Association of Gallbladder Wall Thickening and Haematocrit Values with Severity in Patients of Dengue Fever

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ABSTRACT

BACKGROUND
The word “dengue” originates from the Bantu phrase Ka-dinga pepo, meaning “cramp-like seizure”. Breakbone fever viruses are enclosed in the family Flaviviridae and the virus has four serotypes through-about to as Dengue virus-1, DV-2, DV-3, and DV-4. Breakbone fever virus is a ribonucleic acid virus, encapsulated and is positive-stranded and consists of 3 structural macromolecule genes that encrypt the nuclocapsid or core (c) macromolecule, a membrane-associated (M) macromolecule, an engulfed (E) conjugated protein and 7 non-structural (NS) proteins. Dengue virus is principally transmitted by the dipteron / Aedes aegypti mosquito, two-winged insects and conjointly by the Asian tiger mosquito. The purpose of this study was to find an association of gall bladder wall thickening and haematocrit values with severity in patients with dengue fever admitted to Mahatma Gandhi Medical College & Hospital, Sitapura, Jaipur (a tertiary care unit).

METHODS
It was a hospital-based observational study, conducted on all patients who were positive for dengue NS1 Antigen and IgM serology & who visited the Department of General Medicine in Mahatma Gandhi Medical College & Hospital, Sitapura, Jaipur from January 2020 to June 2021 were included in the study. All data were collected and analyzed by EPI-info software.

RESULTS
The association between gall bladder thickness and PCV was found statistically significant. Associations between PCV and prognosis and that of gall bladder thickness and prognosis were also found statistically significant.

CONCLUSIONS
We concluded that gall bladder wall thickness and haematocrit values are significant contributors to the assessment of the severity of dengue fever. The main advantage of this method is that it is a fast and easily approachable method and can be easily practised in most centres.

KEY WORDS
Dengue, Gall Bladder Thickness, PCV.

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Dengue is the most typical arthropod-borne viral infection of humans. There are about fifty million populations that are infected once a year with breakbone fever and more or less than five lakh people are hospitalized with breakbone fever virus infection, largely in a geographic area. Infections (disease) have been largely urban disease however currently has unfolded conjointly in rural areas of the Republic of India also one. After 1828, the term breakbone fever came into general use.\[1\]

Breakbone fever viruses are enclosed in the family Flaviviridae and the virus has four serotypes through-about to as Dengue virus-1, DV-2, DV-3, and DV-4. It’s transmitted to folks by *Aedes aegypti* or *Aedes albopictus* mosquitoes. Dengue virus is principally transmitted by the dipteran / *Aedes aegypti* mosquito, two-winged insects and conjointly by the Asian tiger mosquito. One serotype produces long immunity against re-infection in humans, however solely partial and temporary immunity against the opposite serotypes.\[2\] Recent estimates indicate that four hundred million folks are infected with breakbone fever worldwide once a year, which makes infectious (disease) the foremost necessary and heavy vector-borne disease of humans.

A recent study was done at the University of Oxford employing a map-based approach to model what percentage of breakbone fever causes were occurring in varied components of the globe, calculable that the Republic of India had the biggest variety of breakbone fever causes, with regarding thirty-three million apparent and another a hundred million infections occurring annually.\[3\] Recent estimates indicate that four hundred million folks are infected with breakbone fever worldwide once a year, which makes infectious (disease) the foremost necessary and heavy vector-borne disease of humans.\[4\]

Though the incidence of breakbone fever in the Republic of India was in 1946, a significant epidemic occurred in 1963-1964 in Kolkata.\[5\] The unwellness profile was modified and the bigger severity was from the late eighties. A characteristic feature of severe infections (disease) beneath each classification is enhanced capillary permeability, delineated by the escape of fluid and simple protein into the extravascular house, resulting in hemoconcentration, symptom and cavitary effusions. Gall bladder wall thickening is one manifestation of enhanced capillary permeability. A thickness bigger than 5 mm might determine breakbone fever in patients with a better risk of developing shock. Gall Bladder wall thickness may be a nonspecific finding associated with several infectious agents, micro-organisms and parasitological diseases.

**Objectives**

- To establish an association between gall bladder wall thickening and haematocrit values.
- To establish an association of haematocrit value and gall bladder wall thickening on dengue fever prognosis.
- To establish the association of haematocrit value and GB wall thickening on dengue complications.

**METHODS**

It is a Hospital-based observational study conducted in the Department of General Medicine, Mahatma Gandhi Medical College and Hospital, Sitapura, Jaipur from January 2020 to June 2021. All patients who were positive for dengue NS1 antigen and IgM serology visiting the department were taken for the study.

**Inclusion Criteria**

All male and female patients in the age group >18 years and who were positive for dengue NS1 Antigen and IgM serology and gave consent for the study were included.

**Exclusion Criteria**

- All other febrile illness
- All dengue IgG +
- Cholecystitis
- Other GB pathologies

The approval was taken from the Institutional and ethical committee of Mahatma Gandhi Medical College & Hospital, before undertaking the study. Written and informed consent was taken from all participants before enrolment into the study.

**Statistical Analysis**

Data were entered into a Microsoft Excel worksheet and analyzed by frequency, percentage, mean, standard deviation (SD), t-test and chi-square tests.

**RESULTS**

**Table 1. General Profile**

<table>
<thead>
<tr>
<th>Mean ± SD</th>
<th>35.33 ±12.14 Yrs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male: Female</td>
<td>127: 93</td>
</tr>
<tr>
<td>Urban: Rural</td>
<td>134: 86</td>
</tr>
<tr>
<td>NS 1, IgM positive</td>
<td>140: 80</td>
</tr>
</tbody>
</table>

A maximum (44.09 %) of dengue patients belonged to 36 to 50 yrs. of age group followed by 34.55 % patients belonging to 19 to 35 yrs. and 21.36 % of patients belonged to more than 50 yrs. age group. 57.53 % of dengue patients were males and 42.27 % of patients were females. 60.91 % of dengue patients were from urban areas and 39.09 % of patients were from a rural areas. 63.63 % of patients were NS 1 antigen-positive and 36.67 % of patients were IgM ELISA positive.

**Table 2. Association between Gall Bladder Thickness and PCV**

<table>
<thead>
<tr>
<th>Gall Bladder Thickness</th>
<th>Normal</th>
<th>PCV Low</th>
<th>High</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3 mm</td>
<td>51</td>
<td>16</td>
<td>0</td>
<td>67</td>
</tr>
<tr>
<td>4-6 mm</td>
<td>53</td>
<td>87</td>
<td>0</td>
<td>140</td>
</tr>
<tr>
<td>&gt;7 mm</td>
<td>1</td>
<td>9</td>
<td>3</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td>105</td>
<td>112</td>
<td>3</td>
<td>220</td>
</tr>
</tbody>
</table>

In our study, the association between gall bladder thickness and PCV was found statistically significant.
In our study, the association between gall bladder thickness and prognosis was found statistically significant.

In the present study, the association between prognosis and PCV was found statistically significant.

In our study, the most common complication was ascites (26.36 %) followed by hepatitis (17.72 %), hepatomegaly (8.64 %), shock (8.64 %), MODS (2.72 %), ARDS (2.72 %), AKI (2.27 %) and splenomegaly (0.45 %).

Dengue is a vector-borne disease that has caused recurrent epidemics throughout the world. This study was conducted at the time of the epidemic in the year 2020. A similar epidemic occurred in 2015 and 2016 which caused a great deal of mortality and morbidity throughout the country. The most crucial part of the treatment of dengue is the monitoring of
the critical phase of dengue. This part is crucial because the patient may be asymptomatic to begin but will be having early features of plasma leakage. Only if the plasma leakage is diagnosed early that the disease can be prevented from further complications. Once the complications set in, dengue will have a high mortality rate. The critical phase of dengue fever is closely monitored by blood investigations mainly hematocrit and platelet count. This is a laborious task, especially at the time of epidemic when the laboratories will be over-flooded. Research has been underway for many years for better, faster methods of assessing plasma leakage. One of the practical approaches is the assistance of radiological techniques namely ultrasound to detect serositis i.e. seepage of fluid in spaces lining internal organs. Many studies have revealed the importance of gall bladder wall thickening in dengue. Although acalculous cholecystitis is a part of the dengue spectrum of diseases, the increase in gall bladder wall thickness has been found to correlate with the severity of plasma leakage. There has been a proven study in many journals and research centres where they used serial ultrasound to assess the gall bladder wall thickness and found out that it is a reliable method to assess disease severity and plasma leakage.

This study was done at Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan. (A Tertiary Care Hospital) where at the time most of the attention was given to the recent dengue breakout and since it was a higher referral centre and most of the cases were already either diagnosed or were in poor condition that required urgent medical attention.

In our study, one-time assessment of 220 patients with confirmed dengue fever was done with signs of bleeding, vials, complete blood count, liver function test, renal function test and ultrasound for gall bladder wall thickness.

In our study, the maximum (44.09 %) dengue patients were from 36 to 50 yrs. of age group followed by 34.55 % of patients belonging to 19 to 35 yrs. and 21.36 % of patients belonging to more than 50 yrs. age group.

A maximum of 57.53 % of dengue patients were males and 42.27 % of patients were females. 60.91 % of dengue patients were from urban areas and 39.09 % of patients were from the rural areas.

These findings are similar to the study of Deshwal et al.[4] In our study, fever (81.81 %) was the most common symptom followed by headache (72.73 %), nausea/vomiting (50.00 %), retro-orbital pain (27.27 %), fatigue (24.55 %), arthralgia (22.73 %) restlessness (10.00 %), epistaxis (6.36 %), diarrhoea (4.54 %), subconjunctival hemorrhage (3.63 %), menorrhagia (2.73 %) and melela (1.36 %).

In our study, 50.90 % of patients had low hematocrit levels, 47.72 % of patients had normal hematocrit levels and 1.36 % of patients' hematocrit levels were high.

In our study, 63.65 % of dengue patients’ gall bladder thickness was (4 - 6 mm) followed by 30.45 % of dengue patients’ gall bladder thickness as (< 3mm) and 5.90 % of dengue patients’ gall bladder thickness was (≥ 7 mm).

The most common complication was ascites (26.36 %) followed by hepatitis (17.7 %), hepatomegaly (8.64 %), shock (8.64 %), MODS (2.72 %), ARDS (2.72 %), AKI (2.27 %) and splenomegaly (0.45 %).

- In our study, out of 220 dengue patients, 4 patients died and 216 dengue patients were alive.
- The increased gallbladder wall thickness also pointed to the high incidence of multi-organ damage as evidenced by the increase in blood urea, serum creatinine, total bilirubin, and liver enzymes. All these variables have statistical significance in comparative data analysis. Also to be noted is the incidence of perinephric collection in select patients who had bleeding manifestations, multi-organ failure and shock all suggestive that this may be a finding associated with severe dengue.

The low platelet count and high haematocrit values were directly proportional to gall bladder thickness and showed statistical significance. This would mean that gall bladder wall thickening can be used as a method of assessing plasma leakage along with haematocrit and platelet count. This will reduce the number of needle pricks, less transmission of infection, and the much lesser need for laboratory assistance.

Jahnvi K et al. also found that in 75 among 100 cases of dengue infections, the platelet count was above 150000 cells/cumm. Most of them had dengue fever. 12 patients showed platelet count between 20000 – 100000 cells/cumm and among them, 10 patients were suffering from dengue hemorrhagic fever, and 2 patients had simple dengue infection. Five patients showed platelet count less than 20000 cells/cumm and among them, 2 patients suffered from dengue hemorrhagic fever and 3 patients suffered from dengue shock syndrome. 17 patients had hepatic dysfunction and improved after fluid resuscitation and an abnormal coagulation profile was noted in 18 % of the patients and 6 % of patients had acute renal failure who improved after fluid resuscitation without dialysis. 4 % of patients developed acute respiratory distress syndrome. But none of them survived in spite of possible treatment.

Chajhiana SPS et al. also related that 119 were found positive for dengue NS1 antigen, 70 were found to be positive by IgG and IgM was positive for 76 cases. Fever was the most common symptom found in all the patients followed by headache (83.1 %), myalgia (77.3 %), orbital pain (74.7 %), bleeding manifestations (31.9 %), like petechiae, melena, epistaxis and gum bleeding. Hypotension was found in 86.5 % of the patients.[7]

The increased gall bladder wall thickness also pointed to the high incidence of multi-organ damage as evidenced by the increase in blood urea, serum creatinine, total bilirubin, and liver enzymes. All these variables have statistical significance in comparative data analysis. Also to be noted is the incidence of perinephric collection in select patients who had bleeding manifestations, multi-organ failure and shock all are suggestive of finding associated with severe dengue.[8]

As was observed in previous studies i.e. Santosh et al.[9] Patil S et al. the most common clinical manifestations presented were fever (100 %), headache (90 %), abdominal pain (72 %), arthralgia (65 %), myalgia (64 %), hepatomegaly (52 %) and splenomegaly (41 %). Thrombocytopenia (84 %) was the most common haematological abnormality observed. Among serology positivity, the majority were positive for NS1 antigen (81 %), followed by IgM antibodies (7 %) and mixed positivity (12 %). The most common complication observed was hepatic dysfunction (33 %). Out of 100 patients, 84 % of the
patients had thrombocytopenia (platelet count < 1.5 lakhs/cu.mm), 55 % patients had leucopenia (TC < 4000 cells/cu.mm), 30 % patients had increased hematocrit (> 45 %), 33 % patients had deranged LFT and 12 % of patients were anaemic (Hb % < 10 g %).[10] The gall bladder thickness and the severity of course of disease were closely related. In our study also, the GB wall thickening and severity were closely related. This correlation between haematocrit, mortality and GB wall thickening was found to be statistically significant.

**CONCLUSIONS**

We concluded that gall bladder wall thickness and haematocrit values are significant contributors to the assessment of the severity of dengue. Many authorized studies have backed up this observation.

The main advantage of this method is that it is a fast and easily approachable one and can be easily practised in most centres. With this added tool, the monitoring of dengue patients becomes more comprehensive and hopefully can be used to curb the onset of dengue associated complications like dengue shock syndrome.

Many other tools for better assessment of dengue severity and monitoring are in research and research for vaccines and drugs is going on. Hopefully, all these will ensure that the morbidity and mortality of dengue will be controlled and someday the disease itself be brought into control.

**REFERENCES**