**ABSTRACT**

**BACKGROUND:** Children with thalassemia are at equal risk of getting dengue. Atypical manifestations of dengue in children with thalassemia are highlighted in studies from South Asia. Burden of suboptimal transfusion and chelation in children with thalassemia prompted us to undertake this study

**OBJECTIVES:** To study the clinical course and short term outcome of children with thalassemia affected by dengue, and compare them to dengue infection in children without chronic illness.

**METHODS:** Retrospective case note review of children with thalassemia, admitted with dengue from April 2013 to April 2018. Comparison group included family without chronic disease admitted with dengue from November 2012 to April 2014. Severity, complication, hematological/ biochemical parameters, treatment given were analysed. Management was according to 'WHO 2009 Guideline on Dengue'.

**RESULTS:** 15 children with Thalassemia (n=207) had confirmed dengue (NSI positive/ Dengue IgM positive), M:F=1:1.1, median age 6 years (interquartile range IQR 3-11). Median duration of hospital stay 6 (IQR 4-6) days. WHO Group A, B and C had 5, 6 and 4 patients respectively. Clinical features included fever in 15 (100%), persistent vomiting in 9 (60%), abdominal pain in 4 (26.7%) and excessive fluid accumulation in 2 (13.3%). 12 (80%) had anemia at presentation, median Hb 83 (IQR 70-101) g/l, while 2 (13.3%) had hematocrit >36%. 14 (93%) patients had platelets <=150,000/µmm, 9 (60%) with severe thrombocytopenia (<=50,000/µmm). TC <=4000/µmm present in 7 (46.7%) patients. AST/ALT elevated in 14 (93.3%) patients, 4 (26.7%) patients required intensive care. 10 (66.7%) children required red cell transfusion. There were no deaths. Comparing with other group, there was significant difference in number of patients with anemia (p=0.0001, 95% CI 5.6 to 3.8) and hemo-concentration (P=0.0001, 95% CI 15.3 to 9.7).

**CONCLUSION:** Children with thalassemia and dengue infection present with anemia requiring red cell transfusion, hence HCT may not be a useful monitoring tool. In comparison to national statistics (INCLEN Study Group data 2014), the proportion of patients in Group B (40 vs 9.5%) and group C (26 vs 5.9%) appears to be higher in children with thalassemia. Such patients require in-patient care as they may be at greater risk of developing severe disease.
cohort included all children aged 1 month-18 years of age admitted with a diagnosis of probable/confirmed dengue, excluding any children with chronic disorders, from November 2012 to April 2014. The severity and complications of disease, haematological and biochemical parameters, and treatment given were analysed. Management was according to the 2009 World Health Organisation (WHO) guideline on Dengue.

The following laboratory results that were performed as per clinical management protocol, were recorded in this study:

- Complete blood count, including serial monitoring of hematocrit.
- Platelet count
- Liver function tests
- Fibrinogen degradation products, D-dimer, prothrombin time and activated thromboplastin time (as clinically indicated)
- Tests for diagnosis of dengue fever (lg M by ELISA and NS1 by rapid antigen detection test)

Institutional Ethics Committee approval obtained. Statistical calculations were done using the software Stata 13.0

RESULTS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Children with thalassaemia &amp; Dengue (n=15)</th>
<th>Children with no chronic illness &amp; Dengue (n=149)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>15 (100%)</td>
<td>149 (100%)</td>
</tr>
<tr>
<td>Persistent vomiting</td>
<td>9 (60%)</td>
<td>146 (98%)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>4 (26.7%)</td>
<td>121 (81.2%)</td>
</tr>
<tr>
<td>Fluid accumulation</td>
<td>2 (13.3%)</td>
<td>109 (73.15%)</td>
</tr>
<tr>
<td>Anemia</td>
<td>12 (80%)</td>
<td>9 (6%)</td>
</tr>
<tr>
<td>Hemo-concentration</td>
<td>2 (13.3%)</td>
<td>120 (80.5%)</td>
</tr>
<tr>
<td>Leucopenia</td>
<td>7 (46.7%)</td>
<td>54 (36.49%)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>14 (93.3%)</td>
<td>148 (99.3%)</td>
</tr>
<tr>
<td>Raised AST/ALT</td>
<td>14 (93.3%)</td>
<td>146 (98%)</td>
</tr>
</tbody>
</table>

Of 207 children with thalassaemia registered at our centre, 15 had probable or confirmed dengue (Dengue IgM positive and/or non structural antigen NS1 positive respectively), M:F = 1:1.1, median age 6 years (interquartile range 3-11).

Group A (dengue without warning signs), B (dengue with warning signs) and C (severe dengue) had 5 (33%), 6 (40%) and 4 (26%) patients respectively. The median duration of hospital stay was 6 days (interquartile range 4-6). Fever was present in all patients, persistent vomiting in 9 (60%), abdominal pain in 4 (26.7%) and excessive fluid accumulation in 2 (13.3%). 12 patients (80%) had anemia at presentation with median Hb 83g/l (interquartile range 7-10.1), and only 2 (13.3%) had haemoconcentration (Haematocrit >36%). 14 (93%) patients had thrombocytopenia (platelets <= 150,000/ cu.MM), and 9 (60%) with severe thrombocytopenia (<= 50,000/cu.MM). Leucopenia (TC <= 4000/cu.MM) was present in 54 (36.49%) patients. Aspartate transaminase (AST)/Alanine Transaminase (ALT) were elevated in 146 (98%) patients.

22 (14.8%) patients required intensive care treatment. 6 (4.03%) required red cell transfusion. 5 (3.4%) patients died.

Comparing the two groups of patients, there was no significant difference in the gender distribution or symptoms of dengue illness, duration of hospital and intensive care stay, or laboratory features such as leucopenia, thrombocytopenia and elevation of liver enzymes. There was a significant difference in the number of patients presenting with anemia (p=0.0001, 95% CI 5.6 to 3.8) and hemo-concentration (P=0.0001, 95% CI 15.3 to 9.7) between the two groups.

DISCUSSION AND CONCLUSION

Dengue inflicts a significant health, economic and social burden on the populations of endemic areas. Children, especially infants and teenagers are at risk of severe dengue. Most patients tend to recover from the illness. Pediatric patients with thalassemia infected by dengue virus frequently present with anemia instead of hemoconcentration. Many require red cell transfusion to maintain adequate intravascular volume. This is congruous with studies on similar populations in Thailand and South East Asia. Our study is limited by part of it being conducted in a retrospective manner, and selection bias of patients with more severe disease being admitted to hospital, particularly in the comparative group. However in comparison to national statistics INCLEN Study Group data 2014(1), the proportion of patients in Group B (40 vs 9.5%) and group C (26 vs 5.9%) appears to be higher in children with thalassemia.

It is prudent to admit all children with thalassemia with suspected dengue infection to hospital for close monitoring and prompt intervention to yield a favorable outcome. Elevated hematocrit is less useful as a tool for guiding treatment in these patients, as they usually present with anemia and require red cell transfusion.

REFERENCES: