*Original Article*

ISSN (Online): 2959-8176
ISSN (Print): 2958-0307

**Journal of Association of Clinical Endocrinologist and Diabetologist of Bangladesh**
*July 2023, Vol. 2, No. 2, pp. 39-45*

# Screening before 24 weeks of gestation may be wise for early detection of abnormal glucose tolerance during pregnancy

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**Abstract**

**Background:** Screening for abnormal glucose tolerance (AGT) before 24 weeks of gestation (WG) is underestimated though its effects on pregnancy outcomes are not negligible.

**Objectives:** To see the frequency of AGT before 24WG and its correlation with maternal risk factors.

**Methods:** In this cross-sectional study, 451 pregnant women (gestational weeks 6-23) were enrolled from July 2013 to June 2017. Study participants underwent 75g OGTT (2 samples, n=451, 3 samples, n=249) to categorize them into normal glucose tolerance (NGT) or AGT following World Health Organization (WHO) criteria both 2013 and non-pregnant criteria. Glucose was measured by the glucose oxidase method.

**Results:** Overt diabetes and prediabetes were 24 (5.3%) and 132 (29.3%) respectively when WHO non-pregnant adult criteria were applied (n=451). Whereas, 11 (4.4%) and 68 (27.3%) were diabetes in pregnancy (DIP) and gestational diabetes mellitus (GDM) respectively according to WHO 2013 criteria (n=249). Age (27.60±4.82 vs. 25.43±4.64, years, p<0.001), BMI (25.90±4.41 vs. 23.56±3.85 kg/m2, p<0.001), systolic blood pressure (105.61±12.18 vs. 100.76±11.90 mm-Hg, p<0.001), diastolic blood pressure (68.75±8.95 vs. 64.85±8.47 mm-Hg, p <0.001) and family history of diabetes (53.8% vs. 35.0 %, p<0.001) were significantly higher in AGT than NGT (n=451). 02h plasma glucose value on OGTT had a positive correlation with age (r=0.268, p<0.001), BMI (r=0.277, p<0.001), and FPG (r=0.551, p<0.001). BMI (B=0.021, p<0.001, CI 95%: 0.010-0.032) was an independent predictor for AGT.

**Conclusions:** High prevalence of AGT was observed before 24WG, and needs careful attention to avoid complications. *[J Assoc Clin Endocrinol Diabetol Bangladesh, July 2023; 2 (2):39-45]*

**Keywords:** Early pregnancy hyperglycemia, gestational diabetes mellitus, diabetes in pregnancy, Bangladesh

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## Introduction

Hyperglycemia in pregnancy (HIP) is a very common medical condition, affecting about one in six pregnancies globally, and about one in four pregnancies in Southeast Asia.[1] According to the World Health Organization (WHO) and the International Federation of Gynecology and Obstetrics, HIP can be categorized as either pre-gestational diabetes, gestational diabetes mellitus (GDM), or diabetes in pregnancy (DIP).[2,3] Pre-gestational diabetes includes women with known diabetes before conception, it may be type 1, type 2 (T2DM), or other forms of diabetes. GDM occurs during or after the second trimester due to hormonal changes in pregnancy which is not expected to persist postpartum. DIP applies to hyperglycemia first diagnosed during pregnancy mainly in the first trimester and meets WHO criteria of diabetes in the non-pregnant state. GDM contributes about 75%-90% of cases of HIP.[4] GDM is associated with not only short-term adverse perinatal outcomes, e.g. large for gestational age (LGA), neonatal hypoglycemia, increased rate of neonatal intensive care unit admission, induction of labor, and cesarean section but also long-term complications by increasing the risk of developing obesity, T2DM, and cardio-metabolic disease at an early age for both mother and offspring.[5-7] DIP represents a serious form of hyperglycemia which is associated with worse maternal and fetal outcomes and warrants more aggressive management.[8,9]

Screening for GDM between 24 and 28 weeks of gestation (WG) is important to reduce the risk for adverse pregnancy outcomes but there is conflicting evidence regarding screening for GDM in early pregnancy.[10,11] The American Diabetes Association (ADA) recommends screening for overt diabetes at the first prenatal visit based on risk factors but no specific guidelines on early screening of GDM and its diagnostic cut-off.[12] Most of the cases of T2DM are often asymptomatic and women with severe hyperglycemia in early pregnancy are at high risk for adverse pregnancy outcomes. So diagnosis and treatment of diabetes during pregnancy are required as early as possible. Therefore, screening for overt diabetes with the same criteria used for non-pregnant adults is recommended by WHO. But the presence of intermediate hyperglycemia which is considered GDM during 24 to 28 WG poses a diagnostic and therapeutic challenge to clinicians when present before 24WG. The International Association for Diabetes in Pregnancy Study Group (IADPSG) recommended using an FPG range of 5.1-6.9 mmol/L before 24 WG to define early GDM (eGDM) and should be referred for immediate care though the evidence to this recommendation is very poor regarding prognosis.[13,14] The IADPSG criteria for the diagnosis of GDM is adopted by the 2013 WHO criteria for GDM.

Pregnancy should be planned in a society where the prevalence of T2DM is high. But in a country like Bangladesh where most of the pregnancies are unplanned, waiting for 24 WG to diagnose HIP would delay the initiation of standard care which potentially lead to serious maternal and fetal complications. Furthermore, the prevalence of fetal malformations was recently reported to be higher in women with DIP compared to women with GDM.[15]

There is some conflicting evidence regarding the diagnostic cutoff for the diagnosis of eGDM. In one study, of women who had eGDM based on the IADPSG/WHO criteria, 39.1% received the diagnosis of late GDM at the second OGTT.[16] Another study reported that in women diagnosed with early-onset GDM, 47% had normal 75 g OGTT values at 24-28 WG.[17] FPG decreased with increasing gestational age, a recent study reported that only 30.3% of women who had an FPG of ≥5.1 mmol/L at early pregnancy still had an FPG of ≥ 5.1 mmol/L at 24–28 weeks whereas it was 66.2% for those having FPG between 6.1-6.9 mmol/L at early pregnancy.[18] This study was designed to see the frequency of abnormal glucose tolerance (AGT) based on WHO criteria for non-pregnant adults and pregnancy-specific 2013 criteria in early pregnancy up to 23 WG and its relationship with maternal risk factors.

## Methods

### Study design and study participants

This cross-sectional observational study included 451 pregnant women aged ≥18 years. Pregnant women with 6 to 23 WG were recruited by consecutive sampling from the antenatal clinic, Department of Gynecology & Obstetrics, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, after approval by the Institutional Review Board (IRB). OGTT was done at the GDM clinic, Department of Endocrinology, BSMMU. Any women with prior history of GDM or DM, or currently getting steroids for any illness were excluded from the study. Two-sample 75-gm OGTT was done in the first 202 participants, whereas the rest (249) underwent 3-sample 75-gm OGTT.

All study participants were categorized as either prediabetes or diabetes or normal glucose tolerance (NGT) according to WHO criteria for non-pregnant adults, where prediabetes included either impaired fasting glucose (IFG) or impaired glucose tolerance (IGT), or a combination of both.[19] On the other hand, 249 participants were also categorized as either DIP, GDM, or NGT based on the availability of 3-samples OGTT according to WHO 2013 criteria for GDM.[2] Demographic and clinical variables including height, weight, body mass index (BMI, kg/m$^2$), and blood pressure (mm-Hg) were recorded in a structured data collection sheet for analysis.

### Analytic method

Plasma glucose was assayed by the glucose oxidase method on the same day in an automated analyzer [RA-50 analyzer (Dade Behring, Germany)].

### Statistical analysis

All data were processed in IBM SPSS Statistics for Windows version 22.0 (IBM Corp, Armonk, NY, USA) and expressed as frequencies or percentages as well as mean (± SD) as applicable. The frequency of AGT and its predictors were assessed by using different test methods (chi-square test, independent samples t-test, Pearson's correlation, and multivariate logistic regression) as applicable. P values < 0.05 were considered statistically significant.

## Results

Our study population was mainly from the housewife occupational category (68.5%) and 57.4% were gestational age 14 to 23 weeks, mean age of 26.2 ± 4.8

years, and BMI of 24.4±4.2 kg/m$^2$ as shown in Table-I. In this study, we observed overt diabetes and prediabetes were 5.3% and 29.3% respectively based on the WHO non-pregnant adult criteria whereas DIP and GDM were 4.4% and 27.3% respectively based on the WHO 2013 criteria for pregnancy (Figure-1). We also observed that among NGT groups by non-pregnant adult criteria, 56 (12.41%) participants had asymptomatic fasting hypoglycemia. Comparing the demographic and clinical variable of the study participants based on glycemic status, we observed the age (27.60±4.82 vs. 25.43±4.64, years, p<0.001), BMI (25.90±4.41 vs. 23.56±3.85, kg/m$^2$, p<0.001), systolic blood pressure (105.61±12.18 vs. 100.76±11.90, mm-Hg, p<0.001), diastolic blood pressure (68.75±8.95 vs. 64.85±8.47 mm-Hg, p <0.001) and family history of diabetes (53.8% vs. 35.0 %, p<0.001) were significantly higher in AGT group than NGT group (Table-II). No significant differences were observed in the percentages of AGT before and after 13 weeks of gestation of the study participants (32.8 % vs. 35.9 %, $\chi 2$=0.467, p=0.548) but the percentages of AGT

**Table-I:** Characteristics of the study participants (n=451)

| Variables | Values |
|---|---|
| Age, years | 26.2 ± 4.8 |
| BMI, kg/m$^2$ | 24.4± 4.2 |
| Systolic BP, mm-Hg | 102.4±12.2 |
| Diastolic BP, mm-Hg | 66.2±8.8 |
| Family history of DM | 187 (41.6%) |
| History of abortion | 144(32%) |
| Gravida | |
| Primigravida | 164 (36.4%) |
| Multigravida | 287 (63.6%) |
| Weeks of gestation | |
| 6-13 weeks | 192 (42.6%) |
| 14-23 weeks | 259 (57.4%) |
| Occupation | |
| Housewife | 309 (68.5%) |
| Service holder | 142 (31.5%) |

Data were expressed in mean±SD or frequency (%) as appropriate
Within parenthesis are percentages over the column total
BMI: body mass index; BP: blood pressure; DM: diabetes mellitus

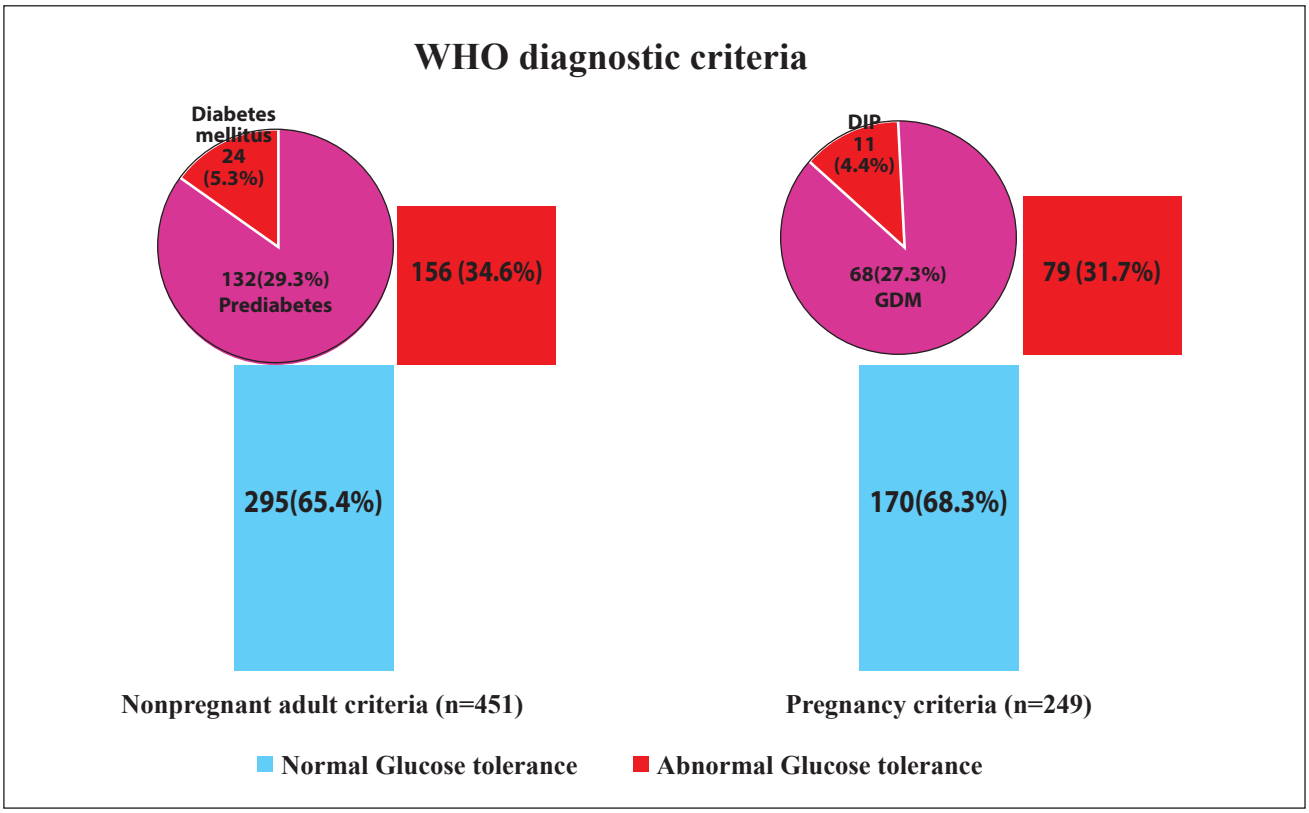


**Figure-1** Glycemic status in pregnancy by WHO non-pregnant (n=451) and Pregnancy specific WHO 2013 criteria (n=249)

GDM: gestational diabetes mellitus, DIP: diabetes in pregnancy
Prediabetes includes impaired fasting glucose, or impaired glucose tolerance or combination of both
Percentages are over the column total

**Table-II:** Characteristics of the study participants based on glycemic profile by WHO criteria for the non-pregnant adults (n= 451)

| Characters/variables | NGT (n= 295) | AGT (n= 156) | P |
|---|---|---|---|
| Age (mean±SD, years) | 25.4±4.6 | 27.6±4.8 | **<0.001** |
| BMI (mean±SD, kg/m$^2$) | 23.5±3.8 | 25.9±4.4 | **<0.001** |
| Systolic BP (mean±SD, mm-Hg) | 100.7±11.9 | 105.6±12.2 | **<0.001** |
| Diastolic BP (mean±SD, mm-Hg) | 64.8±8.5 | 68.7±8.9 | **<0.001** |
| Family history of DM | 103 (35.0%) | 84 (53.8%) | **<0.001** |
| History of abortion | 94 (31.9%) | 50 (32.3%) | 0.932 |
| Gravida | | | |
| Primigravida | 117 (39.7%) | 47 (30.1%) | **0.045** |
| Multigravida | 178 (60.3%) | 109 (69.9%) | |
| Weeks of gestation | | | |
| 6- 13 weeks | 129 (43.7%) | 63 (40.4%) | 0.548 |
| 14-23 weeks | 166 (56.3%) | 93 (59.6%) | |
| Occupation | | | |
| Housewife | 204 (69.2%) | 105 (67.3%) | 0.688 |
| Service holder | 91 (30.8%) | 51 (32.7%) | |

Within parentheses, percentages are over the column total
Numerical data were analyzed by independent sample t-test
Categorical data were analyzed by the Pearson Chi-Square test.
AGT included prediabetes (IFG, IGT, or both) and diabetes mellitus (n= 24) based on WHO non-pregnant adult criteria.

increased with increasing maternal age (≥25 vs. <25, years: 66.7% vs. 33.3%, $X^2$=19.65; p<0.001) (Figure-2). We also observed that both FPG and 02h PG value on OGTT had a positive correlation with maternal age (r=0.17, p<0.001 and r=0.27, p<0.001 respectively) and BMI (r=0.17, p<0.001 and r=0.28, p<0.001 respectively) (Table-III). BMI (B=0.021, 95%CI: 0.01 to 0.032, p<0.0001), positive family history of DM (B=0.121, 95%CI: 0.033 to 0.209, p=0.007,) and age of the

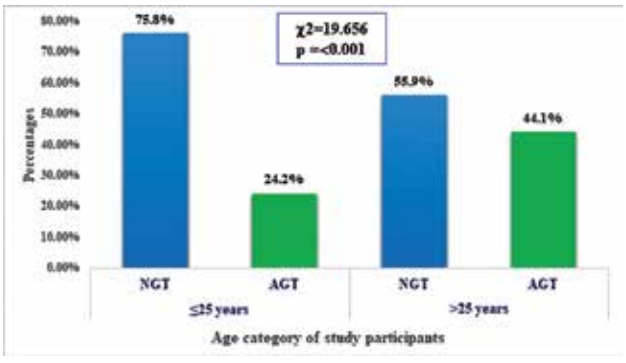


**Figure-2:** Prevalence of NGT and AGT (prediabetes and diabetes) among the study participants using WHO criteria for non-pregnant adults with the age category of 25 years (n= 451)
NGT (normal glucose tolerance), AGT (abnormal glucose tolerance)

**Table-III:** Correlations between glycemic values and clinical variables (n=451)

| Determinant's of 'r' | Study participants r | p |
|---|---|---|
| FPG vs. Age | 0.17 | **<0.001** |
| FPG vs. BMI | 0.21 | **<0.001** |
| FPG vs. Week of gestation | -0.07 | 0.135 |
| 02h PG vs. Age | 0.27 | **<0.001** |
| 02h PG vs. BMI | 0.28 | **<0.001** |
| 02h PG vs. Weeks of Gestation | 0.07 | 0.136 |

BMI: Body mass index, FPG: Fasting Plasma Glucose
02 PG: 02-hour plasma glucose on 75g OGTT
Pearson's correlation test was done

**Table-III:** Multivariate binary logistic regression analysis to see the effects of age, positive family history, BMI on blood glucose among study participants (n=451)

| Variables | B | SE | p | 95% CI |
|---|---|---|---|---|
| Age | 0.01 | 0.005 | **0.025** | 0.004 to 0.02 |
| Positive family history of DM | 0.12 | 0.045 | **0.007** | 0.03 to 0.21 |
| BMI | 0.02 | 0.006 | **<0.001** | 0.01 to 0.03 |
| Constant | -0.63 | 0.163 | **<0.001** | -0.95 to -0.31 |

BMI=Body mass index
CI= Confidence Interval

participants (B=0.013, p<0.025, Cl 95%: 0.004 to 0.023) were independent predictors for AGT (Table-IV).

## Discussion

The observed frequency of AGT before 24 WG in our study was alarmingly high whatever the diagnostic criteria used for diagnosis (34.6% and 31.7% by using non-pregnant adult criteria and pregnancy-specific WHO 2013 criteria respectively, Table-II) which is similar to the frequency observed in a study done in Europe.[20] Egan AM et al. observed the high prevalence of GDM among pregnant mothers in Europe. In his study, the overall prevalence of GDM was 39% and the prevalence of GDM in early pregnancy was 24%.20 Jayasinghe IU et al. in the Anuradhapura district, Sri Lanka observed the prevalence of hyperglycemia in the first trimester was 15%, which is lower than our findings. This may be due to the sampling process, we included pregnant women from 6 weeks to 23 weeks of gestation whereas Jayasinghe IU et al. included pregnant women only in the first trimester of pregnancy.[21] International Diabetic Federation (IDF) also mentioned the high prevalence of hyperglycemia in pregnancy in Southeast Asia. Age-adjusted prevalence of HIP (20-49 years) was reported to be 28% with the highest prevalence of 42.3% in 45-49-year-old women.[22]

Fasting plasma glucose gradually decline from the first trimester onward that's why only 39.1% of pregnant mother who meets the IADPSG or WHO 2013 diagnostic criteria in the first trimester, can meet the same criteria at 24-28 weeks of gestation.[23] So using the cut-off of IADPSG/WHO 2013 criteria at 24-28 weeks of gestation may not be scientific to use the same criteria in early pregnancy. Moreover, over diagnosis and aggressive management of this mild hyperglycemia in early pregnancy were associated with low birth weight and a higher rate of neonatal ICU admission.[24,25] But it is well established that untreated overt diabetes or DIP is associated with serious maternal and fetal complications when present in early pregnancy. A recent study from China reported 66.2 % of women who had an FPG of 6.1-6.9 mmol/L at early pregnancy still had an FPG of ≥ 5.1 mmol/L at 24–28 WG which is required to define GDM.[26] In our study Out of 451 subjects, overt diabetes, and prediabetes were found at 5.3% and 29.3% respectively according to WHO non-pregnant adult criteria which means 34.6% of pregnant women before 24 WG have FPG of ≥ 6.1mmol/L in our population which was alarmingly high. A very recent study reported untreated intermediate hyperglycemia in early pregnancy is also associated with serious maternal and fetal complications similar to that observed in Hyperglycemia and Pregnancy Outcome (HAPO) Study.[21,27,28] The findings of our study indicate the high prevalence of clinically significant hyperglycemia in early pregnancy that require adequate attention and appropriate steps from the national policymaker to avoid unwanted maternal and fetal complications. This research was done at a tertiary care hospital in Dhaka city which does not represent the population of the whole country, so the result of the study does not truly represent the condition of the whole country. We could do 3 samples of OGTT in all subjects which might miss a group of pregnant women with GDM or DIP is also another limitation in our study.

## Conclusions

Early screening is effective in detecting AGT in pregnancy and risk factors were significantly related to AGT. Considering the high prevalence of AGT before 24 weeks of gestation, early screening may be beneficial for the prevention of long-term fetal and maternal complications.

## Declarations

**Acknowledgements**

We are grateful to the study participants and their attendants.

**Conflict of Interest**

The authors have no conflicts of interest to disclose.

**Financial Disclosure**

The author(s) received partial support by University Research and Development, BSMMU.

**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**

This study was approved by the Institutional Review Board (IRB) of BSMMU, Reg: No. BSMMU/2016/2746, Approved on 08-03-2016. All procedures performed in studies involving human participants were in accordance with the ethical standards of the IRB and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed written consent was obtained from each of the participants included in the study.



**How to cite this article:** Hasan MR, Sultana N, Panthi S, Hasan M, Jahan S, Hasanat MA. Screening before 24 weeks of gestation may be wise for early detection of abnormal glucose tolerance during pregnancy. J Assoc Clin Endocrinol Diabetol Bangladesh 2023; 2(2): 39-45

**Publication History**
Received on: 19 April 2023
Accepted on: 01 June 2023
Published on: 01 July 2023

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