Reviewer’s report

Title: Exclusion of pregnancy in dialysis patients: diagnostic performance of human chorionic gonadotropin

Version: 0 Date: 17 Nov 2019

Reviewer: Lawrence McMahon

Reviewer's report:

This is a relatively brief study of the relevance and significance of β-hCG concentrations in women, both fertile and infertile, with ESKD. It is not large enough to provide an epidemiological normal or speak for all nationalities. Nonetheless, as the authors point out, available reports are small and inconclusive, and these data do help address a relevant issue.

Issues and Concerns

1. The reference to diagnosis of primary ovarian failure or menopause in the Discussion (P. 12) is referenced in the Methods section (P.6). Are both necessary?

2. The authors state several times that age was not related to test results. This is a counter-intuitive finding, although might be accounted for either by what patients are excluded or judged infertile. Was there a correlation between infertile patients and age? I think some additional information / discussion should be presented to explain this. The authors might also wish to comment on the general applicability of these data, given the limited demographic context. Would we expect factors such as race and co-morbidities to affect primary failure? At what point might CKD affect menopause and β-hCG concentrations?

3. What about women with a significant degree of intrinsic renal function (especially those commenced on peritoneal dialysis)? I accept that numbers might be too small to predict with confidence but it is of some significance as it is these patients who are more likely to fall pregnant.

4. There is a reference to interfering heterophilic antibodies, especially in patients with autoimmune disease (P.13). Is it known if this interference remains when patients are on regular dialysis, particularly for those with a history of vasculitis?

5. The limitations of the statistics and therefore more moderate conclusions should be drawn. The data are helpful but I am not convinced they are sufficiently robust to be relied upon completely. This particularly applies to the proposed cut-off values: that a 100% predictive value is based on zero samples is a case in point. Similarly, marked caution is advised with respect to the lower limit of β-hCG concentrations in pregnant dialysis patients, given that one of the two pregnancies had a reading of 58 mIU/mL compared to 25 for the highest non-pregnant reading.

6. Tables and Figures: I think these should be simplified and made more relevant.

a. Tables 1 and 2 contain a great deal of data, but they are inherently descriptive and of limited value, in my opinion. Could the authors perhaps address the data again and refine? Options might be to include
only the more essential data and divide it also into the fertile / infertile / and pregnant groups in the one table, as well as cut out extraneous information.

b. Table 3 could be excluded, or potentially included in the table(s) above.

c. Table 4 focusses on hCG concentrations \(>5 \text{ mIU/mL}\), but this value was not found to be of clinical significance in the study. Furthermore, such data seem excessive. I think that the group data (as suggested above) would give us greater insight into what the authors discuss in the text. Conversely, it does not appear to be stated whether the patients were on peritoneal dialysis or haemodialysis. Was a level of intrinsic renal function relevant?

d. Could Figures 1 and 2 be combined?

e. Figure 3. The range between the two pregnant dialysis patients is extreme and contributes to the previously suggested. This deserves some acknowledgement in the text. Was it merely related to the gestational age or were other factors identified?

7. Within the confines of the relatively small numbers, if the \(\beta\)-hCG concentration is elevated, does the degree of elevation indicate the appropriate line of investigation, as would be suggested by the study data? Would an algorithm be possible or are numbers too small?

8. What tests concerning pregnancy/fertility should be performed on women of child-bearing age with ESKD? Is this for every woman? Is it possible to suggest an appropriate frequency of testing (e.g., annual/ pre-op/ pre-transplant … )? This is particularly relevant in the conclusion, which I think should be rewritten.

Please confirm that you have included your review in the ‘Comments to Author’ box?

As a minimum standard, please include a few sentences that outline what you think are the authors’ hypothesis/objectives, their main results, and the conclusions drawn. Your report should constructively instruct authors on how they can strengthen their paper to the point where it may be acceptable for publication, or provide detailed reasons as to why the manuscript does not fulfill our criteria for consideration. Please supply appropriate evidence using examples from the manuscript to substantiate your comments. Please break your comments into two bulleted or numbered sections: major and minor comments.

Please note that we may not be able to use your review if no comments are provided.

Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included as text in the ‘Comments to Author’ box.

Yes
Are the methods appropriate and well described to allow independent reproduction of experiments?
Please state in the ‘Comments to Authors’ box below what you think are the strengths and weaknesses of the methods (study design, data collection, and data analysis), and what is required, if anything, to improve the quality of reporting.

Yes

Does the work include the necessary controls?
If not, please explain in the ‘Comments to Author’ box below.

Yes

Are you able to assess the statistics?

- Are the statistical test(s) used in this study appropriate and well described?

- Is the exact sample size (n) reported for each experimental group/condition (as a number, not a range)?

- Are the description of any error bars and probability values appropriate?

- Are all error bars defined in the corresponding figure legends?

- Has a sample size calculation been included, or a description and rationale about how sample sizes were chosen?

Please confirm which of the following statements apply to your statistical assessment of the manuscript (Please include details of what the authors need to address in the ‘Comments to Author’ box):

I have been able to assess all of the statistics in this manuscript (please refer to checklist above)

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in the ‘Comments to Author’ box below.

No

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

Should the manuscript be highlighted for promotional activity?

Articles that are deemed of interest to a broad audience can be promoted in a variety of ways. This could be through email updates, postings on the BioMed Central homepage, social media, blogs and/or press releases. Please indicate in the text box below whether you think this manuscript
should be considered for promotional activity, indicating your reasons why (e.g. what is the most newsworthy aspect of the research).

No

**Declaration of competing interests**

Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal