Reviewer's report

Title: Congenital toxoplasmosis and prenatal care state programs

Version: 10 Date: 30 September 2013

Reviewer: Martine Wallon

Reviewer's report:

M Avelino and colleagues submit a revised version of their article 'Congenital toxoplasmosis in a prenatal care state program' that compares outcomes in newborns identified by different strategies in Brazil.

Despite the changes made, the methods and results chapters still lack in clarity and several methodological points need to be addressed in the discussion.

Major Compulsory Revisions

The design remains difficult to understand and precision are lacking on several important points.

1. Incidence of congenital infection and clinical outcomes were compared in two groups of newborns. Based on table 1, it seems that

- the 155 newborns in the first group were born from mothers who had a profile of acute Toxoplasma infection at the first prenatal test and were then treated during pregnancy, and,

- that the 74 newborns in second group were born from mothers who tested negative at the first prenatal test, but positive at delivery (true seroconversion), and were not treated during pregnancy. However, the reader is confused by the mention in the text that seroconversions (12/74) were also diagnosed in pregnancy, and that group 2 also included newborns identified through a neonatal screening program? Is this correct? An algorithm is clearly needed.

Describing the methods and the results according to these two groups (Group 1 and 2) would greatly help

2. The authors also need to provide information on possible selection and detection biases and confounders.

   a. How were pregnant women who underwent screening selected? Was testing offered to all of them? Were the 246 cases of maternal infections included in the cohort all consecutive cases? This seems a rather low incidence over a 8-year period, especially considering the high incidence which was previously reported in this area.

   b. What the timing of testing the same in women in both groups?

   c. It is stated on page 6 that the prenatal treatment was started once “fetal infection” was confirmed. Do the authors mean until “pergravidic infection or reinfection” was confirmed or do they mean that mothers were not treated until
infection was confirmed in the fetus? If the latter is true, this would prevent discussing about any impact of treatment on transmission.

d. A large number of children in both groups had clinical signs. How often were they diagnosed in utero in both groups?

e. Also important, is whether the proportions of newborns with clinical signs could have been overestimated in group 2 because those who had clinical signs would be more likely to be tested at birth? In other words, would a child with a subclinical infection be as likely as a child with an overt infection to be tested?

3. All these methodological aspects are also important to address in the discussion.

4. As already mentioned, epidemiological studies that are not controlled cannot allow making interference about treatment efficacy. This is specially the case when the groups are not comparable, which was clearly the case. The criteria for maternal infections were not the same in both groups. As positive IgM and low avidity can be detected for more than one year after the initial infection, there is a risk for underestimating incidence and severity of infection when establishing a pergravidic maternal infection on a serological profile of “acute infection”, rather than on a profile of true seroconversion. Timing of infection might also have been different between mothers in groups 1 and 2 and this would greatly influence outcomes. The authors could state that the outcomes were better in the first group, and discuss the hypothesis that it might be the consequence of prenatal treatment, but they should be careful in not drawing definite conclusions about treatment efficacy.

5. The introduction and discussion are still very lengthy with many repetitions and rather vague statements. They should be revised to be tighter and more concise.

Minor revisions

References are also very abundant and not always appropriate. As an example, 37 references are quoted to illustrate the comment that toxoplasmosis is important even in low incidence areas, but they include articles that stated the opposite. The selection of references should be narrowed down to the most relevant and recent ones.

There are also errors in the text. The screening program in Denmark was discontinued in 2007, retesting is performed every 3 months in Austria.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests