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Original Research Article

Comparison of the inferior vena cava index and inferior vena cava collapsibility index obtained by ultrasound as a measure of body fluid volume status in children with nephrotic syndrome

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ABSTRACT

Background: There is triad of hypoalbuminemia, edema, and hyperlipidemia in nephrotic syndrome patients. Management of nephrotic syndrome includes general measures like fluid restriction, emergency albumin transfusions and diuretics that provide symptomatic relief till steroids act. These measures require an assessment of body fluid volume to avoid circulatory failure which is very difficult in these patients because of edema. The objective of the study was to measure and compare the Inferior Vena Cava (IVC) Index and Inferior Vena Cava Collapsibility (IVCC) Index by ultrasound as a measure of body fluid volume status in children with nephrotic syndrome.
Methods: The present observational study was conducted in all children of age more than 1 year up to 18 year. There were two groups; group 1 was nephrotic syndrome patients-Initial episode or in relapse and group 2 (Control) was age and sex-matched non-nephrotic children. IVC index and IVCC index were measured and compared in both the groups.
Results: Mean value of minimum diameter of IVC during inspiration in cases was 5.91±1.60 mm as compared to 4.53±0.94 mm in controls which was significantly higher in case group {P <0.0001}. Mean value of IVC index in cases was 0.88±0.20 cm/m^2 as compared to 0.93±0.19 cm/m^2 in controls which was non-significant. Mean value of IVCC index in cases (35.61±13.68) was significantly less as compared to controls (52.23±2.01) {P <0.0001}.
Conclusions: The present study concluded that IVCC index is better indicator of body fluid volume status in nephrotic patients as compare to IVC index.

Keywords: Edema, Inferior vena cava index, Inferior vena cava collapsibility index, Nephrotic syndrome

INTRODUCTION

Edema is one of the most common symptoms in nephrotic syndrome.[1] The mechanism of edema formation in the nephrotic syndrome has long been a source of controversy. The major pathophysiological factors which lead to water retention and edema in nephrotic syndrome are primary sodium retention that is directly induced by the renal disease (overfill hypothesis), secondary sodium retention in which the low plasma oncotic pressure due to hypoalbuminemia promotes the movement of fluid from the vascular space into the interstitium, leading to under filling of the vasculature and activation of the renin-angiotensin-aldosterone system (underfill hypothesis).[2] Other probable mechanisms of edema in nephrotic syndrome are increase in vascular permeability and primary increase in renal sodium retention due to increased level of Vasopressin, an impaired response to ANP in nephrotic syndrome which might be caused by over active efferent

sympathetic nervous activity, over activity of the Na^+K^+ATPase and renal epithelial sodium channel in the cortical collecting duct.[2]

There is evidence for both intravascular volume expansion (overfilling) and intravascular volume depletion (underfilling) in patients with nephrotic syndrome.[3] The clinical importance of distinguishing between these mechanisms is the ability to tolerate diuretic therapy.

Diuretics are well tolerated in patients with renal sodium retention but, if underfilling is the primary mechanism, it can lead to worsening of hypovolemia as evidenced clinically by an elevation in serum creatinine. Management includes general measures like fluid restriction, emergency albumin transfusions and diuretics that provide symptomatic relief till steroids act. These measures require an assessment of body fluid volume to avoid circulatory failure.

Clinical assessment (vitals, urine output, skin turgor, blood pressure, pulse, weight changes etc.), central venous pressure (CVP), biochemical laboratory measures (fractional excretion of sodium, vasoactive hormones measurement like atrial natriuretic peptide and vasopressin and plasma renin activity, aldosterone, angiotensin II) and Ultrasound-Doppler/ECHO (Inferior Vena Cava Index, Inferior Vena Cava Collapsibility Index, Inferior vena cava: Aortic Calibre ratio) are the parameters that reflect body fluid volume.[4-7]

Clinical parameters are not accurate and determination of CVP is an invasive method. Biochemical parameters are very costly and not readily available. Echocardiography and ultrasound used Inferior Vena Cava Index (IVCI) and Inferior Vena Cava Collapsibility Index (IVCCI) are utilized in adult patients as these techniques are noninvasive and help in determining intravascular volume load.[2]

Echocardiography is not readily available so ultrasound can be used in place of echocardiography. Therefore, ultrasound which is a non-invasive, cheaper and readily available method enables rapid assessment of body fluid volume and helps in management of cases of nephrotic syndrome. Very few studies were conducted to compare IVCI index and IVCCI index for body fluid volume in children. This study was planned to measure and compare the inferior vena cava index and inferior vena cava collapsibility index by ultrasound as a measure of body fluid volume status in children with Nephrotic syndrome.

METHODS

The present observational study was conducted in both out and in patients of department of Pediatrics, Nephrology division, SPMCHI Hospital, SMS Medical College, Jaipur over a period of 1 year i.e. from March 2016 till April 2017. After approval from institutional ethics committee all children of age more than 1 year up to 18 year with Nephrotic syndrome were recruited for the study. Children with Nephritic-Nephrotic combination pathologies, children who are very sick (on ventilator, with very severe respiratory distress, with shock) and children on diuretics in the last 12 hours were excluded from the study. Age and sex-matched non-nephrotic children were also recruited for control. Nature and the purpose of the study were explained fully to the parents/guardian and written consent was taken from them for all enrolled children.

Complete history, clinical assessment of body fluid volume (by vitals, urine output, skin turgor, CFT, blood pressure, pulse etc.) was done at first contact. Standard laboratory features (including complete blood counts, renal functions tests, serum electrolytes, serum total protein and albumin, serum total cholesterol, urine protein by dip stick, urine complete microscopy and urine protein urine creatinine ratio) supportive of a diagnosis of Nephrotic syndrome [Initial episode or in relapse] were obtained.

A predesigned structural performa was used to collect information. Basic demographic data e.g. age, sex, religion, parents name and age at diagnosis, treatment was collected from all patients. BMI and BSA was calculated by using following formula.

weight (kg)/height $(m)^2$ and

4 × weight (kg) + 7 /90 + weight (kg).

Specific measurement of IVC caliber diameter was measured using an ultrasound-M mode under supervision by a single radiologist. IVC caliber measurement was done during deep inspiration and expiration in supine position after 5 min of rest. The inferior vena cava diameter was measured 2 cm distal to the right atrium along the subcostal long axis by using probes (7-3 MHz, 18-5 MHz) by Hitachi Hi-vison Preiurs ultrasound machine, in M mode.

The following formulas were used to determine the IVC and IVCC index:

$$IVCI = \frac{\text{expiration max. diameter (cm) + inspiration min. diameter (cm)}}{2 \times \text{body surface area}}$$

$$IVCCI = \frac{\text{expiration max. diameter(cm) - inspiration min. diameter (cm)} \times 100}{\text{expiration max. diameter (cm)}}$$

Statistical analysis

All the data was expressed as Mean±SD. Statistical analysis was performed using t test, chi-square test wherever applicable. A P value of <0.05 was considered to be statistically significant.

RESULTS

In present study total number of cases and control were 30 in each group which were age and sex matched (19 males and 11 females).

Table 1: Demographic and laboratory parameters in both cases and controls.

Parameters	Cases (Mean±SD)	Controls (Mean±SD)	P value
Age (year)	7.08±3.47	7.09± 3.47	0.997
Sex (M/F)	19/11	19/11	-
Weight (kg)	24.95±11.03	19.49±6.34	0.022*
Height (cm)	113.11±21.27	115.56±23.03	0.670
Body Surface Area (m^2)	0.89±0.26	0.77±0.18	0.038*
Body Mass Index (kg/m^2)	19.08±4.48	15.31±5.02	0.003*
Systolic blood pressure (mmHg)	110.87±14.42	104.37±6.83	0.03*
Diastolic blood pressure (mmHg)	72.4±12.03	66.13±5.06	0.01*
Urea (mg/dl)	44.56±32.37	23.86±8.65	0.001*
Creatinine (mg/dl)	0.69±0.35	0.68±0.18	0.887
Sodium (meq/l)	141.2±3.73	136±3.53	0.0003*
Potassium (meq/l)	4.2± 0.50	4.38±0.47	0.157
Chloride (meq/l)	106.16±5.60	106.63±5.03	0.735
Total protein (gm/dl)	4.07±0.73	6.16±0.6	0.0006*
Albumin (gm/dl)	2.02±0.48	3.91±0.5	0.0006*
Total cholesterol (mg/dl)	384.5±109.35	104.96±21.99	0.005*

*significant

Table 2: Maximum diameter of IVC in expiration and minimum diameter of IVC in inspiration in cases and controls.

	Cases (Mean±SD)	Controls (Mean±SD)	P value
Maximum diameter of IVC in expiration (mm)	9.31±2.12	9.48±1.87	0.743 (Non significant)
Minimum diameter of IVC in inspiration (mm)	5.91±1.60	4.53±0.94	0.0001* (significant)

Table 3: Distribution of cases and controls according to IVC index and IVCC index.

IVC index (cm/m^2)	Cases N (%)	Controls N (%)	Volume status
<0.8	10 (33.33)	7 (23.33)	Hypovolemic
0.8-1.15	18 (60)	21 (70)	Euvolemic
>1.15	2 (6.66)	2 (6.66)	Hypervolemic
IVCC index			
<50 %	21 (70)	0	Hypervolemic
≥50%	9 (30)	30 (100)	Hypovolemic or euvolemic (fluid responsive)

Demographic and laboratory parameters in both cases and controls groups are shown in Table 1. Mean value of maximum IVC diameter during expiration in cases was 9.31±2.12 mm as compared to 9.48±1.87 mm in controls. Mean value of minimum diameter of IVC during inspiration in cases was 5.91±1.60 mm as compared to 4.53±0.94 mm in controls which was significantly higher in case group (Table 2).

According to IVC index maximum number of cases and controls were in euvolemic groups. In euvolemic group (IVC index 0.8 to 1.15 cm/m^2), there were 18 (60%) cases and 21 (70%) controls (Table 3). According to IVCC index; there were 21 (70%) cases and zero controls in hypervolemic group (IVCC index <50%) (Table 3).

Mean value of IVC index in cases was 0.88±0.20 cm/m2 as compared to 0.93±0.19 cm/m^2 in controls which was non-significant. Mean value of IVCC index in cases (35.61±13.68) was significantly less as compared to controls (52.23±2.01). P value was 0.00003 (Table 4).

Table 4: Mean IVC index and IVCC index in both case and controls.

	Cases (Mean±SD)	Controls (Mean±SD)	P value
IVC index	0.88±0.20	0.93±0.19	0.358 (Non significant)
IVCC index	35.61±13.68	52.23±2.01	0.00003 (Significant)

DISCUSSION

The IVCI is a good indicator of circulating blood volume, and the IVCCI is an accurate determinant of right atrial pressure.8 These techniques are reliable and relatively easy to perform as compare to other invasive methods. However, these techniques can be difficult to carry out on pediatric patients, which increase the possibility of obtaining inaccurate measurements, especially for patients with cardiac insufficiency and/or heart disease. Major variations may be observed depending on the individual performing the technique, making it difficult to obtain any useful information regarding the severity of volume overload.[9] In present study authors measured and compared the Inferior vena cava index and inferior vena cava collapsibility index by ultrasound in children with nephrotic syndrome as a measure of body fluid volume status in children.

Mean value of maximum inferior vena cava (IVC) diameter during expiration in cases was similar to controls. Mean value of minimum diameter of IVC during inspiration in cases was significantly more in cases. These maximum and minimum IVC measurements individually are static parameters but IVCCI is a dynamic parameter, which takes into account variation of IVC diameter over the respiratory cycle.[10] This could be due to that the inferior vena cava (IVC) is a highly compliant vessel with no valves and its size varies with changes in intra vascular pressure, blood volume, right heart function and the degree of collapsibility during the respiratory cycle predicts the fluid status of the patient.[7,11,12]

A study conducted by Ozdemir et al, in children with nephrotic syndrome found that there was no significant difference between the nephrotic syndrome patients (0.66±0.33) and controls (0.60±0.3) for IVCI (P >0.05).[13] The values for the IVCCI in the nephrotic patients (39.4±8.6) were much lower than the values calculated for the control subjects (56.9±8.7) (P <0.05). These results are similar to present study. Mean value of IVC and IVCC index in present study in nephrotic patients (0.88±0.20, 35.61±13.68) and in controls were (0.93±0.19, 52.23±2.01). P value was significant for IVCC index.

Donmez et al, studied Inferior vena cava indices to determine volume load in children with minimal lesion nephrotic syndrome.[2] Twelve children with MLNS (7 boys, 5 girls) and 21 healthy children as a control were included in this study. The patients were classified into three different stages (stage A: edematous; stage B: 50% decrease in weight gain; stage C: edema free) following measurement of their ideal weights. The value of IVCI were 6.1±0.6, 5.6±0.5, 5.9±0.4 and 6.09±0.3 in stage A, B, C and controls group respectively. The values of IVCCI were 57.3±2.6, 58.9±2.5, 62.9±2.6, and 65.0±1.6 in stage A, B, C and control group. There was no significant difference between stage A edematous nephrotic patients and control group in IVCI while there was significant difference in IVCCI. Although in present study we did not divided the edematous patients in groups according to weight loss, we only formed edematous nephrotic patients in relapse and normal age and sex matched children and found similar results.

In a study by Nalcacioglu et al, for assessment of body fluid volume in children with nephrotic syndrome using bioelectrical impedance analysis, NT-Pro BNP and IVCI.[14] In 19 patients with nephrotic syndrome before treatment (group 1) and at remission (group 2) and 25 healthy age and sex matched controls (group 3) the values of IVCI were 6.6±2.82, 6.2±2.54, 5.2±1.30 respectively in group 1, 2, 3 which were not significantly different from each other. They did not calculate IVCCI index but values of IVCI were same in all groups like in present study.

In a study by Ghaffari et al, IVCI and IVCCI were measured to determine the volume status of 30 pediatric patients without edema, 13 patients with moderate edema, and 11 patients with significant edema. The IVCCI was found to be higher in patients without edema, and IVCI values were similar between all groups.[15] In this study, echocardiography had limited utility in determining volume status, particularly for pediatric patients with severe volume overload.[15] However, in present study, IVCI and IVCCI measurements were performed with ultrasound M mode for all patients. The present study found that IVCCI values were lower in children with nephrotic syndrome when compared with the controls. In contrast, values for the IVCI were similar between the patients and the controls.

Tabel et al, conducted a study in which he studied 18 children with minimal change disease either newly diagnosed or relapsed but were steroid free for at least 6 months, during the first week of edema and when edema resolved (5-7 days after initiation of therapy).[16] The volume load of all patients was evaluated, measuring the inferior vena cava indices in each stage by echocardiography. The inferior vena cava index (IVCI) values decreased significantly after diuretic treatment (P

<0.001), while inferior vena cava collapsibility index (IVCCI) values increased in the post-treatment period (P <0.001). Thus, both indices were showed significant changes. The reason of different results could be that in all other studies and present study control group was taken but in Tabel et al, study these values were calculated on same patients in different stage.[16]

CONCLUSION

The present study concluded that IVCCI is better indicator of body fluid volume status in nephrotic patients as compare to IVCI index and thus it can provide a useful guide for intravascular volume status assessment in children. This study had also showed that the majority of nephrotic patients are normovolemic or hypervolemic. Although mechanism of edema formation in nephrotic can be multiple but present study support the overfill hypothesis as evidenced by significant increase sodium concentration in nephrotic patients and IVCC Index value <50% in most of edematous nephrotic patients.

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