Reviewer’s report

Title: Impaired awareness of hypoglycemia in children and adolescents with type 1 diabetes mellitus in North of Jordan

Version: 0 Date: 13 Jan 2019

Reviewer: Neil White

Reviewer's report:

In this manuscript, Alkhatatbeh et al from Jordan report a low rate of Impaired Awareness of Hypoglycemia (IAH) in children and adolescents with type 1 diabetes (T1D). Their reported rate is 15.96%, lower than that reported in many other studies. Importantly, and more important than the rate of IAH, they report that IAH is associated with having reported more hypoglycemia during the preceding 6 months. Based on what we already know about IAH (also known as hypoglycemia unawareness and as a component of hypoglycemia-associated autonomic failure [HAAF]), this is not an unexpected finding and has been reported many times. The only elements of this report that are novel are the report from a different population and the surprising conclusion that IAH was not associated with HbA1c or with the frequency of severe hypoglycemia (SH). I have problems with these latter conclusions.

My problems with some of the conclusions in this manuscript are the lack of association of IAH with HbA1c, the presence of SH during the preceding year, insulin regimen and adherence to the regimen. In all these cases, I think that the sample is too small to reliably conclude that their result are different from prior reports. In the case of HbA1c, the p-value between the Aware and the IAH group is p=0.12; with more subjects this would likely be significant and this study is underpowered to detect the difference. In the case of insulin regimen, only 6 subjects were not using Mixtard; too few subjects not using Mixtard to make any conclusions related to the insulin regimen. In the case of adherence, no definition of the categories are given and there is likely a difference between the groups if the sample size were larger; the p-value (0.06) is approaching significance. Most importantly, in the case of SH, which is an important conclusion, the number of events is small with a p-value of 0.14; again, with a larger number of events, this would likely be significant in the direction expected; IAH would be associated with more SH. To conclude the lack of an association in contrast to other studies, some determination of power for the sample size would be important. I suspect that the power to detect a difference between groups in HbA1c and SH would be low. The studies to which the authors compare their results and came to different conclusion related to duration, HbA1c and SH were much larger studies (Hoi-Hansen et al: N=372; Ly et al: N=656; Abraham et al: N=413).

Secondly, in this manuscript, they have excluded subjects <5 years old who "were not mature enough to express their feeling of hypoglycemia." On one hand, this is an arbitrary age cutoff. In addition, I am not sure that all the other studies to which they compare their results used the same exclusion.

Specific Comments
1. Many of the references, especially #6 and #14 in the Introduction, are certainly not the best references to cite in support of the statements to which they refer. There are much more robust references.

2. They should state specifically whether the cutoffs used on the questionnaires were the same as those used in the other studies. Any differences would certainly make the comparisons weaker if not meaningless.

3. On the first page of the Results section (line 25), they state that self-monitoring was done on a "daily basis". More detail about the frequency of monitoring should be given and there needs to be some analysis of hypoglycemia frequency for different monitoring frequencies. The frequency of monitoring will certainly affect the frequency of hypoglycemia reported.

4. The percentages reported to 2 decimal places is inappropriate (15.96, 18.01, 65.96); one decimal place (16.0; 18.0; 66.0) is more than adequate.

5. Last paragraph of Results (line 20): "lest" should be "least".

6. Were all patients on insulin from the time of diagnosis, as hopefully would be the case for T1D? If so, in Table 1, "duration of DM" and "Duration of insulin therapy" are redundant, and only one is needed.

7. Also, in Table 1, to report a p-value for the difference in age between children and adolescents is meaningless since the groups were defined by age and there would be no overlap.

8. In Table 3, what is meant by "Mean Rank" in the column headers?

**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.

No

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