on the availability of study staff.

Study Protocol

Staff Training. Beginning in early 2008, physicians at all three study hospitals in Rwanda began receiving training in the use of US for diagnosing a variety of conditions. Prior to the start of this study in early 2009, we identified two local physicians at each of the three hospitals who expressed interest in further developing their US skills and recruited them as study coordinators. All of the physicians participating in the study had completed medical school and internship, but none had received specialty training in any field, as residency training is uncommon in Rwanda. Each of the physicians underwent an individualized training with the primary investigator (ACL) of this study in the measurement of IVC and aorta diameter using US. The training included an hour-long didactic presentation followed by hands-on scanning practice in the hospital. Study coordinators each performed at least 10 US examinations of the IVC and aorta under direct observation of the primary investigator before they were considered proficient enough to begin enrolling patients on their own.

Data Collection and Methods of Measurement. Upon arrival of an eligible child, the nurse or physician on duty contacted a study coordinator, who explained the study to the child's parent or guardian and obtained either written or verbal consent in the local language, Kinyarwanda. After enrollment, each child was weighed using a standard scale. The Rwandan nurse or physician admitting the patient noted demographic information, nutritional status, and signs and symptoms of dehydration. The study coordinator then performed a bedside US examination to determine the IVC diameter, the aorta diameter, the IVC inspiratory diameter, and the IVC expiratory diameter for each child using the study protocol.

Afterward, the patient was admitted to the pediatric ward and treated according to standard hospital protocols. US measurements were not used to guide clinical care and were not allowed to delay any immediately necessary interventions, such as delivery of IV fluids.

After volume resuscitation, a repeat weight was obtained at hospital discharge using the same standard scale. Patients discharged between Monday and Friday also received a repeat US exam.

Ultrasound Protocol. Portable Sonosite Micromaxx (Bothell, WA) US machines were already available at each hospital and were used to perform the necessary measurements during this study. For the purpose of the study, the child was laid flat on the bed or in the parent's lap. The study coordinator placed the standard curvilinear low frequency abdominal US probe in the patient's midline, just inferior to the xiphoid process. The probe was oriented in the transverse plane, with the marker pointed to the patient's right. In this position, both the aorta and the IVC were visible just above

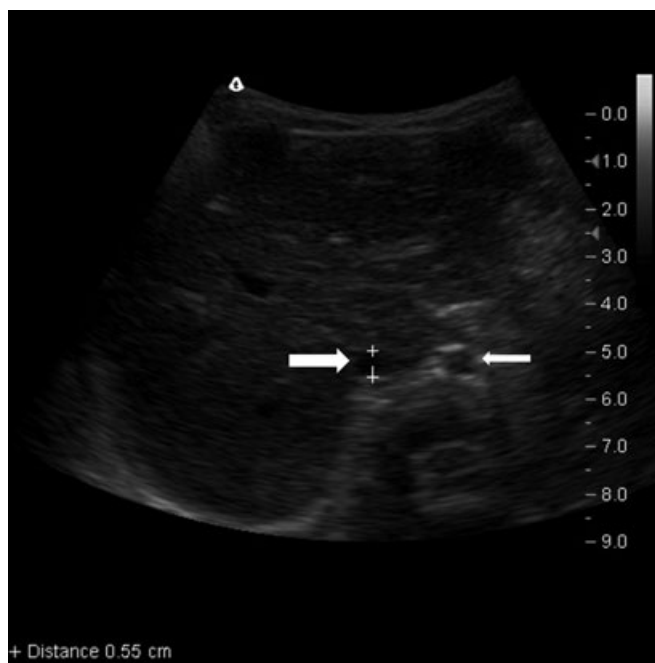


Figure 1. Ultrasound measurement of IVC and aorta. B-mode subxyphoid anterior–posterior plane of measurement for IVC (thick arrow) and aorta (thin arrow), with the probe marker pointed toward the patient’s right. Aortic diameter was measured in systole (widest diameter) and IVC diameter was measured in expiration (widest diameter). IVC = inferior vena cava.

the vertebral shadow. At this point, the study coordinator saved a short video loop for later review.

The study coordinator then froze the image on the screen and scrolled backward frame by frame to find the aorta at its maximal width (in systole). He or she then used the calipers to measure the anterior–posterior aorta diameter (inner wall to inner wall for the purpose of this study). The study coordinator then scrolled back a few more frames to find the IVC at its largest width (in expiration) and used the calipers to measure the anterior–posterior IVC diameter (Figure 1).

Next, the study coordinator placed the probe back on the patient’s abdomen, but with the probe in the longitudinal axis and the probe marker pointed toward the patient’s head. The study coordinator manipulated the probe slightly until he or she could clearly see the IVC empty into the right atrium of the heart. The study coordinator then turned on M-mode and centered the M-mode line about 2 cm inferior to the point at which the IVC crosses the diaphragm and enters the right atrium. While some authors recommend assessing IVC collapse 2 cm below the junction of the hepatic vein and IVC, we felt that this landmark would be more difficult to locate in young children. The study coordinator performed an M-mode measurement of the IVC, which produces an image of a single line spread out over time. The M-mode image was saved at this point for future review. The study coordinator then measured the maximum and minimum width of the IVC on the screen, corresponding to the IVC expiratory and IVC inspiratory diameter, respectively (Figure 2).

Both the video loop and the M-mode images without caliper measurements were saved and brought back to the United States, where two emergency physicians with US fellowship training performed independent measurements of the IVC and aorta diameter as well as the IVC inspiratory and expiratory diameters.

Outcome Measures. An increase of greater than 10% between admit and discharge weight was considered the criterion standard for severe dehydration, based on accepted standards in the pediatric literature.^{5,7} For each subject, we determined the aorta/IVC ratio by dividing the largest aorta diameter (during systole) by the largest IVC diameter (during expiration). We determined the percent collapse of the IVC with inspiration using the equation: $(\text{IVC expiratory diameter} - \text{IVC inspiratory diameter}) / \text{IVC expiratory diameter} * 100\%$.

We collected data on several commonly used signs and symptoms of dehydration. Four of these, including mental status, level of thirst, skin pinch, and sunken eyes, were used to construct the clinical scale recommended by the WHO.⁴

Data Analysis

We begin by reporting basic descriptive statistics regarding our sample population, including the proportion of severely dehydrated children and total rehydration time in the hospital. As support for the underlying physiologic basis of using US of the IVC to determine severity of dehydration, we calculated the mean percent change in IVC diameter between admission and discharge, comparing the population with severe dehydration to the population without severe dehydration. We also calculated the correlation between percent weight change, aorta/IVC ratio, and IVC inspiratory collapse in our sample using Spearman’s rho. To test the interrater reliability of our US data, we calculated the interclass correlation coefficient (ICC) between the US measurements obtained by local physicians in Rwanda and those obtained by US fellowship-trained emergency physicians using a two-way mixed effects model.

To determine the accuracy of US and clinical exam for detecting severe dehydration, we constructed receiver operating characteristic (ROC) curves to evaluate the overall performance of aorta/IVC ratio, IVC collapse, and the WHO scale compared to our criterion standard. In addition, we calculated test characteristics (sensitivity, specificity, and positive and negative likelihood ratios [LR+, LR-]) for the best cut-point determined by the ROC curves for each of the US methods and clinical scales. We chose 0.05 as the family-wise Type I error rate for our statistical comparisons and used the Holm-Bonferroni method to adjust for multiple comparisons. Statistical analyses were performed with SPSS version 16.0 (SPSS Inc., Chicago, IL); we used standard algorithms to calculate likelihood ratios and their confidence intervals (CIs).⁸

Sample Size Calculation. We determined that US examination of the IVC would have to have a sensitivity of at least 90% and a specificity of at least 50% to be clinically useful, corresponding to an LR- of 0.2 and an LR+ of 1.8. This was based on the idea that while it is

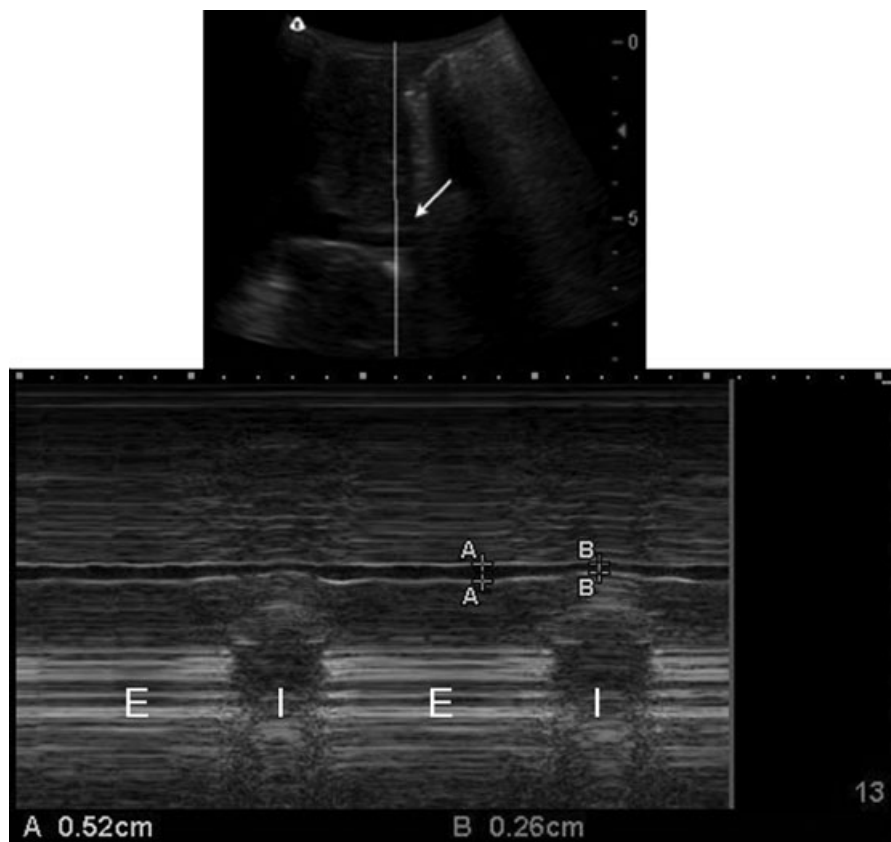


Figure 2. Ultrasound measurement of IVC collapse. M-mode measurement of expiratory (A) and inspiratory (B) phases of IVC diameter, with the probe marker pointed toward the patient's head. The M-mode reference line is applied to the longitudinal view of the IVC (arrow) about 2 cm distal to the IVC–right atrial junction. The letters “E” and “I” demarcate the periods of expiration and inspiration, respectively. IVC = inferior vena cava.

important to limit the use of unnecessary hospitalizations and IV fluids for children without severe dehydration, it is far more important to minimize the number of severely dehydrated children who do not receive life-saving resuscitation. Based on an estimated 33% prevalence of severe dehydration among children with diarrhea at our hospitals and using standard equations in the literature, we calculated we would need to enroll at least 42 children to obtain statistically significant LR+ and LR–.³

RESULTS

We enrolled 73 children between March 2009 and July 2009. Two children who died prior to discharge and seven children who were missing discharge weights were excluded from analysis. Twelve additional children had evidence of severe malnutrition on initial exam requiring protein-energy supplementation during their admission. Since their weight gain could not be completely attributed to rehydration, they were also excluded, leaving 52 children for analysis.

Children ranged in age from 1 month to 10 years, although 95% of children were less than 5 years old. The median percent weight change with rehydration was 4% (interquartile range [IQR] = 1%–12%). Twenty-nine percent of children had greater than 10% weight gain with rehydration and were therefore considered to

have severe dehydration based on our criterion standard. Children spent a median of 4 days in the hospital (IQR = 3–6 days). Ninety-eight percent of children spent at least 24 hours in the hospital, 72% spent at least 72 hours in the hospital, and 87% spent less than 1 week in the hospital.

Figure 3 demonstrates the change in IVC and aorta size with rehydration in the 39 children who received both admit and discharge US. The IVC diameter increased by a median of 13% (IQR = –5% to 25%) in children without severe dehydration, compared to a median increase of 30% (IQR = 19%–45%) in children with severe dehydration ($p < 0.005$). In contrast, change in aorta diameter was not significantly different in the two groups of children. In addition, the IVC-to-aorta ratio correlated significantly with percent weight change ($r = 0.435$, $p < 0.001$). IVC inspiratory collapse did not correlate significantly with percent weight change ($r = 0.114$, $p < 0.42$).

Figure 4 demonstrates the ROC curves for our three different tests of severe dehydration compared to our criterion standard. Only aorta/IVC ratio had an area under the ROC curve statistically different from the reference line (area under the curve = 0.76; 95% CI = 0.62 to 0.90).

Using the best ROC curve cutoff of 1.22, aorta/IVC ratio had a sensitivity of 93% (95% CI = 81% to 100%), specificity of 59% (95% CI = 44% to 75%), LR+ of 2.3

Change in Vessel Size with Rehydration by Category

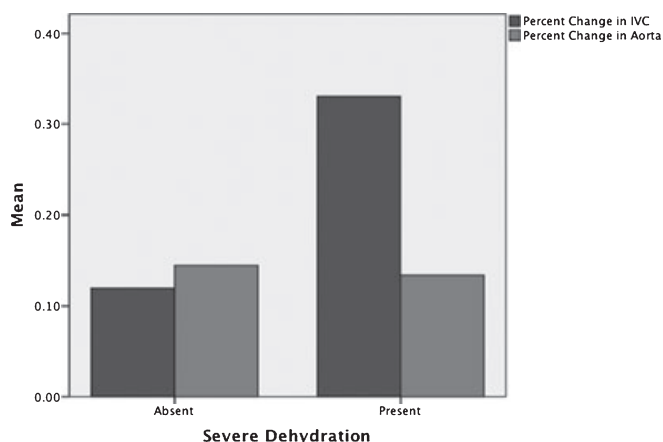


Figure 3. Percent change in vessel size with rehydration. IVC = inferior vena cava.

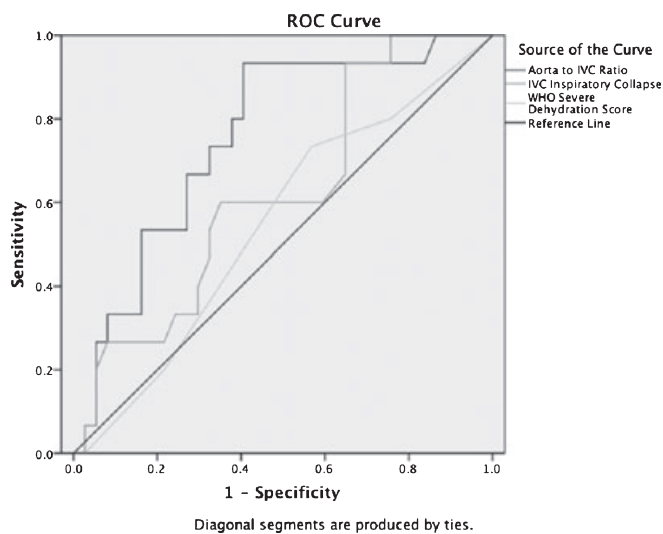


Figure 4. ROC curves. IVC = inferior vena cava; ROC = receiver operating characteristic.

(95% CI = 1.5 to 3.5), and LR⁻ of 0.11 (95% CI = 0.02 to 0.76) for detecting severe dehydration. Using the best cutoff of 27% collapse, IVC inspiratory collapse had a sensitivity of 93% (95% CI = 81% to 100%), specificity of 35% (95% CI = 20% to 51%), LR⁺ of 1.4 (95% CI = 1.1 to 1.9), and LR⁻ of 0.19 (95% CI = 0.03 to 1.3). Using the best ROC curve cutoff of two or more signs, the WHO score had a sensitivity of 73% (95% CI = 51% to 96%), specificity of 43% (95% CI = 27% to 59%), LR⁺ of 1.3 (95% CI = 0.9 to 2.0), and LR⁻ of 0.62 (95% CI = 0.25 to 1.5).

For 36 of the 52 patients analyzed, US images were reviewed by an emergency physician with US fellowship training to determine the reliability of each of our US tests. Images from the remaining 16 patients were lost due to human error in the operation of one of the US machines in Rwanda. Aorta/IVC ratio demonstrated an ICC of 0.723 (95% CI = 0.458 to 0.859). IVC inspiratory collapse demonstrated an ICC of 0.417 (95% CI = -0.143 to 0.703).

DISCUSSION

Acute diarrhea remains the second leading cause of death in children worldwide and a major cause for pediatric admissions in both developed and developing countries. Over the past several decades, appropriate rehydration of children presenting with acute diarrhea has reduced mortality dramatically, but the best method for determining severity of dehydration remains unknown. A variety of clinical signs and symptoms have been proposed as appropriate predictors of dehydration status, but a recent meta-analysis of 13 different studies concluded that while some signs and symptoms performed better than others, no single sign had adequate sensitivity, specificity, and reliability to evaluate pediatric dehydration, including a physician's determination of the child's general appearance.⁵

Although no prior published studies have determined the test characteristics of the most common clinical scale used worldwide, the WHO scale, against a valid criterion standard, several studies have looked at whether other combinations of clinical signs and symptoms may be accurate predictors of dehydration status in children.^{7,9-11} It should be noted that most of these studies were conducted by clinicians with pediatric specialty training in large, urban, pediatric referral hospitals, and their applicability to small, rural hospitals in the developing world or even to small community hospitals in North America is questionable. In addition, while these clinical scales were able to achieve relatively high specificities, resulting in LR⁺ ranging from 3.7 to 8.2, this came at the expense of relatively low sensitivities for the detection of severe dehydration (70% to 82% as reported by the authors), which is below what we would consider acceptable for a life-or-death diagnosis such as severe dehydration.^{7,9-11}

Ultrasound has become a popular tool for evaluating a variety of conditions, both in emergency departments (EDs) in the developed world and in rural hospitals and refugee camps in the developing world.^{12,13} Its relative cost-effectiveness, versatility, portability, and simplicity make it an ideal diagnostic tool in these settings. More recently, US has emerged as a potential tool for diagnosing severe dehydration in children with diarrhea. Several studies have evaluated the use of US measurement of IVC diameter as a predictor of volume status in adult patients. Specifically, studies have found both US measures of IVC diameter and IVC inspiratory collapse to be early predictors of shock in trauma patients, as well as useful for measure of volume status in intensive care unit patients with sepsis or undifferentiated hypotension.^{14,15} Use of US measurement of IVC diameter as a tool for measuring fluid status in pediatric patients has been less well studied. One study found IVC diameter correlated well with hydration status in children on hemodialysis.¹⁶ A single recent study found US measurement of the IVC to aorta ratio in children to be a good test for dehydration, although this study had several limitations, including lack of a valid criterion standard and few children with severe dehydration.⁶

When studying any new diagnostic test, it is important to have a valid criterion standard against which to

measure it. Prior research by Gorelick et al.⁷ has shown that postresuscitation discharge weight correlates almost perfectly with preillness weight; the difference between admit and discharge weight therefore functions as an adequate proxy for the total volume of fluid loss and is currently the accepted criterion standard for most studies of dehydration in the pediatric literature. In the study by Gorelick et al., the median amount of rehydration time required to reach a stable weight for pediatric patients was 24 hours, and nearly all patients had reached a stable weight by 72 hours. Nearly all patients in our study were rehydrated for over 24 hours, and 72% were rehydrated for over 72 hours, making it likely that the vast majority of patients had the opportunity to reach a stable, preillness weight prior to discharge. While it is possible that some of the patients in our study may have gained weight in other ways during their admission, such as through improved nutrition in the hospital compared to their home environment, this is unlikely for two reasons. First, children with evidence of severe malnutrition were excluded from analysis, so none of the children analyzed received any special form of protein-energy supplementation. Second, 87% of children spent less than 1 week in the hospital, so it is unlikely that they would have been able to gain a significant amount of protein-energy weight in that time period while being fed a standard Rwandan diet.

In our study, we determined the test characteristics for two US measures of severe dehydration and one clinical scale for severe dehydration in children with diarrhea and/or vomiting compared to the criterion standard of percent rehydration weight change. Of these, only US of the aorta/IVC ratio had an ROC curve statistically different from the reference line (i.e., better than flipping a coin). Moreover, US of the aorta/IVC ratio was able to achieve a relatively high sensitivity of 93%, while still maintaining an adequate specificity. A high aorta/IVC ratio meant that a child was twice as likely to have severe dehydration, while a low aorta/IVC ratio meant that a child was 10 times less likely to have severe dehydration. In addition, we found that general practice physicians with minimal US training were able to reliably obtain similar measurements of aorta/IVC ratio, compared to US fellowship-trained emergency physicians.

LIMITATIONS

This study included children presenting to rural hospitals in a low-income country with relatively high rates of severe dehydration. Its results should be applied with caution to EDs in North America, where prior studies have found much lower rates of severe dehydration.^{6,7} In addition, we compared US measures of dehydration to the WHO scale, considered the standard of care in many developing countries including Rwanda, but not commonly used in North America. We chose this scale because it is well known to both physicians and nurses practicing at our clinical sites. Several more complex clinical scales have been suggested in the literature, and it is quite possible that these may perform better than the WHO scale.

While we attempted to minimize bias by having separate clinicians performing the US exam and clinical exam of each patient, there was no way to completely blind study coordinators performing the US exam to the clinical appearance of the patient. However, study coordinators were effectively blinded to our criterion standard (percent weight change with rehydration), which is most important for a diagnostic study. We assessed the percent weight change by comparing the admission weight to the discharge weight, but did not standardize the time of day that discharge weights were taken, although discharges generally occurred after morning rounds each day.

Our US measure of IVC collapse may have been compromised by the cranial-caudal movement of the diaphragm over the course of the respiratory cycle, resulting in measurement of two different locations of the IVC during inspiration and expiration. This could have resulted in an underestimation of IVC collapsibility, as the measurement during inspiration would have been closer to the diaphragm where the IVC is less collapsible. Video and still images of most US exams were reviewed by an emergency physician with US fellowship training; however, we were not able to have an US fellowship-trained physician present during the course of the study to perform repeat US exams in real time.

Study subjects were a convenience sample based on investigator availability; overall, we enrolled about half of eligible patients. Essential data were missing for about 10% of enrolled patients, who were therefore excluded from analysis. In addition, study images were lost for about a third of our US exams and could not be reviewed by a clinician with US fellowship training. Because all the data were lost due to random accidents not related to patient or sonographer characteristics, we do not believe that this significantly biased our results.

CONCLUSIONS

We found ultrasound assessment of aorta/inferior vena cava ratio to be a relatively accurate and reliable predictor of severe dehydration in children with diarrhea and/or vomiting. We did not find ultrasound assessment of inferior vena cava inspiratory collapse or the World Health Organization scale to be accurate predictors of severe dehydration in this same population of children. While the numbers of patients enrolled in our study were too small to definitively say that ultrasound performed better than clinical exam for evaluating dehydration status in children, the data suggest that ultrasound may be a useful adjunct to clinical exam in guiding management of these patients.

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