

Clinical Spectrum and Outcome of Dengue fever in children at tertiary care Hospital

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DECLARATIONS

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CONFLICT OF INTEREST

Authors declared no conflict of interest.

ETHICAL APPROVAL

Hospitalized patients with Dengue Fever were enrolled after approval from the ethical review board of Dr. Ziauddin University Hospital (Reference Code: 7620823RMPED) granted on September 14th 2023.

AUTHORS CONTRIBUTIONS

RM (Corresponding Author): Initiated and designed the study, led the research coordination, and played a key role in manuscript writing.

MI: Contributed to the conceptualization of the work, provided expertise in data analysis, and offered critical feedback on the manuscript.

FZ: Conducted detailed literature review, contributed to the interpretation of data, and provided critical revision of the manuscript.

SS: Drafted the manuscript, performed statistical analysis, and provided critical revision for intellectual content.

AA: Collected and organized the data, conducted preliminary analysis, and contributed to the interpretation of results

SA: Assisted in data collection, contributed to the analysis of findings and contributed to the interpretation of results

ABSTRACT**Background:**

Dengue fever has emerged as a major public health issue in recent years, particularly in developing countries like Pakistan. Annual outbreaks of dengue fever occur regularly in Pakistan, resulting in significant morbidity and mortality among children. Understanding the diverse clinical presentations, timely diagnosis, and rapid, correct management are crucial aspects of addressing this health challenge. Therefore, the aim of this study is to identify the different clinical spectrums of dengue fever and its outcomes in children.

Method: We conducted a Retrospective Cohort study between 1st October, 2021 to 30th September, 2022 at Paediatric Department of Dr. Ziauddin Hospital, Karachi. Total 56 patients of both genders aged 1–15 years, with the diagnosis of Dengue fever were included in this study. After taking informed written consent from the parents of children detailed demographics included age, sex, weight, clinical signs like bleeding, joint pain, petechiae and fever. Outcomes among all patients were discharge, left against medical advice (LAMA) and death were assessed. SPSS 21.0 was used to analyze all data.

Results: There were 19 (52.8%) male and 17 (47.2%) females among all children. Mean age of the children was 9.13 ± 7.35 years and mean weight was 20.8 ± 4.27 kg. Most common symptom was fever in 22 (61.1%) followed by bleeding in 8 (22.2%) cases, joint pain in 4 (11.1%) and petechiae in 2 (5.6%) cases. Frequency of Ns1Ag positive patients were 29 (80.6%). 14 (38.9%) cases had platelet count $> 100000/\text{mm}^3$. Mean hospital stay was 19.7 ± 4.13 days. 24 (66.7%) patients were discharged, 6 (16.7%) cases were left LAMA and 2 (5.6%) patients were died.

Conclusion: Males children had a higher prevalence of dengue in the study. Regular check-ups showed that the severity of dengue did not worsen right away after infection, but rather increased

gradually over time. Most patients spent more than two weeks in the hospital, and there was two cases of fatality throughout the research.

Keyword: Dengue, Fever, LAMA, Mortality

INTRODUCTION

Aedes, a mosquito that is primarily found in tropical and subtropical regions, is the vector that transmits the dengue virus, an arboviral (Flaviviridae family) infection. The incubation time is seven days, with an average of three to fourteen days [1]. Dengue virus infections can range in severity from asymptomatic, undifferentiated febrile illness to a severe infection. 2009 saw the development of an updated classification system for dengue fever, dengue hemorrhagic fever, and dengue shock syndrome. This new classification system distinguished between non-severe and severe dengue virus infections. After that, patients with and without warning signs are separated into two subgroups for non-severe dengue [1-3].

In order to help clinicians decide where and how to manage and keep patients for observation, a revised classification system has been implemented [1]. Vaccines or targeted, significant, and therapeutic vector control efforts haven't yet been able to halt its rapid exposure and spread throughout the world [4]. Patients of any age can contract the disease, but children under the age of eighteen account for 90% of cases [6]. The most typical dengue symptoms in children are still fever, which is followed by vomiting and stomach pain [7].

Over the past 20 years, the dengue virus has infected various parts of Pakistan. In 1985, the first report with documentation was given. in which the type-2 Dengue virus was discovered during a sero-epidemiological study on encephalitis [8]. The first massive eruption of an outbreak was documented in 1994–1995. [9, 10] In 2006, Karachi went through a similar Epidemic after a spell of heavy rain. Some material that was kept private indicated children as significant victims. Recent studies have shown that every two to three years, DF epidemics cyclically recur in South-east Asia. It has also been shown that serotype predominance has altered recently. Comparing DEN-3 dengue serotype to DEN-2 dengue serotype, the latter seems to be declining throughout [11]

Depending primarily on the patient's position in the infection process, the clinical criteria for diagnosing dengue can be quite broad. Numerous pathogens can present similarly, giving the impression of a dengue infection, depending on the region of the world in which they occur. Early on in the illness, it may manifest as a moderate "flu-like" fever that shares symptoms with other illnesses like measles, influenza, chikungunya, Zika, malaria, and yellow fever. Accurate clinical diagnosis is challenging due to the wide range of clinical symptoms associated with dengue. In addition to evaluating the clinical presentation, laboratory or point-of-care diagnostics may be utilized. [13, 14]

A high fever (40°C/104°F) combined with two of the following symptoms during the fever phase (2–7 days) raises the possibility of dengue: rash, intense headache, retroorbital pain, muscle and joint pain, vomiting, swollen gums, and nausea. Around the third to seventh day following the start of the illness, a patient typically enters the critical phase. A small number of patients may have shown abrupt worsening of signs and symptoms during the first two days of the critical phase. At that point, warning indicators for severe dengue may appear when the fever lowers to 38°C/100°F. Because of the possibility of severe bleeding, respiratory distress, fluid buildup, organ damage, and plasma leakage, severe dengue is potentially fatal. Prolonged vomiting, intense abdominal pain, exhaustion, fast breathing, agitation, blood in the stool or vomit, liver enlargement, and bleeding gums or nose are warning signs that physicians should watch out for. If there are any warning signs, you must closely monitor the patient for the next two days in order to prevent complications and lower your risk of dying. Throughout the convalescent stage, close observation should also be continued. [12]

There are various types of lab tests available for disease diagnosis, depending on when the patient presents. Both virus isolation and serological techniques can be used to test patient samples that

were taken during the first week of illness. In the early stages of the illness, the virus may be isolated from the blood. Numerous techniques are employed, with RT-PCR being regarded as the gold standard. They do, however, need skilled personnel and specialized equipment. NS-1, a protein generated by the virus, can also be used to identify it. By looking for anti-dengue antibodies, serological techniques such as ELISA can verify the existence of a recent or past infection. The IgM antibodies start to show up about a week after the infection and continue to show up for two to three months. The indication of a recent DENV infection is IgM presence. It takes longer for IgG antibody titres to develop and they can linger in the body for several years. IgG is indicative of a previous infection. [12,14] Thrombocytopenia (platelets $< 100 \times 10^9 /L$), leucopenia (TLC $< 4 \times 10^9 /L$), elevated alanine aminotransferase (ALT), or serum aminotransferase levels (AST) > 39 U/L are additional supportive tests in addition to cut-off values for dengue fever diagnosis.

METHODS

This study was conducted at Paediatric Department of Ziauddin Hospital, Karachi within a duration of 1st Oct 2021-30 Sep 2022. and comprised of 56 children. Our study did not include children who are older than 16 years old, have co-morbid conditions such as typhoid and malaria, or who do not receive hospital admission after visiting the emergency room.

Children of both genders aged 1–15 years, with the diagnosis of Dengue fever were included in this study. Affected children who were admitted to our hospital will have their records reviewed in accordance with the inclusion criteria. Data extraction will involve filling out a structured questionnaire. Age and gender of the child, weight, clinical signs (e.g., bleeding, joint pain, petechiae, fever, convulsions), length of hospital stay, platelet count, and dengue immunoglobulin

M (dengue IgM) and dengue non-structural protein 1 (NS1) will be among our variables. The result will be recorded as discharged, as left against medical advice (LAMA), or as deceased.

For all analyses, SPSS version 21 will be utilized. We will use the Shapiro-Wilk test to determine whether the data are normal. For continuous variables like age, weight, platelets count, Hb, AST, ALT, and HR, descriptive statistics like mean, standard deviation, and range will be computed. Regarding the categorical variables—gender, outcome, vomiting, fever, and rash—frequency and percentages will be determined. To evaluate the relationship between each independent variable and the outcome variable, bivariate analysis will be carried out using the chi-square test.

RESULTS

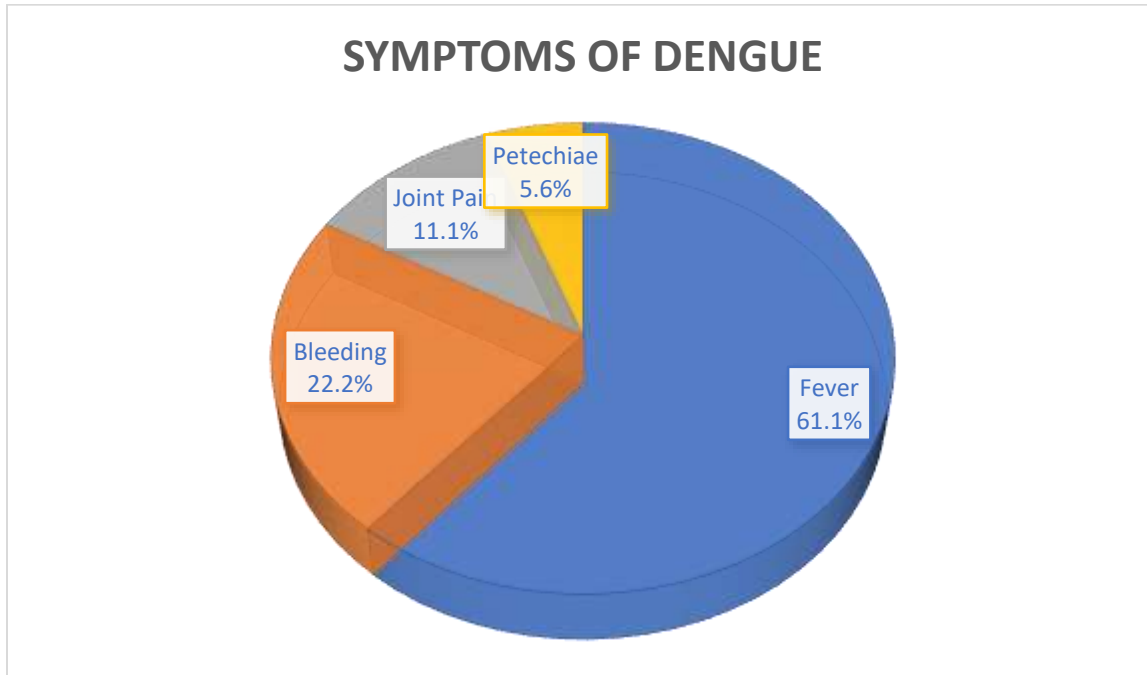
There were 19 (52.8%) male and 17 (47.2%) females among all children. Mean age of the children was 9.13 ± 7.35 years and mean weight was 20.8 ± 4.27 kg. Mean AST was 88.4 ± 2.47 U/L and ALT was 44.5 ± 3.22 U/L.(table 1)

Table-1: Children with baseline details

Variables	Frequency (56)	Percentage
Gender		
Male	19	52.8
Female	17	47.2
Mean age (years)	9.13 ± 7.35	
Mean Weight (kg)	20.8 ± 4.27	
Mean AST (U/L)	88.4 ± 2.47	
Mean ALT (U/L)	44.5 ± 3.22	

Most common symptom was fever in 22 (61.1%) followed by bleeding in 8 (22.2%) cases, joint pain in 4 (11.1%) and petechiae in 2 (5.6%) cases. (figure 1)

Figure-1: Symptoms of fever



Frequency of Ns1Ag positive patients were 29 (80.6%). 14 (38.9%) cases had platelet count > 100000/mm³. (table 2)

Table-2: Distribution of laboratory findings

Results	Frequency	Percentage
Ns1Ag	29	80.6
IgG	3	8.3
IgM	3	8.3
IgG/ IgM	1	2.8
Platelet count		
> 100,000/mm ³	14	38.9

< 100,000/mm ³	22	61.1
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Most common complication was capillary leak followed by liver failure, hemorrhage, fluid refractory shock and renal failure. (table-3)

Table-3: Complications among all cases

Results	Frequency	Percentage
capillary leak	24	42.9
Liver failure	17	30.4
Hemorrhage	7	12.5
Fluid Refractory shock	5	8.9
Renal failure	3	5.4

Mean hospital stay was 19.7±4.13 days. 24 (66.7%) patients were discharged, 10 (27.8%) cases were left against medical advice (LAMA) and 2 (5.6%) patients were died.(table 4)

Table-4: Hospitalization and outcomes of children with dengue fever

Variables	Frequency	Percentage
Hospital stay (days)	19.7±4.13	
Outcomes		
Discharged	24	66.7
LAMA	10	27.8
Died	2	5.6
Total	36	100

DISCUSSION

Even though a large body of literature is being written about the prevalence of dengue in both endemic and non-endemic nations, there is still a dearth of empirical information pertaining to the paediatric population. 60% of kids between the ages of five and ten had at least one dengue infection (immunoglobulin G, or "IgG" seroprevalence positive), according to a sizable multi-center study from India. Multivariate research revealed substantial relationships between seropositivity and household water storage systems and dwelling style [15]. In Puerto Rico, the Passive Dengue Surveillance System (PDSS) has documented almost 4000 cases of dengue in children under the age of 18 months. 33% of hospitalised children had severe dengue, out of all laboratory-positive cases, which required hospitalisation in 58% of cases [16]. Five-year research conducted in India found that 25% of blood samples from suspected dengue patients who were at least 15 years old tested positive for the virus. Male youngsters (58%) and those between the ages of 10 and 15 (46%) had higher prevalence rates [17].

Comparing hospitalised severe dengue cases to the disease from an epidemiological perspective, there is still a dearth of information, despite the illness's high frequency and growing severity with each outbreak. 10% of all fever episodes were serologically confirmed to be dengue in a large cohort study spanning ten Asian and Latin American nations; of these, 11–19% were severe enough to necessitate hospitalisation [18,19]. The percentage of hospitalisations attributed to dengue was high in 2021–2022, according to our analysis. Symptoms like joint pain, fever, and bleeding were frequent. Common complications included bleeding, jaundice, and petechiae. Because of neurological involvement, there was one instance of pleural effusion and fits. In almost all of these studies, fever, abdominal pain, vomiting, and skin rash were the common clinical presentation of dengue fever in children. Thrombocytopenia was also extremely common [20].

The bleeding presentation was commonly reported in the form of petechiae, nose bleeds, hematuria, hemoptysis, bleeding gums, hematemesis, melena, menorrhagia, and subconjunctival hemorrhages [21,22].

Frequency of Ns1Ag positive patients were 29 (80.6%). 14 (38.9%) cases had platelet count $> 100000/\text{mm}^3$. Our children were moving from the acute to the sub-acute and late phases of the illness, as evidenced by the four-day mean time between the start of symptoms and hospital admission. When the illness is at its most acute, DNS1 by itself has been shown to be sufficient. Just DNS1 was negative in all of our kids. The acute and late stages of the disease can be diagnosed with high sensitivity when DNS1 and IgM are both positive.

In our study, the prognosis for children admitted with dengue was extremely encouraging. Very few experienced serious, potentially fatal complications. Prolong hospital stay was observed and mortality rate was 5.6%. This was primarily because most patients had just begun to show symptoms of their dengue infections. Comparable to the observations made by other authors, thrombocytopenia was the most frequently observed laboratory finding in dengue patients reported here. [23,24]

Many earlier studies [25–27] have noted the existence of diarrhoea in dengue infection. Its mechanism hasn't been studied, though. Given that it is most common right before shock sets in, malabsorption-causing plasma leakage may be connected to it. More research is necessary to elucidate the precise nature of the link and mechanism between diarrhoea and DHF.

CONCLUSION

Males' children had a higher prevalence of dengue in the study. Regular check-ups showed that the severity of dengue did not worsen right away after infection, but rather increased gradually

over time. Most patients spent more than two weeks in the hospital, and there were two cases of fatality throughout the research.

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