Original Article

Clinical profile and atypical manifestation of *dengue* fever cases between 2011 and 2018 in Chennai, India

Kamalraj Mohan[1], Jeevan Malaiyan[1], Sowmya Nasimuddin[1], Ravin Sathyaseelan Devasir[2], PradeepRaj Meenakshi-Sundaram[2], Santhiya Selvaraj[1], Bharathi Krishnasamy[3], Sumathi Gnanadesikan[1], Muthulakshmi Karthikeyan[4], Mohanakrishnan Kandasamy[1], Nithyalakshmi Jayakumar[1], Dhevahi Elumalai[1], Gokul G. Ra[2]

Departments of [1]Microbiology and [2]General Medicine, Sri Muthukumaran Medical College Hospital and Research Institute, Affiliated to the Tamil Nadu Dr. M.G.R. Medical University, Chikkarayapuram, Chennai, Tamil Nadu, [4]Department of Microbiology, Meenakshi Medical College Hospital and Research Institute, Meenakshi Academy of Higher Education and Research, Kancheepuram, Tamil Nadu, [3]Institute of Microbiology, Madurai Medical College, Affiliated to the Tamil Nadu Dr. M.G.R. Medical University, Madurai, Tamil Nadu, India

ABSTRACT

Introduction: Dengue fever is a common mosquito-borne viral disease which has reached alarming size in the past few years. It is endemic in more than 100 countries and significant differences were found in clinical profile and atypical manifestation. **Aim of the Study:** A retrospective observational study of clinical profile and atypical manifestations in patients with dengue fever. **Materials and Methods:** Serum samples were collected from clinically suspected cases of dengue fever and it was confirmed by NS1 antigen, IgM, and IgG antibody by ELISA. Clinical details and atypical manifestations were recorded. **Observation:** During the study period, a total of 2502 patients were suspected to have dengue infection, of which 464 (18.5%) samples were found to be positive for dengue viral infection. A majority of the cases were males [268 (57%)] when compared with females [196 (42%)]. Fever was the most common clinical presentation seen in all the patients, followed by headache (78.4%), myalgia (61%), body pain (49.3%), vomiting (40%), joint pain (31.5%), dry cough (19%), nausea (14%), abdominal pain (8%), diarrhea (5.6%), retro-orbital pain (04%), burning micturition (2.4%), and rashes (0.6%). Among atypical manifestations, hepatomegaly [32 (7%)] was the most common, followed by splenomegaly [23 (5%)], bradycardia [18 (4%)], meningitis [6 (1.2%)], hemoptysis [5 (1%)], acalculous cholecystitis [4 (0.8%)], and acute pancreatitis [2 (0.4%)]. The study of hematological parameters showed thrombocytopenia was present in 179 (38.5%) patients, followed by leukopenia [77 (17%)] and raised hematocrit [29 (6.2%)]. **Conclusion:** During ongoing epidemics, the clinical profile and atypical manifestations in clinically suspected dengue patients should be investigated early so that severe forms can be treated promptly.

Keywords: Atypical manifestation, clinical profile, dengue fever, hematological parameters

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Introduction

Dengue, a common mosquito-borne viral disease, occurs in tropical and subtropical countries especially South and Southeast Asia countries, the Caribbean, Central, and South America, and Africa. Dengue virus (DENV) infection is the most rapidly

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spreading disease in the world with a 30-fold increase in incidence in the past 50 years.[1] The first dengue fever in India was reported in 1956 from Vellore and the first dengue hemorrhagic fever occurred in Calcutta in 1963.[2] Dengue is caused by one of the four serotypes of DEVN (DENV-1–DENV-4) belonging to the family *Flaviviridae*.[3] All the four serotypes of the virus have been in circulation and documented in Tamil Nadu.[4] Dengue fever is an acute febrile illness with frontal headache, retro-ocular pain, muscle pain, joint pain, and rash, even though other signs and symptoms could also be present (such as lymphadenopathy, petechiale, nausea, hepatomegaly, and different types of hemorrhagic manifestations).[5] Atypical manifestations are rare and include encephalopathy, encephalitis, seizures, hepatocellular damage, acalculous cholecystitis, myocarditis, pericardial effusion, and severe gastrointestinal hemorrhage.[6,7] The clinical presentation in dengue depends on the virus strain, as well as the age and immune status of the host.[3] This study aims to elucidate the salient clinical feature and laboratory findings of serologically confirmed cases of dengue fever. The elucidation of clinical profile is very important for primary care, management, and thus crucial for saving life.

Aim of the Study

This study aims to study the clinical profile and atypical manifestations in patients with dengue fever.

Materials and Methods

This retrospective observational study was conducted during the period from July 2011 to December 2018 at Sri Muthukumaran Medical College, Hospital and Research Institute, Chennai, India. Informed consent was taken from each patient and the study was approved by Institutional Ethical Committee (obtained on 23.12.2016 (46/IECs)). Serum samples were collected from clinically suspected cases of dengue and were confirmed by NS1 antigen, IgM, and IgG antibody by ELISA (J. Mitra and Co. Pvt. Ltd.). A detailed history was taken and careful clinical examination was performed on all the positive cases. Hematological parameters such as platelet count, hemoglobin, hematocrit (HCT) levels, complete blood count (CBC), and white blood cell count (WBC) were also recorded.

Observation

During the study period, a total of 2502 patients were suspected to have dengue fever, out of which 464 (18.5%) samples were found to be positive. In our study population, the highest numbers of dengue-positive cases were screened in the year 2017 (74.8%), followed by 2013 (27.7%) and 2016 (18.8%) as shown in Table 1. A majority of the cases were males 268 (57.7%) and females were 196 (42.2%). About 45% of positive cases belonged to adult age groups (18–44 years) followed by younger age group <18 years (30%) [Table 2]. Fever was the most common clinical presentation which was found among all the patients, followed by

Table 1: Year-wise distribution of dengue cases during the study period

Year	Total no. of cases	Positive cases
2011	346	9 (2.6%)
2012	463	25 (5.3%)
2013	457	127 (27.7%)
2014	342	72 (21%)
2015	460	85 (18.4%)
2016	90	17 (18.8%)
2017	151	113 (74.8%)
2018	193	16 (8.2%)
Total	2502	464 (18.5%)

Table 2: Age and sex-wise distribution of dengue cases (*n*=464)

Age groups (years)	Males	Females	Total
<18	81	57	138 (30%)
18-44	118	89	207 (45%)
45-60	47	35	82 (18%)
>60	22	15	37 (8%)
Total	268 (57.7%)	196 (42.2%)	

Table 3: Clinical features of *dengue*-positive cases (*n*=464)

Clinical features	No. of cases (%)
Fever	439 (95%)
Headache	364 (78.4%)
Myalgia	284 (61.2%)
Body pain	229 (49.3%)
Vomiting	186 (40%)
Joint pain	144 (31%)
Dry cough	89 (19.1%)
Nausea	63 (13.5%)
Abdominal pain	38 (8.1%)
Diarrhea	26 (5.6%)
Retro-orbital pain	19 (4%)
Burning micturition	12 (2.5%)
Rashes	03 (0.6%)

headache (78.4%), myalgia (61.2%), body pain (49.3%), vomiting (40%), joint pain (31%), dry cough (19%), nausea (13.5%), abdominal pain (8%), diarrhea (5.6%), retro-orbital pain (4%), burning micturition (2.5%), and rashes (0.6%) [Table 3]. In this study, 90 (19.3%) patients had atypical manifestations. Hepatomegaly [32 (7%)] was the most common manifestation, followed by splenomegaly [23 (5%)], bradycardia [18 (4%)], meningitis [6 (1.2%)], hemoptysis [5 (1%)], acalculous cholecystitis [4 (0.8%)], and acute pancreatitis [2 (0.4%)] [Table 4]. The majority of the patients were positive for NS_1 Ag 290 (62.5%) followed by IgG 80 (17.2%), IgM 53 (11.4%), and IgM + IgG 41 (9%) as shown in Table 5. Raised HCT was found in 29 (6.2%) and leukopenia (<4000/mm^3) was found in 77 (16.5%) patients. Thrombocytopenia was observed in 179 (38.5%) cases [Table 6].

Table 4: Atypical clinical manifestations in dengue patients (*n*=90)

Clinical features	No. of cases (%)
Hepatomegaly	32 (7%)
Splenomegaly	23 (5%)
Bradycardia	18 (4%)
Meningitis	6 (1.2%)
Hemoptysis	05 (1%)
Acalculous cholecystitis	04 (0.8%)
Acute pancreatitis	2 (0.4%)
Total	90 (19.3%)

Table 5: Serological marker distribution of dengue cases

Total no. of patients (*n*=464)	Dengue-specific marker			
	NS1 Ag	IgM	IgG	IgG + IgM
Dengue-positive cases	290 (62.5%)	53 (11.4%)	80 (17.2%)	41 (9%)

Table 6: Hematological parameters of dengue-positive cases (*n*=464)

Investigation	No. of cases (%)
Thrombocytopenia (<150,000/mm³)	179 (38.5%)
Leucopenia (<4000/mm³)	77 (16.5%)
Raised hematocrit	29 (6.2%)

Discussion

Dengue is emerging as a major health problem and regular outbreaks of dengue infection have been occurring throughout India.[8,9] The provision of adequate care to patients with suspected dengue in primary care settings requires effective clinical evaluation, laboratory testing, and qualified professionals who know how to recognize warning signs and give appropriate guidance to prevent expended dengue.[10] Rapid urbanization, globalization, increasing population, poor solid waste, and water management have given rise to new habitats for mosquito breeding thereby increasing the number of cases and deaths.[1,11] The identification of dengue cases is possible by distinct clinical features. Studies describe that atypical manifestations in dengue fever are multisystemic and multifaceted with organ involvement, such as liver, brain, heart, kidney, and central nervous system.[12] In this study, we investigated the different clinical profile and atypical manifestations.

Incidences of dengue positivity were increasing for the past few years. In our study, we found that the highest number of dengue-positive cases was reported in the year 2017 (74.8%), 2013 (27.7%), and 2016 (18.8%), which were similar to that of previous studies reported.[13,14] Studies revealed that the majority of the cases were in the age group of 15–44 years, followed by other groups. In this study, males [268 (57.7%)] were predominant than females [196 (42.2%)]. These findings well correlate with previous studies.[15] Fever was the most common clinical presentation which was found among all the presenting patients (100%). Headache (78%) and myalgia (61%)

were seen in the majority of cases, followed by joint pain (31%), dry cough (19%), abdominal pain (8%), diarrhea (5.6%), vomiting (32%), and nausea (14%) which is concordant with the study by Hasan SR *et al*.[16]

Atypical symptoms have been observed in this study, which is low compared with previous study done by Nagarajan N *et al*.[17] Retro-orbital pain as a cardinal feature of dengue fever was seen in few (4%), of our patients, while Denys EF *et al*. had reported 16.1%.[18] Burning micturition (8%), hemoptysis (2%), and rashes (0.2%) were not frequent in our study when compared with other studies.[19] Hepatomegaly is highly specific for the development of both dengue hemorrhagic fever and dengue shock syndrome. In our study, 31 (7%) patients had hepatomegaly which correlates with a previous study done by Row EK *et al*.[20] In our study, splenomegaly was 5% which is concordant with a previous study reported by Anurag Prasad *et al*.[21] Other less common atypical manifestations were bradycardia [18 (4%)], meningitis [6 (1.2%)], hemoptysis [5 (1%)], acalculous cholecystitis [4 (0.8%)], and acute [pancreatitis 2 (0.4%)]. This differs from other studies where bradycardia, meningitis, hemoptysis, and acalculous cholecystitis were detected in higher percentage of confirmed dengue fever.[22-25]

Out of 2038 samples of clinically suspected dengue cases, 464 (23%) were found to be positive by ELISA. The majority of the samples were found positive for NS1 antigen 290 (63%), which indicates high sensitivity of the test for early diagnosis of disease, followed by IgG and IgM antibodies, which is similar to a study conducted by Anand *et al*.[26] In our study, thrombocytopenia was present in 179 (39%) patients <150,000/mm³, which is slightly less than the study conducted by Ahmed NH *et al*. Recent studies have established HCT >40% as a prognostic factor for severe dengue.[26-29] In our study, we have found raised HCT in 29 (6.2%) patients. Low leucocyte count may be due to virus-induced inhibition of myeloid progenitor cells or due to destruction.[30] We found that 11% had leucocyte count <5000, almost similar to a study by Chaloemwong J *et al*.[31] An understanding of the course of disease progression, risk factors, recognition of the warning signs, and look out for clinical problems during the different phases of the disease will enable primary care physicians to manage dengue fever in an appropriate and timely manner to reduce morbidity and mortality.[32] Primary care physician should impart health education about dengue fever to the rural community regularly, through health camps or interpersonal communication based on health awareness programs.[33] Thus, atypical presentations should prompt us to investigate for dengue especially during ongoing epidemics so that primary care and management is very important in preventing expanded dengue syndrome.

Conclusion

To conclude, the clinical profile of the dengue fever cases is changing in different epidemics, even in the same regions and with the period of time. Primary care physician should have a

high index of suspicion to detect and timely manage the atypical manifestations of dengue fever as they are no more a rare entity and will continue to rise so long as they are looked for carefully in dengue patients. This study thus indicates the need for a continuous seroepidemiological surveillance for the early and definite identification of the clinical features and atypical manifestations of dengue infection.

Conflicts of interest

There are no conflicts of interest.

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