Reviewer’s report

Title: Pesticide use, erythrocyte cholinesterase level and self-reported acute intoxication symptoms among vegetable farmers in Nepal: A Cross-sectional Study

Version: 1 Date: 7 June 2014

Reviewer: Leslie London

Reviewer’s report:

This is a well-written paper that communicates important information from a developing country on an important public health problem. However, there are some revisions needed to strengthen it for publication

Major Compulsory Revisions

1. One might have expected to see a comparison of symptoms by ChE level. The discussion states that “… a study found that cholinesterase inhibition was associated with symptoms from the respiratory system, eyes and central nervous system among farmers [16]. Thus, the significantly lower AChE level among farmers compared to controls further suggests that the symptoms could partly be due to pesticide exposures.” However, this study had the data to test that association directly so I would expect to see the results of that testing.

2. Symptoms and Table 4. It isn’t entirely clear to me the symptoms are all equivalent. For example, loss of appetite and back pain are not clearly linked to Cholinesterase inhibition. Was it intentional to include non-pesticide related symptoms as a form of controlling for under-reporting? Or do the authors believe these are pesticide related? If so, I would like to see some motivation in the methods for the choice of these symptoms. The methods are rather thin on describing the symptoms assessed and seem to borrow from an instrument used in Bolivia but it is only in the results that one gets to see what they are and some of the symptoms are rather puzzling. Backache can certainly be associated with farming, but not mediated by pesticide exposure, for example. I would rather call the title of the table ‘Odds Ratio for symptoms…’ and leave the interpretation to the discussion. Please make sure the choice of symptoms and the rationale is clear in the methods.

3. Could the authors elaborate on the statement “The use of dust masks, caps and long-sleeve shirts by the majority of farmers suggests an opportunity to introduce similar but more effective equipment against pesticide exposure…?”

If I understand correctly, they are implying that even if dust masks are ineffective (which they are), the fact that farmers are willing to wear them might signal their willingness to adopt other, more evidence-based measures. If so, could the authors make their intention clearer?

I feel this is quite an important message and perhaps something unique in this
4. The authors argue that 50% of symptomatic farmers seeking health care is low utilization of health care services. This is rather relative. Compared to some studies this is quite high, actually. The impression I get is that farmers in Nepal are actually quite model farmers – they use PPE much more than their colleagues in other countries and seek health care more frequently! (see for example, Lekei et al, 2014). I think this aspect should be examined with a bit more care in the discussion.

5. I am not sure I feel entirely comfortable with the conclusion as stated in the main manuscript. It is different to the conclusion as stated in the abstract (which is more modest). It is true that the study has shown “...Inadequate use of PPE, poor hygienic practices, improper handling of pesticides and the use of moderately toxic pesticides among Nepalese farmers” but I am not sure the analyses presented are sufficient to claim that these factors “...may explain lower AChE levels and increased number of acute intoxication symptoms among Nepali vegetable farmers compared to a control group.” The analyses conducted were on the basis of farmer versus control, not on the basis of inadequate PPE use as an association with lower AChE levels, etc. If the authors want to claim this conclusion, they have the data to test it, should do the testing and then make the relevant conclusions. There may well be power issues in the results, and then this should be discussed, but I feel the statement as made in the conclusion is not supportable without evidence.

Minor Essential Revisions

1. Table 2 has n=90 in the title line but the n implied by the %s in the table is 65. Please clarify this

2. Selection of controls: Blood donors were chosen as having never been occupationally exposed to pesticides and they were matched for sex, age group and district to the exposed group. However,

   a. Blood donors in other countries may be persons of lower SES if they are paid for donation. This may introduce confounding. Could the authors clarify if this is the case? In the limitations, it is stated that donors are generally more healthy, which may be true in relation to reasons for rejecting donors. But the SES may still play a role.

   b. Presumably, the same criteria for exclusion of exposed subjects applied to the controls?

   c. Age seemed different even though matched (Table 1). Was statistical testing done to confirm no significant difference?

3. Table 3 is rather confusing. There are two columns for farmers’ symptom percentage. One appears to be for symptoms in the past month and the other does not have a clear label, but seems to be symptoms after pesticide use. Then, the column for controls has a heading after pesticide use. This must surely be an error and the ‘after pesticide use’ is probably the header for the second farmer column. Can you clarify in the table what is being compared to what? Farmers
reporting symptoms in past month to controls reporting symptoms after pesticide use? Or Farmers compared to controls for symptoms in past month.

4. Table 5 – the text cites the ChE and adjusted ChE values as having significant differences but the table doesn’t include the statistical testing – please include a footnote to the table to indicate significance.

5. The authors seem to make a lot of the Haemoglobin level differences. I would avoid making too much of this. Firstly, in my experience, the TestMate OP kit is not a very accurate device for Hb estimation, unless more recent versions have improved. Secondly, if the authors are going to suggest pesticide-related hepatic or renal damage as the reason for the Hb differences, then they have introduced a serious possibility of confounding to their ChE results. The Test mate measures Hb simply to adjust for anaemia and I don’t think it is justified or in the researchers’ interests to treat the Hb results as an outcome. I would delete this paragraph.

6. A few minor typos have not been corrected
   a. A ‘?’ sitting after the p value in line 3 of page 9
   b. In the first paragraph of the discussion, a phrase (“The practice of hygienic measures”) seems to have been left over from a previous edit

Discretionary Revisions
1. It would be helpful to describe what kind of sickness self-management was practiced?
2. There were 4 professional sprayers. Presumably, they had the most intense exposure. Was that explored?
3. Ability to read is quite a crude measure of education but it is interesting to note that it is associated with PPE usage. Did the authors also explore whether it was related to safety practices (disposal) or storage? There is more recent data (Lekei et al, BMC Public Health 2014; 14:389) suggesting that education is linked to a range of safety practices amongst farmers in Tanzania.
4. Related to education is knowledge, but a number of studies seem to indicate that for many developing countries, farmers may be aware of risks (have the knowledge) but continue to practice unsafe hygiene measures because of pressures of production and income generation. Was knowledge about risks explored in this study? If so, it would be interesting to see whether the Nepalese farmers are different to their counterparts in many other developing countries and to suggest further research direction as to why this would be the case.
5. The comments about suicide are true. But there is also some literature suggesting that exposure to pesticides, particularly OP’s, may increase the risk for suicide, whether through the use of pesticides as agent or through other methods.
6. The limitations:
   a. In fact, if controls had undocumented exposure to pesticides, it would only bias
the study to the null, so the true measure of effect would have been larger. The authors might want to make that observation.

b. Recall bias – would ‘dummy’ questions have helped to reduce the impact of recall bias?

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests