

## Persistent dysglycemia and associated risk factors at 6-12-week post-partum in mothers with gestational diabetes mellitus

\*Aktar Y<sup>1</sup>, Jahan S<sup>2</sup>, Shrestha S<sup>3</sup>, Sultana N<sup>4</sup>, Hasan M<sup>5</sup>, Panthi S<sup>6</sup>, Hasanat MA<sup>7</sup>

<sup>1</sup>Yasmin Aktar, Assistant Professor, Department of Endocrinology, Bangladesh Medical College Hospital (BMCH), Dhaka, Bangladesh;

<sup>2</sup>Sharmin Jahan, Associate Professor, Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh; <sup>3</sup>Sradha Shrestha, Ex-Resident, Department of Endocrinology, BSMMU, Dhaka, Bangladesh; <sup>4</sup>Nusrat Sultana, Assistant

Professor, Department of Endocrinology, BSMMU, Dhaka, Bangladesh; <sup>5</sup>Mashfiqul Hasan, PhD student, Department of Endocrinology, BSMMU, Dhaka, Bangladesh; <sup>6</sup>Sandesh Panthi, Ex-Resident, Department of Endocrinology, BSMMU, Dhaka, Bangladesh;

<sup>7</sup>Muhammad Abul Hasanat, Professor, Department of Endocrinology, BSMMU, Dhaka, Bangladesh

### Abstract

**Background:** Despite the fact that gestational diabetes mellitus (GDM) typically goes away after delivery, women who have already been diagnosed with the condition are at a higher risk of having long-term metabolic disorders like type-2 diabetes. Upon delivery, women with a history of GDM should be observed for glycemic status.

**Objective:** The objective of this study was to observe the persistence of glucose intolerance and associated risk factors of GDM mothers at 6-12 weeks post-partum.

**Methods:** This cross-sectional study included 222 mothers from December 2011 to December 2018 who had a history of GDM based on 2013 World Health Organization criteria. Mothers who fulfilled the criteria for diabetes in pregnancy (DIP) were excluded from the analysis. They were recruited consecutively at 6-12 weeks post-partum from 'GDM Clinic' as applicable with the elapse of time. GDM mothers were assessed by 75-gm oral glucose tolerance test (OGTT) for the persistence of glucose intolerance. The risk factors associated with the persistence of glucose intolerance were also recorded.

**Results:** Out of 222 GDM, 150 (67.6%) had normal glucose tolerance (NGT) while 72 (32.4%) had abnormal glucose tolerance (AGT) [impaired fasting glucose IFG: 16 (7.2%), IFG-IGT: 20 (9%), impaired glucose tolerance IGT: 24 (10.8%) and diabetes mellitus (DM): 12 (5.4%)] following American Diabetes Association (ADA) criteria. The age of the mother was significantly different from AGT to normal glucose tolerance.

**Conclusion:** A good number of GDM mothers express AGT at 6-12 weeks post-partum, which suggests it is necessary to follow GDM mothers after child birth. [*J Assoc Clin Endocrinol Diabetol Bangladesh, January 2023; 2 (1): 02-07*]

**Keywords:** Gestational diabetes mellitus; Abnormal glucose tolerance; Post-partum persistence

\***Correspondence:** Dr. Yasmin Aktar, Assistant Professor, Department of Endocrinology, Bangladesh Medical College Hospital, Dhanmondi, Dhaka-1207, Bangladesh; Phone- 880-(0)1614121143, e-mail: yasminaktar18@gmail.com

### Introduction

Mothers with gestational diabetes mellitus (GDM) are at risk of developing type 2 diabetes mellitus (T2DM) or prediabetes during post-partum follow-up.<sup>1</sup> An oral glucose tolerance test (OGTT) should be performed to disclose this dysglycemia.<sup>2</sup> About two-thirds of GDM usually resolves after delivery, but one-third of affected women will have diabetes or impaired carbohydrate metabolism at post-partum screening.<sup>3</sup> It has been estimated that eventually, 15-50% of GDM mothers will develop T2DM in later life.<sup>4,5</sup> The conversion of GDM to T2DM ranges from 6% to 92%, depending on diagnostic criteria, race/ethnicity, and particularly, the duration of surveillance (from 6 months to 28 years).<sup>1</sup>

The risk of glucose intolerance after delivery of a GDM mother may persist for 15 years in the study by Linne et al., 20 years in the study by Gunderson et al., and up to 28 years in the most extended follow-up to date, with the historical O'Sullivan, study.<sup>6-8</sup> Following delivery, the persistence of glucose intolerance is related to several well-known risk factors like race, age, parity, family history of diabetes, pre-pregnancy weight, post-partum obesity, and weight gain. Some other risk factors like medication used during pregnancy, previous GDM, and blood glucose level in diagnostic OGTT of GDM are described in several studies.<sup>9,10</sup> It has been observed in an Australian retrospective cohort study that a nine-fold increase in T2DM after 15 years of delivery among the

GDM mother who had a family history of diabetes, high glucose value at diagnosis, and insulin use during pregnancy.<sup>11</sup> The prediabetes group should be identified earlier to reduce the future risk of diabetes. This population group also has a higher risk of cardiovascular disease.<sup>12</sup> From this point of view; several studies have shown a 2-5-fold increase in the incidence of metabolic syndrome after GDM.<sup>13</sup> A Danish cohort study conducted by Lauenborg et al. observed the incidence of metabolic syndrome ten years after GDM; it was 36% compared to 13% in the control group.<sup>14</sup> A systemic review analysis by Kims et al. showed a higher rate (30-84%) of recurrence in the subsequent pregnancy depending on the country.<sup>15</sup> Several factors, including ethnicity, maternal age, parity, body mass index (BMI), OGTT report & need for insulin treatment, were important factors related to recurrence.<sup>1</sup> Several hospital-based studies in Bangladesh observed an alarming frequency of GDM.<sup>16,17</sup> In a study on the persistence of dysglycemia at post-partum, nearly 50% of mothers with hyperglycemia in pregnancy had some form of glucose intolerance. However, the study encompassed both GDM and diabetes in pregnancy (DIP).<sup>18</sup> Therefore, the rate of persistence of glucose intolerance of GDM in Bangladeshi mothers is not yet clear. In this background, the study was conducted to observe the persistence of glucose intolerance and related risk factors in mothers with a history of GDM.

## Methods

### Study participants:

It was a cross-sectional observational study carried out from December 2011 to December 2018 by the GDM study group of the Department of Endocrinology of a tertiary care hospital. GDM mothers recruited consecutively from 'GDM Clinic' were diagnosed based on World Health Organization (WHO) criteria either in 1999 or 2013 as applicable with the elapse of time. Mothers who fulfilled the criteria for DIP throughout the whole series, including those recruited based on WHO 1999 criteria, were excluded from the analysis (Figure-1). Informed written consent was duly taken from each of the participants.

### Study design:

The patient series of this study was encompassed as and when a study on GDM was carried out by our GDM study group and over the participants willing for follow-up and management. BMI was calculated over the weight taken at the time of visit during post-partum. At 6-12 weeks post-partum, GDM mothers were assessed by 75-g-OGTT for the persistence of glucose

intolerance. These women had been on an unrestricted carbohydrate diet for three days and came to the GDM clinic after an overnight fast (at least 8 hours but not more than 14 hours) for 75-g-OGTT. The samples were assayed on the same day for glucose. Before the commencement of this study, the research protocol was approved by the Institutional Review Board (IRB).

### Analytic method:

RA-50 analyzer (Dade Behring, Germany) was used to assay plasma glucose. A fixed, known concentration for low level (5.21 mmol/l) as well as high level (16.1 mmol/l) was used in every assay run to assess inter-assay Co-efficient of variation (CV) of glucose which were 5.78% and 5.59%, respectively.

### Statistical analysis:

Data were analyzed by the SPSS program (version 22.0) and expressed as mean ( $\pm$ SD) or frequency (percentage) as applicable. Comparison of qualitative data between groups was done by chi-squared test. Multivariate binary logistic regression was used to assess the potential risk factors' ability to predict the persistence of abnormal glucose tolerance (AGT). P-values  $\leq 0.05$  were considered statistically significant.

## Results

The study recruited 222 mothers who agreed to check their glycemic status by OGTT at 6-12-week post-partum (age:  $29.0 \pm 4.8$  years, BMI:  $26.5 \pm 3.8$  kg/m<sup>2</sup>, mean $\pm$ SD; Table-I).

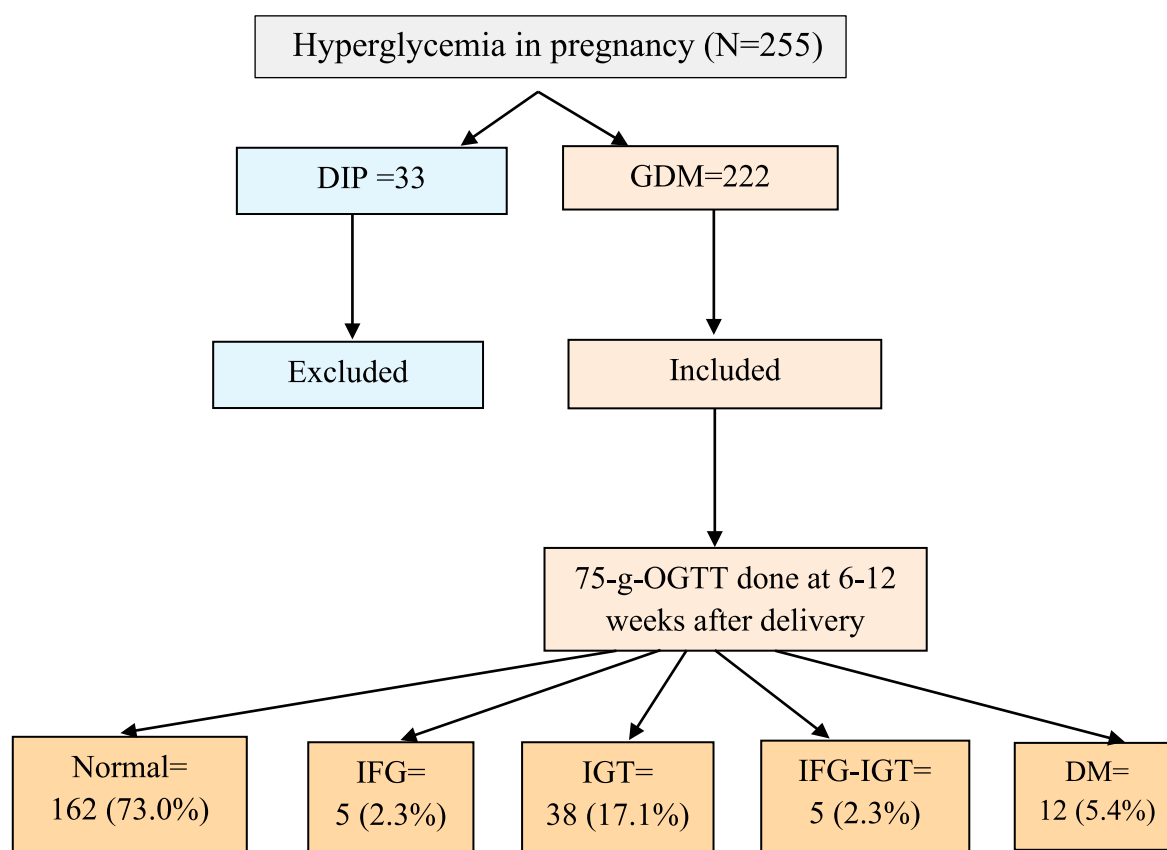
**Table-I:** Demographic characters of the studied mothers

Variables	All subjects
N	222
Age in years (mean $\pm$ SD)	29.0 $\pm$ 4.8
BMI in kg/m <sup>2</sup> (mean $\pm$ SD)	26.5 $\pm$ 3.8
Family history of T2DM (%)	147 (66.2)
Occupation (%)	
Housewife	142 (64.0)
Service	33 (14.9)
Medical professional	27 (12.2)
Student	20 (9.0)
Parity (%)	
Nulliparous	21 (9.5)
Multiparous	201 (90.5)
Use of insulin during pregnancy (%)	34 (15.3)

(Within parenthesis are percentages over column total)

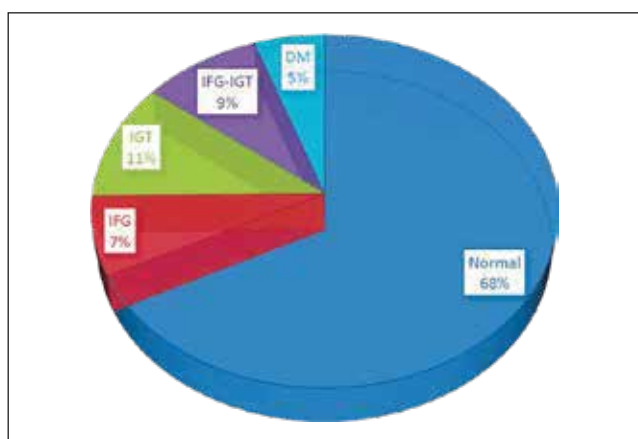
T2DM: type 2 diabetes mellitus BMI: body mass index

As shown in Figure-2, 73.0% of participants were found to be normal glucose tolerance (NGT) while 2.3%



**Figure-1:** Post-partum glycemic status of the studied mothers under WHO criteria

WHO: World Health Organization  
 IFG: Impaired fasting glucose  
 IGT: Impaired glucose tolerance  
 DM: Diabetes Mellitus



**Figure-2:** Glycemic status at 6-12 weeks of post-partum among the subjects (n=222) according to ADA criteria  
 ADA: American Diabetes Association

5.4% diabetes mellitus (DM) by WHO criteria. Their frequencies, according to ADA standards, were NGT 67.6%, IFG 7.2%, IGT 10.8%, IFG-IGT 9.0%, and DM 5.4%. Glucose abnormality was more in advanced age groups ( $p<0.001$ ) with relatively higher frequencies in the age group  $>35$  years showing 68.8% AGT (Table-II).

**Table-II:** Glycemic status (according to ADA) at post-partum among the age groups having GDM (n=222)

Age group (year)	Normal	AGT	Total
< 25 year	33 (86.8)	5 (13.2)	38
25-35 year	112 (66.7)	56 (33.3)	168
>35 year	5 (31.5)	11 (68.8)	16
<b>Total</b>	<b>150</b>	<b>72</b>	<b>222</b>

(Within parenthesis are percentages over row total)

$P<0.001$ ,  $\chi^2=16.135$

ADA = American Diabetes Association

GDM = Gestational diabetes mellitus

AGT = Abnormal glucose tolerance

showed impaired fasting glycemia (IFG), 17.1% impaired glucose tolerance (IGT), 2.3% IFG-IGT, and

Multiple regression analysis to see the persistence of glucose intolerance at 6-12-week post-partum of the

GDM mothers revealed only the age of the mother to be an independent predictor of persistence (Table-III). With every 1-year increase in age, the risk of persistence increased by 12% (OR 1.12; 95% CI: 1.04-1.21,  $p=0.004$ ).

**Table-III:** Multivariate binary logistic regression for the persistence of abnormal glucose intolerance (AGT) at 6-12 weeks post-partum in mothers with GDM

Independent variables	OR	95% CI	P
Age (per year increase)	1.12	1.04-1.21	0.004
BMI (per kg/m <sup>2</sup> increase)	1.05	0.97-1.15	0.224
Gestational age at GDM detection (per week increase)	0.99	0.95-1.04	0.674
Parity (per unit increase)	1.12	0.87-1.44	0.370
Family History of DM	0.97	0.49-1.92	0.920
Use of insulin	1.35	0.60-3.06	0.473
FPG during pregnancy (per mmol/L increase)	1.62	0.94-2.78	0.082
Post OGTT 2hr glucose in pregnancy (per mmol/L increase)	1.18	0.88-1.59	0.268

GDM= Gestational diabetes mellitus

BMI= Body mass index

DM= Diabetes mellitus

FPG= Fasting plasma glucose

OGTT= Oral glucose tolerance test

## Discussion

The current study revealed that around one in four mothers with GDM had some degree of glucose intolerance at 6-12 week post-partum. The commonest category of AGT was IGT (17.1%) followed by DM (5.4%), IFG (2.3%), and IFG-IGT (2.3%). Among those who had AGT, most were in the prediabetic range i.e., IFG, IGT, or both IFG and IGT. Although the frequency of persistence at post-partum is observed to be less than 10% in different studies, it may differ according to the study design & criteria used.<sup>19</sup> However, in a previous study conducted in the same institute by Sharmin-Jahan et al., the frequency of persistent glucose intolerance was significantly higher (43%). This disparity could be explained by the fact that the previous study did not exclude mothers with DIP. Furthermore, maternal age and BMI were higher in the previous study.<sup>18</sup> Maternal age was significantly higher in this study among those who demonstrated post-partum persistence, which was also illustrated in another study.<sup>20</sup> BMI and family history of diabetes also did not show any significant difference in our study. A similar observation was also noticed in other studies.<sup>7,20</sup> It is noteworthy that our

previous study revealed a significant difference in the rate of persistence of glucose intolerance which might have been attributable to some extent to higher maternal age, BMI, and increased family history of diabetes in those studied subjects.<sup>21</sup> In the majority of GDM mothers, hyperglycemia is managed with lifestyle changes; with only 15% to 30% requiring insulin.<sup>2</sup> In our study 15.3% of mothers required insulin but in multiple regression analysis, the use of insulin did not independently predict the persistence of AGT. The use of insulin did not show a higher rate of glucose intolerance persistence than those managed with lifestyle intervention only also evident in another study conducted on Ethiopian women.<sup>22</sup> But most of the studies observed that the use of insulin during the antenatal period is a predictor of post-partum persistence of glucose intolerance.<sup>21,23,24</sup> Multivariate binary logistic regression for the persistence of glucose intolerance in context to the probable risk factor showed none of the factors like BMI, parity, gestational age at detection of GDM, use of insulin, FPG, or 2-hr glucose during detection of GDM at pregnancy showed any independent predictability over the persistence of glucose intolerance at post-partum. But, a study observed the risk of developing diabetes was 3.5 times higher for mothers with GDM than for general population even after adjustment for confounding factors like age, family history of diabetes, education level, and smoking history.<sup>25</sup> Following the first diagnosis of GDM, the probability of acquiring diabetes was 6.9% at five years and 21.1% at 10 years.<sup>26</sup> The cumulative risk of developing T2DM in GDM was 25.8% after 15 years of the index pregnancy.<sup>27</sup> In our country, this type of follow-up study has not yet been done to detect the persistence of glucose intolerance among mothers with GDM. Still, a long-term follow-up study is needed to find out the rate of development of DM in our GDM mothers. A study from Edmonton, Alberta found that only 50% of women adhered to post-partum testing recommendations.<sup>9</sup> While conducting this study on our post-pregnant population, we confronted multiple obstacles, most notably poor adherence to post-partum testing. A convenient window period of 6-12 weeks post-delivery was offered for the benefit of the mothers, yet many failed to respond. Probable factors leading to non-adherence to testing were lack of awareness, superstition, and difficulty in time management with a small baby.

## Conclusion

A significant number of GDM mothers exhibit AGT between 6 and 12 weeks after delivery. It is prudent to follow-up GDM mothers for an extended period of time because the NGT may convert to AGT in the future.

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## Conflict Of Interest

There is nothing to disclose by authors for conflict of interest.

## Financial Disclosure

The author(s) received no specific funding for this work.

## Data Availability

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.

## Ethics Approval and Consent to Participate

Ethical approval for the study was obtained from the Institutional Review Board, BSMMU. The written informed consent was obtained from all study participants. All methods were performed in accordance with the relevant guidelines and regulations.

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