ANALYTICAL STUDY OF VIRAL FEVER CASES ADMITTED IN A TERTIARY CARE HOSPITAL, NELLORE, A.P.

Cherukuri Nirmala¹, Moturi Ratna Manjula², Chinta Lakshmi Prasanna³, Gottumukkala Ravi Prabhu⁴

¹Associate Professor, Department of Paediatrics, ACSR Government Medical College, Nellore.

²Associate Professor, Department of Paediatrics, ACSR Government Medical College, Nellore.

³Assistant Professor, Department of Paediatrics, ACSR Government Medical College, Nellore.

⁴Professor and HOD, Department of Community Medicine, ACSR Government Medical College, Nellore.

ABSTRACT

BACKGROUND

Viral fevers are the cause for admission in the hospital during certain seasons of the year. Commonly, the hospitalisations often increase in the monsoon period during the months of July to November in most of the regions across the world due to seasonal changes. The vector-borne diseases especially Malaria, Dengue increase with changes in the humidity, temperature, rainfall and pooling of water in the households. In this present study, an attempt is made to find out the probable cause of fever among admitted cases of viral fever.

MATERIAL AND METHODS

This study was a retrospective study carried out in the Paediatric Department at a newly commissioned Medical College Hospital at Nellore, Andhra Pradesh, during August 2015 to November 2015 as obtained from the medical records and admission registers.

RESULTS

Of the total 596 cases, 201 children were with a diagnosis of viral fever. There was a male preponderance which was however not statistically significant. The viral fever cases accounted for 6% and 43.8% of the total admitted cases in the months of August and October 2015 respectively. Laboratory investigations revealed thrombocytopenia in 57.5% of the children and leucopenia in only 5.5% of them. NS₁ antigen testing in 17 cases showed 88.8% positivity. IgM antibody against Dengue in 109 cases showed positivity in 37.6% of cases. Thrombocytopenia was more frequently seen among children admitted in PICU. There was a correlation of thrombocytopenia and positivity of either NS₁ antigen or Dengue IgM antibody.

CONCLUSION

In view of these findings, it can be concluded that the surge in viral fever cases may be probably due to Dengue fever.

KEYWORDS

Viral Fevers, Thrombocytopenia, NS₁ antigen, IgM Antibody.

HOW TO CITE THIS ARTICLE: Nirmala C, Manjula MR, Prasanna CL, et al. Analytical study of viral fever cases admitted in a tertiary care hospital, Nellore, A.P. J. Evolution Med. Dent. Sci. 2016;5(67):4774-4778, DOI: 10.14260/jemds/2016/1088

INTRODUCTION

There are seasonal outbreaks in disease occurrence depending upon the endemic conditions and environmental influences. In developing countries, infectious diseases contribute to significant morbidity and mortality. Climate plays an important role in the transmission of infectious diseases and its impact can be attributed to the human behaviour, the disease pathogen and the vector.^{1,2}

Though respiratory infections and diarrheal diseases are the common causes of mortality and morbidity in children under five years, viral fevers are also the cause for admission in the hospital during certain seasons of the year. Commonly, the hospitalisations often increase in the monsoon period during the months of July to November in most of the regions

across the world due to seasonal changes.³ Community acquired pneumonia has a seasonal peak in hospitalisations during winter, spring and the months of December and January.⁴ The vector borne diseases especially Malaria and Dengue increase with changes in the humidity, temperature, rainfall and pooling of water in the households. Despite panic like situation in outbreaks, medical professionals attempt to find out the aetiology of the outbreak, which though possible may not be feasible due to deficiency in the diagnostic facilities. In this present study, an attempt is made to find out the probable cause of fevers that occurred in the months of October and November 2015 in the district of Nellore in comparison to the months of August and September 2015.

METHODS

This study was a retrospective study carried out in the Paediatric Department at a newly commissioned Medical College Hospital at Nellore, Andhra Pradesh, with overall 750 beds and 100 paediatric beds. The data collection and analysis of results was carried out from December 2015 to February 2016. All the admitted children with a diagnosis of viral fever during August 2015 to November 2015 were included in the study. The information regarding age, gender, laboratory investigations were analysed to study the probable cause and its effect among admitted children and their outcome. The

Financial or Other, Competing Interest: None.

Submission 26-06-2016, Peer Review 20-07-2016,

Acceptance 26-07-2016, Published 20-08-2016.

Corresponding Author:

Dr. Cherukuri Nirmala,

Flat No. 3, Esteem Villa,

Behind Bhavan's School,

Vivekanandapuram North,

Sainikpuri, Secunderabad-500094.

Telangana, India.

E-mail: cnirmala06@yahoo.com

DOI: 10.14260/jemds/2016/1088

details were retrieved from the medical records and admission registers.

RESULTS

A total of 596 children were admitted for various ailments during the period between August and November 2015 in Department of Paediatrics at Government General Hospital, Nellore attached to ACSR Government Medical College, Nellore. Out of the total 596 cases admitted, about 201 cases were diagnosed to be suffering from viral fever based on clinical criteria. Out of these total 201 cases, analysis of the age and gender distribution of children showed no gender discrimination in care seeking behaviour among parents. Majority of the children were above the age of 5 years. Overall, there is preponderance of male children (53.2%) compared to female children (46.8%). In all the age groups also, a higher proportion of male children was found compared to that of female children. However, the differences in the proportions of gender among various age groups was not statistically significant ($\chi^2=1.50$; 0.90; NS) (Table 1 and Fig. 1).

The number of cases per month revealed that viral fever cases accounted for only 6% of the total in the month of August and peaked in the month of October to 43.8%. This sudden increase in the cases is mainly attributed to an epidemic of viral fevers in the surrounding areas. Proportionately, the outpatient department of paediatrics has also seen a surge in the cases to three fold (Table 2 and Fig. 2).

Out of a total of 201 cases, blood analysis for leucopenia and thrombocytopenia was done in 145 suspected individuals. It was found that out of these 145 cases, leucopenia was found in 8 cases (5.5%), thrombocytopenia in 75 cases (51.7%), while in 5 cases (3.4%) both leucopenia and thrombocytopenia was found. Investigation for NS1 antigen was done in 17 cases (8.5%), out of which 15 cases were positive (88.2%). Investigation for IgM antibodies against dengue was done in 109 cases (54.2%), out of which 41 cases (37.6%) were positive. The summary of the investigative findings are as depicted in Table 3.

Analysis of platelet count and its co-relation with NS1 antigen positivity and IgM antibodies against Dengue was carried out. It was found that the thrombocytopenia was found to be significantly higher in those cases with NS1 Ag positivity or IgM positive cases and also in the group of cases in whom either NS1 Ag or IgM is positive or both. Thus, NS1 Ag and IgM positivity was significantly associated with thrombocytopenia (Table 4).

The mean platelet count was found to be lower in those with ICU admission (95,711) compared to those without ICU admission (1,24,880), but the difference however was not statistically significant ($P=0.08$; NS) (Table 5).

To conclude, the occurrence of more cases of viral fever during the rainy season co-relates to increased incidence of the same due to seasonal changes. Further, during an outbreak in focal areas, the possibility of common viral fevers that had existed in the previous year should be kept in mind. The availability of the appropriate investigations during the outbreaks without loss of continuity shall enable us to know the incidence, involvement if any of other systems and the serotype of the dengue. The data can be utilized to take steps to prevent, limit the mortality or to control the outbreak.

Age Group (Years)	Male (%)	Female (%)	Total (%)
Less than 1 Year	6 (66.7)	3 (33.3)	9 (100.0)
1 – 2	5 (62.5)	3 (37.5)	8 (100.0)
2 – 3	8 (61.5)	5 (38.5)	13 (100.0)
3 – 4	8 (53.3)	7 (46.7)	15 (100.0)
4 – 5	8 (53.3)	7 (46.7)	15 (100.0)
5 & Above	72 (51.1)	69 (48.9)	141 (100.0)
Total	107 (53.2)	94 (46.8)	201 (100.0)

Table 1: Age and Gender Distribution of Children

$\chi^2=1.50$; 0.90; NS

Month	No. of Cases	Percentage
August 2015	12	6.0
September 2015	24	11.9
October 2015	88	43.8
November 2015	77	38.3
Total	201	100.0

Table 2: Prevalence of Cases by Month

Sl. No.	Parameter	No. of Cases	Percentage
1	Total Number of Viral Fever Cases	201	---
2	Blood Investigation done for Leucopenia and Thrombocytopenia	145	72.1
3.	No. of cases with Leucopenia	8/145	5.5
4.	No. of cases with Thrombocytopenia	75/145	51.7
5.	No. of cases with both Leucopenia and Thrombocytopenia	5/145	3.4
6.	Investigation done for NS1	17/201	8.5
7.	No. of cases with NS1 Positivity	15/17	88.2
8.	No. of cases Investigated for IgM	109/201	54.2
9.	No. of cases with IgM Positivity	41/109	37.6

Table 3: Summary of Certain Laboratory Findings

Sl. No.	Group Investigated	No. of Cases Investigated	No. of Cases Positive	%	P value
1.	NS 1 Ag Positive	15	11	73.3	0.003; S
2.	IgM Positive against Dengue	41	23	56.1	0.005; S
3.	Either NS 1 Ag or IgM Positive	55	33	40.0	<0.001; S

Table 4: Analysis of the Thrombocytopenia among NS1 or IgM Positive Cases

ICU Admission	No. of Cases	Platelet Count		P value
		Mean	SD	
Yes	59	95,711	82,439	0.08; NS
No	142	1,24,880	1,16,463	

Table 5: Analysis of Mean Platelet Count with ICU Admission

Fig. 1: Age & gender distribution of children **Fig 2: Trend of cases over the various months**

DISCUSSION

An epidemic is the occurrence of more cases of disease than expected in a given area or among a specific group of people over a particular period of time.⁵ In contrast, a cluster is an aggregation of cases in a given area over a particular period without regard to whether the number of cases is more than expected. Outbreaks of fever due to various aetiologies occur during the months of July to November in various regions all over the world. Whenever there is a sudden surge in the children attending the outpatient clinics, it is indicative of the impending rise in hospitalisation of the sick children. In the present study, it was found that viral fever is the most common cause of hospitalisation during the months of October and November in contrast to August and September months. Kalyani and Shankar also found viral fever to be the commonest cause of disease burden.⁶ In order to identify the most probable cause of these viral fevers during the present study, the causative agents in the previous years have been considered.

In view of the rainy season and with the occurrence of Dengue or Chikungunya outbreaks in and around the region in the past, the possibility of Dengue was considered based on the symptoms. The common symptoms in the present study among viral cases were fever, myalgias, headache, vomiting followed by recovery or progress to severe Dengue, which includes Dengue Shock Syndrome and Dengue Haemorrhagic Fever. As per the WHO guidelines, the symptoms mentioned above correlate to the classification as probable Dengue.⁷ In older children, retro-orbital pain is also a significant symptom. The laboratory investigations in the present study revealed that around 51.1% cases had thrombocytopenia and a few cases had leucopenia. Laboratory diagnosis of confirming dengue is by detection of virus, viral nucleic acid, antigens or antibodies or both. During the early stages, virus isolation or antigen detection is helpful in diagnosis. NS₁ is a marker of acute dengue infection, which is a non-structural protein detected in both primary and secondary infection cases during

first 6 days of the illness.⁵ Dengue specific IgM antibody starts rising from 3-5 days of the onset of illness and peaks by 2 weeks after onset and persists till 3 months. IgM ELISA offers reliable diagnosis as done in the current study.⁸

Dengue serotype confirmation is done by RT PCR (reverse transcriptase), which allows for a rapid identification.⁹ There are four distinct serotypes of dengue, which can cause infection (DENV-1, DENV-2, DENV-3 and DENV-4). In India, all four serotypes are identified of which the most widespread are DENV-1 and DENV-2.¹⁰ Dengue infection on recovery provides lifelong immunity against that particular serotype. Cross-immunity is only partial. There is an increased risk of development of severe dengue with subsequent infections by other serotypes. Irrespective of the serotypes of dengue virus, it was found that the NS₁ antigen rises in the early phase of infection.¹¹

In the present study, NS₁ antigen detection and IgM antibody levels to dengue infection were determined depending on the availability of the kits. The NS₁ antigen was found to be positive in 15 of the 17 cases tested and IgM positivity was 41 of the 109 cases tested. In a study by Kassim et al, it was found that a combination of NS₁ antigen and serology detection against dengue was comparable to PCR and serology. They concluded that the diagnostic efficiency in early diagnosis of dengue can be enhanced by combining NS₁ antigen with serology.¹² In a study by Datta and Wattal, it was found that NS₁ antigen assay has high specificity in diagnosing dengue fever and dengue haemorrhagic fever during the first 4 days of illness. It was also noted that NS₁ in combination with MAC-ELISA on a single serum sample is effective in diagnosing dengue fever without the need of the paired sera.¹³ In the present study, a co-relation of NS₁ antigen and IgM positivity to thrombocytopenia was analysed and it was found that the degree of thrombocytopenia was higher where either of the above was positive. It was observed that high titre of NS₁ antigen in the first 3 days of fever correlated with platelet count of less than one lakh and DHF.¹⁴ In a study by Paronavitane et al, it was concluded that NS₁ antigen has been associated with severe dengue. Hence, the positivity to NS₁ antigen should alert the treating clinician to closely monitor these children for early detection of the complications.^{14,15} Thrombocytopenia was more commonly seen among children who were admitted in intensive care unit in comparison to those in the paediatric wards. Thrombocytopenia is defined as a platelet count below 1,50,000/cumm.¹⁶ Dengue is mostly a self-limiting illness diagnosed clinically and confirmed by laboratory investigations. Mortality is high among severe dengue.¹⁷

In the present study, 2 children died due to severe dengue. As per WHO, 100 countries were found to be endemic for dengue. South East Asia and Western Pacific account for >70% of the disease burden.¹⁸ An estimated 390 million dengue infections occur per year, of which clinically manifested cases were about 96 million.¹⁹ Dengue is transmitted by the bite of a female *Aedes aegypti* mosquito, which is a daytime feeder with peak time of biting being early in the morning and in the evening before dusk. It breeds in fresh water and in water stored for drinking, bathing and in rain water collected in containers around the households. Urbanisation, limited flight range of the vector facilitates the outbreaks of infection during seasonal variation and these outbreaks can be explosive.²⁰ Though *Aedes Albopictus* transmits dengue, it is not very

common. Dengue is an RNA virus with a peak incidence during the rainy season. There is a co-relation between incidence of dengue cases and high larval index of *Aedes aegypti* during the same time. Anticipation of the possibility, early detection and confirmation may reduce the mortality in children.²¹ When cases are reported with similar symptoms in a cluster or different areas in a district, adequate measures can be taken to control by taking anti-larval measures, vector control and reducing the transmission. It has been found in a study by Wongkoon et al that higher incidence of dengue corresponded with increased *Aedes* larvae.²² In dengue endemic areas, the children are most affected.²³ Worldwide, dengue virus is the most widespread of the arboviruses in the tropical and subtropical regions. There has been progress in prevention and control of infectious diseases with improvement of environmental conditions, hygiene, sanitation and use of vaccines.²⁴ There is a seasonal rise in cases mostly during rainy season, which was noted in our study with more cases requiring admission during the months of October and November.

Development of climate-based dengue early warning systems may in future predict the probable epidemics and measures can be taken to contain the situation.²⁵ Strengthening of the surveillance system for communicable and non-communicable diseases shows the seasonal trends. This knowledge may allow the administrators to take measures in preventing the occurrence and to contain the outbreaks in future.²⁶

Seasonal variation of communicable diseases is commonly observed in various parts of the world. This present study highlights the need to investigate when more cases are reported than the previous months and to keep in mind the pattern of fevers, environmental conditions and the possibility of vector-borne diseases while investigating.

Limitation of the Study

Dengue virus isolation or serotype identification could not be done in the cases of viral fever due to lack of availability of the appropriate diagnostic facilities. The serology and NS1 antigen tests were done in few cases.

REFERENCES

1. WHO using climate to predict Infectious disease outbreaks: a review. Geneva: World Health organization 2004.
2. Fares A. Factors influencing the seasonal patterns of infectious diseases. *Int J Prev Med* 2013;4(2):128-32.
3. Kumari R, Nath B, Midha T, et al. Morbidity profile and seasonal variation of diseases in a primary health center in Kanpur district: a tool for the health planners. *J Family Med Prim Care* 2012;1(2):86-91. doi:10.4103/2249-4863.104943.
4. Murdoch KM, Mitra B, Lambert S, et al. What is the seasonal distribution of community acquired pneumonia over time? A systematic review. *Australas Emerg Nurs J* 2014;17(1):30-42. doi: 10.1016/j.aenj.2013.12.002.
5. Park K. Park's Textbook of preventive and social medicine. 23rd edn. India: M/S Banarsidas Bhanot, chapter 3,5 2015:92-94, 246-55.
6. Kalyani D, Shankar K. Assessment and seasonal variations of communicable diseases: 3-year study. *Int J Res Med Sci* 2016;4(4):1186-92. doi:10.18203/2320-6012.
7. WHO. Dengue guidelines for diagnosis, treatment, prevention and control, new edition 2009.
8. Kapil A. Ananthanarayan and Paniker's textbook of microbiology. 9th edn. Published by universities press 2013:523.
9. Brooks GF, Carroll KC, Butel JS, et al. Arthropod borne and rodent borne viral diseases. In: Jawetz, melnick & adelberg's medical microbiology. 26th edn. New York: McGraw-Hill Medical 2013:564-6.
10. WHO. Comprehensive guidelines for prevention and control of dengue and dengue haemorrhagic fever. Revised and expanded edition, regional office of South-East-Asia 2011.
11. Bessof K, Delorey M, Sun W, et al. Comparison of two commercially available dengue virus (DENV) NS1 capture enzyme-linked immunosorbent assays using a single clinical sample for diagnosis of acute DENV infection. *Clin Vaccine Immunol* 2008;15(10):1513-8.
12. Kassim FM, Izati MN, TgRogayah TA, et al. Use of dengue NS1 antigen for early diagnosis of dengue virus infection. *Southeast Asian J Trop Med Public Health* 2011;42(3):562-9.
13. Datta S, Wattal C. Dengue NS1 antigen detection: a useful tool in early diagnosis of dengue virus infection. *Indian J Med Microbiol* 2010;28(2):107-10.
14. Libraty DH, Young PR, Pickering D, et al. High circulating levels of the dengue virus non-structural protein NS1 early in dengue illness correlate with development of dengue haemorrhagic fever. *J Infect Dis* 2002;186(8):1165-8.
15. Paranavitane SA, Gomes L, Kamaladasa A, et al. Dengue NS1 antigen as a marker of severe clinical disease. *BMC Infectious Diseases* 2014;14(1):570.
16. WHO. Dengue haemorrhagic fever: diagnosis, treatment, prevention and control. World Health Organization Geneva, Switzerland 1997.
<http://www.who.int/csr/resources/publications/dengue/Denguepublication/en/>
17. Balasubramanian S, Ramachandran B, Amperayani S. Global child health. Dengue viral infection in children: a perspective. *Arch Dis Child* 2012;97(10):907-12. doi:10.1136/archdischild-2012-301710.
18. WHO. Dengue and severe dengue. Fact sheet updated 2016.
19. Bhatt S, Gething PW, Brady OJ, et al. The global distribution and burden of dengue. *Nature* 2013;496(7446):504-7.
20. Behrman RE, Kliegman R, Nelson WE. Nelson textbook of paediatrics. Dengue fever and dengue hemorrhagic fever. 18th edn. Philadelphia: W.B. Saunders Co 2002:1412-5.
21. Bhatnagar S, Lal V, Gupta SD, et al. Forecasting incidence of dengue in Rajasthan using time series analyses. *Indian J Public Health* 2012;56(4):281-5.
22. Wongkoon S, Jaroensutasinee M, Jaroensutasinee K. Distribution, seasonal variation and dengue transmission prediction in Sisaket, Thailand. *Indian J Med Res* 2013;138(3):347-53.
23. Wilder-Smith A, Ooi EE, Vasudevan SG, et al. Update on dengue: epidemiology, virus evolution, antiviral drugs, and vaccine development. *Curr Infect Dis Rep* 2010;12(3):157-64.

24. Jones KE, Patel NG, Levy MA, et al. Global trends in emerging infectious diseases. *Nature* 2008;451(7181):990-3.
25. Kuhn K, Campbell-Lendrum D, Haines A, et al. WHO. Using climate to predict infectious disease epidemics 2005.
26. Detels R, Mceven J, Beaglehole R, et al. Oxford text book of public health. 4th edn. New York: Oxford University Press 2002.