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ORIGINAL ARTICLE

CLINICAL PROFILE OF DENGUE INFECTION IN PEDIATRIC AGE GROUP IN WEST INDIA

Jayant M. Deshmukh[1], Sudhir Mavadiya[2]

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ABSTRACT: INTRODUCTION: Dengue viral infections are among the most important mosquito-borne diseases of the Indian subcontinent and have become a major global public health concern. Spread of disease has led to increased recognition of atypical manifestations, apart from the classical clinical features of dengue infection. **METHODOLOGY:** This case study was conducted at the department of Pediatrics in collaboration with the Microbiology Department of Dr. Ulhas Patil Medical College, Jalgaon District of Maharashtra in West India during the period of 2 years from July 2012 to June 2014. Clinically suspected and serologically confirmed cases of dengue fever were included in the study. Clinical and biochemical parameters were compared between the two groups of dengue fever and dengue hemorrhagic fever. **RESULTS:** 247 patients clinically suspected and serologically confirmed cases of dengue infection were enrolled in the study. One sixty one (65%) patients were males and 86 (35%) were females. One seventy three (70%) patients had a classical dengue fever while 74 (30%) had dengue hemorrhagic fever. The most common symptoms were headache (212, 86%), skin rash (163, 66%), abdominal pain (131, 53%), vomiting (119, 48%), and hemorrhagic manifestations were present in 84 (34%) patients. Atypical manifestations were recorded. Notably, 9% of patients had neurological involvement and 5% had multi-organ failure. Overall mortality was 4.5%. **CONCLUSION:** Dengue infection poses a huge burden to the healthcare system; its spectrum ranges from mild self-limiting illness to severe fatal disease. It can have varied and multi-systemic manifestations which can go unrecognized. Deaths occurred in 55% (6/11) cases were associated with dengue neurological manifestations needs support to the clinicians should have a high index of suspicion for atypical manifestations in dengue endemic countries.

KEYWORDS: Dengue infection; dengue hemorrhagic fever; atypical manifestations of dengue; CNS involvement and multiorgan failure.

INTRODUCTION: Dengue is the most important arthropod-borne viral infection of humans. In recent years, dengue has become a major global public health concern. Approximately 2.5 billion people, living mainly in urban areas of tropical and subtropical regions, are estimated to be at risk of acquiring dengue infection.[1] Dengue virus has 4 serotypes and transmitted by the day time biting mosquito Aedes aegypti, that has been highly urbanized.[2] Dengue infections vary in severity, ranging from influenza-like self-limiting illness to life-threatening dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) which, if left untreated, are associated with mortality as high as 20%. [3]

We undertook this prospective study in the Department of Pediatric collaboration with Microbiology department at Dr. Ulhas Patil Medical College, Jalgaon District of Maharashtra in West India from July 2012 to June 2014 to assess the clinical profile of dengue infection in hospitalized patients as well as to observe rare manifestations of dengue infections.

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METHODOLOGY: Clinically and serologically confirmed cases of Dengue were included in the study. Patients of 0 - 12 years old admitted to pediatrics wards and I.C.U. who appeared to have acute febrile illness with myalgia, arthralgia, headache, retro orbital pain, abdominal pain, nausea and vomiting, bleeding, hypotension or thrombocytopenia and serologically positive for dengue virus seromarkers NS1 antigen, IgM and IgG antibody by chromatographic strip method and confirmed by micro plate ELISA.[4]

Only IgG positive cases were not included in the study. Detailed history was collected as well as a general and systemic clinical examination (including the tourniquet test) was done. Haematological profiles and biochemical investigations were done at the time of admission and were followed by daily (or bi-daily) investigations as required until discharge.

Clinical diagnosis of dengue hemorrhagic fever was based on the presence of the following four criteria: (i) continuous high-grade fever lasting for 2 to 7 days; (ii) hemorrhagic tendency as shown by a positive tourniquet test, petechiae or epistaxis; (iii) thrombocytopenia < 100, 000/µl; (iv) evidence of plasma leakage manifested by hemoconcentration (an increase in hematocrit 20% above the average for age, sex and population); pleural effusion and ascites, etc. Signs of plasma leakage were assessed by chest radiograph and abdominal ultrasonography.[5]

Specific investigations were performed in patients who presented with neurological involvement (cerebrospinal fluid analysis, neuroimaging, electrodiagnostic studies or muscle biopsy) or hepatic failure (viral markers, peripheral smear and serology for plasmodium falciparum, typhoid fever and leptospirosis) and blood culture in all cases.

STATISTICAL ANALYSIS: Statistical analysis was performed by 'Z' test done by using the Statistical Package Social Sciences (SPSS) , p value < 0.05 taken as statistically significant.

RESULTS: The study enrolled 247 cases confirmed to have dengue infection out of whom 161 (65%) patients were males and 86 (35%) were females. 173 (70%) patients had classic dengue fever while 74 (30%) fulfilled the criteria of dengue hemorrhagic fever [Graph: 1]. Of those patients with dengue hemorrhagic fever, twenty one patients had developed dengue shock syndrome and death occurred in eleven patients (4.5%). The most common symptoms were headache (212, 86%), abdominal pain (131, 53%), vomiting (119, 48%), skin rash (163, 66%), and haemorrhagic manifestations were present in 84 (34%) patients in which epistaxis was the most common symptom fallowed by GI bleed [Table: 1].

Per laboratory parameters, 220 (89%) patients had thrombocytopenia; 225 (91%) had elevation of liver enzymes; an altered coagulation profile was found in 92 (37%) patients; and 2% (5) patients developed multiorgan failure. In our study the mortality rate was 4.5 % (11/247) and maximum fatal cases were due to neurological involvement (six cases) and rest of due to multi-organ failure (five cases) [Table: 2]. Apart from the classical manifestations of the dengue infection, we particularly observed certain rare and atypical manifestations.

Neurological complications were found in 9 % of our patients compared to the previously reported 0.5-6%.[6] Neurological involvement was present in the form of convulsions (eleven), encephalopathy (six), and meningitis (seven). This neurological involvement can be related to the neurotrophic effect of the virus, the systemic effects of dengue infection, or the host immune response.[7]

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DISCUSSION: Liver enzyme elevation, a common feature in dengue infection [8] was also apparent in our study. In this study, AST levels were equal to or greater than those of ALT levels in all of dengue infected patients, a finding that has also been reported earlier.[9]

A significant proportion of patients (84%) with classical or uncomplicated dengue fever had thrombocytopenia and 17% of them had an altered coagulation profile as well. Overall, an altered coagulation profile was observed in 37% patients in our study and is indicative of the activation of both coagulation and fibrinolysis during acute dengue infection, which is found to be particularly greater in patients with dengue hemorrhagic fever.[10]

Although the etiology of abdominal pain remains obscure in Dengue fever but it could be due to raised amylase level and enlarged pancreas and in shock due to hypoperfusion to gut.[11] One of the cardinal features of severe dengue is capillary leakage resulting into accumulation of fluids in various body cavities.[12]

Thrombocytopenia was the consistent finding in our patients 84% in classical dengue and 100% in dengue hemorrhagic fever and most of the patients had counts between 20, 000 100, 000/cmm. Many studies report that thrombocytopenia is the commonest but not the constant finding in Dengue fever.[13] Dengue virus -2 induces apoptotic cell death in a subpopulation of early megakaryocytic progenitors which may contribute to thrombocytopenia in dengue disease.[14]

Twenty two cases associated with neurological involvement. The incidence of neurological manifestations in patients diagnosed with Dengue Haemorrhagic Fever (DHF) and severe Dengue has been documented to vary from 3% (24/858) in prospective DHF studies to 25% in retrospective studies.[15,16] Encephalitis is known to be one of the more frequent presenting manifestations of dengue neurological disease.[16] Seizures occurring in dengue-infected patients have been documented to be associated with intracerebral haemorrhages.[17]

Kamath et al also noted that most neurological events were unrelated to the perfusion status (shock or otherwise) of subjects studied and were found to be the commonest cause of death in complicated dengue infections.[15] In this study, the fatality among dengue-infected patients with neurological manifestations was 27%. Most dengue infections were detected in September and October. This finding corresponds to the expected dengue seasonal trend and the stronger relation of dengue infection to temperature changes rather than rainfall.[18]

Infection with one of these serotypes provides lifelong immunity (IgG) to that particular serotype only. Therefore, persons can acquire a second dengue infection from a different serotype which can lead to more severe form of the disease i.e. dengue hemorrhagic fever.[19]

In the present study all patients were either NS1 or IgM positive but only 7% in classical dengue and 66% in dengue haemorrhagic fever were positive for both NS1/IgM and IgG. In dengue serological interpretation seromarkers NS1 antigen or IgM antibody indicate recent infection and only IgG antibody associated with chronic or late stage of dengue infection. When a dengue infection occurs in individuals who have experienced a previous dengue infection, a secondary immune response occurs, which generates high levels of IgG through the stimulation of memory B cells from the previous infection.[20]

CONCLUSION: Dengue disease continues to involve newer areas, newer populations and is increasing in magnitude. No vaccine is yet available for protection and the vector control measures are inadequate.[21] The application of WHO the classification system is not as simple and straightforward

as it seems and clinical features may overlap among different categories. The WHO classification system of dengue does not include unusual manifestations such as encephalopathy, meningitis, convulsions, acute hepatic failure, cardiomyopathy and acute respiratory distress syndrome, which might be life-threatening.

Although these manifestations are rare, they have been reported from endemic regions.[22,23] Therefore, clinicians should have a high index of suspicion and knowledge of these atypical manifestations, particularly in view of the increasing burden of dengue on the health-care system.

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	Total dengue positive (n=247)	**Dengue fever (n = 173)**	**Dengue hemorrhagic fever (n =74)**	**P value**
Headache/Myalgia	212 (86%)	137(79%)	47(63%)	0.014*
Abdominal pain	131 (53%)	68 (39%)	63 (85%)	0.000*
Hemorrhagic manifestations	84 (34%)	10 (6%)	74 (100%)	0.000*
Skin Rash	163 (66%)	140 (81%)	23 (31%)	0.000*
Hepatomegaly	142(58%)	86 (50%)	56 (76%)	0.000*
Cholecystitis (by USG)	29 (12%)	--	29 (39%)	--
Sign of plasma leakage	74 (30%)	--	74 (100%)	--
Convulsions	11 (4.5%)	--	11 (15%)	--
Oliguria	2 (0.8%)	--	2 (3%)	--

Table 1: Comparison of clinical parameters between dengue fever and dengue hemorrhagic fever

* $p < 0.05$

	Total dengue positive (n = 247)	**Dengue fever (n = 173)**	**Dengue hemorrhagic fever (n =74)**	**P value**
Thrombocytopenia (Platelet count < 100, 000/ul)	220 (89%)	146 (84%)	74 (100%)	0.000*
Abnormal PT/APTT	94 (38%)	29 (17%)	63 (85%)	0.000*
Elevation of transaminases	225 (91%)	155 (90%)	70 (95%)	0.154
Both NS1/IgM and IgG positive	61 (25%)	12 (7%)	49 (66%)	0.000*

Table 2: Comparison of biochemical parameters and serological markers between dengue fever and dengue hemorrhagic fever

PT- Prothrombin time, APTT- Activated partial thromboplastin time, * $p < 0.05$

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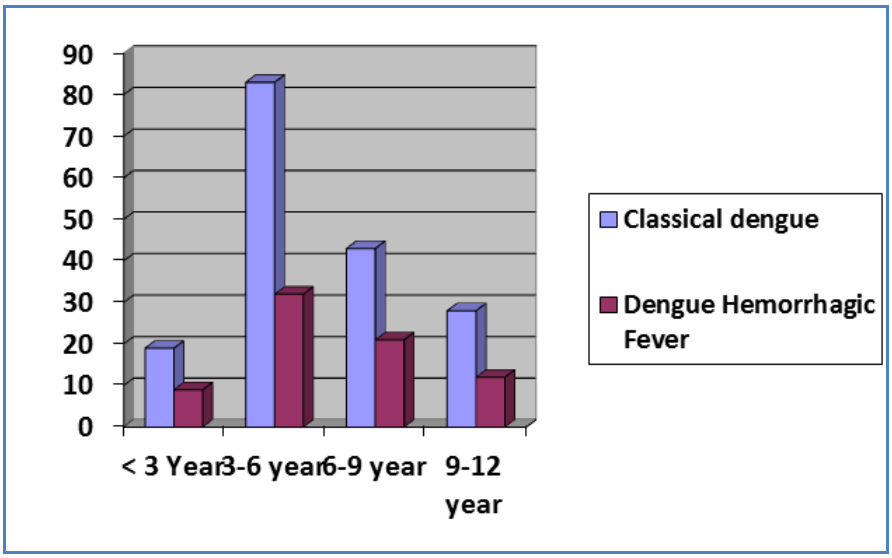
Graph 1: Showing Age-group wise Distribution of Classical Dengue and Dengue Hemorrhagic Fever.



Graph 1

AUTHORS:

1. Jayant M. Deshmukh
2. Sudhir Mavadiya

PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Microbiology, Dr. Ulhas Patil Medical College & Hospital, Jalgaon Kh (M.H.)
2. Assistant Professor, Department of Pediatrics, Dr. Ulhas Patil Medical College & Hospital, Jalgaon Kh (M.H.)

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Jayant Mahadeorao Deshmukh,
Associate Professor,
Department of Microbiology,
Dr. Ulhas Patil Medical College &
Hospital, Jalgaon (Khurd-425309),
M. H, India.
Email: jayantmdeshmukh@yahoo.co.in

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