Gestational Diabetes Mellitus in Early Pregnancy: Evidence for Poor Pregnancy Outcomes Despite Treatment

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OBJECTIVE

Recent guidelines recommend testing at <24 weeks of gestation for maternal dysglycemia in “high-risk” women. Evidence to support the early identification and treatment of gestational diabetes mellitus (GDM) is, however, limited. We examined the prevalence, clinical characteristics, and pregnancy outcomes of high-risk women with GDM diagnosed at <24 weeks of gestation (early GDM) and those with pre-existing diabetes compared with GDM diagnosed at ≥24 weeks of gestation, in a large treated multiethnic cohort.

RESEARCH DESIGN AND METHODS

Outcomes from 4,873 women attending a university hospital antenatal diabetes clinic between 1991 and 2011 were examined. All were treated to standardized glycemic targets. Women were stratified as pre-existing diabetes (n = 65) or GDM diagnosed at <12 weeks of gestation (n = 68), at 12–23 weeks of gestation (n = 1,247), or at ≥24 weeks of gestation (n = 3,493).

RESULTS

Hypertensive disorders in pregnancy including pre-eclampsia, preterm delivery, cesarean section, and neonatal jaundice (all P < 0.001) were more prevalent in women with pre-existing diabetes and early GDM. Macrosomia (21.8% vs. 20.3%, P = 0.8), large for gestational age (39.6% vs. 32.8%, P = 0.4), and neonatal intensive care admission (38.5% vs. 39.7%, P = 0.9) in women in whom GDM was diagnosed at <12 weeks of gestation were comparable to rates seen in women with pre-existing diabetes.

CONCLUSIONS

Despite early testing and current best practice treatment, early GDM in high-risk women remains associated with poorer pregnancy outcomes. Outcomes for those in whom GDM was diagnosed at <12 weeks of gestation approximated those seen in pre-existing diabetes. These findings indicate the need for further studies to establish the efficacy of alternative management approaches to improve outcomes in these high-risk pregnancies.

Gestational diabetes mellitus (GDM) is associated with significant transgenerational maternal and neonatal morbidity (1–3). The prevalence of GDM is rising, in part reflecting the changing demographics of women of childbearing age, with an increasing incidence of both obesity and advanced maternal age (4–6). These observations have important implications for the current GDM testing paradigm.
The seminal Hyperglycemia and Adverse Pregnancy Outcomes study (1) unequivocally demonstrated a continuous positive relationship between maternal blood glucose levels (BGLs) and several adverse maternal and neonatal outcomes, while intervention studies (7,8) have shown that treatment of GDM after 24 weeks of gestation significantly ameliorates this risk. This evidence formed the basis for the recently revised International Association of Diabetes and Pregnancy Study Groups and World Health Organization (WHO) recommendations for the diagnosis and classification of GDM (9,10).

Screening for maternal dysglycemia prior to 24 weeks of gestation is now recommended for “high-risk” women, with the purpose being primarily to identify “overt diabetes during pregnancy” (International Association of Diabetes and Pregnancy Study Groups terminology) (9) or “diabetes mellitus in pregnancy” (WHO terminology) (10); that is, to identify women with likely undiagnosed pre-existing diabetes early in pregnancy. It is important to note that women in whom GDM is diagnosed rather than diabetes mellitus in pregnancy at this early time point may also represent a cohort of women with a similar high risk, as evidenced by early dysglycemia. Furthermore, at present, there is a paucity of evidence with regard to the efficacy of a strategy of early identification and treatment of GDM prior to 24 weeks of gestation to further support these guideline recommendations.

A compelling rationale for the identification of dysglycemia early in pregnancy arises from the effect of early maternal hyperglycemia on excessive fetal growth in women with type 1 diabetes (11,12). The existing literature on early GDM has reported similarly poor pregnancy outcomes, but interpretation is confounded by the presence of pre-existing diabetes within this cohort. Importantly, a recent Israeli observational study (13) explicitly excluded pre-existing diabetes, and still found an association between GDM and milder first trimester fasting BGLs and adverse outcomes.

To date, no studies have addressed whether this early maternal dysglycemia, at thresholds less than that of diabetes mellitus in pregnancy, is associated with adverse pregnancy outcomes in a multi-ethnic cohort and critically whether it is attenuated by early intensive intervention. Indeed, recent GDM screening and intervention guidelines (14,15) have explicitly acknowledged this as a priority area for research.

The aim of the current study was to determine the prevalence, clinical characteristics, and pregnancy outcomes among high-risk women in whom GDM was diagnosed before 24 weeks of gestation and among women with pre-existing diabetes compared with women in whom GDM was diagnosed after 24 weeks of gestation, in a large treated multiethnic cohort.

**RESEARCH DESIGN AND METHODS**

Women (N = 4,873) attending the Royal Prince Alfred Hospital Antenatal Diabetes Clinic between 1991 and 2011 were studied. GDM was defined by the Australasian Diabetes in Pregnancy Society (ADIPS) diagnostic criteria, with universal testing between 24 and 28 weeks of gestation implemented since 1991 (16,17). At our institution, women deemed to be at high risk have been advised to undergo early testing for GDM since the 1970s, generally soon after the first antenatal appointment. High-risk criteria consisted of the following: previous GDM, macrosomia, or unexplained stillbirth; family history of type 2 diabetes; and the later addition of maternal age (≥35 years) and obesity (BMI ≥30 kg/m²) in 1991. High-risk ethnicity (i.e., non-Caucasian) has also been a consideration for early testing since the 1980s (18). Thus, the prevailing clinical practice at Royal Prince Alfred Hospital of early testing determined by risk factors is aligned with the recent ADIPS recommendations for early testing (15).

To identify women with pre-existing diabetes or diabetes mellitus in pregnancy, as distinct from “true GDM,” two approaches were taken. For the primary analysis, pre-existing diabetes was defined as known type 2 diabetes diagnosed prior to the index pregnancy. For the secondary analysis, WHO diagnostic criteria for diabetes mellitus in pregnancy were retrospectively applied and were defined as follows: fasting BGL ≥7.0 mmol/L (126 mg/dL); 2-h BGL ≥11.1 mmol/L (200 mg/dL) after a 75-g oral glucose load or random BGL of ≥11.1 mmol/L (200 mg/dL) in the presence of diabetes symptoms (10). In total, six women in whom GDM was diagnosed prior to 24 weeks of gestation met the WHO criteria for diabetes mellitus in pregnancy and were excluded in the secondary analysis, as follows: five women in the <12 weeks of gestation cohort and one woman in the 12–23 weeks of gestation cohort. Women with known type 1 diabetes were excluded. Baseline maternal clinical and biochemical data taken at the time of GDM diagnosis were collected prospectively in a standardized manner (18). Ethics committee approval and informed consent were obtained.

Treatment involved the following multidisciplinary approach: lifestyle (diet and exercise) intervention and the addition of insulin therapy if BGL targets were not achieved with lifestyle modification alone. Women undertook home blood glucose monitoring four times daily aiming to achieve a capillary fasting BGL target of <5.2 mmol/L (93.6 mg/dL) and a 1-h postprandial BGL target of <7.5 mmol/L (136 mg/dL) (prior to 1998, a capillary fasting BGL target of <5.5 mmol/L [100 mg/dL] and a 2-h postprandial BGL target of <6.7 mmol/L [120 mg/dL] were used). Although there is no consensus as to treatment targets in GDM, all subjects were treated to standardized BGL targets with similar insulin intervention thresholds across all groups. Importantly, the efficacy of this management approach was recently validated in an independent audit (19) at our institution, which found a neonatal body fat percentage in the offspring of women with well-controlled GDM that was similar to that in normoglycemic women.

Data were analyzed using NCSS 2007. Continuous data were checked for normality and presented as the mean or median. Data not normally distributed were transformed for analysis. ANOVA or Kruskal-Wallis tests were used to compare means or medians. The post hoc q test with Bonferroni or Kruskal-Wallis z tests were used to adjust for multiple comparisons. Categorical data were presented as a percentage. The χ² test was used to compare groups. Data were grouped according to 1) type of diabetes and 2) the timing of GDM diagnosis at <12, 12–23 (collectively referred to as “early GDM”), or ≥24 weeks.
Nearly one-third of GDM diagnosis occurred prior to 24 weeks of gestation (27.4%) (early GDM). Compared with women in whom GDM was diagnosed at or after 24 weeks of gestation (later GDM), women with early GDM were older, had a higher prepregnancy BMI, and were more likely to have an immediate family history of diabetes and to be multiparous, essentially reflecting the selection criteria used for early testing at our institution.

Gestation at GDM diagnosis was also associated with differential treatment requirements; specifically, a greater need for early intensive insulin therapy, reflecting the more severe baseline dysglycemia seen in early GDM (Table 2). The earlier the diagnosis of GDM, the more likely that insulin therapy was required (75.0%, 59.1%, and 42.7% [P < 0.0001], respectively, for GDM at <12, 12–23, and ≥24 weeks of gestation) and at a higher median total daily dose at confinement (median 48 units [range 20–89 units], 33 units [range 16–62 units], and 20 units [range 10–38 units] [P < 0.0001], respectively, for GDM diagnosed at <12, 12–23, and ≥24 weeks of gestation) and at a higher median total daily dose at confinement (median 48 units [range 20–89 units], 33 units [range 16–62 units], and 20 units [range 10–38 units] [P < 0.0001], respectively, for GDM diagnosed at <12, 12–23, and ≥24 weeks of gestation), albeit much lower than that for women with type 2 diabetes (106 units [range 69–165 units]), following our treat-to-target approach. Despite a higher prepregnancy BMI, there was less GWG among the early GDM cohorts (median weight gain 6.4 kg [range 3.5–13.0 kg], 10.5 kg [range 7.4–14.0 kg] vs. 12.5 kg [range 9.0–16.0 kg] [P < 0.0001], respectively, for GDM diagnosed at <12, 12–23, and ≥24 weeks of gestation).

Association Between Early GDM and Adverse Maternal and Neonatal Outcomes
Despite this intensive treatment regimen, our results demonstrate a continuum of risk for adverse maternal outcomes according to the type and timing of diabetes diagnosis (Table 3). Women with type 2 diabetes had the highest rates of preterm delivery, cesarean section, and hypertensive disorders of pregnancy. The next highest incidence of adverse outcomes was seen in women with early GDM, followed by women diagnosed with later GDM.

The risk associated with early GDM was even more pronounced for neonatal outcomes (Table 4), such that outcomes for GDM diagnosed at <12 weeks of gestation were as poor as those for women with type 2 diabetes. Notably, there was no difference in the incidence of macrosomia (21.8% vs. 20.3%, P = 0.8), LGA (39.6% vs. 32.8%, P = 0.4), and neonatal intensive care admission (38.5% vs. 39.7%, P = 0.9), respectively, in women with type 2 diabetes and GDM diagnosed at <12 weeks of gestation. Alarmingly, the highest rate of stillbirth was seen in women in whom GDM was diagnosed at <12 weeks of gestation rather than (as would be expected) in women with type 2 diabetes (1,21).

Conversely, later GDM was associated with the lowest risk of adverse neonatal outcomes. Reassuringly, the incidence of SGA (5.2% and 8.5% vs. 7.3% [P = 0.2], respectively, for GDM diagnosed at <12, 12–23, and ≥24 weeks of gestation) was not increased in women with early GDM despite their greater insulin treatment regimen, suggesting that our early intensive treatment approach is not associated with excessive growth restriction. We note also that the incidence of neonatal hypoglycemia was not different between the cohorts of GDM diagnosed at <12 weeks of gestation and later GDM.

Importantly, the adverse outcomes associated with early GDM diagnosis are not due to an over-representation of diabetes mellitus in pregnancy in this cohort. Specifically, although the diagnostic OGTT values and HbA1c and AUC glucose levels were higher in women with early GDM compared with later GDM (Table 2), these glucose thresholds were still much lower than those for diabetes mellitus in pregnancy or that seen in the type 2 diabetes cohort (9). Moreover, of the early GDM cohort with available follow-up data, diabetics did not persist postpartum in the majority, further supporting the absence of pre-existing diabetes in this cohort. Secondary analysis, which specifically excluded women who fulfilled WHO diagnostic criteria for diabetes mellitus in pregnancy (n = 6), yielded similar results (i.e., P values as for primary analysis) for adverse pregnancy (Supplementary Table 1) and neonatal outcomes (Supplementary Table 2), except for neonatal jaundice and respiratory distress syndrome, which were no longer statistically different between the GDM diagnosed at <12 weeks of gestation and the later GDM cohorts.
Exploring the Independent Role of Early Versus Late GDM Diagnosis on Adverse Outcomes

To examine the independent contribution of the timing of GDM diagnosis on the significant fetal outcomes of LGA and macrosomia, we performed multivariate regression analysis and included known risk factors for both LGA and macrosomia in the models. This showed that the timing of GDM diagnosis was not an independent risk factor for adverse outcomes; rather, the risk associated with early GDM was encompassed by the known high-risk factors of prepgnancy BMI, GWG, fasting OGTT values, and cesarean section for macrosomia (Supplementary Table 3); while prepgnancy BMI, GWG, cesarean section, and hypertensive disorders of pregnancy were significant independent associates of LGA (Supplementary Table 4).

CONCLUSIONS

In this large multiethnic cohort study, we found that despite early testing and intensive intervention, early GDM diagnosis in high-risk women was still associated with adverse pregnancy outcomes, including preterm delivery, cesarean section and hypertensive disorders of pregnancy, macrosomia, LGA, neonatal intensive care admission, and stillbirth, which are more comparable to those of women with type 2 diabetes than those with GDM diagnosed after 24 weeks of gestation. Importantly, we also showed that this risk was not accounted for by women with diabetes mellitus in pregnancy captured within the early GDM cohort, which has confounded the interpretation of the evidence to date. Specifically for the important outcomes of LGA and macrosomia, this excess risk appears...
Table 3—Maternal outcomes for type 2 diabetes and GDM stratified by timing of diagnosis

<table>
<thead>
<tr>
<th>Maternal outcomes</th>
<th>T2DM (n = 65)</th>
<th>GDM &lt;12 weeks (n = 68)</th>
<th>12–23 weeks (n = 1,247)</th>
<th>≥24 weeks (n = 3,493)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestation at delivery (weeks)</td>
<td>37.4 ± 1.9*</td>
<td>37.5 ± 3.2*</td>
<td>38.3 ± 2.4*</td>
<td>38.8 ± 1.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Preterm delivery (%)</td>
<td>25.9*</td>
<td>16.7*</td>
<td>11.2*</td>
<td>6.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cesarean section (%)</td>
<td>57.9*</td>
<td>30.7</td>
<td>36.2*</td>
<td>28.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hypertensive disorders in pregnancy (%)</td>
<td>34.6*</td>
<td>26.3*</td>
<td>13.8*</td>
<td>11.2</td>
<td>&lt;0.0002</td>
</tr>
<tr>
<td>Postpartum OGTT (%)# (N = 28)</td>
<td>79*</td>
<td>71*</td>
<td>85</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>11</td>
<td>24</td>
<td>14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IGT</td>
<td>11</td>
<td>5</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2DM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data are presented here as the mean ± SD, unless otherwise indicated. Hypertensive disorders in pregnancy, either pre-eclampsia or systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg in a previously normotensive pregnant woman whose pregnancy is at ≥20 weeks of gestation and has no proteinuria or new signs of end-organ dysfunction; preterm delivery, <37 weeks of gestation. IGT, impaired glucose tolerance; T2DM, type 2 diabetes mellitus. *Different from GDM diagnosed after 24 weeks of gestation (comparator group). #Performed 3 months postpartum, IGT was defined as a fasting BGL of 6.1–6.9 mmol/L and/or a 2-h BGL of 7.8–11.0 mmol/L, and T2DM was defined as a fasting BGL of ≥7.0 mmol/L and/or a 2-h BGL of ≥11.1 mmol/L.

predominantly due to the higher rates of maternal adiposity and early dysglycemia, which characterize the early GDM cohort. This finding reflects that of the observational Hyperglycemia and Adverse Pregnancy Outcomes study (22), which identified the independent effect of both maternal adiposity and higher OGTT values in later pregnancy on LGA and macrosomia.

Our findings are also consistent with those of the single prospective cohort study in this field (23). This showed that women in whom GDM was diagnosed early (before 24 weeks of gestation) were more likely to be hypertensive, to have poorer glycemic control, and to have greater need for insulin therapy, with all cases of neonatal morbidity and mortality occurring in this cohort (23). Similar findings have been reported in retrospective cohort studies (24–27); however, all these studies were limited by the heterogeneity of their early GDM cohorts. In contrast, our data, by removing the confounder of pre-existing diabetes from the early-onset cohort, convincingly demonstrate that early GDM persists in high-risk women represents a particularly high-risk subset.

Although the true prevalence of early GDM is unknown, due to the differing diagnostic criteria used and the population screened, our rate of ~30% is consistent with those of other studies reporting early GDM prevalence in both unselected and high-risk cohorts of 29–42% (23,28–30), although, notably, rates have been as high as 62–66% in certain high-risk populations (25,31). Thus, early GDM is a frequent finding, and the application of systematic testing in early pregnancy will identify a substantial number of women and potentially affect their pregnancy outcomes.

In contrast to the improvement in outcomes seen in intervention studies after 24 weeks of gestation (7,8), we found a consistent magnitude of difference in outcomes for early GDM despite an effective within-clinic, previously validated approach (19) and a consistent standard of care. A limitation of our study was that the efficacy and compliance of glycemic intervention throughout pregnancy was not assessed, although the smaller GWG in the early GDM cohort would suggest some degree of treatment efficacy. In addition, the similarly low rates of neonatal hypoglycemia among the cohorts of women with <12 weeks of gestation and later GDM, as an index of perinatal glycemic exposure, would also suggest the efficacy of attained maternal glycemia. There is a paucity of evidence that the diagnosis and treatment of GDM before 24 weeks of gestation affects pregnancy outcomes. However, if we surmise that our glycemic management strategy was uniformly applied across the GDM cohorts, why might

Table 4—Neonatal outcomes for type 2 diabetes and GDM stratified by timing of diagnosis

<table>
<thead>
<tr>
<th>Neonatal complications</th>
<th>T2DM (n = 65)</th>
<th>GDM &lt;12 weeks (n = 68)</th>
<th>12–23 weeks (n = 1,247)</th>
<th>≥24 weeks (n = 3,493)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macrosomia</td>
<td>21.8*</td>
<td>20.3*</td>
<td>9.0</td>
<td>10.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LGA</td>
<td>39.6*</td>
<td>32.8</td>
<td>21.5</td>
<td>22.8</td>
<td>0.008</td>
</tr>
<tr>
<td>Stillbirth</td>
<td>1.8</td>
<td>3.4</td>
<td>0.8</td>
<td>0.3</td>
<td>0.2</td>
</tr>
<tr>
<td>Jaundice</td>
<td>41.7*</td>
<td>28.1*</td>
<td>24.8</td>
<td>19.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Neonatal intensive care admission</td>
<td>38.5</td>
<td>39.7</td>
<td>38.3*</td>
<td>34.0</td>
<td>0.04</td>
</tr>
<tr>
<td>Respiratory distress syndrome</td>
<td>12.3*</td>
<td>7.4*</td>
<td>3.8</td>
<td>4.0</td>
<td>0.005</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>14.9</td>
<td>20.7</td>
<td>20.2*</td>
<td>17.2</td>
<td>0.1</td>
</tr>
<tr>
<td>SGA</td>
<td>0.0</td>
<td>5.2</td>
<td>8.5</td>
<td>7.3</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Data are reported here as %. LGA/SGA were defined as sex- and gestational age–specific neonatal birth weight >90th centile (LGA) or <10th centile (SGA) for New South Wales, Australia, population (20); macrosomia was defined as ≥4,000 g; neonatal hypoglycemia was defined as a BGL<2.5 mmol/L. *Different from GDM diagnosed after 24 weeks of gestation (comparator group).
this residual risk have been incompletely attenuated?

There are several possible explanations for the poorer outcomes seen in our early GDM cohort despite intensive intervention. First, given their higher prepregnancy BMI and antenatal glycemic parameters plus corresponding greater insulin requirements and higher rates of hypertensive disorders of pregnancy, this cohort may be characterized by a more insulin-resistant phenotype compared with later GDM. Therefore, similar to those with type 2 diabetes, their dysglycemia was potentially more difficult to manage. This possibility is supported by a recent study assessing the pathophysiological characteristics of early (median diagnosis 16 weeks of gestation) versus late (≥24 weeks of gestation) GDM, which found significant differences in β-cell function and insulin sensitivity relating to the timing of GDM onset, even after accounting for maternal BMI (32). Conversely, our glycemic intervention may well have been effective throughout pregnancy (19); however, even earlier and more aggressive glycemic management may be required in this early GDM cohort, given that the mean (±SD) gestation at which insulin was commenced was 15.2 ± 8.9 weeks. Additionally, an excess of free fatty acids associated with maternal adiposity may have fueled the excess growth seen in the early GDM neonates (33), given the known impact of maternal overweight and obesity on adverse neonatal outcomes, particularly LGA (34). Despite the lower GWG seen in the early GDM cohort, it may be that even earlier intervention (i.e., at preconception) is required to ameliorate the higher prepregnancy maternal BMI in that cohort and/or that even tighter GWG targets are needed. Finally, there may be genetic aspects and socioeconomic determinants associated with the heterogeneity of the GDM phenotype that account for the disparate outcomes seen in women with early versus late GDM.

Some potential limitations require discussion. First, the early GDM cohort was a preselected high-risk group, and we lacked a control cohort to assess outcomes among women with early GDM without early intervention. Further, we acknowledge that the selection and early testing of high-risk women in our study encompasses the prevailing clinical practice at our institution and as such represents a “real-world” setting; accordingly, there will have been variable application of these testing recommendations over time, despite the strategy at our institution since the 1970s to test early for GDM in high-risk women. The relatively small number of women with pre-existing type 2 diabetes reflected the lack of systematic recording of this cohort in the database, which was primarily developed to capture GDM. Reassuringly, however, our findings for these women are consistent with the literature (35). Finally, there was significant loss to follow-up for the postpartum OGTT values throughout the GDM cohort; however, those with undiagnosed pre-existing diabetes are less likely to contribute to the findings, given that normoglycemia occurred postpartum in the majority of women, which was substantiated by the subthreshold antenatal glycemic parameters throughout the early GDM cohort.

In summary, this is the first large, multicentric data set comparing outcomes in women with treated GDM diagnosed in early pregnancy and pre-existing diabetes in comparison with those with GDM diagnosed after 24 weeks of gestation. This study demonstrates that, despite intensive intervention, early GDM in high-risk women is associated with suboptimal outcomes, and that this increased risk is associated with dysglycemia lower than the threshold for diabetes mellitus in pregnancy. Moreover, outcomes for those women in whom GDM was diagnosed at <12 weeks of gestation are the worst of the GDM cohort and approximate those of women with pre-existing diabetes. Thus, women with early GDM represent a high-risk cohort requiring systematic early identification and intensive surveillance. Given the persistence of poor outcomes in this cohort, despite early testing and current best practice treatment, prospective studies are needed to address residual risk factors and establish the efficacy of alternative glycemia and lifestyle management approaches in these high-risk pregnancies.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

Author Contributions. A.N.S. researched the data and wrote the article. G.P.R. contributed to the discussion, and reviewed and edited the article. J.H. reviewed and edited the article. L.M. researched the data, and reviewed and edited the article. M.C. researched the data. A.J.H. compiled the data. J.W. researched the data, contributed to the discussion, and reviewed and edited the manuscript. A.N.S. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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