Original Research Article

Study of honeycomb pattern of gallbladder wall thickening for early diagnosis of severe dengue fever

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Abstract

Background: Dengue fever (DF) and its severe forms dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) have become major international public health concerns. Early recognition is crucial for any efforts at curative therapy. In present study we aimed to evaluate honeycomb pattern of gallbladder wall thickening for early diagnosis of severe dengue fever at our tertiary hospital. **Material and Methods:** Present study was an observational study, conducted in patients with confirmed diagnosis of dengue fever either by NS1 antigen test or Dengue IgM or IgG antibody test. Sonography done on day 2/3 and repeated on day 5/6 of admission. Honeycomb pattern of gallbladder wall thickening was identified as multiple hypoechoic areas separated by multiple echogenic layers. **Results:** In present study, 108 patients of dengue fever were underwent serial ultrasonography abdomen on day 2/3 and repeated on day 5/6 of admission. Most common age group was more than 50-59 years age (21%) followed by 19-29 years (20 %) and 30-39 years age group (18 %). Male (63%) patients were more than female (37%) patients. Out of 108 patients considered in study, 49 progressed to dengue hemorrhagic fever (DHF) and/or dengue shock syndrome (DSS). Gall bladder wall thickening (94%), gall bladder wall thickening with pericholecystic fluid (94%), ascites (45%), splenomegaly (29%) and pleural effusion (24%) were common findings in those patients. Honeycomb pattern of gall bladder wall thickening (94%), gall bladder wall thickening with pericholecystic fluid (94%) were more specific for progression of dengue fever to dengue hemorrhagic fever (DHF) and/or dengue shock syndrome (DSS). Honeycomb pattern of gall bladder wall thickening was noted in 52 patients, 46 later diagnosed with dengue hemorrhagic fever (DHF) and/or dengue shock syndrome (DSS), while 6 patients were stable with dengue fever. Honeycomb pattern of gallbladder wall thickening had sensitivity (93.87%), specificity (89.83%), positive predictive value (88.46%), negative predictive value (94.64%), accuracy (91.66%) for early diagnosis of severe dengue fever (dengue hemorrhagic fever and/or dengue shock syndrome). **Conclusion:** "Honeycomb" pattern of gallbladder wall thickening in abdominal ultrasound examination is a reliable sign in patients with suspected DHF/DSS to detect early signs that are suggestive of the disease prior to obtaining serologic confirmation test results, especially in a dengue fever epidemic area.

Key Words: gallbladder wall thickening; honeycomb pattern; severe dengue fever; ultrasound examination

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INTRODUCTION

Dengue is one of the most important and fastest growing, mosquito-borne viral diseases affecting tropical and subtropical regions in the world, particularly the Asia Pacific region.[1] Dengue fever (DF) and its severe forms dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) have become major international public health concerns In 2009, WHO reclassified dengue fever according to severity: DF without warning signs; DF with warning signs (abdominal pain, persistent vomiting, fluid

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accumulation, mucosal bleeding, lethargy, liver enlargement, increasing hematocrit with decreasing platelets); and severe DF (dengue with severe plasma leakage, severe bleeding or organ failure).[2] Hypovolemic shock due to the leakage of plasma into serosal cavities is prominent feature of severe dengue. Clinically it is difficult to determine leakage of plasma and quite often serum hematocrit is used as an adjunct to detect significant plasma leak. Gallbladder wall thickening due to significant plasma leakage is one of the commonest findings in dengue fever.[3,4] Specific treatment for dengue is not available, but early detection and fluid replacement therapy and use of analgesics and antipyretics with good nursing care ensures marked reduction of the mortality rates 20% to less than 1% due to severe cases.[5] In present study we aimed to evaluate honeycomb pattern of gallbladder wall thickening for early diagnosis of severe dengue fever at our tertiary hospital.

MATERIAL AND METHODS

Present study was an observational study, conducted in patients with confirmed diagnosis of dengue fever. Study was conducted in Department of Radiodiagnosis, Pacific Institute of Medical Sciences, Udaipur during January 2019 to September 2019. Institutional scientific research committee approval was taken for present study.

Inclusion criteria-

- Patients with confirmed diagnosis of dengue fever either by NS1 antigen test or Dengue IgM or IgG antibody test.
- Patients willing to participate and follow up.

Exclusion criteria-

- Patients with dengue haemorrhagic fever (grade I to IV), dengue shock syndrome.
- Patients with known liver parenchymal disease, hepatobiliary disease, renal parenchymal disease, and cardiac failure.

Study was explained to patients in local language and written informed consent was taken. Demographic data, clinical details, laboratory investigations and USG findings were noted in proforma. The clinical manifestations of DF included fever, headache, retro-orbital pain, muscle- joint pain, nausea-vomiting, rash, leukopenia, and thrombocytopenia. Abdominal ultrasound was done in patients with dengue fever, after 4 hours of fasting for better visualization of the gallbladder (GB). Abdominal ultrasound was done by senior radiologist, performed on a GE LOGIQ P5 unit, equipped with a 4C wide bandwidth (1.5 to 4.6 MHz) convex probe and 11L wide bandwidth (4 to 12 MHz) linear probe. The linear probe was used for pediatric patients. Sonography done on day 2/3 and repeated on day 5/6 of admission. For present study, thickened GB wall was defined as being ≥ 3 mm and was measured by placing calipers between the two layers of anterior wall. Honeycomb pattern of gallbladder wall thickening was identified as multiple hypoechoic areas separated by multiple echogenic layers. Other additional findings on abdominal ultrasound examination such as hepatomegaly, splenomegaly, pancreatic enlargement, ascites, pleural effusion were recorded. Clinical diagnosis at the time of discharge/death were noted and compared with radiological findings. Statistical analysis was done for honeycomb pattern of gallbladder wall thickening for early diagnosis of severe dengue fever (dengue hemorrhagic fever and/or dengue shock syndrome).

RESULTS

In present study, 108 patients of dengue fever were underwent serial ultrasonography abdomen on day 2/3 and repeated on day 5/6 of admission. Most common age group was more than 50-59 years age (21%) followed by 19-29 years (20 %) and 30-39 years age group (18 %). Male (63%) patients were more than female (37%) patients.

Table 1: Age and gender distribution

AGE (yrs)	Male	Female	Total
19-29	13 (12%)	9 (8%)	22 (20%)
30-39	11 (10%)	8 (7%)	19 (18%)
40-49	11 (10%)	6 (6%)	17 (16%)
50-59	15 (14%)	8 (7%)	23 (21%)
60-69	10 (9%)	4 (4%)	14 (13%)
≥ 70	8 (7%)	5 (5%)	13 (12%)
Total	**68 (63%)**	**40 (37%)**	**108**

Out of 108 patients considered in study, 49 progressed to dengue hemorrhagic fever (DHF) and/or dengue shock syndrome (DSS). Gall bladder wall thickening (94%), gall bladder wall thickening with pericholecystic fluid (94%), ascites (45%), splenomegaly (29%) and pleural effusion (24%) were common findings in those patients. Honeycomb pattern of gall bladder wall thickening (94%), gall bladder wall thickening with pericholecystic fluid (94%) were more specific for progression of dengue fever to dengue hemorrhagic fever (DHF) and/or dengue shock syndrome (DSS).

Table 2: USG abdomen finding in patients with dengue hemorrhagic fever (DHF) and/or dengue shock syndrome (DSS) (n=49)

USG abdomen finding	Day 2/3 (n=49)		Day 5/6 (n=49)	
	No. of patients	Percentage	No. of patients	Percentage
Honeycomb pattern of gallbladder wall thickening	39	80%	46	94%
Gall bladder Wall thickening with pericholecystic fluid	17	35%	46	94%
Ascites	8	16%	22	45%
Splenomegaly	11	22%	14	29%
Right sided pleural effusion	9	18%	12	24%
Left sided pleural effusion		0%	10	20%
Hepatomegaly	1	2%	7	14%
Pericardial Effusion	1	2%	4	8%

Honeycomb pattern of gall bladder wall thickening was noted in 52 patients, 46 later diagnosed with dengue hemorrhagic fever (DHF) and/or dengue shock syndrome (DSS), while 6 patients were stable with dengue fever.

Table 3: Honeycomb pattern of gall bladder wall thickening in study patients

Confirmed diagnosis	Honeycomb pattern of gall bladder wall thickening		Total
	Present	Absent	
dengue hemorrhagic fever (DHF) and/or dengue shock syndrome (DSS)	46	3	49
Dengue Fever only	6	53	59
Total	**52**	**56**	**108**

Honeycomb pattern of gallbladder wall thickening had sensitivity (93.87%), specificity (89.83%), positive predictive value (88.46%), negative predictive value (94.64%), accuracy (91.66%) for early diagnosis of severe dengue fever (dengue hemorrhagic fever and/or dengue shock syndrome).

Table 4: Statistical analysis

Parameter	Value
Sensitivity	93.87
Specificity	89.83
Positive Predictive Value	88.46
Negative Predictive Value	94.64
Accuracy	91.66

DISCUSSION

The pathophysiology of dengue fever is that the virus especially attacks the capillary endothelium, resulting in increased permeability and causing plasma leakage and serous effusion with a high protein content (mostly albumin). 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.[6,7] Clinically dengue manifests with sudden onset of high fever with chills, intense headache, muscle and joint pain, retro-orbital pain and severe backache. Fever usually lasts for about 5 days, rarely for more than 7 days. Early recognition is crucial for any efforts at curative therapy. Abdominal pain developing in dengue patient mimics many of surgical emergencies like cholecystitis, pancreatitis and appendicitis. The pathophysiology for the abdominal inflammatory signs is due to leakage of plasma into the tissues, lymphadenitis or lymphatic follicular hyperplasia. In cholecystitis gall bladder is thick walled, oedematous usually without any calculus. The presence of gallbladder wall oedema has been proved to have prognostic significance in various conditions like hypoalbuminemia, cholecystitis, acute hepatitis and liver cirrhosis.[8] 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. Early detection of DHF/dengue shock syndrome (DSS) can go a long way in managing these patients and reducing morbidity and mortality, especially in DHF and DSS cases. A simple ultrasound examination will effectively expedite the diagnosis and justifies initiation of specific treatment for dengue fever pending serological confirmation. Sonographic features of thickened GB wall, pleural effusion (bilateral or right side), ascites, hepatomegaly and splenomegaly should strongly favor the diagnosis of dengue fever in patients presenting with fever and associated symptoms, particularly during an epidemic.[9] "Honeycomb" pattern of gallbladder wall thickening is one of the most common ultrasound (USG) finding in patients with dengue fever. Few earlier studies have confirmed that gallbladder wall thickening can play a significant role in assessing patients at risk of developing severe dengue fever.[10,11] Similar findings were noted in present study.

Oliveira GA *et al.*,.[12] reported transient reticular gall bladder wall thickening in severe DF due to plasma leakage in the wall and the author identified four distinct gall bladder wall thickening patterns as striated pattern of multiple hypoechoic layers separated by echogenic zones, asymmetric pattern with echogenic tissue projecting into the gall bladder lumen, central hypoechogenic zone separated by two echogenic layers; and a uniform echogenic pattern. Sachar *et al.* found "Honeycomb" pattern in 19 out of 20 patients of severe DF (95%), whereas Parmar J *et al.* demonstrated "Honeycomb" pattern in 71.4% of severe DF cases. Parmar J *et al.* noted sensitivity of 71.4%, specificity of 94.37%, PPV of 86.95%, and NPV of 86.28% and concluded that "Honeycomb" pattern of GBWT can favor diagnosis of severe DF in epidemic areas of DF with appropriate clinical scenario.[13,14] James Colbert *et al.*.,[15] showed a high negative predictive value for detecting Dengue haemorrhagic fever/Dengue Shock Syndrome using ultrasound dependably in the hospital settings to rule out severe dengue in cases presumed to have suspected dengue as well as to determine the patients who needed to be monitored closely as well as which ones to hospitalize. Sonography is a good tool for early diagnosis in clinically suspected cases of dengue fever, before serological studies are known, especially when dengue NS1 is not available.[16] Dengue fever with sonography findings of thickened gallbladder wall, ascites, splenomegaly, and pleural effusion in an acute febrile patient with thrombocytopenia in an area of recurrent dengue fever could be used as an additional diagnostic modality for early diagnosis of suspected dengue fever in endemic areas.[17] Ultrasonography (USG) is a cheap, rapid and widely available non invasive imaging modality. It can be used as a first-line imaging modality in patients with suspected DF to detect early signs suggestive of the disease prior to obtaining serologic confirmation test results, especially in a DF epidemic area.[18]

CONCLUSION

"Honeycomb" pattern of gallbladder wall thickening in abdominal ultrasound examination is a reliable sign in patients with suspected DHF/DSS to detect early signs that are suggestive of the disease prior to obtaining serologic confirmation test results, especially in a dengue fever epidemic area.

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