IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 21, Issue 9 Ser.4 (September. 2022), PP 52-56
www.iosrjournals.org

Clinico-epidemiological, Biochemical and Radiological predictors of Severe Dengue in Children

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Abstract

Background

Dengue fever is a major public health issue and its incidence has grown over decades. Children are at risk of developing severe disease and complications. Early prediction of this complication is crucial for timely management and favourable outcome. This study is intended to identify clinical, biochemical, and laboratory predictors of severe dengue in children admitted in a tertiary care hospital.

Material and Methods

An observational study conducted in paediatric ward, fever ward and Intensive Care Unit of a tertiary care teaching hospital in Tamil Nadu over a period of 1 year. A total of 170 children aged 2 months to 12 years who were diagnosed as dengue were included in the study. Detailed history, anthropometry, vitals and systemic examination were done. Blood investigations were sent. The data were analysed using SPSS software.

Results

Our study included a total of 170 children, of which 89 (52.3%) had severe dengue. Majority of children with severe dengue were in the age group of more than 5 years (79.8%). The male to female ratio of children with severe dengue was 1:1.Fever was present in all cases with severe dengue. The next most common presenting feature was arthralgia (83.1%) followed by Retro-orbital pain (80.8%). High haematocrit value, leukopenia and lymphocytosis were significantly associated with severe dengue (p value <0.05). Low total cholesterol levels, high triglyceride levels (>200mg/dl), elevated SGOT levels (>1000 IU/L), elevated SGPT levels (>400 IU/L), prolonged prothrombin time, prolonged aPTT had statistically significant association with severe dengue in our study. High serum ferritin levels (>500ng/dl) and thrombocytopenia did not have significant association with severe dengue.

Conclusion

With the available parameters a scoring system can be developed to predict the severity of dengue infection early in the course of illness.

Key words: *Severe dengue, haematological profile, biochemical profile, scoring system*

Date of Submission: 03-09-2022 Date of Acceptance: 17-09-2022

I. Introduction

Dengue fever is a major public health issue among all vector borne viral diseases. It is one of the leading causes of hospitalization and death among children with communicable disease. The incidence of dengue fever increases every year globally for the past 5 decades. About half of the world's population are now at risk. There are an estimated 390 million infections each year and about 2.5% of those affected do not survive[1]. Early diagnosis and volume replacement of lost plasma with crystalloid solution can reduce the severity of dengue fever and prevent shock. At times, in the absence of hall mark clinical symptoms and signs, diagnosis of impending shock/hemorrhage may be difficult. Early prediction of this complication is crucial for timely management and favourable outcome. This study is intended to identify clinical, biochemical, and laboratory predictors of severe dengue in children admitted in a tertiary care hospital.

II. Material and Methods

An observational study conducted in paediatric ward, fever ward and Intensive Care Unit of a tertiary care teaching hospital, Tamil Nadu, India over a period of 1 year (March 2018 – February 2019). A total of 170 children aged 2 months to 12 years who were diagnosed as dengue based on clinical symptomatology and Dengue IgM /NS1 ELISA positivity were included in the study.

Study Design: Descriptive observational study
Study Location: This was a tertiary care teaching hospital done in paediatric ward, fever ward and Intensive care unit of Institute of Child Health & Hospital for Children, Egmore, Chennai, Tamil Nadu.
Study duration: March 2-18 – February 2019
Sample Size: 170 children
Sample size calculation: $4pq/d^2$
P – prevalence
Q – 1-p
D – Attrition

The prevalence of severe dengue was found to be 13% from a study done by SudhagarHegdeet al[2], D – 5 (constant), the sample size was calculated to be 170.

Inclusion Criteria
All children aged 2 months to 12 years who were diagnosed as dengue based on clinical symptomatology and Dengue IgM /NS1 ELISA positivity.

Exclusion Criteria
Patients who had underlying chronic liver disorder, hematological or endocrine disorders.

Procedure:

Institutional ethical clearance was obtained. After getting informed written consent from parents, detailed history was taken including sociodemographic details and symptoms pertaining to dengue fever. Detailed clinical examination including anthropometry, vital signs and Systemic examination were done. Chest X ray and Ultra sonogram were done for all children with dengue fever. Approximately 5 ml of blood were collected from peripheral veins under aseptic precautions and were sent for complete blood count, liver function test, coagulation profile (prothrombin time, activated partial thromboplastin time, INR), Serum ferritin and lipid profile. The data were analysed using SPSS software. P value <0.05 was considered statistically significant.

III. Results

Our study included a total of 170 children, of which 89 (52.3%) had severe dengue. Majority of children with severe dengue were in the age group of more than 5 years (79.8%). The male to female ratio of children with severe dengue was 1:1 in our study as shown in table 1.

Table 1: Demographic details of Children included in the study

Category		Dengue Fever N (%)	Dengue with warning signs N (%)	Severe Dengue N (%)
Total		22 (12.9)	59 (34.8)	89 (52.3)
Age in years	< 1years	1 (4.5)	2 (3.4)	5 (5.6)
	1 – 5 years	3 (13.6)	7 (11.9)	13 (14.6)
	> 5 years	18 (81.8)	50 (84.7)	71 (79.8)
Sex	Male	9 (40)	21(35.6)	45 (50.5)
	Female	13 (60)	38 (64.4)	44 (49.5)

Among the severe dengue cases, 89.8% presented with dengue shock syndrome, 1.1% with bleeding and 8.9% with organ dysfunction. Fever was present in all cases with severe dengue. The next most common presenting feature was arthralgia (83.1%) followed by Retro-orbital pain (80.8%) as shown in table 2.

Table 2: Clinical symptoms experienced by children included in our study

Symptoms	Frequency (N)	Percentage (%)
Fever	100	100
Arthralgia	74	83.1
Retro-orbital pain	72	80.8
Headache	70	78.6

Myalgia	69	77.5
Abdominal Pain	65	73
Vomiting	55	61.7
Respiratory distress	51	57.3
Rashes	21	23.5
Loose stools	10	11.2

Hematological Profile

High haematocrit value (PCV value >39 in less than 5 years and >43 in more than 5 years), leukopenia and lymphocytosis were significantly associated with severe dengue (p value <0.05). There was no statistically significant association between the presence of thrombocytopenia and severe dengue in our study as shown in table 3.

Table 3: Hematological parameters of children

Parameter	Value	Dengue fever N (%)	Dengue fever with warning signs N (%)	Severe Dengue N (%)	P value
Hematocrit	High	1 (4.5)	1 (1.7)	88 (98.9)	<0.05
WBC count	<4000 cells/mm3	21(95.5)	55(93.2)	85 (95.5)	<0.05
Lymphocytosis	Present	7 (31.8)	11(18.6)	83 (93.3)	<0.05
Platelet count	<1,50,000 cells/mm3	21(95.5)	58 (98.3)	85(95.5)	>0.05

Low total cholesterol levels, high triglyceride levels (>200mg/dl), elevated SGOT levels(>1000 IU/L), elevated SGPT levels(>400 IU/L), prolonged prothrombin time, prolonged aPTT were the other laboratory parameters which had statistically significant association with severe dengue in our study. High serum ferritin levels(>500ng/dl) did not have significant association with severe dengue as shown in table 4.

Table 4: Lab parameters of children

Parameter	Value	Dengue fever N (%)	Dengue fever with warning signs N (%)	Severe Dengue N (%)	P value
Total cholesterol	Low	11(50)	31 (52.5)	85 (95.5)	<0.05
Triglycerides	High	11(50)	31 (52.2)	85 (95.5)	<0.05
SGOT	>1000 IU/L	7 (31.8)	15 (25.4)	85 (95.5)	<0.05
SGPT	>400 IU/L	3 (13.6)	3 (5)	83 (93.3)	<0.05
PT/aPTT/INR	Prolonged	9 (40.9)	25 (42.4)	85 (95.5)	<0.05
Serum Ferritin	>500ng/dl	19 (86.4)	49 (83)	85 (95.5)	>0.05

The presence of pleural effusion in chest X-ray did not have significant association with severe dengue in our study as shown in table 5. Gall bladder wall edema was the most consistent finding in USG which was present in 96% children.

Table 5: Imaging studies of children

Parameter	Findings	Dengue fever N (%)	Dengue fever with warning signs N (%)	Severe Dengue N (%)	P value
Chest X ray	Normal	6 (27.3)	11 (18.6)	5 (5.6)	>0.05
	Presence of pleural effusion	16 (72.7)	48 (81.4)	84 (94.4)	

Among the 89 severe dengue cases, 81 children (91%) had complete recovery. Ten children developed hemophagocyticlymphohistiocytosis and required short term steroids. All these 10 children recovered completely. 8 children (9%) who presented with organ dysfunction succumbed to illness.

IV. Discussion

This study was conducted in a single centre with the aim of identifying clinical, biochemical, and laboratory predictors of severe dengue in children. A total of 170 children were included in the study, of which 89 children had severe dengue. Most children who presented with warning signs and severe dengue were more than 5 years of age. Similar observations were made in studies by Pomgpan et al[3], Shivathanu et al[4]. In our study there was no sex predilection for severe dengue. A similar observation was seen by SivathanuS et al[4] who observed equal sex distribution. Fever was present in all the children included in our study and the mean fever duration was 3-5 days in 80% cases. Other common symptoms were arthralgia (83.1%), retro-orbital pain (80.8%), head ache (78.6%), myalgia (77.5%), abdominal pain (73%), vomiting (61.7%), respiratory distress (57.3%), rashes (23.5%) and loose stools (11.2%). GopalakrishnanSet al[5] observed fever (100%), headache (95.7%), myalgia/arthralgia (92.1%), retro-orbital pain (78%), hemorrhagic manifestations (29.7%), respiratory distress (12.7%), and altered sensorium (4.5%). The mean duration of fever in our study was 3-5 days. TirumaniHB et al[6] reported a shorter fever duration of 1-5 days. In our study, severe dengue was present in about 52% cases. Balakrishnan V et al[7] analysed 306 cases of children admitted with dengue fever and reported 42.8% were dengue fever without warning signs, 38.8% were dengue fever with warning signs and 18.4% were severe dengue. The reported incidence of severe dengue varies from 5% to 18% in various studies. The higher proportion of severe dengue reported in our study may be due to the fact that being a tertiary care institute most children are referred and admitted with severe forms of the disease.

In our study, severe dengue was associated with 14.4% anemia, 98.9% elevated haematocrit values and 96.6% leukopenia. Lymphocytosis was present in 92.2%. Although most patients had thrombocytopenia, there was no significant association with the presence or severity of thrombocytopenia and disease severity. Malathesha MK et al[8] have reported a similar profile. AST elevation more than 1000 was seen in 94.4% cases of severe dengue while ALT elevation more than 400 was observed in 92.2% cases of severe dengue. A similar finding was reported by Tirumana HB et al[6], out of 55 cases admitted , liver function tests showed AST levels elevated more than 45 U/L in 20 (86.9%)DF , 29 (100%) DHF, 3(100%) DSS patients. ALT levels were elevated more than 45 U/L in 16(69.5%) DF, 24 (82.75%), 3 (100%) DSS patients. PT, INR and aPTT prolongation was observed in 94.4% of severe dengue in thisstudy. In 2010 Chuansumrit et al[9], from a study done in Thailand, found a positive correlation between abnormal coagulation studies and dengue shock. In Indonesia, Budastra et al[10] concluded that APTT can be used as a predictor of bleeding manifestations in DHF.

The lowest levels of total cholesterol(TC) (94.4%) and highest levels of triglycerides (94.4%) were found in severe dengue ($p<0.05$) in our study. Liver damage caused by DENV infection could be contributing to the lower cholesterol levels we observed in dengue patients. Elevated triglycerides may be due to secondary HLH. Van Gorpet al[11] also reported the lowest levels of TC,HDL,LDL and highest levels of triglycerides in severe dengue than mild dengue ($p<0.05$). Elevated serum ferritin levels did not correlate with the severity of dengue. However several studies suggest that serum ferritin levels are useful predictor of disease severity.

In our study, Gall bladder wall edema was the most consistent finding in USG which was present in 96% children. Gopalakrishnan S et al[5] observed that GB wall edema in USGwas the most consistent finding seen in 95.03% of cases followed by pleural effusion (70.92%), ascites (65.24%) and hepatomegaly (55.3%).

Limitations of the study were the serotype of dengue virus was not part of study protocol and may have had a influence on the prognosis. Since IgG ELISA for dengue is not done routinely as part of instituitional protocol in all cases, differentiation between primary and secondary dengue was not possible.

V. Conclusion

Headache, arthralgia, retro-orbital pain, abdominal pain and persistent vomiting were the symptoms commonly associated with severe dengue. Any child presenting with the above symptoms should be referred to tertiary centres. Elevated haematocrit, absolute lymphocytosis, low cholesterol, high triglycerides, elevated liver enzymes, prolonged prothrombin time and aPTT were all associated with severe dengue in children. With these parameters a scoring system can be developed to predict the severity of dengue infection early in the course of illness.

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Inkarsal Vaithilingam, et. al. "Clinico-epidemiological, Biochemical and Radiological predictors of Severe Dengue in Children." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 21(09), 2022, pp. 52-56.