

CORRELATION OF ULTRASOUND (USG) FINDINGS WITH SEROLOGICAL TESTS IN DENGUE FEVER

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ABSTRACT

INTRODUCTION

Dengue is an endemic and epidemic disease of the tropical and subtropical regions. Between September & October 2012, there was an established outbreak of dengue in Hoskote, near Bangalore. Dengue results in serositis, which can be imaged by ultrasonography.

OBJECTIVE

To correlate the USG findings with the serological tests in paediatric and adult patients.

MATERIALS AND METHODS

110 patients with clinical suspicion of dengue fever during the above period underwent serological tests-NS1, IgM and IgG and were evaluated with USG of the abdomen and thorax. The USG findings were correlated with serological tests.

RESULTS

67 Patients were seropositive, 43 were seronegative. The USG findings in seropositive paediatric patients (n=32) and adult patients (n=35) respectively were gall bladder (GB) wall edema-27 & 31, hepatomegaly-12 & 14, ascites-16 & 12, splenomegaly-15 & 9, right pleural effusion-14 & 13, left and bilateral pleural effusion-7 & 5.

CONCLUSION

In our study GB wall edema significantly correlated with seropositivity (p value=0.032). Thus ultrasound is an efficient screening tool in a case of dengue outbreak.

KEYWORDS

Ultrasound, Dengue, GB wall edema and Seropositive.

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INTRODUCTION: India is one of the seven identified countries in South East Asia reporting epidemics of dengue fever and soon may transfer into a major niche for dengue infection. Community awareness, early diagnosis and management and vector control measures needs to be strengthened during monsoons to curb the infection rate.¹

Radiologic findings of dengue fever have not yet been clearly elucidated in relation to clinical and serological findings, despite two fifths of world population living in endemic areas.^{2,3}

In resource constraint environment these serological tests are not widely available and even if available the results of the confirmatory tests reach the treating consultant late. There is not much literature regarding the correlation of USG findings with serology. So we tried to correlate the USG findings with serology in a dengue endemic developing country to predict the pattern of dengue.

MATERIALS AND METHODS: Our institutional review board approved this study; data was collected prospectively but analysis was done retrospectively after the outbreak. Between September and October 2012, 110 patients who were clinically suspected of having dengue fever and dengue like illness were referred for ultrasound scanning of both abdomen and thorax. Ultrasound examination was done using GE Voluson® 730 Pro (GE Healthcare Austria GmbH & Co OG) using curvilinear probe (1.5-6 MHz) for the abdomen and pelvic examination and linear probe (6-10 MHz) for thoracic examination. All patients were examined for GB wall

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edema, pleural effusion (right/left/bilateral), ascites, hepatomegaly and splenomegaly. USG examination was done both by the Consultants and by the residents. Serological tests were done using a rapid solid phase immunochromatographic test for qualitative detection of dengue NS1 antigen and differential detection of IgM and IgG antibodies to dengue virus in serum samples. Dengue day 1 kit (J. Mitra & Co. Pvt. Ltd) was used for the serological tests. It consists of two devices; one device for the detection of dengue NS1 antigen and the second device for the differential detection of dengue IgM/IgG antibodies in serum samples. Seropositive patients were divided into paediatric (age <18) and adult groups. Ultrasound findings were compared in both these groups. The findings were also correlated with all the three serological tests in combination and with each individual test in isolation. Statistical analysis was done using SPSS Software version 17.0.

RESULTS: Total number of patients in the study was 110. Males constituted 69.4% and females constituted 29.7%. The minimum age of the patient was 2yrs and the maximum age was 80yrs. The median age was 41yrs. 26 % of the patients were in the age group of 0-10yrs another 26% were in the age group of 11-20yrs. 22.7% were in the age group of 21-30yrs. The least number of patients were in the age group of 60-80 (6.4%). Maximum number of patients was in the age group of 0-20 (52.7%). [Table 1] Seropositivity was seen in 60.9%. Serology was negative in 39.11%. Out of the seropositive patients, NS1 test positivity was seen in 50.9%. IgM positivity was seen in 44.5%. IgG positivity was seen in 28.2%. All the three serological tests in combination were positive in only 20 cases.

All patients were subjected to ultrasound examination. Ultrasound findings in seropositive patients were GB wall oedema in 86.5%, right pleural effusion in 40.2%, ascites in 41%, hepatomegaly in 38.8%, splenomegaly in 35.8%, left and bilateral pleural effusion in 17.9%. [Table 2] Out of the 110 patients, 67 were found to be serologically positive for NS1, IgG or IgM and the remaining 43 were negative. The seropositive patients (n=67) were then sorted into two groups based on the age. Group I (n=32) included patients who were below 16 years of age (paediatric). Group II (n=35) included patients who were more than 16 years of age (adult). The ultrasound findings in the seropositive paediatric patients (n=32) were gall bladder wall thickening in 27, hepatomegaly in 12, ascites in 16, splenomegaly in 15, right pleural effusion in 14, left pleural effusion in 7 and bilateral pleural effusion in 7. The findings in seropositive adult patients were gall bladder wall thickening in 31,

hepatomegaly in 14, ascites in 12, splenomegaly in 9, right pleural effusion in 13, left pleural effusion in 5 and bilateral pleural effusion in 5 cases. [Table 3] In cases of acute infection (NS1 and/or IgM positivity, n=55), gall bladder wall thickening was seen in 49, ascites in 24, hepatomegaly in 22, splenomegaly in 19, right pleural effusion in 28, left pleural effusion in 11 and bilateral pleural effusion in 11. [Table 4] In all the groups, the finding of GB wall oedema was found to be statistically significant in acute infection (p value 0.032). The ultrasound findings in the 43 seronegative patients. [Table 5]

Age group	No. of patients (%)
0-10	29(26%)
11-20	29(26%)
21-30	25(22.7%)
31-40	11(10%)
41-50	3(2.7%)
51-60	6(5.5%)
61-70	6(5.5%)
71-80	1(0.9%)

Table 1: Age distribution

USG Findings	No. of cases (%)
GB wall oedema	58(86.5%)
Ascites	28(41.7%)
Right pleural effusion	27(40.3%)
Hepatomegaly	26(38.8%)
Splenomegaly	24(35.8%)
Left pleural effusion	12(17.9%)
Bilateral pleural effusion	12(17.9%)

Table 2: Ultrasound findings in seropositive patients

USG Findings	≤18YRS (n=32)	>18YRS (n=35)
GB wall oedema	27(84.3%)	31(88.6%)
Right pleural effusion	14(43.7%)	13(37.1%)
Ascites	16(50%)	12(34.3%)
Splenomegaly	15(46.8%)	9(25.7%)
Hepatomegaly	12(37.5%)	14(40%)
Bilateral pleural effusion	7(21.9%)	5(14.3%)
Left pleural effusion	7(21.9%)	5(14.3%)

Table 3: Ultrasound findings in the paediatric and adult age group

USG Findings	NS1, IgM, IgG positivity (n=20)	NS1, IgM positive, IgG negative (n=18)	NS1 positive, IgM, IgG negative (n=10)	IgM positive, NS1, IgG negative (n=7)	NS1, IgG positive, IgM negative (n=7)	IgG Positive, NS1, IgM negative (n=2)
GB wall oedema	17(85%)	16(88.9%)	10(100%)	6(85.7%)	5(71.4%)	2(100%)
Ascites	9(45%)	8(44.4%)	3(30%)	4(57.1%)	1(14.3%)	1(50%)
Hepatomegaly	8(40%)	10(55.6%)	2(20%)	2(28.6%)	2(28.6%)	1(50%)

Splenomegaly	8(40%)	4(22.2%)	3(30%)	4(57.1%)	1(14.3%)	1(50%)
Right pleural effusion	5(25%)	10(55.6%)	10(100%)	3(42.9%)	2(28.6%)	2(100%)
Left pleural effusion	2(10%)	3(16.7%)	4(40%)	2(28.6%)	1(14.3%)	0
Bilateral pleural effusion	2(10%)	3(16.7%)	4(40%)	2(28.6%)	1(14.3%)	0

Table 4: Correlation of ultrasound findings with the various combinations of serological tests

USG Findings	Number Of Cases
GB wall oedema	30
Ascites	16
Hepatomegaly	13
Splenomegaly	14
Right pleural effusion	20
Left pleural effusion	11
Bilateral pleural effusion	11

Table 5: Ultrasound findings in the 43 serologically negative patients

DISCUSSION: Dengue is an infectious disease caused by the Arbovirus (Flaviviridae family), having its maximum incidence at the end of the rainy season. Four serotypes have been identified for this virus (Serotypes-DEN1, DEN2, DEN3, DEN4), there being a scarce cross-immunity between the antibodies generated by these serotypes. As a result, when a person suffers from this disease, he/she becomes immune only to a specific serotype.

Classic Dengue infection has an incubation period ranging from three to 14 days, its average period being 5-8 days. After this phase, a fever develops abruptly with temperatures in the 39-40°C range, chills, heavy and widespread osteomuscular pain, especially in the lumbar region, neck and shoulders, as well as in the knees and hips. Haemorrhagic Dengue symptoms are similar to those of the classic form, but are also associated with bleeding with an intensity that varies depending on the severity of the clinical manifestations.

The Severity of This Disease Falls into Four Degrees:

Degree I: Fever, general symptoms and positive tourniquet test.

Degree II: Degree I plus spontaneous haemorrhage on the skin, gums, gastrointestinal tract, and other areas.

Degree III: Degree II plus circulatory shortage and agitation.

Degree IV: Shock.

In all phases, there is thrombocytopenia and hemoconcentration. Degrees III and IV are related to DHF (Dengue haemorrhagic fever).⁴

Testing algorithm for Dengue fever.⁵

1. PCR (polymerase chain reaction): DENV (dengue virus) can be detected in the serum from patients for approximately the first 5 days of symptoms. Current tests are 80-90% sensitive and more than 95% specific. A positive PCR result is a definite proof of current infection and confirms the infecting serotype as well.
2. MAC (Human membrane attack complex) ELISA: IgM antibody capture ELISA (MAC-ELISA) is most widely used

- in diagnostic laboratories and is available as diagnostic kits. The sensitivity is 100% and specificity is 99.89%. The main limitation is cross reactivity between other Flaviviruses like West Nile virus, Japanese encephalitis virus, yellow fever virus and St. Louis encephalitis virus.
3. IgG (Immunoglobulin G) ELISA: It is used for detection of past dengue infection. The sensitivity is 100% and specificity is 99.89%.
 4. NS1 (Non structural protein 1) ELISA: it is shown to be a useful tool for diagnosing acute infection. The main advantage of this test is it can be used as soon as one day after the onset of symptoms and it is most specific. The sensitivity is 100% and specificity is 99.94%.⁶
 5. PRNT: Plaque reduction and neutralisation test. It is the most specific serological tool for determination of dengue antibodies. It is used in determination of the infecting serotypes.

Ultrasound Findings: The reported changes vary according to the severity of each case. In adults with DHF Degree III, pleural effusion has been observed in 53% of cases, thickening of gall bladder walls in 43%, and mild ascites in 15% of case. In paediatric patients with Degree I-II disease, ultrasound findings are pleural effusion in 30% of cases, ascites in 34%, thickening of gall bladder walls in 32%, and pancreatic enlargement in 14% of cases. In Degree III and IV cases, reported findings are pleural effusion, ascites, and thickening of vesicular walls in 95% of cases, peri- and pararenal collections in 77% of cases, hepatomegaly 56%, pancreatic enlargement 44%, and splenomegaly 16%, hepatic or splenic sub capsular collections 9%, and pericardial effusion in 8% of cases.⁴ An index was recently prepared based on ultrasound findings that have a shock-predictive value (DHF-dengue haemorrhagic fever). The score is 0-12 as given by the ultrasound alterations observed (pleural effusion, liquid within the Morrison’s pouch, thickening of gall bladder walls, etc.), with a “cut-off” a value of 5. Patients over this value have a higher risk of developing the most severe form of this disease.⁷ According to a study by Venkata Sai et al during an epidemic ultrasound findings of GB wall thickening with or without polyserositis in a febrile patient should suggest the possibility of dengue fever.⁸ Severe forms of the disease are characterized by fluid collection in the perirenal and pararenal region, hepatic and splenic sub capsular fluid, pericardial effusion, pancreatic enlargement and hepatosplenomegaly. These findings have been demonstrated in studies by Pramuljo HS, Harun SR⁹ and by Joshi et al.⁷ Based on these results, ultrasound can be useful in the estimation of severity of dengue fever.

The main limitations of this study are, this is a retrospective study, the number of seropositive paediatric and adult patients are less. Serological tests were not done using the standard ELISA kits. Further prospective studies are required to evaluate and compare ultrasonological findings in the paediatric and adult patients.

CONCLUSION: To conclude, there are no statistically significant changes in the ultrasound findings in the seropositive paediatric and adult patients. GB wall oedema appears to be statistically significant in cases of acute infections (p value 0.032). The ultrasound finding of GB wall oedema correlates with NS1 antigen and IgM antibody positivity in 88.9% in our study. Rest of the findings like hepatomegaly, splenomegaly and left pleural effusion are seen in less than 50% of serologically positive cases. The findings of GB wall oedema is also seen in serologically negative cases which needs further evaluation in prospective studies.

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