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LETTER TO EDITOR

High Potential Risk of Zika Virus Infection Outbreak in Dengue Suspected Cases in Nepal

Yogendra Shah^{1,2,*}, Kishor Pandey^{1,3}, Dhan K. Pant², Krishna P. Panta⁴ and Basu D. Pandey^{1,5}

¹Everest International Clinic and Research Center, Kathmandu, Nepal

²National Zoonoses and Food Hygiene Research Centre, Kathmandu, Nepal

³Nepal Academy of Science and Technology (NAST), Lalitpur, Nepal

⁴Department of Microbiology, Far-Western University, Bhimduttanagar, Nepal

⁵Sukraraj Tropical and Infectious Disease Hospital, Teku, Kathmandu, Nepal

DEAR EDITOR,

The viruses in the genus *Flavivirus*, family Flaviviridae, cause disease in humans, including dengue, yellow fever, West Nile and Zika viruses [1]. Zika virus (ZIKV) infection is considered as one of emerging international public health problems worldwide. Dengue virus (DENV) and Zika virus (ZIKV) infection are an arthropod-borne virus that transmitted to human by the bite of infected female mosquito mainly *Aedes aegypti* and *Aedes albopictus* [2 - 4]. The same mosquitoes' species also transmit the chikungunya virus (CHIKV) and yellow fever [5]. DENV is the causative agents for Dengue Fever (DF) and of chronic cases called Dengue Hemorrhagic Fever (DHF), which may lead to Dengue Shock Syndrome (DSS) in humans. Four DENV serotypes *viz* DENV-1, DENV-2, DENV-3 and DENV-4 are mainly responsible for the disease [6]. According to WHO, DENV infection was reported as most emerging global public health problems with 390 million dengue infections per year globally including the Americas, South-East Asia and the Western Pacific region [7, 8]. Recently research studies revealed that ZIKA infection had similar epidemiology, transmission cycles and also same dispersal routes like DENV and CHIKV infections [9]. Till date, 85 countries has been reported laboratory verification of mosquito-borne ZIKA transmission around the world [10]. For instance, our open porous border country with three sites i.e. India has first reported three laboratory confirmed cases of ZIKV infection in May 2017 and one site border with China also documented first case in 2016 [10]. According to DENV, CHIKV and ZIKV mosquitoes are rapidly widespread throughout the tropical and subtropical developing nations strongly associated with human migration, genotypes increased

the virulence, influenced by climates, such as temperature/rainfall, unplanned urbanization and also the growing global trade and travel [5, 11, 12]. ZIKV can cause infection results in microcephaly with severe brain malformations and other birth defects from pregnant women to the fetus. ZIKV also characterized similar clinical signs and symptoms with DENV and CHIKV like fever, chills, headache, vomiting, rashes, joint pain and conjunctivitis *etc.* [13]. Therefore, there is high risk of miss-diagnosis or under-reporting of ZIKV and CHIKV infection by the physician during the treatment of DENV in endemic areas [14].

The first DENV infection was documented in Nepal from Chitwan district in 2006 followed by sporadic reports [16]. However, DENV large outbreak has also been reported from India in 2006 affected Delhi state with at least 3613 confirmed DF and 50 deaths [14 - 16]. Nepal is open porous bordered by India in the eastern, western and southern therefore infected person may be easy across the border and possible virus might be transmitted by DENV, CHIKV and ZIKV infected vector with several pieces of evidences in border districts to terai region of Nepal. All four serotypes are responsible for causing DENV infection throughout the country. There were only a few cases of DENV recognized between 2007 and 2009. In contrast, the 2010 DENV large outbreak occurred in the central and western parts of Nepal with circulating DENV-1/2 serotypes followed by DENV-2 serotypes in 2014 [16 - 19, 23, 24]. Potentially, a high risk threat of ZIKV infection outbreak as already reported and established of human biting mosquito vectors *i.e.* *Aedes aegypti* and *Aedes Albopictus* causing DENV and CHIKV infections in Nepal.

Nepal is one of vulnerable countries in South East Asian region recognized for several outbreaks reported from DENV infection in including hilly districts last 10 years' period [15 - 33]. In 2014, the first CHIKV infection in Nepal was

* Address correspondence to this author at the Everest International Clinic and Research Center, Kathmandu, Nepal; Tel: +977-9849610127; E-mail: yogendra90@hotmail.com

confirmed by molecular analysis (FRNT50) [28 - 30]. Some of the South Asian countries already reported ZIKV cases, mainly Bangladesh and Myanmar in 2016, and India in 2017 [34, 35]. Nepal has open porous bordered by India in the Eastern, Western and Southern regions, therefore, DENV, CHIV and ZIKV infected person can easily cross the border from India to Nepal. Nepal being high risk for possible ZIKA outbreak due to open border with India and International travel from other countries [36]. Due to the lack of information on the diagnosis of ZIKV infection in DENV endemic regions in Nepal were unreported previously. Therefore, early differential molecular diagnosis of ZIKV from suspected DENV infections is an urgent need in Nepal. Highly specific and sensitive molecular methods are required because the high percentage of cross-reactivity among the flaviviruses when serological approaches are used [37, 38].

Government of Nepal should take quick and urgent action to prevent the flavivirus infection including (DEN, ZIKV, CHIKV) by initiate surveillance mechanism integrated with vector control program to abate from an outbreak of particular flavivirus infection especially in every year monsoon season. The responsible health authorities should trace out the possible high risk of ZIKV infection hotspot region of both diseases in Nepal and neighboring countries. The government of Nepal, Ministry of Health and Population should provide molecular testing facilities for RT-PCR and Triplex RT-PCR in each regional hospital and also strong recommended to policymaker and planner for the further strategy to diagnosis, vector-borne control and prevention in the future outbreak of DENV and ZIKA infections throughout Nepal by applying One Health approaches.

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