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Value of lung ultrasound in detection of volume overload in children chronic kidney disease on regular hemodialysis: prospective cohort study

Enas M. Sweed^{1*} , Ashraf S. Shafei¹, Afaf A. Mohamed², Soha A. El-Gendy³ and Wesam E. Afifi³

Abstract

Background Several methods have emerged to predict the occurrence of early volume overload (VO) in pediatric patients with chronic kidney disease undergoing regular hemodialysis (HD). Nevertheless, achieving an accurate assessment remains challenging. Consequently, this study aimed to identify VO in pediatric HD patients using lung ultrasound (LUS). Additionally, the study sought to investigate the relationship between various clinical parameters employed to detect VO and the ultrasonographic B-line score.

Methods This prospective observational cohort study was conducted on 30 pediatric patients with end-stage renal disease undergoing a maintenance HD program for 4 months. The clinical evaluation of the fluid status of pediatric patients involved using LUS pre-, intra, and post-HD. The study included the dry weight (DW) and non-DW groups; within these groups, the B-line scores were evaluated pre-, intra, and post-HD sessions. Tabulations were conducted to document the variations in body weight and B-line scores during pre-, intra-, and post-dialytic periods.

Results The results of the LUSs performed on the 30 pediatric patients pre-, intra, and post-HD revealed that the B-line scores significantly reduced post-HD in all pediatric patients with more significant reduction in non-dry weight group ($p < 0.001$). There was a positive relation between the total number of B-lines pre-HD and inter-dialytic weight gain, pre-dialytic blood pressure, and clinical fluid score ($r = 0.811, p < 0.01$; $r = 0.59, p < 0.001$; and $r = 0.75, p < 0.001$, respectively) and also post-dialysis. Eventually, dialytic weight loss exhibited a significant direct positive correlation to B-line score reduction ($r = 0.891, p < 0.01$).

Conclusions LUS is an innovative, simple noninvasive bedside method that provides real-time evaluation of fluid volume alterations in pediatric HD patients with chronic conditions. LUS shows excellent potential as a viable approach for assessing DW and non-dry weight in pediatric HD patients.

Keywords CKD, Dry weight, Hemodialysis, Lung ultrasound, Non-dry weight, Ultrasonographic B-line, Volume overload

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Background

Chronic kidney disease (CKD) refers to enduring kidney structural or functional impairment for a duration exceeding three months [1]. The criteria for diagnosing and staging pediatric CKD were published by Kidney Disease: Improving Global Outcomes (KDIGO) in their clinical practice guidelines [2]. Using the KDIGO



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diagnostic criteria and staging classification standards are prevalent in clinical settings, research endeavors, and public health initiatives pertaining to pediatric CKD. Determining dry weight (DW) is a critical and frequently complex aspect of hemodialysis (HD) aimed at preventing volume overload (VO) or depletion.

Dry weight was defined as the lowest tolerated post-dialysis weight achieved via a gradual change in post-dialysis weight at which patients experienced minimal signs or symptoms of either hypovolemia or hypervolemia [3].

The presence of hypovolemia and hypervolemia adversely affects the quality of life and contributes to the development of chronic cardiovascular complications [4]. Abnormal fluid status increases blood pressure (BP) and cardiac preload, causing left ventricular (LV) hypertrophy and congestive heart failure [5]. Therefore, it is of almost importance to prioritize the optimization of the target weight in the HD prescriptions of children to minimize VO. This can be achieved through the utilization of clinical judgment, as well as the evaluation of various parameters, including the presence of intra-dialytic symptoms, inter-dialytic weight gain (IDWG), physical examination findings, and BP measurements [5].

Numerous methodologies are available for conducting a comprehensive clinical assessment of hydration status. These include the cardiothoracic index, derived from chest X-ray assessment, echocardiography, biomarkers, and plasmatic volume variation monitoring, besides the most recent method, lung ultrasound (LUS) [4]. LUS entails examining the lungs across various regions, precisely 28 zones, to identify and analyze various sonographic artifact categories and patterns. B-lines, characterized as vertical hyperechoic reverberation artifacts, are observed to extend from the pleural line to the lowermost portion of the screen. The presence of more than three to four B-lines in an interspace between ribs indicates the presence of alveolar interstitial syndrome. Additionally, quantifying the B-line number enables a semi-quantitative assessment of the VO degree in pediatric populations [6]. This study aimed to identify VO in pediatric patients with CKD undergoing HD through LUS. Additionally, we sought to investigate the relationship between various clinical parameters commonly employed to detect VO and the ultrasonographic B-line score.

Methods

Study design

This prospective observational cohort study included pediatric patients with end-stage kidney disease (ESKD) on a maintenance HD program in the pediatric nephrology unit of the Benha University Hospital from period of April 2022 to August 2022.

The Local Ethical Committee of the Medical Faculty of Benha University approved the study, besides obtaining

written informed consent from the parents. Three out of the 33 pediatric patients undergoing regular HD in this particular unit were unable to be included due to exclusion criteria. These criteria comprised one case of acute respiratory distress syndrome (ARDS), one case of interstitial pneumonia, and one case of cardiac failure. Meanwhile, the cohort of 30 patients CKD exhibited no indications of heart failure, ARDS, pulmonary fibrosis, lung atelectasis, or interstitial lung disease, all of which could influence the LUS results. Every patient had an examination before and after four distinct HD sessions. Each patient received three HD sessions/week, each lasting 4 h and median follow-up of these patients is 4 months.

All participants went through a comprehensive process of gathering medical information, encompassing factors including age, gender, place of residence, the underlying cause of CKD, utilization of antihypertensive medications, and a thorough physical examination. This examination included the assessment of vital signs, i.e., blood pressure, urine output, DW, laboratory measurements, and echocardiography (ECHO) results. Measurements were recorded using both departmental and bedside ultrasonography techniques to detect B-lines [7]. The VO degree was clinically assessed pre-HD using a clinical score of 0–10 [8, 9]. This evaluation was conducted by the attending physician, taking into consideration various clinical indicators such as dyspnea at rest, orbital edema, weight gain, hypertension, and chest crepitation.

Patients were divided into two groups: dry weight group, which is usually determined on the basis of blood pressure (BP) control in children, remains normotensive during the inter-dialytic period without the use of antihypertensive medications [10] and a non-dry-weight group.

Ultrasonographic examinations

The water content of the lung interstitium, known as extravascular lung water (EVLW), is a body fluid compartment that holds considerable significance [11].

LUS examinations were conducted for CKD children 15 min pre-, intra-dialytic (1 h after the beginning of the dialysis session), and 15 min post-HD using a G.E LOGIC 6 ultrasound device at the Benha radiology department. A convex 5 MHz probe and a linear 8–12 MHz superficial probe were utilized for the examinations. The intra-HD procedure involved using a portable device (SonoSite S-ICU) with a 10 MHz linear probe operating in B-mode. The quantification of B-lines was performed in 14–28 intercostal positions for most patients. All patients underwent lung ultrasound in the supine position. The scanning procedure for older children involved positioning them either in a semi-supine posture or in an upright seated position, based on the preference of each patient. The lung scans were conducted bilaterally, with the examination extending from the second to the fifth intercostal

space on the right side and from the second to the fourth intercostal space on the left side. The transducer was positioned along the parasternal, mid-clavicular, anterior axillary, and mid-axillary lines [12].

B-lines were quantified in 14 intercostal positions on the anterior and lateral chest wall for patients weighing less than 20 kg and 28 positions for patients over 20 kg.

B-lines were quantified on a scale of 0–10 in each position [12]. The recorded data included the maximum B-line number visualized at each site. The evaluation of maximal B-line density was conducted employing a freeze-frame analysis of the obtained images. A cumulative B-line score was computed for each evaluation [13] (Fig. 1).

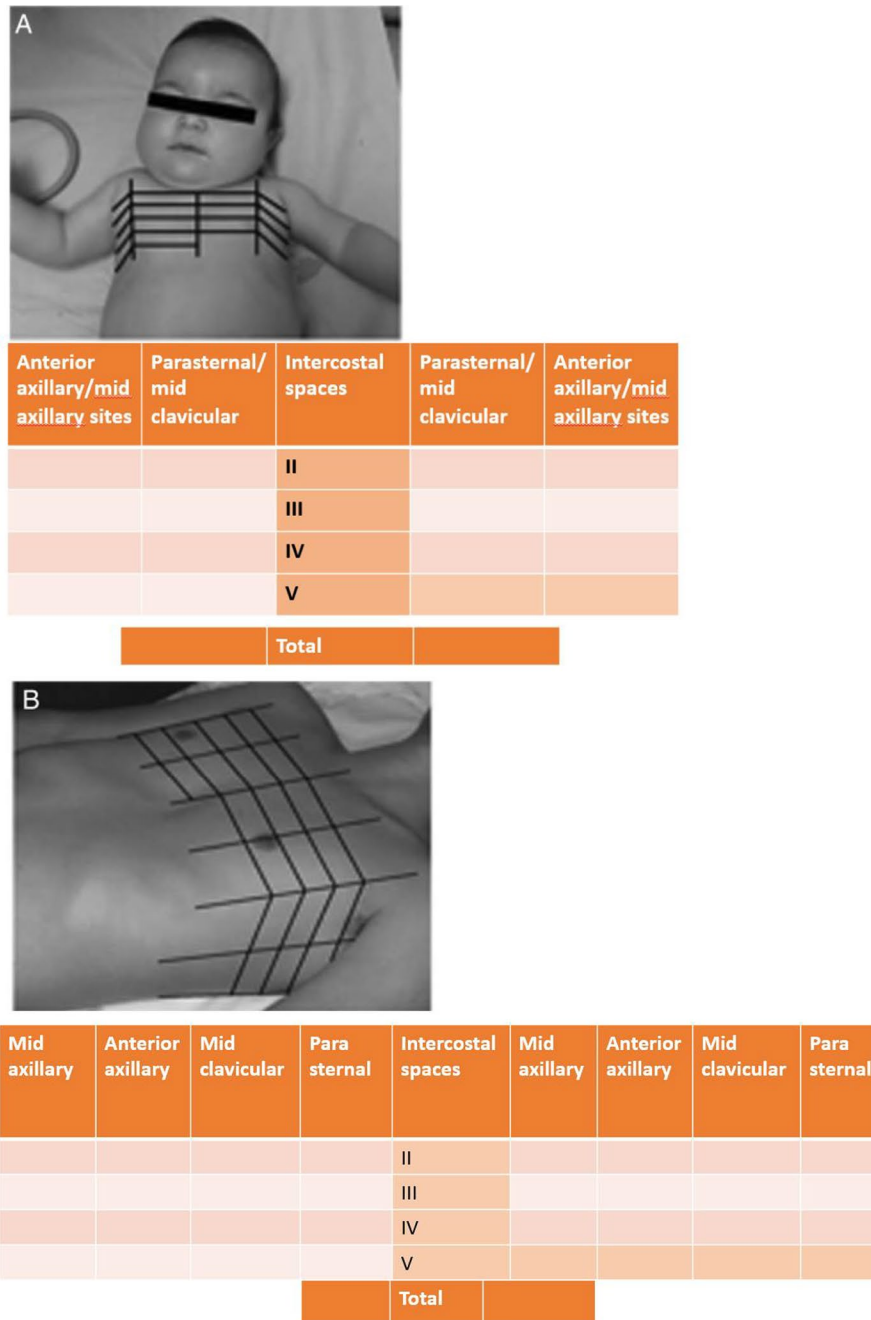


Fig. 1 Anatomical sites and data sheets for sonographic B-line measurements. **A** 14 position assessments in patients under 20 kg (parasternal/mid-clavicular and anterior axillary/mid-axillary sites), and **B** 28 position assessments in patients over 20 kg (parasternal, mid-clavicular, anterior axillary, and mid-axillary sites)

The patient weighed more than 20 Kilogram. The posterior axillary, scapular, and paraspinal lines were incorporated. A standardized methodology was employed to ascertain and measure B-lines in every anatomical location. The characteristics that define B-lines include hyper-echogenic lines that are perpendicular to the probe surface, originating at the pleural line, extending to the lower field limit, being independent of A-lines, and exhibiting synchronous movement with pleural sliding [6]. The measurements following the HD sessions were re-conducted after 15 min post-HD sessions for most patients and median follow-up was for 4 months.

Statistical analysis

Data analysis was conducted using IBM SPSS Statistics (V. 26.0, IBM Corp., USA), reporting the quantitative parametric data as mean \pm SD and as number and percentage for categorized data. Descriptive statistics for quantitative measures include the number of cases, mean, standard deviation, range (minimum to maximum), and the number and percentage for qualitative measures. The study compared two dependent groups with parametric data employing the paired t test (compare the mean of B-lines, weight and blood pressure in dry and

non-dry weight pre- and post-dialysis sessions). The Spearman correlation test was utilized for examining the potential correlation between pairs of variables within each group, specifically for nonparametric data (it was utilized to correlate B-lines, blood pressure, and weight in non-normally distributed data). A significance level of 0.05 was deemed statistically significant, whereas significance levels of 0.01 and 0.001 were highly significant.

Results

Patient baseline characteristics

The study enrolled 30 patients with CKD on regular HD. Those 30 patients were with equal gender distribution. The median age was 11.66 years (6.5–18) from Benha and its surrounded suburbs. Idiopathic CKD accounted for the highest proportion, precisely 30%, as the leading etiology. The median follow-up time was four months (1–13).

Pre- and post-HD characteristics and hydration status of the patients

The observed variables exhibited significant differences in their values pre- and post-HD ($p < 0.01$, Table 1). Figure 2 illustrates the correlation between the total B-line number post-HD and clinical parameters.

Table 1 Volume load measurements recorded pre- and post-HD

Measurements	Min–Max	Mean \pm SD
I. Volume load measurements recorded pre-hemodialysis		
1. Inter-dialytic weight gain (Kg)	0.4–2.8	1.2163 \pm 0.6701
2. Systolic blood pressure (mmHg)	100–140	120.5 \pm 13.022
3. Diastolic blood pressure (mmHg)	60–95	79.17 \pm 7.777
4. Clinical overhydration score	2–10	4.53 \pm 2.46
5. B-line score pre-hemodialysis	9–160	59.633 \pm 42.811
II. Volume load measurements recorded post-hemodialysis		
1. Post-dialytic weight loss (Kg)	0.1–1.7	0.645 \pm 0.4764
2. Dry weight (Kg)	12.1–42.95	28.356 \pm 8.6488
3. Difference between post-hemodialysis (actual) weight and dry (target) weight (Kg)	0.05–1.4	0.4373 \pm 0.398
4. B-line score post-hemodialysis	4–100	32.7 \pm 27.9

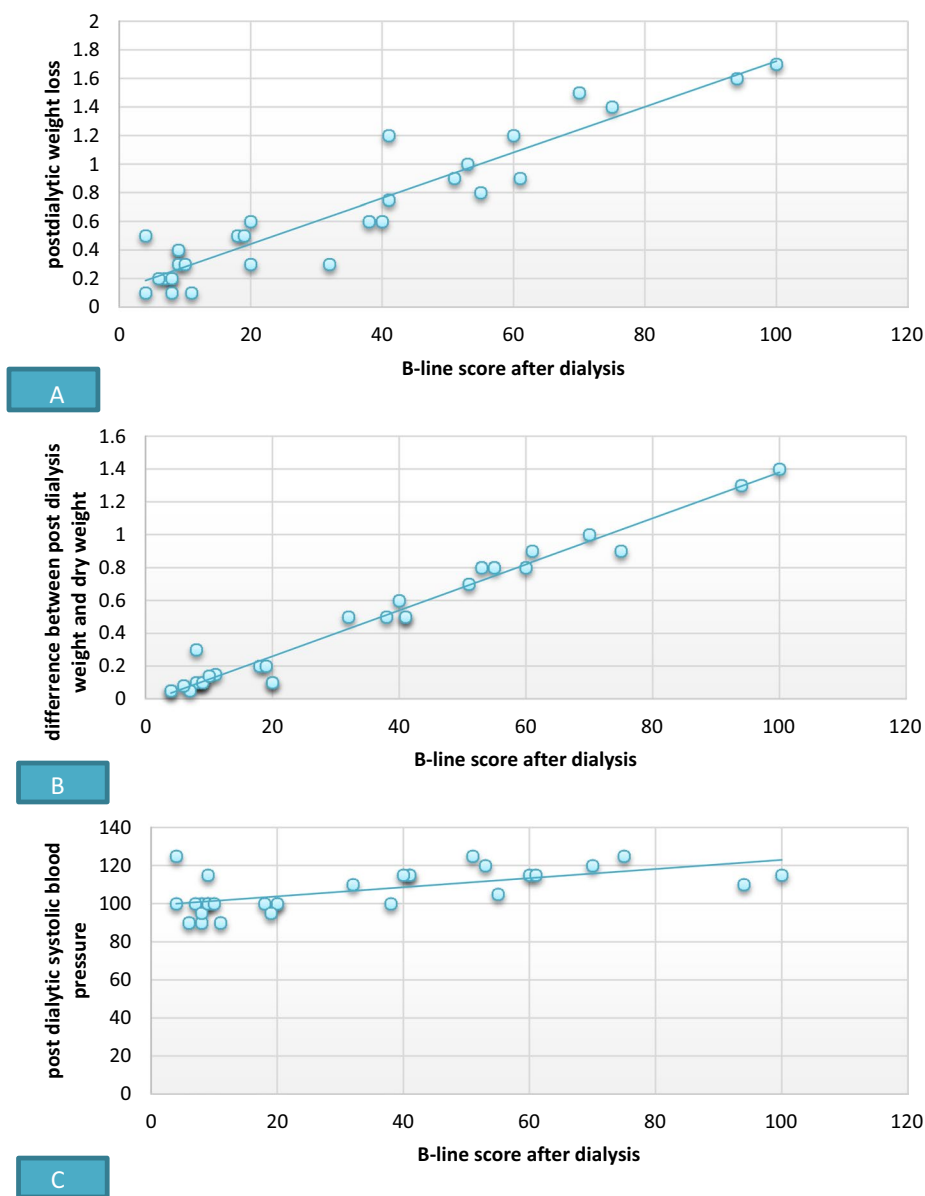


Fig. 2 The correlation between the total B-line number post-HD and clinical parameters. **a** Correlation between the total B-line number post-HD and post-dialytic weight loss; **b** Correlation between the total B-line number post-HD and the difference between post-HD weight and DW; **c** Correlation between the total B-line number post-HD and post-dialytic systolic blood pressure (SBP)

B-line scores exhibited significant reduction post-HD in the DW and non-DW groups, with more significant decreases in the non-DW groups (Table 2) (Figs. 3 and 4). Herein, more posterior lines, i.e., posterior axillary, scapular, and paraspinal lines, were added for more acquisition, exhibiting significant decreases in DW and non-DW groups.

Table 2 Comparison between ultrasonographic B-line scores pre- and post-HD in both DW and non-DW groups

B-line scores	Dry weight group (n = 14)	Non-dry weight group (n = 16)
Pre-hemodialysis	29.142 ± 12.629	86.312 ± 42.169
Post-hemodialysis	11.9286 ± 5.876	51.5 ± 26.087
t test	7.1318	8.369
P value	< 0.01	< 0.01

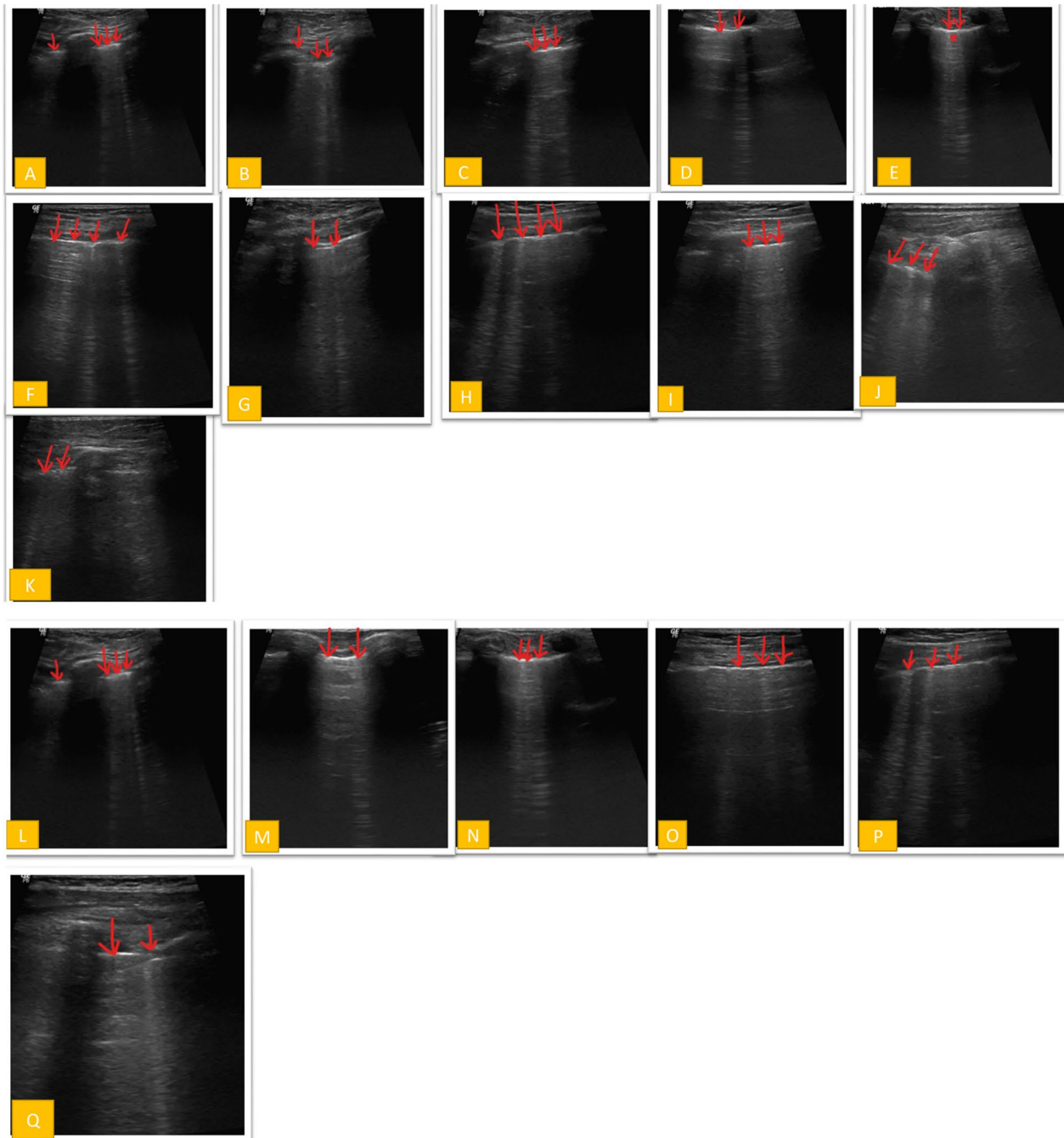


Fig. 3 Case illustrative for non-dry weight CKD child: Female patient, 15 years old, CKD on regular hemodialysis, weighted 32.5 KG at pre-dialysis session (increased in weight by 4 KG), blood pressure = 140/90, presented tachypneic, tachycardia, dyspneic with puffy eye lid, with multiple B-lines are seen at different intercostal spaces at pre-dialysis session denoting VO, **A–C** 10 B-lines seen at MCL lines, **D, E** 5 B-lines seen at parasternal lines, **F, G** 6 B-lines detected at mid-axillary, **H, I** 7 B-lines at posterior axillary line and **J, K** 4–5 B-lines at paraspinal lines. Post-dialysis weight is 28 KG, blood pressure is 100/70 with significant reduction in number of B-lines (**L–Q**). **L, M** 5 B-lines at right MCL, **N** 3 B-lines at parasternal line, **O, P** 3 B-lines at mid-axillary as well as at posterior axillary lines and **Q** 2 B-lines at paraspinal line

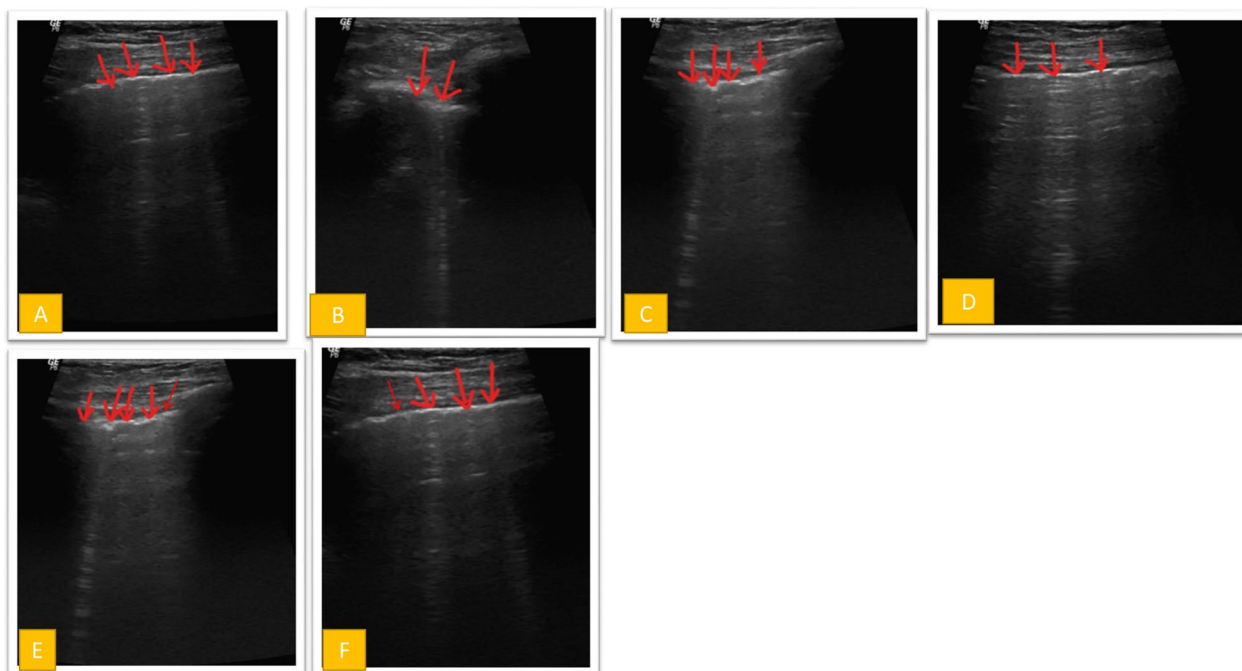


Fig. 4 Case illustrative for dry weight CKD child. Female patient, 6 years old normotensive, weighted 18 KG at pre-dialysis session with B-lines detected at intercostal spaces, **A, B** shows 6 B-lines A at MCL, **C, D** shows 6–7 B-lines at anterior/mid-axillary line. Post-dialysis mild reduction in number of B-lines with 4–5 B-lines seen at MCL **E** and 4 B-lines at anterior/mid-axillary line **F**. Post-dialysis weight is 17.5 KG

The results during intra-dialytic period were insignificant. Moreover, the correlation between the total B-line numbers and other fluid status parameters are clarified in Table 3

Table 3 Correlation between the total number of B-lines and overhydration status parameters (pre-HD)

Parameter	Pre-hemodialysis volume overload determined by the total number of B-lines	
Inter-dialytic weight gain	<i>r</i>	0.811
	<i>p</i>	>0.01
Pre-hemodialysis systolic blood pressure	<i>r</i>	0.593
	<i>p</i>	<0.01
Pre-hemodialysis diastolic blood pressure	<i>r</i>	0.674
	<i>p</i>	<0.01
Fluid score	<i>r</i>	0.7516
	<i>p</i>	<0.01

Discussion

The clinical evaluation of fluid status exhibits inaccuracies in its diagnostic capabilities and lacks precision. To investigate this matter, this study examined the link between other clinical measures to identify VO and the ultrasonographic B-line score in CKD pediatric patients receiving HD [14].

In line with previous research [15, 16], the present study assessed the impact of increased hydration status pre-HD (VO), specifically focusing on pre-HD indicators such as inter-dialytic weight gain, BP, clinical fluid scoring, and B-line scoring. HD patients typically receive 3–5 h of HD three times a week. Therefore, they gain weight in the intervals between their treatments almost exclusively due to fluid retention. Therefore, the amount of fluid ultra-filtrated during the subsequent HD (i.e., the difference between the pre- [wet] and post-HD [dry] weights) is similar to the amount of weight increase [17]. This study revealed that the mean of inter-dialytic weight gain observed in this period was (1.2163±0.6701 kg). This result coincided with previous studies, reporting

that the inter-dialytic BP fluctuations in children on chronic HD exhibited significant variability, with a significant correlation to corresponding changes in body weight [18, 19]. Specifically, elevations in systolic blood pressure (SBP) were positively correlated to increase in inter-dialytic weight.

Herein, 53.3% of patients showed hypertension requiring antihypertensive medicines during the inter-dialytic interval. Measurement of BP pre-HD reveals that mean SBP and diastolic blood pressure (DBP) were 120.5 ± 13.022 and 79.17 ± 7.777 mmHg, respectively. The results coincided with prior research, indicating that patients with VO had increased BP more frequently than patients without VO (78.6% vs. 45.7%, $p=0.037$), despite using antihypertensive medicines [20]. Only 48.6% of children without VO and 85.7% of those with VO reported using two or more antihypertensive drugs ($p=0.017$). The correlation between volume load and BP has been substantiated in multiple studies. A study conducted on 13 pediatric patients undergoing HD has demonstrated a significant correlation between increased IDWG and elevated BP load as measured by 44-h ABPM [21]. In children receiving peritoneal dialysis, both SBP and DBP are positively linked with daily ultrafiltration and residual urine output [22]. However, previous studies showed that a significant proportion exceeding 50% of children with high BP exhibited no VO, indicating that other factors may be involved in hypertension. Therefore, it is necessary to employ alternative objective techniques, such as B-line scoring, to assess the efficacy of fluid removal during HD [13, 23]. The primary factors contributing to hypertension in individuals receiving HD include salt and VO, arterial stiffness, activation of the sympathetic and renin-angiotensin-aldosterone systems, and endothelial dysfunction [24].

Herein, above-mentioned BP and weight gain measurements are used with other clinical parameters (dyspnea at rest, orbital edema, and chest crepitation) to clinically assign VO with a score of 1–10 by the attending physician, revealing a mean fluid score of 4.53 ± 2.46 . The clinical hydration score demonstrates a satisfactory level of diagnostic performance, accompanied by acceptable inter-observer reliability. Consequently, it can be conveniently employed in regular clinical practice to make adjustments to DW, therefore establishing its current status as the primary method for pediatric HD patients [25]. LUS examinations have been observed to be well tolerated and readily accepted by pediatric patients owing to their rapid nature [26].

This study conducted LUS assessments on 30 children pre- and post-HD. The total B-line number visible on the LUS picture was measured in each session. Commonly, up to five B-lines indicate a standard characteristic.

Based on earlier-reported findings, it was observed that the B-line score for individuals in good health ranged from 0 to 5 [27]. Specifically, out of the total sample size, 77 patients had a B-line score of 0, while five patients had a B-line score of 5. The results showed that the mean B-line score pre-HD was (59.633 ± 42.811). These results are consistent with previously documented results which evaluated the patient hydration status by conducting 30 pre-HD measurements; the total number of pre-HD B-line scores was 10.5 (8–18) [16]. Moreover, 30 and 48 LUS examinations were performed in the DW and non-DW groups, respectively [25]. All patients had ultrasonographic B-lines in the lungs with pre-HD B-line scores of 23.5 (10–45) and 56.5 (14–176) in the DW and non-DW groups, respectively. Conversely, a study demonstrated a diminished efficacy of ultrasonographic B-line score in CKD due to the presence of a stronger linear relation between the B-line score and VO in children with acute kidney injury (AKI) than in those with CKD [24]. The observed difference could be attributed to the fact that CKD children have target weights that are determined through experimental means by the clinical team rather than relying on a universally accepted benchmark known as the gold standard DW. On the other hand, the baseline weight of individuals with AKI was objectively measured after the resolution of fluid excess, making it more likely to represent their physiological DW accurately.

Consistent with previous research, we assessed the efficacy of HD in terms of volume removal by evaluating post-HD weight loss, DW, and B-line scores. This study showed rapid weight loss during the dialytic period. There was a high significant decrease in weight post-HD than pre-HD (29.4383 ± 8.61693 kg), with a post-HD mean weight loss of 0.645 ± 0.4764 . Meanwhile, the weight gain between dialytic sessions (1.2163 ± 0.6701 kg) was more than the weight loss post-HD (0.645 ± 0.4764 kg). This coincides with [28], which reported that HD practices that help people reach lower post-HD weights minimize their chance of developing cardiomyopathy, hypertension, and chronic VO. The body weight was found to be significantly decreased from 32.276 kg pre-HD to 30.576 kg post-HD [27]. The median weight loss post-HD was 5%, with a range of 0.26%–24.05%. The occurrence of dyspnea, edema, and a simultaneous decrease in SBP and DBP post-HD significantly decreases as the body weight of patients is reduced. According to the results, the mean DW was 28.356 ± 8.6488 . Attaining the patient's DW was not possible throughout every HD session. This resulted from pre-HD weight exceeding the maximum permitted ultrafiltration volume per HD session and prematurely halting ultrafiltration due to intra-dialytic discomfort, with 14 patients (46.7) achieving the DW. The mean

difference between the post-HD weight achieved and the DW targeted was (0.4373 ± 0.398). Regarding mean B-line scores, post-HD sessions showed a significant decrease in the total B-line number. The mean total B-lines decreased from 59.633 ± 42.811 pre-HD to 32.7 ± 27.994 post-HD. B-line scores were high and significantly decreased in both the DW ($p < 0.001$) and non-DW groups post-HD ($p < 0.001$). Regarding Pre-HD, the DW group exhibited lower mean B-line scores (29.142 ± 12.629) than the non-DW group (86.312 ± 42.169). Regarding post-HD, the DW group exhibited lower mean B-line scores (11.9286 ± 5.876) than the non-DW group (51.5 ± 26.087), revealing a significant difference between the two groups ($p < 0.001$). Consistent with [25], the mean B-line scores decreased from 23.5 pre-HD to 8.5 post-HD in the DW group while decreasing from 56.5 pre-HD to 32 post-HD in the non-DW group.

Mean blind scores in non-dry weight groups decreased from 56.5 before hemodialysis to 30 following hemodialysis, even though in non-dry weight group

As their patient's blind scores were significantly the highest (median 24 (4–93) before dialysis and median 16 (5–55) post-dialysis. These results were constituent with data from 29. (27) (pre-dialysis: 24 to 25 and post-dialysis: 9 to 10). (28) reported median pre- and post-dialysis values of 10 and 4, respectively, which were greater than those of 29) (3.5 4 pre- and 1.7 3.1 post-dialysis).

The study aimed to evaluate the relationship between VO detected by all physical examination measures pre-HD and B-line line score. Pre-HD total B-line number was positively correlated to IDWG, BP, and clinical fluid score ($r = 0.811$, $p < 0.01$; $r = 0.59$, $p < 0.001$; $r = 0.75$, $p < 0.001$, respectively). Moreover, the post-HD total B-line number was positively correlated to post-dialytic weight loss ($r = 0.89$, $p < 0.001$). Additionally, the total B-line number post-HD was significantly positively correlated to residual volume calculated based on the difference between post-dialytic weight and DW ($r = 0.943$, $p < 0.001$). Meanwhile, the post-HD total B-line number exhibited a significant positive correlation to post-HDSBP ($r = 0.598$, $p < 0.001$) and post-HDDBP ($r = 0.663$, $p < 0.001$) (Table 3). A study conducted on overhydrated patients discovered a more significant correlation between the total B-line number and VO as measured by weight gain ($r = 0.764$, $p < 0.001$) [16]. The linear regression demonstrated a direct and positive correlation between changes in both B-line scores (B-line) and interdialytic weight gain ($r = 0.517$, $p = 0.002$) and dialytic weight reduction ($r = 0.558$, $p < 0.001$) [24]. However, all post-HD measurements were made 15 min post-HD sessions, a moderately positive correlation was found between VO post-HD and the total B-line number [11]. Conversely, prior research has shown that it takes 2–3 h

for the fluid balance in intravascular and extravascular compartments to return to normal post-HD. They consequently assumed that the post-HD assessments showed a decline in the correlative power of the overall number of B-lines.

Limitations

On portable device during the intra-dialytic session, we cannot store the images due to technical problems.

Conclusions

LUS is a noninvasive and emerging method that can be performed at the patient's bedside in a real-time manner. This technique is employed for the purpose of diagnosing hypervolemia and quantifying B-lines. Therefore, LUS serves as a valuable technique for monitoring DW and optimizing the target weight in cases of pediatric HD.

Recommendation

Further research is warranted to investigate the potential utility of LUS in identifying VO in cases of AKI and peritoneal dialysis.

Abbreviations

ABPM	Ambulatory blood pressure monitoring
AKI	Acute kidney injury
ARDS	Acute respiratory distress syndrome
BP	Blood pressure
CKD	Chronic kidney disease
DBP	Diastolic blood pressure
DW	Dry weight
ECHO	Echocardiography
ESKD	End-stage kidney disease
EVLW	Extravascular lung water
HD	Hemodialysis
IDWG	Inter-dialytic weight gain
KDIGO	Kidney Disease: Improving Global Outcomes
LUC	Lung ultrasound
LV	Left ventricular
SBP	Systolic blood pressure
VO	Volume overload

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Not applied.

Author contributions

ES and WA authored the manuscript and handled correspondence with the journal. AM and WA were responsible for collecting and processing patient data and images. ES, AS, and SE contributed to the study's design and conducted the statistical analysis. The study was conceptualized by ES and WA, who also contributed to its design and coordination. Eventually, ES and WA reviewed the draft from a clinical perspective. All authors have read and approved the manuscript.

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Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

The Institutional Review Board (IRB) of the Faculty of Medicine, Benha University, approved the study with ethical committee approval dated 26.10.2022, Code:MS-1-2019. Informed written consent was taken from all subjects.

Consent for publication

All patients included in this research gave written informed consent to publish the data contained within this study.

Competing interests

No financial or non-financial competing interests.

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