Reviewer's report

Title: Molecular epidemiology of a hepatitis C virus epidemic in a haemodialysis unit: outbreak investigation and infection outcome.

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Reviewer: Jean-Claude Desenclos

Reviewer's report:

This is a well conducted and comprehensive investigation of an outbreak of HCV in a dialysis setting. Authors used a multidisciplinary complementary approach through descriptive and analytical epidemiology, audit of care and hygiene practices and phylogenetic analysis of HCV strains. They were able to identify the source of infection and the major mode of transmission. They also did a clinical follow up of those infected and could document the rate of viral clearance at one year of follow up in these very vulnerable patients.

Review of BMC criteria:

1. Is the question posed by the authors well defined: Two questions are posed: 1) what was the mode of transmission in this outbreak (main question)? 2) what is the rate of HCV chronic infection among hemodialyzed patients one year after acute infection (secondary question)?

2. Are the methods appropriate and well described? The methods are appropriate and quite well described (see specific comments below).

3. Are the data sound? The data are sound and allow to draw clear conclusions.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition? The authors indicated that they followed the ORION guidelines for reporting outbreak investigation. It also follows relatively well the STROBE guidelines.

5. Are the discussion and conclusions well balanced and adequately supported by the data?

Yes in general

6. Are limitations of the work clearly stated?

Some are acknowledged. A few additional should be discussed as well. See specific comments below.

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?

Not sufficiently.
The authors make reference only to US work. They are missing several recent European references of investigation of HCV outbreak that occurred 1) in dialysis unit (Delarocque-Astagneau et al, ICHE, 2002; and Savey et al, ICHE, 2005) or 2) was linked to sharing multiple dose vial (Germain JM, ICHE, 2005).

What do the authors mean exactly by “lacks in infection control measures”. They should be more specific. Transmission of HCV through hands of HCW has been discussed in several outbreak investigation reports (see Delarocque-Astagneau E et al, ICHE, 2002; Savey A et al, ICHE, 2005). The authors do not mention this as a possibility for the 2 extra cases. What were hand hygiene procedures in this unit?

Also, what was the ratio of patients to HCW as compared to standard of care in Italy? This is a critical point since the probability of contacts of HCW to patients increases when this ratio decreases (see Savey A et al, ICHE, 2005). Also how this ratio evolved over time, particularly at the time HCV transmission occurred?

8. Do the title and abstract accurately convey what has been found?

Yes.

The abstract: why adding discussion after the conclusion?

9. Is the writing acceptable? There are several grammatical errors that need to be corrected.

10) Other specific comments:

10.1. Figure 2 and 3 do not bring anything important and should be ignored for the final paper.

10.2. The authors do not give criteria for the definition of an incident case. They should be more precise on this issue. Why were they not able to date incident HCV infection based on last HCV test, ALD elevation, date of PCR and HCV antibody positivity?

10.3. As the reviewer understood, the authors defined symptomatic cases as those that had elevated ALT. This is not appropriate. Patients may have elevated ALT and have no symptoms. In practice, were the authors able to document symptoms such as jaundice, fatigue, digestive symptoms, fever...among the 13 newly infected patients and, if yes, how many had really symptoms?

10.4. Since the incidence rate is high the odds ratio (OR) is not an appropriate estimate of the relative risk (RR). In such a situation the OR over estimates the RR. Since the authors used a cohort study design they should report RR as the measure of association in univariate analysis. For instance, for the shift MWF-pm the univariate RR (that the reviewer calculated) is 6.95 (95% CI: 2.66-18.20 while the OR calculated by the authors is 33.75 (5.23-215.43) ! So it is recommended that authors report univariate RR and not OR. For MLR there is no other way than having OR; However, modified Poisson regression models with robust error

10.5. In the audit practice, did the authors searched for flooding of blood into the double filter on the arterial pressure tubing set. This has been described as a possible mode of transmission from patient to patient using the same dialysis machine.

10.6. The use of Multi dose vials has been implicated in many HCV and HBV outbreaks. Why not banning them? Authors should discuss this issue.

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

**Declaration of competing interests:**

'I declare that I have no competing interests'