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Mini Review

An Account of Dengue Epidemics in Central India

Abstract

Dengue virus is one of most rapidly growing arthropod born viral disease in the world which has serious health and economic implications. Dengue infection can lead to life threating condition with no specific drug or vaccine currently available for its treatment or prevention. The scenario of dengue infections in developing and under developed countries is very grim with increase in the number of endemics and poor health care infrastructure. The situation in central India needs more attention because it is backward, underdeveloped and tribal dominated region of India. Over the past five decades there have been various outbreaks of dengue in central India. An overview of reported outbreaks has been presented here and many outbreaks have not even been scientifically studied and validated, which is essential to get a real picture of the prevalence of dengue in central India.

Introduction

Dengue virus (DENV) is a RNA virus belonging to Flavivirus genus and is transmitted by Aedes mosquitos. Upto 75% of DENV infections are subclinical or can cause self-limiting mild dengue fever (DF) whereas the rest could lead to severe life threatening condition described as dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS) which is characterized by capillary leakage resulting in skin and gastrointestinal bleeding. Four DENV serotypes (DENV-1-4) are currently responsible for dengue viral disease [1,2].

Dengue disease has recently emerged as one of the biggest public health concerns globally with 390 million infections annually and with more than half of the world population at risk of infection [3]. Dengue infections are endemic to Africa, Asia and South America. However, the incidences of dengue infections and outbreaks have gradually increased in Africa and India. In addition, it is difficult to estimate the real burden of dengue disease in India and in other developing or under developed countries due to lack of proper health care infrastructure [4]. National Vector Borne Disease Control Program reported 20,474 average annual dengue cases in India from 2006 to 2012. However, various studies have reported that this number significantly underestimates dengue burden in India [5]. Cases with clinical presentations similar to dengue disease in India were first reported in 1780. Virologically confirmed dengue epidemic in India were first reported in 1963-64 and since then epidemiology and spread of dengue infections has been very complex with the involvement of all four serotypes throughout the country [6]. In this review virologically and/or serologically confirmed dengue infection epidemics that occurred so far in central India will be summarized. The review will provide an overview of dengue burden in underdeveloped central India which has a significant amount of tribal population.

Dengue burden in central India

Dengue epidemics in central India started in 1966 and since then, they have been occurring regularly and more frequently. First outbreak of dengue in central India occurred in Jabalpur during October to July 1966. An epidemiology study indicated that approximately 25% of Jabalpur, Madhya Pradesh (MP) population was affected [7]. Virological and serological analysis of 69 patient samples from the epidemic demonstrated that 31 samples had dengue infection and DENV-3 was the major causative agent of the outbreak [8]. DENV-3 outbreak also occurred in Saugor (Sagar), MP in 1966 but the number of infections was not reported. Similarly, an outbreak in 1970 occurred due to DENV-1 and 3 in Gwalior, MP but details of the number of infected individuals were not reported [9]. Several dengue epidemics were reported in Chirimiri area of Sarguja district, MP in 1990 followed by an epidemic in June and July of 1992. Using MAC ELISA, 13 out of 25 samples collected from 1992 outbreak were found to be dengue positive. Isolation of DENV-2 from female *Aedes aegypti* mosquitoes suggested it could be the etiological agent of the epidemic [10]. A major dengue epidemic occurred in Gwalior, MP from September to November 2001 during which 312 patients were admitted to the hospital with clinical presentation of dengue viral disease. Serological analysis of 312 patients revealed that 206 patients were positive for the presence of antibodies against

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dengue. RT-PCR using dengue group specific primers was positive for 13 samples and type specific primers found DENV-2 in the samples although sample were negative for dengue antibodies [11]. This outbreak was followed by another major outbreak in Gwalior from October to December 2003. A total of 76 cases (which included 12 cases from Delhi outbreak) were analyzed for dengue specific antibodies using Dipstick ELISA and the results showed 53 cases were positive. Group specific RT-PCR of all samples resulted in 4 dengue positive samples (2 from Gwalior and 2 from Delhi), which were negative for the presence of antibodies against dengue. Further, serotype specific RT-PCR identified the dengue virus as type-3 [12]. In September and October of 2009 an outbreak of dengue occurred which involved Bhopal, Indore and adjoining 8 districts of MP. In this epidemic 620 samples from patients suspected with dengue infection were tested positive for dengue antibodies by ELISA [13]. A study was performed from August to December 2010 to investigate the prevalence of dengue infections when there was no outbreak. In this study 89 samples were collected from Jabalpur, MP and adjoining villages and also from nearby Narsinghpur district, MP. Out of 89 samples 18 samples were positive for IgM dengue antibodies and 7 samples were positive for IgG dengue antibodies. RT-PCR of positive sample showed presence of dengue in only one sample and by nested PCR it was identified as DENV-4 [14]. Based on media reports of high incidence of febrile illness a clinical investigation team collected samples from Churcha Colliery of Korea district, Chhattisgarh (CG) state and from villages of Narsinghpur district, MP respectively, in August and November 2012. The investigation found that 53 of 142 samples from Churcha and 62 of 105 samples from Narsinghpur were positive for dengue infection by ELISA for dengue IgM or NS1 protein. IgG ELISA showed that 96% of infections were primary. RT-PCR results identified dengue serotype I as the etiological agent of the outbreak [15]. Dengue outbreaks in central India mostly occurred in urban areas until an epidemic in June 2013 occurred in 18 tribal villages in Mandla district of MP. Rapid Response Team from National Institute for Research in Tribal Health, Jabalpur was intimated by the State authorities about the rapid increase of cases with dengue viral disease like symptoms. The team collected a total of 648 samples from June to September 2013 and diagnosed for dengue by ELISA to detect dengue antibodies or dengue NS1 protein or by RT-PCR. It was found that 321 samples were positive for dengue and RT-PCR identified DENV-2 from both patient samples and from mosquitoes collected from the area. The isolated DENV-2, sequence showed high degree of homology with urban DENV-2 suggesting the importance of travel in the spread of dengue virus [16]. Table 1 provides the summary of the epidemics that were clinically analyzed and reported from central India. The location and intensity of the epidemic with etiological agent are shown in figure 1. Since 2013 there have been various media reports for dengue outbreaks in central India. However, no reported clinical study was found in literature.

Conclusion

The reported clinical studies indicate that the frequency and intensity of dengue epidemics have been increasing gradually with decreasing interval time between epidemics. The epidemics, which usually occurred in urban areas, recently started to occur in remote tribal areas as seen in the 2013 outbreak in Mandla district, MP. The DENV-2 isolated in this study shows high sequence homology to DENV-2 isolated from Jammu and Pondicherry indicating that travel might contribute to the spread of the virus. Increase access to transportation and movement of people may be one of the reasons for the occurrence of epidemics in rural areas. It is also possible that dengue epidemics that might have occurred in rural or tribal areas have gone unreported. DENV-2 and 3 seem to be prevalent in the epidemics of central India with only two epidemics caused due to DENV-1. DENV-4 was identified in only sample from a study in 2010, which was not performed during an epidemic or outbreak. DENV-4 isolated in this study showed 99% similarity to virus isolated from Andhra Pradesh again suggesting the possible role of travel in spreading the virus. Although most of the studies have reported the age distribution of the dengue patients a comprehensive analysis of age distribution is not possible because age grouping of patients is not uniform in all the studies. Therefore, a standard age grouping criterion should be followed during epidemiology studies in future. As there are no specific drugs or treatment for dengue viral disease it becomes crucial to diagnose dengue early for proper management of the disease. Moreover, epidemiology studies should cover all dengue endemics to provide more insights into the spread and transmission of the disease. Such information will enable the scientific and health care system to implement measures to control dengue spread and transmission through vector control and other means. Currently there are no specific drugs or vaccine against dengue virus. International Centre for Genetic Engineering and Biotechnology, India with collaboration with Ranbaxy isolated highly active ingredient that is active against all four dengue serotypes from *Cissampelos pareira* [17]. Recently TV003 vaccine has shown protection against dengue challenge in 100% subjects. The vaccine is promising but it was tested only against

Table 1: Summary of all the clinically reported dengue epidemics.

Sl. No.	District and Year	Suspected Dengue Infections	Confirmed Dengue Infections	Etiological agent	Reference
1	Jabalpur, Madhya Pradesh (MP)-1966	69	31	DENV-3	[8]
2	Sarguja, MP-1992	25	13	DENV-2	[10]
3	Gwalior, MP-2001	312	206	DENV-2	[11]
4	Gwalior,MP-2003	76	57*	DENV-3	[12]
5	Bhopal, Indore and adjoining 8 districts, MP-2009	620	620	-	[13]
6	Jabalpur and Narsinghpur, MP-2010	89	25#	DENV-4	[14)]
7	Korea, Chhattisgarh (CG) and Narsinghpur, MP-2012	142 (Korea) 105 (Narsinghpur)	53(Korea) 62 (Narsinghpur)	DENV-1	[15]
8	Mandla, MP- 2013	648	321	DENV-2	[16]

* This study included 12 samples from Delhi
# This study was done when there was no outbreak

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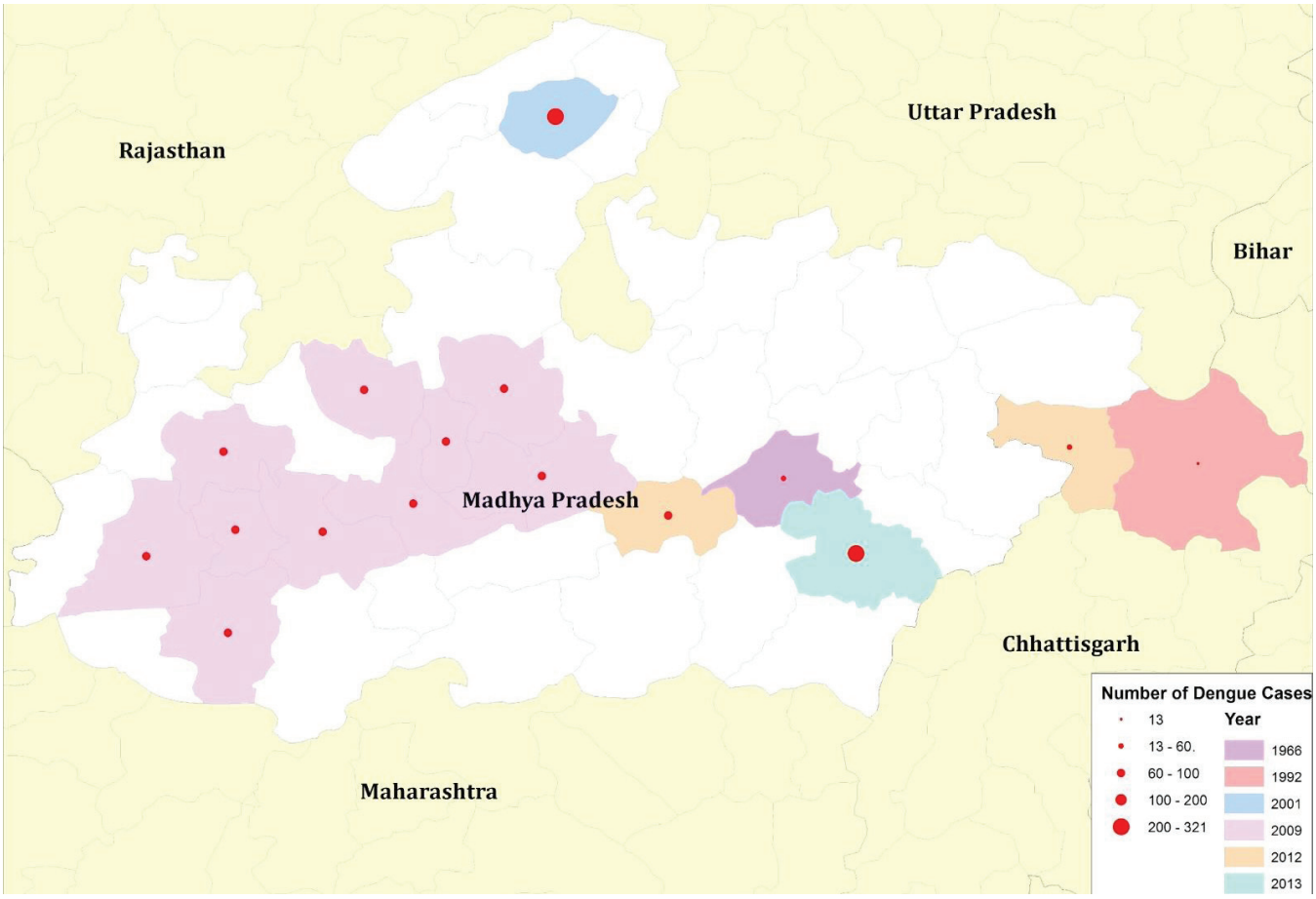

Figure 1: Summary of recorded dengue epidemics in central India indicating the year, area and number of patients.

DENV-2 and large scale trials need to be done to validate its efficacy [18]. Interestingly in India, Pakistan, Sri Lanka and some south Asian countries papaya leaf juice was reported to be beneficial in dengue disease management by increasing platelet count. Scientific validation of papaya leaf juice benefits and determination of mechanism of action is essential before exploring it as a potential option for dengue treatment or management [19]. We have to explore all the possibilities to counter dengue which is one of largest spreading viral disease.

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