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A prospective study of role of portal venous doppler in predicting capillary leakage in dengue fever patients

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Abstract

Aim

- To evaluate the ultrasonographic features of capillary leak syndrome in dengue fever patients.
- To investigate the role of Doppler study of the portal vein as a predictor for capillary leakage in dengue fever serology positive patients.
- To compare and correlate the portal venous Doppler findings with the laboratory findings and clinical outcome.

Materials and Methods: A Prospective Cohort Study was conducted in 100 Patients with Acute fever, clinical symptoms and signs of dengue with laboratory evidence of thrombocytopenia, NS1 and IGM Positivity for a period of 6 months in Department of Radiodiagnosis, S.P Medical College Hospital, Bikaner, Rajasthan. Grey scale and colour Doppler ultrasound were performed in patients with 4-6 hrs at the time of admission.

Acute Fever patients with thrombocytopenia, IGM positive and NS1 positive were included and Patient with Chronic liver disease, MP/Mf positive, known case of Hypoalbuminemia, and Hypotension, were excluded from the study sample.

Portal vein diameter, Flow velocity, Cross sectional area were measured at the level of liver hilum. Congestive Index was calculated by Cross sectional area / portal venous velocity. Check was made of associated features like Ascites, Pleural effusion, Gallbladder wall edema.

Results: 90% of the patients developed capillary leak syndrome and showed mean portal diameter of 12.88mm, mean portal velocity of 18.27cm/s and mean congestive index of 0.0972. The sensitivity and specificity of congestive index (0.07 as cut off) were 56% and 100%, portal diameter (>11.2cm as cut off) were 75% and 70%, PV velocity (<25 cm /s as cut off) were 93% and 60%.

Conclusion: Dengue fever patients with evidence of decreased portal venous velocity, Increased portal vein diameter and increased congestion index were more prone for developing capillary leak syndrome. These measurements predicted CLS earlier than clinical and laboratory evidence thus aiding in early treatment and thus decreasing mortality.

Keywords: dengue, ultrasound, fever, haemorrhage, index, velocity

Introduction

Dengue Fever / Dengue Haemorrhagic fever is increasingly recognized as one of the world's major emerging infectious tropical diseases having the potential of causing large scale outbreaks^[1]. According to WHO, Dengue fever or Dengue haemorrhagic fever is considered as the second most important tropical disease next to malaria^[2]. It is endemic in > 100 countries in the tropical and subtropical regions of the world^[3]. In India, the first evidence about the occurrence of dengue fever was reported during 1956 from Vellore district in Tamil Nadu. The first DHF outbreak occurred in Calcutta (Kolkata, West Bengal) in 1963 with 30% of cases showing haemorrhagic manifestations.

The risk of dengue has shown an increase in recent years due to rapid, urbanization, life style changes and deficient water management. Annually there are 100 million new dengue viral infections reported worldwide with 5 lakh cases of Dengue haemorrhagic fever (DHF) and Dengue shock syndrome (DSS)^[4]. Clinically Dengue infection manifests as wide spectrum of illness ranging from undifferentiated dengue fever, fatal Dengue haemorrhagic fever and Dengue shock syndrome which can finally lead to death through increased vascular permeability and shock^[5]. One of the primary problems in management of dengue is misinterpretation of the term haemorrhagic fever, which implies a significant haemorrhagic component to the patho-physiology and thus overshadowing the capillary leak syndrome

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occurring due to increased permeability, which causes depletion of the intravascular component.

Capillary leak syndrome /CLS is the principal pathologic event in causation of DHF and dengue shock syndrome (DSS). CLS broadly is characterized by hypotension with hemoconcentration, hypoalbuminemia without albuminuria and generalized edema [6].

Ultrasound can be used as an early predictor as well as an important prognostic sign for severe dengue infection especially during an epidemic. The common ultrasonographic features that were significantly associated with severe dengue infection were gall bladder wall thickening, ascites, pleural effusion, pericardial effusion, peritoneal fluid, hepatomegaly, splenomegaly and mesenteric adenopathy [7].

In addition to the above features, in view of hepatosplanchic circulatory dysfunction in acute hepatic infection in cases of dengue hemorrhagic fever, portal venous changes are anticipated. Early diagnosis of CLS is essential to start volume replacement and avoid progression to DSS. Thus this study is intended to evaluate the ultrasonographic features of capillary leak syndrome and investigate the role of Doppler study of the portal vein as a predictor for capillary leakage in these patients.

Materials & Methods

Source of Data

The prospective study was performed in the Department of Radiodiagnosis, S.P Medical College, Bikaner, Rajasthan, on patients with dengue fever.

Study Design

Prospective Cohort Study

Study Population

Patients with Acute fever, clinical symptoms and signs of dengue with laboratory evidence of thrombocytopenia, NS1 and IGM Positivity

Study Period

From March 2020 to September 2021 , for a period of 7 months

Sample Size

100

Study Centre

Department of Radiodiagnosis, S.P Medical College, Bikaner, Rajasthan

Sampling Technique: Convenience Sampling.

Inclusion Criteria

- Acute Fever patients with thrombocytopenia and with
- IGM positive
- NS1 positive

Exclusion Criteria

- Patient with Chronic liver disease / tumours.
- Known case of Hypoalbuminemia
- Known case of Hypotension
- MP/Mf positive
- Known case of portal vein / splanchnic vessel thrombosis.

- Patients who don't give consent for the study.

Method of Collection of Data

A structured pre-prepared case proforma was used to enter the patient details, clinical history and serological status of patients who met the inclusion criteria. Ultrasonography was performed as an initial imaging examination, followed by portal venous Doppler and the findings were recorded.

Methodology

Study Technique

- The study was started after obtaining institutional ethical committee clearance. All the included cases were subjected to imaging after obtaining written consent.
- Ultrasonography of the abdomen and chest wall was performed in real time, in grey scale and color Doppler modes, using 3.5- 5 MHz convex curvilinear probe in Toshiba Aloka Prosound Alpha machine at the time of admission.
- The patient was usually scanned in 4 -6 hours fasting, in supine or left decubitus position.
- General examination of the liver was done to rule out chronic liver pathologies.
- Check was made of sonographic features like
- Gall bladder wall edema
- Gall bladder wall thickness
- Ascites
- Pleural effusion
- Splenomegaly.

Portal Doppler Study

- The portal vein was interrogated either in subcostal approach pointing posterocephalad or in right intercostal approach pointing medially.
- Grey scale assessment of portal vein was done and the following were recorded:
 - Portal vein diameter
 - Cross sectional area.
 - Colour and spectral Doppler assessment of portal vein is done with appropriate machine settings to evaluate the following:
 - Flow velocity
 - Flow direction
 - Congestive Index is then calculated with the formula: Cross sectional area (cm²) / portal venous velocity (cm/sec).

Assessment

- The ultrasonographic features and Doppler findings were then correlated with Clinical outcome and laboratory findings.

Case 1

- 23-year-old male patient presenting with complaints of high-grade fever for 3 days, retroorbital pain and abdominal pain with melena.
- Laboratory investigations showed thrombocytopenia with platelet count 44000.
- Portal venous doppler was done at the time of admission



Fig 1: Grey scale USG subcostal right paramedian approach showed, portal vein diameter measured at the level of hilum - 11.1 mm **Fig 2:** Right subcostal oblique sonogram showed increased GB wall thickness measures 10.4 mm which is measured along the liver parenchyma



Fig 3: Spectral Colour doppler image showed normal portal vein flow.portal vein colour uptake appeared normal with normal hepatopetal flow pattern and normal respiratory variation and the flow velocity is 15.2 cm/sec.

Case 2

- A 45-year-old female complaints of fever with chills for 5 days Nausea, Vomiting and Abdominal pain

- Lab investigations showed platelet count 64000, IGM positive.
- Portal venous doppler was done at the time of admission.



Fig 4: USG abdomen showed portal vein diameter measuring 10.9 mm **Fig 5:** GB wall thickening measured 5.8 mm



Fig 5: USG Chest showed minimal fluid collection noted in right pleural cavity

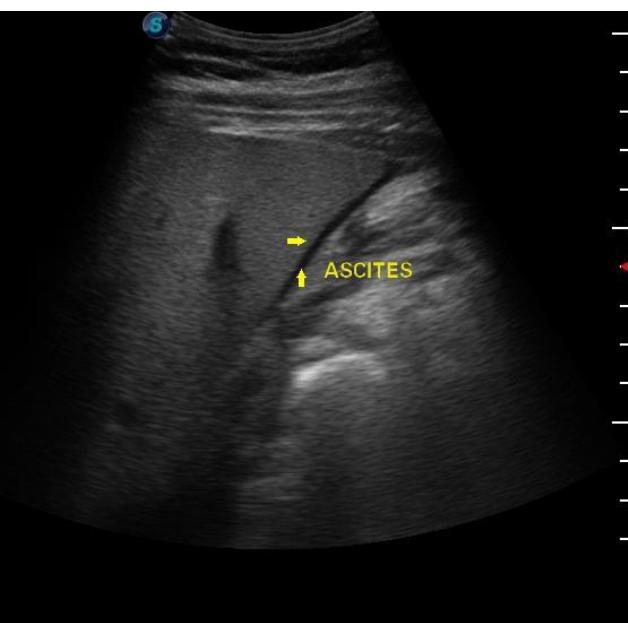


Fig 6: USG Abdomen showed minimal fluid collection noted in hepatorenal pouch

Statistical Analysis

The Data was entered in a excel worksheet and double checked. Both descriptive and inferential statistics were employed for data analysis. IBM SPSS version 22 software was used for statistical analysis.

Descriptive Statistics

The descriptive statistics procedure displayed uni-variate summary statistics for several variables in a single table and calculated standardized values. Variables were ordered by the size of their mean, alphabetically, in ascending or descending order or in any other suitable order. Descriptive analysis was carried out using mean and standard deviation for quantitative variables. In the present study following descriptive statistics have been employed

- Frequencies
- Percentages

The frequencies procedure provides statistics and graphical displays that are useful for describing many types of variables.

Data was also represented using appropriate diagrams like bar diagram, pie diagram and box plots. For a frequency report and bar chart, the categories were arranged in order, by their frequencies.

Crosstabs

Using the crosstabs procedures, two-way and multiway tables were formed and measures of association were determined for two-way tables. The sensitivity, specificity, positive and negative predictive values and diagnostic accuracy of Portal venous doppler in predicting the development of the capillary leak syndrome in dengue fever patients, correlated and confirmed with clinical findings and laboratory investigations along with their 95% CI (Confidence Interval) were computed and presented. Reliability of the test was assessed by kappa statistics along with its 95% CI and P Value. P value < 0.05 was considered statistically significant.

Results and Conclusion

In our study, the sensitivity of GB wall edema, ascites and pleural effusion were 60%, 36.6% and 48.9 % while the specificities were 90%, 100% and 100% respectively. All the ultrasonographic features had a high specificity and positive predictive value, 98.1%, 100%, 100% and since the false negative frequencies were high, the features showed a less negative predictive value, 20%, 15%, 17.8% and the diagnostic accuracies yielded were 63%,43%, and 54% for GB wall edema, ascites and pleural effusion respectively.

The sensitivity of PV diameter, PV Velocity, cross sectional area and congestive index were 75.6%, 93.3%, 61.1% and 55.6 % while the specificities were 70%, 60%, 80% and 100% respectively.

Comparing the ultrasonographic features and portal Doppler features, it was found in our study that Ultrasonographic features had an increased specificity, but low sensitivity, while, portal Doppler features showed increase in sensitivity, thus revealing the reduction in false negative rate. Thus the diagnostic accuracy would increase when the ultrasonography is combined with portal venous Doppler to predict the Capillary leak syndrome in dengue fever patients.

The area under ROC curve of ultrasonographic features were higher than the laboratory findings, thus revealing the higher efficiency of imaging features than laboratory findings in predicting the occurrence of capillary leak syndrome.

The area under ROC curve of Portal Doppler features ranged from 0.718 to 0.827, but the area under curve for haematocrit and haemoglobin were 0.666 and 0.667, which was significantly less than Portal Doppler venous features.

Thus revealing the importance of portal Doppler study in early prediction of the capillary leak syndrome than the laboratory values like haematocrit and haemoglobin.

Thus, imaging has an important role in the early diagnosis of capillary leak syndrome in dengue fever patients. Ultrasonography aids in the early detection of manifestations of plasma leak. Combined use of USG and

Portal Doppler study features like portal vein diameter, velocity, cross sectional area and congestive index increases the detection rate and thus aids in the early treatment of capillary leak syndrome, thereby reducing the morbidity and mortality of dengue fever, inspite of normal haematocrit and haemoglobin values.

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