

# Clinical Characteristics, Outcomes, and Progression to Type 2 Diabetes in Women with Hyperglycemia in Pregnancy

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## Abstract

**Context:** Women with hyperglycemia in pregnancy (HIP) are at increased risk of developing type 2 diabetes (T2D). **Aim:** The present study intended to study the incidence of postpartum diabetes among HIP women and predict its risk factors. **Settings and Design:** This was a prospective observational study done on 178 women with HIP diagnosed after the first trimester, attending the tertiary care hospitals between December 2018 and March 2020. **Materials and Methods:** Demographics, clinical variables, and fetomaternal outcomes were recorded. The postpartum glycemic status was determined using a 75 g oral glucose tolerance test (OGTT) at 1 and 6 months. **Statistical Analysis:** All analyses were performed with SPSS software (version 21.0). **Results:** The mean age of women with HIP was  $30.2 \pm 6.1$  years, with 38% having a family history of diabetes. Eighty percent of the women delivered full-term babies and 71.3% underwent a cesarean section. Gestational hypertension was present in 21.9% of patients. Macrosomia was present in 4.6% of the babies, hypoglycemia in 6.7%, and spontaneous abortion occurred in 7.7%. Postpartum OGTT at 6 months was completed by 76.4% of participants. The incidence of diabetes and glucose intolerance postpartum was 11.7 and 16.2%, respectively at 6 months. Logistic regression analysis showed that maternal obesity, diagnosis of HIP at an earlier trimester (<24 weeks), need for insulin treatment during pregnancy, signs of insulin resistance and fasting and 2-h plasma glucose >100 (>5.6 mmol/L) and >195 mg/dL (>10.9 mmol/L), respectively, and glycated hemoglobin > 6.5% (>48 mmol/mol) increased the risk of having postpartum diabetes significantly. **Conclusion:** The incidence of postpartum glucose intolerance in women with HIP is high. Prospective diabetes evaluation is required and intervention should be considered in women with HIP who have obesity, diagnosis of HIP at an earlier trimester, signs of insulin resistance, and require insulin treatment during pregnancy.

**Keywords:** Gestational diabetes mellitus (GDM), glucose intolerance, hyperglycemia in pregnancy (HIP), oral glucose tolerance test (OGTT), outcome, postpartum diabetes, type 2 diabetes

## INTRODUCTION

Diabetes has reached a pandemic level and has become a major health challenge. Worldwide around 415 million people have diabetes. As per the International Diabetes Federation (IDF) 2019 report, India has 77 million patients with diabetes and is expected to be 134.2 million by 2045.<sup>[1]</sup> IDF Atlas revealed that around 15.8% (20.4 million) of live births are affected by hyperglycemia in pregnancy (HIP) worldwide, whereas 24% (6.6 million) are affected in South East Asia.<sup>[1]</sup> HIP is the most common metabolic disorder during pregnancy and is increasing worldwide due to advanced maternal age and increasing prevalence of obesity.<sup>[2]</sup> American Diabetes Association (ADA) in 2019 defines gestational diabetes mellitus (GDM) as diabetes diagnosed in the second or third trimester of pregnancy and is not either preexisting type 1 or type 2 diabetes (T2D).

The importance of GDM is that two generations are at risk of future development of diabetes. Nutrigenetics and epigenetics changes in women with GDM increase the subsequent risk of various diseases, including diabetes in offspring.<sup>[3,4]</sup> Women with GDM are not only at higher risk of T2D but also cardiometabolic disorders, including cardiovascular disease, hypertension, and metabolic syndrome.<sup>[5]</sup> Women with GDM

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have 10 fold odds of having T2D as early as 1 year following delivery than those with normoglycemia during pregnancy.<sup>[6]</sup> Various risk factors for developing T2D in GDM are age, race, parity, family history of diabetes, prepregnancy weight, weight gain, and postpartum obesity.<sup>[7]</sup>

Screening for diabetes in pregnancy facilitates better care during pregnancy and provides an opportunity to identify women with future risk of developing T2D.<sup>[8]</sup> The ADA guidelines recommend that women with GDM should undergo screening for persistent diabetes using the 2-h oral glucose tolerance test (OGTT) at 4–12 weeks postpartum.<sup>[9]</sup>

Ethnicity is one of the main determinants of increasing risk for postpartum dysglycemia. South Asians have an earlier and higher postpartum conversion to T2D following GDM than other ethnic groups and varying from 35 to 60%, within 5 years after the index delivery.<sup>[9-13]</sup> The percentage varies with the criteria used for diagnosing GDM, trimester of screening, and postpartum screening rate. The Indian study revealed dysglycemia in 57.7%, diabetes in 10.5%, and prediabetes in 47.2% by ADA criteria at a median of 20 months following the index delivery.<sup>[10,14]</sup> The screening rate was <50% at 6–12 weeks postpartum and the long-term follow-up rate was even less.<sup>[15]</sup> However, the later studies have revealed a lower dropout rate if the protocols are strictly adhered.

Previously, studies from India had studied outcomes and progression of women in GDM but with multiple limitations of being retrospective, using older criteria for diagnosing GDM and small sample size.<sup>[16-18]</sup> Thus, women with GDM are at high risk for reproductive and subsequent metabolic derangements, and early identification will improve health outcomes with the help of both prevention and intervention strategies. So, it would be desirable to identify women at the most significant risk of postpartum T2D during their pregnancy. Therefore, the present study was conducted with the objectives of studying clinical characteristics, outcomes, and the incidence of postpartum diabetes and its risk factors among women with HIP.

## MATERIALS AND METHODS

### Study design and setting

This was a prospective observational study of Indian women aged >18 years diagnosed as HIP and attending the tertiary care hospitals in India. The institutional ethical committee approved the study and informed consent was obtained from all the recruited subjects.

### Sample size and study subjects

The study recruited 178 women diagnosed with HIP, after the first trimester following the Department of Endocrinology and Obstetrics at two centers in India. This study was conducted from December 2018 to March 2020. GDM was diagnosed by the International Association of Diabetes and Pregnancy Study Group (IADPSG) criteria adopted by ADA as 1/2/3 abnormal values ( $\geq 92/180/153$  mg/dL ( $\geq 5.1/10/8.5$  mmol/L) at 0, 1, and 2 h, respectively) on a

75 g OGTT performed in a fasting state after 12 weeks of pregnancy. Blood was also collected for other biochemical parameters, including glycated hemoglobin (HbA1c). For plasma glucose, samples were collected in a fluoride vial, centrifuged immediately, and transported to the laboratory within 1 h of collection. Plasma glucose was analyzed using the hexokinase method with DiaSys (Sysmex BX-3010). HbA1c was measured by high-performance liquid chromatography (D-10TM Hemoglobin A1c Program; Bio-Rad Laboratories). Overt diabetes in pregnancy was defined as fasting plasma glucose (FPG)  $\geq 126$  mg/dL ( $\geq 7$  mmol/L) or 2-h postload glucose (PG)  $\geq 200$  mg/dL ( $\geq 11.1$  mmol/L) and/or HbA1c of  $\geq 6.5\%$  ( $\geq 48$  mmol/mol). The exclusion criteria were: (i) women with preexisting diabetes, (ii) essential hypertension, (iii) medical/surgical conditions that alter glucose metabolism, such as post pancreatectomy, acromegaly, and Cushing's syndrome, (iv) patients on steroids or drugs which affect glucose metabolism including antiepileptics, antiretroviral therapy, antitubercular therapy, (v) preexisting PCOS, and (vi) pregnancy at the time of postpartum OGTT.

All the patients were interviewed regarding demographic details, history of GDM in previous pregnancies, relevant obstetric history, family history of diabetes, parity, and gestational age at diagnosis. Prepregnancy weight was used to calculate the body mass index (BMI). Obesity was defined as a BMI of  $\geq 25$  kg/m<sup>2</sup> based on World Health Organization (WHO) Asia Pacific guidelines. For assessing obesity during pregnancy, the revised Institute of Medicine recommendations define obesity as a BMI  $\geq 30$  kg/m<sup>2</sup>.<sup>[19]</sup> The presence or absence of insulin resistance (acanthosis nigricans/skin tags) was noted. Detailed general and physical examinations were recorded. Ultrasonography (USG) for fetal well being was done.

All women with HIP received nutrition counseling and individualized exercise protocol and oral antidiabetic therapy or insulin treatment. These women had self-monitoring of blood glucose using a glucometer and underwent periodical clinical and biochemical evaluations. The goals of treatment were the same as those recommended by ADA.<sup>[9]</sup>

### Outcome measures

Feto-maternal outcomes were recorded. Maternal outcomes accessed were gestational hypertension, preeclampsia, eclampsia, gestational age at delivery, preterm delivery, antepartum hemorrhage, and postpartum hemorrhage. Uses of insulin or oral antihyperglycemic drugs during HIP were recorded. Birth outcomes recorded were route of delivery (vaginal or cesarean section), fetal birth weight, small for gestational age (SGA), large for gestational age (LGA), neonatal intensive care unit (NICU) admission, hypoglycemia, spontaneous abortion, and stillbirth.

### Postpartum glycemic status

HIP women returned for follow-up and postpartum glycemic status was determined using 75 g of OGTT at 1 and 6 months. Plasma glucose was measured at 0 and 2 h after 75 g of anhydrous glucose dissolved in 250 mL of water

and consumed over 5–10 min. Individuals were classified to have normoglycemia (FPG <100 mg/dL (<5.6 mmol/L), 2-h PG <140 mg/dL (<7.8 mmol/L), and HbA1c <5.7% (<39 mmol/mol)), postpartum impaired glucose as both impaired fasting glucose (IFG) and impaired glucose tolerance (IGT), i.e., FPG between 100 and 125 mg/dL (5.6–6.9 mmol/L) and 2-h PG between 140 and 199 mg/dL (7.8–11 mmol/L) and/or HbA1c 5.7–6.4% (39–47 mmol/mol), while WHO criteria for IFG are FPG between 110 and 125 mg/dL (6.1–6.9 mmol/L) and postpartum diabetes as FPG  $\geq$ 126 mg/dL ( $\geq$ 7 mmol/L) and/or 2-h PG  $\geq$ 200 mg/dL ( $\geq$ 11.1 mmol/L) and/or HbA1c  $\geq$ 6.5% ( $\geq$ 48 mmol/mol).<sup>[9]</sup> HbA1c estimation was done at 6 months postpartum. HbA1c for diagnostic purpose was used only at 6 months. Dysglycemia was defined as IFG or IGT or diabetes.

### Definitions

Gestational hypertension is a systolic blood pressure  $\geq$ 140 mmHg or a diastolic blood pressure  $\geq$ 90 mmHg, on two occasions at least 4-h apart in previously normotensive women, without significant proteinuria and diagnosed after 20 weeks of gestation. Preeclampsia was defined as gestational hypertension with a 24-h urine protein of  $\geq$ 300 mg. Eclampsia was defined as preeclampsia with seizures that could not be attributable to other causes. Polyhydramnios was diagnosed when the amniotic fluid index was  $>$ 95<sup>th</sup> percentile for a given gestational age on USG. Preterm delivery was defined as delivery  $<$ 37 weeks of gestation; neonatal hyperbilirubinemia as plasma levels exceeding 12 mg/dL. Antepartum hemorrhage is bleeding from the vagina that occurs after 20 weeks of pregnancy but before delivery, while postpartum hemorrhage was defined as  $>$ 500 mL of blood loss within the first 24 h after childbirth.

Loss of fetus  $\leq$ 20 weeks of pregnancy was referred to as a spontaneous abortion, while stillbirth refers to the loss of a baby  $>$ 20 weeks of gestation. SGA is a birth weight that is below the 10<sup>th</sup> percentile for a given gestational age or weighs  $\leq$ 2500 g at birth. LGA refers to neonatal birth weight  $>$ 90<sup>th</sup> percentile for a given gestational age. The newborn weighing  $>$ 3.5 kg was considered macrosomia as per Indian consensus.<sup>[20]</sup> Neonatal hypoglycemia was defined as capillary glucose  $<$ 45 mg/dL. The neonatal capillary glucose monitoring was done via glucometer for the first 24 h.

### Statistical analysis

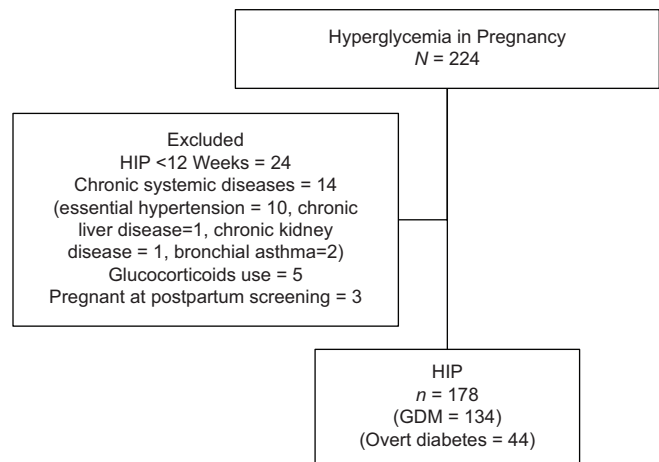
Qualitative variables were expressed as a proportion, while quantitative variables were expressed as means  $\pm$  standard deviation. Descriptive and univariate analytic techniques were used to analyze the data. Chi-square test or Fisher's exact tests were used to compare categorical variables, whereas Student's *t*-test for independent observations was used for continuous variables. Binary logistic regression analysis was carried out to calculate multivariate *P* value for various independent variables. *P* values  $<$  0.05 were considered statistically significant. All the analyses were performed by the statistical software SPSS Version 21 (IBM SPSS Statistics for Windows, version 21 Armonk, NY, USA: IBM Corp.).

## RESULTS

After applying the exclusion criteria, there were 178 participants, as shown in Figure 1. GDM was present in 134 (75.3%) and overt diabetes in 44 (24.7%) of study cohort. Table 1 shows the demographic and laboratory profile of women with HIP. The mean age was  $30.2 \pm 6.1$  years at the time of diagnosis. Prepregnancy obesity was present in 29.2% and the previous history of GDM was present in 20.2% of subjects.

### Perinatal outcome

Table 2 shows the maternal outcome in women with HIP. Gestational hypertension was present in 21.9%. Polyhydramnios was present in 9% and preterm delivery



**Figure 1:** Flow diagram of study participants. HIP: hyperglycemia in pregnancy; GDM: gestational diabetes mellitus

**Table 1: Demographic and laboratory profile of patients with hyperglycemia in pregnancy (n=178)**

Variables	No. of patients
Maternal age (years)	30.2 $\pm$ 6.1
Prepregnancy weight (kg)	62.7 $\pm$ 9.2
Prepregnancy obesity	46 (25.8)
Obesity in pregnancy	52 (29.2)
Primigravida	94 (52.8)
Multigravida	84 (47.0)
Singleton pregnancy	161 (90.5)
Twin pregnancy	17 (9.5)
History of abortion	29 (16.3)
Family history of diabetes	69 (38.7)
Previous history of GDM	36 (20.2)
Laboratory	
FPG (mg/dL) [mmol/L]	110.8 $\pm$ 23.7 [6.6 $\pm$ 1.3]
1-h PG (mg/dL) [mmol/L]	204.2 $\pm$ 40.8 [11.3 $\pm$ 2.3]
2-h PG (mg/dL) [mmol/L]	189.6 $\pm$ 48.1 [10.5 $\pm$ 2.7]
HbA1c (%) [mmol/mol]	6.6 $\pm$ 1.7 [48.6]
GDM	134 (75.3)
Overt diabetes	44 (24.7)

*Categorical variables [n (%)] and Continuous variables [mean $\pm$ SD].*  
GDM: gestational diabetes mellitus, FPG: fasting plasma glucose, PG: postload glucose, HbA1c: glycated hemoglobin

occurred in 20.2%. Full-term delivery occurred in 79.8%, with LSCS in 65.7%, while only 18.5% had a normal vaginal delivery.

Table 3 shows the fetal outcomes, which was accessed in 195 cases as 9.5% of HIP women had twin pregnancy. The stillbirths, macrosomia, and NICU admissions occurred in 4.6, 4.6, and 9.2%, respectively. The spontaneous abortion and hypoglycemia was 7.7 and 6.7%, respectively.

### Postpartum glycemc outcome (1, 6 months)

Table 4 reveals the postpartum glycemc status of HIP women at 1 and 6 months. One hundred forty-eight (83.1%) and 136 (76.4%) HIP women followed at 1 and 6 months, respectively. Normal glycemc was present in 81.8 and 72.1% of HIP women at 1 and 6 months, respectively. Postpartum dysglycemc occurred in 27 (18.2%) and 38 (27.9%) at 1 and 6 months, respectively. As per WHO criteria, postpartum impaired glucose (IFG + IGT) was present in 8.1 and 13.9%, respectively, whereas as per ADA, impaired glucose was seen in 10.8 and 16.2%, respectively, at 1 and 6 months. Postpartum diabetes was present in 7.4 and 11.7% at 1 and 6 months, respectively.

### Factors predictive of postpartum diabetes

Table 5 reveals the factors predicting postpartum diabetes at 6 months. These factors are maternal age at diagnosis, obesity in pregnancy, diagnosis of HIP early in pregnancy (<24 weeks), overt diabetes at diagnosis, need for insulin treatment during pregnancy, signs of insulin resistance, FPG and HbA1c predict postpartum diabetes at 6 months ( $P < 0.05$ ). HIP screening using the IADPSG criteria for glycemc at 1 and 2 h, a correlation was observed with 2-h PG only for postpartum diabetes. No correlation was observed for the previous history of GDM, family history of diabetes, and gravidity.

Table 6 shows the variables predictive of postpartum diabetes on multiple logistic regression analysis. Obesity in pregnancy, diagnosis of HIP early in pregnancy, need for insulin treatment during pregnancy, signs of insulin resistance, FPG >100 mg/dL (>5.6 mmol/L), 2-h PG >195 mg/dL (>10.9 mmol/L), and HbA1c >6.5% (>48 mmol/mol) predict postpartum diabetes at 6 months ( $P < 0.05$ ). We used cutoff values of 100 mg/dL (area under the curve [AUC] 0.62), 195 mg/dL (AUC 0.58), and 6.5% (AUC 0.70) for FPG, 2-h PG, and HbA1c, respectively, which were derived from the ROC. The sensitivity of FPG cutoff was 70.4%, with specificity of 64% and positive predictive value of 78.6%, while for 2-h PG and HbA1c, sensitivity, specificity, and positive predictive values were 71.1, 60.8, and 71.8% and 82, 100, and 100%, respectively.

## DISCUSSION

HIP is linked to adverse perinatal outcomes and detrimental long-term health events in mothers and offspring. There is a global variation in the risk of T2D after HIP. A conversion rate to postpartum diabetes varies from 2.6 to 70%, depending on diagnostic criteria, protocols used, duration of follow-up, and

**Table 2: Maternal outcome in patients with hyperglycemia in pregnancy (n=178)**

Variables	No. of patients n (%)
Gestational hypertension	39 (21.9)
Preeclampsia	12 (6.7)
Eclampsia	2 (1.1)
Polyhydramnios	16 (9.0)
Preterm delivery	36 (20.2)
Antepartum hemorrhage	19 (10.7)
Postpartum hemorrhage	15 (8.4)
Mode of delivery	
LSCS	117 (65.7)
Instrumental	28 (15.8)
Normal vaginal delivery	33 (18.5)
Full-term delivery	142 (79.8)

GDM: gestational diabetes mellitus; LSCS: lower-segment caesarian section

**Table 3: Neonatal outcome in patients with hyperglycemia in pregnancy (n=195)**

Variables	No. of cases n (%)
Baby birth weight (g)	3061±586
NICU admission	18 (9.2)
SGA	28 (14.3)
LGA	23 (11.7)
Macrosomia	9 (4.6)
Hyperbilirubinemia	17 (8.7)
Hypoglycemia	13 (6.7)
Spontaneous abortion	15 (7.7)
Stillbirth	9 (4.6)

NICU: neonatal intensive care unit; SGA: small for gestational age; LGA: large for gestational age

**Table 4: Postpartum glycemc status of hyperglycemia in pregnancy patients at 1 and 6 months**

Diagnosis	1 month n=148	6 months n=136
Normal	121 (81.8)	98 (72.1)
Postpartum impaired glucose	16 (10.8)	22 (16.2)
Postpartum diabetes	11 (7.4)	16 (11.7)

ethnicity.<sup>[21]</sup> GDM is the risk factor for T2D and may even represent an impending stimulus in the natural course of T2D, which occurs as a result of acquired insulin resistance along with a defect in beta-cell compensation. Also, women with GDM and T2D have many similar environmental and genetic risk factors.<sup>[22]</sup> One-third of women with T2D have preceding GDM occurrence.<sup>[23]</sup> Thus, ADA and the ACOG recommend that women with GDM be tested for glucose intolerance from 4 to 12 weeks postpartum and then followed. Therefore, this study analyzed the perinatal outcome, incidence of postpartum diabetes, and its risk factors among women with HIP.

In our study, gestational hypertension was present in 21.9%, polyhydramnios in 9%, and preterm delivery occurred in 20.2%



**Table 5: Factors predicting postpartum diabetes at 6 months**

Parameters	Normal n=98	Postpartum diabetes n=16	P*
Maternal age at diagnosis (years)	29.4±4.5	32.1±5.3	0.032
Maternal age ≥35 years	20 (20.4)	8 (50.0)	0.011
Prepregnancy obesity	20 (20.4)	7 (43.8)	0.057
Previous history of GDM	16 (16.3)	5 (31.2)	0.155
Family history of diabetes	36 (36.7)	9 (56.3)	0.138
Parity			
1	49 (50.0)	9 (56.2)	0.647
2	32 (32.7)	4 (25.0)	0.540
3	17 (17.3)	3 (18.7)	0.892
Signs of insulin resistance	11 (11.2)	7 (43.8)	0.001
Gestational age at diagnosis (weeks)	22.7±5.2	19.2±4.9	0.013
Diagnosis of HIP early in pregnancy (<24 weeks)	26 (26.5)	10 (56.3)	0.017
Overt diabetes	24 (24.9)	8 (50.0)	0.039
Need for insulin treatment during pregnancy	41 (41.8)	13 (81.3)	0.003
Obesity in pregnancy	21 (21.4)	8 (50.0)	0.015
Twin pregnancy	7 (7.1)	3 (18.7)	0.292
Macrosomia	4 (4.1)	2 (12.5)	0.165
Polyhydramnios	8 (8.2)	3 (18.7)	0.185
Gestational hypertension	15 (15.3)	4 (25.0)	0.336
Gestational age at delivery (weeks)	38.6±1.8	37.9±1.4	0.141
Stillbirth	5 (5.1)	2 (12.5)	0.255
FPG (mg/dL) [mmol/L]	88.8±19.3 [4.9±1.1]	120.7±26.2 [6.7±1.5]	<0.001
1-h PG (mg/dL) [mmol/L]	197.9±24.1 [11.0±1.3]	211.3±32.7 [11.7±1.8]	0.053
2-h PG (mg/dL) [mmol/L]	172.1±23.7 [9.6±1.3]	214.8±41.4 [11.9±2.3]	<0.001
HbA1c (%) [mmol/mol]	5.9±1.1 [41.0]	7.8±2.3 [61.7]	<0.001

Categorical variables [n (%)] and Continuous variables [mean±SD]. \*P<0.05 is considered statistically significant. GDM: gestational diabetes mellitus; HIP: hyperglycemia in pregnancy; FPG: fasting plasma glucose; PG: postload glucose, HbA1c: glycated hemoglobin

**Table 6: Variables predictive of postpartum diabetes on multiple logistic regression analysis**

Variables	P*	Odds ratio (95% CI)
Maternal age ≥35 years	0.115	1.03 (0.96-1.31)
Obesity in pregnancy	0.033	1.42 (1.07-3.32)
Diagnosis of HIP early in pregnancy (<24 weeks)	0.044	1.24 (1.03-2.35)
Overt Diabetes	0.126	0.98 (0.94-1.23)
Need for insulin treatment during pregnancy	0.021	1.72 (1.13-4.24)
Signs of insulin resistance	0.019	2.50 (1.24-8.70)
FPG >100 mg/dL	0.017	2.72 (1.82-12.36)
2-h PG >195 mg/dL	0.019	2.35 (1.20-10.40)
HbA1c >6.5%	0.007	5.62 (3.02-19.44)

\*P<0.05 is considered statistically significant. HIP: hyperglycemia in pregnancy; FPG: fasting plasma glucose; PG: postload glucose; HbA1c: glycated hemoglobin

of study participants. Caesarian section was required in 65.7% of women. The stillbirths, macrosomia, and NICU admissions occurred in 4.6, 4.6, and 9.2%, respectively. The spontaneous abortion and hypoglycemia was 7.7 and 6.7%, respectively. Perinatal outcome varies with the characteristics of studied population, early identification, aggressive management, and achievement of glycemic goal. The study by Kumari et al.<sup>[18]</sup> revealed cesarean delivery occurred in 50%, gestational hypertension in 13.5%, LGA babies in 28.2%, and neonatal

hypoglycemia in 20.6%. Another Indian study revealed that 25% developed gestational hypertension, 9% developed preeclampsia, 44% required cesarean section, 16.4% babies were LGA, 2.1% babies were macrosomic, 4.1% developed neonatal hypoglycemia, and 20% required NICU admission.<sup>[17]</sup> Spontaneous abortion, stillbirth, preterm delivery, and neonatal hypoglycemia occurred in 8.7, 2.8, 11, and 10.4%, respectively, whereas 65% underwent a cesarean section in another study.<sup>[16]</sup>

The postpartum glucose tolerance outcomes studies from South Asia have reported dysglycemia rates of 15–58% at varying follow-up, ranging from 6 weeks to 20 months using IADPSG criteria.<sup>[10,14,24]</sup> The cumulative incidence of postpartum T2D among women with GDM is relatively high in South Asia.<sup>[11]</sup> In our study, postpartum dysglycemia occurred in 18.2 and 27.9% at 1 and 6 months, respectively. An Indian study revealed that 15.5% of women had dysglycemia by 12 weeks, while 38.1% were detected to have dysglycemia between 12 weeks and 1 year of delivery.<sup>[10]</sup> Similarly, 33.8% developed an abnormal OGTT at 6 weeks postpartum in another study.<sup>[24]</sup> This indicates the importance of early screening for T2D in HIP women. It also shows the value of screening within 1-year window period in women who missed the screening or screened negative at 12 weeks postpartum.<sup>[10]</sup> Furthermore, these women will need lifelong follow-up at various intervals as recommended by multiple guidelines.

In our study, the overall incidence of T2D was 7.4 and 11.7% at 1 and 6 months, respectively, on postpartum screening. The study on Asian Indian women revealed that 1.2% developed postpartum diabetes between 6 and 12 weeks and 11.9% developed diabetes within a year of follow-up, which is lower than ours at 1 month, but similar at later follow-up.<sup>[10]</sup> Another Indian study found that 6.4% had T2D at 6 weeks postpartum.<sup>[21]</sup> Our results confirm previous findings from India, indicating that women with GDM are at high risk of either prediabetes or T2D in the early postpartum period.<sup>[10,12,14,24]</sup> ATLANTIC-DIP study reported dysglycemia in 26% as per ADA criteria at a mean interval of 2.6 years in 270 Irish women.<sup>[25]</sup> Our study cohort had a similar dysglycemia (27.9%) compared to European population, despite the study population being younger (mean age 30.2 vs. 36.6 years) but followed up at a shorter postpartum interval (6 vs 30 months).

### Factors related to postpartum diabetes

T2D is a vital sequel of HIP, so close postpartum follow-up is essential. It is critical to identify women at the most significant risk of postpartum T2D to help plan prevention and intervention strategies to improve health outcomes, as proper postpartum follow-up protocol is lacking. In our study, the variables predictive of postpartum diabetes at 6 months are obesity in pregnancy, diagnosis of HIP early in pregnancy, need for insulin treatment during pregnancy, signs of insulin resistance, FPG >100 mg/dL, 2-h PG >195 mg/dL, and HbA1c >6.5% [Table 6].

Other global and South Asian studies have shown that increased maternal age at the time of testing, obesity, positive family history of diabetes, previous history of GDM, insulin use during the index pregnancy, higher FPG and HbA1c, weight gain during pregnancy, and birth weight of the baby were found to predict glucose intolerance at the follow-up testing.<sup>[14,16,26]</sup>

Many of the predictors identified in this study have been evaluated previously, although with varying results. Age is the important risk factor for the development of GDM and T2D<sup>[27]</sup>; however, not all studies have described an association between age at diagnosis of GDM and an increased risk of postpartum glucose intolerance.<sup>[10,28-30]</sup> Studies have observed that women in whom GDM is diagnosed at early gestational had an increased risk of postpartum diabetes than those diagnosed late in pregnancy.<sup>[28,31]</sup> Insulin requirement in GDM management has been inconsistently associated with postpartum diabetes. The use of insulin in women with GDM depends on protocols followed and doctor/patient preference. Therefore, the association is inconsistent in different study populations, but as the GDM is diagnosed at earlier gestational age and diabetes is overt, the use of insulin is obvious, as was seen in our study.<sup>[24,30,31]</sup> Several studies have revealed maternal BMI and obesity at baseline as an independent risk factor for postpartum dysglycemia in global and South Asian women.<sup>[30,32]</sup> A study from India reported that BMI of  $\geq 25$  kg/m<sup>2</sup> was one of the main predictors of postpartum glucose abnormalities.<sup>[10]</sup>

Similarly, FPG during OGTT was predictive of postpartum glucose intolerance in most of the studies.<sup>[28,31,33,34]</sup> One study reported that FPG of >102 mg/dL was predictive of abnormal postpartum glucose metabolism.<sup>[35]</sup> Two-hour PG after OGTT<sup>[29,31,36]</sup> and HbA1c are also reported to predict diabetes following GDM.<sup>[14,29,36]</sup> Although other traditional risk factors demonstrated a trend toward an increased risk for postpartum diabetes. Our study found no statistically significant association between previous GDM,<sup>[10,33,34]</sup> family history of diabetes,<sup>[10,33]</sup> gravidity,<sup>[33]</sup> and prepregnancy BMI.<sup>[30,34]</sup> This could probably be due to the smaller sample size.

In our study, 83.1 and 76.4% of women with HIP followed at 1 and 6 months, respectively, for OGTT, whereas other Indian studies revealed 95.8 and 82.7% follow-up rates, which surpasses typically expected rates of follow-up seen in global studies.<sup>[10,24]</sup> The higher follow-up rates could be because these HIP women were constantly reminded to return for postpartum screening during their pregnancy.

The main limitation of our study is the lack of a defined control group against which comparisons could be drawn. The relatively small number of women with T2D in this study should be considered when interpreting our findings. Another limitation is that we did not include postpartum diet, physical activity, and breastfeeding assessment in the protocol as it could influence the risk of T2D and also the postpartum follow-up duration was short. Other limitation was that the sensitivity analysis comparing the characteristics of women who participated and those who did not participate in the study was not carried out, which will have helped reduce selection bias.

### CONCLUSION

To conclude, Indian women with HIP remain at significantly high risk and rapid conversion to diabetes in the early postpartum follow-up, confirming and extends previous observations. Identification of antepartum risk factors in advance is crucial for preventing prediabetes and the onset of T2D. Early screening in the postpartum period, particularly in women with HIP having obesity during pregnancy, diagnosis of HIP at an earlier trimester (<24 weeks), signs of insulin resistance, and require insulin treatment during pregnancy, will identify these women and help in the implementation of targeted intervention. Future strategies should focus on to improve postpartum screening rates and introduction of alternative methods to cumbersome OGTT for glycemia evaluation and implementation of a lifestyle intervention program in women with GDM to reduce the risk of postpartum dysglycemia.

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## Conflicts of interest

There are no conflicts of interest.

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