The burden of dengue infection in some vulnerable regions of Nepal

A Poudel,[1] Y shah,[3] B Khatri[1] DR Joshi,[1] DR Bhatta[1] and BD Pandey[2, 3]

[1]Central Department of Microbiology, Tribhuvan University, Kirtipur, Kathmandu, Nepal, [2]Sukra Raj Tropical and Infectious Disease Hospital, Teku, Kathmandu, [3]Everest International Clinic and Research Centre, Kathmandu,

Corresponding author: Mr. Asia Poudel, Central Department of Microbiology, TU, Kathmandu, Nepal; e-mail: azp_cozy@yahoo.com

ABSTRACT

Dengue is an emerging mosquito borne disease of public health importance in Nepal. A descriptive cross sectional study was carried out to estimate sero-prevalence and distribution pattern of dengue in certain vulnerable regions of Nepal from June to September 2009. A total of 460 venous blood samples were collected from individuals experiencing a febrile illness clinically consistent with dengue infection visiting nearby hospitals of Kanchanpur, Kailali, Banke, Dang and Chitwan districts. The sero-prevalence of dengue virus specific IgM was determined by enzyme linked immunosorbent assay (ELISA) kit. The anti-dengue IgM positivity was found to be 12.17 %. The higher frequency of positive cases (16.4 %) were from age group 20-40 years followed by < 20 years age group with 9.7 % and 5.3% from >40 years age group. The association between dengue infection and age is found to be statistically significant ($p<0.05$). The male:female ratio was determined as 1.3:1 in IgM positive population. Among sampling areas, Kanchanpur showed highest prevalence of dengue infection (15.5%) followed by Chitwan (11.7%), Kailai (11.1%), Banke (10.7%) and Dang (8.3%). Similarly, 94.6% of the positive cases were indigeneous and had no history of travel to other countries. Dengue is firmly established in terai region with increasing trends of infection and expansion into newer areas raising a public health threat. Regular epidemiological studies are suggested which could further reveal the contributing factors associated with dengue virus infection and help in formulating strategies in reducing the transmission rate and control of the infection.

Keywords: Dengue, ELISA, burden, Nepal.

INTRODUCTION

Dengue is an acute viral disease affecting tropical and subtropical regions worldwide, predominantly in urban and suburban areas. It is a vector borne disease transmitted to humans primarily by *Aedes aegypti* (*A.aegypti*).[1] The four antigenically distinct serotypes of dengue virus (DEN-1, DEN-2, DEN-3 and DEN-4) are responsible in causing the infection to humans.[2] The viral infection causes a spectrum of illness ranging from asymptomatic or mild febrile illness, Dengue Fever (DF), to severe and fatal hemorrhagic diseases, Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS).[3] Moreover, secondary infection with another serotype is considered to be a major risk factor for developing dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).[4]

The prevalence of dengue viral infection has been increasing dramatically in the recent years around the world. It has been estimated that over 2.5 billion people live in the areas of risk with an incidence of 50-100 million cases per year and several thousands of deaths are estimated to occur annually worldwide.[5] It has been identified as one of the most important re-emerging vector-borne viral disease in the region of tropics and likely to increase due to the expanding geographic distribution of both viruses and vectors, increased frequency of epidemics, demographic changes, rapid urbanization, global travel and environmental change, the co-circulation of multiple virus serotypes and the emergence of DHF in new areas.[2,3,6]

In Nepal, DF is an emerging disease appeared since 2004 although it has been already observed in foreign visitor earlier.[7,8] Nepal had experienced dengue outbreak in November 2006 for the first time during which 23 confirmed cases were reported and many patients had travel history to India.[9] This outbreak had occurred following the Indian epidemic of DF/DHF suggesting that Nepal, being bordered by India in the eastern, western and southern belts, has increasing spread of the epidemic DF/DHF.[7] Furthermore, the occurrence of all four serotypes and the evidence of vector has enhanced the possibility of local disease transmission and increased the public health threat in these areas.[9,10] The evidence of major DF cases in Terai belt and the prevalence of *A. aegypti* in this region imply the expanding occurrence of dengue viral infection and its vulnerability to dengue outbreaks.

This study aims to determine the sero-prevalence and distribution pattern of Dengue in certain dengue vulnerable regions of Nepal.

MATERIALS AND METHODS

The study was designed as a descriptive cross-sectional study. The study was carried from June to September 2009. The total of 460 suspected cases from Bharatpur Hospital, Chitwan; Bheri Zonal Hospital, Banke; Nepalgunj Medical College, Banke; Rapti Zonal Hospital, Dang; Seti Zonal Hospital, Kailai and Mahakali Zonal Hospital, Kanchanpur were enrolled.

Venous blood samples were collected from individuals experiencing a febrile illness clinically consistent with dengue infection. Contributing factors of disease (sex, age, travel history and region) were recorded through a questionnaire. A case was included if there was high fever with clinical symptoms suggestive of dengue infection.[11] A case was excluded, if routine laboratory testing suggested bacterial or any other febrile diseases. IgM in serum was detected by IgM-capture ELISA through JE-Dengue IgM Combo ELISA assay (Panbio).

Chi-quare test (at 5% level of significance) was applied to observe any statistical significance between disease occurrence and the variables. The binary logistic regression analysis was done to determine the risk factors associated with positive dengue IgM. Odds ratios and their 95% confidence intervals were provided as estimates of the effect sizes. The collected data were analyzed using Statistical Package for Social Science (SPSS) Software (version 13.0).

RESULTS

IgM antibody was detected in 56 (12.17%) out of 460 suspected cases with 9.7% (16/165) in the age group of less than 20 years, 16.4% (36/219) in the group of 20-40 years and 5.3% (4/76) in the age group of more than 40 years. The mean value for the age group less than 20 years was 11.5, and 26.06 and 58.8 for the age group 20-40 years and more than 40 years respectively, however the overall mean age value was found to be 26.8. The positive cases age ranged from 1 to 75 years with median 24.50. The prevalence of positive anti-dengue IgM for males was 32 in 247 (13.0%) and 24 in 213 for females (11.3%). The male: female ratio was found to be 1.3:1. Among the sampling region, Kanchanpur had a dengue prevalence of 22 in 142 (15.5%), similarly Chitwan, Kailai, Banke and Dang showed dengue prevalence of 11.7% (9/77), 11.1% (9/81), 10.7% (12/112) and 8.3% (4/48) respectively. 94.6% (53/418) of positive cases had no travel history whereas 7.1% (3/42) among the positive result had travel history in past two week period prior to clinical manifestation.

In chi-square and binary logistic regression analysis only the age group was found to be statistically significant with the positive anti-dengue IgM ($p<0.05$). The odds ratio of dengue seroprevalence according to the age of the cases were found to be 2.022 (95% CI: 1.055-3.875) for age group 20-40 years compared with below 20 years age ($p=0.034$) and 0.586 (95% CI: 0.186-1.849) for the age group above 40 years compared with below 20 years age ($p=0.362$) (Table-1 and 2).

Table-1: Sex and Age wise result of IgM capture ELISA (n= 460)

		No.of Cases	IgM Positivity (%)	Statistics
Sex	Male	247	32 (13.0)	p>0.05
	Female	213	24 (11.3)	
Age Group	<20	165	16 (9.7)	
	20-40	219	36 (16.4)	p<0.05
	>40	76	4 (5.3)	

DISCUSSION

Nepal had encountered sporadic dengue cases since 90's in foreigners and the first case of DF was reported in Nepal in the year 2004[12] whose report suggested that dengue infections are being misdiagnosed for other related infections and its importance is underestimated. The exact dengue burden in the country is under reported due to the lack of proper knowledge about it in the society as well as among the majority of health staff and lack of proper laboratory facilities.

Present study was based on IgM capture ELISA (MAC-ELISA) for the laboratory diagnosis which is the most widely used serologic test for dengue diagnosis. It has been found to be as a reliable, useful and inexpensive indicator of primary infection and becomes the frontline diagnostic test in situation where speed is required or demonstration of rising titer is not possible.[13] This technique has sensitivity and specificity of approximately 90% and 98% respectively.[14] IgM capture ELISA can be applied to the sero-diagnosis of dengue virus infection when both Japanese encephalitis (JE) and dengue virus co-exist because ELISA was highly specific as only 10.7 % dengue virus infection cross reacted with JE antigen.[15] Cross-reactivity with other circulating flaviviruses does not seem to be a problem as subjects with previous JE immunizations were excluded from the study, thus the chances of false positive results due to cross reactivity is minimal.

Our study estimated 12.7% of dengue sero-positivity among the suspected cases in the certain dengue vulnerable areas of central and western terai region of Nepal. The result suggests the increasing trends of dengue infections

Sampling Districts

in these areas based on the previous literature.[15] Globally, the rate of dengue occurrence have been rising significantly; the order of dengue infection in South East Asia Region is also found to be increasing as the number of dengue reported cases and deaths have increased by 18% and 15% respectively.[5] The ratio of dengue positive cases in male to female was estimated as 1.3:1 in the present study which indicates the risk of having dengue infections is almost unbiased among males and females i.e. both the sexes are equally susceptible to the infection.

The age wise distribution of suspected dengue cases revealed that the highest number of suspects and the positive cases were from the age group 20-40 years, the productive age group. The result is in harmony with some of the previous findings in South East Asian regions including Nepal.[9,16-18] In this study, age is found to be statistically significant to the occurrence of infection ($p<0.05$). The result suggests that the chance of having anti-Dengue IgM is higher in 20-40 age groups than in others. The odds ratio showed that the risk of having dengue infection was 2.022 times higher in productive age compared to age below 20 years ($p<0.05$). It may be due to the fact that the individuals in this age group are economically active; they may get involved in outdoor as well as household activities which may enhance the chances of exposing to the vectors and may cause infection. However, it is not known that all the age groups population may not have equal access to participating health facilities.

There was a difference in age distribution characteristic of dengue cases worldwide in earlier periods of epidemics. It was reported that the incidence of DF and DHF is higher in adults in American region whereas in South East Asia it predominates and occur more often in children than in adults.[19, 20] There are several factors associated with this epidemiological pattern which are still under study, among them circulation of multiple serotypes and underreporting of DF cases are considered to be the significant ones.[19] However some of the recent studies suggest that there is a shift in age distribution in these regions. There are reports on increasing mean age of dengue infection and adults are found to be frequently infected in some South East Asian countries.[21-24] It is now clear that the chance of having dengue infections is not limited to any age group instead all population is vulnerable to it irrespective of the affected regions. Despite its complex epidemiology, further study is needed to determine the relationship between the age and dengue virus infection.

Among the study areas, the higher numbers of positive cases were from the hospitals of Kanchanpur district followed by Banke, Kailai, Chitwan and Dang, however there was no relation between the infection and the region ($p>0.05$). The first dengue case in Nepal has been reported from Chitwan district since then dengue is expanding in other areas, and now entire terai region including some adjoining hilly areas are susceptible to the disease.[9] All the districts involved in this study are found to be associated with some level of dengue burden which is suggestive of expanding dengue transmission.

Table-2: District/Region and travel history wise result of IgM ELISA (n= 460)

		No.of Cases	IgM Positivity (%)	Statistics
District/Region	Kanchanpur	142	22 (15.5)	
	Kailai	81	9 (11.1)	
	Banke	112	12 (10.7)	p>0.05
	Dang	48	4 (8.3)	
	Chitwan	77	9 (11.7)	
Travel History	Yes	42	3 (7.1)	p>0.05
	No	418	53 (12.7)	

Out of 56 positive cases only 3 had travel history to India. It indicates that majority of positive cases were indigenous which may cause outbreaks and possible secondary infection in future, it is suggestive of existence of endemic cycle in these areas. The transmission scenario of dengue infections has been dramatically changing in recent years as it has been evidenced that the dengue transmission areas have expanded significantly worldwide and all the four serotypes are now found to be circulating in dengue affected countries creating a global threat.[3,19] In Nepal, the evidence of vectors and circulation of multiple serotypes has increased the range of disease transmission in newer areas.[10] Furthermore, the increasing pattern of temperature, favorable climatic conditions for vectors, porous border to India along with unmanaged urbanizations and overcrowding city areas are enhancing the transmission rate of dengue in Nepal.[7,9]

This prospective study has revealed the emergence of Dengue and its firm establishment in the terai region of Nepal. Furthermore, increasing pattern of observation and almost positive cases with no travel history along with the circulation of multiple serotypes and the occurrence of vectors have also highlighted on the possible outbreaks in future which would create a public health threat and increase the dengue burden in newer areas particularly the entire terai region and its adjoining hilly regions. The age related significance described in this study indicates the importance of comparing wide range of ages in future studies of dengue. Therefore, regular epidemiological study is needed which could further reveal the distribution factors associated with DVI and would help in making strategies in abating the dengue morbidity and mortality and its negative socio economic impacts. In addition, it would be helpful to adopt appropriate diagnostic tools, case management, vector surveillance and control to forecast any future outbreaks.

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