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CLINICAL MANIFESTATION AND PATTERN OF DENGUE CASES ADMITTED IN TERTIARY CARE HOSPITAL KARACHI

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Abstract

Objective: *Clinical manifestation and pattern of dengue cases admitted in tertiary care hospital, Karachi.*

Patients and methods: *Prospective observational study was conducted in the Department of Pediatric, Civil Hospital, Karachi. Children who presented in OPD or Emergency with clinical symptoms suggestive of dengue fever and age between 1 years to 15 years were included in this study. Baseline and clinical variables were collected through a structured questionnaire to collect the data such as age, clinical manifestations, laboratory parameters, and outcome. Data was analyzed using SPSS version 26.*

Results: *Of the 249 patients, 127 (51.0%) were females. The overall mean age was 11.18±4.87 years. The most common clinical manifestations were fever (n = 249, 100%), followed by headache (n = 188, 75.5%), and irritability (n = 136, 54.61%). Most of the patients with dengue fever recovered (n = 185, 74.29%) and did not require admission (n = 64, 25.70%). Patients with rashes (n = 41, 64.06%), joint pain (n = 36, 56.25%), bleeding from nose (n = 20, 31.25%), bleeding from gums (n = 15, 23.43%), patients who had bruises (n = 22, 34.75%), patients with difficulty of breathing (n = 5, 7.81%), patients with low systolic blood pressure (mean difference 12.26±3.71 mmHg), low platelets count (mean difference 56.03±21.5 x 10^3), and patients with raised alanine aminotransferase (mean difference 20.77±4.31 IU/l) had significantly higher chances of hospitalization, p value <0.05.*

Conclusion: *Dengue fever is common among young females with most of the patients presented with fever, headache, and irritability. Factors such as bleeding, thrombocytopenia, raised ALT, and shortness of breath were associated with higher rates of hospitalization.*

INTRODUCTION

Global public health is now concerned about dengue, particularly in most tropical and subtropical nations. The dengue virus has spread to over 130 countries in the last 60 years, resulting in 100 million symptomatic cases and close to 10,000 fatalities annually. In addition, over 50% of the world's population is susceptible to dengue transmission, with Asia accounting for the bulk of cases, followed by Africa and America (1). The World Health Organization (WHO) estimates that 400 million cases of dengue fever occur each year with Asian nations accounting for the majority of these occurrences (2). Currently known as endemic in Pakistan (3), dengue poses a risk to public health, particularly for children (4). Superimposed variables include low socioeconomic status, low public health knowledge, inadequate cleanliness, and unsanitary circumstances lead to a more severe type of dengue fever in Pakistan (5, 6).

In a previously published study authors have observed that children aged 12.5 years and over who had dyspnea and plasma leakage had a 92.9% predictive likelihood of developing severe dengue (7). In Southeast Asia, it ranks among the top causes of mortality for children. Nearly 95% of dengue cases in youngsters occur in those under the age of 15 years. Children, especially newborns, are more susceptible to severe dengue fever because to their undeveloped hemodynamic system (8). Asian nations' national surveillance statistics consistently indicate that children 4–9 years old and newborns under 1 year old are most at risk for severe dengue sickness (9).

The first dengue fever epidemic in Pakistan was documented in Karachi in 1994. Large outbreaks with 6376 cases and 23 fatalities were later reported from Swat in 2013, Lahore in 2011, and Karachi in 2005. The two serotypes that were found to be most common in Pakistan were DEN-2 and DEN-3 (10). Studies have indicated that a warm, humid climate is conducive to mosquito vector reproduction. Certain risk factors for dengue fever have also been documented by a number of research. Vectors seem to favor small, stagnant water puddles found in tires, plants, and ditches as their preferred breeding grounds. The best ways to avoid dengue disease are wearing long sleeves and legs, applying insect repellent, and controlling the vectors via thermal fogging and insecticide residual spray (11). Considering the significance of dengue in Pakistan and also lack of clinical studies in children and adolescents, this study aims to determine the clinical manifestations and pattern of dengue cases admitted in a tertiary care hospital Karachi, Pakistan

Methodology:

A prospective observational study was conducted during the dengue outbreak that lasted from 3rd March 2022 to 10th November 2022. The study was conducted in the Department of Pediatrics, Civil Hospital, Karachi. All the patients between the ages of one and fifteen (01 - 15) years, history of fever lasting more than 48 hours without any obvious infection-related foci, fever lasting more than 24 hours along with symptoms like headache, eye pain, joint pain, vomiting, or altered consciousness with a positive dengue NS1 antigen test, and presented with signs & symptoms indicative of dengue fever in the out-patient department (OPD) or emergency were included in this study. The exclusion criteria for this study were; children with established chronic disorders such as chronic liver and kidney disease, fever with a clear infection focus, or negative NS1 antigen, children with concomitant malaria or bleeding diathesis, and those who did not consent to participate. An informed consent in the language of understanding was provided to the parent or caregiver of patient.

A structured questionnaire was used to collect the baseline and clinical data including age, gender, and area of residence. Laboratory investigations was performed including alanine transferase (ALT), NS1 antigen, total leukocyte count (TLC), total platelet count (PLT), hemoglobin (Hb), and hematocrit (HCT) measured at the hospital's laboratory. Where indicated, an abdomen ultrasound, a chest x-ray, and a coagulation profile were also performed. Clinical data included signs & symptoms indicating dengue fever such as abdominal pain or tenderness, prolonged vomiting (incapable of being tolerated orally), 4-6 hours voiding interval, petechiae on the skin, hepatomegaly, evidence of mucosal bleed, clinical fluid accumulation (pedal edema, ascites, or pleural effusion), and an increase in hematocrit with a rapid decrease in platelets were the warning signs. Severe bleeding, shock symptoms (cold, clammy skin, prolonged capillary refill, weak pulse, low blood

pressure), signs of fluid accumulation (tender liver >2 cm or pedal edema or pleural effusion), and signs of organ damage (liver; AST or ALT ≥1000, neurological and renal impairment) were considered as cases of severe dengue. Narrow pulse pressure (less than 20 mmHg) or hypotension for age (systolic pressure less than 80 mmHg for children under five, or less than 90 mm Hg for those five years of age and above) were the two criteria used to characterize hypotension. Fast breathing was measured as follows: >50 breaths/min in children over 2–12 months, >40 breaths/min in children 1–5 years, and >30 breaths/min in children over 5 years. ≥40% was considered high HCT. Less than 4000 × 103/μL was considered to be leukopenia. The definition of thrombocytopenia was PLT <150,000/mm^3. The threshold for severe thrombocytopenia was PLT of 50,000/mm^3 or lower. The difference between hematocrit maximum minus hematocrit minimum divided by hematocrit minimum multiplied by 100 was used to calculate the percent change in hemoconcentration.

Oral rehydration, antipyretics, and antiemetic medications were administered to the outpatients as symptomatic care. The inpatient group requested for admission to the tertiary care government hospital at Pakistan. In accordance with the recommendations, the patients monitored as outpatients until day 14 for symptoms, clinical examinations to check for warning indications, clinical worsening, or recovery. For the first two follow-ups, the temperature readings, blood counts (Hb, HCT, TLC, and PLT), and any other tests that the treating physician deemed essential were performed every day. After that, the tests were repeated every two days until the patients start to improve and recover. According to the conventional procedure, being afebrile for 48 hours, improving appetite, clinical well-being, and rising trends in PLT were consider as the requirements for recovery. Patients who failed to show up for follow-up were tracked down over the phone, and inquiries and notes about their clinical symptoms and reason for defaulting were made. Follow-up was done at day 14. Recovery or hospitalization was the major outcome measure.

Data Analysis method:

Statistical Package for Social Sciences (SPSS) version 26 was used to enter and analyze the data. To determine the frequency and percentages of categorical variables, descriptive statistics was performed. For continuous variables, the mean and standard deviation (SD) was performed. Where appropriate, the independent t-test and the x^2 test was employed to determine the statistical significance between various variables. A P-value of less than 0.05 was considered as significant.

Results:

A total of 249 children & adolescents with dengue fever were analyzed. The overall age of enrolled patients was 11.18±4.87 years in which mostly belongs to age group ≥7 – 15 years (n = 156, 62.65%). Females were predominant as compared to males, 51.0% (n = 127) and 48.99% (n = 122), respectively. The most common clinical manifestations were fever (n = 249, 100%), followed by headache (n = 188, 75.5%), and irritability (n = 136, 54.61%). While serious complications of dengue such as bleeding from nose and difficulty in breathing found in 8.83% (n = 22) and 2.4% (n = 06) of the patients with dengue fever. Patients with dengue fever were anemic (11.31±3.17 - gm/dL), low platelets count (79.26±29.66 x 10^3), and raised alanine transaminase levels (79.26±29.66 – IU/l). Table 1, 2 and graph 1.

Most of the patients with dengue fever recovered (n = 185, 74.29%) and did not require admission (n = 64, 25.70%). Table no. 3 and 4 shows association of clinical manifestations and laboratory parameters with outcome among patients with dengue fever. Patients with rashes (n = 41, 64.06%), joint pain (n = 36, 56.25%), bleeding from nose (n = 20, 31.25%), bleeding from gums (n = 15, 23.43%), patients who had bruises (n = 22, 34.75%), patients with difficulty of breathing (n = 5, 7.81%), patients with low systolic blood pressure (mean difference 12.26±3.71 mmHg), low platelets count (mean difference 56.03±21.5 x 10^3), and patients with raised alanine aminotransferase (mean difference 20.77±4.31 IU/l) had significantly higher chances of hospitalization as compared to patients without these clinical manifestations, p value <0.05. Table 3 & 4.

Discussion:

Dengue fever usually presents as fever, nausea, vomiting, body ache, headache, joint pain, and weakness but in severe cases it may present as bruises,

bleeding from gums, bleeding from nose, sometimes as difficulty in breathing, and shock (12). Children are more prone to severe form of dengue fever (13) that is why they need to be diagnosed and manage at the earliest. Pakistan is prone to dengue fever due to multiple reasons such as favorable mosquito breeding conditions and hot & humid summer climate. In our study the most common clinical manifestation was presence of fever (100%) which was found among all patients. While, headache, irritability, and nausea were the common clinical manifestations after fever and accounts for 75.5%, 54.61%, and 51.8%, respectively. The same findings were observed in a previously conducted study on children with dengue fever (14). Another previously conducted study by Verhagen LM and colleagues is in agreement and also emphasized that children are more prone to severe form of dengue disease (15). Serious complications of dengue fever such as bleeding from nose, gums, difficulty in breathing is less common but cannot be ignored. In our study bleeding from nose, gums, and difficulty in breathing are as follows, 8.83%, 7.22%, and 2.4%, respectively. In a recently published study from multiple cities of Pakistan also observed pleural effusion and hepatomegaly in children with dengue fever (16).

Dengue fever is usually subsided by itself but in severe cases it may need hospitalization. In Pakistan, despite the high prevalence and increasing severity with every outbreak, there still is lesser data explaining the characteristics and outcomes of hospitalized severe cases of dengue as compared to the epidemiological perspective of the illness. In a large cohort conducted across 10 Asian and Latin American countries, 10% of all febrile episodes were serologically proven to be dengue; of these 11-19% were severe enough to require hospitalization (17). Study conducted by Alejandria MM has observed in his study review that dengue fever among children is rarely fatal and fatality rate is less than 1% (18). Bodinayake CK and colleagues observed 0.2% mortality rate while rate of hospitalization was 14.3% (19). On the other hands, in our study we did not observed mortality among children but rate of hospitalization was higher (25.70%) as compared to previously mentioned study. This difference could be due to area where the studies were conducted. Previously published study was conducted in Sri Lanka where the healthcare facilities are comparatively better than Pakistan. Another reason could be time period when the studies were conducted like, our study was conducted at the time of dengue outbreak while previously conducted study was conducted without any outbreak of dengue fever. While another recently conducted study from Bangladesh by the Gosh K and colleagues observed that during the dengue season more than 70% of the patients stayed at hospital (9). Study from Karachi Pakistan also favors findings of our study as they observed 16.1% hospitalizations in 2019, 33.3% in 2018, and 50.5% in 2017 (20).

In our study we also observed the factors leading to hospitalization of children with dengue fever. Patients with rashes (64.06%), joint pain (56.25%), bleeding from nose (31.25%), bleeding from gums (23.43%), patients who had bruises (34.75%), patients with difficulty of breathing (7.81%), patients with low systolic blood pressure (mean difference 12.26±3.71 mmHg), low platelets count (mean difference 56.03±21.5 x 10^3), and patients with raised alanine aminotransferase (mean difference 20.77±4.31 IU/l) had significantly higher chances of hospitalization, p value <0.05. The same factors were also observed in previously conducted international studies from Indonesia (21), Mexico (22), India (23), Vietnam (24), Brazil (25), and Pakistan (26).

Most of our study subjects had mean age of 11.18±4.87 years and most of them were females (51.0%). Different studies have shown different mean age of children infected with dengue fever. Such as study conducted by Mishra S and colleagues have observed mean age was 8.7 years at the time of admission while most of the children presented at the age of 11 years (27), which is similar to our study. This is also confirms by the study conducted at Thailand in which authors have observed higher prevalence of dengue fever among children having age less than 15 years (28).

Limitations

We identify key study limitations and suggest directions for future research on this topic: (1) this is a single center study and only included patients presented at Civil Hospital, Karachi (2) seasonal variations have not been considered. A longer duration of study is required to interpret accurately for it; (3) a study comprised of a small number of patients larger sample may be a true representative.

Conclusion:

The present study observed and provides scientific data regarding dengue fever among children. Dengue fever is common among young females with most of the patients presented with fever, headache, and irritability. Factors such as bleeding, thrombocytopenia, raised ALT, and shortness of breath were associated with higher rates of hospitalization.

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Table 1: Baseline parameters of study subjects (n = 249)

Parameters		
Age - years		
Mean±SD	11.18±4.87	
Age groups	**Frequency**	**Percentage**
1 - 7 years	93	37.34
≥7 - 15	156	62.65
Gender		
Male	122	48.99
Female	127	51
Area of residence		
Urban	162	65.06
Rural	87	34.93

Graph 1: Clinical manifestations of patients with dengue fever (N = 249)

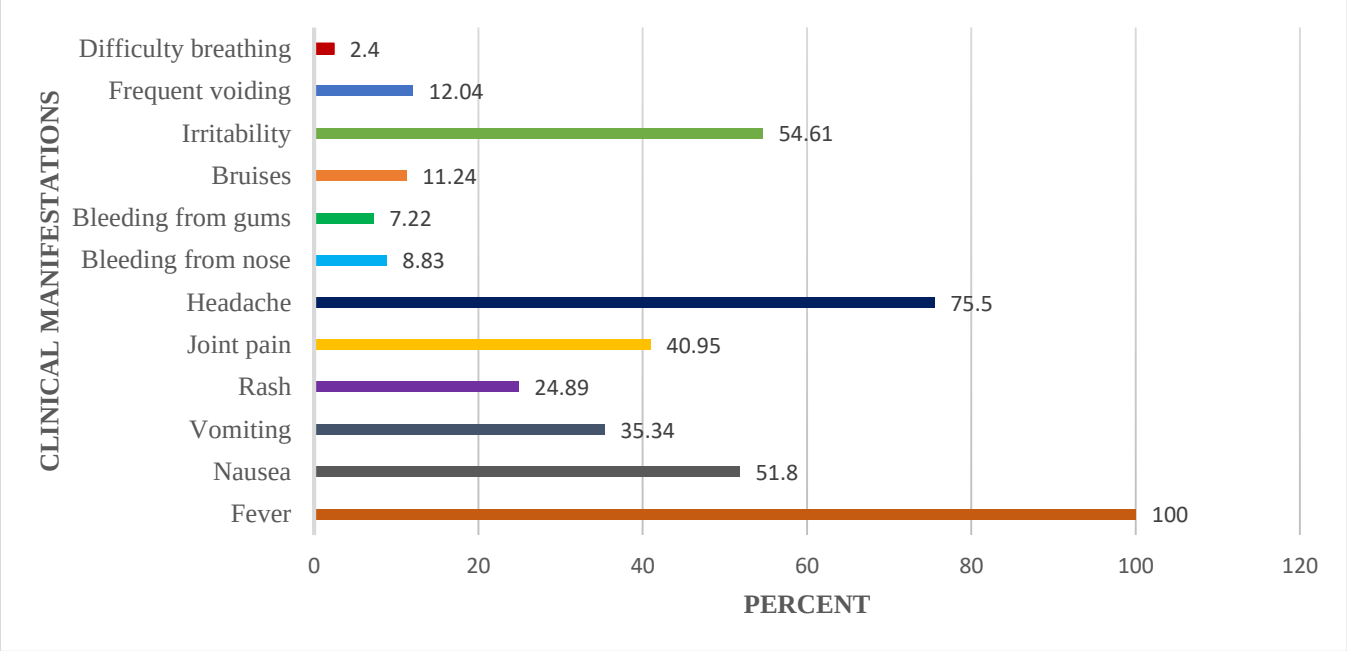

Table 2: Vital signs and laboratory parameters of study subjects with dengue (N = 249)

Parameters	Minimum	Maximum	Mean±SD
Systolic blood Pressure - mmHg	65	135	115±10.87
Diastolic blood pressure - mmHg	50	90	65±8.34
Hemoglobin - g/dL	7	14	11.31±3.17
Platelets - 103/**µ**L	20	230	79.26±29.66
Hematocrit - %	40	60	51.76±5.91
Alanine transaminase - IU/L	25	256	106.42±16.77

Table 3: Association of clinical manifestations & pattern of dengue fever with outcome (N = 249)

Parameters	Total	Outcome		p value
	(N = 249) n, %	Recovered (n = 185)	Hospitalized (n = 64)	
Fever	249 (100%)	185 (100%)	64 (100%)	0.09
Nausea	129 (51.8%)	99 (53.51%)	30 (46.87%)	0.24
Vomiting	88 (35.34%)	66 (35.67%)	22 (34.75%)	0.39
Rash	62 (24.89%)	21 (11.35%)	41 (64.06%)	0.02*
Joint pain	102 (40.95%)	66 (35.67%)	36 (56.25%)	0.001*
Headache	188 (75.5%)	138 (75.59%)	50 (78.12%)	0.91
Bleeding from nose	22 (8.83%)	2 (1.08%)	20 (31.25%)	0.01*
Bleeding from gums	18 (7.22%)	3 (1.62%)	15 (23.43%)	0.001*
Bruises	28 (11.24%)	6 (3.24%)	22 (34.75%)	0.04*
Irritability	136 (54.61%)	90 (48.64%)	46 (71.87%)	0.65
Frequent voiding	30 (12.04%)	24 (12.97%)	6 (9.37%)	0.37

Difficulty breathing	6 (2.4%)	1 (0.54%)	5 (7.81%)	0.001*

*p value <0.05 considered statistically significant

Table 4: Association of laboratory parameters of dengue fever with outcome (N = 249)

Parameters	Overall	Outcome			p value
	n = 249 Mean±SD	Recovered (n = 185) Mean±SD	Hospitalized (n = 64) Mean±SD	Mean difference	
Systolic blood Pressure - mmHg	115±10.87	118.6±5.28	106.34±8.99	12.26±3.71	**0.02***
Diastolic blood pressure - mmHg	65±8.34	64.71±2.45	61.22±4.27	3.49±1.82	0.91
Hemoglobin - g/dL	11.31±3.17	12.11±2.65	11.29±3.01	0.82±0.36	0.08
Platelets - 103/**µ**L	79.26±29.66	101.10±18.24	45.07±39.74	56.03±21.5	**0.001***
Hematocrit - %	51.76±5.91	46.08±5.43	50.49±1.12	4.41±4.31	0.73
Alanine transaminase - IU/L	106.42±16.77	85.62±12.43	106.39±8.12	20.77±4.31	**0.03***

*p value <0.05 considered statistically significant