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Radiology Section

Role of Ultrasonography in Diagnosis and Evaluation of Dengue Fever

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ABSTRACT

Introduction: Dengue Fever (DF) is endemic to Southeast Asian region and poses a major public health problem with increasing incidence of epidemics over the past few years.

Aim: This study intends to evaluate ultrasonographic findings in patients with DF during an epidemic in south India and their accuracy in diagnosis.

Materials and Methods: This is a prospective observational study performed in tertiary care hospital in Tirupati, Andhra Pradesh, India. A total 310 patients seropositive for dengue, referred to Radiology department for sonography were screened for ascites, gall bladder wall thickening, pleural effusion, pericardial effusion, hepatomegaly and splenomegaly. These findings were correlated with patient demographics, serological tests for dengue and platelet count.

Results: Mean age of the study population was 48.9 years. The male: female ratio was 1.46:1. Total 302 patients (97.4%) had at least one positive ultrasound finding supportive of DF. Ascites (93.8%) was the most common finding, followed by right pleural effusion (78.7%), gall bladder wall thickening (64.8%), left and bilateral pleural effusion (64.1%), splenomegaly (42.6%) and hepatomegaly (28.0%). Patients were classified into four groups based on degree of thrombocytopenia. Ascites was the most common finding in all the groups of patients. Gall bladder wall thickening was seen in 63.2%, 70.5%, 73.0% and 27.7% in four groups respectively. Ascites was the most sensitive finding, while gall bladder wall thickening was the most specific finding. This study showed statistically significant correlation of ultrasound findings with platelet counts (p=0.00001). No statistically significant correlation was noted between age group of the patients and sonographic findings (p=0.908).

Conclusion: Constellation of sonographic findings like ascites, gall bladder wall thickening, pleural effusion, hepatomegaly and splenomegaly, when used together, are useful not only in early diagnosis of the disease, but also in assessment of severity of the disease.

Keywords: Gall bladder, Hemorrhagic fever, Oedema sonography

INTRODUCTION

Dengue is a mosquito-borne acute febrile viral infection caused by the Dengue virus belonging to the family Flaviviridae, transmitted by *Aedes aegypti*. DF is endemic to more than 100 countries, with Southeast Asia being the one of the most seriously affected regions. The incidence of dengue has grown dramatically around the world in recent decades, with 390 million new dengue infections every year and prevalence estimates of 3.9 billion people in more than one hundred endemic countries [1,2].

DF is caused by one of the four serotypes of Dengue virus (DEN1, DEN2, DEN3 and DEN4). The clinical presentation can differ widely from a simple non-specific febrile illness called as Dengue Fever (DF) to a severe life threatening form known as Dengue Hemorrhagic Fever (DHF) with features of capillary extravasation, plasma leaking, fluid accumulation, respiratory distress, severe bleeding, or organ impairment. Rarely, patients with DHF develop hypotension and progress into dengue shock syndrome, that can be fatal if not managed appropriately [3,4].

Serology remains the mainstay for diagnosis of DF. Capillary extravasation and plasma leakage, hallmark features of DHF, lead to development of pleural effusion, ascites, pericardial effusion, fluid in perirenal space. These findings also correlate well with severity of DHF in children. Non-specific findings like splenomegaly, hepatomegaly and volumetric increase of pancreas can be observed. Many studies have observed that, though these findings are non-specific, ultrasonography is

useful for early diagnosis in patients with DHF and might help to differentiate from other febrile diseases [5,6]. Many studies have evaluated various findings in DF with varying sensitivities and specificities. In the year 2016, there was an outbreak of dengue epidemic in Chittoor district of Andhra Pradesh state of South India. The purpose of this study was to evaluate prospectively the patients presenting with DF during the epidemic to our tertiary care hospital, in correlation with lab parameters, and to evaluate if ultrasound can act as useful adjunct in reliable diagnosis of DF.

MATERIALS AND METHODS

The prospective observational study was performed in Tertiary Care Hospital in Tirupati, Andhra Pradesh, India. The institutional review board and ethical committee approved the study. All the patients who were referred to Radiology Department with acute febrile illness for ultrasound of abdomen and thorax between April 2016 to December 2016 were included in the study. The patients who were not willing for ultrasound or who did not undergo serological testing for characterization of febrile illness were excluded from the study.

Radiologist having at least five years experience in ultrasound performed all the studies. All ultrasound examinations were performed Seimens Acuson X 300 ultrasound machine with 3.5 to 5 MHZ convex probe. The patients were screened for ascites. The gall bladder wall thickening was measured by placing the callipers between the two layers of anterior sub-hepatic wall of gall bladder in a longitudinal section. A thickness measures > 3.0 mm was considered positive for gall bladder wall thickening [7-9]. Thoracic sonography was performed either in supine or sitting posture and screening was done through intercostal or subcostal approach for pleural or pericardial effusions. Liver span of more than 15 cm was considered as hepatomegaly. Spleen measuring more than 12 cm was considered as splenomegaly [10].

All the patients were subjected to laboratory investigations including serological tests for dengue like NS-1 antigen test and dengue Ig G and Ig M tests for confirmation of diagnosis. Platelet counts in the patients were also observed on the same day of ultrasound for correlation with severity of ultrasound findings. A total of 732 patients who presented with fever to our hospital and were referred to Radiology Department during the study period were included in the study. Among them, 310 patients were found seropositive for dengue, which accounted for 42.3% of total fever patients during the epidemic. These patients who tested positive for dengue were included in the study and were later divided into four groups based on platelet count for correlation with sonographic findings. Group I had patients with platelet count <40,000 (severe thrombocytopenia); Group II with platelet count of 40,000-80,000 (moderate thrombocytopenia); Group III with platelet count of 80,000-1,50,000 (mild thrombocytopenia) and; Group IV with patients having platelet count > 1,50,000 (normal platelet count).

All qualitative variables and categorical data were reported as absolute number of patients and percentage of the group studied. The accuracy of each of the findings in the differentiation of benign and malignant lesions was evaluated by calculating sensitivity and specificity. Pearson χ^2 test was used to compare categorical data and determine the association between the sonographic findings and platelet count or age group of the population. The p-value < 0.05 was considered as statistically significant.

RESULTS

Of the 732 patients who presented with fever, 310 patients were found seropositive for DF and were included in the study. Dengue accounted for 42.3% of total fever patients during the epidemic. The male: female ratio in present study was 1.46:1. Mean age of the study population was 48.9 years.

Of the 310 patients included in the study, 302 patients had at least one positive ultrasound finding supportive of DF (97.4%). Eight patients had normal ultrasound study. Ascites was the most common finding in present study and is seen in 93.8% of patients [Table/Fig-1] followed by right pleural effusion in 78.7% and gall bladder wall thickening in 64.8% of patients. Left pleural effusion was seen in 64.1% patients, with all these patients showing bilateral pleural effusion. None of the patients had isolated left pleural effusion without right sided effusion in present study. Splenomegaly and hepatomegaly were seen in 42.6% and 28.0% patients respectively. Only four patients (1.3%) had pericardial effusion.

Most common age group of patients included in the study was 30-49 years [Table/Fig-2]. Findings were similarly distributed among various age groups of patients. Most common finding in all age groups was ascites followed by right pleural effusion and gall bladder wall thickening. No statistically significant difference was found in incidence of findings among various age groups (p-value=0.908).

Finding	No. of Patients	Percentage (%)
Ascites	291	93.8%
Gallbladder Wall Thickening	201	64.8%
Right Pleural Effusion	244	78.7%
Left Pleural Effusion	199	64.1%
Bilateral Pleural Effusion	199	64.1%
Hepatomegaly	87	28.0%
Splenomegaly	132	42.6%
Pericardial Effusion	4	1.3%

[Table/Fig-1]: Incidence of ultrasound findings in patients with DF.

Findings	Age group of patients				Total
	<10	10-29	30-49	>50	
GBWT	14	65	79	43	201
Ascites	15	101	116	59	291
Right pleural effusion	13	84	96	51	244
Left pleural effusion	10	64	72	53	199
Bilateral pleural effusion	10	64	72	53	199
Hepatomegaly	8	28	33	18	87
Splenomegaly	9	44	58	21	132
Pericardial effusion	0	0	2	2	4
Total	16	108	121	65	310

[Table/Fig-2]: Distribution of ultrasound findings in various age groups of patients (p-value=0.908).

Correlation of ultrasound findings with platelet count of the patients on the day of the study is shown in [Table/Fig-3]. Patients were categorised into 4 groups based on platelet count. Group I had patients with platelet count < 40,000 (severe thrombocytopenia); Group II with platelet count between 40,000-80,000 (moderate thrombocytopenia); Group III with platelet count between 80,000-1,50,000 (mild thrombocytopenia); and Group IV with platelet count of > 1,50,000 (normal platelet count). About 50% of the patients (155 of 310) belonged to Group 1. 27.4%, 16.7 % and 5.8% patients respectively belonged to Groups II, III and IV respectively. Ascites was the most common finding in Groups I, II and III with 99.3%, 98.8% and 96.1% incidence respectively. Right, bilateral pleural effusions were the second most common finding in sonography in Groups I and II. All the patients with left pleural effusion had bilateral effusion in present study. Isolated left pleural effusion was not seen in any of the patients in this study.

Findings	Platelet Count				Total
	Group I <40,000	Group II 40,000-80,000	Group III 80,000-1,50,000	Group 4 >1,50,000	
GBWT	98 (63.2%)	60 (70.5%)	38 (73.0%)	5 (27.7%)	201
Ascites	154 (99.3%)	84 (98.8%)	50 (96.1%)	3 (16.6%)	291
Right Pleural Effusion	132 (85.0%)	65 (76.4%)	39 (75%)	8 (44.4%)	244
Left Pleural Effusion	121 (78.0%)	50 (58.8%)	20 (38.4%)	8 (44.4%)	199
Bilateral Pleural Effusion	121 (78.0%)	50 (58.8%)	20 (38.4%)	8 (44.4%)	199
Hepatomegaly	24 (15.4%)	26 (30.5%)	28 (53.8%)	9 (50.0%)	87
Splenomegaly	32 (20.6%)	45 (52.9%)	44 (84.6%)	11 (61.1%)	132
Pericardial Effusion	4 (2.6%)	-	-	-	4
Total no. of Patients	155	85	52	18	310

[Table/Fig-3]: Correlation of ultrasound findings with platelet count in patients with Dengue fever. (p-value = 0.00001).

Gall bladder wall thickening was seen in 63.2%, 70.5%, 73.0% and 27.7% in four groups respectively. Splenomegaly was the most common finding in Group IV patients (normal platelet count) and seen in 61.1% respectively. It was the second most common finding in Group III (84.6%). Hepatomegaly was second most common finding in patients showing normal platelet count (50%). All the four patients with pericardial effusion were in Group I (severe thrombocytopenia). Of the eight patients with normal sonography, seven patients had normal platelet count (Group IV) and one patient had mild thrombocytopenia (Group III). This study showed statistically significant correlation of imaging findings with platelet counts (p-value= 0.00001).

Ascites was the most sensitive finding in the study population (93.87% sensitivity) followed by right pleural effusion, gall bladder wall thickening and bilateral pleural effusion (78.7%, 64.9% and 64.1% sensitivity respectively). Gall bladder wall thickening was the most specific finding for diagnosis of DF in study population (98.6% specificity). Right sided pleural effusion and ascites had specificity of 89.3% and 77.9% respectively. Hepatomegaly was the least sensitive finding (28.6% sensitivity), and splenomegaly was the least specific finding (36.97 % specificity) in this study.

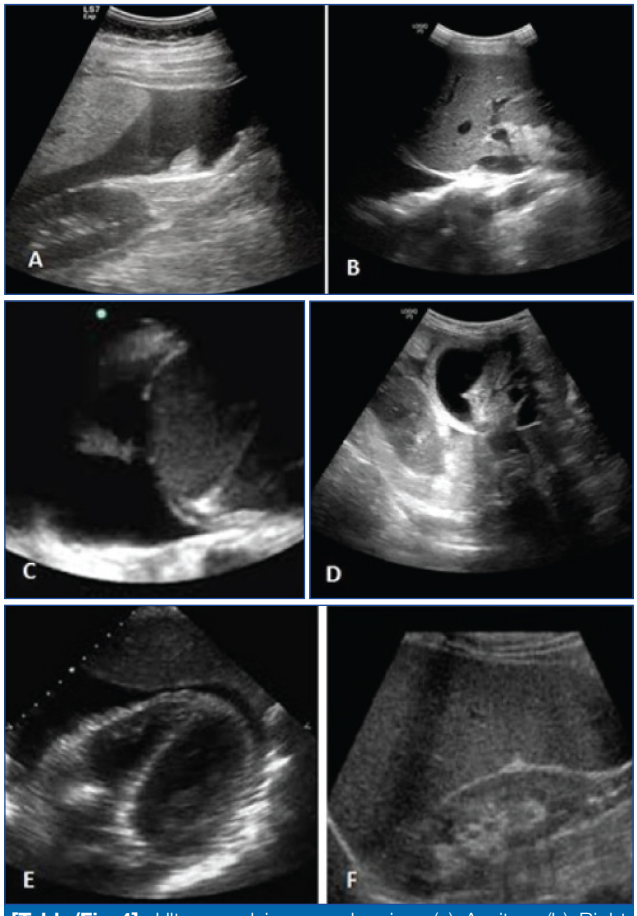
DISCUSSION

Dengue is the most common arboviral disease caused by dengue virus. Factors like rapid urbanization, life-style changes and poor water management, coupled with lack of awareness in general public has contributed to significant increase in the risk of DF [11]. In the last 50 years, incidence has increased 30-fold with increasing expansion to new countries. DF is endemic in many tropical and subtropical regions, like Southeast Asia (including India). Dengue was endemic in 23 states in 2011-12 in India [12]. In 2015, Delhi, India, recorded its worst outbreak since 2006 with over 15,000 cases [13].

The diagnosis of DF is suspected on the basis of clinical manifestations. However, appropriate laboratory and radiological investigations are needed to distinguish the DF from other common etiological agents of acute febrile illness in India like malaria, typhoid and enteric fever [14,15]. Serological tests are still the mainstay for confirmation of diagnosis in dengue, but can delay the diagnosis. Hence, additional diagnostic modalities are often sought for early detection of dengue. The early ultrasonographic findings favouring the

diagnosis of dengue have been reported in the literature with varying combination of gall bladder wall thickening, ascites, pleural, pericardial effusions and organomegaly [Table/Fig-4a-f]. Previous studies have reported different levels of accuracy of various individual sonographic findings. Hence, in present study we tried to prospectively evaluate the incidence and accuracy of these findings during an epidemic of DF in South India.

Ascites was the most common finding in present study (93.8%), followed by right pleural effusion (78.7%), gall bladder wall thickening (64.8%) and bilateral pleural effusion (64.1%). Splenomegaly and hepatomegaly were seen in 42.6% and 28.0% patients respectively and were least common. However, in patients with normal platelet count (Group IV), Splenomegaly and hepatomegaly were the most common findings. Most of the patients with thrombocytopenia (97.3%) had evidence of sonographic findings of plasma leakage, which suggests that sonography can be used for early evaluation of DHF. Presence of these findings also helps to assess the severity, early in the course of disease, as all the patients with evidence of ascites or effusion had some degree of thrombocytopenia. Ascites was the most sensitive finding and the gall bladder wall thickening was the most specific finding in this study for diagnosis of dengue.



[Table/Fig-4]: Ultrasound images showing; (a) Ascites; (b) Right pleural effusion; (c) Left pleural effusion; (d) Gallbladder wall thickening; (e) Pericardial effusion and; (f) Splenomegaly in 48 years old male patient with severe thrombocytopenia (platelet count: 13,000).

The findings of our study are in concordance with previous studies by Motla M et al., [16] which also showed ascites as most common finding (74.6%). Studies by Venkata sai PM et al., (100%) [17], Vedaraju et al., (83.3%) [18] and Sachar et al., (100%) [19], have shown that gall bladder wall thickening was the most common finding. However, gall bladder wall thickening was seen in only 64.8% in our study. The reason for this difference can be multifactorial. Firstly, the degree and proportion of severe thrombocytopenia was significantly higher in present study when compared to previous studies, which could have contributed to significantly higher incidence of ascites. The difference in the antigenic strains and patient susceptibility might also have contributed for the difference in incidence of various sonographic findings.

Studies by Asghar J et al., [20] and Chandak S et al., [21] have found hepatomegaly and splenomegaly as most common findings. On the contrary, these were the least common findings in our study, except in patients with normal platelet count where splenomegaly was the most common finding. Higher proportion of patients with severe thrombocytopenia could have increased the incidence of ascites, making organomegaly least sensitive finding. This study has also shown that isolated hepatosplenomegaly is non-specific for diagnosis of DF (specificities of 36.9% and 63.0% respectively). Few previous studies have found abnormal liver parenchymal echotexture in dengue, which has been attributed to intraparenchymal and subcapsular hemorrhages. None of these findings were found in our study. These differences might also suggest the changing trend of dengue infection. Of the 310 patients included in the study, 308 patients recovered from dengue. While a total of fourteen patients developed dengue shock syndrome, two patients died of dengue shock syndrome, with ages of 6 years and 74 years, which suggests that children and elderly patients might have poor prognosis in dengue shock syndrome.

LIMITATION

The study had few limitations. Being a Tertiary Care Centre, the findings were recorded on the day patient presented to the Department (2 to 7 days of onset of fever). Hence, it was not possible to correlate the findings with timing of symptoms, which might have helped to better understand the pathophysiologic process. Patients could not be followed up for resolution of the findings.

CONCLUSION

Constellation of sonographic findings like ascites, gall bladder wall thickening, pleural effusion, hepatomegaly and splenomegaly are useful not only in the early diagnosis of the disease, but also in assessment of severity of the disease.

Though in isolation these findings are non-specific, when seen together, should strongly suggest the diagnosis of DF, especially during an epidemic. Hence, abdominal ultrasonography should be a routine investigation in suspected cases of DF.

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