Reviewer’s report

Title: Febrile patients admitted to remote hospitals in Northeastern Kenya: seroprevalence, risk factors and a clinical prediction tool for Q-Fever

Version: 0 Date: 01 Mar 2016

Reviewer: Dimitrios Frangoulidis

Reviewer's report:

Reviewer comments to „Febrile patients admitted to remote hospitals in Northeastern Kenya: prevalence, risk factors and a clinical prediction tool for Q-Fever"

The here presented article draft describes a serostudy of febrile patients in Kenya according to their Q fever status. The benefit of the study is to enhance the data of Q fever epidemiology in this part of Africa. In addition the authors are trying to calculate an algorithm to support Q fever diagnostics without laboratory work.

Although the general idea to screen sera for Q fever and to make fever diagnostics in this underdeveloped area easier the study shows two major constraints which make a publication doubtful.

1. Development of an algorithm/score to support microbiological diagnosis in fever of unknown origin.

Due to the unspecific symptoms of acute Q fever it is a difficult approach to generate a symptom driven score for Q fever diagnosis. The major problem of the here presented study is the lack of checking relevant differential diagnosis. No information was given if relevant bacterial diseases like Mycoplasma pneumoniae, Chlamydia pneumoniae or Legionella pneumonia were studied. Also Brucellosis, Cholera and Typhus-disease should be excluded. In addition relevant viral diseases like Rift Valley-fever, Dengue, West Nile and Chikungunya and so one are also missing. On top of that the authors are trying to identify a very difficult to diagnose infectious disease in their study population. Q fever diagnostics is relying of antibody detection and/or DNA detection. These special issues are the basis of the second problem of the here presented data.

2. Determination and Interpretation of serological data:

The authors are defining an acute Q fever disease when IgG Phase 2 Antibodies are >= 1:128 or Coxiella specific DNA is detected. Both definitions must be seen critical and used carefully. The
authors are relying to a publication from Anderson et al. (2013) but in this paper it is clearly written that the above used criteria (IgG phase II > 1:128) indicates a PROBABLE acute infection and it is also stated from the authors that interpretation must be done with caution "especially in patients with rural or farming backgrounds"! This is explained by existing baseline antibodies acquired as a result of previous exposure to Q fever. This is obviously the case in the here studied region/population of Kenya (citation from the abstract "pastoralist population").

Therefore it is not possible to reproduce the diagnosis of acute Q fever in the here presented data. So all extracted and generated conclusions are not proven and validated! According to the 10 sera which are PCR positive the situation is in principle better, but it is not excluded to find Coxiella DNA in the chronic form of the disease. So the author have to check the exact antibody combination of phase I and II too.

There are also some minor errors/discrepancies in the general text, but before looking for this, the general problems of the paper must be solved and clarified.

Summary:

The paper is in the actual form not acceptable for publication.

It should be generally checked according to study design and diagnostic protocols. The authors must check relevant bacterial and viral differential diagnostics pathogens before relying on Q fever. And in addition the results from their Q fever diagnostics should be interpreted more carefully.

By the way: the authors mentioned the support of the German Consulting Laboratory for Q fever - does this means, that all ELISA positive results had been checked and confirmed by IFA including the interpretation of the results in cooperation with this Consulting Laboratory?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?
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