International Journal of Science and Healthcare Research
Vol.4; Issue: 1; Jan.-March 2019
Website: www.ijshr.com
Original Research Article *ISSN: 2455-7587*

Recent Trends in Clinical Presentation in Cases of Dengue Presenting At Tertiary Care Hospital

Dr. Manoj Kumar[1], Dr. Rajesh Kumar Verma[2], Dr. Deepak Kumar[3], Mr. Bishal[4]

[1]Research Scientist, [2]Professor& Head, [3]MD student (Junior Resident), [4]Research Assistant,
Department of Microbiology, UP University of Medical SciencesSaifai, Etawah U.P., India-260130.

Corresponding Author: Dr. Rajesh Kumar Verma

ABSTRACT

Introduction: The dengue virus is transmitted to man by the bite of the mosquito (*Aedes aegypti and Aedes albopictus*). The cases are increasing year on year basis with significant rate of morbidity and mortality in different parts of the country. These cases often present with varied spectrum of clinical signs and symptoms during the course. Recently it has been observed that these classical symptoms are shifting to less common ones with increase in their severity.
Objective: To study the shift in paradigm of clinical presentations and their severity in the cases presenting to this Tertiary Care Hospital.
Materials and Methods: All clinically suspected cases during study period 2016-17, attending different OPDs or admitted to indoor of different clinical departments, were enrolled in this study and their sera samples were subjected to NS1 antigen and IgM antibody ELISA. Of the total 562 suspected cases, 119 cases were positive either by NS1 antigen or IgM ELISA or both.
Results: The majority of these cases were males 92 (77.3%) and the most susceptible age group was 19-25 years followed by 26-35 years. The fever was commonest presentation in 118 (99.2%) cases followed by headache and abdominal pain in 76 (63.8%), myalgia in 52 (43.7%), vomiting in 44 (37%), and joint pain in 36 (30.2%) cases. In present study we observed 89 (74.8%) cases of dengue with fever, 26 (21.8%) cases with hemorrhagic manifestations and 4(3.4%) cases with presentations of shock.
Conclusion: Upon the analysis of the results, it was observed that there is shift in clinical presentations of the cases. Beside fever being the predominant symptom, abdominal pain, headache and vomiting are next common.
Key words: Dengue, NS1 antigen and IgM antibody

INTRODUCTION

Dengue fever has become one of the most important mosquito-borne viral diseases with a steady increase in global incidence including the India. [1] Dengue virus (DENV) is the etiological agent of this condition which belongs to the genus *Flavivirus*, family flaviviridae and has been classified into four (DENV1-4) serotypes. [2] Our country frequently encounters this infection significantly throughout the country especially during and post monsoon, the outbreaks frequency in Uttar Pradesh and Delhi becomes severe. [3]

Dengue has a varied clinical spectrum ranging from asymptomatic disease to undifferentiated fever (or viral syndromes), classical dengue fever (DF), dengue hemorrhagic fever (DHF), or dengue shock syndrome (DSS). [4] The diagnosis is based on serology mainly by NS1 antigen and IgM antibody ELISA. These methods are accurate having high sensitivity and specificity in diagnosis of acute dengue fever. [5] The combination of both types of ELISA enhances the accuracy of results because it encompasses the NS1 protein present in early 3-6 days and further extending to IgM antibody present up to 5-14 days post infection. [6]

The primary clinical signs and symptoms mainly include fever, petechial rashes and bony or joint pain with decreased platelet count. [7] Although these signs and symptoms with corroborative laboratory evidences are most important for making clinical decision for better management of the condition. Although, the clinical picture

gives a clue to the diagnosis but due to paradigmal shift in symptomatology, the patients now frequently present with less common signs and symptoms like headache, vomiting etc. as suggested by few recent studies. Thus, the present study is aimed to analyze this variation in clinical picture of the cases presenting to this Hospital.

MATERIALS AND METHODS

Study design and setting: The present study is a cross sectional study and was conducted at this Tertiary Care Hospital of Western Uttar Pradesh India. All the clinically suspected cases attending different OPDs or/and admitted to indoor of different department of our hospital, were enrolled in this study during study period 2016-17. The blood samples were collected and their sera separated and tested for NS1 antigen and IgM antibody ELISA.

Inclusion criteria:

a) All cases clinically suspected of dengue, visiting OPDs or admitted in this Hospital.
b) Cases who gave consent to participate in this study.

Exclusion criteria:

a) Cases of fever diagnosed for other than dengue like malaria, typhoid, or other febrile illness etc.
b) Suspected cases in which serology was found to be negative.

Laboratory diagnosis: The diagnosis of cases was established by two types of ELISAs, Non Structural Protein 1 (NS1) Antigen (QUALISA Dengue NS1 (Qualpro diagnostics Pvt. Ltd., Goa, India), and IgM antibody capture ELISA (MICROLISA IgM, J. Mitra& Co, New Delhi). All the sera samples were subjected to these ELISAs same day as per the manufacturer's instructions as described below in brief.

NS1 ELISA

50µL sample diluent was added to each well and 100µL of negative, positive controls were also added followed by serum samples in the corresponding wells. The plate was incubated for 30 minutes at 37^{o}C. It was then washed to remove any unwanted and unbound antigens and blot dried. Further, 100µL of conjugate was added to each well and plate was again incubated for 60 minutes at 37^{o}C followed by washing and drying. Further, 100 µL of substrate was added and plate incubated for 15 minutes in dark at room temperature. Finally, 100µL of stop solution was added and absorbance was read at 450nm.

IgM (MAC) ELISA

100µL of negative and positive controls, calibrator and 100 µL diluted serum samples (1:100) were added to corresponding wells and incubated at 37^{o}C for 60 minutes. The plate was washed five times and dried. Further, 100µL of conjugate was then added and plate incubated for 60 minutes at 37^{o}C. After incubation washing was done followed by 100µL of substrate being added and incubated in dark for 30 minutes at 37^{o}C. Finally, 100µL of stop solution was added and absorbance was read at 450nm.

Statistical Methods: The data entry and results analysis were done with the Microsoft Excel Version 10. All the relevant variables were analyzed by descriptive statistics.

Ethical Approval: This study was approved by University Ethics Committee "408 UPUMS/Dean/2018-19 E.C. No.2017/82".

RESULTS

A total of 562 clinically suspected cases of dengue were enrolled during study period 2016-17. Out of these, 119 (21.1%) cases were laboratory confirmed on the basis of serological diagnosis either by Non-Structural antigen 1 assay (NS1) antigen or IgM antibody ELISA. Of the total 119 positive cases, the NS1 antigen was positive in 100 (84%) cases and 30 (25.2%) cases were positive for IgM, however, a total 11 (9.2%) cases were also positive by both assays (NS1 antigen and IgM antibody ELISA). The majority of these cases were males 92 (77.3%) and the most common age groups among all cases was 19-25, followed by 26-35 years as observed in this study (Table1).

Of all the 119 seropositive cases, 118 (99.2%) had fever. Only one case didn't have fever despite it was IgM positive, which might be in early phase of the disease. The next common clinical presentation observed after fever, was headache as seen in 76 (63.8%) cases followed by abdominal pain in 76 (63.8%), myalgia in 52 (43.7%), vomiting in 44 (37%),ascites in 40 (33.6%) and joint pain in 36 (30.2%)cases. The distribution of 15 most common clinical signs and symptoms in terms of frequency of occurrence among these seropositive cases is depicted in Table 2. In this study the average platelet count recorded was 46508/mm^3 and range was between 14000-143000/mm^3.

In present study we observed 89 (74.8%) cases of DF, 26 (21.8%) cases of DHF and 04 (3.4%) cases of DSS. Thus, total hemorrhagic manifestations were observed in 30/119 (25.2%) cases. Among the spectrum of the symptomatology, commonest hemorrhagic manifestations were presented as body rashes 30/30 (100%), melena in 24/30 (80%) cases, epistaxis 12(40%) and gum bleeding 12 (40%) cases (Table3).

Table 1: Age wise distribution of seropositive dengue male and female cases

Age groups	Male (%)	Female (%)	Total (%)
0-18	14 (11.8)	04 (3.4)	18 (15.1)
19-25	32 (26.9)	10 (8.4)	42 (35.3)
26-35	26 (21.8)	07 (5.9)	33 (27.7)
36-45	12 (10.1)	03 (2.5)	15 (12.6)
46- 60	08 (6.7)	03 (2.5)	11 (9.2)
Total	92 (77.3)	27 (22.7)	119 (100)

Table 2: Clinical presentations of dengue fever among seropositive cases (*n*=119)

S.No	Symptoms	Total
01	Fever	118 (99.2%)
02	Headache	76 (63.8%)
03	Abdominal pain	76 (63.8%)
04	Myalgia	52 (43.7%)
05	Vomiting	44 (37%)
06	Ascites	40 (33.6%)
07	Joint pain	36 (30.2%)
08	Body itching	28 (23.5)
09	Back pain	26 (21.8%)
10	Chest pain	22 (18.5%)
11	Retro orbital pain	21(17.6%)
12	Dyspnea	18 (15.1%)
13	Pleural effusion	12(10%)
14	Diarrhea	08 (6.7%)
15	Hepatomegaly	04 (3.3%)

Table 3: Hemorrhagic dengue Fever (*n* = 30)

Symptoms	DHF (n=26)	DSS (n=4)
Body Rashes	30 (100%)	
Melena	24 (80%)	
Epistaxis	12(40%)	
Gum bleeding	12(40%)	

DISCUSSION

Dengue is an acute viral infection presenting with wide spectrum of clinical presentations, ranging from classical to fatal dengue hemorrhagic fever. [8] WHO estimated that 3.9 billion people, in 128 countries, are at risk the of infection with dengue. The number of cases reported has increased from 2.2 million in 2010 to 3.2 million in 2015 in member states of WHO. [9] The reports from various national surveillance agencies suggest that dengue fever outbreaks from different parts of India have increased in last few years. [10] The outbreaks frequency in some states of North India including Uttar Pradesh and Delhi has become more frequent with dengue fever. [3] Increase in social awareness about dengue, its annual epidemics and availability of rapid diagnostic tools in hospitals have helped in the improved case detection. The present study has attempted to describe the changing trends of clinical profile of dengue infected patients admitted at this Tertiary Care Hospital in rural area of Uttar Pradesh India.

A total of 119 patients were found seropositive during (2016-17) study period; among them, 77.3% were male. The similar frequency of male subjects was reported by many other authors, e.g. one study done by Kale *et.al.,* [11] 63% were male, while another study by Karoli *et al.,* [12] 58% were male and 42% female. The male: female ratio was 3.4:1 found in the present study and this is supported by study of Bansal *et.al.* [13] who reported similar ratio of 3:1.

Thus, it might be stated that high number of male cases might be due to their more outdoor activity and more susceptibility to other environmental risks. [14] The most common age groups affected in this study were19-25 years, followed by 26-35 years (Table1). These age groups reflect most active age groups which

actually may actually indirectly affect economic and GDP loss in the country. Many national and international studies do support our findings of the age range of15 to 45 years. [8,15]

Dengue biomarkers that have been targeted for diagnosis, include viral products (detection of the secreted NS1 protein), and/or the host immune response to virus infection virus specific antibody IgM/IgG. [16] In developing countries the diagnosis of dengue fever mainly based on serodiagnosis NS1 and IgM ELISA. In present study total 119 dengue cases detected either by NS1 and/or IgM ELISA. Out of these 84% cases were detected by NS1 ELISA and 25.2% cases by IgM ELISA method. To maintain the precision in diagnosis and to achieve maximum cases, all samples were processed same day of sample receipt and tested for NS1 antigen and IgM antibody. The NS1 had higher sensitivity in present study. The higher sensitivity of NS1 assays is also supported by many other studies. [17,18]

The clinical spectrum of dengue revealed that fever was present in99.2% of cases, and it was the principal presentation. Similar findings were reported by several other studies from India which substantiates fever as being the most common presenting symptom in dengue patients. [19,20]

In the present study the second most common symptoms after fever, were headache, abdominal pain and myalgia (Table2).A recent Indian study by Thaher *et.al*., [21] reported myalgia, abdominal pain and headache as second most common symptoms after fever. A high number cases in our study had vomiting (37%), which might be due to liver injury by viral products and deranged liver functions due altered enzyme levels. In a study by Kumar *et.al.,* [8] abdominal pain was found in 37% and vomiting in 47% cases, while according to Arunagirinathan *et.al.,* [22] abdominal pain and vomiting were observed in 61% cases. Another Indian study by Kale *et.al.,* [11] 64% cases had vomiting as main presentation. These studies support our findings that report abdominal pain and vomiting as predominant symptoms after fever, in dengue patients. It may be interpreted here that although, fever and other gastrointestinal symptoms may be caused by other infections such as typhoid, leptospirosis, enteroviral infections which are common in India but cases of fever with vomiting should be undergo testing for dengue and be kept as one of the differential diagnosis, especially in seronegative cases for dengue. [8,23] In the present study we observed joint pain in 30.2% cases, pruritus in23.5% and retro orbital pain in 17.6% cases. A study by Laul *et. al.,* [24] reports pruritus in 19% of case which slightly lower than our findings.

The present study thus concludes that 89 (74.8%) cases had DF, 26 (21.8%) DHF and 4 (3.4%) DSS and these findings are nearly similar to study by Parmar *et.al.,* [25] which reported DF in 80%, DHF in 16%, and DSS in 4% patients. In another study by Daniel *et al.,* [26] DHF/DSS rate was 33% and Karoli *et al.,* [12] found, DF rate as 70% and DHF 30%.The finding of present study were similar to above mentioned studies. The common hemorrhagic manifestations observed, include body rashes 100% and 80% melena (Table 3). The most common bleeding manifestations observed were petechial rashes and other symptoms (epistaxis, gum bleeding, hematemesis, melena, hypermenorrhea, hemoglobinuria) which helped in identifying early suspected cases of dengue hemorrhagic fever. [7]

CONCLUSION

Our study concludes, that apart from usual manifestations, sometimes unusual but clinically extremely important manifestations can occur which, if not detected early, can prove fatal. So, a vigilant and timely approach is warranted with all clinical parameters. Epidemics occurs post monsoon season thus requiring extensive preventive measures clinical diagnosis and vector control.

ACKNOWLEDGEMENT

We are thankful to Mrs. Suchitra Nirjhar and Miss Monika Singh for her technical support and the Department of Health Research (DHR), Ministry of Health & Family Welfare and ICMR for financial support under establishment of a Network of Laboratories for Managing Epidemics and Natural Calamities (Viral Research and Diagnostic Laboratory).

REFERENCES

1. Cecilia D. Current status of dengue and chikungunya in India. WHO South East Asia J Public Health. 2014;3(1):22-26.
2. Pyke AT, Moore PR, Taylor CT *et al.* Highly divergent dengue virus type 1 genotype sets a new distance record. Sci Rep. 2016; 6:22356.
3. Jain S, Mittal A, Sharma SK *et al.* Predictors of dengue-related mortality and disease severity in a tertiary care center in North India. Open Forum Infect Dis. 2017; 4(2):ofx 056
4. R Senaka. Dengue shock. J Emerg Trauma Shock. 2011;4(1):120-7.
5. Bhattacharya N, Mukherjee H, Naskar R*et al.*Serological diagnosis of dengue in laboratory practice in Kolkata. Indian J Med Microbiol. 2014;32(3):277-80.
6. Anand AM, Sistla S, Dhodapkar R *et al.* Evaluation of NS1 antigen detection for early diagnosis of dengue in a tertiary hospital in southern India. Journal of clinical and diagnostic research: J ClinDiagn Res. 2016; 10(4):1-4.
7. Kalayanarooj S. Clinical Manifestations and Management of Dengue/DHF/DSS. Trop Med Health. 2011;39(4 Suppl):83-87.
8. Kumar A, Rao CR, Pandit V *et al.* Clinical manifestations and trend of dengue cases admitted in a tertiary care hospital, udupi district, karnataka. Indian J Community Med. 2010;35(3):386-90.
9. World Health Organization (WHO); Dengue and severe dengue [Internet]. 2018 [updated 2018 Sept. 13; cited 2019 Feb. 24]. Available from http://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue.
10. Mutheneni SR, Morse AP, Caminade C *et al.* Dengue burden in India: recent trends and importance of climatic parameters. Emerg Microbes Infect. 2017; 6(8):e70.
11. Kale AV, Haseeb M, Reddy S *et al.* Clinical Profile and Outcome of Dengue Fever from a Tertiary Care Centre at Aurangabad Maharashtra India. J. Dent. Med. Sci. 2014; 13(9):14-19.
12. Karoli R, Fatima J, Siddiqi Z *et al.* Clinical profile of dengue infection at a teaching hospital in North India.J Infect Dev Ctries. 2012;6(7):551-54.
13. Bansal N, Uniyal N, Khrime D *et al.* Clinical profile and outcome of dengue fever in tertiary level hospital in Uttarakhand, India. Trans world Med J 2014;2(3):165–69.
14. Prasith N, Keosavanh O, Phengxay M *et al.* Assessment of gender distribution in dengue surveillance data, the Lao People's Democratic Republic. Western Pac Surveill Response J. 2013;4(2):1-9.
15. Thai KT, Nishiura H, Hoang PL *et al.* Age-specificity of clinical dengue during primary and secondary infections. *PLoS* Negl Trop Dis.2011;5(6):e1180.
16. Muller DA, Depelsenaire AC, Young PR. Clinical and laboratory diagnosis of dengue virus infection. J. Infect. Dis.2017;215 (suppl-2):S 89-95.
17. Tricou V, Vu HT, Quynh NV *et al.* Comparison of two dengue NS1 rapid tests for sensitivity, specificity and relationship to viraemia and antibody responses. BMC Infect Dis 2010;10:142.
18. Debnath F, Ponnaiah M, Acharya P. Dengue fever in a municipality of West Bengal, India, 2015: An outbreak investigation. Indian J Public Health. 2017;61(4):239-42.
19. US Department of Health and Human Services, Centers for Disease Control and Prevention. Dengue and Dengue Hemorrhagic Fever: Information for Health Care Practitioners.[Internet]. 2010 [updated 2010; cited 2019 Feb. Available at http://www.cdc.gov /ncidod/ dvbid/dengue/dengue-hcp.htm
20. Mandal SK, Ganguly J, Sil K*et al.* Clinical profiles of dengue fever in a teaching hospital of eastern India. National J Med Res. *2013*; 3(2): 173-76.
21. Thaher MA, Ahmad SR, Chandrasekhar A.Clinical presentation and outcome of dengue cases in a tertiary care hospital, Hyderabad. Int J Med Sci Public Health 2016;5(10):2009-12.
22. Arunagirinathan A, Thirunavukarasu B, Narayanaswamy DK *et al.* Clinical profile and outcome of dengue fever cases in children by adopting revised WHO

guidelines: A hospital based study. Int J Sci Stud. 2015;3(2):174-78.
23. Khan E, Siddiqui J, Shakoor S*et al*. Dengue outbreak in Karachi, Pakistan, 2006: experience at a tertiary care center. Trans R Soc Trop Med Hyg. 2007;101(11):1114-19.
24. Laul A, Laul P, Merugumala V *et al.* Clinical profiles of dengue infection during an outbreak in Northern India. J Trop Med. 2016;5917934:1-7.
25. Parmar K, Amin B, Hadiyel I *et al.* A Study of Symptomatic and Clinical Profile in Dengue Patients. Natl J Integr Res Med, 2013;4(6):94–96.
26. Daniel R, Philip AZ. A study of Clinical Profile of Dengue Fever in Kollam, Kerala, India. Dengue Bull 2005;29:197–202.

How to cite this article: Kumar M, Verma RK, Kumar D et. al. Recent trends in clinical presentation in cases of dengue presenting at tertiary care hospital. International Journal of Science & Healthcare Research. 2019; 4(1): 356-361.

******