



## EARLY GESTATIONAL DIABETES MELLITUS: UNRAVELING RISK FACTORS AND THEIR INFLUENCE ON PERINATAL OUTCOMES

### Endocrinology

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### ABSTRACT

**Background:** Early gestational diabetes mellitus (GDM) is associated with maternal and perinatal complications. Identification of clinical and biochemical predictors in early pregnancy may facilitate timely screening and intervention. **Objective:** To identify maternal clinical and biochemical risk factors in the first trimester associated with the development of GDM and to determine independent predictors of GDM. **Methods:** A logistic regression analysis was performed to evaluate the association between maternal clinical and biochemical parameters measured in the first trimester and subsequent development of GDM. Univariate analysis was initially performed, followed by multivariate logistic regression incorporating clinically relevant and statistically significant variables. **Results:** On univariate analysis, family history of diabetes (OR: 2.10; 95% CI: 1.05–4.20;  $p = 0.035$ ), previous macrosomia (OR: 2.80; 95% CI: 1.20–6.50;  $p = 0.018$ ), and previous GDM (OR: 3.20; 95% CI: 1.30–7.80;  $p = 0.011$ ) were significantly associated with GDM. Among biochemical parameters, HbA1c (OR: 2.10;  $p = 0.035$ ), fasting blood sugar (OR: 1.18;  $p < 0.001$ ), fasting insulin (OR: 1.08;  $p = 0.010$ ), and HOMA-IR (OR: 2.45;  $p = 0.009$ ) showed significant associations. On multivariate analysis, HbA1c (adjusted OR: 2.35; 95% CI: 1.02–5.41;  $p = 0.044$ ), fasting blood sugar (adjusted OR: 1.21; 95% CI: 1.12–1.31;  $p < 0.001$ ), and HOMA-IR (adjusted OR: 2.67; 95% CI: 1.27–5.62;  $p = 0.010$ ) remained independent predictors of GDM. **Conclusion:** First-trimester HbA1c, fasting blood sugar, and HOMA-IR were independent predictors of GDM. These biochemical parameters may help identify women at increased risk of GDM early in pregnancy and support timely screening and management.

### KEYWORDS

Gestational diabetes mellitus; first trimester; HbA1c; fasting blood sugar; HOMA-IR; insulin resistance; risk factors.

### INTRODUCTION

Early gestational diabetes mellitus (GDM) refers to hyperglycemia detected before 20 weeks of gestation in women without pre-existing diabetes. However, there is no clear consensus regarding its diagnostic criteria or screening strategies [1]. Commonly used tests include fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), and the oral glucose tolerance test (OGTT). The World Health Organization (WHO) 2013 criteria, based on the International Association of Diabetes and Pregnancy Study Groups (IADPSG), are widely used and diagnose GDM when one or more values on a 75-g OGTT are abnormal (FPG  $92\text{--}125\text{ mg/dL}$ , 1-hour  $\geq 180\text{ mg/dL}$ , 2-hour  $153\text{--}199\text{ mg/dL}$ ) [2]. Although GDM is conventionally diagnosed at 24–28 weeks (late GDM), metabolic abnormalities often begin earlier. The prevalence of early GDM varies widely (0.7–36.8%) due to heterogeneity in populations and diagnostic criteria [3]. Established risk factors include higher body mass index, family history of diabetes, prior GDM, and multiparity [3]. The STRiDE India study reported a prevalence of 18.4% using FPG-based screening [4], while a meta-analysis by Li et al. showed that 11–60% of GDM cases are identified in the first trimester and 28–55% before 24 weeks [5]. Despite this, data from South Asian populations using WHO 2013 criteria remain limited.

Pathophysiologically, early GDM is characterized by increased insulin resistance and impaired  $\beta$ -cell function. The SPRING trial demonstrated reduced insulin sensitivity with compensatory hyperinsulinemia in early pregnancy [6]. A lower pregnancy insulin physiology score predicts early GDM and is associated with greater postpartum  $\beta$ -cell dysfunction [7], while elevated HbA1c and studies such as Harreiter et al. further support impaired insulin secretion and increased insulin resistance [8].

Screening recommendations vary considerably. FIGO and the Australasian Diabetes in Pregnancy Society recommend WHO OGTT criteria [9], while IADPSG suggests selective screening using FPG  $92\text{--}125\text{ mg/dL}$  [11]. The American Diabetes Association recommends FPG  $\geq 110\text{ mg/dL}$  or HbA1c  $\geq 5.9\%$  [13], whereas the American College of Obstetricians and Gynecologists advocates a two-step approach [12]. In contrast, the Diabetes in Pregnancy Study Group of India recommends universal screening using a 2-hour value  $\geq 140\text{ mg/dL}$  [15], and NICE suggests FPG  $\geq 100\text{ mg/dL}$  or 2-hour  $\geq 140\text{ mg/dL}$  [14]. Notably, 30–50% of women diagnosed with early GDM revert to normal glucose tolerance at 24–28 weeks [16]. The TOBOGM study showed that such “regressor GDM” cases have outcomes comparable to normoglycemic pregnancies, suggesting possible overtreatment [17]. This regression may reflect physiological changes in early pregnancy, variability in OGTT, and lifestyle

interventions [18], while the “fetal steal” hypothesis appears unlikely due to the lack of increased adverse outcomes [19]. Persistence of GDM is more likely in women with polycystic ovary syndrome and higher baseline glycemia [18]. Evidence on early screening remains conflicting. Some studies show no improvement in perinatal outcomes with early screening [20], whereas a meta-analysis by Immanuel et al. reported increased risks of perinatal mortality, neonatal hypoglycemia, and insulin requirement in early-onset GDM [21].

Given the lack of consensus on early GDM diagnosis, wide variability in prevalence, and conflicting outcome data, there is a need for standardized, population-specific evidence. This is particularly important in South Asian populations, where data using WHO 2013 criteria remain limited. The present study aims to identify the prevalence, predictors and maternal and neonatal outcomes of early GDM.

### METHODOLOGY

After receiving institutional ethics committee approval, this prospective observational study was carried out over a two-year period at a primary health center connected to Osmania Medical College. The study included 349 pregnant women who presented at or before 20 weeks of gestation. The study included pregnant women with singleton pregnancies who were  $\leq 20$  weeks gestation and willing to give informed permission; those with severe systemic illnesses or pre-existing diabetes mellitus were excluded. As part of the screening procedure, each participant had a 75 g oral glucose tolerance test (OGTT). The International Association of Diabetes and Pregnancy Study Groups (IADPSG) classified early gestational diabetes mellitus (GDM) as hyperglycemia detected before 20 weeks of gestation. A standardized proforma was used to gather baseline maternal clinical and demographic information, including age, parity, body mass index (BMI), mid-upper arm circumference (MUAC), socioeconomic status, and educational status. Prior GDM, polycystic ovarian syndrome (PCOS), poor obstetric outcomes, and a history of macrosomia were among the pertinent medical and obstetric histories that were recorded. BMI was computed as weight in kilograms divided by height in meters squared ( $\text{kg/m}^2$ ) after anthropometric measurements were obtained using standardized procedures. Complete blood pictures, liver and renal function tests, lipid profiles, thyroid function tests, glycated hemoglobin (HbA1c), serum uric acid, and insulin resistance and  $\beta$ -cell function indices, HOMA-IR and HOMA- $\beta$ , were among the laboratory investigations. Neonatal outcomes included macrosomia, preterm birth, and hospitalization to the neonatal intensive care unit (NICU); maternal outcomes included the development of gestational hypertension and the mode of delivery. SPSS version 26 was used for statistical analysis, with continuous data

represented as mean  $\pm$  standard deviation and categorical variables as frequencies and percentages. Logistic regression analysis was utilized to find independent predictors of early GDM, and the Chi-square test was employed to evaluate relationships between categorical variables. Statistical significance was defined as a p-value of less than 0.05.

## RESULTS

A total of 349 pregnant women were included. The prevalence of early GDM was 6%. 92.2% of the participants had Normal 75gm OGTT. 1.8% of the participants had IGT. 6.0% of the participants had GDM.

**Table 1 - Distribution of the Participants in Terms of '75gm OGTT**

| 75gm OGTT (First Trimester) | Frequency | Percentage | 95% CI        |
|-----------------------------|-----------|------------|---------------|
| Normal                      | 401       | 92.2%      | 89.1% - 94.5% |
| IGT                         | 8         | 1.8%       | 0.9% - 3.7%   |
| GDM                         | 26        | 6.0%       | 4.0% - 8.7%   |

**Table 2 - Association between 75gm OGTT and Parameters**

| Parameters                                    | 75gm OGTT         |                   |                   | p value            |
|-----------------------------------------------|-------------------|-------------------|-------------------|--------------------|
|                                               | Normal (n = 401)  | IGT (n = 8)       | GDM (n = 26)      |                    |
| Age (Years)                                   | 25.23 $\pm$ 4.12  | 25.00 $\pm$ 5.21  | 25.69 $\pm$ 3.83  | 0.699 <sup>1</sup> |
| Age Group                                     |                   |                   |                   | 0.308 <sup>2</sup> |
| 18-25 Years                                   | 238 (59.4%)       | 5 (62.5%)         | 12 (46.2%)        |                    |
| 26-30 Years                                   | 122 (30.4%)       | 2 (25.0%)         | 11 (42.3%)        |                    |
| 31-35 Years                                   | 34 (8.5%)         | 0 (0.0%)          | 3 (11.5%)         |                    |
| 36-40 Years                                   | 7 (1.7%)          | 1 (12.5%)         | 0 (0.0%)          |                    |
| Parity                                        |                   |                   |                   | 0.227 <sup>2</sup> |
| P1                                            | 149 (37.2%)       | 4 (50.0%)         | 5 (19.2%)         |                    |
| P2                                            | 147 (36.7%)       | 3 (37.5%)         | 10 (38.5%)        |                    |
| $\geq$ P3                                     | 105 (26.2%)       | 1 (12.5%)         | 11 (42.3%)        |                    |
| Weight (Kg)                                   | 54.78 $\pm$ 11.48 | 58.00 $\pm$ 13.33 | 58.92 $\pm$ 14.83 | 0.252 <sup>1</sup> |
| Height (cm)                                   | 154.05 $\pm$ 4.78 | 156.25 $\pm$ 7.03 | 152.96 $\pm$ 4.67 | 0.414 <sup>1</sup> |
| BMI (Kg/m <sup>2</sup> )                      | 22.68 $\pm$ 4.46  | 23.24 $\pm$ 3.98  | 24.17 $\pm$ 4.69  | 0.171 <sup>1</sup> |
| BMI Grading***                                |                   |                   |                   | 0.023 <sup>2</sup> |
| Normal                                        | 186 (46.4%)       | 2 (25.0%)         | 5 (19.2%)         |                    |
| Underweight                                   | 46 (11.5%)        | 1 (12.5%)         | 3 (11.5%)         |                    |
| Overweight                                    | 73 (18.2%)        | 4 (50.0%)         | 8 (30.8%)         |                    |
| Obese                                         | 96 (23.9%)        | 1 (12.5%)         | 10 (38.5%)        |                    |
| MUAC (cm)                                     | 27.15 $\pm$ 2.90  | 29.12 $\pm$ 3.44  | 28.23 $\pm$ 3.19  | 0.056 <sup>1</sup> |
| Literacy Status                               |                   |                   |                   | 0.841 <sup>2</sup> |
| Illiterate                                    | 13 (3.2%)         | 0 (0.0%)          | 0 (0.0%)          |                    |
| Reads & Writes                                | 1 (0.2%)          | 0 (0.0%)          | 0 (0.0%)          |                    |
| Primary                                       | 237 (59.1%)       | 4 (50.0%)         | 18 (69.2%)        |                    |
| Secondary                                     | 87 (21.7%)        | 2 (25.0%)         | 6 (23.1%)         |                    |
| High Secondary                                | 23 (5.7%)         | 0 (0.0%)          | 1 (3.8%)          |                    |
| Intermediate                                  | 16 (4.0%)         | 1 (12.5%)         | 1 (3.8%)          |                    |
| Graduate                                      | 21 (5.2%)         | 1 (12.5%)         | 0 (0.0%)          |                    |
| Post Graduate                                 | 3 (0.7%)          | 0 (0.0%)          | 0 (0.0%)          |                    |
| Occupation                                    |                   |                   |                   | 0.758 <sup>2</sup> |
| House Wife                                    | 342 (85.3%)       | 7 (87.5%)         | 22 (84.6%)        |                    |
| Employee                                      | 29 (7.2%)         | 1 (12.5%)         | 1 (3.8%)          |                    |
| Laborer                                       | 12 (3.0%)         | 0 (0.0%)          | 2 (7.7%)          |                    |
| Service                                       | 10 (2.5%)         | 0 (0.0%)          | 1 (3.8%)          |                    |
| Professional                                  | 4 (1.0%)          | 0 (0.0%)          | 0 (0.0%)          |                    |
| Teacher                                       | 2 (0.5%)          | 0 (0.0%)          | 0 (0.0%)          |                    |
| Business                                      | 1 (0.2%)          | 0 (0.0%)          | 0 (0.0%)          |                    |
| Pharmacist                                    | 1 (0.2%)          | 0 (0.0%)          | 0 (0.0%)          |                    |
| Socioeconomic Status                          |                   |                   |                   | 0.938 <sup>3</sup> |
| Low Income                                    | 316 (78.8%)       | 6 (75.0%)         | 21 (80.8%)        |                    |
| Middle Income                                 | 85 (21.2%)        | 2 (25.0%)         | 5 (19.2%)         |                    |
| History Of Gestational Hypertension (Yes) *** | 15 (3.7%)         | 0 (0.0%)          | 5 (19.2%)         | 0.009 <sup>2</sup> |
| Family History Of Diabetes (Yes) ***          | 53 (13.2%)        | 0 (0.0%)          | 8 (30.8%)         | 0.037 <sup>2</sup> |
| Past History Of Pcos (Yes)                    | 6 (1.5%)          | 0 (0.0%)          | 2 (7.7%)          | 0.123 <sup>2</sup> |
| Past History Of Gdm (Yes)***                  | 12 (3.0%)         | 1 (12.5%)         | 3 (11.5%)         | 0.030 <sup>2</sup> |

|                                     |                       |                         |                       |                     |
|-------------------------------------|-----------------------|-------------------------|-----------------------|---------------------|
| History Of Macrosomic Baby (Yes)*** | 11 (2.7%)             | 0 (0.0%)                | 4 (15.4%)             | 0.015 <sup>2</sup>  |
| Bad Obstetric History (Yes)         | 11 (2.7%)             | 0 (0.0%)                | 0 (0.0%)              | 1.000 <sup>2</sup>  |
| Thyroid Status                      |                       |                         |                       | 0.342 <sup>2</sup>  |
| Euthyroid                           | 331 (82.5%)           | 6 (75.0%)               | 19 (73.1%)            |                     |
| Hypothyroid                         | 70 (17.5%)            | 2 (25.0%)               | 7 (26.9%)             |                     |
| Hemoglobin (g/dL)                   | 11.31 $\pm$ 1.29      | 11.79 $\pm$ 1.42        | 11.47 $\pm$ 0.91      | 0.500 <sup>1</sup>  |
| TLC (/mm <sup>3</sup> )             | 9326.40 $\pm$ 6005.23 | 18323.62 $\pm$ 24131.08 | 9418.69 $\pm$ 1575.19 | 0.309 <sup>1</sup>  |
| Neutrophil Count                    | 6075.41 $\pm$ 1830.25 | 6612.88 $\pm$ 3025.83   | 6432.19 $\pm$ 1370.64 | 0.380 <sup>1</sup>  |
| Lymphocyte Count                    | 2249.22 $\pm$ 1104.70 | 2504.62 $\pm$ 548.95    | 2254.92 $\pm$ 739.43  | 0.269 <sup>1</sup>  |
| N/L Ratio                           | 2.89 $\pm$ 0.86       | 2.65 $\pm$ 0.84         | 3.23 $\pm$ 1.05       | 0.441 <sup>1</sup>  |
| Blood Urea                          | 17.74 $\pm$ 5.66      | 18.12 $\pm$ 1.96        | 18.35 $\pm$ 5.99      | 0.730 <sup>1</sup>  |
| S Creatinine                        | 0.75 $\pm$ 1.89       | 0.52 $\pm$ 0.10         | 0.55 $\pm$ 0.15       | 0.738 <sup>1</sup>  |
| Uric Acid                           | 3.58 $\pm$ 1.07       | 3.35 $\pm$ 0.91         | 4.01 $\pm$ 1.18       | 0.083 <sup>1</sup>  |
| AST                                 | 20.53 $\pm$ 6.54      | 17.88 $\pm$ 4.55        | 20.62 $\pm$ 5.10      | 0.625 <sup>1</sup>  |
| ALT                                 | 19.30 $\pm$ 6.72      | 17.25 $\pm$ 4.46        | 17.73 $\pm$ 6.66      | 0.545 <sup>1</sup>  |
| Albumin                             | 3.69 $\pm$ 0.39       | 3.67 $\pm$ 0.50         | 3.80 $\pm$ 0.48       | 0.413 <sup>1</sup>  |
| Globulin                            | 3.35 $\pm$ 0.48       | 3.34 $\pm$ 0.27         | 3.40 $\pm$ 0.46       | 0.872 <sup>1</sup>  |
| A G Ratio                           | 1.15 $\pm$ 0.28       | 1.11 $\pm$ 0.16         | 1.15 $\pm$ 0.24       | 0.994 <sup>1</sup>  |
| Total Cholesterol***                | 177.70 $\pm$ 39.70    | 210.38 $\pm$ 30.15      | 189.27 $\pm$ 37.50    | 0.005 <sup>1</sup>  |
| Triglycerides                       | 138.77 $\pm$ 40.68    | 166.38 $\pm$ 40.02      | 149.50 $\pm$ 41.61    | 0.070 <sup>1</sup>  |
| LDL                                 | 104.54 $\pm$ 25.10    | 112.38 $\pm$ 22.80      | 113.85 $\pm$ 26.54    | 0.092 <sup>1</sup>  |
| HDL                                 | 49.92 $\pm$ 10.68     | 55.25 $\pm$ 12.10       | 47.88 $\pm$ 11.53     | 0.298 <sup>1</sup>  |
| LDL HDL Ratio                       | 2.18 $\pm$ 0.63       | 2.06 $\pm$ 0.28         | 2.50 $\pm$ 0.83       | 0.087 <sup>1</sup>  |
| TG HDL Ratio                        | 2.89 $\pm$ 0.99       | 3.11 $\pm$ 0.83         | 3.25 $\pm$ 1.02       | 0.177 <sup>1</sup>  |
| CH HDL Ratio***                     | 3.65 $\pm$ 0.90       | 3.89 $\pm$ 0.54         | 4.14 $\pm$ 1.16       | 0.032 <sup>1</sup>  |
| Hba1C***                            | 4.96 $\pm$ 0.63       | 5.19 $\pm$ 0.42         | 5.63 $\pm$ 0.67       | <0.001 <sup>1</sup> |
| T3                                  | 1.76 $\pm$ 0.62       | 1.92 $\pm$ 0.71         | 1.75 $\pm$ 0.58       | 0.740 <sup>1</sup>  |
| T4                                  | 11.46 $\pm$ 3.49      | 14.50 $\pm$ 3.37        | 11.74 $\pm$ 4.30      | 0.072 <sup>1</sup>  |
| Tsh                                 | 3.09 $\pm$ 3.51       | 3.68 $\pm$ 1.60         | 2.58 $\pm$ 1.52       | 0.186 <sup>1</sup>  |
| Fasting Insulin***                  | 7.24 $\pm$ 3.04       | 8.79 $\pm$ 2.26         | 11.73 $\pm$ 2.15      | <0.001 <sup>1</sup> |
| HOMA IR***                          | 1.48 $\pm$ 0.60       | 1.98 $\pm$ 0.72         | 2.50 $\pm$ 0.48       | <0.001 <sup>1</sup> |
| QUICKI Score***                     | 0.37 $\pm$ 0.03       | 0.36 $\pm$ 0.03         | 0.32 $\pm$ 0.02       | <0.001 <sup>1</sup> |
| FBS (First Trimester)***            | 77.50 $\pm$ 7.23      | 81.88 $\pm$ 5.59        | 95.69 $\pm$ 8.58      | <0.001 <sup>1</sup> |
| 1 Hour PPBS (First Trimester)***    | 102.85 $\pm$ 18.82    | 132.88 $\pm$ 28.81      | 144.46 $\pm$ 32.05    | <0.001 <sup>1</sup> |
| 2 Hours PPBS (First Trimester)***   | 93.44 $\pm$ 17.11     | 145.25 $\pm$ 2.25       | 132.46 $\pm$ 26.66    | <0.001 <sup>1</sup> |
| EARLY GDM(First (Present)***        | 0 (0.0%)              | 8 (100.0%)              | 26 (100.0%)           | <0.001 <sup>2</sup> |
| PERINATAL OUTCOMES                  |                       |                         |                       |                     |
| Gestational HTN (Yes)***            | 29 (7.2%)             | 0 (0.0%)                | 10 (38.5%)            | <0.001 <sup>2</sup> |
| Preterm Delivery (Yes)***           | 23 (5.7%)             | 0 (0.0%)                | 12 (46.2%)            | <0.001 <sup>2</sup> |
| Cesarean Delivery (Yes)***          | 32 (8.0%)             | 1 (12.5%)               | 9 (34.6%)             | <0.001 <sup>2</sup> |
| Macrosomic Baby (Yes)***            | 33 (8.2%)             | 2 (25.0%)               | 18 (69.2%)            | <0.001 <sup>2</sup> |
| NICU Admission (Yes)***             | 41 (10.2%)            | 2 (25.0%)               | 12 (46.2%)            | <0.001 <sup>2</sup> |

There were no statistically significant variations across the groups in terms of age (p = 0.5131) parity (p = 0.1062), weight (p = 0.5081), height (p = 0.3561), or BMI (p = 0.2211). Grading of BMI was on the verge of significance (p = 0.0532), where obesity was higher among the GDM group (40.0%). Socio-demographic variables like literacy

status ( $p = 0.6042$ ), occupation ( $p = 0.6342$ ), and socioeconomic status ( $p = 0.6512$ ) had no variation across groups. Past history of gestational hypertension was more frequently seen in the GDM group (20.0%) as compared to Normal (3.7%) ( $p = 0.0152$ ). Past history of macrosomic baby was more in GDM (15.0%) as compared to Normal (2.2%) ( $p = 0.0372$ ). The total cholesterol was highly increased in the IGT group ( $222.50 \pm 23.50$  mg/dL) when compared to Normal ( $175.14 \pm 37.37$ ) and GDM ( $186.90 \pm 41.11$ ) ( $p = 0.0031$ ). HbA1c increased progressively from Normal ( $4.96 \pm 0.63$ ) to IGT ( $5.20 \pm 0.50$ ) and highest in GDM ( $5.62 \pm 0.72$ ) ( $p < 0.001$ ). Fasting insulin, HOMA-IR, QUICKI score, had statistically significant differences, with GDM women having higher markers for insulin resistance (all  $p < 0.001$ ). Fasting blood sugar (FBS), 1-hour and 2-hour postprandial blood sugars (PPBS) were significantly elevated in GDM as compared to Normal and IGT groups ( $p < 0.001$ ). There were significant differences in pregnancy outcomes as well: Gestational hypertension occurred more in the GDM group (45.0%) compared to Normal (7.4%) ( $p < 0.001$ ). Preterm delivery rates (45.0% vs 5.6%), Caesarean section rates (40.0% vs 8.0%), macrosomic infants (70.0% vs 9.0%), and NICU discharges (50.0% vs 9.9%) were all increased in GDM versus Normal (all  $p < 0.001$ ).

**Table 3 - Association Between EARLY GDM and 'Gestational HTN'**

| Gestational HTN | 75gm OGTT    |            |             |              | Fisher's Exact Test |         |
|-----------------|--------------|------------|-------------|--------------|---------------------|---------|
|                 | Normal       | IGT        | GDM         | Total        | $\chi^2$            | P Value |
| Yes             | 24 (7.4%)    | 0 (0.0%)   | 9 (45.0%)   | 33 (9.5%)    | 31.688              | <0.001  |
| No              | 299 (92.6%)  | 6 (100.0%) | 11 (55.0%)  | 316 (90.5%)  |                     |         |
| Total           | 323 (100.0%) | 6 (100.0%) | 20 (100.0%) | 349 (100.0%) |                     |         |

**Table 4- Association Between EARLY GDM and 'Preterm Delivery'**

| Preterm Delivery | 75gm OGTT (First Trimester) |            |             |              | Fisher's Exact Test |         |
|------------------|-----------------------------|------------|-------------|--------------|---------------------|---------|
|                  | Normal                      | IGT        | GDM         | Total        | $\chi^2$            | P Value |
| Yes              | 18 (5.6%)                   | 0 (0.0%)   | 9 (45.0%)   | 27 (7.7%)    | 41.529              | <0.001  |
| No               | 305 (94.4%)                 | 6 (100.0%) | 11 (55.0%)  | 322 (92.3%)  |                     |         |
| Total            | 323 (100.0%)                | 6 (100.0%) | 20 (100.0%) | 349 (100.0%) |                     |         |

**Table 5 - Association Between EARLY GDM and 'Caesarean Delivery'**

| Caesarean Delivery | 75gm OGTT (First Trimester) |            |             |              | Fisher's Exact Test |         |
|--------------------|-----------------------------|------------|-------------|--------------|---------------------|---------|
|                    | Normal                      | IGT        | GDM         | Total        | $\chi^2$            | P Value |
| Yes                | 26 (8.0%)                   | 1 (16.7%)  | 8 (40.0%)   | 35 (10.0%)   | 21.606              | <0.001  |
| No                 | 297 (92.0%)                 | 5 (83.3%)  | 12 (60.0%)  | 314 (90.0%)  |                     |         |
| Total              | 323 (100.0%)                | 6 (100.0%) | 20 (100.0%) | 349 (100.0%) |                     |         |

**Table 6-Association Between EARLY GDM and 'Macrosomic Baby'**

| Macrosomic Baby | 75gm OGTT (First Trimester) |            |             |              | Fisher's Exact Test |         |
|-----------------|-----------------------------|------------|-------------|--------------|---------------------|---------|
|                 | Normal                      | IGT        | GDM         | Total        | $\chi^2$            | P Value |
| Yes             | 29 (9.0%)                   | 2 (33.3%)  | 14 (70.0%)  | 45 (12.9%)   | 64.712              | <0.001  |
| No              | 294 (91.0%)                 | 4 (66.7%)  | 6 (30.0%)   | 304 (87.1%)  |                     |         |
| Total           | 323 (100.0%)                | 6 (100.0%) | 20 (100.0%) | 349 (100.0%) |                     |         |

**Table 7-Association Between EARLY GDM and 'NICU Admission'**

| NICU Admission | 75gm OGTT (First Trimester) |            |             |              | Fisher's Exact Test |         |
|----------------|-----------------------------|------------|-------------|--------------|---------------------|---------|
|                | Normal                      | IGT        | GDM         | Total        | $\chi^2$            | P Value |
| Yes            | 32 (9.9%)                   | 1 (16.7%)  | 10 (50.0%)  | 43 (12.3%)   | 28.131              | <0.001  |
| No             | 291 (90.1%)                 | 5 (83.3%)  | 10 (50.0%)  | 306 (87.7%)  |                     |         |
| Total          | 323 (100.0%)                | 6 (100.0%) | 20 (100.0%) | 349 (100.0%) |                     |         |

**Table 8 - Predictors of GDM Using Logistic Regression Analysis**

| Variable                      | Unadjusted OR | 95% CI    | p-value | Adjusted OR | 95% CI    | p-value |
|-------------------------------|---------------|-----------|---------|-------------|-----------|---------|
| Age (years)                   | 0.96          | 0.86–1.07 | 0.420   | 0.94        | 0.83–1.07 | 0.358   |
| Age group (>25 yrs)           | 1.28          | 0.62–2.65 | 0.500   | 1.10        | 0.50–2.40 | 0.810   |
| Weight (kg)                   | 0.99          | 0.95–1.03 | 0.560   | 0.98        | 0.94–1.03 | 0.475   |
| BMI (kg/m <sup>2</sup> )      | 1.12          | 0.98–1.28 | 0.090   | 1.05        | 0.90–1.22 | 0.520   |
| Family history of diabetes    | 2.10          | 1.05–4.20 | 0.035   | 1.72        | 0.82–3.60 | 0.150   |
| History of macrosomic baby    | 2.80          | 1.20–6.50 | 0.018   | 1.95        | 0.78–4.85 | 0.150   |
| Past history of GDM           | 3.20          | 1.30–7.80 | 0.011   | 1.85        | 0.70–4.90 | 0.210   |
| Past gestational hypertension | 1.65          | 0.70–3.90 | 0.250   | 1.30        | 0.50–3.40 | 0.580   |
| HbA1c (%)                     | 2.10          | 1.05–4.18 | 0.035   | 2.35        | 1.02–5.41 | 0.044   |
| FBS (mg/dL)                   | 1.18          | 1.10–1.27 | <0.001  | 1.21        | 1.12–1.31 | <0.001  |
| 1-hour PPBS (mg/dL)           | 1.02          | 1.00–1.03 | 0.060   | 1.01        | 0.99–1.03 | 0.180   |
| 2-hour PPBS (mg/dL)           | 1.01          | 0.99–1.03 | 0.120   | 1.00        | 0.98–1.02 | 0.600   |
| Fasting insulin               | 1.08          | 1.02–1.15 | 0.010   | 1.04        | 0.98–1.11 | 0.180   |
| HOMA-IR                       | 2.45          | 1.25–4.80 | 0.009   | 2.67        | 1.27–5.62 | 0.010   |

Univariate logistic regression analysis was performed to assess the association between maternal clinical and biochemical parameters in the first trimester and the development of gestational diabetes mellitus (GDM). Among clinical variables, family history of diabetes (OR: 2.10; 95% CI: 1.05–4.20;  $p = 0.035$ ), history of macrosomic baby (OR: 2.80; 95% CI: 1.20–6.50;  $p = 0.018$ ), and past history of GDM (OR: 3.20; 95% CI: 1.30–7.80;  $p = 0.011$ ) were significantly associated with GDM. Age, weight, BMI, and past history of gestational hypertension were not statistically significant. Among biochemical parameters, HbA1c (OR: 2.10;  $p = 0.035$ ), fasting blood sugar (FBS) (OR: 1.18;  $p < 0.001$ ), fasting insulin (OR: 1.08;  $p = 0.010$ ), and HOMA-IR (OR: 2.45;  $p = 0.009$ ) showed significant association with GDM. Postprandial glucose values were not significantly associated. Variables with clinical relevance and/or statistical significance were included in multivariate logistic regression analysis. On multivariate analysis, HbA1c (adjusted OR: 2.35; 95% CI: 1.02–5.41;  $p = 0.044$ ), fasting blood sugar (adjusted OR: 1.21; 95% CI: 1.12–1.31;  $p < 0.001$ ), and HOMA-IR (adjusted OR: 2.67; 95% CI: 1.27–5.62;  $p = 0.010$ ) emerged as independent predictors of GDM. Although clinical risk factors such as family history of diabetes, history of macrosomic baby, and past history of GDM were significant on univariate analysis, they did not retain statistical significance after adjustment.

## DISCUSSION

The current study assessed the predictive value of first trimester biochemical and clinical indicators for gestational diabetes mellitus (GDM). Our results show that HbA1c, HOMA-IR, and fasting blood glucose (FBS) are independent predictors of GDM, while traditional clinical risk factors like prior macrosomia, family history of diabetes, and past GDM were significant on univariate analysis but lost significance after adjustment. FBS was found to be the best predictor of all the factors, and an increase of one unit was linked to a substantial increase in the probability of developing GDM. This result is in line with other research that demonstrated hepatic insulin resistance and  $\beta$ -cell dysfunction are the causes of high fasting glucose in the early stages of pregnancy [22, 23]. Before the traditional diagnosis of GDM at 24–28 weeks, early fasting hyperglycemia probably indicates a preclinical stage of glucose intolerance.

Additionally, HbA1c was shown to be an independent predictor, suggesting that women at higher risk can be identified by even slight increases in early glycemic exposure. Several studies have shown the usefulness of HbA1c in early risk stratification, even if it is not officially advised as a stand-alone diagnostic tool in pregnancy [24, 25].

Insulin resistance plays a key role in the pathophysiology of GDM, as evidenced by the substantial independent connection between GDM and HOMA-IR, a measure of insulin resistance. This is consistent with research that shows early metabolic impairment occurs in women with GDM even before a clinical diagnosis is made [26]. It's interesting to note that after multivariate correction, clinical risk variables such as prior GDM, history of macrosomic babies, and family history of diabetes were not independent predictors. This implies that although these variables are helpful in identifying high-risk groups, biochemical markers may be more accurate in predicting the actual onset of disease. Other studies that found that clinical risk variables alone had low predictive accuracy have revealed similar findings [27, 28]. The comparatively maintained postprandial insulin response during early gestation may be the cause of the lack of correlation with postprandial glucose readings in early pregnancy, with fasting abnormalities manifesting earlier in the illness trajectory. Overall, our results lend credence to the idea that metabolic changes occur before clinical symptoms, and early biochemical screening could offer a more impartial and trustworthy way to identify women who are at risk for GDM.

### CLINICAL IMPLICATIONS

The findings of this study have important implications for clinical practice. First, even before the typical screening window of 24 to 28 weeks, early pregnancy screening utilizing straightforward biochemical indicators like FBS and HbA1c can assist identify women at high risk for GDM. This makes it possible to implement early lifestyle changes that may lower the chance of developing GDM, including as dietary changes and increased physical activity. Second, a more pathophysiology-based risk assessment is made possible by the addition of HOMA-IR, which sheds light on underlying insulin resistance rather than depending solely on demographic characteristics. Third, the findings imply that risk stratification models that include biochemical indicators might be better than conventional risk factor-based screening methods, especially in societies like India that have a high baseline risk. Lastly, early detection of high-risk individuals may enable improved maternal and fetal outcomes, early therapeutic interventions, and closer monitoring, potentially lowering complications including macrosomia, preeclampsia, and cesarean birth.

### CONCLUSION

This study concludes that HbA1c, HOMA-IR, and first trimester fasting blood glucose are important independent predictors of gestational diabetes mellitus. After correction, clinical risk variables such as past obstetric history and family history of diabetes do not independently predict GDM, despite their correlation. These results highlight the significance of early biochemical screening during pregnancy and encourage the creation of a risk prediction model that takes first trimester metabolic markers into account for prompt detection and treatment.

### Author Contributions

**[Author 1]:** Conceptualization, methodology, study design, data collection, data curation, formal analysis, and manuscript preparation. Statistical analysis, interpretation of data, and critical review of the manuscript.

**[Author 2]:** Data collection, investigation, data curation, and literature review.

All authors contributed to the study, reviewed and critically revised the manuscript, approved the final version, and agreed to be accountable for all aspects of the work.

### CONFLICT OF INTEREST – NO

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