



**SDI Review Form 1.6**

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| Journal Name:            | <a href="#">International Journal of TROPICAL DISEASE &amp; Health</a>                                                    |
| Manuscript Number:       | Ms_IJTDH_30612                                                                                                            |
| Title of the Manuscript: | <b>Burden of Dengue Virus Infection in Chitwan and Peripheral Districts: An Emerging Disease in Terai Region of Nepal</b> |
| Type of the Article      | <b>Original Research Article</b>                                                                                          |

**General guideline for Peer Review process:**

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

(<http://www.sciencedomain.org/page.php?id=sdi-general-editorial-policy#Peer-Review-Guideline>)



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**PART 1: Review Comments**

|                                            | <b>Reviewer's comment</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | <b>Author's comment</b> <i>(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)</i>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
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| <b><u>Compulsory</u></b> REVISION comments | <p>This is a description of a study on dengue illnesses seen in 2015 in a Nepalese city in the Terai. Dengue viruses spread to Nepal from India. This report should not be written as if dengue springs up in Nepal spontaneously. The timing and severity of annual outbreaks is undoubtedly responsive to dengue epidemiology in bordering India. The Discussion should describe accurately what was observed. This is a single year study of patients seen at the Chitwan Hospital. But, were they admitted to hospital or seen as out-patients? If the latter, then this is predominantly a description of an outbreak of dengue fever. If this is occurring in a seronegative population, then children experiencing a first dengue infection usually have silent or mild infections. In many virgin soil outbreaks of dengue adult males seek medical care more frequently than females. The discussion is far too long and should be tightly focused on what was observed here and not generalized to dengue illness experience in countries where multiple dengue viruses have circulated for many years.</p> | <p>We greatly appreciate the constructive comments of the reviewer and respond as follows to their concerns:</p> <p>We agree, dengue virus spread to Nepal from India due to open border and trade between the neighbouring countries. I have tried to explain some part in discussion. Our teaching hospital is situated in a location where people from Chitwan as well as people from peripheral district visit here seeking for medical help. In this study samples were collected from patients suspected to be suffering from dengue virus infection both from inpatients and outpatient departments. I have tried to explain focussing on the findings of this study in short.</p> |



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|  | <p>AS diagnostic sera may not have been collected correctly, this may not be an accurate study of the incidence and etiology of febrile patients seen at Chitwan Hospital in 2015. See comments below.</p> <p><b>Must be revised. If issue of collection of diagnostic sera cannot be resolved.</b></p> |  |
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| <p><b>Minor</b> REVISION comments</p> | <p>Line 15. What is a “descriptive cross-sectional study?” This seems to be a study of individuals presenting for clinical care. From the outset the nature of the illness observed and the disposition of patients (hospitalized, treated and sent home?) should be described.</p> <p>Line 37. There are FOUR dengue viruses. The news article cited does not reflect consensus of scientific opinion. The authors must find a report of a fifth dengue virus in a peer reviewed publication that is fully and accurately titled.</p> <p>Line 48. The authors should consult more recent estimates of global dengue burden. The information contained here is obsolete.</p> <p>Line 75. Aedes aegypti seldom breeds in tree holes. This species generally breeds in man-made containers (big and small, artificial or natural) that fill with water both in urban, suburban and rural areas.</p> <p>Line 88. DHF/DSS occurs in only a small subset of individuals who experience sequential heterotypic dengue infections.</p> <p>Line 116. Sorry, this reviewer does not know what is meant by a “cross-sectional study.” Where were patients observed and how were they recruited into study? Who made the diagnosis of “dengue” and when? Was this all done on a single day? If the patient was then sent home how was it possible that blood</p> | <p>Line 15. This is a prospective study and samples were collected from patients suspected to be suffering from dengue virus infection both from inpatient and outpatient departments.</p> <p>Line 37: Since there are no reports in peer reviewed journal regarding 5 serotypes of dengue viruses, I have corrected the statement as 4 serotypes of dengue viruses.</p> <p>Line 48: The reference on Global burden of dengue has been taken from journal published in 2016. Shrestha R, Pant ND, GC G, Thapa S, Neupane B, Shah Y, et al. (2016) Serological and Entomological Study of Dengue in Dang and Chitwan Districts of Nepal. PLoS ONE 11(2): e0147953.doi:10.1371/journal.pone.0147953. I thought this estimates are correctly reported.</p> <p>Line 75: We have corrected the statement that Aedes species generally breeds in water accumulated in containers.</p> <p>Line 88: We have corrected the statement and explained only about immunity not DHF/DSS.</p> |
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|  | <p>samples were collected for dengue IgM testing on day 5 or later. This timing of collection of early convalescent serum is crucial. Normally, dengue IgM does not become positive until the 5<sup>th</sup> day after onset of fever. This may have been a study among patients who attended the Chitwan Hospital, but were the patients HOSPITALIZED? If all the patients studied were hospitalized, please describe the nature of the disease that resulted in hospitalization. From the very vague descriptions provided, it seems that most of the patients studied had a mild illness.</p> <p>Line 175. Better check the accuracy of this statement with recent estimates of the global disease burden of human dengue infections.</p> <p>Line 217. This is not a prevalence study. The authors observed an incidence of dengue illness among patients (in-patients? Out-patients?) It is not clear that some randomization scheme was used to recruit patients for study. So, is this an accurate incidence rate?</p> <p>Line 222. Are the authors speaking of serological surveys or studies on patients, if so, in-patients or out-patients? These incidence numbers must all occur during a specific period of observation. This period must be identified.</p> <p>Line 269. Aedes aegypti do not breed in “marshy places.” There appear to be several authors of this manuscript. They should agree on</p> | <p>Line 116: It is a prospective study and samples were collected from patients suspected to be suffering from dengue virus infection both from inpatients and outpatient departments. We have corrected this aspect.</p> <p>Line 217: Samples were collected from all patients visiting Chitwan Medical College Teaching Hospital, suspected to be suffering from dengue virus infection both from inpatients and outpatient departments. This study was undertaken to determine the prevalence of dengue virus infection in Chitwan where patients visit CMCTH from districts peripheral to Chitwan seeking for medical care.</p> <p>Line 222: This study is basically focussed on seroprevalence of dengue virus infection infection both from inpatients and outpatient departments.</p> <p>Line 269: We have corrected this part, Aedes aegypti do not breed in marshy places.</p> <p>Line 285: Yes, Sanofi’s dengue vaccine has been introduced but it is not available for use in Nepal. So, we have corrected this statement.</p> |
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|                                         | standard descriptions of dengue epidemiology.<br>Line 285. Sanofipasteur has licensed in<br>tetravalent dengue vaccine in 20 countries. |                                 |
| <b><u>Optional/General</u></b> comments |                                                                                                                                         | Thank you for all the comments. |