Reviewer’s report

Title: Elevated lipase levels in patients with Hantavirus-induced Nephropathia epidemica - should we think about acute pancreatitis?

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Reviewer: Marco Goeijenbier

Reviewer’s report:

Kitterer et al. describe the lipase levels in acute NE patients in a large cohort in Germany and a potential relation to acute pancreatitis. This paper follows multiple (interesting) papers published from this specific cohort, of which multiple attempted to discover new usable biomarkers in NE. Although many limitations of the chosen study design could be mentioned, still the message can be of interest for people working in the hantavirus field and especially clinicians.

Abstract:
Background is not a background but seems an objective.
P value is not written with a capital p

Major Compulsory Revisions

Title:
In my opinion the title is misleading and incorrect. Actually it may even cause confusion among people who only screen title and abstract. A title must represent the data in the article. I would suggest something in line with Evaluation of lipase levels in acute hantavirus patients in Germany, no evidence for acute pancreatitis. Also hantavirus is without a capital as is nephropathia epidemica.

Background:
The beginning paragraph of the background is not of proper scientific quality. It actually states things that are not true and reads not easily.

Couple of examples

1) Frist two sentences do not read well and are actually not correct. HCPS is indeed caused by new world hantaviruses but these do not only circulate in the USA as a matter of fact most infections in recent years are due to Andes virus infection in South America. Furthermore only pathogenic hantaviruses cause disease which currently are 23 out of the 43 known hantaviruses. I would suggest to rewrite to:

- Pathogenic hantaviruses are able to cause disease in humans and after inhalation of virus containing aerosols to known syndromes may arise: haemorrhagic fever with renal syndrome (HFRS), with the milder subtype nephropathia epidemica (NE) and the hantavirus cardiopulmonary syndrome
(HCPS). HFRS is endemic in large parts of Eastern and Northern Europe and Asia, while small clustered outbreaks of HCPS have been reported in North and South America. I think the current references can be used to back up this introduction. I am quite sure that a reference from 1989 doesn’t hold through for what is known today about hantavirus epidemiology.

2) Much higher case fatality rates have been reported. See Goeijenbier et al. Crit. Rev. Microbiol. 2013, 39(1):26-42

3) “Along with norovirus, rotavirus, influenza and 77 hepatitis C, hantavirus infections are associated with the five most common viral diseases [5]”

This is wrong in so many ways. What do the authors want to say? I really hope this statement if about Germany but even that I doubt. Now it reads like it is about the world. How about HIV, dengue and hep a and B????

Methods:

1) There should be also a case definition for the diagnosis of acute Puumala hantavirus infection. What is considered as an acute hantavirus case by the Robert Koch institute? Since hantavirus serology done by ELISA (especially Progen or Focus) and/or IFA (especially Euroimmun mosaic) results in a remarkably high number of false positive test result I doubt if all patients included in this study are actually hantavirus infected patients.

2) On what ground was the Lipase level cut off decided? Preferably backed up with a reference.

3) ‘at the treating physician’s discretion’ is a huge selection bias. This is not a deal breaker since still the data could be of interest for physicians in infectious diseases but this should be clearly stated in the discussion.

4) Definition were there amylase levels from any patient?

Results:

The result section does not read well. First of all there is duplication of the results (Abdominal ultrasound was performed in 88% of the 153 patients with elevated serum lipase but without signs of acute pancreatitis. In two patients, CT 154 scans of the abdomen were performed, revealing no signs of pancreatitis.) is written twice (first and third paragraph)

1) I thought that in the PCT paper from the same group and the same cohort also PCT levels where available in 166 out of the 456 patients (correct me if I’m wrong). Where this the same patients? Is it still the physicians choice to test either amylase or PCT or are we looking at a in depth studied cohort of 166 patients in a total of 456 reported cases?

Table 1:

Is there anything known about level of lipase in serum and correlation to age or to creatinine levels?

Table 2:

Does not read well consider turning it to a landscape page and try to be more
comprehensive

**Level of interest:** An article of importance in its field

**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