ORIGINAL ARTICLE

Sonographic Features of Polyserositis as an Adjunct to Clinico-Pathological Parameters in Diagnosing and Predicting the Severity of Dengue Fever

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ABSTRACT

Aims & Objectives: We aimed to demonstrate sonographic features as an adjunct to clinico-pathological parameters in diagnosing and predicting the severity of dengue fever or dengue hemorrhagic fever.

Methodology: Transabdominal ultrasound scanning was performed on 171 patients (93 male, 78 female; age range 12–70 years, mean age 29 years) between August and December 2010, besides serological confirmation of clinical diagnosis of dengue fever. 13 patients were excluded on negative serological results. Initial ultrasound scans were done on day of presentation (first 3 days of fever), with a follow up scan after one week of fever (7^{th} day).

Results: Out of 158 patients, 99 patients (62.65%) demonstrated sonographic features of serositis during initial scanning (first 3 days of fever). Follow up scanning on 7^{th} day confirmed previous findings with additional findings in overall 147 patents (93%). In 11 cases (7%), we didn't demonstrate any sonographic evidence of serositis. Gall bladder wall thickening was the most consistent finding in all the serologically positive cases of dengue fever, 99 cases (62.65%) on initial scanning and 139 cases (88%) on follow up scan. Itwas almost exclusively associated with pericholecystic edema. 72 patients demonstrated right-sided unilateral pleural effusion (45.6%) on initial scan. None had ascites or left sided pleural effusion or pericardial effusion during the first 3 days of fever. On follow-up scan (day 7), minimal to mild ascites were noted in 37 patients (23.41%), right sided pleural effusion was found in 91 (58%) and bilateral pleural effusion in 48 patients (30.37%). Pericardial effusion depicted in 16 patients (10%). Hepatomegaly, splenomegaly and diffused pancreatic enlargement were found in 17 (10.75%), 12 (7.6%) and 9 (5.7%) cases respectively. Subcapsular fluid collection in liver and spleen was found in 8 (5%) and 2 (1.2%) cases respectively, suggestive of serous fluid rather than hemorrhage. No pararenal and perirenal space fluid collections were found in any of the cases. Joint effusion was demonstrated in elbow and knee joints in 2 patients (1.2%).

Conclusion: Transabdominal ultrasound is an important diagnostic tool to clinical profile in diagnosing Dendue fever early in its course compared with other modes of diagnosis before the severe form of disease is clinically apparent, thus ameliorating various complications. Sonographic surveillance is necessary besides clinical and laboratory correlation due to the high risk of aggravation of dengue fever into its more severe forms.

Key words: Ultrasound, dengue fever, polyseositis, gall bladder wall thickness.

INTRODUCTION

Dengue fever (DF) is an acute febrile viral (arbovirus) disease. It is one of the major health problems, particularly, in the tropical and subtropical areas including South East Asia. Dengue fever is endemic in Pakistan with seasonal rise in cases. However, recently, the transmission of dengue fever has intensified in the country with increased incidence and geographic expansion. The recent Pakistan floods may have contributed to this upsurge as a result of changes in risk factors for these diseases.

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The incidence of dengue has grown dramatically around the world in recent decades. Some 2.5 billion people ($2/5^{th}$ of the world's population) are now at risk from dengue. World Health Organization (WHO) currently estimates there may be 50 million dengue infections worldwide every year. In 2007 alone, there were more than 890,000 reported cases of dengue in the Americas, of which 26 000 cases were Dengue Hemorrhagic Fever (DHF). The disease is now endemic in more than 100 countries in Africa, the Americas, the Eastern Mediterranean, South-east Asia and the Western Pacific. In developed countries, dengue usually presents in the benign form, but sudden aggravation is always possible. An estimated

500,000 people with DHF require hospitalization each year, a very large proportion of who are children. About 2.5% of those affected die. Without proper treatment, DHF fatality rates can exceed 20%.

The spread of dengue is attributed to expanding geographic distribution of the four dengue viruses and their mosquito vectors, the most important of which is the predominantly urban species Aedes aegypti. It manifests clinically with acute onset of fever, severe headache, retro-ocular pain and pain involving the muscles and joints. According to WHO criteria, DHF is defined by the presence of fever, a hemorrhagic tendency, thrombocytopenia and some evidence of plasma leakage due to increased vascular permeability. Most severe cases are categorized as dengue shock syndrome (DSS) when circulatory failure is present (hypotension for age, or narrow pulse pressure i.e. <20 mmHg). Hemorrhagic diasthesis and thrombocytopenia with concurrent hemoconcentration is a constant finding. The diagnosis is based on clinical appearance in combination with serology, which takes approximately 7 to 10 days to give a positive result.

Radiological findings mostly suggest polyserositis. Similar feature have been reported by pediatric groups during dengue outbreaks in Asia. Autopsies performed on cases of DHF reported that the most frequent pathological findings were fluid collections in the thorax, abdomen, pericardial sac and other body compartments and petechial hemorrhages. Keeping this fact and delayed results of serological tests, we aimed to determine sonographic findings as an important adjunct to clinico-pathological parameters in diagnosing and predicting the severity dengue fever or dengue haemorrhagic fever.

METHODOLOGY

This cross-sectional study was done at Department of Radiology in collaboration with Department of Medicine (Medical Unit IV) between August and December 2010. We included 171 subjects (93 male, 78 female; age range 12–70 years, mean age 29 years) who were clinically suspected of having Dengue fever. The patients were referred after registration from a Unit of Infectious and Communicable diseases for transabdominal ultrasound scanning. Common clinical manifestations were quite variable. Fever was the most common symptom found in the entire patients (n=158), which was either associated with severe headache (n=115), body aches and joint pain (n=98), retro-ocular pain (n=54), and purpuric spots on the body (n=20). Hematological investigation in almost all the patients revealed thrombocytopenia with concurrent raised hematocrit (hemoconcentration) in severe cases. Based on the clinical/ laboratory findings and to correlate severity of the disease with ultrasound findings, patients were categorized in three major groups according to WHO classification (based on severity of the disease); classical dengue fever (CDF), dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS). These patients were confirmed serologically, 158 cases were found positive. We excluded the record of remaining 13 patients from our data. Clinical categorization included 103 cases of CDF (65%), 49 cases of DHF (31%) and 6 cases of DSS (4%).

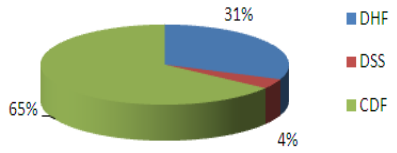


Figure 1: Clinical categorization percentages of the patients (based on severity of the disease according to WHO classification); classical dengue fever (CDF), dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).

Transabdominal ultrasound scans were performed using Toshiba Xario (SSA 660A; Tokyo, Japan) with 3.5 MHz transducer. Primarily, the emphasis was made on gallbladder wall thickness, any measurement greater than 3 mm was considered as abnormal. Liver, spleen, pancreas and any free fluid in the peritoneal or pelvic cavity were also recorded. The scan also included lower thoracic scanning done in supine posture to evaluate pleural cavity for any free pleural fluid. Both the pleural spaces were evaluated through an intercostal approach. Pericardial space was also evaluated for effusion subcostally. Besides all sonographic examination mentioned above, joint swelling was also evaluated through high frequency transducer for the presence of joint effusion. The patients were scanned during first 3 days after onset of fever. Follow up scan wa

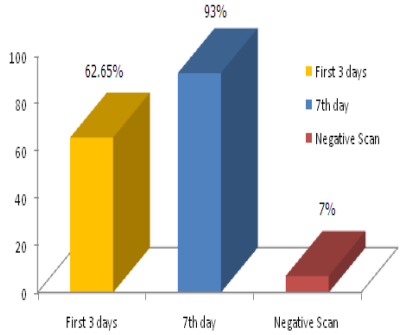
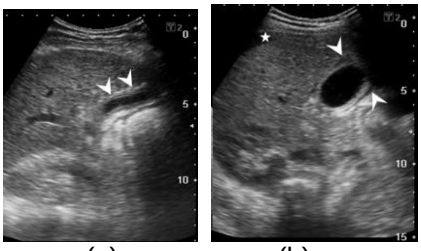


Figure 2: Percentage of positive and negative scans according to the Days of examination.

RESULTS

We demonstrated that thickened GB wall along with pericholecystic edema was the most common and consistent ultrasound finding on initial as well as later scans followed by pleural effusion, ascites and pericardial effusion. Hepatomegaly, splenomegaly and pancreatic enlargement were noted in few patients with severe disease.

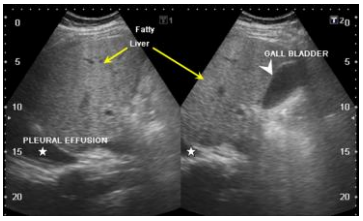
Out of 158 patients, there were 99 patients (62.65%) in whom sonographic features of serositis were found on the transabdominal scanning during the first 3 days of onset of fever. However, a follow up scanning on 7th day confirmed previous findings as well as demonstrated additional findings in 147 patents (93%). In total, 11 cases (7%) didn't demonstrate any of the sonographic evidence of serositis (figure 2). The sonographic features according to the days of examination are given in table 1.



(a) (b)

Fig. 1: (a&b). Transverse sonogram demonstrating thickened gall bladder wall with mild preicholecystic edema besides intrinsically normal gall bladder lumen. (b). Note mild free peritoneal fluid (star) in the subphrenic space.

Patients scanned during first 3 days after onset of fever revealed that gall bladder wall thickening in 99 cases (62.65%), the most consistent finding in all the serologically positive cases of dengue fever ranging from mild to severe form. It was measured by placing the calipers between the two layers of anterior wall. GB wall thickening was almost exclusively associated with pericholecystic fluid (n=88, 89%). There were 72 patients with right-sided unilateral pleural effusion (45.6%), found more in the mild and moderate severity of the disease rather than in DSS. None had ascites or left sided pleural effusion or pericardial effusion during the first 3 days of fever.



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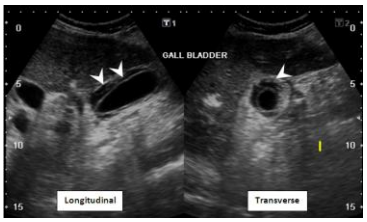

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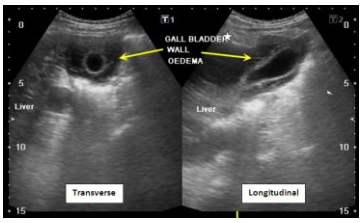


(c)

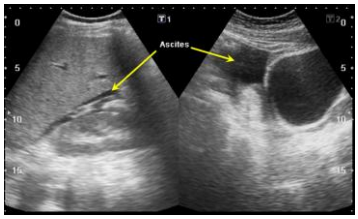
Fig. 2: (a). Sonogram of a patient with 2 days history of dengue fever demonstrates mild right pleural effusion (star), however gall bladder wall thickness is normal. Hepatic steatosis is documented. (b&c). Marked gall bladder wall thickness with moderate pericholecystic edema is demonstrated.

Table 1: Summary of ultrasound findings according to the Days of examination.

Sonographic Features	**Day 1-3**	**Day 7**
Gallbladder wall thickening	99 (62.65%)	139 (88%)
Right sided pleural effusion	72 (45.6%)	91 (58%)
Bilateral pleural effusion	-	48 (30.3%)
Ascites	-	37 (23.4%)
Pericardial effusion	-	16 (10%)
Hepatomegaly	-	17(10.7%)
Splenomegaly	-	12 (7.6%)
Pancreatic enlargement	-	9 (5.7%)
Hepatic subcapsular fluid collection	-	8 (5%)
Splenic subcapsular fluid collection	-	2 (1.2%)
Joint effusion	-	2 (1.2%)

On follow-up scan (day 7), gall bladder wall thickening with pericholecystic edema was consistent and demonstrated in 139 cases (88%). In addition, minimal to mild ascites were noted in 37 patients (23.41%). Right sided pleural effusion increased in overall cases, found in 91 (58%); bilateral pleural effusion was demonstrated in 48 patients (30.37%). We didn't find isolated left sided pleural effusion in our study. Pericardial effusion depicted in 16 patients (10%). Hepatomegaly, splenomegaly and diffused pancreatic enlargement were found in 17 (10.75%), 12 (7.6%) and 9 (5.7%) cases respectively. Subcapsular fluid collection in liver and spleen was found in 8 (5%) and 2 (1.2%) cases respectively, suggestive of serous fluid rather than hemorrhage. These findings were more common in severe form of disease. Renal appearances were normal in all cases. No pararenal and perirenal space fluid collections were found in any of the cases. We

demonstrated joint effusion in the elbow and knee joints in 2 patients (1.2%); this feature is not documented so far in the literature in relation to dengue fever.



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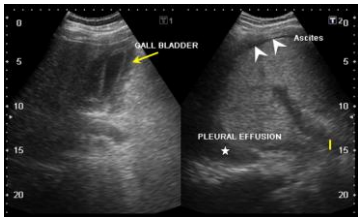


(b)

Fig. 3: (a&b). Sonogram demonstrating free clear ascites besides thick walled gall bladder and pleural effusion (star) in two different patients.

We found that gall bladder wall thickening and right sided pleural effusion were the most sensitive sonographic markers in the early course of dengue fever, i.e. in the milder form of disease. These features remain consistent with moderate and severe form of dengue fever. However, other forms of serositis have predilection towards moderate form of disease.

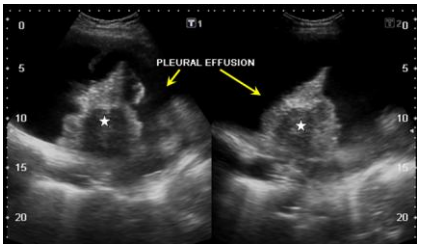
Table 2: Various sonographic pathological features in mild moderate and severe forms of dengue fever.

Sonographic Features	CDF (n=103)	DHF (n=49)	DSS (n=6)
Gallbladder wall thickening	83 (80.5%)	49 (100%)	6 (100%)
Right sided pleural effusion	72 (69.9%)	48 (97.9%)	6 (100%)
Bilateral pleural effusion	6 (5.8%)	43 (87.7%)	5 (83.3%)
Ascites	3 (2.91%)	31(63.26%)	6 (100%)
Pericardial effusion	-	12(24.49%)	4 (66.6%)
Hepatomegaly	4 (3.88%)	14(28.57%)	6 (100%)
Splenomegaly	3 (2.91%)	10 (20.4%)	5 (83.3%)
Pancreatic enlargement	1 (0.97%)	7 (14.2%)	2 (33.3%)
Hepatic subcapsular fluid collection	-	5 (10.2%)	3 (50%)
Splenic subcapsular fluid collection	-	-	2 (33.3%)
Joint effusion	-	2 (4.1%)	-

Joint effusion was a rare but important cause found in the patients having moderate form of disease associated with painful joint movements at elbow and knee. Global polyserositis was almost exclusively found in the severe form of disease. These features are given in table 2.

DISCUSSION

The increase in the incidence of DF is due to uncontrolled growth rate of under developed world and absence of appropriate water management. Global spread of dengue strains via travel and trade is another factor. In Pakistan, the situation is alarming because of outbreaks reported by the National Institute of Communicable diseases in the recent past. Over 1500 laboratory-confirmed cases of dengue fever including 15 deaths have also been reported from Pakistan in the year 2010.



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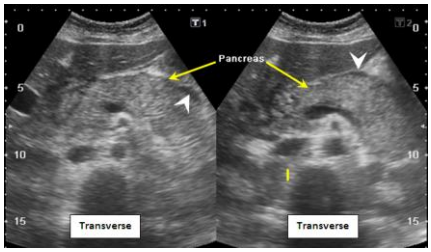


(b)

Fig. 4: (a) Massive pleural effusion demonstrated in a patient with DSS confirming extensive serositis. (b). Transverse sonogram demonstrating swollen pancreatic parenchyma with increased dimensions of head and body besides minimal peripancreatic fluid streak (arrow heads) suggestive of pancreatic parenchymal inflammation due to dengue fever.

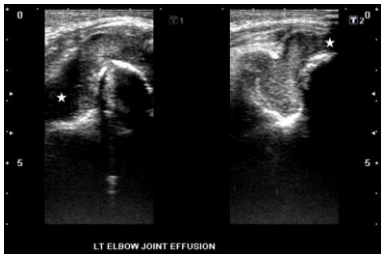
Dengue viruses are transmitted to humans through the bites of infective female Aedes mosquito. The incubation period of the disease is 3–14 days. The onset of the disease is recognized by the sudden onset of high fever, retro-orbital pain, thrombocytopenia and haemorrhagic manifestations. The major pathophysiological feature of DHF is an increased vascular permeability, giving rise to loss of plasma and albumin from the vascular compartment. Common laboratory findings include pancytopenia,

neutropenia, increased hemoconcentration, thrombocytopenia and prolonged bleeding time. These findings are consistent with increased vascular permeability, plasma leakage, abnormalities of hemostasis and protein losing shock syndrome, which commonly occur in DF pathogenesis. Serology is the mainstay in the diagnosis of DF. Hemagglutination inhibition antibodies usually appear at detectable level by day 5 to 6 of febrile illness. The diagnosis of DF is often delayed owing to time taken for availability of results.

Ultrasound can be used to detect small amounts of transudate in serous cavities in the patients with DF. Physical examination allows detection of ascites only in volumes above 1000--1500 ml, while ultrasound can demonstrate as little as 100 ml. The sonographic findings in early milder form of DF are polyserositis including GB wall thickening, pericholecystic edema, minimal to mild ascites and pleural effusion. Severe forms of the disease are characterized by pericardial effusion, hepatic and splenic subcapsular fluid, fluid collection in the perirenal and pararenal region, pancreatic enlargement and hepatosplenomegaly. The abnormal liver parenchyma is attributed to intraparenchymal and subcapsular haemorrhages. However, we could not find any significant parenchymal echo pattern change of the liver. Previous studies also suggested GB wall thickening as the initial finding in DF, followed and pleural effusion.

Gall bladder wall thickening in DF is due to decrease in intravascular osmotic pressure. This finding may also occur in other viral infections, enteric fever and leptospirosis. But in other viral infections, the symptom complex evolution and physical findings do not mimic those of DF. Sonographic features of enteric fever include splenomegaly, intra-abdominal lymphadenopathy, bowel abnormalities in the form of intramural thickening of the terminal ileum and caecum, renal abnormalities like arteriectasis and perinephric fluid collection in addition to GB wall thickening and polyserositis. Leptospirosis also shows gross abnormalities involving hepatic and renal parenchyma. GB wall thickening also occurs in association with other conditions such as ascites, hypoalbuminaemia, congestive cholecystopathy and in patients with cirrhosis of liver and portal hypertension. Due to this non-specific nature of abnormal GB wall thikness in isolation, we recommend that ultrasound features in conjunction to clinical suspicion of Dengue fever is an important diagnostic tool which also helps to evaluate the severity of the disease. GB wall thickness can be relied upon as an additional but important criterion to support the clinical diagnosis and predicting the severity/ poor prognosis of DHF. Likewise, positive correlation between the amount of pleural effusion and severity of the disease was also found in our study.

WHO is raising the awareness campaigns regarding dengue fever exposure risks and preventive measures for the general public, strengthening clinical and case management of patients with hemorrhagic fevers, stockpiling appropriate drugs and personal protective equipment, and implementing targeted vector control activities. WHO is mobilizing experts in the clinical management of severe dengue fever and in infection control in health care settings through the Global Outbreak Alert and Response Network (GOARN). WHO is also assisting our country with resource mobilization, strengthening disease surveillance, laboratory diagnostics, and training of health care providers.



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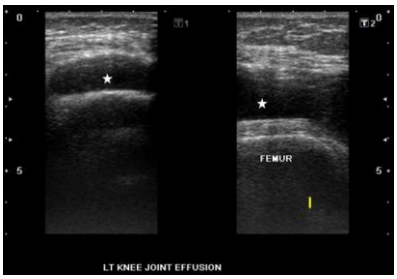

(b)

Fig. 5. Sonograms through elbow (a) and knee (b) demonstrating effusion (star) in the joint space.

CONCLUSION

Transabdominal ultrasound is an important diagnostic tool to clinical profile in diagnosing Dengue fever early in its course compared with other modes of diagnosis before the severe form of disease is clinically apparent, thus ameliorating various complications of the disease in the form of hemorrhage, hypovolemia and shock. Sonographic findings of gall bladder wall thickening with or without polyserositis in a febrile patient should raise the suspicion of DF/DHF. Sonographic surveillance is necessary besides clinical and laboratory correlation due to the high risk of aggravation of dengue fever into its more severe forms.

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