Reviewer's report

Title: Simultaneous Exposure to Multiple Heavy Metals and Glyphosate May Contribute to Sri Lankan Agricultural Nephropathy

Version: 3 Date: 30 April 2015

Reviewer: Keith Levine

Reviewer's report:

Major Compulsory Revisions

Sri Lanka's emerging chronic kidney disease epidemic is a public health crisis and is of significant interest to the Sri Lankan and international scientific communities. The authors of this manuscript are to be commended for drawing further attention to this serious public health issue. Reports of the association between chronic, low-level exposure to heavy metals and other persistent environmental chemicals and non-communicable disease genesis and progression are becoming more frequent in the literature. As a result, biosample data from a broad panel of metals and a frequently used pesticide (glyphosate) are of potential interest.

The primary limitation of this study is the limited sample size for the case and two control groups. The authors acknowledge this in the Discussion section of the paper, but it should be stated in the abstract section and emphasized elsewhere in the paper. Even though the sample size was limited, some interesting data were obtained that may warrant further study. Additional information about the study participants would be of interest if data are available (for example, stage of CDK, BMI, other risk factors, dietary recall prior to spot urine sample, etc.). It would also be helpful to summarize criteria for assignment to case/control groups in table 1 (i.e. biochemical marker levels, medical criteria, etc.).

From data tables 2 and 3, it was noted that no values were flagged as less than detection or quantitation limit. It would be of interest to compare collected data with these method detection/quantitation limits to put reported data into context. For this broad panel of analytes, however, it seems unlikely that measurable values would be obtained at high confidence for all samples. Additional information on sample preparation, quality control, and analysis procedures may be helpful for both ICP-MS and kit-based assays, as appropriate.

Minor Essential Revisions

There are editorial changes throughout the manuscript that should be made prior to publication. For example, 'manufacturer’s' on line 148, potentially repeated text on line 179, and so on. It may be of benefit for the authors to review the manuscript looking for these minor items.

The manuscript would also benefit from an expansion of the background about
heavy metals (lines 69 - 80) with additional references.

Discretionary Revisions

The authors discuss similarities with other international CKD epidemics and mention other confounding factors (i.e. chronic dehydration). It would add value to this manuscript if these discussions could be expanded with additional references added.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.