

Clinical and Sonographic Evaluation of Dengue Fever in Bangladesh: A Study of 100 Cases

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Dengue has become a major international public health concern in recent years. Its mortality ranges from 1-5% in treated patients to maximum of 50% of untreated or poorly treated patients. The aim of this study was to evaluate the clinical and sonographic findings of dengue fever in Bangladesh which may be useful in the early diagnosis and proper management of dengue fever. This cross sectional study was carried out in the department of Radiology and Imaging Dhaka Medical College Hospital and BSMMU during the period of March 2008 to February 2009 in patients suspected to have Dengue fever. All patients underwent serological examination for Dengue IgG and IgM antibodies. Ultrasonographic findings of dengue fever were - thickened gall bladder wall, pericholecystic fluid, hepatomegaly, hepatic intraparenchymal fluid, splenomegaly, pancreatic enlargement, ascites, and pleural and pericardial effusion. The study concluded that abdominal and thoracic sonography can be used as first line of imaging modality in patients with suspected dengue fever to detect early signs suggestive of the disease prior to obtaining serologic confirmation specially in dengue fever epidemic areas and early prediction or severity of the disease.

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Introduction

Dengue is a mosquito-borne acute febrile infectious disease caused by flavivirus. Dengue fever (DF) has been known for more than a century in the tropical areas of South East Asia and the Western Pacific regions. A significant increase in the incidence of this infectious disease has taken place in the last 20 years and Dengue has become a major international public health concern in recent years. In 1998, it was deemed to be the most important tropical mosquito-transmitted infectious disease, surpassed only by malaria.¹ It is now endemic in more than 100 countries and threatens the health of more than 2500 million i.e. 40% of the world's population. It is estimated that 10 million classic dengue infections occur each year with 500,000 cases of dengue hemorrhagic fever. Its mortality ranges from 1-5% treated patients to a maximum of 50%

for untreated or poorly treated patients resulting in at least 12,000 deaths annually mainly among children.²

The disease occurs in two forms: classic dengue, the milder form of the disease and dengue hemorrhagic fever (DHF), the severe form. The severity of this disease falls into four grades. Grade I is characterized by fever, general symptoms and positive tourniquet test. Grade II shows sign and symptoms of grade I plus spontaneous hemorrhage on the skin, gums, gastrointestinal tract, and other areas. Sign and symptoms of grade III include those of grade II plus circulatory shortage and agitation. Grade IV shows shock and non-detectable artery pressure. In all phases, there is thrombocytopenia and haemoconcentration. Since there is no other tests that can be used to diagnose the condition with a reasonable

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degree of accuracy and reliability, the diagnosis of dengue fever is based on clinical appearance in combination with serology. Positive serology (anti dengue antibody) is the mainstay in the diagnosis of DF.³ But serology takes approximately 7 days to give a positive result.⁴ The diagnosis of DF is often delayed owing to time taken for availability of serology test results.² Moreover, this test is expensive and not widely available all over Bangladesh.

Ultrasonography (USG) is a cheap, rapid and widely available non-invasive imaging method. In recent years several studies concluded that ultrasonography of the chest and abdomen can be an important adjunct to clinical profile in diagnosis DF and diagnosis can be made early in the course of disease compared with other modes of diagnosis.² It can be used as a first-line imaging modality in patients with suspected dengue fever to detect early signs suggestive of the disease prior to obtaining serologic confirmation test results, especially in a dengue fever epidemic area.⁵

Sonographic findings of dengue fever have been described in several previous literatures. Some authors concluded that during an epidemic the ultrasound findings of gall bladder wall thickening with or without polyserositis in a febrile patient should suggest the possibility of DF/DHF.² The reported changes vary according to the severity of each case. According to the previous studies ultrasound findings in milder form include pleural effusion, ascites, gall bladder wall thickening, hepatomegaly, splenomegaly, pancreatic enlargement, pericholecystic fluid and pericardial effusion. Severe form of the disease is characterized by fluid collection in the perirenal and pararenal region, hepatic and splenic subcapsular fluid collections, pericardial effusion, pancreatic enlargement, pleural effusions, ascites, gallbladder wall thickening, hepatomegaly,

splenomegaly, hepatic intraparenchymal haemorrhages, and pancreatic enlargement.^{1,2,5,7-11} These findings may also occur in other viral infections and enteric fever but in other viral infections the historical profile, symptom complex evolution and physical findings do not mimic those of DF.² One study attempted to investigate whether gall bladder wall thickening (GBWT) measured by ultrasonography can be used as a reliable criterion to predict the onset of severe dengue hemorrhage fever. It is found that a GBWT 5 mm is useful as a criterion for identifying DHF patients at high risk of developing hypovolumic shock.⁸ The aim of this study was to evaluate the clinical and sonographic findings of dengue fever in Bangladesh which may be useful in the early diagnosis and proper management of DF.

Methods

This cross-sectional observational study was carried out in the department of Radiology and Imaging of Bangabandhu Sheikh Mujib Medical University, Dhaka and Dhaka Medical College Hospital, Dhaka during the period of March 2008 to February 2009 on consenting patients suspected to have dengue fever who were referred from the outpatient department and indoor of these hospitals for ultrasound scanning of both abdomen and thorax. Relevant clinical information was collected systematically. Then all of them underwent sonography first by the investigator which was then confirmed by a senior radiologist and the sonographic findings were noted. All patients underwent serological examination for dengue virus IgG and IgM antibodies by a pathologist for final diagnosis.

Initially 134 patients underwent ultrasonography. Among them 3 patients died before serological confirmation, 5 patients refused to undergo serological investigation, 24 patients did not have dengue antibodies in serological studies, and serological report of 2

patients could not be collected. They were excluded from the study. So, finally the rest 100 patients were the study population. Then the demographic, clinical, laboratory and sonographic data of these 100 patients of dengue fever were analyzed.

Inclusion Criteria - Patients of dengue fever of all grades of severity and of all age groups and in both sexes.

Exclusion Criteria - The followings were excluded from the study: a) Patients who did not undergo serological test for dengue fever b) whose serological reports were not available and c) who were seronegative for dengue fever.

Study Variables - (a) Demographic variables - age and sex of the patients (b) Clinical variables - clinical symptoms and signs, related investigations and clinical grade of severity of the patients (c) Sonographic variables - 1) Thickened GB wall : present/absent 2) Pericholecystic fluid : present/absent 3) Hepatomegaly present/absent 4) Hepatic subcapsular and/or Intraparenchymal fluid: present/absent 5) Splenomegaly 6) Splenic subcapsular fluid 7) Pancreatic enlargement 8) Pancreatic enlargement 9) Peripancreatic fluid 10) Ascites 11) Pleural effusion 12) Pericardial effusion and 13) Others

Serological examination

Serological test (anti dengue antibody) was performed by a pathologist to confirm the final diagnosis of dengue fever. A case of dengue was defined as a febrile patient with ≥ 40 antibody units by IgG or IgM. Serology is generally positive as of the fifth day after onset of disease. Reports were collected and serologically negative patients were excluded from this study.

Data Collection

After explaining all the necessary information regarding the research study data were collected in predesigned structured data collection sheets.

Statistical analysis of data

Collected data was checked for consistency and to remove any minute error. All the relevant collected data were compiled on a master sheet first and was then organized by using scientific calculator and standard statistical formulae. Percentages were calculated to find out the proportion of the findings. The results were presented in tables, graphs and diagrams using computer based software Microsoft Excel.

Results

Among 100 patients included in this study the age ranged between 6 to 67 years. Age distribution of the study population is shown in table I. There were 58 men (58%) and 42 women (42%).

Table I: Age distribution of the study population (n = 100)

Age group (years)	No. of patients	Percentage
0-10	14	14%
11-20	22	22%
21-30	26	26%
31-40	16	16%
41-50	12	12%
51-60	08	08%
61-70	02	02%
Total	100	100%

Clinical symptoms of the study population are shown in table II. The table shows that fever is the most common clinical manifestation followed by nausea/vomiting and musculoskeletal pain. Analysis of the clinical signs showed that most common clinical sign is hepatomegaly followed by positive tourniquet and subconjunctival hemorrhage (table III).

Table II: Clinical symptom of patients with dengue fever.

Clinical symptoms	No. of patients	Percentage
Fever	98	98%
Nausea / Vomiting	76	76%
Musculoskeletal pain	61	61%
Melena	39	39%
Headache	34	34%
Anorexia	32	32%
Generalized weakness	31	31%
Abdominal pain	14	14%
Retro-ocular pain	13	13%
Restlessness	11	11%
Hematemesis	07	07%
Gum bleeding	05	05%
Loss of consciousness	04	04%
Epistaxis	03	03%

Table III: Clinical signs of the study population (n=100).

Clinical signs	No. of patients	Percentage
Hepatomegaly	48	48%
Positive tourniquet test (\geq 20/sq inch)	24	24%
Subconjunctival hemorrhage	17	17%
Hypotension	17	17%
Splenomegaly	13	13%
Skin rash	11	11%
Bradycardia	10	10%
Lymphadenopathy	09	09%
Anaemia	07	07%
Shock	05	05%
Dehydration	04	04%

Important investigation findings of the study population are shown in table IV. Elevated liver enzymes, thrombocytopenia and haemoconcentration were common investigation findings. Patients were divided into the four grades of clinical severity based on the clinical and laboratory findings of the patients and according to the WHO criteria (Table V). Majority of the patients were in grade II (46%).

Table IV: Investigation findings of the study population (n=100)

Investigation findings	No. of patients	Percentage
Elevation of liver enzyme (s) level (s)	61	61%
Thrombocytopenia (platelet count < 100.000/mm ³)	57	57%
Haemoconcentration (Haematocrit fall > 20%)	27	27%
Prolongation of PT and/or PTT	21	21%
Anaemia	09	09%
Leucopenia	05	05%
Chest X-ray:		
Pleural effusion	18	18%
Bronchopneumonia	09	09%

Table V: Clinical severity grading of the study population (n=100).

Severity grade	No. of patients	Percentage
Grade I	37	37%
Grade II	46	46%
Grade III	12	12%
Grade IV	05	05%

Ultrasonographic findings of the study population are shown in table VI. Sonographic findings in different grades of clinical severity of dengue fever are also shown in this table. The table shows that pleural effusion, ascites, thickened GB wall, hepatomegaly and splenomegaly is present in all grades of clinical severity but their number increases with the degree of clinical severity. Pericardial effusion, pericholecystic fluid, hepatic intraparenchymal fluid, splenic subcapsular fluid, pancreatic enlargement, peripancreatic fluid collection, and perinephric fluid collection are mainly present in dengue patients of higher degree of clinical severity.

Table VI: Ultrasonographic findings of the study population

Sonographic Characteristics	Total N=100 No. of patients (Percentage)	Severity grade			
		Grade I N=37 No. of patients (Percentage)	Grade II N=46 No. of patients (Percentage)	Grade III N=12 No. of patients (Percentage)	Grade IV N=05 No. of patients (Percentage)
Thickened GB wall	38 (38%)	11 (29.7%)	15 (32.6%)	07 (58.3%)	05 (100%)
Pericholecystic fluid	02 (02%)	00 (00%)	01 (2.1%)	01 (8.3%)	00 (00%)
Hepatomegaly	54 (54%)	14 (37.8%)	27 (58.6%)	09 (75%)	04 (80%)
Hepatic Intraparenchymal fluid	02 (02%)	00 (00%)	00 (00%)	01 (%)	01 (20%)
Splenomegaly	18 (18%)	05 (13.5%)	09 (19.5%)	03 (00%)	01 (20%)
Splenic subcapsular fluid	03 (03%)	00 (00%)	00 (00%)	02 (16.6%)	01 (20%)
Pancreatic enlargement	11 (11%)	00 (00%)	4 (8.6%)	05 (41.6%)	02 (40%)
Peripancreatic fluid	01 (01%)	00 (00%)	00 (00%)	01 (8.3%)	00 (00%)
Parirenal fluid collections	15 (15%)	00 (00%)	03 (6.5%)	08 (66.6%)	04 (80%)
Ascites	41 (41%)	05 (13.5%)	23 (50%)	08 (66.6%)	05 (100%)
Pleural effusion	42 (42%)	08 (21.6%)	19 (41.3%)	10 (83.3%)	05 (100%)
Pericardial effusion	06 (06%)	00 (00%)	04 (8.6%)	01 (8.3%)	01 (20%)

Discussion

Dengue fever is an acute febrile viral disease caused by flavivirus. Dengue has become a major international public health concern in recent years. Large-scale yearly outbreaks during the rainy season have been occurring in Bangladesh since the year 2000 and are straining the limited healthcare resources of this country.³ Hence, it will be useful in the proper management of dengue fever if symptoms, signs and laboratory parameters and sonographic findings associated with the disease are identified early and the clinical severity is known. The main objective of their study was to identify symptoms, signs, laboratory values and other investigation findings of dengue fever and the sonographic findings of dengue fever in different grades of clinical severity in Bangladesh.

Out of 100 patients included in this study the age ranged from 6 to 67 years. There were 58 (58%) men and 42 (42%) women. This is consistent with previous study findings that dengue fever occurs more in male sex.²

The present study findings were compared with those previous studies. The clinical symptoms, signs, investigation and sonographic findings of dengue fever found in this study are similar to those found in some of the previous studies^{1,2,57}. Some differences exist between some previous study findings and the present study. For example, Gonzalez et al found that most common bleeding site in dengue fever was the vaginal bleeding (64%).¹² But no patient in the present study complained of vaginal bleeding. Setiawan et al and Pramuljo and Harun reported hepatic subcapsular fluid collections in dengue fever which was not seen in this study.^{9,13} There are investigation and sonographic findings between different previous study findings as well between previous study findings and the present study findings. For example, Quiroz-Moreno et al found gallbladder thickening in 86% of the patients, Sai et al in 56% patients, Gonzalez et al in 35.1% but it was present in this study in 38% patients^{2,6,7}. This may be due to serotype of the causative dengue virus, secondary antibody patterns of the patients

due to previous exposure to dengue viruses, race of the patients and other factors yet to be known.^{12, 13}

In this study it was found that, chest x-ray diagnosed pleural effusion in 18 patients whereas ultrasonography diagnosed pleural effusion in 42 cases. Similar findings have been also demonstrated in previous studies.⁷ There were also mild to moderate amount of ascites in the studied patients. As a result neither pleural effusion nor ascites was apparent on clinical examination in any of them. But sonography diagnosed all of them correctly. Moreover hepatomegaly in 6 patients and splenomegaly in 5 patients could not be diagnosed by clinical examination but were diagnosed correctly by ultrasonography. So this study clearly demonstrates the importance of abdominal and thoracic sonography in the accurate and complete clinical evaluation and management of dengue fever. This study also shows that certain sonographic findings are more common in higher grades of clinical severity of dengue fever. Obviously this means that ultrasonography can also give the clinicians some idea about the severity of the disease process and thus help in more meticulous management of the patients. It should also be noted that serological confirmation of dengue fever needs about 5 days after its onset. Most of the manifestations of this disease can be visualized by ultrasonography before this period of time.

The study concludes that abdominal and thoracic sonography can be used as a first-line imaging modality in patients with suspected dengue fever to detect early signs suggestive of the disease prior to obtaining serologic confirmation test results especially in a dengue fever epidemic area and may be useful for early prediction of the severity of the disease.

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