Reviewer's report

Title: Zika virus disease, microcephaly and Guillain-Barré syndrome in Colombia: epidemiological situation during 21 months of the Zika virus outbreak, 2015-2017

Version: 0 Date: 31 May 2017

Reviewer: Henry Kyobe Bosa

Reviewer's report:

This is a very good piece of work and I would like to congratulate the authors for the innovation of the concepts to update the global scientific niche of the ZVD in Colombia and the enormous amount of work put in the manuscript.

From the three case definitions; it is not clear what was included in the ‘total number of cases of ZVD’

Using percentage in age distribution means little in the distribution of ZVD in Columbia. This would better be presented as Attack Rates (AR) for those age-groups. Possible tabular presentation of this is more informative. Using AR may change the distribution.

If Bogota DC is excluded as no transmission area being on a higher altitude, there are certainly variations of vector distribution and characteristic at different altitudes. Thus, there is a need to re-analyze the ZVD case distribution at the different altitudes.

Using an appropriate altitude ranges, the distribution of ZVD cases should be analyzed accordingly not only for AR but also age-group/gender distribution. This by proxy will unmask intra-altitude variations in the distribution of case.

There is a need to disaggregate GBS and microcephaly cases by; (1) age, (2) gender and geographical location to investigate variations and possible (intra-regional or gender-related) drivers.

To understand the GBS and microcephaly distribution this needs to be presented as a proportion of births (i.e. xx per 100,000 births) in the respective territories not as simple percentages.

The same needs to be done on the pregnant women and later expressed as a proportion pregnant women, i.e. yy per 100,000 women (depending on the trimester).
The strongest evidence of ZVD is in the confirmed cases. Separate confirmed ZVD case (alongside overall number of cases) intra-territorial, intra-altitude, age-group distribution by both percentage and attack rate (AR) will appropriate represent the actual distribution of ZVD in Columbia.

The two paragraphs in results section---the language here appears like discussion. In practice, this discussion needs to be moved to the ‘discussion’ section of the manuscript and here we only present results as they’re.

The ‘density’ of cases, as highlighted in yellow needs to be presented in qualitative terms to ease comparison.

The graphic representation of ZND cases is very informative as cases/Km2. The danger here is the population distribution which may be masked by land area. I envisage here that the population distribution is not homogenous across the country. Density (cases/Km2) may not necessarily represent Attack rate. In light of that, together with density distribution the authors need to plot the distribution of cases by attack rate per geographical location.

Like in the previous comment, presentation of GBS and ZVD cases needs to be presented as attack rates not as percentages.

Similarly, the clustering requires to be fully described and if there is any emerging pattern highlighted. Any emerging pattern can then be explained, if not (like in case of paucity of data) then it needs to be noted.

To make this conclusion, we needed to have used the population level measures like attack rates not simple percentages. The most affected age-groups may be different.

Many assertions in the discussion are not backed by any reference. This needs to be developed further and referenced.

The overall 0.22% (Attack Rate) can be presented in non-fractional terms like xxx/100,000 or xxx/1,000,000 etc.

The comment “This is an alarming situation because of congenital defects associated with ZIKV infection” needs to be well developed in spatio-temperol aspects. Thus the intra-country (Columbia) and regional (Latin America) distribution, and in time series.
One of the possibilities could be the increased reporting and active surveillance in the CNS congenital manifestations since ZIKV infection began sweeping in the region.

These (suspected cases) have not been referred to in the results section and here they’re not referenced.

Similarly, early on it was assumed the case definitions of microcephaly and GBS were generic. From the above, there is need offer a case definition of suspected and confirmed cases of the each.

The authors need to describe what they term as association. Otherwise it is better be put the increase of microcephaly cases during ZIKV transmission………

Are the microcephaly trends increasing in the wake of decreasing cases of ZVD? This has to be developed in relation to baseline or histological data or evidence.

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