

Continuous Glucose Monitoring System Profile of Women with Gestational Diabetes Mellitus Missed Using Isolated Fasting Plasma Glucose-Based Strategies Alternative to WHO 2013 Criteria: A Cross-Sectional Study

Authors

Yashdeep Gupta D.M.¹, Charandeep Singh D.M.¹, Alpesh Goyal D.M.¹, Mani Kalaivani PhD², Juhi Bharti M.D.³, Seema Singhal M.D.³, Garima Kachhawa M.D.³, Vidushi Kulshrestha M.D.³, Rajesh Kumari M.D.³, Reeta Mahey M.D.³, Jai B Sharma M.D.³, Neena Malhotra M.D.³, Neerja Bhatla M.D.³, Rajesh Khadgawat D.M.¹, Nikhil Tandon PhD¹

¹Department of Endocrinology & Metabolism, All India Institute of Medical Sciences, New Delhi, India

²Department of Biostatistics, All India Institute of Medical Sciences, New Delhi, India

³Department of Obstetrics and Gynaecology, All India Institute of Medical Sciences, New Delhi, India

Corresponding author

Yashdeep Gupta,

Email: yashdeep@aiims.edu

Supplementary Material

Appendix S1

Anthropometry and biochemical measurements

Weight and height were recorded in a fasting state using standard methods. Weight was measured with a portable weighing scale (Seca 813) with a capacity of 200 kg and sensitivity of 0.1 kg. Height was measured with a portable stadiometer (Seca 217) with the measurement corrected to the nearest 1 mm. BMI was calculated from measurements of height and weight as per formula ($\text{BMI} = \text{weight in kg} / \text{height in meters}^2$). Blood pressure (BP) was measured using a digital BP apparatus [Omron HEM-7124] after 15 minutes of rest.

A 75 g OGTT with measurement of plasma glucose at 0, 60 and 120 min was performed using 83.3 g glucose monohydrate* (equivalent to 75 g anhydrous glucose) dissolved in 300 ml water and consumed over 5–10 min. The time from the first sip of the glucose solution was counted for 60 and 120 min sampling. For plasma glucose, samples were collected in a fluoride vial, centrifuged immediately, separated and transported to the laboratory within 1 h of collection in cool boxes. Glucose was analyzed using the hexokinase method with the Cobas Integra 400 plus auto-analyzer (Roche Diagnostics, Mannheim, Germany). Blood for HbA1c was collected in ethylenediaminetetraacetic acid (EDTA) vials and measured by ion-exchange high performance liquid chromatography (HPLC) method (Tosoh HLC-723 G8 HbA1c analyzer, Tosoh Corp., Tokyo, Japan).

*The molecular weight of glucose and glucose monohydrate is 180 and 198, respectively. The formula we used for inter-conversion was: multiplication of glucose monohydrate amount by 0.9 to obtain the desired amount of anhydrous glucose. Since we aimed to use 75 g anhydrous glucose, the approximate amount of glucose monohydrate needed was 83.3 g ($83.3 \times 0.9 = 75$).

Procedure of CGMS insertion and instructions to the study participants

Enlite sensor with iPro2 recorder (Medtronic MiniMed Northridge, CA 91325, USA) which records interstitial fluid glucose every 5 min was installed on the lateral half of mid abdomen between 1200 and 1500 hours (after completion of OGTT). The insertion was done on the side opposite to the one which woman preferred to turn while sleeping. Women were provided with a blood glucose meter (Contour Plus, Bayer HealthCare LLC) for monitoring blood glucose four times a day (pre-meals and after dinner) to facilitate CGMS calibration. For initial calibration, additional monitoring was done at 1-h and 3-h after the installation. Study participants were instructed to note exact timings of meals and snacks intake and

blood glucose check. This was periodically reinforced by the research staff during the period of data acquisition. In case of any query, contact number of the staff and one of the study investigators was provided. No diet modification was advised, however, for proper reporting of meal-related parameters, women were instructed not to consume meals or snacks 2-h before and 2-h 30 min after a major meal. CGMS was removed four days after the installation (five days if patient was not able to come after four days, or it was a holiday) and data were uploaded using Medtronic Care Link Software. After removal of CGMS, standard dietary advice was provided based on OGTT diagnosis of normoglycemia or GDM.

Definition of CGMS-based parameters

CGMS-based parameters were reported as per suggestions by Hernandez et al [1]. The indices and their definitions have been elaborated in table S1. The criteria for deciding valid meals have been reported ahead. For all valid meals, we calculated mean values of each meal-related parameter (preprandial, 1-h and 2-h postprandial glucose values, 1-h postprandial glucose excursion, and peak glucose value).

Criteria for valid meals

The timings of meal entry were completely dependent on the study participants. The data were captured for their usual diet habits without influencing the choice of food, or its quantity. We observed that after each meal, the glucose values started to rise within 5 minutes of beginning the meal. Therefore, we calculated meal-related parameters, assuming the point of inflection (rise of glucose value) as the meal point. We included meal-related segments in which rise in glucose was within 20 minutes of documentation of meal timing, dropping the other highly unreliable meal segments

Meal segments with absolute relative difference (between the pre-meal glucose value of CGMS and glucometer) of $\geq 20\%$ were also considered invalid. In addition, we excluded the segments where the women did not consume a major meal, or there was an apparent effect of the food consumed prior to a major meal (documented or undocumented, but apparent). The details on the number of invalid meal segments (189/864, 21.9%) and reasons for the same have already been reported in our previous work [2].

Table S1: Criteria for analysis of CGMS data

CGMS variables	Criteria
Fasting glucose	Mean of six consecutive values starting at 0600 h and/or after at least 7 h fasting
Preprandial glucose	Mean of three consecutive values directly before breakfast, lunch, and dinner meal start time during BG stability
1 h-postprandial glucose	Mean of three consecutive measures 1 h after the meal start time
2 h- postprandial glucose	Mean of three consecutive measures 2 h after the meal start time
1-h postprandial glucose excursion	(1-h PP BG) – (preprandial BG) (calculated)
24-h mean glucose	Mean of all measures in 24 h: 2330–2330 h
Peak postprandial glucose	Highest PP glucose within 2 h of meal start time

CGMS: Continuous glucose monitoring system

References

1. Hernandez TL, Barbour LA. A standard approach to continuous glucose monitor data in pregnancy for the study of fetal growth and infant outcomes. *Diabetes Technol Ther* 2013; 15:172–9.
2. Singh C, Gupta Y, Goyal A, et al. Glycemic profile of women with normoglycemia and gestational diabetes mellitus during early pregnancy using continuous glucose monitoring system. *Diabetes Res Clin Pract* 2020;169:108409.