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LETTER

Medicalising pregnancy with new diagnostic criteria for gestational diabetes mellitus: do we need more evidence? Reply to Venkataraman H and Saravanan P [letter]

Sarah H. Koning[1] · Jelmer J. van Zanden[2] · Klaas Hoogenberg[3] · Helen L. Lutgers[4] · Alberdina W. Klomp[1] · Fleurisca J. Korteweg[5] · Aren J. van Loon[5] · Bruce H. R. Wolffenbuttel[1] · Paul P. van den Berg[6]

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Abbreviations

2HG	2 h plasma glucose
GDM	gestational diabetes mellitus
LGA	large for gestational age
NGT	normal glucose tolerance

To the Editor: We thank doctors Venkataraman and Saravanan for their letter and supportive comments [1].

The authors express their concerns about the reported differences in crude birthweight and not sex- and gestational-age-adjusted birthweight *z* scores. In our paper we reported a significantly lower birthweight in the WHO 1999 2HG only group compared with the normal glucose tolerance (NGT) group upon testing [2]. This is to be expected, as women classified with gestational diabetes mellitus (GDM) according the WHO 1999 criteria were treated with diet and/or insulin therapy. Venkataraman and Saravanan comment that it is likely that these differences were insignificant if birthweight *z* scores adjusted for gestational age and sex were used.

To make a correction for birthweight in relation to gestational age/time of delivery and sex, we reported the lowest and highest birth percentiles in our paper (small for gestational age: birthweight <10th percentile and large for gestational age (LGA): birthweight >90th percentile). The birth percentiles are corrected for gestational age, parity, ethnicity and sex. After these corrections we observed no differences in LGA neonates between the GDM classification groups and NGT group. It was a notable finding of our study that the women with NGT also had high rates of LGA neonates. This finding shows that even women with NGT who underwent an OGTT because of risk factors for GDM are also at increased risk of giving birth to an LGA neonate. Since these women with NGT were not representative of healthy pregnancies not affected by GDM, we reported a large difference in LGA rates between the general obstetric population and the classification groups. Women classified as having GDM according to the WHO 2013 fasting glucose guidelines only had a twofold higher rate of LGA neonates than the general obstetric population (21% vs 11%) [2].

It also needs to be borne in mind that the women diagnosed according the national guidelines benefit from treatment (WHO 1999 group and WHO 1999 2HG only group). The WHO 1999 2HG only group (2HG ≥7.8 but ≤8.4 mmol/l) had the lowest LGA rate of 15.4%. These women were actively treated with dietary modifications, and 20.5% needed insulin therapy [2]. These interventions normalised their glycaemic profiles and pregnancy outcomes. Not treating these women would be likely to result in higher LGA rates.

✉ Bruce H. R. Wolffenbuttel
bwo@umcg.nl

[1] Department of Endocrinology, University of Groningen, University Medical Center Groningen, HPC AA31, P.O. Box 30.001, 9700 RB Groningen, the Netherlands

[2] Laboratory of Clinical Chemistry, Certe, Medical Laboratory North, Groningen, the Netherlands

[3] Department of Internal Medicine, Martini Hospital, Groningen, the Netherlands

[4] Department of Internal Medicine, Medical Center Leeuwarden, Leeuwarden, the Netherlands

[5] Department of Obstetrics and Gynaecology, Martini Hospital, Groningen, the Netherlands

[6] Department of Obstetrics and Gynaecology, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands

A further criticism was that the statistical analyses were not adjusted for potential confounders such as pre-gestational BMI or gestational age. Obesity is a major risk factor and confounder in the association between mild hyperglycaemia and adverse pregnancy outcomes, including LGA [3]. Therefore, we additionally analysed the unadjusted and adjusted ORs for the associations between the WHO 2013 fasting glucose only group (i.e. women with fasting glucose ≥5.1 but ≤6.9 mmol/l) and the most important pregnancy outcomes with sufficient statistical power for multivariable adjustment (Table 1). Analyses were performed using logistic regression models in which the unadjusted and adjusted ORs (adjusted for pre-gestational BMI, maternal age, ethnicity, parity and gestational age) for the WHO 2013 only fasting glucose group were calculated using the NGT group as reference group (these data were not reported in our original paper). After correction, ORs for the incidence of induction of labour and admission to neonatology were still significantly higher in the untreated WHO 2013 only fasting glucose group, however, the planned Caesarean section rate was no longer significantly increased. It should be noted that we have incomplete data about what should be the comparator population: pregnant women without risk factors for GDM.

GDM and obesity are also both associated with insulin resistance and hyperglycaemia [3, 4]. In our GDM populations, the majority of the women were overweight or obese. To reduce the risks related to GDM there is an urgent need for effective lifestyle interventions. We support the policy that women with obesity receive standard lifestyle interventions before pregnancy, including advice about a healthy diet to obtain and maintain a healthy BMI. This is supported by Zang et al, who showed that adherence to a healthy lifestyle before pregnancy was associated with a reduced risk of GDM [5].

Our main reason for choosing to present the outcomes of this subset of 4431 women was that we retrospectively collected all the data by hand from written medical and obstetric records at midwives offices in primary care and at two hospitals. This was a representative sample: as mentioned in the results section of our article, the fasting glucose, 2HG and maternal age of these 4431 women were similar to the values obtained for the other 6211 women who completed a 75 g OGTT [2].

The authors are correct that universal testing is now recommended in several guidelines around the world. Our national guidelines still advocate targeted testing, and we do not have

Table 1 ORs for pregnancy outcomes in the WHO 2013 fasting glucose only group

	NGT	WHO 2013 only fasting glucose
Criteria (mmol/l)	Fasting glucose <5.1 and 2HG <7.8	Fasting glucose ≥5.1 but ≤6.9 and 2HG <7.8
Pregnancy outcomes		
n	2851	667
Treated for GDM, *n*	0	0
Induction of labour		
No. of cases, *n* (%)	793 (28.0)	230 (34.8)
Unadjusted OR	1.00 (Ref)	1.38 (1.15, 1.65)**
Multivariable-adjusted OR	1.00 (Ref)	1.22 (1.00, 1.48)*
Planned Caesarean section		
No. of cases, *n* (%)	185 (6.5)	68 (10.3)
Unadjusted OR	1.00 (Ref)	1.64 (1.23, 2.20)**
Multivariable-adjusted OR	1.00 (Ref)	1.36 (0.98, 1.88)
LGA[a]		
No. of cases, *n* (%)	514 (18.0)	140 (21.0)
Unadjusted OR	1.00 (Ref)	1.21 (0.98, 1.49)
Multivariable-adjusted OR	1.00 (Ref)	1.22 (0.97, 1.53)
Admission to neonatology		
No. of cases, *n* (%)	315 (11.1)	100 (15.0)
Unadjusted OR	1.00 (Ref)	1.42 (1.12, 1.81)**
Multivariable-adjusted OR	1.00 (Ref)	1.36 (1.04, 1.77)*

Data are expressed as OR (95% CI)

Multivariable adjustment included maternal age, pre-gestational BMI, ethnicity, parity and maternal smoking

[a] LGA was adjusted for maternal age, pre-gestational BMI and maternal smoking

p values were derived from logistic regression models: *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$ compared with NGT group

data on universal testing. In addition, there is a lot of controversy in connection with the diagnostic criteria and numerous different criteria are in use. The WHO 1999 criteria are currently recommended in the Dutch national guidelines, and we therefore reported these data. As mentioned in our reply to Ng et al [6, 7], a prospective study comparing both WHO 1999 and WHO 2013 cut-off criteria is needed.

In addition, Venkataraman and Saravanan suggest reporting the data of the modified WHO 1999 criteria (fasting glucose ≥6.1 and 2HG ≥7.8 mmol/l) [1]. We have to take into consideration the data indicating that even women who were screened for GDM and had a normal OGTT had higher LGA rates. We therefore hope to be able to make such a meaningful analysis once we have solid data on pregnancy outcomes in healthy women, i.e. those women who were not eligible for GDM screening in the absence of risk factors.

Finally, the authors express their concerns about medicalisation of pregnancy [1]. We agree completely that unnecessary medicalisation of pregnancy should be avoided. However, we clearly showed that the women classified as having GDM based only on the WHO 2013 criteria for fasting glucose (i.e. women with fasting glucose ≥5.1 but ≤6.9 mmol/l) had significantly higher rates of gestational hypertension and induced labour and their neonates were more likely to have an Apgar score <7 at 5 min and to be admitted to the neonatology department [2]. According to our national guidelines these women would not have been diagnosed with GDM. Labelling this group as having GDM can help these women to reduce the short- and long-term risk connected to GDM, and also to prevent obesity, excess weight gain and the long-term risk of type 2 diabetes. Even universal screening for GDM using an OGTT can be considered as medicalisation when compared with targeted screening. Nevertheless, additional collaborative research is needed to establish whether treatment of mild GDM is beneficial and cost-effective.

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