Section: Medicine

Original Research Article

USEFULNESS OF IVC COLLAPSIBILITY INDEX IN ADULTS WITH DENGUE FEVER WITH AND WITHOUT WARNING SIGNS

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Abstract

Background: Dengue is characterized by damage to capillaries leading to plasma leakage resulting in hypovolemia Intravascular volume status is a major determinant of the severity of the disease. Intravascular volume can be assessed by clinical parameters, electrocardiogram (ECG), echocardiogram, and Inferior Vena Cava Collapsibility Index (IVCCI). The IVCCI is a relatively simple ultrasonographic non-invasive measure of the intravascular volume status the aim of this study the relationship between IVCCI, a marker of intravascular volume, and clinical grading in adults with dengue with or without warning signs. **Materials and Methods:** This hospital based prospective observational study was conducted in a Medical College hospital among adults older than 18 years with dengue with or without warning signs. Intravascular volume was assessed by ECG, transthoracic echocardiography, and IVCCI. Measurement of agreement between the various methods was assessed using Cohen's kappa. **Result:** One hundred and one participants were enrolled, 53 had dengue without warning signs while 48 had warning signs. The most common presenting feature was fever which was universally present. ECG changes were uncommon and the most common finding was sinus tachycardia. Grade 1 diastolic dysfunction was the most common abnormal echocardiographic finding and was present in 21 (20.8%) of the study population. Thirty one out of 101 patients had abnormal IVCCI. Cohen's kappa statistical analysis showed values of 0.053 for IVCCI and Diastolic Dysfunction and 0.091 for IVCCI and clinical grading. **Conclusion:** IVCCI is not a useful tool for the assessment of intravascular hypovolemia in adults with dengue with or without warning signs.

INTRODUCTION

Dengue fever is an arboviral illness that is transmitted among humans by infected female Aedes aegypti mosquito and is a major public health problem in tropical and subtropical regions of the world.[1,2] Dengue infection is typically mild in more than 80 % of the infected population, but it can occasionally progress to severe dengue, which is a life-threatening condition.[3] Clinical Dengue infection can be classified into two categories: dengue with or without warning signs and severe dengue.[4] Clinical dengue is typically characterised by damage to capillaries leading to plasma leakage which can lead to loss of fluid from the vascular compartment into the interstitium resulting in hypovolemia and fluid accumulation in the third space progressing to shock, respiratory distress, severe bleeding, organ failure, and in some cases, death. Intravascular volume status is a major determinant of the severity of the disease. Therefore, it is important to identify intravascular volume depletion at the earliest in patients with dengue fever and provide fluid therapy as needed.

Intravascular volume can be assessed by clinical parameters such as blood pressure, pulse rate, and urine output. However, these parameters do not reflect the volume status accurately. Electrocardiogram (ECG), and Echocardiogram can be useful in assessing vascular volume. ECG provides clues to intravascular volume status by reviewing the preload of the heart. ECG changes seen in hypovolemia include decreased amplitude of the QRS complex, prolonged QTc interval and increased heart rate.[5] Echocardiogram is useful to evaluate the size and shape of the chambers of the heart, as well as the cardiac output, which helps in the estimation

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of vascular volume. Echocardiographic changes depend on the degree of hypovolemia and the most commonly seen findings are reduced cardiac output, decreased right ventricular filling, and ventricular dysfunction. But these techniques are not as accurate as methods, such as vascular ultrasound. The Inferior Vena Cava Collapsibility Index (IVCCI) is a non-invasive measure of the intravascular volume status and is a useful predictor of fluid responsiveness in critically ill patients. The IVCCI is a relatively simple ultrasonography measure that can be used in a variety of settings, including the emergency department and the intensive care unit. Studies in children have shown that IVCCI is a useful non-invasive method for assessment of intravascular fluid status.[6] The aim of this study is to usefulness of IVCCI as a marker of intravascular volume in adults with dengue with or without warning signs.

MATERIALS AND METHODS

This hospital based prospective observational study was conducted in the Department of Medicine of a tertiary care government hospital in South India and was approved by the Institute Ethics Committee. Subjects who were 18 years and above with fever without focus and positive diagnostic test (NS1 antigen by non-ELISA based test or dengue IgM by ELISA test) for dengue infection with the clinical classification of dengue with or without warning signs were included in the study. After informed consent, basic demographic parameters – age, sex, height, weight, abdominal circumference, and blood pressure, were entered in a predesigned proforma. Those who presented with fever of less than five days underwent Dengue NS1 antigen testing, while those who presented after 5 days of fever were investigated for dengue IgM using ELISA. Patients with severe dengue, coinfection with scrub typhus, enteric fever, and those with pre-existing cardiac illness and rhythm disturbances were excluded from the study. The cases were classified according to the WHO Guidelines for Clinical Management of Dengue Fever (2015) into dengue with or without warning signs and severe dengue. Standard 12-lead ECG with standardizations for each of the 12 leads was recorded at 25 mm/s and 10 mm/mV using CARDIART 6108T (manufactured by BPL Electronics Ltd) in the supine position. All patients underwent ECHO within 24 hours of admission by a trained physician using Philips cardiac machine using a 4 MHz phased array transducer. An M mode scan of the left ventricular (LV) is obtained from a standard parasternal long-axis view at the level of the mitral valve (MV) tip in all patients. Systolic function was assessed by Left ventricular ejection fraction (LVEF). LVEF was calculated by Teichholz formula $LVEF = 7LVID^3/ (2.4+LVID)$ where LVID is the Left Ventricular Internal Dimension [7]. The LV function was considered mildly reduced if the LVEF was 54–45%, moderately reduced if the LVEF was 44–31%, and significantly reduced if it was less than 30%. Diastolic function was assessed by E/A ratio, a measure of the early diastolic filling of the left ventricle. It is the ratio of peak velocity blood flow from left ventricular relaxation in early diastole (the E wave) to peak velocity flow in late diastole caused by atrial contraction (the A wave). Transmitral Pulse wave Doppler velocities (peak E and A wave velocities) were measured in the apical four-chamber view with the sample volume positioned at the MV. The E/A ratio < 1 and > 2 were considered as diastolic dysfunction.

IVC measurements were done in the subcostal view below the level of the hepatic veins. The IVCCI is calculated by dividing the difference between the maximum IVC diameter on expiration and the minimum IVC diameter on inspiration by the maximum IVC diameter on expiration and was expressed as a percentage [8]. The IVC collapsibility of more than 50% and less than and equal to 20% were considered to be abnormal. Patients were managed as per the standard WHO protocol for the management of Dengue. Data were compiled and tabulated using the Microsoft Excel sheet. Analysis of the data was performed by using the statistical software SPSS version 17. Measurement of agreement between the various methods was assessed using Cohen's kappa and was interpreted as follows: values ≤ 0 as indicating no agreement and 0.01–0.20 as none to slight, 0.21–0.40 as fair, 0.41– 0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as almost perfect agreement.

RESULTS

One hundred and one participants were enrolled, 55 (54.5%) were males and the rest were females. The majority of subjects were in the age group 20 to 29 years, with the youngest being 18 years and the oldest patient being 74 years. Nearly half of the patients (51) were only positive for NS1 antigen and the rest were either IgM antibody or both NS1 and IgM antibody positive. Fifty Three patients had dengue without warning signs while 48 had dengue with warning signs [Table 1). None of the patients had any clinical signs of shock and all the patients survived without any long term morbidity. The most common presenting feature was fever which was universally present in all the subjects. The next common clinical features were myalgia, vomiting, and headache. Though 82 of the 101 patients had thrombocytopenia, bleeding manifestations such as gastrointestinal bleeding, petechiae, and subconjunctival haemorrhage were uncommon [Table 2]. Hemoconcentration (Hematocrit > 50.3% for males and > 44.3% for females) was present in only two patients. Leucopenia (WBC < 3,500 cell/ ml) was found in 27 (26.7%) of the study population. Abnormal abdominal ultrasound findings were found in 51 of the 101 patients and included ascites, hepatomegaly, splenomegaly, pleural effusion, and

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gall bladder edema. ECG changes were uncommon and the most common finding was sinus tachycardia. Sinus bradycardia was the next common finding. Other findings which were seen include ST segment elevation, inverted T wave in the chest leads, and low voltage complexes [Table 3]. Grade 1 diastolic dysfunction was the most common abnormal echocardiographic finding and was present in 21 (20.8%) of the study population. Other findings include grade 2 (2) and 3 (2) diastolic dysfunction, hypokinesia (5) and pericardial effusion (1) [Table 4]. [Figure 1] shows the distribution of the IVC collapsibility index in the study population. Thirty One out of 101 patients had abnormal IVCCI. Agreement statistics was applied for the relationship between IVCCI, clinical severity, and diastolic dysfunction. Cohen's kappa statistical analysis showed values of 0.053 for IVCCI and Diastolic Dysfunction and 0.091 for IVCCI and clinical grading. This indicates that there is no agreement between IVCCI and diastolic dysfunction and clinical grading. Based on these values, we conclude that IVCCI assessment does not have clinical value in patients with dengue fever with or without warning signs.

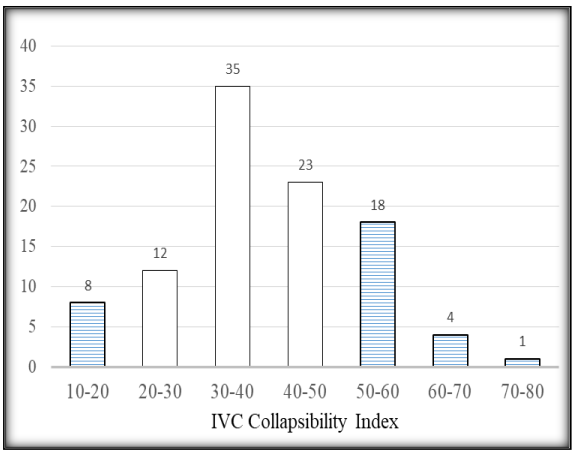

Figure 1: Distribution of IVCCI

Table 1: Demographics of Study Population

	Male	Female	Total
Study Population	55 (54.5 %)	46 (45.5 %)	101 (100 %)
Age Wise Category			
19 years & below	4 (4 %)	4 (4 %)	8 (7.9 %)
20-29 years	27 (26.7 %)	9 (8.9 %)	36 (35.6 %)
30-39 years	10 (9.9 %)	13 (12.9 %)	23 (22.8 %)
40-49 years	9 (8.9 %)	11 (10.9 %)	20 (19.8 %)
50 - 59 years	0 (0 %)	6 (5.9 %)	6 (5.9 %)
60 - 69 years	2 (2 %)	2 (2 %)	4 (4 %)
70 years & above	3 (3 %)	1 (1 %)	4 (4 %)
BMI Stature			
< 15	1 (1 %)	3 (3 %)	4 (4 %)
15 – 24.9	29 (28.7 %)	22 (21.8 %)	51 (50.5 %)
25 – 29.9	19 (18.8 %)	19 (18.8 %)	38 (37.6 %)
30 – 34.9	5 (5 %)	1 (1 %)	6 (5.9 %)
≥ 35	1 (1 %)	1 (1 %)	2 (2 %)
Waist circumference (≥ 90 for men & ≥ 80 cm for women)			
Normal	23 (22.8 %)	6 (5.9 %)	29 (28.7 %)
Increased	32 (31.7 %)	40 (39.6 %)	72 (71.3 %)
Diagnostic Test			
NS1 positive	31 (30.7 %)	20 (19.8 %)	51 (50.5 %)
IgM positive	18 (17.8 %)	19 (18.8 %)	37 (36.6 %)
NS1 and IgM positive	6 (5.9 %)	7 (6.9 %)	13 (12.9 %)
Type of Presentation			
Dengue Fever	26 (25.7 %)	27 (26.7 %)	53 (52.5 %)
Dengue with warning signs	29 (28.7 %)	19 (18.8 %)	48 (47.5 %)

Table 2: Clinical Presentation

	Male	Female	Total (Percentage)
Fever	55	46	101(100 %)
Myalgia	35	25	60(59.4 %)
Vomiting	22	24	46(45.5 %)
Headache	22	16	38(37.6 %)
Abdominal Pain	9	10	19(18.8 %)
Diarrhoea	10	8	18(17.8 %)
Lower GI Bleeding	4	1	5(5 %)
Upper GI Bleeding	3	1	4(4 %)
Retroorbital Pain	3	1	4(4 %)
Menorrhagia	0	4	4(4 %)
Giddiness	2	1	3(3 %)
Petechiae	3	0	3(3 %)
Breathlessness	1	0	1(1 %)
Subconjunctival Hemorrhage	1	0	1(1 %)

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Table 3: ECG Findings in the Study Population

Parameter	Finding	Number (%)
ECG Voltage	Normal	99 (98 %)
	Low	2 (2 %)
Rate	Normal rate	69 (68.3 %)
	Sinus Tachycardia	22 (21.8 %)
	Sinus Bradycardia	10 (9.9 %)
ST Segment	Normal	99 (98 %)
	Elevation	2 (2 %)
T wave Morphology	Normal	96 (95 %)
	Inverted, V1 - V6	2 (2 %)
	Inverted, V1 to V4	1 (1 %)
	Inverted, V4 to V6	1 (1 %)
	Isoelectric	1 (1 %)

Table 4: Echo Findings in the Study Population

Parameter	Finding	Number (%)
Diastolic Dysfunction	Normal	76 (75.2 %)
	Grade 1	21 (20.8 %)
	Grade 2	2 (2 %)
	Grade 3	2 (2 %)
Ejection Fraction	> 54	96 (95 %)
	44-53	5 (5 %)
Pericardial Effusion	No	100 (99 %)
	Yes	1 (1 %)

DISCUSSION

Though dengue is usually a mild illness, it can progress to severe, life threatening disease in some patients. The core pathophysiological problem in dengue fever is increased vascular permeability, which is caused by a complex interaction between viral and host factors, including direct damage to blood vessels by the dengue virus itself and immune response to the virus, causing bystander injury to blood vessels, particularly due to antibody-dependent enhancement. Increased vascular permeability leads to clinically significant problems, such as hypovolemic shock and haemorrhage.[9]

Management of dengue is supportive and aimed at relieving the symptoms and treating the complications, as there is no specific treatment.[10] The best approach to improve the outcome is to identify intravascular hypovolaemia during the early stages. However, the severity of the decrease in intravascular volume varies depending on the severity of the dengue infection.[11] Unfortunately, the clinical signs of decreased intravascular volume in the early stages are subtle. In mild cases, the decrease in intravascular volume may be only slight and may not cause any symptoms. Since the clinical signs are inaccurate in identifying intravascular hypovolaemia, we studied IVCCI which is gaining popularity for this purpose in acute care.

The IVCCI is a noninvasive tool to assess intravascular volume status and is measured by the percentage decrease in the IVC diameter during a brief inspiratory pause. It is based on the principle that the IVC collapses during inspiration as a result of decreased intrathoracic pressure. In hypovolemic patients, the IVC is less compliant and does not collapse as much during inspiration. A study published in 2016 found that the assessment of intravascular volume status by determining IVC collapsibility using bedside USG is a helpful non-invasive tool in children with dengue fever.[12] However, the IVCC can be affected by factors other than intravascular volume status, such as the patient's position, the respiratory rate, and the presence of abdominal distension. Additionally, the IVCC may not be accurate in patients with right heart failure or pericardial effusion.

The IVCCI has been shown to be a reasonably accurate predictor of intravascular hypovolemia in adults in some studies.[13] However, other studies have found that the IVCC is not as accurate in diagnosing hypovolemia in adults.[14] In our study, we found that the agreement between IVCCI, clinical severity, and diastolic dysfunction, another marker of intravascular hypovolemia in patients with dengue fever and dengue fever with warning signs was poor. The limitations of our study are that this was a single centre study and further studies in a larger population are needed before ruling out the usefulness of IVCCI. Also, blinding of the clinical status was not possible due to logistical reasons.

CONCLUSION

Based on our findings, we conclude that IVCCI is not a useful tool for the assessment of intravascular hypovolemia in adults with dengue with or without warning signs.

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