Reviewer's report

Title: Follow-up study of neurodevelopment in 2-year-old infants who had suffered from neonatal hypoglycemia

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Reviewer: Denis Azzopardi

Reviewer's report:

This manuscript reports the neurodevelopmental outcome of a group of newborn infants born to diabetic mothers who suffered at least one episode of hypoglycaemia soon after birth compared with a control group of healthy newborns. Infants with neonatal hypoglycaemia were subdivided into three groups according to the severity and duration of hypoglycaemia. The infants were examined at 2 years corrected age by the Gesell Developmental schedule. The authors report that there were no difference in developmental scores between the hypoglycaemic and control groups but hypoglycaemic infants in the more severe groups had lower "adaptability" scores than the least severe hypoglycaemic group and controls. Other Gesell test measures were not significantly different among the groups.

The study findings are consistent with generally accepted views that prolonged neonatal hypoglycaemia can cause brain injury and impair neurodevelopment. The authors also report that infants with more severe hypoglycaemia were more likely to be born to mothers who needed insulin therapy and had more weight gain during pregnancy consistent with views that poor glucose control in pregnancy is associated with more severe neonatal hypoglycaemia.

There are a number of weaknesses with the study. As noted by the authors the group sizes were small, and loss to followup relatively high, which reduces the statistical power of the study and increases risk of error. In addition I have the following concerns: It seems blood glucose was measured by a micro glucose meter and not confirmed in the laboratory; Neurodevelopment was tested by the Gesell method but it is not stated which version was used. The reference to the assessment given in the manuscript (reference 24) is not a valid reference for the test. The Gesell Developmental Observation- Revised is the validated version and is only applicable from 2 years 9 months of age but followup in this study was at 2 years corrected age. There is no description of the clinical course of the infants admitted to the neonatal unit, such as the need for assisted ventilation or oxygen therapy, or feeding difficulties, which might influence neurodevelopment.

There are a number of errors such as the less than (<) and more than (>) signs are not always given correctly, eg in the definitions of hypoglycaemia and subgroups; The statement at lines 82-84 that neurodevelopment of infants suffering neonatal hypoglycaemia has not been performed is incorrect; the formula for scoring assessment items in lines157-161 is not clear and needs to be checked.
The primary outcome of the study needs to be clearly stated and the conclusion needs to relate to the primary outcome and objective of the study. In the manuscript the conclusion in the abstract and main manuscript differ.

The manuscript requires revision and language corrections.

**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?**
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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