Original Article

Clinical and Demographic Characteristics of Dengue Patients in Public Sector Hospital

Azizullah Khan Dhiloo[1*], Madiha Sattar Ansari[1], Sana Tanzil[2], Nazima Zain[3], Amanullah Abbasi[4]

ABSTRACT

OBJECTIVE: To determine the patterns of demographics, clinical presentation, and outcome among dengue patients treated at Dr. Ruth K.M. Pfau Civil Hospital, Karachi.

METHODOLOGY: This retrospective cross-sectional study comprised 1003 suspected dengue cases presented at Dr. Ruth K. M. Pfau Civil Hospital, Karachi, between September 2019 and February 2020. Medical records of 328 patients who tested positive for dengue infection on immune chromatographic technique (ICT) for recombinant NS1 antigen and/or IgM serology were included in the analysis.

RESULTS: Among 1003 suspected cases, 328 cases were laboratory-confirmed dengue fever; 82.3% (n=270) presented with acute dengue infection as they were positive for NS1 antigen only. 13.1% (n=43) of the patients were IgM-positive, whereas 0.9% (n=3) were positive for IgG. 3.6% (n=12) of the laboratory -confirmed dengue patients were positive for both NS1antigen and IgM. The majority of the dengue patients were from the district of South Karachi. Among all in-patients, 77 % (n=94) of the patients presented uncomplicated dengue fever, while 21.3% (n=26) of hospitalized dengue patients presented with dengue hemorrhagic fever. However, 1.6% (n=2) of hospitalized patients presented with dengue shock syndrome. Mortality was 1.6% (n=2).

CONCLUSION: We conclude that the epidemiology of dengue infection and seasonal disease variability in Pakistan's urban settings has not changed over the last decade but warrants continuous monitoring due to climate change. The disease is still more prevalent among young males with a classic presentation of dengue fever. Dengue hemorrhagic fever is relatively less common, while very few patients develop dengue shock syndrome, contributing to mortality.

KEYWORDS: Dengue virus, Fever, Karachi, Seasonal variation.

INTRODUCTION

The dengue epidemic is a global public health and social problem and inflicts a significant health, social, and economic burden on the populations of endemic areas. In recent decades, the incidence of dengue virus infection has increased dramatically. Dengue, also known as Break –Borne disease, represents one of the most emerging public health challenges throughout the World[1].

The bite of infected arthropod species such as mosquitoes, tritons, ticks, bugs, black flies and sand flies mainly transmits vector-borne infections. The diseases transmitted by mosquitoes include Dengue, Chikungunya, Malaria, West Nile virus, Yellow fever, Zika virus, Filariasis, Tularemia, Japanese encephalitis, and Saint Louis encephalitis. These diseases are common problems in tropical and sub-tropical areas with poor water, sanitation, and hygiene (WaSH)[2].

Dengue virus is a single-stranded positive-sense RNA virus with four different serotypes (DEN-1 to 4) and belongs to the genus Flavivirus, Flaviviridae family. The Dengue virus is spherical with three structural proteins. It is a vector-borne disease, mainly caused by the bite of an infected mosquito, particularly Aedes Aegpti, and is found in tropical and subtropical regions. It usually breeds during warmer climates[3].

Since the Second World War, dengue has become a global problem and is endemic in more than 100 countries, including Southeast Asia. In 2015, America reported more than 2 million dengue cases, leading to 1181 deaths; in 2016, dengue cases increased to 3.34 million throughout America, Southeast Asia and Western Pacific[4, 5].

In 2013, the World Health Organization (WHO) reported over 370 million cases of dengue fever worldwide. Dengue Fever has worsened the health-

[1]*Department of Infectious Diseases (Isolation ward), Dow University of Health Sciences, Dow Medical College, Dr. Ruth K M Pfua, Civil Hospital, Karachi, Sindh-Pakistan.*
[2]*Department of Community Medicine, Dow Medical College, Dow University of Health Sciences, Karachi, Sindh-Pakistan.*
[3]*Department of Gyne & Obs. Dr. Ruth K M Pfua, Civil Hospital, Karachi, Sindh-Pakistan.*
[4]*Department of Medicine, Dow University of Health Sciences, Dow Medical College, Dr. Ruth K M Pfua, Civil Hospital, Karachi, Sindh-Pakistan.*
***Corresponding:** azizullah.khan@duhs.edu.pk*
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related mortality and morbidity in Pakistan as the country has been facing an unprecedented intensity for the last few years, which has adversely affected both social and psychological grounds. In 1995, Karachi reported 145 cases, out of which one died. In recent years, Karachi has been the worst affected region in Pakistan, and the transmission of dengue fever has intensified with geographic expansion [6,7]. In Pakistan, the highest numbers of confirmed dengue cases were recorded for two consecutive years, i.e. 2010 and 2011. In 2011, the largest dengue outbreak was reported in Lahore with 22,562 dengue cases and 363 deaths and in 2013 (Swat KP province) reported 8343 dengue cases and 57 deaths with predominant dengue serotype DENV-2 & 3 [8,9]. Hence, dengue causes many cases and contributes to morbidity related to infectious diseases in various regions of Pakistan[10].

Dengue infection causes 20% symptomatic infection, usually a mild flu-like illness called dengue fever. The mild disease is associated with intense body aches and retro-orbital and joint pain. However, the disease can lead to severe manifestations like hemorrhage and subsequent vascular leakage, which present with bleeding, thrombocytopenia and pleural effusion known as dengue hemorrhagic fever, some of the individuals presented with warning signs like abdominal pain, persistent vomiting, and change in mental status or marked temperature change. Subsequent plasma leakage can lead to shock, respiratory distress, organ impairment and critical bleeding, known as dengue shock syndrome[12].

The Laboratory diagnosis of Dengue virus includes detection of the virus by viral culture technique, viral nucleic acid by Real-time PCR, detection of viral antigen by immune chromatographic technique (ICT) for recombinant NS1 antigen and detection of IgM / IgG antibodies by Enzyme link immunoassay ELISA technique. In the acute phase, the virus, viral nucleic acid or NS1 antigen can be used to diagnose the disease. After the acute phase of infection is resolved, a serological method is used to confirm the diagnosis. It takes three to five days to develop IgM antibodies after the onset of symptoms. The antibodies increase to 80% in five days, while the antibody titer reaches 99% on the 10th day. However, the highest antibody titer levels are achieved two weeks after the onset of symptoms. The antibodies remain in patients' blood for the next two to three months, and a decline in titer is followed by development and a rise in serum IgG levels after several months. Secondary dengue infection is another serotype of dengue virus that has previously infected a host, and the predominant antibody is IgG, which is detectable at high levels, even in the patient presented in the acute phase of infection [13]. Dengue is a self-limiting disease, so treatment is symptomatic with oral rehydration, antipyretics and, in severe cases, blood products. The treatment may require intravenous fluids and blood transfusion in case of serious illness such as Dengue Hemorrhagic Fever[14-17].

There were 54,000 cases of dengue fever in 2019, of which 14,000 were in Sindh, with 40 deaths with a mortality rate of 0.28%. Over time, the rise in dengue cases in Sindh warrants a review of the current situation regarding the disease's sociodemographic and clinical presentation.

Therefore, the objective of our study was to determine the Patterns of demographic and clinical presentation among Dengue Patients treated at Dr. Ruth K.M. Pfau Civil Hospital, Karachi. This information will help better understand and plan to manage Karachi's dengue outbreaks.

METHODOLOGY

A retrospective cross-sectional study was conducted at Dr. Ruth K.M. Pfau Civil Hospital, Karachi. Data of all the suspected dengue cases (in-patients as well as outpatients) who were investigated for dengue infection and tested positive on immune chromatographic technique (ICT) for recombinant NS1 antigen and/or IgM serology between September 2019 and February 2020 was included in this study. Hence, a total of 1003 blood samples, including in-patients and outpatients who presented at Dr. Ruth K.M. Pfau Civil Hospital, Karachi, with dengue symptoms and were sent to the laboratory to confirm the presence of dengue infection in the blood, 328 tested positive for dengue fever. All the tests were performed at Ruth K.M. Pfau Civil Hospital laboratory, a well-equipped laboratory with a state-of-the-art facility. The Civil hospital laboratory has a well-established computerized patient information and management system. However, the information regarding demographic characteristics, signs and symptoms such as fever, mucosal bleeding, hemorrhagic shock and outcomes like death and recovery or hospital discharge (in case of in-patient) from in-patients was collected by reviewing the medical records. All the information gathered from patients` records was recorded in writing with the help of a specifically designed structured proforma. Among all the patients who tested positive for dengue infection, those with incomplete medical records or missing demographic information were excluded from the study. As the study was based on available laboratory or health records, all the available data was included in the analysis, and no specific sample size or sampling strategy was calculated.

Moreover, no further information was gathered from outpatients due to the unavailability of their medical records at the hospital. Hence, the study mainly focused on in-patients admitted with dengue at Civil Hospital Karachi. The ethical approval for this study was obtained from the Institutional Review Board (IRB) of Dow University of Health Sciences Ref: IRB-1728/DUHS/ Approval/2020.

Data on confirmed dengue cases was further analyzed using the Care Us Combo dengue kits for Non-structural protein 1 antigen and antibody. The

sensitivity and specificity of kits were 92.1% and 75.8%, respectively. The study achieved a response rate of around 98% for the information collected from the outpatients.

All the data was entered and analyzed using Statistical Package for Social Science SPSS 16. Descriptive statistics were calculated for demographic information and health-related characteristics. Median and IQR (inter-quartile range) were calculated for quantitative continuous variables, while proportions were calculated for qualitative categorical variables. A chi-square significance test was applied with a 5% significance level to compare the characteristics of patients with different disease outcomes.

RESULTS

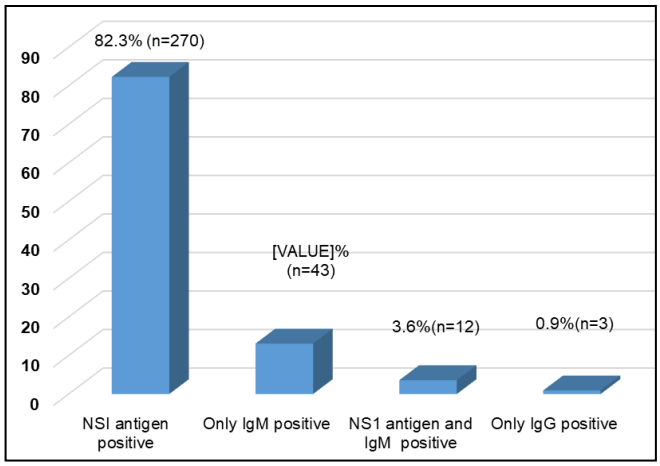
Only 32.7% (n=328) of 1003 samples from suspected patients were positive for dengue infection. The median age of patients with laboratory-confirmed dengue infection was 30 years (IQR =25 years). Among all the laboratory-confirmed dengue cases, 68.6% (n=225) were males, and 31.4% (n=103) were females. Among all the dengue patients included in this study, 62.8% (n=206) were outpatients, and 37.2% (n=122) were in-patients admitted to medical wards of civil hospital Karachi. Most confirmed dengue cases were reported from District South and District West of Karachi, with a proportion of 45.1% and 23.0%, respectively. However, the most confirmed dengue cases were reported in October 2019 (**Table I**).

Table I: Sociodemographic characteristics of dengue patients (n =328)

Variable	Frequency (n)	Percentage (%)
Median Age (IQR) 30 years (25 years)		
Age (in completed years)		
18 years or younger	43	19.5
19-25 years	69	30.0
26 years and above	114	50.5
Sex		
Male	225	68.6
Female	103	31.4
Patient status		
Outpatient	206	62.8
In-patient	122	37.2
Area of Residence		
South	148	45.1
West	75	23.0
East	40	12.1
Central	38	11.6
Korangi and Malir	27	8.2
Time distribution of cases		
September	87	26.5
October	168	51.2
November	50	15.2
December	17	5.2
January	04	1.3
February	02	0.6

Most of the laboratory-confirmed dengue cases (including outpatients and in-patients), i.e. 82.3% (n=270), were presented with acute dengue infection as they were positive for NS1 antigen only. 13.1% (n=43) of the patients were positive for IgM, whereas 0.9% (n=3) were positive for IgG. 3.6% (n=12) of all the laboratory-confirmed dengue patients were positive for both NS1antigen and IgM (**Figure I**)

Figure I: distribution of serology markers for Dengue Infection (n-328)



Out of 122 hospitalized or in-patients, 77.0% (n=94) of the patients presented uncomplicated dengue fever, while 21.3% (n=26) of the dengue in-patients presented with dengue fever and mucosal hemorrhage. However, 1.6% n=2) of dengue in-patients presented with dengue shock syndrome.

Among all the in-patients, 84.4% (n=103) dengue cases presented with fever, 12.2% (n=15) cases presented with mucosal bleeding from different sites, whereas 31.9% (n = 39) cases presented with myalgia, 2.4% (n=3) presented with arthralgia. 25.4% (n=31) of dengue complained of vomiting, and 10.6% (n=13) complained of headache respectively. The petechial rash was seen in 9% (n=11) of in-patient dengue cases, abdominal pain in 4.9% (n=6) cases, altered consciousness in 2.4% (n=3), and diarrhea was present in 1.6% (n=2) of in-patient laboratory-confirmed dengue cases. The median length of hospital stay was four days (IQR=2 days), and mortality was 1.6%(n=2). (**Table II**)

Table II: Distribution of disease presentation, symptoms and outcome among Dengue in-

Variable	Frequency (n)	Percentage (%)
Dengue presentation		
Dengue Fever	94	77.1
Dengue Hemorrhagic Fever	26	21.3
Dengue Shock Syndrome	02	1.6
Symptoms reported*		
Fever	103	84.4
Abdominal Pain	6	4.9
Altered Consciousness	3	2.4
Petechial Rash	11	9.0
Myalgia	39	31.9

Symptoms reported*		
Arthralgia	03	2.4
Vomiting	31	25.4
Headache	13	10.6
Diarrhea	02	1.6
Per orbital pain	03	2.4
Gum Bleed	07	5.7
Epistaxis	04	3.2
Malena	02	1.6
Hemoptysis	01	0.8
Hematuria	01	0.8
Disease outcome		
Fully recovered	120	98.4
Mortality	02	1.6
Median Length of Hospital Stay (IQR) 4 days (2 days)		

**Multiple responses possible*

DISCUSSION

This study determined the burden of dengue cases and their clinical and demographic presentation pattern in one of the largest tertiary care public hospitals in Karachi. The study found that 32.7% of all suspected dengue cases were confirmed as confirmed dengue cases when investigated in the laboratory. However, most cases of dengue infection were presented in the South district, which can be explained by the presence of many densely populated squatter settlements and slums. Moreover, the proximal location of the hospital to the district south is another explanation for the dominant representation of the district south in the data. The majority of the dengue patients were male. This finding can be explained by the sociocultural dynamics of the community, where men have relatively more frequent and prolonged outdoor exposures than females. This finding is supported by previous studies conducted in India and Pakistan [18-21]. However, the other possible reasons for these sex-based differences in the epidemiology of dengue and various other infectious diseases need further research [22]. This study found a median age of 24 years for confirmed dengue cases. This finding is consistent with the conclusions of a previous study from Karachi conducted in 2007 by Khan E. and colleagues [18]. Hence, it can be stated that over the last decade, there has been no change in the average age of presentation among dengue patients in Karachi.

Moreover, this study found a gradual rise in dengue cases in September, with a peak in October followed by a decline afterwards; this indicates that dengue cases tend to rise post-monsoon season, and this conclusion is in line with the findings of previous studies from Pakistan[18,23].

This study reported fever as the most typical symptom of dengue infection, which is in line with the known clinical manifestations of this disease. Our study reported many other symptoms like vomiting, headache, myalgia, abdominal pain, diarrhea, altered mental status and rash. However, only two patients presented with dengue hemorrhagic shock. The present study reported bleeding tendencies in gum bleeding, petechial rash, epistaxis, hemoptysis, hematuria, and melena[24]. However, our study cannot conclude the pediatric population because the sample mainly comprised adult dengue patients. All the manifestations of dengue reported in our study population are already identified as part of the natural history of this disease[12,13].

Furthermore, the literature reports that the clinical features of dengue infection may vary according to the age group[19]. The typical clinical manifestations of dengue infection among the pediatric population are fever, vomiting, abdominal pain and skin rash. However, in Pakistan, there is still a scarcity of local evidence determining the clinical features and outcomes of dengue infection in the pediatric population.

Most patients presented with acute dengue infections with positive NS1 antigen, and 13.1% were positive for IgM, whereas 3.65% were positive for both NS1antigen and IgM, whereas 0.91% were presented with secondary dengue infection. Acute dengue infection can be diagnosed by detecting NS1 antigen or IgM antibodies in serum and secondary dengue infection with predominant antibody IgG, which is detectable at high levels in serum[12,25]. The higher frequency of acute infection cases, as represented by serology markers, validated the new seasonal surge in dengue cases between September and November 2019. The literature supports the use of NSI antigens to diagnose acute infections[25].

This study has limitations, such as providing information from only one public sector tertiary care hospital in Karachi, which limits its generalizability. Since this was a hospital-based study, it cannot reflect the actual situation at a community level. Moreover, the sociodemographic characteristics of the population in this study might be notably different from those presenting with dengue in private hospitals. This further limits the generalizability of the study findings. Furthermore, due to the retrospective nature of this study, analysis was confined to available patient data, which resulted in the inclusion of limited sociodemographic variables, affecting the overall scope of this study. However, these kinds of small-scale studies are an essential source of evidence in countries like Pakistan, which lack a hospital-based surveillance system for continuous surveillance and monitoring of the change in disease patterns in the catchment population. Such evidence also helps guide and plan integrated vector management to prevent outbreaks as required.

CONCLUSION

This study concludes that the epidemiology of dengue infection and seasonal disease variability in Pakistan's urban settings has not changed over the last decade. The disease is still more prevalent among young males with the classic presentation of dengue fever, followed by dengue hemorrhagic fever, and very few

patients developed dengue shock syndrome with low mortality. Climate change is an emerging issue that can change dengue fever from a seasonal disease to a year-round infection, and this needs continuous monitoring of disease trends in future large-scale studies.

Ethical permission: Dow University of Health Sciences IRB letter No. IRB-1728/DUHS/ Approval/ 2020.

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Data Sharing Statement: The corresponding author can provide the data proving the findings of this study on request. Privacy or ethical restrictions bound us from sharing the data publically.

AUTHOR CONTRIBUTIONS

Dhiloo AK: Concept, data collection, manuscript writing, revision and final approval
Ansari MS: Concept proposal, data collection, manuscript writing, data analysis and final approval
Tanzil S: Data analysis, manuscript writing, revising and review for the final approval
Sain N: Data collection, manuscript writing, results revision, reference setting and final approval
Abbasi A: Manuscript concept, proposal review, writing of paper including discussion on the topic with conclusion and final approval

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