Reviewer’s report

Title: Seroprevalence of hepatitis C and associated risk factors in urban areas of Antananarivo, Madagascar.

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Reviewer: George Strickland

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General
This descriptive paper by 13 biomedical scientists in Madagascar reports the prevalence of, and analyzes risk factors for HCV antibodies (anti-HCV) and RNA in a stratified sample of 2,169 subjects in an urban area. Twenty-five (1.2%) subjects met their criteria for being antibody positive and 17 (68%, not the 47.2% noted by the authors) were also HCV-RNA positive. Ten (58.8%, not the 59.2% noted by the authors) of these were genotype 1b, 6 were 2b and one was 2a. The assessed risk factors for seropositivity using both univariate and multivariate methods. In univariate analyses anti-HCV was significantly associated with age, hospitalization, previous injections, dental treatment, scarification (although the data and P value in table 2 suggest this is not significant), IV drug use (although this was rare), and abnormal AST and ALT (which I prefer to ASAT and ALAT which they use). Multivariate analysis showed that only age and AST were independently associated with anti-HCV. Although not significant following adjustment, all 25 cases had a history of previously receiving therapeutic injections. Age appears to be such an important risk that when included in the model, other exposures became less important,

The above is what the authors found. It should be included in the abstract and should be the basis of the introduction, methods, results and discussion sections. Discussions of papers and research that are not directly related to this are not appropriate in a descriptive paper such as theirs. Therefore, this would be best as a precise publication. The most interesting finding is that the prevalence of HCV is low in younger individuals in this LDC urban population (although they miss this point) suggesting that either (or both) the reservoir levels of the virus in the blood is locally low or they have been fairly good at following safe medical practices. The low prevalence of those admitting to IV drug abuse and receiving blood transfusions can partially explain this.

Before, I discuss the details of the paper; the authors need to share reference 24. Entitled Hepatitis C virus infection and genotypes in ..... which is in press for the J Medical Virology with the editors since the title describes this paper.

The paper will require considerable editorial work. Some examples of these problems follow:
(1) In abstract, they say Anti-HCV positivity "seemed" to increase with age. It
doesn't seem, it does. I do not like their closing two sentences in the abstract, they should present their findings and say something like: "XXXX is a community that has a low prevalence of HCV infection." They can hypothesize why this is the case, but their data certainly doesn't lead to "Research in this field will need to be continued." What does that mean?

(2) In the first sentence of the Introduction they say "Hepatitis C virus (HCV) continues to be a major health burden worldwide." It is a health burden. Sentences that "set the table" for the importance of the paper need to be precise and straightforward since they are only leading the reader to the paper itself. One could also argue that it is not HCV that is the health burden, but it is the disease it causes, which is usually called hepatitis C. However, we often interchange the agents and the diseases they cause. Towards the end of the same paragraph, the authors use "anti-HCV Ab". Since this is the first time the use this word, I believe they should use "antibodies to HCV (anti-HCV)."

(3) Methods. In the statement were they describe the city, "of which it occupies only a small part" adds nothing but words. Since they are the basis of study, I think they need more description of their methods for detecting HCV antibodies and RNA. I assume that the Desican Plus HCV assay is like a RIBA, but do not know that for sure. (Also I would be interested to know the results of the testing for HCV- RNA on the 8 serum samples that were indeterminate by the test with exclusion of these patients.) It is inadequate to describe the test use for "... screened for viral RNA as described previously" when the paper has not been published. Did they use RT-PCR? They don't define the type of test they used. They also need to include something about their genotyping methods.

(4) Results could be made more concise. The figure should be dropped and the numbers and percentages of anti-HCV (and HCV-RNA) positives and total in the group could be added to table 2. This marked increase with age, with a maximum of only one case less than 24 years old, strongly suggests a cohort effect which they deny without explaining. They don't show the data but what is seen is that exposures are occurring in older adults that or not occurring in children and young adults and/or exposures occurred in the past that are not occurring recently. Table 1 provides considerable useful information. It could be more precisely described in the results. All the specific data must not be in both places. I have already made the point about injections being universal in those who were anti-HCV positive although when adjusted for age and the fact that a large proportion of those not having anti-HCV also had injections, it is not a significant risk. That does not mean that many of those infected were infected by medical injections. As mentioned earlier additional columns could be added to table 2.

(5) Discussion. The data presented here does not warrant an extensive discussion of the prevalence of anti-HCV in other countries or what are the factors for transmission of HCV in Antananarivo other than mentioning some of the examples of transmission in specific areas, particularly in Africa and some thoughts on the transmission pattern. That is why it is now so low in those under age 24. For instance, has the local health department put a strong campaign in past 15-or-20 years that reduced transmission of blood-borne infections. How does this relate to HIV transmission?
The way they present their study design and the data analysis is very good and this component appears to be outstanding. I think this paper could be a contribution as a short description of the prevalence of HCV in Antananarivo, IF IT DOES NOT INCLUDE THE SAME MATERIAL IN THE PAPER THAT IS IN PRESS FOR THE JOURNAL OF MEDICAL VIROLOGY.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
see above

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
see above

Discretionary Revisions (which the author can choose to ignore) none

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of limited interest

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

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I have no competing interests.