Reviewer's report

Title: Reference intervals for thyroid stimulating hormone and free thyroxine derived from neonates undergoing routine screening for congenital hypothyroidism at a university teaching hospital in Nairobi, Kenya: A cross sectional study

Version: 0 Date: 12 Jan 2016

Reviewer: Jennifer Yee

Reviewer's report:

In this manuscript "Reference intervals for thyroid stimulating hormone and free thyroxine derived from neonates undergoing routine screening for congenital hypothyroidism at a university teaching hospital in Nairobi, Kenya: A cross sectional study," the authors' main objective was to determine reference ranges for TSH and fT4 in African infants using the Roche e601 analyzer. The authors' rationale for the study is that population-specific references intervals are needed for this analyzer method which was based on a very different population from theirs. The statistical method used was a publicly available software to determine the reference ranges, and which has been cited in at least 8 other articles on PubMed. Otherwise, the statistical methods appear reasonable. In general, the study accomplished its stated aims. The study determined that the references ranges for TSH and fT4 were overall similar to the published range, but their ranges were more narrow. Strengths for the study include a large number of subjects on which the reference intervals are based. Areas for manuscript improvement include needing more information on several aspects of the study methodology along with a few additional comments below.

The pages are not numbered, so the following lines are referred to by the author line numbering.

Questions: It is always challenging to define a reference population, and my questions center around the approach to defining the reference population in this study.

1) The methods section should include more information about the approach to collection of data. For example, were the laboratory databases examined first to identify infants, or were the clinical records used to identify them?
2) Would like to know additional details about the infants included in the reference population. Were there any predetermined inclusion or exclusion criteria for data to be included? Additional information I would like know include, for example, what was the average gestational age of the infants? How many were preterm?

3) Along the same lines, would like to know more about chart reviews that were conducted. These were mentioned in the discussion section, but not in the methods. In particular, I would like to know the extent to which chart reviews were performed, e.g. how many chart reviews? And what were the aims of the chart reviews?

4) There is also mention of examination of the charts of the outliers, and some might have non-thyroidal disease, but how many? What if infants had sick euthyroid syndrome, which is when non-thyroidal illness could certainly affect thyroid function transiently.

5) Also, the analysis was repeated in a "parametric analysis" without the outliers, and there was supposedly no change. This additional analysis should be discussed in the methods section.

6) Would suggest some discussion about how using the new reference range might impact clinical detection and screening for congenital hypothyroidism.

Minor

6) Background line 91, "commonest" should be changed to "most common."

7) Line 110, "…population-specific and derived from…” (add a hyphen before "specific", and add "and.")

8) Line 122, should read "This population was comprised of primarily…” (add "was" and "of")

9) Line 123, should read"…which is largely comprised of black…”

10) Line 135 -Please write out what ISO stands for

11) Line 141, "Newborn" is one word


13) Results line 192. For neonates age 8-14 days, is the lower limit 7 or 8? Some places in the manuscript say 7, and some say 8.

14) Results line 201, instead of "not within," suggest saying "outside."
15) Discussion, line 262 and 265, please clarify what RI is being discussed. I presume TSH.

16) Discussion line 289, suggest adjusting sentence to "in the first week of life, which was probably not sufficient…"

17) The Conclusion also needs editing for missing articles

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.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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

Needs some language corrections before being published

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