

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Iron intake, haemoglobin and risk of gestational diabetes: a prospective cohort study
AUTHORS	Kinnunen, Tarja ; Helin, Annika; Raitanen, Jani; Ahonen, Suvi; Virtanen, Suvi; Luoto, Riitta

VERSION 1 - REVIEW

REVIEWER	Bo Simona Dept Internal Medicine, University of Turin, Italy I have no competing interests
REVIEW RETURNED	20-Jul-2012

GENERAL COMMENTS	Total energy intake and nutrient intake (in particular increased saturated fat intake and reduced fibre and magnesium intake) might impact on GDM incidence. It cannot be excluded that the women with higher iron intake were also those with a more unfavourable dietary pattern. These nutritional data should be provided. Furthermore, weight gain during pregnancy is another important risk factor, worthy to be considered.
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REVIEWER	Karen Chan Clinical associate professor Dept of Obstetrics and Gynaecology University of Hong Kong Hong Kong I have no conflict of interest
REVIEW RETURNED	31-Jul-2012

THE STUDY	The authors used only information from 1 questionnaire to determine the participants' iron intake. This is only a snap shot of the pregnancy and may not be reflective of the true situation. Furthermore, there is no report of the compliance (eg did all women completed all 181 items ?) and accuracy of filling the questionnaire (eg was the ability to complete the questionnaire correctly checked in at least a proportion of the participants.). Also, there were no objective evidence of their iron intake or status eg serum Fe measurement, TIBC etc
RESULTS & CONCLUSIONS	The results are generally well presented, except : The authors mentioned that after excluding women with low Hb (< 12 g) the odd ratio become significant. How many women had Hb > 12 g and what is the mean Hb in this group of women ?

	Why did the authors choose to divide the groups into fifths for comparison ?
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VERSION 1 – AUTHOR RESPONSE

Reviewer: Bo Simona
Dept Internal Medicine,
University of Turin, Italy

I have no competing interests

Total energy intake and nutrient intake (in particular increased saturated fat intake and reduced fibre and magnesium intake) might impact on GDM incidence. It cannot be excluded that the women with higher iron intake were also those with a more unfavourable dietary pattern. These nutritional data should be provided. Furthermore, weight gain during pregnancy is another important risk factor, worthy to be considered.

Authors' response:

These were very relevant comments. We have compared dietary intake between the iron intake groups (20, 60 and 20%) and added data on macronutrient and fibre intake and gestational weight gain in Table 1 and in the text (page 10). The chapter 'Statistical methods' has also been updated. We found a few statistically significant differences in dietary intake between the iron intake groups: The women in the lowest iron intake group had lower total energy and dietary fibre intakes than the other women whereas women in the highest iron intake group had higher intake of saturated fatty acids than the other women. We added these three dietary variables as confounders in the multivariate logistic regression models (Table 3). As a consequence, the association between iron intake and the risk of GDM became slightly stronger.

Gestational weight gain did not differ statistically significantly between the iron intake groups (Table 1), but it was statistically significantly associated with the risk of GDM and was included in the multivariate models (Table 3).

The women in the lowest iron intake group had lower magnesium intake (mean 361 mg/day, sd 74) than women in the mid (445 mg/day, sd 115) or the highest iron intake groups (435 mg/day, sd 112) (Kruskal-Wallis test, $p < 0.001$). However, magnesium intake was not associated with the risk of GDM in any of the multivariate model and was not therefore included in the final models shown in Table 3. We also assessed the effect of including total fat and carbohydrate intakes in these multivariate models. Since the results were essentially similar and total fat or carbohydrate intakes were not associated with the risk of GDM, they were also not included in the final models.

Reviewer: Karen Chan
Clinical associate professor
Dept of Obstetrics and Gynaecology
University of Hong Kong
Hong Kong

I have no conflict of interest

The authors used only information from 1 questionnaire to determine the participants' iron intake. This is only a snap shot of the pregnancy and may not be reflective of the true situation. Furthermore, there is no report of the compliance (eg did all women completed all 181 items ?) and accuracy of filling the questionnaire (eg was the ability to complete the questionnaire correctly checked in at least a proportion of the participants.). Also, there were no objective evidence of their iron intake or status eg serum Fe measurement, TIBC etc

Authors' response:

The reviewer is right in pointing out that it would be relevant to estimate iron intake for a longer time period during pregnancy. We have discussed this limitation as follows in the manuscript on pages 10-11 (WORDS IN CAPITALS ARE ADDED INTO THE REVISED MANUSCRIPT):

“A limitation of this kind of study is that estimating iron intake during pregnancy can be challenging because dietary habits and use of supplements can vary a lot during pregnancy due to nausea and other changes in wellbeing. Iron intake was assessed at a certain point in time (AT 26-28 WEEKS' GESTATION COVERING THE PREVIOUS MONTH), thus it does not cover the intake during the whole pregnancy. In our study we decided to use information on iron intake in mid-pregnancy to get the best estimation on iron intake during pregnancy and before the onset of GDM. We did not use information of iron intake abstracted in the beginning of pregnancy because it covered only dietary habits and supplement use during one month before the pregnancy when use of supplemental iron is rare. However our information on iron intake covers only one month in the mid-pregnancy.”

We have reported data related to compliance and accuracy of completing the questionnaire in Methods on page 6 as follows:

“The completed questionnaires were checked by a nutritionist and those with more than ten missing values in the frequency data were completed after consulting the participant on the phone.”

We also state the following in the beginning of the same paragraph:

“Information on diet and supplement use was obtained by a validated 181-item food frequency questionnaire (Erkkola et al. 2001) ALTHOUGH THE VALIDITY OF THE SUPPLEMENT DATA WAS NOT ASSESSED IN THE STUDY BY ERKKOLA ET AL.”

No further efforts to check the validity of the completed questionnaires were made in this study.

We agree with the reviewer on that objective measurement of iron intake or status would be more valuable than self-reported data. In addition to the Hb data, we have taken blood samples from the participants and are planning to analyse markers of iron status in our further studies.

Reviewer: Karen Chan

The results are generally well presented, except: The authors mentioned that after excluding women with low Hb (< 12 g) the odd ratio become significant. How many women had Hb > 12 g and what is the mean Hb in this group of women?

Authors' response:

The numbers of women with Hb >120 g/l or ≤120 g/l are shown in Table 2. We have added the number of women with Hb >120 g/l and their mean Hb level in the text. The sentence on page 9 is revised as follows:

“When including women with haemoglobin levels >120 g/l in early pregnancy (n=321, mean Hb 135, SD 9), the difference between the groups was even larger but still not statistically significant (P=0.11).”

Reviewer: Karen Chan

Why did the authors choose to divide the groups into fifths for comparison?

Authors' response:

We first divided the groups into fifths to be able to assess a possible dose-response relationship in more detail than when comparing thirds or fourths. We then compared women in the highest fifth to the other women as they seemed to be at increased risk of GDM. We also did sensitivity analyses using different cut-off points for categorising the women, as reported in Statistical methods (page 8) and Results (page 9).

REVIEWER	Karen Chan Clinical associate professor Dept of O&G University of Hong Kong
REVIEW RETURNED	30-Aug-2012

- The reviewer completed the checklist but made no further comments.