

## SHORT ARTICLES

# High Incidence of Dengue Fever in Karachi and the Benefits of Ultrasound for Diagnosis of Complications

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## ABSTRACT

**Background:** Dengue fever presentations are from asymptomatic fever to most serious complications. Acute high-grade fever, muscle and joint pain, myalgia, skin rashes, hemorrhage and circulatory shock are the common symptoms. There has been reported increase in number of dengue fever and last few years. Urgent diagnosis is critical to avoid complications like liver injury, cardiomyopathy, pneumonia, orchitis, oophoritis, seizures and encephalopathies. This study aimed to determine the complication caused by dengue fever after the diagnosis by clinical and laboratory investigation by performing ultrasound abdomen and thorax.

**Methods:** In this study one hundred and twenty one (121) patients diagnosed with dengue fever and laboratory investigations done from Jinnah Medical Hospital (JMH) and Pathological and Molecular Laboratories from August to November 2019. Ultrasound of abdomen and thorax was performed for diagnosing complications such as ascites, pleural and pericardial effusion through Xario-100 sonography machine.

**Results:** Out of one hundred and twenty one (121) patients diagnosed with dengue fever forty-three (43) were found to have developed the complications such as ascites, pleural and pericardial effusion by performing ultrasound abdomen and chest.

**Conclusion:** We found 35 % patients with dengue fever complications by ultrasound, which is most convenient diagnostic tool. Therefore, by performing early ultrasound scan of abdomen and thorax in these patients can reduce the risk of morbidity and mortality.

**Keywords:** Dengue; ELISA; Antigen; Ultrasound; Ascites; Pleural; Pericardial Effusion.

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## INTRODUCTION

This study was performed to find out the significance of ultrasound imaging in evaluating the complications caused by dengue fever (diagnosed on clinical and laboratory findings) to determine the severity. High grade fever is the initial symptom caused by dengue virus which gets transmitted by Aedes mosquito's sting. Clinical findings include from high grade fever to most serious symptoms life

threatening hemorrhages and shock. Along with fever, muscular pain, joint pain, myalgia, rashes are the common symptoms<sup>1,2</sup>. Dengue has emerged as a worldwide life-threat to public health, affecting population in more than hundred countries. Thus, the physician should be aware about the symptoms of this viral fever and ensure an early and adequate treatment plan. The incidence of dengue has increased dramatically in the last few years. The infection is now endemic in various countries.

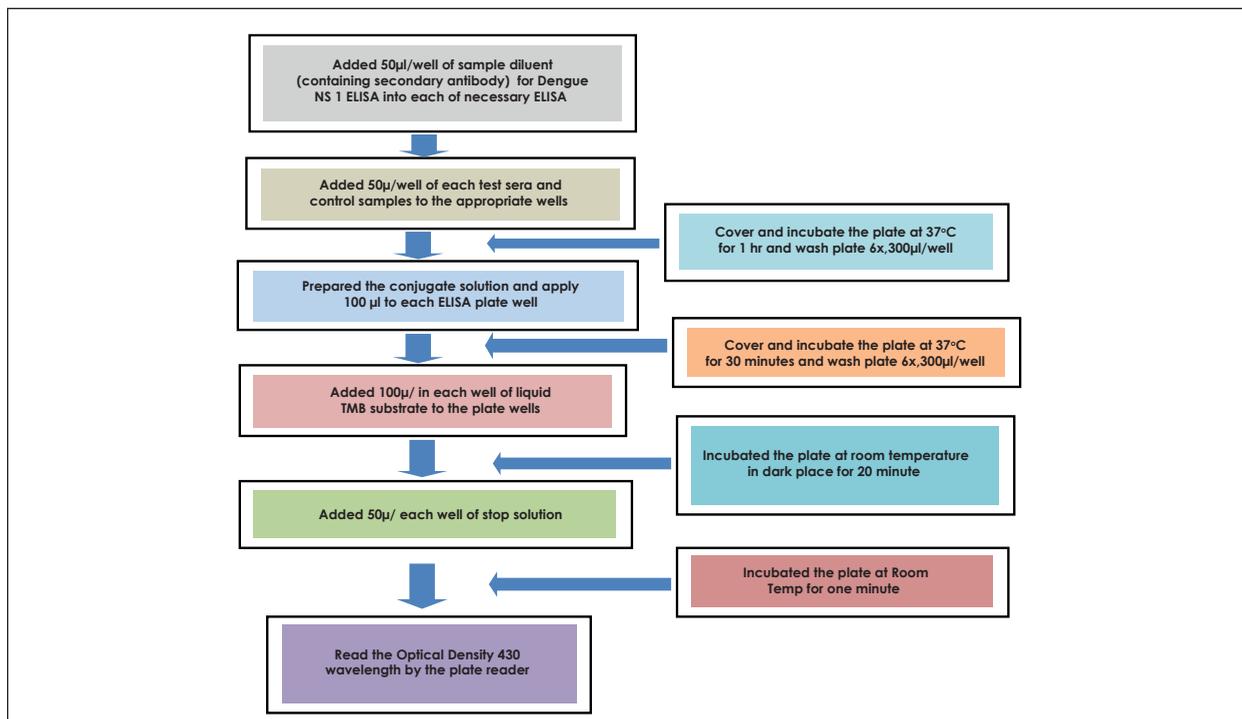
Patients develop dengue hemorrhagic fever who were previously infected with one subspecies of the dengue virus develop severe capillary permeability and bleeding after being infected with another subspecies of the dengue virus<sup>3</sup>. The dengue virus is an arthropod-borne virus transmitted by *Aedes aegypti* having four serotypes (DENV1-4)<sup>2</sup>. Dengue was first introduced in Pakistan at Karachi port through the importation of tiers containing eggs of infected mosquitoes. Thus dengue fever spread rapidly all over the country in the last few years. This infection is endemic in various countries worldwide and diagnosis of dengue virus done by ELISA<sup>3,4</sup>. Study has also shown high incidence of dengue fever, and complication in 45% patients out of which 100 % patients shown gall bladder wall thickness and hepatomegaly<sup>5</sup>. The other complications of dengue fever are liver injury, complications of dengue virus cardiomyopathy, pneumonia, orchitis, oophoritis, seizures, encephalopathy, and encephalitis<sup>5</sup>. The complications of dengue fever such as abdominal complications such as liver injury, ascites, also cardiomyopathy, and pleural effusion may get confirmed diagnosis by performing ultrasound scan<sup>6</sup>. This study was performed to find out the significance of the role of ultrasound in the diagnosis of complications associated with dengue fever (diagnosed on clinical and laboratory findings) to determine the severity.

**METHODS**

In this study One hundred and twenty one (121) dengue fever patients having clinical findings along

with Laboratory investigations were done (CBC, ICT-MP, Dengue NS-1 by ELISA) from blood samples collected from patients visiting Medicare cardiac and General Hospital and Dr. Rubina Ghani molecular and pathology Laboratory. Oral consent was taken from the patients. Blood samples were collected for complete blood count (CBC) and ICT (immunochromatographic assay) was performed to rule out the presence of malarial parasite. Oral informed consent was taken from the patients and ERC of Jinnah Medical and Dental College took ethical approval.

The ethical review committee, Jinnah Medical and Dental College approved the use of human samples in the study protocol referenced above from 01-08-2019 to 01-11-2019. ELISA was performed by using MyBioSource Elisa Kit by adding 50µl/well of sample diluent (containing secondary antibody) for Dengue NS 1 ELISA into each of necessary ELISA<sup>3</sup>. All the diagnosed cases of dengue fever had ultrasound examinations done by using Xario-100 sonography machine using probe with frequency 2.5-3.5 MHZ to for determine the complications associated with dengue fever. All abdominal ultrasounds were performed after 6-8 hours of proper fasting to allow better distension of gallbladder, also examined liver, spleen, kidneys, for ascites. Thoracic ultrasound was performed in sitting posture. Steps for ELISA as given in following Flow chart (Figure 1) by Pal et al., Evaluation of Dengue NS1 Antigen Rapid Tests and ELISA Kits using clinical samples<sup>3</sup>.



**Figure 1: Enzyme-linked immunosorbent assays (ELISAs) targeting NS1 antigen (Ag).**

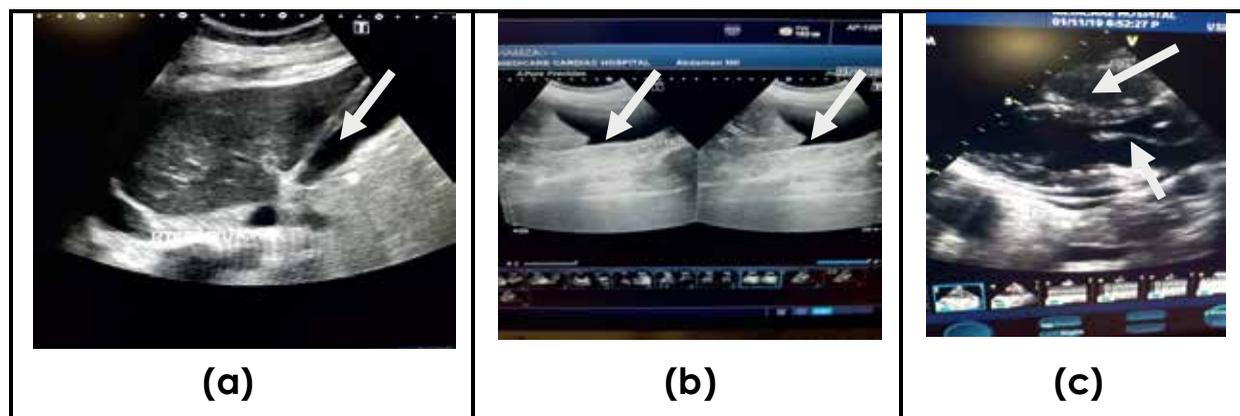
## RESULTS

Out of total of 121 patients diagnosed with dengue fever (with fever, headache, myalgia, dizziness and vomiting), 43 were found to have developed the complications. These include hepatomegaly, splenomegaly, ascites and pleural effusion by performing ultrasound abdomen and chest. After diagnosis of dengue fever by clinical signs and symptoms, ELISA was performed. Ultrasound abdomen was performed after 6-8 hours fasting.

We found Gall bladder wall thickness in 43 consistent finding in all serologically positive cases. Hepatomegaly was finding in 5 and splenomegaly was finding in 5, mild to moderate ascites in 30 cases (Table 1). Thoracic ultrasound performed in sitting posture, one patient with pericardial and bilateral mild to moderate pleural effusion was seen in 25 patients with dengue fever. Ultrasound images of abdomen in patient with dengue fever show gall bladder wall thickness, ascites, and pericardial effusion shown in Figure 2a-c.

**Table 1: Ultrasound findings of the patients diagnosed with Dengue fever.**

No.	Ultrasound of patients with dengue fever (N=121)	No. of cases with various complications (n=43)	Percentage (%) of patient with specific complication
<b>Abdominal and Pelvis Ultrasound</b>			
1	G.B Wall thickness	43	36%
2	Hepatomegaly	5	4%
3	Splenomegaly	5	4%
4	Ascites	30	25%
<b>Ultrasound Chest</b>			
5	Pericardial effusion	01	1%
6	Pleural effusion	25	20%



**Figure 2: (a) Ultrasound findings of abdomen in patient with dengue fever, arrow show thickened Gall Bladder wall. (b) Ultrasound findings of abdomen in-patient with dengue fever show ascites. (c) Ultrasound findings of thorax inpatient with dengue fever show pericardial effusion.**

## DISCUSSION

In this study 43 (forty three) patients were found to have developed the complications such as ascites, pleural and pericardial effusion was confirmed by performing ultrasound abdomen and chest. Dengue fever (DF) can present as an asymptomat-

ic infection or simple high grade fever or dengue hemorrhagic fever (DHF) with multi-organ failure, due to increase in capillary permeability with leakage of fluids during the critical phase of dengue fever<sup>7-12</sup>. A study done in teaching hospital of Sri Lanka during epidemic of dengue fever in 2016. The age range 12-51 years, comprising six

females and four males. The group of patients included seven cases of hemorrhagic fever, three of dengue fever and two patients with primary dengue infections had severe bleeding into gut. Other life threatening problems were acute severe hepatitis, severe septic shock, myocarditis, intracranial bleeding, and diarrhea and decompensated dengue shock. Blood transfusions and other empirical therapeutic methods were used along with fluid replacement to manage each patient. Bedside ultrasound scanning helped early detection of critical phase. All of these patients recovered completely<sup>13</sup>. In another study done to determine utility of ultrasound for patients with dengue fever symptoms lasting for a weeks, had reported gall bladder wall thickness in all patients, hepatomegaly (21%), splenomegaly (7%), ascites (96%) pleural effusion (87%). Hemorrhagic fever and shock syndrome are the most severe complications of dengue infection. Acute renal failure is one of the complications of severe dengue infection (2-5%) of cases and is associated with hypotension, rhabdomyolysis, or hemolysis. Mesangial proliferation and immune complex deposition is the characteristic feature of dengue-associated glomerulonephritis<sup>14</sup>. Liver dysfunction is commonest in both dengue fever and with DF complaints of abdominal pain, nausea, vomiting and anorexia.

Also a study shown that due to direct effects of the virus or host immune response on liver cells, circulatory compromise, metabolic acidosis and/or hypoxia caused by hypotension or localized vascular leakage inside the liver are possible cause of liver dysfunction<sup>15,16</sup>. Bleeding is common complication both dengue fever and dengue hemorrhagic fever. Pathology of the dengue fever is not very well understood. Thrombocytopenia is most common in the laboratory finding in this viral fever. Abnormal platelet functions results in rapid peripheral destruction of platelets<sup>17,18</sup>. A study also suggests that bleeding is more common in patients with severe thrombocytopenia. Such patients having platelet count less than 20,000/cumm and high risk of bleeding require platelet transfusion whereas patients with platelet count 21-40,000/cumm required platelet transfusions only with hemorrhagic episodes<sup>17-18</sup>.

Study done in Sri Lanka on dengue fever patients had shown high incidence of cardiac complications during dengue fever outbreak<sup>19</sup>. Studies have reported neurological complications associated with DF and DHF<sup>20,21</sup>. A retrospective cross-sectional done at Dr. Soliman Fakeeh Hospital in Jeddah, Saudi Arabia between January 2010 and June 2014, five hundred and sixty seven patients had been diagnosis of dengue fever or dengue hemorrhagic fever/shock syndrome. Also there were associate complications of thrombocytopenia, plasma leakage syndrome (pleural effusion or ascites) or bleeding<sup>22</sup>. Furthermore, thrombocytopenia occurs maybe due to altered

megakaryocytopoiesis causing malfunction of platelets thus leading to hemorrhages<sup>23-28</sup>.

The Dengue vaccine (DV) attacks the monocytes, dendritic cells and macrophages. In addition, the DV non-structural protein (NS1) causes damage to endothelial cells and platelets. Moreover, abnormal activity of T-cells results in increase in vascular permeability<sup>28-29</sup>. Most serious complications of DF /DHF include hepatic dysfunction leading to acute hepatic failure, muscle disorder such as myositis, rhabdomyolysis, gastrointestinal and intracranial bleeding. Also may include endocrine disorders such as Diabetes ketoacidosis and Guillain-Barre syndrome<sup>30</sup>. Early and proper diagnosis of dengue fever and complications has improved the survival but still more efforts for prevention and appropriate management of such patients. As found in the study done in Pakistan, due to overpopulation and poor sanitation the incidence this viral disease is very high in larger cities<sup>30</sup>.

This indicated high incidence of dengue fever in last few months and evolved appropriate diagnosis of dengue and effective ultrasound scans had been able to diagnose complications such as ascites, pericardial and pleural effusion enabling better patient care to reduce mortality.

## CONCLUSION

The study had shown high incidence of dengue fever in Karachi, Pakistan. If fever develops early diagnosis is most important in reducing complications and mortality. By determine the complication by ultrasound scan in dengue fever, which is most convenient diagnostic tool, early and appropriate management, can reduce the risk of morbidity and mortality.

## ACKNOWLEDGMENTS

We are highly thankful to Medicare Cardiac and General hospital and patients to provide us approval for carrying out this study.

## CONFLICTS OF INTEREST

The authors declared no conflict of interest.

## ETHICS APPROVAL

The ethical review committee of Jinnah Medical and Dental College approved the use of human samples in the study protocol referenced above from 01-08-2019 to 01-11-2019.

## PATIENT CONSENT

Verbal consent was obtained from all the patients.

## AUTHORS' CONTRIBUTION

SI and SK contributed in providing ultrasound findings, SPK contributed in the concept of study design and article writing and RG contributed for providing samples of blood test and ELISA.

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