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Sero- Epidemiological trends of Dengue Fever in Jammu Province of J&K State

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ABSTRACT

Dengue, an arthropod-borne arboviral disease is becoming a major public health concern, both in the tropical and subtropical regions of the world. In view of exponential increase in dengue positive cases reported in 2013, this study to follow the emerging trends of the disease over a period of five years from 2011 to 2015 was planned. The laboratory records of clinically suspected Dengue patients from 2011 to 2015 were analyzed retrospectively for the results of IgM anti dengue antibodies tested by Dengue IgM capture ELISA (MAC ELISA) along with demographic features, and seasonal variations. A total of five thousand nine hundred fifty (5950) samples from patients suspected of dengue infection were received and screened for the presence of dengue specific IgM antibodies.1891/5950 (31.78%)of the samples were found to be positive. The association between serum samples and different age groups was found to be highly significant (p=0.0000).Dengue infection has recently become an endemic disease in this region occurring annually. In absence of specific treatment and vaccine for dengue fever (DF), early diagnosis is important in management of infection. This also demands continuous seroepidemiological surveillance for the timely formulation and implementation of effective dengue control programme. Moreover, serological crossreactivity with other Flaviviruses was unexpected in Jammu, for their absence.

Key words: Seroepidemiology, Dengue fever, IgM antibody capture enzyme linked immune sorbent assay(MAC ELISA), India, Vector.

INTRODUCTION

Dengue virus (DV) is a positive-stranded encapsulated RNA virus of the family *Flaviviridae*. There are four serotypes of the virus referred to as DV-1, DV-2, DV-3 and DV-4[1]. It is transmitted mainly by *Aedes aegypti* mosquito and also by *Aedes albopictus*. All four serotypes can cause the full spectrum of clinical illness, ranging from an asymptomatic or mild febrile illness to classic dengue fever (DF) to the most severe type of illness i.e. Dengue Hemorrhagic Fever (DHF) &Dengue Shock Syndrome (DSS) [2]. Global epidemiology of dengue is showing a discernible upward trend in recent years and the disease is associated with increasing frequency of outbreaks. In India first epidemic was experienced in Kolkata during1963-64. Since then DV infection has occurred in many places in India [3, 4]. One of the largest outbreaks in North India occurred in Delhi in 1996, followed by another in 2003[5]. The South East Asia region is currently experiencing an upsurge in reported cases of dengue in a number of countries, including India, Sri Lanka and Thailand [6]. Approximately 2.5 billion people are estimated to be at risk of acquiring dengue infection and 50 to 100 million people are believed to be infected worldwide annually, with half a million life-threatening infections requiring hospitalization, resulting in approximately 12,500 to 25,000 deaths (6).Treated DHF/DSS is associated with 3% mortality , while untreated is with 50 % mortality [7]. Thus, early laboratory diagnosis of dengue virus infection is important for management of the cases and is routinely done by serological tests. This study was designed to observe the trends of the serologically positive cases of dengue infection at Jammu, a town of North India from July to December over the period of five years from 2011-2015.

MATERIALS AND METHODS

Before the start of this study permission was taken from the Institutional Ethical Committee (IEC), Government Medical College Jammu. In our study, blood samples were received from the various district hospitals and also from out-patient department and wards of medicine and paediatrics specialties of Govt. Medical College, Hospital, Jammu, a tertiary care teaching hospital and processing of samples was done at Department of Microbiology, GMC, Jammu. Cases with high fever and clinical symptoms suggestive of dengue infection (as per WHO criteria) were included in the study. 2 to 3 ml of blood was collected from each patient by nursing personnel or physicians using strict aseptic precautions and serum was collected using standard methods. Serum collected was tested for IgM anti dengue antibodies by Dengue IgM capture enzyme linked immune sorbent assay (MAC ELISA)(PanbioPty limited, Queensland, Australia or kits by National Institute of Virology, Pune). Briefly, the procedure was done as follows: 125 µl of peroxidase-labelled antidengue monoclonal antibody conjugate was added in the microwell containing dengue 1 to 4 antigens (antigen plate), resulting in the formation of antigen antibody complex. Within 10 min of addition of conjugate to the antigen plate, 100 µl of 1:100 diluted serum and control were added to another plate (assay plate) containing antihuman IgM antibodies or IgM antibodies attached to microwell test strips. The assay plate was incubated at 37°C for one hour and then washed. After that, 100 µl of complexed antigen conjugate solution was transferred from the antigen plate to assay plate which was further incubated for one hour. After incubation, the microwells were washed and 100 µl of tetramethyl-benzidine/ hydrogen peroxide (TMB/H_20_2) substrate solution was added to each well. After 10 min of incubation at room temperature, stop solution was added to each well and the colour density of the residue (optical density) was read within 30 min at the wavelength of 450 nm. Patients with positive anti dengue IgM were considered positive cases for dengue viral infection. For the year 2015, depending upon the duration of illness diagnosis of DV infection was done by demonstration of NS1Antigen (fever <5 days) or anti DV IgM antibodies (fever =/>5 days).The data was collected, tabulated and analysed. Pearson's chi-square test was used as test of significance and $p<0.05$ was considered significant.

RESULTS

The results have revealed that during five years of the study period, a total of 5950 serum samples were examined. It was further found that 1891/5950 samples were positive for IgM antibodies thus giving a positivity rate of 31.78%. The seasonal trend of the dengue fever for the month of July to December in the successive years of 2011-2015 is shown in Table-1. The state of Jammu and Kashmir has two provinces for administrative purposes, Jammu and Kashmir. Jammu province has ten districts under its jurisdiction and district wise distribution of serum samples is depicted in Table- 2. Sex wise distribution of the serum samples is shown in the Table- 3 and no association was found between sex and year of serum sample collection ($p>0.05$).

The serum samples were further analyzed on the basis of age where it was found that 87.6% (1657/1891) of the serum samples belonged to age group≥12years. This association between yearly serum samples and different age groups was found to be highly significant ($p=0.0000$).

DISCUSSION

Dengue is one of the most important emerging public health care problem of tropical and sub tropical region and in the last decade, a regular occurrence with periodic upsurges has been noted [8] in most parts of India. In our study, an increase in number of dengue patients has been observed in year 2013 and 2015. Maximum seropositivity was reported in the year 2013 i.e.36% followed by 16.9% in the year 2015. The dengue positive cases were seen to be on the lower side in the year 2011,2012 and 2014 as only few cases were reported i.e., 4.5%,3.5%and 1.29% respectively.

In the current study, 31.78% samples were serologically positive for dengue infection while Ekta etal reported a slightly higher rate of 44.56% of seropositivity in their study. Other studies associated in India from Delhi and Gwalior reported much higher seropositivity rates to the tune of 95%, and 65% respectively [9, 10]. However the results of present study are in agreement with a study from Brazil, which also reported a seropositivity of 30% [11]. The higher seropositivity in other studies could be best explained because of the heavy load of migratory floating population from dengue endemic states of India and higher dengue virus activity resulting into higher rate of transmission. Another factor which could contribute to higher rates of transmission could be temporary shelters for

construction workers who do not have adequate water supply and are forced to store water for construction as well for human use which could act as breeding grounds for the mosquitoes.

However, dengue was hypoendemic in the Jammu province despite the fact that the climate of Jammu is favourable for growth and spread of virus. Three plain districts of Jammu province Kathua, Samba and Jammu, adjoin the state of Punjab and climate is similar in both the regions. District wise distribution of seropositive samples show a clear trend of more number of cases from these three districts in comparison to the rest of districts of Jammu province which usually have a hilly terrain. Dengue infection is no more an urban area infection but it has affected the rural areas also as positive samples were found to be present in patients residing in rural areas also. Human migration patterns disperse vectors and viruses in the new areas. Further, the rise found in the year 2013 may be partially attributed to the rapid unplanned urbanization with unchecked construction activities and poor sanitation facilities contributing fertile breeding grounds for mosquitoes. It is also true that an increase in the alertness among medical fraternity following the initial epidemics in North India and the availability of diagnostic tools in the hospital have contributed to the increased detection of cases.

A monthly distribution of the cases in the current study shows an increase from the month of September onwards which concurs with other outbreaks in India [12]. To correlate the seasonal variation of the disease, analysis of the data on monthly basis was done. A gradual increase in cases was noticed from August with a peak in October, during the study. The correlation between occurrence of dengue and monsoon season is clearly evident in this study and is further supported by similar findings from Delhi, Ludhiana, Chandigarh and Karachi [12-15]. It may be because this season is very favorable for high breeding of the vector, that is, *Aedes aegypti*. This seasonal outbreak of disease transmission is very important at local level for effective control measures and that preventive measures against dengue infection should come into full swing during water stagnation periods after the initial bouts of rainfall and at the end of monsoon.

Fig 1.Distribution of positive and total serum samples on an yearly basis

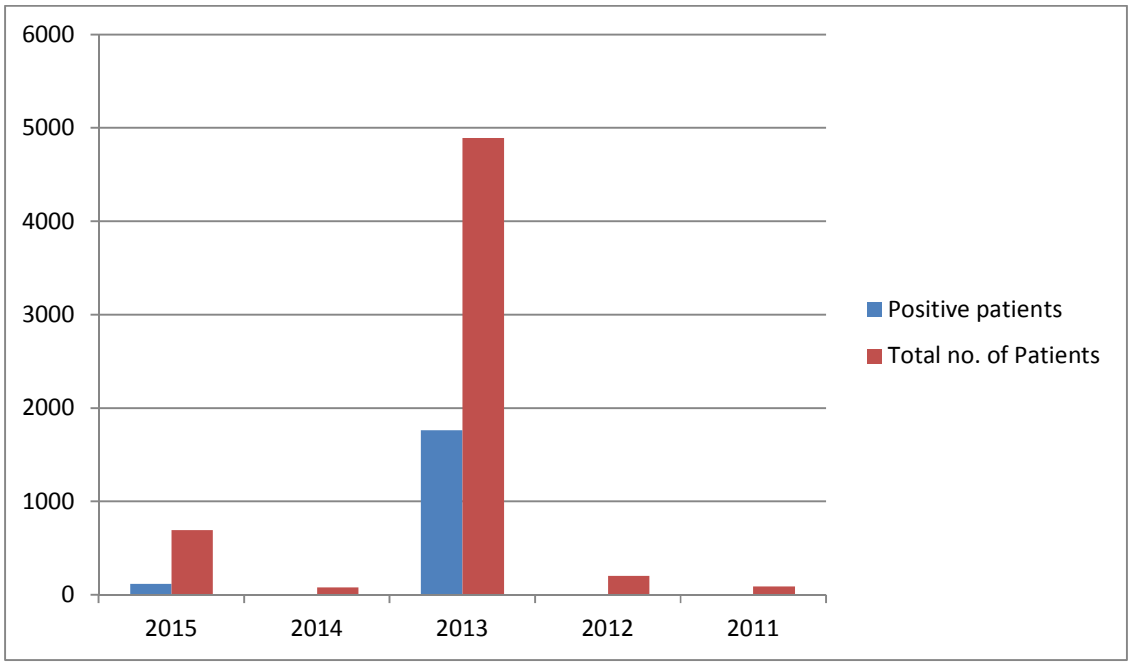

Table1: Year and month-wise Distribution of the collected samples from 2011-2015

Year	July	Aug	Sept	Oct	Nov	Dec	Total
2015	0(1)	3(37)	26(166)	80(339)	8(127)	0(22)	117 (692)
2014	0(5)	0(15)	0(26)	0(18)	1(11)	0(2)	1(77)
2013	-	0(16)	213(766)	1186(3668)	109(680)	7(29)	1762(4891)
2012	0(8)	0(41)	2(70)	4(47)	1(34)	0(0)	7(200)
2011	0(0)	0	0	0(18)	4(42)	0(29)	4(90)

Table2: District-wise distribution of dengue cases in Jammu Province

Year	Jammu	Samba	Kathua	Udhampur	Reasi	Poonch	Ramban	Rajouri	Doda	Kishthwar	
2015	77(474)	7(36)	20(84)	2(26)	3(18)	1(8)	1(6)	2(20)	3(18)	1(2)	117(692)
2014	1 (77)	-	-	-	-	-	-	-	-	-	1 (77)
2013	1265 (3387)	405 (1201)	56(190)	8(33)	6(22)	5(10)	6(13)	9(15)	2(15)	0(5)	1762(4891)
2012	7(200)	-	-	-	-	-	-	-	-	-	7(200)
2011	4(90)	-	-	-	-	-	-	-	-	-	4(90)

Table 3: Year & Sex-wise distribution of dengue cases

Year	Male	Female	Total
2015	90 (469)	27 (223)	117(692)
2014	1(43)	0(34)	1(77)
2013	1350(3160)	412 (1731)	1762(4891)
2012	4(116)	3(76)	7(200)
2011	2(55)	1(35)	4(90)

Chi-square (x^2) = 1.952
Df = 4
p = 0.7445

Fig.2 Distribution of cases on the basis of sex

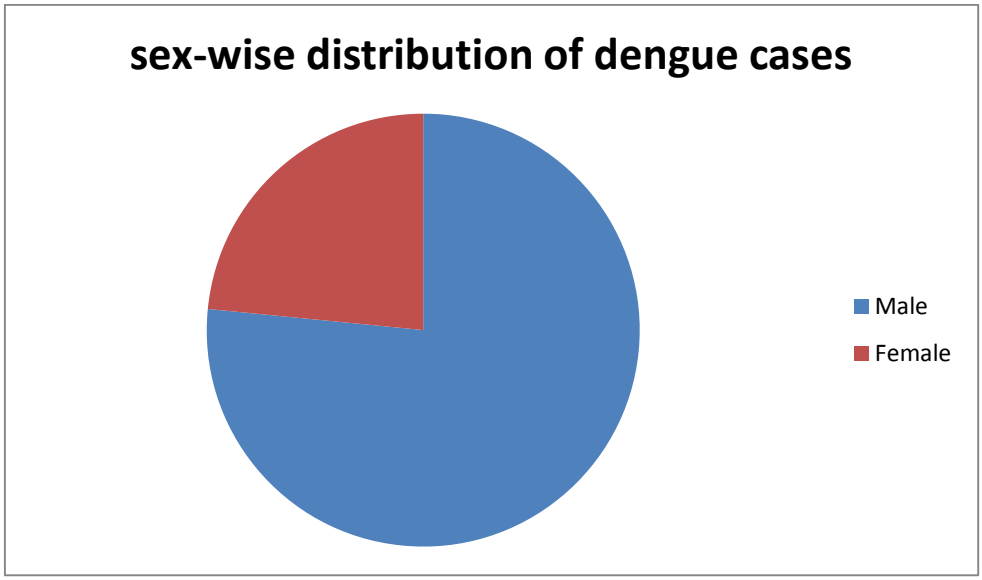

Table 4: Distribution of the dengue Positive cases on the basis of age& year

Year	0 <12yrs	≥ 12 and above	Total
2015	35	82	117(692)
2014	0	1	1(77)
2013	198	1564	1762(4891)
2012	0	7(200)	7(200)
2011	1(3)	3(87)	4(90)

Chi-square (x^2) = 37.02
Df = 4
p = 0.0000

Sex wise analysis revealed a male predominance, which is consistent with observations in other Indian studies [16, 17]. Males are associated with more outdoor activities leading to increased proneness to mosquito bite during the day time. Our study revealed that only 12.37% (234 /1864) children below the age of 12 years were found to be positive and majority of the cases were present in age group beyond 12 years. These findings are consistent

with other Indian studies, as most of the other Indian studies have reported 12 to 45 years as the most affected age group [16-18]. On the contrary, several international studies, dengue has been reported to mainly a pediatric public health problem for example a study from Cambodia further reported large number of pediatrics admission for dengue fever in a National Pediatric Hospital [19].

The main limitation of the current study was that all the serum samples were collected from the government hospitals / institutions .So, the patients going to private hospitals or private practioners could not be included in the study for the obvious reasons. Thus it would be pertinent to admit that the trends of dengue fever in this study may not be truly representative of the Jammu province.

CONCLUSION

Dengue continues to be a global challenge as public health problem, both in underdeveloped and developing countries. There is no available antiviral therapy and management is mainly supportive. Early detection of DF can help to reduce morbidity and mortality especially in DHF and DSS cases. Thus, tests to detect NS1 antigen and IgM antibodies should be available at primary health centers, so that cases can be diagnosed early and thus properly managed. Also, implementation of vector control strategies is essential to prevent such outbreaks. This will also be beneficial in controlling the other mosquito borne diseases like Chikungunya, Japanese Encephalitis, West Nile, Zika, Yellow Fever encephalitis etc and even the vector borne parasitic disease like Malaria and Filaria.

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