



PREDICTIVE DIAGNOSTIC VALUE OF SERIAL ULTRASONOGRAPHY IN EVALUATING SEVERITY OF DENGUE INFECTION.

Radiodiagnosis

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ABSTRACT

Identification of dengue patients at risk for progressing to severe disease is difficult. Significant plasma leakage is a characteristic of severe dengue infection which can suddenly lead to hypovolemic shock around the time of defervescence. It is hypothesized that the detection of subclinical plasma leakage may identify those at risk for severe dengue. The aim of the study was to determine the predictive diagnostic value of serial ultrasonography for severe dengue. Serial USG, in contrast to existing markers such as hematocrit, may better identify patients at risk for development of severe dengue. Patients with evidence of subclinical plasma leakage and/or an edematous gallbladder wall by ultrasonography merit intensive monitoring for development of complications. Ultrasound is also useful for early prediction of the severity of dengue fever, thus helps in triage and prevention of those cases which will further progress to dengue haemorrhagic fever or dengue shock syndrome.

KEYWORDS

Plasma Leakage, Serial Usg, Hematocrit.

INTRODUCTION

Dengue virus infection is one of the most rapidly spreading mosquito-borne viral disease in the world. Symptomatic dengue patients usually present with a self-limiting febrile illness, called dengue fever. However, a proportion of dengue patients develops severe complications around the time of defervescence. Transient plasma leakage into serosal cavities, which may progress to life-threatening hypovolemic shock, is a hallmark of severe dengue [1,2]. In the former World Health Organization (WHO) classification (1997), severe dengue characterized by fever, thrombocytopenia, plasma leakage and hemorrhagic tendency, is referred to as dengue hemorrhagic fever (DHF) and, when accompanied by circulatory failure, as dengue shock syndrome (DSS) [3]. The most recent WHO classification (2009) defines severe dengue infection in case plasma leakage leading to shock or respiratory failure, severe bleeding or severe organ failure is present [4]. However, in clinical practice severe bleeding and severe organ failure are relatively uncommon and rarely occur without plasma leakage [5,6]. Hence, plasma leakage is an essential element of severe dengue, regardless whether the WHO 1997 or 2009 classification is used.

STUDY DESIGN

For this prospective observational study, we included patients with dengue infection, belonging to different age groups, who were admitted to New civil hospital, Surat, a tertiary care centre in South Gujarat. All patients who had a clinically suspected dengue infection followed by its serological confirmation were subjected to serial USG on Philips Affiniti 50G machine and were classified as non-severe or severe dengue according to WHO criteria from the guidelines edition 2009 [4].

The aim of our study was to determine the predictive diagnostic value of serial ultrasonography for severe dengue. We compared the ability to detect plasma leakage by serial ultrasonography. The presence of plasma leakage detected by ultrasonography was compared with frequently used clinical and laboratory parameters for plasma leakage and related to severe dengue as a clinical outcome.

The presence of plasma leakage was confirmed by a significant hematocrit change (minimal 20%) and/or single high hematocrit values (.50 and .44% for men and women respectively), and/or by plasma leakage seen during ultrasonography.

OBSERVATIONS AND ANALYSIS

Clinical characteristics

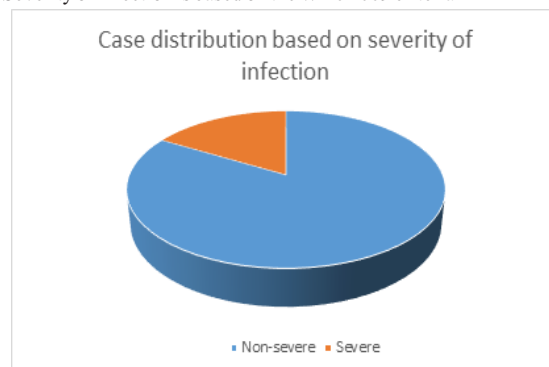
Among the 70 patients with clinically suspected dengue infection, 60 patients had a positive PCR and/or serology and were included.

50(83%) patients were retrospectively classified as non-severe dengue and 10 (17%) as severe dengue according to the 2009 WHO classification [4]. All patients with severe dengue had plasma leakage with vascular collapse; none of the patients had severe bleeding or organ failure. The first day of fever was defined as the first day of illness.

CASE DISTRIBUTION ACCORDING TO SEVERITY OF INFECTION*

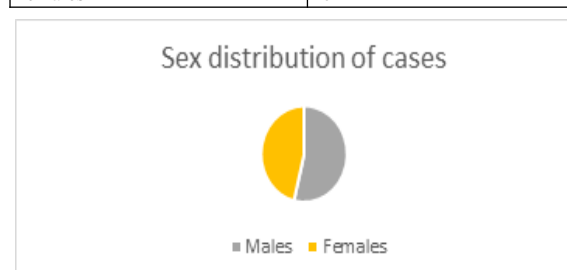
	No. of cases
Non-severe	50
Severe	10

*Severity of infection is based on the WHO 2009 criteria



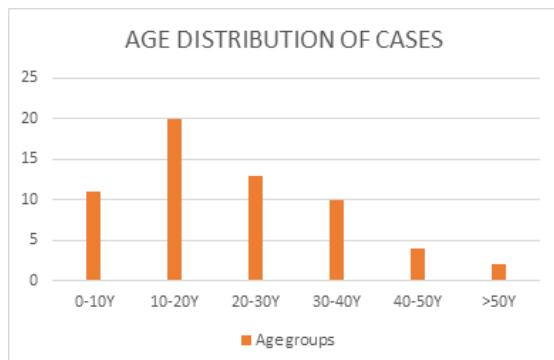
GENDER DISTRIBUTION OF CASES

	No. of cases
Males	40
Females	20



AGE DISTRIBUTION OF CASES

AGE GROUP(in years)	No. of cases
1-10	11
10-20	20
20-30	13
30-40	10
40-50	4
>50	2

**CASE DISTRIBUTION BASED ON E/O PLASMA LEAKAGE**

	Non-severe	Percentage values	Severe	Percentage values
ENROLLMENT				
Cases with E/o plasma leakage (Ascites and/or pleural effusion) at enrollment	10	20%	6	55%
FOLLOW-UP				
Newly detected cases with E/o plasma leakage (Ascites and/or pleural effusion) at follow-up	4	11%	2	36%
Total no. of cases with plasma leakage at any time	14	28%	8	80%

At enrollment, ascites and/or pleural effusion were found by ultrasonography in 10/50 (20%) patients in the nonsevere dengue group and in 6/10 (55%) patients of the severe dengue group. As 6 of 16 patients with ascites or pleural effusion at enrollment developed severe dengue, the positive predictive value (PPV) of detection of plasma leakage by ultrasonography for development of severe dengue was 35%.

4 of the 40 patients without ultrasonographic evidence of plasma leakage at enrollment, eventually developed severe dengue, yielding a negative predictive value (NPV) of 90%. Two of these patients already had a narrow pulse pressure at enrollment without further clinical evidence for plasma leakage.

After admission, 4 patients developed ultrasonographic findings of plasma leakage, mainly in the critical phase. In total, 14/50 (28%) patients in the non-severe and 8/10 (80%) in the severe dengue group developed ultrasonographic evidence of plasma leakage. The diagnosis of plasma leakage in the patient with severe dengue without ultrasonographic evidence of plasma leakage was based on an >20% increase in hematocrit values. Ascites was more frequently detected by ultrasonography than pleural effusion, which was found either right-sided or bilateral.

CASE DISTRIBUTION BASED ON GB WALL THICKNESS AT ENROLLMENT AND FOLLOW-UP USG

	Non-severe	Percentage values	Severe	Percentage values
ENROLLMENT				
Cases with GB wall thickening at enrollment	33	65%	9	90%
Average GB wall thickness	0.27-0.50cm	0.35-0.75cm		
FOLLOW-UP				

Newly detected cases with GB wall thickening at follow-up	1	5%	1	100%
Total no. of cases with thickened GB wall at any time	34	68%	10	100%

A thickened gallbladder wall was found in 33/50 (65%) of nonsevere and 9/10 (90%) of severe dengue patients at enrollment. The median thickness of the gallbladder wall at enrollment was 0.36 cm (IQR, 0.27–0.50 cm) in patients with non-severe dengue versus 0.54 cm (IQR, 0.35–0.75 cm) in those with severe dengue.

Eventually, a thickened gallbladder wall was detected in 34/50 (68%) of the non-severe dengue and 10/10 (100%) of the severe dengue patients. Detection of a thickened gallbladder wall at enrollment had a PPV of 21% and a NPV of 91% for severe dengue. In patients who developed ascites or pleural effusion, thickening of the gallbladder preceded the detection of ascites or pleural effusion by 1 to 3 days in 60% of the non-severe and in 67% of the severe patients. Multiple layers were frequently visible in thickened gallbladder walls suggesting the presence of a sub-serosal fluid layer.

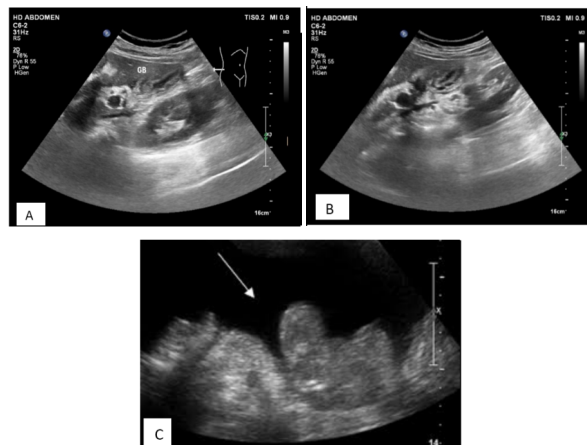
Patients with subclinical plasma leakage at enrollment had a thicker gallbladder wall than those without plasma leakage with median values of 0.59 cm and 0.35 cm respectively. There was an inverse correlation of gallbladder wall thickness with platelets counts at enrollment.

Regarding the timing of the ultrasonographic abnormalities in relation to the day of illness, in patients developing pleural effusion or ascites and gallbladder wall thickening during the study, these findings were already detectable on the first ultrasonography performed at enrollment in 16/22 (72%) and 42/44 (95%) of patients, respectively.

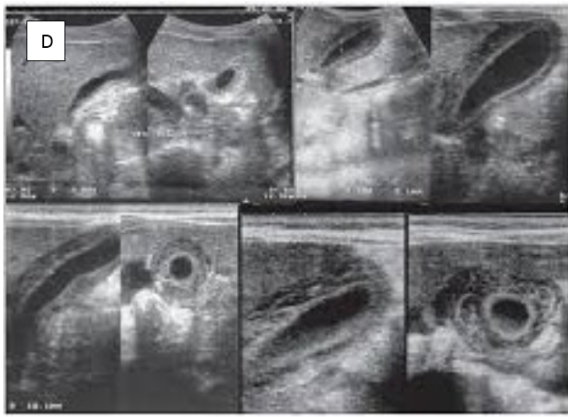
On the other hand, an elevated hematocrit value was found in only 4/60 (7%) of patients at enrollment. Single hematocrit values at enrollment were not helpful in discriminating between patients with and without ultrasonographic plasma leakage and between patients classified as non-severe or severe dengue. The change in hematocrit values was also not helpful for this purpose. Thus, haematocrit is a poor indicator of plasma leakage as compared to ultrasonography.

More than 1 out of 3 patients (35%) with ultrasonographic evidence of subclinical plasma leakage at enrollment developed shock, in contrast to only 1 out of 10 patients (10%) without subclinical plasma leakage.

The reported proportion of dengue patients with gallbladder thickening in earlier studies varied from 28% to 100%, while pleural effusion and ascites was found in 32% to 100% and 15% to 96%, respectively [7,8,9,10,11].



- A. USG image of a case showing thickened GB wall with pericholecystic fluid collection.
 B. USG image of another case showing pericholecystic fluid
 C. USG image depicting free fluid in peritoneal cavity in a patient with DHF
 D. Different patterns of pericholecystic edema as observed in the study.



CONCLUSION

In conclusion, serial handheld ultrasonography holds promise as a diagnostic and prognostic tool in dengue. Compared to serial hematocrit values, serial ultrasonography had a better predictive value in identification of those patients at risk for severe dengue. Moreover, it may improve monitoring of circulatory status and enable timely adjustments in fluid balance to avoid hypovolemic shock or iatrogenic fluid overload.

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