Reviewer's report

Title: Birth weight by gestational age and congenital malformations in Northern Ethiopia

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Reviewer: Giuseppe Puccio

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This paper presents data about births in Northern Ethiopia that are certainly of potential interest, given the very special nutritional problems of the population in that area, and the obvious consequences on pregnancies and births. Any data which can improve our understanding of the conditions of mother and child health in such a context is certainly precious, especially in the perspective of possible nutritional and socio-sanitary intervention in the area.

That said, unfortunately the paper has many serious flaws, especially for what concerns the presentation, description and analysis of data, and therefore also the discussion and conclusions are unclear and ill defined. I will try to focus on the main methodological problems.

Major Compulsory Revisions

1) In the background section, there is this strange statement:
   “From all live births worldwide 16% are LBW, >90% of which occur in the low-income sub-Saharan African countries”

   As it seems unlikely that what is meant is that >90% of all LBW births worldwide occur in the low-income sub-Saharan African countries, I suppose there is some error here. Moreover, IUGR is not defined here, so I will assume that it is meant in the usual sense of “birth weight below the 10th percentile of some birth-weight-for-gestational-age reference curve”.

2) As the sample in the study is from the births in two hospitals, which are only a small percentage of the general births (most of which occur at home), there is potential selection bias, which should be at least addressed in the discussion: what kind of mothers preferentially recur to birth in hospital, in the local context?

3) In the Results section, it is not clear why in Table 1 the sex ratio of “neonates without malformations”, and not of all neonates, is shown. It should be clarified also what the p value refers to. Is it a one proportion test? A simple chi square test would show that the percentage of females is 55.5% in neonates without malformations, and only 31.2% in neonates with malformations, which is probably more interesting, and that the difference is significant (p = 0.006312).
   Table 1 also shows the sex ratio in SGA babies, but there is no definition, here or elsewhere, of how those SGA babies are defined (what percentile reference chart has been used?).

Moreover, it seems that SGA babies are 49 in all. In a population of 1516 births,
without any excess of IUGR, 151 would be expected. What do these numbers mean?

If a reference percentile chart has been used, why not give the numbers of SGA, AGA and LGA in the whole sample? If not, what does “SGA” mean, in the paper?

4) Let’s go to Figure 1, which is specially unclear. What do the green diamonds represent? Is this a scatterplot of the individual case? Are they medians, means, or what else? How is it possible that all babies from 26 to 36 weeks of GA have practically the same birthweight of about 1000 grams? And babies weighing less than 100 grams at 36 weeks of GA are not SGA? That makes no sense.

5) Figure 2 is more clear, but nowhere in the discussion about parity are the numbers or rates of different parities given. Why?

6) There is no mention of the distribution of GA in the sample. How many babies were born at each GA? How many were pre-term? Figure 3, panel B, shows percentage of babies with malformations for each GA, but those cannot be correctly interpreted if the total number of babies born at each GA is not shown.

7) In Figure 3, panel B, C and D are regressions on percentages and counts, of which R squared are given, but not p values. That seems not the best way to analyze frequencies. For GA, an analysis of the distribution of GA in the two groups (with or without malformations), for example by a Wilcoxon test, would be more appropriate. Counts of babies with malformations per parity class could be analyzed by a chi square test. The different relationship between GA and malformations according to sex is interesting, but without some appropriate inferential analysis it’s difficult to discuss it.

8) The text says: “Table 4 shows that the babies with congenital anomalies died intrauterinely in almost 38% of cases,”, but the data about intrauterine deaths are missing in the Table. Moreover, as the 32 babies with malformations apparently included 12 intrauterine deaths, it is not clear if intrauterine deaths are also included in the group without malformations.

9) The discussion cannot be well evaluated, given the many inconsistencies and the incompleteness in data presentation.

10) The text says: “Furthermore, the offspring sex ratio declined dramatically to ~20% males if the neonates were born to mothers with at least 3 completed pregnancies, which, as far as we are aware, was not reported earlier.” That is interesting, but what kind of explanation do the authors suggest for that?

11) The comparison with the Netherlands curves seems obscure. Again, the distribution of weight for GA should be better described, in terms of percentiles (even with the Netherland curves, if others are not available). The data about LBW and VLBW are more clear, and confirm the extreme conditions of malnutrition in pregnant women in the area. Here too, the problem of a possible selection bias for hospitalized women should be considered.

12) The comment “The very high prevalence of severely underweight small-for-gestational-age neonates after 3-4 offspring (~60%) is also noticeable.” But again, the data shown in Figure 2 make no reference to SGA infants and
their number or prevalence, but only to absolute birth weight. Again, there is the impression that the authors do not make a clear distinctions between absolute weight and weight for GA. 

13) The data about the prevalence of malformations are obviously biased by the methodology, as the authors correctly admit, and certainly show a very high prevalence of malformations, especially of the CNS. The nutritional explanations proposed seem credible enough, although they are not well supported by the data themselves. A better analysis of the relationship between malformations and IUGR (weight percentile at birth) could provide some hints.

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

In the past five years I have received reimbursements and fees for some consultancy work from the following organisation: NESTEC LTD.

However, I have no reason to believe, as far as I know, that the above mentioned organization may in any way gain or lose financially from the publication of this paper, either now or in the future.

I declare that I have no other competing interests