Original Article

Sonological Markers for Assessment of Dengue Fever with Serological Correlation

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Abstract

Background: Dengue, a viral infection has become a major public health problem with epidemic outbreaks worldwide. Ultrasound (US) is used as screening modality in all patients presenting with fever and abdominal pain. The study was to establish the Ultrasound features of dengue fever and correlate Ultrasound findings with platelet counts in serologically positive cases. **Subjects and Methods:** A cross sectional study of 104 patients carried out during dengue epidemic in 2015 in Delhi and NCR. Patients of all age groups were included in the study. Ultrasound of abdomen and chest was performed on 3- 7th day of fever and sonographic features were recorded. **Results:** Mean age of patients was 29.9 ± 15 years with 48 (47 %) males and 56 (53 %) females. Maximum number of patients belonged to age group of 21-30 years (32%). The Gall bladder (GB) wall thickening was noted in majority 81 (77.8 %) of the study subjects followed by Ascites in 64 (62.7%), bilateral pleural effusion 32 (31.3 %), unilateral pleural effusion 24 (23.5 %), Splenomegaly in 16 (15.0%) subjects and Hepatomegaly in 10 (9.8%). The sonographic abnormalities including Gall bladder wall thickening, ascites, pleural effusion, Splenomegaly, Hepatomegaly were significantly higher in study subjects with decreased platelet count. Although Gall Bladder wall thickening was the commonest finding in 77.8 % subjects, Ascites was the commonest finding in 48 (82.7%) study subjects with platelet count between 0-50000 indicating that ascites was a better prognostic indicator than Gall bladder thickening in cases of dengue fever. **Conclusion:** Its rapidity, ready and widespread availability not only makes Ultrasound as a primary modality of diagnosing dengue fever before the results of serological tests are available, it can also be used as mainstay investigation in epidemic regions for recognizing critically ill patients requiring early and prompt management.

Keywords: Dengue, Ultrasound, Fever, platelets, Edematous Gall bladder wall.

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Introduction

Dengue virus is single stranded RNA virus belonging to the falviviridae family with infection transmitted to humans via Aedes Aegypti mosquitoes.[1] A disease of the tropics dengue fever is gradually becoming a global threat with seasonal outbreaks in Southeast Asia, Central and South America, and the Western Pacific regions.[2] Clinically these patients can present as asymptomatic or present with acute onset fever, headache, body ache, retro-orbtial pain, muscle and joint pain. Severe forms like dengue hemorrhagic fever (DHS) and dengue shock syndrome (DSS) may show features of thrombocytopenia, hemconcentration and plasma leakage.

Although the diagnosis of dengue fever is based on clinical, laboratory and serum NS I test. Ultrasound serves as an important adjunct to clinical and laboratory findings. Its rapid availability, non invasive nature and cost effectiveness serves as a potent means to assess and monitor the presence and degree of plasma leakage in various body compartments. The primary objective of this study is to demonstrate the US findings of dengue fever and to predict the prognosis thus identifying critically ill-patients requiring early and prompt management.

Subjects and Methods

After obtaining formal approval from the institutional ethical committee the study was carried from July 2015 to November 2015 at Santosh Hospital and medical college Delhi NCR. Informed consent was taken from all patients participating in the study.

Selection of study subjects

The following cross sectional observational study was conducted during a period of 5 months from (July 2015 to November 2015 during the dengue epidemic outbreak).

Patients of all ages presenting in the medicine and pediatrics outpatient and inpatient Department with complaints of abdominal pain and fever and clinically suspected to have

dengue fever were referred to Department of Radiology for evaluation by ultrasound.

Equipment facilities– Siemens Acuson X 300 USG machine

A. **Inclusion Criteria**
- Patients with fever, abdominal pain and vomiting.
- Patients with clinical suspicion of Dengue.

B. **Exclusion criteria**
- Pregnant subjects.
- Subjects whose serological reports were not available.

All ultrasound examinations were performed with the Siemens Acuson X 300 USG machine using 3.5MHz and 5 MHZ probes. In addition to this Ultrasonography of the thorax was performed to assess for pleural effusion.

Abdominal scanning was done preferably after 4 hours of fasting to allow better distension of gall bladder (GB) and better visualization of solid organs. Sonographic parameters of GB wall thickening, ascites and pleural effusion, pericardial effusion, hepatomegaly, splenomegaly was recorded. In all patients serological tests for dengue were performed using dengue nonstructural protein 1 (NS1) antigen and for detection of immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies against dengue virus in human serum/plasma. Hematological parameters including platelet count were recorded. Patient's symptoms were recorded and patients were divided into mild and severe cases based on features of hypotension and thrombocytopenia like rapid weak pulse, petechie and bleeding from body cavities. Additionally the patients with platelet count less than 20,000 were also classified as severe cases even in the absence of features of hypotension and thrombocytopenia.

Results

Total number of dengue cases was 104, out of which 64 cases were of mild form of disease and 40 cases were suffering from severe dengue.

Table 1: Total number of dengue cases studied

Total number of cases	Mild disease	Severe disease
104	64	40

Out of the 104 cases 47 % were male patients and 53 % were female patients with a female: male ratio of 1.1:1

Table 2: Gender distribution of disease

Gender	Mild Disease (N=64)	Severe disease (N=40)
Male	33	15
Female	31	25

Maximum number of patients belonged to 21-30 yrs of age (32.6 %). Mean age of patients was 29.9 ± 15 years. Mean age of male patients was 29.7 ± 14 yrs. Mean age of female patients was 30.5 ± 16 years.

Table 3: Age Distribution

Age Group (years)	Male	Female	Total
0-10	3	7	10
11-20	8	8	16
21-30	15	19	34
31-40	8	12	20
41-50	6	6	12
51-60	4	5	9
61-70	0	2	2
>70 YRS	0	1	1
TOTAL	48	56	104

Table 4: Incidence of various Ultrasound findings in dengue

USG Findings	No of patients
GB wall edema	81
Ascites	64
Bilateral Pleural effusion	32
Pleural effusion (R)	24
Pleural effusion (L)	0
Splenomegaly	16
Hepatomegaly	10
Pericardial Effusion	0
Normal USG	2

Table 5: Correlation of USG Findings and Platelet Count

USG Findings	0-50000	50000-100000	100000-150000	>150000
Total	58	28	13	5
GB wall thickening	45	26	10	0
Ascites	48	10	6	0
Pleural Effusion	25	4	3	0
Splenomegaly	10	4	3	1
Hepatomegaly	6	4	0	0
Pericardial effusion	0	0	0	0
Normal	0	0	0	2

Discussion

Dengue is a common rapidly spreading mosquito borne acute febrile illness affecting almost 50 million people annually with 2.5 billion people living in endemic zones[3]. Although a disease of the tropics and subtropics, rapidly increasing population with urbanization and inadequate management of water resources and waste disposal have lead to global outbreaks. Dengue is caused by a single stranded RNA virus of flaviviridae family, of which 4 serotypes exists. Among those serotype 2 and 3 are considered with frequently associated with severe disease.[4,5] These seroypes are transmitted to humans by the bite of infected Aedes mosquitoes, principally Aedes Aegypti.[6]

After the incubation period of 5-10 days the disease classically presents as sudden onset high grade fever, rigors with chills, retro orbital pain , muscle and joint pain. Primary infection is thought to induce lifelong immunity to the infecting serotype.[7]

Individuals suffering an infection are protected from illness with a different serotype within 2-3 months of the primary infection but with no long-term cross-protective immunity. Recovery is usually complete

within one week , however a small proportion of the population go on to develop a more severe form of infection if affected by more than one serotype. Dengue hemorrhagic fever and dengue shock syndrome are the two most severe forms of infection related to increased vascular permeability and hemoconcentraion These two severe forms can manifest as circulatory collapse and bleeding daisthesis.

Serology remains the main stay of diagnosis of the disease, however haem agglutination inhibition antibodies usually appears at detectable level by day 6 of febrile illness , hence the The diagnosis of dengue fever often delayed owing to time taken for availability of results.[8] Morever no separate test for detection of severe forms such as (DHF and DSS) exists. Ultrasound is very sensitive to detection of fluids in body cavities as well as visceral changes such as GB wall edema, ascites, pleural/pericardial effusions, organomegaly which can suggest the diagnosis of dengue fever much before the serological reports arrive.

This viral illness is divided into 3 phases; the febrile phase (1-3 days) characterized by fever, myalgia and vomiting. The critical phase (4-6 days) characterized by increased capillary permeability and fall in haemotocrit level and thrombocytopenia. The capillary leakage is responsible for GB wall edema, ascites and pleural effusion. Studies conducted by Balasubramian et al and Srikiatkachorn et al have shown that Ultrasonographic findings of plasma leakage are seen before significant changes in the Hematocrit. Hence, ultrasonography has a high negative predictive value in the diagnosis of dengue hemorrhagic fever.[9,10]The last phase (recovery phase) beyond the 6th day is characterized by generalized sense of well being of the patient and absorption of the fluid from the extra vascular compartment.

Maximum number of patients belonged to 21-30 yrs of age (32.6 %). Mean age of patients was 29.9 years. Mean age of male patients was 29.7 yrs. Mean age of female patients was 30.5 years.

The incidence of females affected was slightly more than the number of males affected 1:1.1 (M: F). This is different from observation made by Setiwan M W et al and Venkatasai PM et al.

Table 6: Gender distribution in various studies

Study	Year	Place	Number of cases	M:F ratio
Setiwan et al[11]	1990-1994	Jakarta	148	1.20: 1
Venkatasai PM et al[12]	2005	Chennai	88	1.6: 1
Mehdi S et al[13]	2011	Faisalabad	50	1.94: 1
Present study	2015	Delhi NCR	104	1:1.1

The commonest ultrasound findings in our study was GB wall cdcma sccn in 81 of thc 104 (77.8 %) of thc study subjects. The striated appearance of the GB wall measured along the anterior wall was due to increased fluid accumulation.[14] The generalized cutoff level

accepted for GB wall thickening was 3 mm. Our findings correlated with a similar study conducted by Venkata Sai et al[12] and Santhosh et al[15] with gall bladder wall thickening being the most frequent finding present in 100 % and 66.7 % of the cases[15]

Table 7: GB wall Edema in various studies

Study	Place	GB wall edema
Venkatasai PM et al[12]	Chennai	100%
Chatterjee et al[16]	Loni, Maharashtra	83.33 %
Santhosh et al[15]	Chennai	66.7%
Present study	Delhi NCR	77.8%

GB wall thickening was also associated with decreased platelet counts as seen in our study.87 % of the patients with GB wall thickening had a platelet count of less than 100,000. This is comparable to study by Vedaraju et al[17] where 96 % of the patients with GB wall edema had platelet less than 80,000.

Ascites was the second most common finding in our study seen in 62.7 % of the patients. The incidence of ascites in various others studies include 77 % in Chatterjee et al[16], and 53.2 in Venkatsai et al.[12] Setiwan et al[11] also noted 95 % of ascites in severe dengue. They also concluded that ascites is a good indicator to –predict the severity of dengue fever. These findings comparable with our present study.

Table 8: Ascites in various Studies

Study	Place	Incidence of Ascites
Chatterjee et al[16]	Loni, Maharashtra	77 .08 %
Venkatasai PM et al[12]	Chennai	53 %
Mia M WET et al[18] Dhaka	Dhaka	41%
Present study	Delhi NCR	62.7 %

Pleural effusion was the next most common finding in our study seen with bilateral effusion seen in 31.3 % and unilateral right pleural effusion in 23.5 % of the patients. In none of the cases isolated left side pleural effusion was seen. Our study is in agreement with Pramuljo and Harun SR et al[19] and Sudhir Sachar et al[20] that states that pleural effusion can be found on the right and in bilateral pleural spaces but no isolated left pleural effusion is seen. However there are reports in literature like the one by Vedaraju at al,[17] S . Kanaga Durga et al[21] and Motla M et al[22] which show isolated left side pleural effusion can be seen in dengue patients. Although the author believes that isolated left side pleural effusion can be seen in dengue patients, however this may be only seen in conjunction with other features of plasma leakage such as ascites and GB wall edema and presence of isolated left pleural effusion as an only findings would be exceedingly rare in dengue and warrant an alternate diagnosis.

Of the 14 pediatric patients, none of the patients in our study had pericardial effusion. This finding is in disagreement with studies conducted by S. Kanaga Durga et al[21] where pericardial effusion was seen in

all pediatric patients with platelet count less than 20000, but the author cannot confirm or oppose these findings with the current study as none of the pediatric patients in our study has a platelet count of less than 20000 and the pericardium is a potential site for extravascular fluid leakage.

In present study organomegaly was seen in 25.8 % of cases with hepatomegaly seen in 9.8 % of the cases and splenomegaly seen in 15 % of cases. Splenomegaly was found to be more common than hepatomegaly. Mild splenomegaly has been attributed as a high risk factor for significant morbidity and hypovolemic shock in dengue fever.[23]

None of the patients had altered echotexture of liver which has been attributed by some authors due to intraparenchymal and subcapsular hemorrhages.[24] Difference in incidence of hepatomegaly as compared to the other study may be due to inter observer variability However organomegaly does not seem to correlate well with severity of the disease.

Table 9: Incidence of Hepatomegaly and splenomegaly compared to other studies

Study	Hepatomegaly	Splenomegaly
Chandak .S et al[25]	62%	45%
Javed et al[26]	35.5%	25.9%
Present study	9.8 %	15%

Conclusion

As incidence of dengue epidemic continues to rise, the author concludes that ultrasound feature of GB wall thickening, ascites, pleural effusion and organomegaly can be used as ultrasound features to establish diagnosis in suspected cases of dengue fever. In our study, GB wall thickening was the most common finding (77.8%), followed by ascites (62.7 %) and pleural effusion (54.8 %), Furthermore, GB wall thickening, ascites, and pleural effusion were more common in patients with platelet count less 100,000. Thus, severity of the disease, which is usually assessed by clinical features and platelet count, can also be assessed by sonography presenting where antigen assay are not available. Furthermore degree of abnormal findings also correlated well with the severity of disease, thus aiding in better and early management of severe cases.

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