

CLINICAL PROFILE OF DENGUE INFECTION IN PEDIATRIC AGE GROUP AT SOCIAL SECURITY TEACHING HOSPITAL, LAHORE

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ABSTRACT

Background: Dengue viral infection is a significant tropical disease and have become a major global public health concern.

Objective: To sketch the evolving clinical spectrum of dengue especially highlighting the unusual manifestations.

Methods: Data of 120 suspected dengue fever cases was collected, compiled, and analysed during the monsoon and post-monsoon seasons in the year 2021 at the Department of Pediatric Medicine, Social Security Teaching hospital, Lahore. Patients with serological confirmation of dengue infection were classified according to Dengue Good Clinical Practice (GCP) Guidelines 2020. Clinical parameters were studied.

Results: Out of 120 suspected patients with dengue fever enrolled in the study, 48 (40%) had serologically confirmed dengue infection. Out of 120 cases, 68 (56.66%) patients were males and 52(43.33%) were females. 66.66 % patients had classical dengue fever while 33.33% had dengue hemorrhagic fever. DHF grade I/II was seen in 25 % cases and grade III DHF in 8.33% The most common symptoms after fever were vomiting (85.4%), abdominal pain (68.75%), headache (37.5%), rash (20.83%) and itch (16.66%). Hemorrhagic manifestations were observed in 43.75% patients. Atypical manifestations were documented in 4 patients (8.33%) patients. Overall outcome in this study was good with no mortality.

Conclusion: Dengue infection has posed a huge burden to the health-care system with spectrum ranging from mild self-limiting disease to severe fatal disease. It usually presents with common manifestations as shown by this study but may also have varied and multi-systemic manifestations like encephalitis and acute respiratory distress syndrome which may go unnoticed. Pediatricians should have a high index of suspicion for atypical manifestations so revelation of the exact clinical profile is significant for patient effective management.

Key words: Dengue infection, hemorrhagic fever, shock syndrome, atypical manifestations of dengue fever.

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INTRODUCTION

Dengue infection is caused by dengue virus that is a mosquito-borne flavivirus.^{1,2} Dengue virus is transmitted by *Aedes aegypti* and *Aedes albopictus*. The word “Dengue” is a derivative of Swahili phrase *kadungapepo* which means “cramp like seizure”. In 1780,

Benjamin Rush reported dengue for the first time in Philadelphia and defined it as “break-borne disease.”²

Epidemiologic surveys have revealed younger age, female gender, higher body-mass index, type of virus strain and genetics of the human host like major histocompatibility complex class I related sequence B and phospholipase C epsilon 1 genes as risk factors for severe dengue.³

Dengue ranks now a days as the most significant mosquito-borne viral ailment in the world, which has undergone a 30-fold rise in the global incidence over past fifty years.⁴ Outbreaks put an enormous burden on populations in many tropical areas of the world. Although the true global burden of this infection is still not known, the patterns are pretty alarming for human health and economy. According to report of WHO, nearly 3.9 billion people living in 128 countries are having risk of dengue.^{1,5}

In the last few years, the incidence of dengue virus (DENV) infection has raised globally due to geographic expansion to new countries. The leading factors for rapid rise in dengue incidences are unplanned urbanization, poor sanitation facilities leading to fertile breeding areas for mosquitoes, improper vector control and change in climate, increased rate of trade and in travel, global warming and lack of proper vaccination and specific antiviral therapy.^{3, 6} The seasonal transmission of dengue infection is noticed more in monsoon and after the monsoon period. Although the true influence of dengue is difficult to measure due to insufficient disease surveillance, deficiency of diagnostic facilities and poor system of reporting. The load of dengue is expected to get further high due to these contributing factors.

The first confirmed DHF outbreak happened in Karachi Pakistan in 1994 showing up 145 cases and one fatality report. Punjab has faced this disease for two decades now and will be passing on to hyperendemicity by 10 to 15 years more. Dengue infection is expected to be quite rampant in younger population rather than the middle age population group. The overall case fatality rate (CFR) of Dengue infection in Punjab during 2013-2017 was found to be 1.86/ 1000 confirmed cases.^{3,5,7}

The incubation period of dengue infection is typically between 4-7 days (range 3-14). The profile of clinical manifestations differs from asymptomatic disease to the severe infection, with or without evidence of plasma leakage or organ dysfunction.^{3,8,9}

Infection caused by any of the four dengue virus serotypes can be asymptomatic or can lead to classic dengue fever (DF) or more severe disease known as dengue hemorrhagic fever (DHF). DHF is sub-grouped as mild (grades I and II) or severe (grades III and IV), on the basis of the presence of shock due to volume leakage. Grades III and IV are also

known as Dengue Shock Syndrome. About 90% of the dengue infections happen in children with risk of death during the secondary attack which is about 15-fold more than that of adults.^{3,9,10}

The present study was conducted with the objective to document the clinical spectrum of dengue infections in pediatric age group. Many manifestations of this infection do not have a discrete demarcation line apart from the classic feature. The reports of rare manifestations of dengue infection are becoming more common. Some features that are not included in the World Health Organization (WHO) definitions might be potentially alarming leading to high morbidity and mortality of this disease. Many of these signs may remain undocumented due to lack of knowledge amongst primary care providers.

There are not much studies documenting the infrequent clinical manifestations of dengue. The present study was done to observe the variable clinical presentation of dengue patients admitted in a teaching hospital specially focusing the unusual manifestations.

METHODS

The study involved 120 suspected cases of Dengue fever and were followed prospectively at Social Security Hospital, Multan Road Lahore in the department of Pediatric Medicine. It was a simple comparative study. This was done during the dengue outbreak occurring between the months of September to November 2021.

Patients were selected through convenient purposive sampling technique. These 120 patients of age group 1-15 years were labelled as suspected, probable and confirmed dengue as per Dengue GCP guidelines. Confirmed dengue patients were then further classified as dengue fever, dengue hemorrhagic fever (grade I – IV) according to Dengue GCP guidelines.

Dengue fever was suspected on the basis of the presence of fever for > 2 days and <10 days along with any two of these symptoms: 1) headache 2) ocular pain 3) myalgia 4) arthralgia/ bone pain/ backache 5) rash 6) bleeding manifestations 7) abdominal pain 8) oliguria. All suspected cases with supporting laboratory evidence (in form of leucopenia / thrombocytopenia) were labelled as “Probable Dengue”.

All probable cases with confirmatory evidence (in the form of positive NS-1 antigen or positive serology) were considered as “Confirmed Dengue”.

A pre designed proforma mentioning the detailed epidemiological, clinical and laboratory parameters documented during the hospital stay, was used as a tool for data collection.

All clinical and laboratory parameters were observed daily and atypical manifestations were also documented. A detailed history as well as a general and systemic

clinical examination was taken and recorded. Clinical presentation (fever), pattern of temperature, nausea or vomiting, rash, abdominal pain, myalgia, headache and hemorrhage were documented. Hematological parameters and biochemical investigations were performed at the phase of admission and were followed by daily (or bi-daily) as per need. Signs of plasma leakage were monitored by chest X ray and abdominal USG. More specific investigations were also done in some patients as required like serum albumin, cerebrospinal fluid analysis, neuroimaging, viral serology/markers, peripheral smear for plasmodium falciparum, blood culture/ sensitivity. Cases with positive NS-1 antigen or positive serology were labelled as confirmed dengue fever. Patients were then further grouped as dengue fever, dengue hemorrhagic fever (Grade I–IV) as per Dengue GCP guidelines.

Variables in demography like age were presented as mean and standard deviation and variables like sex were presented as percentage. All the categorical variables like clinical features and biochemical parameters were stated as numbers and percentages.

Statistical analysis was executed by Chi Square test done by the Statistical Package for Social Sciences (SPSS 15.0) with $p < 0.05$ declared as statistically significant.

The study protocol was approved by the Institutional Ethics and Research Committee of the hospital and a written formal consent was taken from the parents or guardians for using their personal data in the study.

RESULTS

Out of 120 enrolled suspected dengue cases 56.66% were male while 43.33% were female. Majority of the confirmed dengue patients were male (60.41%) and 39.58% of the patients were female. The most dominant age group among the suspected and confirmed dengue patients was >10-15 yrs.

Out of these 120 suspected Dengue cases, 75 % were labeled as probable dengue but 40% were later confirmed to have dengue infection. Patients included were grouped as dengue fever (DF), dengue hemorrhagic fever (DHF grade I–IV) as per Dengue GCP guidelines. DSS includes patients with DHF grade III and IV. Of the confirmed dengue fever patients, 66.66% patients had classic dengue fever while 33.33% satisfied the criteria of dengue hemorrhagic fever (DHF). Of these 16 patients with dengue hemorrhagic fever, 25% patients were of DHF grade I/ II, 8.33% patients were of DHF grade III and none with DHF grade I (Table 1)

The most frequently found clinical manifestation was fever seen in all (100%) patients. The mean duration of fever was 6.32 days. Other common symptoms were headache (37.5%), abdominal pain (68.75%), vomiting (85.4%), rash (20.83%), and itch (16.66%). Hemorrhagic manifestations were present in 21

(43.75%) patients in which epistaxis was the most common symptom. Signs of plasma leakage / serositis was seen in 41.66% cases (Table 2 & 3).

Apart from these typical manifestations of the dengue infection, we observed some atypical manifestations in this study. Neurological complications in the form of encephalitis were found in 2.08% patients. Neurological involvement can be related to the neurotropic effect of the virus, the systemic effects of dengue infection, or the host immune response. Myositis was another atypical presentation observed in 2 (4.16%) of patients. Acute respiratory distress syndrome was observed in 2.08% patients (Table 4).

Among the laboratory parameters, 77.08% patients had leucopenia; 45.83% had thrombocytopenia; 62.5% had elevated liver enzymes; an altered coagulation profile was found in 10.41% patients and hypoproteinemia was observed in 8.33% cases (Table 5).

Table 1: Distribution of patients as DF, DHF I/II, DHF III/IV (DSS).

Confirmed Dengue	DF	DHF (n =16)		
		DHF I/II IV	DHF III	DHF IV
n= 48	32	12	4	0
% age	66.66%	25%	8.33%	0%

Table 2: Comparison of Clinical parameters in DF and DHF.

Clinical Parameter	Confirmed Dengue n=48	DF n=32	DHF n=16	p Value
Fever	48 (100%)	32 (100%)	16 (100%)	p>0.05
Vomiting	41 (85.4%)	27 (84.37%)	14 (87.5%)	p>0.05
Abdominal pain	33 (68.75%)	18 (56.25%)	15 (93.75%)	p>0.05
Body pains/ Myalgia	25 (52.08%)	13 (40.62%)	12 (75%)	p>0.05
Diarrhea	19 (39.58%)	9 (28.12%)	10 (62.5%)	p>0.05
Headache	18 (37.5%)	8 (25%)	10 (62.5%)	p>0.05
Ocular pain	11 (22.91%)	7 (21.87%)	4 (25%)	p>0.05
Rash	10 (20.83%)	6 (18.75%)	4 (8.33%)	p>0.05
Itch	8 (16.66%)	5 (15.62%)	3 (6.25%)	p>0.05
Bleeding Manifestations	21 (43.75%)	7 (21.87%)	14 (87.5%)	p< 0.05*
Signs of plasma leakage	20 (41.66%)	7 (21.87%)	13 (81.25%)	p>0.05

*p value <0.05 is considered to be significant.

Table 3: Clinical parameters in Dengue Hemorrhagic Fever grade I_ IV

Clinical Parameter	DHF n=16	DHF n = 16	
		DHF I/II n = 12	DHF III/IV (DSS) n = 4
Fever	16 (100%)	12 (100%)	4 (100%)
Vomiting	14 (87.5%)	10 (83.33%)	4 (100%)
Abdominal pain	15 (93.75%)	12 (100%)	3 (75%)
Body pains/ Myalgia	12 (75%)	9 (75%)	3 (75%)
Diarrhea	10 (62.5%)	8 (66.66%)	2 (50%)
Headache	10 (62.5%)	8 (66.66%)	2 (50%)
Ocular pain	4 (25%)	3 (25%)	1 (25%)
Rash	4 (8.33%)	3 (25%)	1 (25%)
Itch	3 (6.25%)	2 (16.66%)	1 (25%)
Bleeding Manifestations	14 (87.5%)	10 (83.33%)	4 (100%)
Signs of plasma leakage	13 (81.25%)	9 (75%)	4 (100%)

Table 4: Atypical manifestations of Dengue patients.

Atypical presentation	No. of patients
Encephalitis	1
Myositis	2
Acute Respiratory Distress Syndrome	1

Table 5: Laboratory parameters of Dengue patients.

Laboratory Parameter	n =48 (Percentage)
Leucopenia (WBC < 4000/mm ³)	34 (70.83%)
Thrombocytopenia (<150, 000 /mm ³)	45 (93.75%)
Elevation of Transaminases	33 (68.75%)
Abnormal PT/ APTT	13 (27.08%)
Hypoproteinemia	11 (22.91%)

DISCUSSION

Dengue is a significant emerging problem of our region. The epidemics of dengue fever have been reported during September to November.^{1, 3} Our study population was also selected during this period which was in accordance with various other studies. These findings guide that preventive campaign against dengue virus infection must be initiated efficiently after the initial spells of rainfall and at the end of monsoon.

In our study, more than 50% of the subjects were males. Several other studies have also depicted a male

dominance.^{5,8,9} A study from eastern India done by Chatterjee et al, however, showed an equitable gender distribution.¹¹ The majority of subjects in this study were belonging to age group 10-15 yrs. Patil from Maharashtra¹² Chaturvedi et al¹³ also stated a higher incidence in young population.

Out of 120 suspected cases, dengue confirmed cases were 40%. The study revealed 66.66% cases with DF, 25% with DHF I/II, 8.33% with DHF III but none was noticed with DHF IV.³

The commonest presenting symptoms after fever (100%), followed by vomiting (85.4%) and abdominal pain (68.75%). Similar results were observed in various other studies. Abdominal pain was also a common presentation (64%) in a study by Payal Jain.¹⁴ Similar high incidence of gastrointestinal symptoms was also described in a study from Kerala¹⁵ attributed to hepatomegaly and serositis. It is essential to note that other infections causing fever and gastrointestinal symptoms like typhoid fever are very common in Pakistan leading to a diagnostic dilemma.

Serositis presenting with ascites and pleural effusion from capillary leak were frequently reported in many studies.^{8,10,11} In this study, radiological indication of serositis was seen in 41.66% cases in contrast to 16.67% cases observed by Payal Jain.¹⁴ But Chatterjee et al¹¹ found serositis in 43% subjects that was in concordance to our finding.

Cutaneous manifestations in DF usually varies from maculopapular rash, petechial rash, flushing and itching. In our study, rash was observed in 20.83% and itch in 16.66% cases. Payal Jain¹⁴ observed itching in 9.56% cases and rash in 17.54% patients. In a north Indian study by Karoli et al¹⁶, rash was reported in 26% cases and cutaneous hypersensitivity in 16% patients. In another study from eastern India rash was found in 37.84% cases.¹¹

Bleeding diathesis is a well-known feature of dengue illness due to low platelet count and leaking from blood vessels. 45 out of 48 children had platelet count below 150,000 cell/mm³. 62.5% cases in our study had platelet count below 100,000/mm³. Bleeding manifestations were noticed in 21 (43.75%) patients which was mostly in the form of mucosal bleeding like, epistaxis and gum bleed. This is in contrast to 63% and 69% of bleeding evidence noticed by Horvath from Australia¹⁷ and Sharma from India¹⁸ respectively. Payal Jain¹⁴ reported bleeding in 22.8% patients that is in accordance with our study. In a Hyderabad based study conducted by Khan et al¹⁹, just 5% cases showed evidence of bleeding while 40% of the patients had thrombocytopenia. Severity of bleeding did not show any correlation with platelet count, implicating many other contributory factors except for thrombocytopenia like platelet dysfunction, endothelial dysfunction and consumption coagulopathy. Similarly, many other studies also did not observe any direct relationship between the platelet counts and bleeding tendency.

Elevated levels of transaminases were observed in 68.75% of the patients.

In study conducted by Payal Jain,¹⁴ neurological manifestations were seen in 5 (4.38%) patients like hypokalemic paralysis, Guillain-Barre syndrome and encephalitis, but in our study only one case with encephalitis was noticed. In contrast, Misra et al²⁰ described 11 encephalopathy patients having CSF lymphocytic pleocytosis, suggestive of viral meningoencephalitic. Other atypical manifestations of diseases were also seen like acute respiratory distress syndrome and myositis.²¹

The outcome of this disease is variable as depicted by various studies; however, outcome of patients in this study was very good with no mortality and majority of the patients recovering finally.

The limitations of our study were that some cases exhibiting symptoms and signs indicative of dengue infection were not involved because they were negative for dengue infection after laboratory testing. Facility for detection of specific dengue virus serotype was also not available at our institutional.

CONCLUSION

Dengue infection is attaining an alarming situation in Pakistan which is compounded by the increasing population, poor diagnostic facilities, inadequate medical care, insufficient measures for mosquito control and other factors favoring the multiplication of the vector. In view of the rise in the number of cases in pediatric population and emerging clinical spectrum of the disease, this study will help to develop a high index of suspicion to timely diagnose and treat dengue fever in pediatric population. Future studies must be conducted to help pediatricians in triaging patients in the period of outbreak as dengue infection is no more area occurrence in this population.

Ethical Approval: Submitted

Conflict of Interest: Authors declare no conflict of interest.

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