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Trend in Sero-Prevalence of Dengue Infection in Rural Kerala, India

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A B S T R A C T

Currently, dengue virus infection has become one of the major public health problem in India. The dengue virus infection which was primarily urban centric is now encroaching to rural parts of India. A three year trend study of dengue virus infection was carried out from January 2015 to December 2017 in the rural part of Kerala. Serological markers for dengue virus infection like NS1 (non-structural protein) antigen, Ig M, Ig G along with socio-demographic variables were analyzed. The overall year wise prevalence of dengue (at least one test positive) infection was 31.5%, 18.1% and 36.7% in 2015, 2016 and 2017 respectively Most of the individuals were above the age of 30 years in the study population. The peak of epidemic was seen from the month of June to September except for the year 2016. Our study has shown increasing number of dengue virus infections in rural part of Kerala with some fluctuations year on year. More emphasis should be stressed on the preventive aspects of dengue virus infections.

Introduction

Dengue has become the fastest emerging arboviral vector borne disease in the world (WHO, 2013). Dengue virus is transmitted by the bite of the mosquitoes *Aedes aegypti* and *Aedes albopictus*. In recent decades the world has witnessed significant rise in the incidence of dengue cases (WHO, 2018).

In 128 countries 3.9 billion people are at risk of infection with dengue viruses (Brady *et al.*, 2012). Globally 96 million people manifest clinically with dengue (Bhatt *et al.*, 2013). Over the past five decades the number of dengue cases has increased 30-fold globally (WHO, 2009). Dengue which was mainly restricted to urban areas has now extended its presence to rural regions (Arunachalam *et al.*, 2004). Almost 75 % of the global dengue cases are contributed by South-East Asian regions together with western pacific region (Garg *et al.*, 2011). The resources of most of these nations are limited which are also faced with multiple public health problems and combating the increasing number of dengue cases will not be easy (Halstead; Gubler and Meltzer; Halstead).

Dengue which was earlier a national concern has now become a global threat because of certain factors like change in the climate, global trade, urbanization, expansion of dengue vectors to new geographic regions and

increasing human movement across borders (Bhatt *et al.,* 2013; Murray *et al.,* 2013; Gupta *et al.,* 2012; Rochlin *et al.,* 2013; Schwartz *et al.,* 2008; Wilder-Smith and Gubler, 2008). Global collaboration is the most important in managing & controlling dengue epidemic which are imported from endemic countries to non-endemic areas (Adalja *et al.,* 2012; Effler *et al.,* 2005). There is under reporting and misclassification of lot of dengue cases.

The spread of dengue to peri-urban, rural areas and progression to hyper-endemicity are the trends in recent decades that indicate larger and more frequent dengue outbreaks occurring with geographic expansion to new states along with increased case severity and deaths seen in dengue cases (National Vector Borne Disease Control Programme, 2013; Chakravarti *et al.,* 2012; Gupta and Reddy, 2013). The complications of dengue fever can be avoided by early diagnosis. This study was done to analyze the trend of the dengue fever during 2015-2017 in a tertiary care hospital in a rural set up.

Materials and Methods

Patients and hospital setting

This study was done at a tertiary referral hospital with 750 beds. In this retrospective study, all of the patients with history of febrile illness and suspected to have dengue infections either from outpatient or inpatient (including ICU) admitted to the Medicine and Pediatric ward were enrolled between 1st January 2015 and 31st December, 2017.

Sample collection and laboratory analysis

Laboratory technicians from department of microbiology collected blood samples from the study participants. They centrifuged collected blood to obtain serum for dengue serologic tests. Serum specimens were taken for sero-diagnostic laboratory and tested for non-structural protein 1 antigen test (NS 1 Ag), dengue immunoglobulin-M (IG M) and dengue immunoglobulin-G (Ig G) antibodies by commercially available rapid card tests.

As early as day 1 from the onset of dengue virus infection the NS1 antigen can be detected from the cases which will last until 18th day (http://www.cdc.gov/dengue/clinicallab/laboratory). Ig M is also the early marker for recent infection of dengue virus which can be detected as early as day 3 up to 60th day (Vijayakumar *et al.,* 2005). The sensitivity & specificity of the rapid dengue test varies from 68.9% to 69.2% and 96% to 96.7% respectively. The sensitivity increases to 93% when the dengue early rapid test is performed along with the Ig M/Ig G test (Fry *et al.,* 2011).

Variables measured

The following information age, gender, and source of referral (Outpatient, inpatient, IUC), along with the laboratory test for the dengue infection was collected in a structured excel sheet.

Definitions

The case definition for a febrile study patient was, a patient who came to either the inpatient (including ICU) or outpatient department and to either the medicine or pediatric unit at the P K Das Institute of Medical hospital with fever > 38°C, or who reported a history of fever with onset within the preceding 10 days were considered as suspected dengue cases and were advised laboratory test for dengue diagnosis.

Laboratory-diagnosed dengue cases included those with at least one of the following positive laboratory results: NS 1 Ag, Ig M and

Ig G.

Statistical analysis

Continuous variables are expressed as means and range. Simple proportions were calculated to estimate the hospital-based prevalence of dengue infection. SPSS version 17.0 for Windows (SPSS, Inc., Chicago, IL) was used for all data analysis.

Results and Discussion

During 2015 to 2017, a total of 2289 patients had presented with fever in outpatient, in patient and intensive Care unit of tertiary care hospital. Based on duration of fever and clinical suspicion patient were screened for dengue viral infection.

Those patients who had presented in the early stage of infection were advised NS1 antigen test and those presented in late stage to the hospital were advised dengue Ig M and Ig G.

Thus, 4469 dengue diagnostic test were done for the dengue diagnosis. Out of 4469 dengue diagnostic test, 2155 (48%) was NS1 antigen test, followed by Ig M 1248 (28%) and Ig G 1066 (24%).

Among those tested for dengue as shown in table 1, one fourth of the patients were below the age of 14 and another one forth were between 15 to 30 years. Rest of the patient (50%), who was tested were above the age of 30 years. Wide range of patients from 1 year to 93 years was tested for dengue and mean age of patient was 33 years.

Out of 2289 patients majority 1781 (77.8%) were referred from in patient department, followed by 469 (20.5%) were referred from outpatient department and 39 (1.7%) were from intensive care unit.

Year wise data of 3 years, as shown in table 3, shows that 37.6% of patients were positive for dengue antigen test in year 2017, followed by 94 (34.4%) in year 2015 and 94 (21.1%) in 2016.

As shown in table 3, overall for 3 years, only 2.3% patients were positive for dengue Ig M and 0.5% were positive for dengue Ig G test.

The overall year wise prevalence of dengue (at least one test positive) infection was 31.5%, 18.1% and 36.7% in 2015, 2016 and 2017 respectively. Indicating rising trend of dengue infection in the community, compared to baseline year 2015. The period prevalence for 3 years was 28.8 %. The month wise analysis of the data for 3 years indicate that infections are seen throughout the year, with slight decline in prevalence in the month of February and March and then tend to rise from the month of April to October. The peak of epidemic is seen from June to September (except for year 2016).

However, for year 2015, dengue positivity cases were high in the month of Jan 2015.

In recent years India has seen the increase in the trend of dengue virus infections and the worst affected state is Kerala which reported the highest number of dengue virus infections in 2013 (Mittu Thomas and Pradeep Kumar, 2015). The commonest serological marker which was noted in our study was NS1 antigen (33.7%), the second one was Ig M (2.3%) followed by Ig G (0.5%). In our study most of the dengue virus infections were detected in the early stage. This explains the availability of health care facilities and utilization of these facilities by the local population is good. A higher occurrence of dengue infection was noted among males in our study which is similar to studies conducted earlier (Garg *et al.,* 2011; Kumar *et al.,* 2010). However, this was discordant with the other study where a female predominance was noticed

(Gunasekaran *et al.*, 2011).

Figure 1. Type of dengue diagnostic test used in 3 years

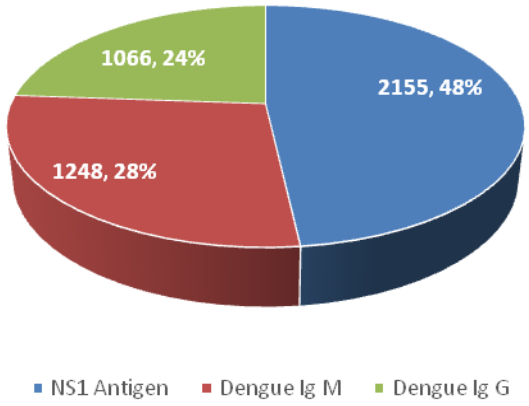

Figure 2. Trend of Dengue Infection Prevalence from 2015 to 2017

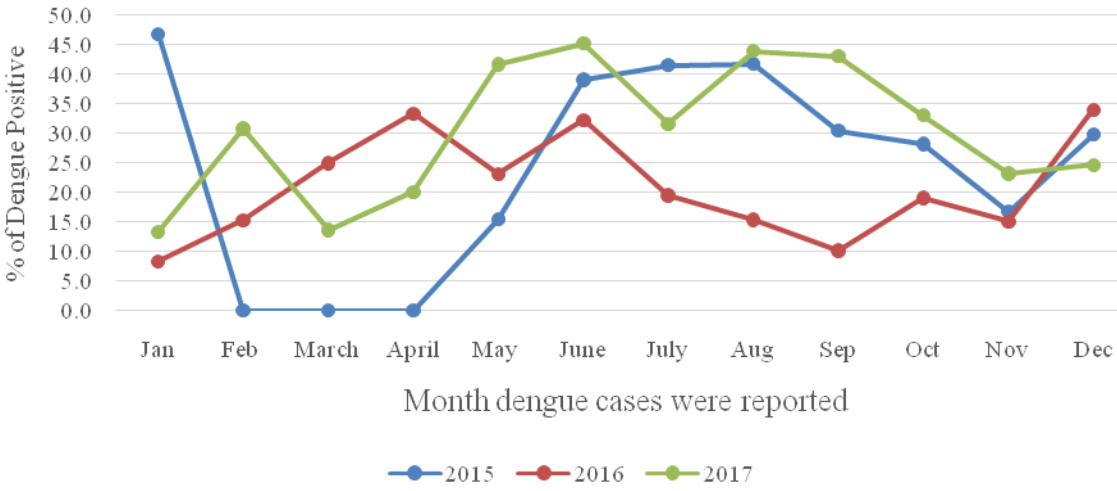

Table.1 Age wise distribution of patient tested for dengue infection

Age group	No. of Male patient (%)	No. of Female patient	Total	Percent(age group)
Less than 14 years	310	260	570	24.9
15 to 30 years	321	251	572	25
31 to 45 years	221	252	473	20.7
46 to 60 years	182	187	369	16.1
61 to 75 years	136	109	245	10.7
More than 75 years	36	24	60	2.6
Total	**1206 (52.7)**	**1083 (47.3%)**	**2289**	100

Table.2 Gender distribution of source of patients tested for dengue infection

	Male	Female	Total
Out Patient	230	239	469 (20.5%)
In Patient	953	828	1781 (77.8%)
Intensive Care Unit	23	16	39 (1.7%)
Total	**1206**	**1083**	**2289**

Table.3 Year wise prevalence of dengue infection by different serological markers

	No. Positive (%)	No. Negative (%)	Total tested
Type of Test	**NS1**		
2015	94 (34.4 %)	179 (65.6 %)	273
2016	94 (21.1%)	402 (78.9%)	445
2017	521 (37.6%)	865 (62.4%)	1386
Sub Total NS1	709 (33.7%)	1446 (66.3%)	2104
Type of Test	**Dengue Ig M**		
2015	20 (11.1%)	160 (88.8%)	180
2016	6 (1.5%)	381 (98.4)	387
2017	16 (2.3%)	665 (97.6%)	681
Sub Total Ig M	42	1206	1248
Type of Test	**Dengue Ig G**		
2015	3 (2.4%)	120 (97.5%)	123
2016	1 (0.2%)	351 (99.7%)	352
2017	3 (0.5%)	588 (99.4%)	591
Sub Total Ig G	7 (0.5%)	1059 (99.4%)	1066

In our study the most common age group affected were above 30 years where as in earlier studies the age group varied from 0 to 30 years (Garg *et al.,* 2011; Kavita, 2007; Sukri *et al.,* 2003; Chakravarti and Kumaria, 2005). As majority of the individual affected in this study are from in patient and above the age of 30 years and majority of them being males in our study. Out of these male members majority of them might be the sole earning member of the family. The number of working days lost due to illness and the recovery from the illness is more and the economic impact imposed by the illness on some of these families may not be sustainable. In this three year trend study the maximum number of dengue virus infections occurred in the month of June for all three years. Earlier studies from other parts of India have reported maximum number of cases in the month of September (Gupta *et al.,* 2005; Ukey *et al.,* 201; Sanghamitra Padhi *et al.,* 2014). We observed in our study the variation in the number of DF cases for the period spanning between January-April in each year. In 2015 the maximum number of cases was recorded in the month of January where as in the year 2016 and 2017 it was in the month of February, March and April. This can be explained by the fact that dengue virus transmission and vector-pathogen interaction is highly influenced by daily temperature

variations (Chan *et al.*, 2015; Lambrechts *et al.*, 2011). There is significant increase in the seasonal mean temperature over the past 100 years in India, during the post-monsoon it is 0.9℃ and in winter it is 1.1 ℃ (Arora *et al.*, 2005). At higher temperatures the external incubation period of the mosquito shortens and also increases the infectivity aiding the dengue virus replication in the mosquito which explains the month wise variation seen in the number of dengue virus infections in this three year trend study (McLean *et al.*, 1974; Watts *et al.*, 1987).

Due to the limited resources the genotyping of the dengue virus was not possible. We were also not able to study the economic status and also due to loss to follow up the clinical outcome of the cases was not possible.

To conclude our study highlighted the increasing trend of DF cases in rural area. The vector control measures should be round the year and it should be strengthened by intra and inter sectoral coordination. Community should be educated about the feeding habits of the mosquito. The availability of dengue vaccine in future will be a boon to India.

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