Reviewer’s report

Title: The role of haematological indices in predicting early iron deficiency among pregnant women in an urban area of Sri Lanka

Version: 0 Date: 30 Jun 2018

Reviewer: Philip Crispin

Reviewer’s report:

Thank you for asking me to review this manuscript. The study prospectively examins the haemoglobin and red cell indices haematological indices as measured on the Celltac E analyser for detecting iron deficiency as determined by serum ferritin. Although a small study, the intent to identify a surrogate for iron deficiency in pregnancy rather than iron deficiency anaemia would improve screening for increased intervention. I think the results would be of interest, especially in areas of limited resources, but also in many high resource areas due to the lack of widespread acceptance of ferritin screening in pregnancy.

The major issue with the paper is the set points for each of the individual indices, which are presumably based on non-pregnant levels (but can't be determined as the reference (22) appears to be to a book review (although I can't find this review at JAMA on line). It is unclear whether the a priori cut offs are suitable for this analyser, or for pregnancy. The results show fairly similar ROC AUCs for MCV, MCH and MCHC, however marked differences in the sensitivity and specificity at the a priori cut-offs despite acknowledging that MCV increases in pregnancy. The lower sensitivity and higher specificity suggest that the cut-off of 80fL for MCV might be too low. An optimum MCV cut-off based on the ROC is not stated. The stated MCHC optimum is very close to the a priori cut-off. Do these results therefore suggest the MCV range should be changed in pregnancy for improved detection of iron deficiency rather than the MCHC being vastly superior> Is the mildly better ROC AUC significant? It would be useful to compare the ROC curves directly and determine from the data rather than from standard normal ranges the ideal MCV for iron deficiency detection.

Minor issues:

There could be improved clarity between iron deficiency and iron deficiency anaemia, for example on page 7, the validity of haemoglobin for detection of "iron deficiency anaemia" is questioned. This may be reasonable for iron deficiency, but iron deficiency anaemia would require a low haemoglobin.

Page 5, L40 the authors assert that functional consequences of iron deficiency are not apparent in the early stages, which is contrary to the later well-developed argument that early iron deficiency without anaemia may have an impact on foetal outcomes. I presume this assertion relates to the effect of anaemia only.
At L46 "severe" is defined as 2SD below the mean healthy population. This definition is un referenced and is problematic as ferritin is not normally distributed and a "healthy" population of women includes a high proportion with iron deficiency both in developed and emerging economies.

It is implied that UK guidelines recommend screening with ferritin, whereas the guidelines (Pavord 2012) recommend ferritin in early pregnancy for high risk women only. This is relevant as there is a reluctance even in high resource settings to undertake universal ferritin screening in pregnancy despite increasing understanding of the relevance of iron deficiency and high prevalence. This increases the relevance of the study.

The relevance of marital status with respect to iron deficiency is unclear (Table 1). If there are cultural reasons why this association was suspected they should be stated.

The reference formatting needs to be thoroughly checked - for example, the use of month for book chapter, first author only, follow by et al, is not consistent with journal guidance. Reference 22 also appears to be incorrect.

The article would benefit from assistance with English. There are occasional changes in form also suggested, for example P8, L21 Celltac E (Nihon Kohden Corp. Tokyo).

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

Yes

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

Yes

**Are the conclusions drawn adequately supported by the data shown?**
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