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ORIGINAL ARTICLE

Continuous glucose monitoring system profile of women diagnosed as gestational diabetes mellitus by International Association of Diabetes and Pregnancy Study Groups criteria and labeled as normoglycemic by alternate criteria in early pregnancy

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Keywords
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ABSTRACT

Aims/Introduction: We aimed to evaluate and compare continuous glucose monitoring system (CGMS)-based glycemic parameters in women in early pregnancy (<20 weeks of gestation) who were classified as: (i) gestational diabetes mellitus (GDM) by the International Association of Diabetes and Pregnancy Study Groups (IADPSG), but normoglycemia by alternate (UK National Institute for Health and Care Excellence, Canadian Diabetes Association and Diabetes in Pregnancy Study group of India) criteria; and (ii) normoglycemia by both (IADPSG and alternate) criteria.

Material and Methods: In this cross-sectional study, eligible women underwent standard 75-g oral glucose tolerance test, followed by the placement of a CGMS. Glycemia-related parameters were calculated using the standard approach for CGMS data in pregnancy.

Results: We enrolled 96 women at 14.0 ± 3.2 weeks of gestation. Of the women diagnosed as GDM by IADPSG criteria, 34.2%, 26.3% and 44.7% were classified as normoglycemic by UK National Institute for Health and Care Excellence, Canadian Diabetes Association and Diabetes in Pregnancy Study group of India criteria, respectively. Mean 1-h postprandial glucose and time above range were significantly higher in women who were GDM by IADPSG, but normoglycemia by Canadian Diabetes Association criteria, compared with women with normoglycemia using both criteria. Similarly, mean 1-h postprandial glucose, 2-h postprandial glucose, peak postprandial glucose, 1-h postprandial glucose excursion and time above range were significantly higher in women who were not identified as GDM by the UK National Institute for Health and Care Excellence criteria. Finally, women missed by the Diabetes in Pregnancy Study group of India criteria had significantly higher mean 1-h postprandial glucose, 2-h postprandial glucose, peak postprandial glucose, postprandial glucose excursion, 24-h glucose and time above range parameters.

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Conclusions: More than one-quarter of women diagnosed as GDM by IADPSG criteria are not identified by alternate criteria. Such women are significantly different from normoglycemic women in terms of several CGMS-based glycemic parameters of clinical significance.

INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as hyperglycemia diagnosed for the first time during pregnancy, which is not overt diabetes[1,2]. The body of evidence generated over the years has paved the way for 'universal screening' for GDM at 24–28 weeks of gestation, which is now advocated by most major professional organizations in their respective guidelines[3]. However, a significant disagreement still exists on the most appropriate criteria for the diagnosis of GDM[4]. The more recently introduced International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria define GDM in terms of perinatal outcomes, in contrast to the previous criteria, which were based on the future risk of type 2 diabetes[3,5,6]. Although most professional organizations have now adopted the IADPSG criteria, there are many who still recommend other criteria. For instance, the National Health Service England recommends the National Institute for Health and Care Excellence (NICE) criteria[7], Canadian Diabetes Association (CDA) criteria are followed in Canada[8], and Diabetes in Pregnancy Study group of India (DIPSI) criteria are widely used in South Asia[9]. All these criteria tend to underdiagnose GDM, identifying only a fraction of women diagnosed with IADPSG criteria[10,11]. However, the UK NICE and DIPSI criteria also diagnose some women categorized to have normoglycemia according to the IADPSG criteria as GDM; that is, those with 2-h post-oral glucose tolerance test (OGTT) plasma glucose value of 7.8–8.4 mmol/L (140–152 mg/dL)[7,9].

There is clear evidence to suggest that hyperglycemia is associated with adverse pregnancy outcomes, with no distinct glycemic threshold above which this risk increases[6]. Given this association, it is of vital importance to avoid a missed diagnosis of GDM in a potentially treatable patient. However, it is also desirable to avoid a disease label, and unnecessary treatment for an apparently normal pregnant woman[12]. In our previous work, we presented data on the magnitude of differences in various CGMS parameters between women with normoglycemia and GDM in early pregnancy, as per IADPSG criteria[13]. We have used the same dataset to answer separate novel and relevant research questions: are glycemic parameters different among women classified as normoglycemic by one criteria, and GDM by the other, and if yes, what is the magnitude of difference? This question has significant clinical implications, considering the heterogeneity in the diagnostic criteria for GDM, not only globally[14], but also within the same country, such as India[10]. To the best of our literature review, this is the first study that evaluates and compares CGMS parameters in women diagnosed as GDM and normoglycemic during early pregnancy using multiple and commonly practiced diagnostic criteria.

MATERIALS AND METHODS

Settings, study design, participant identification and recruitment

We carried out the present cross-sectional study between July 2017 and June 2019 at the All India Institute of Medical Sciences, a public tertiary care hospital in New Delhi, India. The work started after the study protocol was approved by the institutional ethics committee, and conforms to the provisions of the Declaration of Helsinki (as revised in Fortaleza, Brazil, October 2013). Written informed consent was obtained from all study participants.

Inclusion and exclusion criteria

We included women with singleton pregnancy and <20 weeks period of gestation. Women with pre-existing diabetes, overt diabetes in pregnancy and GDM on dietary modifications for >1 week were excluded. We also excluded women with a history of major systemic disease or use of drugs known to cause hyperglycemia.

Diagnostic criteria for GDM

For the main analysis[13], we defined GDM as per the World Health Organization (WHO) 2013 criteria. These criteria extrapolate the use of IADPSG-recommended thresholds during the course of the entire pregnancy[15]. In the present analysis, we evaluated differences in CGMS-based glycemic parameters between women who were diagnosed as GDM by IADPSG (WHO 2013) criteria, but were normoglycemic by alternate diagnostic criteria (UK NICE, CDA and DIPSI criteria).

Thus, women diagnosed as GDM by IADPSG criteria, but normoglycemic by: (i) UK NICE criteria; (ii) CDA criteria; and (iii) DIPSI criteria were compared with normoglycemic women. For each comparison, 'normoglycemic women' was defined as those who had normal test results according to both criteria being compared.

Definition of GDM based on different diagnostic criteria

GDM was defined by the IADPSG criteria as the presence of any one of the following abnormal values on a 75-g OGTT carried out in a fasting state: 0 h, ≥5.1 mmol/L (92 mg/dL); 1 h,

≥10.0 mmol/L (180 mg/dL); and 2 h, ≥8.5 mmol/L (153 mg/dL)[5]. GDM was defined by UK NICE criteria as any one of the two abnormal values (≥5.6, or 7.8 mmol/L [100 or 140 mg/dL] at 0 and 2 h, respectively)[7], by CDA criteria, as any one of the three abnormal values (≥5.3, 10.6 or 9.0 mmol/L [95, 191 or 162 mg/dL] at 0, 1 and 2 h, respectively) and by DIPSI criteria if the 2-h plasma glucose value after a 75-g OGTT carried out in fasting state was ≥7.8 mmol/L (140 mg/dL)[8,9]. The diagnosis of GDM by CDA criteria is a two-step process, and involves a screening 50-g glucose challenge test, followed by a 75-g OGTT for those with an abnormal result. However, for the purpose of the present study, comparison between different diagnostic criteria was made on the basis of the 75-g OGTT alone.

Procedure on the day of testing

We invited women in a fasting state (minimum 8 h). On the day of the study visit, we filled a detailed questionnaire and carried out a 75-g OGTT using 83.3 g glucose monohydrate with measurement of venous plasma glucose at 0, 60 and 120 min. The details on OGTT, anthropometric measurements, estimation of biochemical parameters, process of CGMS insertion and instructions to participants, and definition of CGMS parameters have been provided in detail as supplementary data (Appendix S1) and Table S1, and has also been covered in our previous publications[13,16,17].

Briefly, weight and height were measured using a portable weighing scale (Seca 813; capacity, 200 kg; sensitivity, 0.1 kg; Hamburg, Germany) and a portable stadiometer (Seca 217; measurement corrected to the nearest 0.1 cm), respectively. Body mass index was calculated as weight in kilograms divided by height in meters squared. Blood pressure was measured using a digital blood pressure apparatus (Omron HEM-7124; Kyoto, Japan) after 15 min of rest. For the OGTT, 83.3 g glucose monohydrate (75 g anhydrous glucose) load was consumed over 5–10 min, and samples for plasma glucose were collected at 0, 60 and 120 min. Plasma glucose was measured using the hexokinase method in a Cobas Integra 400 plus autoanalyzer (Roche Diagnostics, Mannheim, Germany). Glycated hemoglobin was analyzed using the ion exchange high-performance liquid chromatography method with a Tosoh HLC-723 G8 HbA1c analyzer (Tosoh Corp., Tokyo, Japan). Enlite sensor with iPro2 recorder (Medtronic MiniMed, Northridge, CA, USA), a type of retrospective CGMS, was used in the present study. The sensor was installed on the abdomen on the same day after completion of the OGTT (between 1,200 and 1,500 h). We did not advise any diet modifications; however, to enable better reporting of meal-related parameters, the participants were instructed not to consume meals or snacks 2-h before and 2-h 30 min after a major meal. For monitoring and calibration of the CGMS device, participants were provided with a blood glucose monitoring device (Contour Plus, Ascensia Diabetes Care; Basel, Switzerland). The sensor was removed 4 days after the installation, and data were uploaded using the Medtronic Care Link Software.

CGMS data collection

A total of 780 values were collected over 65 h, starting from 06.30 h on the day subsequent to CGMS insertion[18]. Mean values of each meal-related parameter (pre-prandial, 1-h and 2-h postprandial glucose [PPG] values, 1-h PPG excursion, peak glucose value and time to peak value) were calculated for each valid meal. The mean glucose value and time range (in, below and above)-related parameters were reported from last 48 h of the data captured. Time in range was defined as the percentage of readings within the recommended target of 3.5–7.8 mmol/L (63–140 mg/dL), whereas time below and above (TAR) range were defined as the percentage of readings below (<3.5 mmol/L or 63 mg/dL) and above (>7.8 mmol/L or 140 mg/dL) the target range, respectively[19].

Statistical analysis

Stata15.0 (Stata Corp, College Station, TX, USA) was used for statistical analyses. Quantitative variables were assessed for normality using the Shapiro–Wilk test. For comparison between two groups, we used Student's *t*-test for variables with normal distribution and the Wilcoxon rank-sum test for variables without normal distribution. Data are presented as *n* (%), mean ± standard deviation or median (interquartile range). A *P*-value of <0.05 was considered statistically significant.

RESULTS

Baseline characteristics

We evaluated 96 women (58 with normoglycemia and 38 with GDM according to IADPSG criteria) at 14.0 ± 3.2 weeks of gestation and at a mean age of 28.5 ± 4.5 years. The mean body mass index at the time of testing and before conception were 26.4 ± 4.6 and 25.0 ± 4.4 kg/m^2, respectively. Of all participants, 33 (34.4%) were enrolled in the first trimester, 33 (34.4%) were primigravida, 19 (19.8%) were employed and 60 (62.5%) were educated up to graduation or beyond (Table 1).

CGMS data for women with GDM by IADPSG criteria, but normoglycemia by UK NICE criteria

Of 38 women diagnosed as GDM by the IADPSG criteria, 13 (34.2%) were normoglycemic by the UK NICE criteria. The mean 1-h PPG (6.9 ± 0.9 vs 6.2 ± 0.6 mmol/L, $P < 0.001$), 2-h PPG (6.2 ± 0.5 vs 5.7 ± 0.5 mmol/L, $P = 0.006$), peak PPG (7.2 ± 0.9 vs 6.5 ± 0.6 mmol/L, $P = 0.001$), 1-h PPG excursion (2.0 [1.4–2.6] vs 1.4 [0.9–1.8] mmol/L, $P = 0.009$) and TAR (2.1 [0.0–5.6] vs 0.0 [0.0–2.6]%, $P = 0.034$) were significantly higher among such women, compared with those with normoglycemia by both criteria (Table 2).

CGMS data for women with GDM by IADPSG criteria, but normoglycemia by CDA criteria

There were 10 (26.3%) women who had GDM by IADPSG criteria, but were normoglycemic using CDA criteria. The mean 1-h PPG (6.7 ± 0.7 vs 6.2 ± 0.6 mmol/L, $P = 0.018$) and TAR

Table 1 | Baseline characteristics of study participants

Variable	Total (n = 96)
Age (years)	28.5 ± 4.5
Period of gestation	14.0 ± 3.2
8–12 weeks	33 (34.4)
13–16 weeks	40 (41.7)
17–20 weeks	23 (24.0)
BMI at time of testing (kg/m^2)	26.4 ± 4.6
Pre-pregnancy BMI (kg/m^2)†	25.0 ± 4.4
Gravida	
1	33 (34.4)
2	24 (25.0)
>2	39 (40.6)
Parity	
0	63 (65.6)
≥1	33 (34.4)
Education, graduate or above	60 (62.5)
Working status, employed	19 (19.8)
Past history of GDM	
Yes	8 (10.7)
No	67 (89.3)
Family history of diabetes	32 (33.3)
Plasma glucose 0-h (mmol/L)	4.8 ± 0.6
Plasma glucose 1-h (mmol/L)	8.1 ± 2.1
Plasma glucose 2-h (mmol/L)	7.0 ± 1.5

Data are mean ± standard deviation, median (quartile 25–quartile 75) or n (%). †n = 80 BMI, body mass index; GDM, gestational diabetes mellitus.

(3.1 [0.0–5.6] vs 0.0 [0.0–1.9]%, P = 0.038) were significantly higher among such women, compared with those with normoglycemia by both criteria (Table 3).

CGMS data for women with GDM by IADPSG criteria, but normoglycemia by DIPSI criteria

A total of 17 (44.7%) women diagnosed as GDM by the IADPSG criteria were normoglycemic by the DIPSI criteria. Such women had significantly higher 1-h PPG (7.0 ± 0.9 vs 6.2 ± 0.6 mmol/L, P < 0.001), 2-h PPG (6.3 ± 0.7 vs 5.7 ± 0.5 mmol/L, P < 0.001), peak PPG (7.3 ± 1.0 vs 6.5 ± 0.6 mmol/L, P < 0.001) and 1-h PPG excursion (2.0 [1.3–2.6] vs 1.4 [0.9–1.8] mmol/L, P = 0.011), compared with women with normoglycemia by both criteria. The mean 24-h glucose (5.7 ± 0.5 vs 5.3 ± 0.4 mmol/L, P = 0.004) and TAR (4.0 [0.0–6.4] vs 0.0 [0.0–2.6]%, P = 0.008) were also significantly higher in these women (Table 4).

DISCUSSION

The present study highlights differences in CGMS parameters between South Asian women classified as GDM by IADPSG, but normoglycemic by alternate criteria, and those with normoglycemia with both criteria. A large proportion (CDA 26.3%, UK NICE 34.2% and DIPSI 44.7%) of women with GDM were not identified by diagnostic criteria other than IADPSG. Such women were significantly different from their normoglycemic counterparts in terms of several CGMS-based glycemic parameters of clinical significance.

The WHO, in 2013, adopted the IADPSG criteria for diagnosis of GDM, and subsequently the updated UK NICE criteria were introduced in 2015[7,15]. The WHO 2013 criteria were based on extrapolation of pregnancy outcomes derived from the Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study to the entire pregnancy[6], whereas the UK NICE criteria were derived based on a cost-effective analysis[7,20]. For the first time, we evaluated absolute differences in various CGMS-based

Table 2 | Comparison of continuous glucose monitoring system-based glycemic data between women with normoglycemia by both the International Association of Diabetes and Pregnancy Study Groups and UK National Institute for Health and Care Excellence criteria, and those with gestational diabetes mellitus by the International Association of Diabetes and Pregnancy Study Groups, but normoglycemia by the UK National Institute for Health and Care Excellence criteria

Variable	Women with normoglycemia by both criteria (n = 53)	Women with GDM by IADPSG criteria but not identified by UK NICE criteria (n = 13)	P-value
Fasting (mmol/L)	4.7 ± 0.5	4.8 ± 0.6	0.437
Total			
Preprandial (mmol/L)	4.7 ± 0.3	4.8 ± 0.4	0.513
1-h postprandial (mmol/L)	6.2 ± 0.6	6.9 ± 0.9	<0.001
2-h postprandial (mmol/L)	5.7 ± 0.5	6.2 ± 0.5	0.006
Peak value (mmol/L)	6.5 ± 0.6	7.2 ± 0.9	0.001
Time to peak (min)	59.6 ± 11.9	63.1 ± 11.3	0.343
1-h excursion (mmol/L)	1.4 (0.9–1.8)	2.0 (1.4–2.6)	0.009
24-h glucose (mmol/L)	5.3 ± 0.4	5.5 ± 0.4	0.059
Time in range, 3.5–7.8 mmol/L (%)	98.1 ± 2.8	94.9 ± 5.3	0.003
Time below range, <3.5 mmol/L (%)	0.3 ± 1.1 (0 [0–0])	0.7 ± 1.2 (0 [0–1.4])	0.167
Time above range, >7.8 mmol/L (%)	1.6 ± 2.6 (0 [0–2.6])	4.4 ± 5.5 (2.1 [0–5.6])	0.034

CGMS, continuous glucose monitoring system; GDM, gestational diabetes mellitus; IADPSG, International Association of Diabetes and Pregnancy Study Groups; NICE, National Institute for Health and Care Excellence.

Table 3 | Comparison of continuous glucose monitoring system-based glycemic data between women with normoglycemia by both the International Association of Diabetes and Pregnancy Study Groups and Canadian Diabetes Association criteria and those with gestational diabetes mellitus by the International Association of Diabetes and Pregnancy Study Groups, but normoglycemia by the Canadian Diabetes Association criteria

Variable	Women with normoglycemia by both criteria (n = 58)	Women with GDM by IADPSG criteria but not identified by CDA criteria (n = 10)	P-value
Fasting (mmol/L)	4.7 ± 0.4	4.7 ± 0.7	0.827
Total			
Preprandial (mmol/L)	4.7 ± 0.3	4.8 ± 0.4	0.627
1-h postprandial (mmol/L)	6.2 ± 0.6	6.7 ± 0.7	0.018
2-h postprandial (mmol/L)	5.8 ± 0.5	5.9 ± 0.5	0.595
Peak value (mmol/L)	6.6 ± 0.6	7.0 ± 0.8	0.063
Time to peak (min)	60.0 ± 12.3	58.8 ± 10.2	0.772
1-h excursion (mmol/L)	1.4 (0.9–1.9)	2.0 (1.3–2.5)	0.057
24-h glucose (mmol/L)	5.3 ± 0.4	5.4 ± 0.4	0.408
Time in range, 3.5–7.8 mmol/L (%)	98.2 ± 2.7	95.5 ± 4.0	0.010
Time below range, <3.5 mmol/L (%)	0.3 ± 1.1 (0 [0–0])	0.8 ± 1.3 (0 [0–2.6])	0.216
Time above range, >7.8 mmol/L (%)	1.5 ± 2.5 (0 [0–1.9])	3.6 ± 3.9 (3.1 [0–5.6])	0.038

Data are mean ± standard deviation, median (quartile 25–quartile 75) or n (%). CDA, Canadian Diabetes Association; CGMS, continuous glucose monitoring system; GDM, gestational diabetes mellitus; IADPSG, International Association of Diabetes and Pregnancy Study Groups.

Table 4 | Comparison of continuous glucose monitoring system-based glycemic data between women with normoglycemia by both the International Association of Diabetes and Pregnancy Study Groups and Diabetes in Pregnancy Study group of India criteria and those with gestational diabetes mellitus by International Association of Diabetes and Pregnancy Study Groups, but normoglycemia by the Diabetes in Pregnancy Study group of India criteria

Variable	Women with normoglycemia by both criteria (n = 53)	Women with GDM by IADPSG criteria but not identified by DIPSI criteria (n = 17)	P-value
Fasting (mmol/L)	4.7 ± 0.5	4.9 ± 0.6	0.248
Total			
Preprandial (mmol/L)	4.7 ± 0.3	4.9 ± 0.4	0.115
1-h postprandial (mmol/L)	6.2 ± 0.6	7.0 ± 0.9	<0.001
2-h postprandial (mmol/L)	5.7 ± 0.5	6.3 ± 0.7	<0.001
Peak value (mmol/L)	6.5 ± 0.6	7.3 ± 1.0	<0.001
Time to peak (min)	59.6 ± 11.9	63.0 ± 12.6	0.314
1-h excursion (mmol/L)	1.4 (0.9–1.8)	2.0 (1.3–2.6)	0.011
24-h glucose (mmol/L)	5.3 ± 0.4	5.7 ± 0.5	0.004
Time in range (3.5–7.8 mmol/L) (%)	98.1 ± 2.8	93.6 ± 6.9	<0.001
Time below range (<3.5 mmol/L) (%)	0.3 ± 1.1 (0 [0–0])	0.7 ± 1.2 (0 [0–1.4])	0.161
Time above range (>7.8 mmol/L) (%)	1.6 ± 2.6 (0 [0–2.6])	5.7 ± 6.7 (4.0 [0–6.4])	0.008

Data are mean ± standard deviation, median (quartile 25–quartile 75) or n (%). CGMS, continuous glucose monitoring system; DIPSI, diabetes in pregnancy study group of India; GDM, gestational diabetes mellitus; IADPSG, International Association of Diabetes and Pregnancy Study Groups.

glycemic parameters for women with normoglycemia by both criteria and those diagnosed to have GDM by one criteria, and normoglycemia by the other. We found that a large proportion (34.2%) of women diagnosed as GDM by IADPSG criteria were not identified by UK NICE criteria, and such women had significantly higher mean 1-h PPG, 2-h PPG, peak PPG, 1-h PPG excursion and TAR compared with those with normoglycemia by both criteria. Elevated PPG during pregnancy is predictive of macrosomia[21,22], as the fetal pancreas is most sensitive to the height of glucose excursions that occur in the postprandial period.

We could not compare pregnancy outcomes between different groups in the present study. However, data to support a higher frequency of adverse outcomes among women not identified as GDM by UK NICE criteria are available in the literature. Meek *et al.* reported that untreated women who tested negative for GDM by UK NICE criteria, but positive by IADPSG criteria, were at a significantly higher risk of having

polyhydramnios, cesarean delivery and large for gestational age infants. Furthermore, the risk for large for gestational age infants was highest among women with fasting plasma glucose 5.1–5.5 mmol/L[23]. Djelmis *et al.*[11] also reported an increased risk of adverse perinatal outcomes in women with elevated fasting plasma glucose (5.1–5.5 mmol/L), who were identified as normoglycemic by the UK NICE criteria. Similarly, Bashir *et al.*[24] and Todi *et al.*[25] found that the frequency of adverse pregnancy outcomes, such as hypertension, pre-term delivery and cesarean section was significantly increased in women who were diagnosed as GDM by IADPSG criteria, but labeled as normoglycemic by NICE criteria. However, the converse was not true; that is, women missed by the IADPSG criteria and diagnosed as GDM by the UK NICE criteria were not at increased risk of adverse pregnancy outcomes[24,25].

Just 10 (26.3%) women diagnosed as GDM by the IADPSG criteria were not identified using the CDA criteria. There were just two parameters (mean 1-h PPG and TAR) that were substantially different in such women from their normoglycemic counterparts. The CDA criteria uses plasma glucose measurement at three time points, as in the IADPSG criteria, but thresholds for diagnosis at each point are higher than in the IADPSG criteria. Compared with the UK NICE criteria, these criteria use an additional 1-h glucose value, and the threshold for diagnosis using fasting plasma glucose value is lower[7,8]. Thus, the CDA criteria are less likely to miss a diagnosis of GDM, and differences in glycemic parameters are less prominent among women who are not identified by these criteria compared with those who are not identified by UK NICE criteria. A study by Agarwal *et al.*[26] compared eight different diagnostic criteria for diagnosis of GDM, and found that the CDA criteria showed maximum diagnostic agreement with the IADPSG criteria.

We also compared the DIPSI criteria, which is used widely in South Asia, with the IADPSG criteria. Among all the alternative criteria compared, the DIPSI criteria missed the highest proportion (44.7%) of women who were diagnosed as GDM by the IADPSG criteria. Such women had significantly higher mean 1-h PPG, 2-h PPG, peak PPG, PPG excursion, 24-h glucose and TAR compared with the normoglycemia group. Mohan *et al.*[27] previously reported poor sensitivity (22.6%) of DIPSI compared with the IADPSG criteria in a cohort of women evaluated at a median period of gestation of 24 weeks. A recent meta-analysis also found that the DIPSI criteria tends to underdiagnose GDM in Indian women, with the reported prevalence being 7.4% by the DIPSI criteria and 19.2% by the IADPSG criteria[10]. The present study found differences in several glycemic parameters among such women who were not identified by DIPSI criteria. These findings could have significant clinical implications, given the established relationship between hyperglycemia and pregnancy outcomes[6].

There were certain strengths of the present study. To the best of our knowledge, this is the first study that provides insights on differences in various CGMS-based glycemic parameters between women diagnosed with GDM using different criteria in early pregnancy and those with normoglycemia. We evaluated a number of diagnostic criteria that are of immediate relevance to the South Asian population, including the women of this ethnicity residing in the UK, Canada and South Asian countries other than India, where these criteria are widely followed. The data lend support in favor of the widely recommended IADPSG criteria, and strengthens the view, that women missed by alternate criteria have adverse glycemic profile than normoglycemic women. The sample size was fairly large for a CGMS study. There were certain limitations to this work. We studied pregnant women in early gestation. The diagnosis of GDM in early pregnancy (<20 weeks) is not standardized and is a matter of debate[14]. Not all women diagnosed with GDM in early pregnancy have abnormal blood glucose values when tested at 24–28 weeks of gestation. For example, a study from China reported that approximately just 40% of women diagnosed with GDM in early pregnancy had abnormal glucose tolerance at 24–28 weeks of gestation[28]. However, emerging evidence suggests that a diagnosis of GDM in early pregnancy is associated with an increased risk of adverse maternal and neonatal outcomes[29], making this an important area of research. Furthermore, recent studies reported that in pregnancies affected by GDM, fetal growth acceleration and fat mass accretion are already detectable at 20 weeks of gestation[30–34], suggesting that screening should begin before the conventional timeframe of 24–28 weeks. We did not evaluate pregnancy outcomes in study participants. The CGMS data were reported for a shorter duration than what is recommended; that is, 10–14 days[19]. The short shelf life (6 days) of the CGMS sensor used in the present study implied that at least three visits for sensor insertion would have been required in a single participant. Clearly, this was technically demanding, cost-prohibitive and could have adversely affected the study recruitment. The need for frequent CGMS calibration using a glucose meter was another barrier, especially in normoglycemic women. Finally, the parameter for TIR has not been validated in GDM. The target range has been extrapolated from evidence generated among pregnant women with type 1 diabetes, and many experts believe that the target for GDM should be more stringent[19]. However, this has more therapeutic implications, and does not have a bearing on the principal findings of the present study.

The present study evaluated differences in glycemic patterns between women diagnosed with GDM using different criteria in early pregnancy and those with normoglycemia. More than one-quarter of women diagnosed to have GDM by the IADPSG criteria are not identified by the UK NICE, CDA and DIPSI criteria. Such women are significantly different from normoglycemic women in terms of several CGMS-based glycemic parameters of clinical significance.

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DISCLOSURE

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Informed consent: Written informed consent was obtained from all participating women.
Registry and the registration no. of study/trial: N/A.
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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Appendix S1 | Supplementary data.