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Research article

# Comparison of risk factors, management and outcome between early and lately detected gestational diabetes mellitus patients

**Mohammad Moin Shahid[1]*, Richmond Ronald Gomes[2], KM Thouhidur Rahman[3], ABM Kamrul Hasan[4], and Shah Mohammad Fahim[5]**

[1]Associate Professor, Endocrinology, Ad-din Women's Medical College Hospital, Dhaka, Bangladesh

[2]Associate Professor, Medicine, Ad-din Women's Medical College Hospital, Dhaka, Bangladesh

[3]Lecturer, Department of Community medicine, Ad-din Women's Medical College, Mogbazar, Dhaka, Bangladesh

[4]Assistant Professor, Department of Endocrinology, Mymensingh Medical College & Hospital, Mymensingh, Bangladesh

[5]Research physician, Nutrition and Clinical service division, International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B)

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***Corresponding author:** Dr. Md. Moin Shahid, Associate Professor, Department of Endocrinology, Ad-din Womens Medical College Hospital, 2 Bara Maghbazar, Dhaka-1217, Bangladesh, Tel: 8801817028202;
E-mail: dr.moin.shahid@gmail.com

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## Abstract

**Aim:** The aim of this study is to compare the risk factors, management and pregnancy outcome between the Gestational Diabetes Mellitus (GDM) patients who were diagnosed at early and late stage of pregnancy.

**Methods:** We randomly selected 250 newly detected GDM patients and examined them. They were divided into two groups considering the gestational age at the time of diagnosis: early group (13 to 28 weeks) and late group (after 28 weeks).

**Results:** Data of 150 cases from early group and 100 cases from late group were analyzed. Incidence of nulliparous GDM patient (24% vs 36%, P – 0.04),weight at the time of GDM diagnosis (66.0 ± 11.067 vs 69.93 ± 9.865, P - 0.004) were significantly higher in late group and so was the excess body weight from ideal body weight (14.13 ± 10.147 vs 17.94 ± 8.535, P - 0.002). Prevalence of pre pregnancy obese/ overweight patients (68.7% vs 80.0%, P - 0.047), maternal H/O of DM (45.3% vs 32%, p - 0.035) and H/O unexplained fetal loss (24% vs 10%, p - 0.005) were higher in early group. There were no significant differences of blood sugar values (SMBG) between the groups except fasting blood sugar at 2nd visit (F2) (5.557 ± 1.045 vs 5.167 ± 0.960, P - 0.01).

**Conclusion:** This study suggests that range of screening should be broader to detect high risk and undiagnosed GDM mothers. Beside that it has also showed that only early diagnosis and intervention will not be enough to prevent the complications if the patients fails to understand and participate in GDM management.

## Introduction

Gestational diabetes is termed as development of glucose intolerance of pregnant women during 2nd& 3rd trimester who were previously known to be normoglycemic. The increased risk of hyperglycemia – GDM was first described by DR.J.P.Hoet in 19541. At the time there was a dilemma regarding diagnostic procedure and criteria of GDM [1]. In early 1960s Dr. John.B.



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O'Sullivan along with statistician Clarie Mahan published the criteria for detecting diabetes during pregnancy following performing 100g OGTT on 752 pregnant women during 2nd& 3rd trimester of pregnancy1.This criteria was considered standard for detection of diabetes during pregnancy in next 40 years. At present there are multiple criteria which are followed at different parts of the world e.g. IADPSG, WHO, DIPSI.

Bangladesh has the 2nd largest diabetic population in south-east Asia where every 1 in 4 live births are affected by hyperglycemia during pregnancy [2]. GDM patients have increased risk of developing preeclampsia, fetal loss during pregnancy and T2DM as well as cardiovascular diseases in later life [3]. The fetus of GDM affected mothers are always at high risk of IUD; developing macrosomia; suffering IUGR, shoulder dystocia, neonatal hypoglycemia, neonatal jaundice, respiratory distress, hypocalcaemia are more prone to develop childhood obesity, impaired glucose tolerance & cardiovascular diseases in later stages of life [3].

Despite rising prevalence, many remain undetected during their course of pregnancy. In this study we compared the risk factors, management & pregnancy outcome of GDM patients diagnosed at 13 – 28 weeks of pregnancy and after 28 weeks of pregnancy.

## Methods

### Study design and settings

This descriptive observational study was carried out from 1st July, 2018 to 30th June, 2019. 250 newly diagnosed GDM cases were randomly selected who were referred to Endocrine OPD. Patients underwent for OGTT (75 gm glucose) irrespective of the presence of the risk factors of GDM during 2nd& 3rd trimester of pregnancy. Diagnoses were made according to IADPSG criteria. GDM was diagnosed if any of the following plasma glucose values were met or exceeded [4,5] –

Fasting (0 hour) ≥ 5.1 mmol/L

1 hour ≥ 10.0 mmol/L

2 hours ≥ 8.5 mmol/L

Preexisting cases of diabetes, patients with any acute or chronic diseases or patients taking any drugs which may alter the blood sugar level, were excluded from the study. Patients were divided into two groups considering the gestational age at the time of diagnosis: early group (13 to 28 weeks) and late group (after 28 weeks).

People of this subcontinent are always at high risk of developing GDM due to ethnicity. South-east Asia is the home of one fifth diabetic population of the world & Bangladesh is 2nd amongst them [2]. Age was documented as per patient's confirmation. Family history of diabetes was recorded in 4 categories – 1. Father's history of diabetes, 2. Mother's history of diabetes, 3. Paternal family member's history of diabetes, 4. Maternal family member's history of diabetes. Clinical information such as: Previous diagnosis of polycystic ovarian syndrome (PCOS), GDM, polyhydramnios, macrosomic baby, history of fetal loss (abortions, MR, stillbirths, IUD), parity, anthropometric measurement (height, weight, excess body weight from ideal body weight) were documented. Patients were instructed regarding diet, exercise, SMBG and insulin management technique (when advised). They were advised to write down the SMBG results and the data were collected at the following visits. A cut-off of 4 kg was used to define a macrocosmic baby [6]. Large for Gestational Age (LGA) infants were defined as those with a birthweight within or above the 90th percentile of the birthweight. Small-for-gestational-age infants were defined as those with a birthweight less than the 10th percentile of the birthweight. Neonatal hypoglycemia was defined as blood glucose levels <2 mmol/L. Neonatal hyperbilirubinemia was defined when phototherapy was required.

## Results

Table 1 is presenting the clinical characters of both group. The average age at diagnosis were above safe age (above 25 years) but there was no significant difference. Weight and excess body weight from ideal body weight at the time of diagnosis were higher in late group (66.0 ± 11.067 vs 69.93 ± 9.865, P - 0.004; 14.13 ± 10.147 vs 17.94 ± 8.535, P - 0.002). Incidence of nulliparous patients was higher in late group 24% vs 36%, P – 0.04)

The risk factors are summarized in Table 2. Prevalence of obesity/ overweight is higher in 'late group' (68.7% vs 80.0%, P - 0.047). Maternal history of DM is higher in 'early group' (45.3% vs 32%, p - 0.035). Unexplained fetal loss (E.g. - abortion, IUD) is higher in 'early group' (24% vs 10%, p -

**Table 1:** Clinical characters.

| Variables | Early group (n – 150) | Late group (n – 100) | P value |
|---|---|---|---|
| Maternal age (Year) | 27.91 ± 4.282 | 27.63 ± 4.029 | 0.596 |
| Weight (Kg) at time of diagnosis | 66.0 ± 11.067 | 69.93 ± 9.865 | 0.004 |
| Excess body weight (Kg) from ideal body weight at time of diagnosis | 14.13 ± 10.147 | 17.94 ± 8.535 | 0.002 |
| Number of nullipara | 36 (24%) | 36 (36%) | 0.04 |

**Table 2:** Risk factors.

| Risk factors | Early group | Late group | P value |
|---|---|---|---|
| | Percent of cases (%) | Percent of cases (%) | |
| Pre pregnancy obesity or overweight | 68.7% | 80.0% | 0.047 |
| Mother's history of DM | 45.3% | 32.0% | 0.035 |
| Father's history of DM | 41.3% | 37.4% | 0.532 |
| Maternal family history of DM | 27.6% | 18.0% | 0.127 |
| Paternal family history of DM | 26.9% | 26.0% | 0.883 |
| H/O unexplained fetal loss (abortion, IUD) | 24% | 10.0% | 0.005 |
| H/O_GDM | 8.0% | 5.1% | 0.366 |
| Previous baby's birth Weight (>4 KG) | 1.3% | 1.0% | .813 |
| Age | | | |
| Age (up to 25years) | 62.7% | 64.0% | .830 |
| Age (above 25years) | 37.3% | 36.0% | |



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0.005). Difference of other risk factors between the groups were insignificant.

A Variables taken in regression analysis: Pre pregnancy obesity or overweight, Mother's history of DM, Father's history of DM, Maternal family history of DM, Paternal family history of DM, H/O unexplained fetal loss (abortion, IUD), H/O GDM, Previous baby's birth Weight (>4 KG).

Table 3 is showing the result of regression analysis considering pre pregnancy obesity or overweight, mother's history of DM, father's history of DM, maternal family history of DM, paternal family history of DM, H/O unexplained fetal loss (abortion, IUD), H/O GDM, previous baby's birth Weight (>4 KG) as variables. According to the table, participants with mother's history of DM and history of unexplained fetal loss had 1.7 times (OR 1.7, 95% CI 1.0-3.0, p=0.046) and 3.3 times (OR 3.3, 95% CI 1.5-7.2, p=0.002) higher risk of being diagnosed of GDM at early stage of pregnancy, respectively. Participants with pre pregnancy obesity or overweight had 2.1 times (OR 2.1, 95% CI 1.1, 3.9, p=0.019) higher risk of being diagnosed of GDM at later stage of pregnancy.

The mean values of OGTT of both groups are shown in Table 4. The values were insignificantly different in spite of OGTT underwent at different periods of gestation.

Table 5 is showing 72.4% of total cases were managed only with lifestyle modification and there wasn't any significant difference between the groups regarding this (70% vs 77%, P – 0.184). Though average advised daily dietary energy requirement was higher in "early" group but wasn't statistically significant (1719.2±173.0 vs 1662.3±172.5, P - 0.533). Despite early diagnosis, prevalence of insulin usage was higher in early group (30% vs 23%, P - 0.130 and 10% vs 2%, P - 0.502). Necessity of short acting insulin was higher than longer acting insulin in both groups.

Table 6 is presenting the mean values of sugar profile – Fasting (F), after breakfast (ABF), after lunch (AL) and after dinner (AD), showing blood sugar changes after starting GDM management at different follow up visits. Only the fasting blood sugar at 2nd visit (F2) was significantly different (5.557 ± 1.045 vs 5.167 ± 0.960, P - 0.01) and the rest differed insignificantly.

Reported antenatal, perinatal & postnatal complications of GDM of the study population are shown in Table 7. Though there were no significant difference of complications between 2 groups but the "early" group had more complications than the "late" group.

**Table 3:** Regression analysis.

| Variables[a] | *Early Group* | |
|---|---|---|
| | Adjusted OR (95% CI) | P-value |
| Mother's history of DM | | |
| No | Ref | |
| Yes | 1.7 (1.0, 3.0) | 0.046 |
| H/O unexplained fetal loss (abortion, IUD) | | |
| No | Ref | |
| Yes | 3.3 (1.5, 7.2) | 0.002 |
| **Variables[a]** | ***Late Group*** | |
| | **Adjusted OR (95% CI)** | **P-value** |
| Pre pregnancy obesity or overweight | | |
| No | Ref | |
| Yes | 2.1 (1.1, 3.9) | 0.019 |

**Table 4:** OGTT values.

| OGTT | Early group | | Late group | | P value |
|---|---|---|---|---|---|
| | Total respondents | Mean ± SD | Total respondents | Mean ± SD | |
| Fasting(0 hour) blood Sugar in OGTT | 147 | 6.11 ± 1.55 | 100 | 6.12 ± 1.50 | 0.972 |
| Blood Sugar at 1 hour in OGTT | 13 | 11.31 ± 1.49 | 17 | 10.85 ± 2.45 | 0.533 |
| Blood sugar at 2 hours in OGTT | 149 | 10.18 ± 2.37 | 99 | 10.26 ± 2.58 | 0.801 |

**Table 5:** Management of cases.

| Variables | Total respondents | | Early | Late | P value |
|---|---|---|---|---|---|
| **Participants managed with lifestyle modification** | | | | | |
| Lifestyle modification – diet and exercise | 182(72.4%) | | 105 (70%) | 77 (77%) | 0.184 |
| Advised daily dietary energy requirement (kcal) Mean ± SD | | | 1719.2±173.0 | 1662.3±172.5 | 0.533 |
| **Participants managed with insulin (multiple response)** | | | | | |
| Rapid(R)/Rapid-analogue (Ra)/Premixed (P) Insulin | 68 | R | 31 | 15 | 0.130 |
| | | Ra | 14 | 6 | |
| | | P | 0 | 2 | |
| | | Total | 45(30%) | 23(23%) | |
| NPH (N)/Long acting (L) Insulin | 18 | N | 13 | 2 | 0.502 |
| | | L | 3 | 0 | |
| | | Total | 16(10%) | 2(2%) | |

## Discussion

The subjects those who have risk factors of GDM are more prone to develop GDM than others [4,7,8]. Although the mean age of both groups at the time of GDM diagnosis were above the safe age (up to 25 years) but both groups showed higher incidence of GDM below 25 years which suggests that the safe age margin for this region could be lower [9]. Its been reported that incidence of GDM in nulliparous women is higher as age increases [10]. The result of this study is also in agreement with that report. Obesity causes insulin resistance which may result in GDM at any stage during gestation [11,12]. Some reports have shown that obese patients are more prone to develop early GDM but this study showed higher prevalence of obesity in 'late' group [13]. Though excess body weight from ideal body weight measurement is not a common practice but in this study we have observed that it may have a role for GDM screening. McLean M et al. reported that maternal history of DM is related to higher incidence of early GDM [14]. Our study observed the similar result. Unexplained fetal loss (UEFL) is often associated with glucose intolerance [15-17]. Craig LB, et al. reported that patients with history of recurrent abortion have higher insulin resistance even at non pregnant state [18]. This may explain our observation that patients with UEFL are more prone to develop early GDM.



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**Table 6:** Sugar profile (SMBG) at follow up visits after starting treatment.

| Sugar profile | Early group | | Late group | | P value |
|---|---|---|---|---|---|
| | Total respondents | Mean ± SD | Total respondents | Mean ± SD | |
| F2 | 106 | 5.557 ± 1.045 | 75 | 5.167 ± 0.960 | 0.01 |
| ABF2 | 106 | 7.284 ± 1.977 | 74 | 7.223 ± 2.283 | 0.852 |
| AL2 | 75 | 7.535 ± 2.102 | 62 | 7.124 ± 1.623 | 0.210 |
| AD2 | 71 | 7.659 ± 2.089 | 62 | 7.686 ± 2.049 | 0.940 |
| F3 | 75 | 5.132 ± 1.099 | 27 | 5.107 ± 1.099 | 0.897 |
| ABF3 | 75 | 6.853 ± 1.596 | 28 | 6.932 ± 1.145 | 0.811 |
| AL3 | 66 | 6.924 ± 1.466 | 28 | 6.968 ± 1.023 | 0.887 |
| AD3 | 68 | 7.410 ± 1.632 | 29 | 7.417 ± 1.444 | 0.984 |
| F4 | 44 | 5.225 ± 0.824 | 11 | 5.073 ± 0.517 | 0.563 |
| ABF4 | 44 | 7.118 ± 1.325 | 11 | 6.900 ± 1.738 | 0.649 |
| AL4 | 42 | 6.922 ± 1.149 | 11 | 7.727 ± 1.558 | 0.133 |
| AD4 | 40 | 7.477 ± 1.289 | 11 | 7.891 ± 1.309 | 0.366 |
| F5 | 21 | 5.181 ± 0.883 | 6 | 4.967 ± 0.850 | 0.605 |
| ABF5 | 23 | 7.052 ± 1.761 | 6 | 6.917 ± 2.076 | 0.885 |
| AL5 | 22 | 6.745 ± 1.382 | 6 | 7.483 ± 1.809 | 0.375 |
| AD5 | 22 | 6.536 ± 1.582 | 6 | 6.967 ± 2.283 | 0.679 |
| F6 | 14 | 5.250 ± 0.858 | 3 | 5.133 ± 0.115 | 0.822 |
| ABF6 | 15 | 6.400 ± 1.382 | 3 | 6.967 ± 0.305 | 0.595 |
| AL6 | 14 | 6.850 ± 0.978 | 3 | 8.067 ± 1.069 | 0.174 |
| AD6 | 14 | 6.836 ± 0.978 | 3 | 7.000 ± 0.755 | 0.764 |

**Table 7:** Complications.

| Reported complications | Early group (n - 83) | Late group (n – 62) | P value |
|---|---|---|---|
| | Number (percentage) | Number (percentage) | |
| Abortion | 4(4.81%) | 0 | 0.08 |
| IUD | 1(1.2%) | 1(1.61%) | 0.835 |
| Macrosomia | 3(3.61%) | 4(6.45%) | 0.430 |
| SGA | 1(1.2%) | 0 | 0.386 |
| Neonatal Jaundice | 3(3.61%) | 4(6.45%) | 0.670 |
| Hypocalcaemia | 0 | 0 | 0 |
| Respiratory distress | 0 | 0 | 0 |
| Birth injury | 0 | 0 | 0 |
| Neonatal hypoglycemia | 1(1.2%) | 0 | 0.218 |
| Congenital anomaly | 0 | 0 | 0 |
| Polyhydramnios | 4(4.81%) | 3(4.84%) | 0.430 |
| PROM | 3(3.61%) | 0 | 0.130 |
| Pre- eclampsia/ eclampsia | 1(1.2%) | 0 | 0.386 |

Like other reports this study also showed that despite early diagnosis and intervention more patients required insulin in 'early group' than 'late group' [19]. But it is also true that 'early' group was at higher risk than the 'late' group due to presence of multiple risk factors. Because of that those patients underwent an OGTT earlier. This study failed to show any significance of early management of GDM reducing the adverse outcomes comparing to late management as GDM related complications were higher in 'early' group. Some of previously conducted studies also had the same result [20]. However, considering individual assessment of patients this study can't reflect the actual importance of early diagnosis and management of GDM. It's obvious that earlier diagnosis will decrease the chances of GDM related complications, only if the blood sugar is controlled. Most of the cases with complications were found to be irregular in follow up visits as well as in following instructions. This points out the significance of patient's role in managing GDM.

One of the limitations of this study is all of the subjects presented some of the histories regarding the risk factors recalling their memories. So there are chances of getting biased.

In this study, it was observed that there was a gradual loss of participant numbers during follow-up visits. Our maximum expected visit to endocrine department of each subject was 8. As diagnosis of GDM happened at different period of gestation, patients visit varied accordingly- maximum 7 & minimum 1. One of the main reasons behind that is, not all the participants were diagnosed as GDM patients at the same time. Some were diagnosed in the earlier stage of pregnancy, and some were even in the last month. So, the follow-up visit number was not the same for all of them. Moreover, there was a loss of patient numbers as some of them were not able to visit multiple times due to their socio-economic conditions or lack of knowledge and interest in repetitive follow-up visits during pregnancy. These reasons also affected the average glucose profile of both groups.

We couldn't contact all of the subjects after the gestational period to know the outcome & fate of GDM.

## Conclusion

Diabetes is now a global epidemic resulting in adverse health outcomes. The prevalence of GDM is increasing day by day, so are the complications. The after effects of GDM causing huge economic burden for the society. Early screening and proper education can reduce GDM related complications at huge scale. More studies are required on this issue so that a proper screening tool can be established to identify the mothers who are at risk of developing GDM and an education strategy can be developed where more people become aware about GDM.

Compliance with ethical standards: None of the authors declared any conflict of interest. Ethical approval was taken and informed written consents were obtained from all enrolled participants.

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