

## GESTATIONAL DIABETES: PERINATAL AND MATERNAL COMPLICATION IN 24-28 WEEKS

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### ABSTRACT

**Background:** Gestational diabetes mellitus (GDM) is a glucose tolerance disorder that occurs or is diagnosed for the first time during pregnancy. Perinatal morbidity is more and women with GDM have more risk of developing diabetes. Uttar Pradesh is a state of India with one of the highest rate of infant as well as maternal mortality which might be, at least partially, due to GDM. Thus, appropriate assessment and management of GDM can improve the outcomes.

**Aims & Objectives:** Primary objective of this study was to determine the prevalence of GDM and evaluate the maternal and fetal outcome in and around Kanpur. Thus, this study was undertaken to know the extent of burden on the healthcare, before scope of intervention could be defined.

**Materials and Methods:** A prospective study (September, 2012 - October, 2014) was done at 198 healthcare facilities. 24,656 mothers were screened (24<sup>th</sup>- 28<sup>th</sup> weeks of pregnancy) as per guidelines of Diabetes in Pregnancy Study Group India (DIPSI) and Federation of Obstetric and Gynecological Societies of India (FOGSI).

**Results:** > 94% pregnant women did not know about GDM. Prevalence of GDM was 14.42%. Stillbirth, Perinatal & neonatal mortality were respectively 2, 3.3 & 6 times higher in GDM. Most of the GDM were diagnosed in primigravida (62%). Congenital Malformation was 8 times higher. Low Birth Weight (LBW) was 35% in GDM (16% in Non GDM). GDM positive cases had 20.6% positive family history of diabetes (compared to 6.5% in non-GDM). Relative risks for PBU (post birth unit), LGA (large for gestational age), LBW (low birth weight), pre-eclampsia and jaundice were also higher.

**Conclusion:** A well predictive screening criteria is needed. As the ignorance about GDM among pregnant ladies is high, to reduce the risk, awareness can be an area of thrust.

**Key Words:** Pregnancy; Gestational Diabetes; Perinatal Complication; Maternal Complication; 24-28 Weeks

### Introduction

Gestational diabetes mellitus (GDM) is a glucose tolerance disorder that occurs or is diagnosed for the first time during pregnancy and is one of the most common pregnancy complication.<sup>[1]</sup> The prevalence of GDM has increased in all racial/ethnic groups.<sup>[2]</sup>

During the next 2 decades, the world population is expected to increase by 37%, but the prevalence of diabetes would increase by 114%. More bothersome is a 151% projected increase in number of people with diabetes vis a vis just a 40% projected increase in population of India during the same period.<sup>[3]</sup>

In GDM, perinatal morbidity is more and, in the long-term, women with GDM have an almost sevenfold increased risk of developing type 2 diabetes after pregnancy.<sup>[4]</sup> Gestational impaired glucose tolerance (IGT) is also associated with both pregnancy complications and subsequent diabetes and cardiometabolic risk.<sup>[1]</sup>

It is therefore highly important that these mothers are diagnosed during pregnancy, and that they have a regular postpartum follow-up for identification and treatment of any complications.

The factors that have been postulated to influence the risk of GDM among mothers include a positive family history of diabetes, treatment for infertility, recurrent, urinary tract infections, macrosomic infant, unexplained neonatal death, prematurity, pre-eclampsia, diabetes in previous pregnancy, and advancing maternal age.<sup>[5]</sup>

But race/ethnicity and obesity are the two strongest independent risk factors for GDM. Asians and Philippines are most effected races while blacks are least vulnerable.<sup>[1]</sup> It is also seen that Asians had a higher reported prevalence of diabetes at lower BMI levels than all other racial/ethnic groups.<sup>[6]</sup>

However, the demographic distribution of obesity (highest among African Americans and lowest among Asians) does not mirror the demographic distribution of GDM (lowest among African Americans and highest

among Asians)<sup>[1]</sup> – might be due to interference of other confounding factors like race/ ethnicity.

Even the definition of obesity is debated. The World Health Organization proposed a BMI cutoff of 23.0 kg/m<sup>2</sup> for overweight among Asians in 2000, compared with a cutoff of 25.0 kg/m<sup>2</sup> for non-Asian populations.

The same is true for the definition of GDM – if Asians have higher post-challenge glucose levels than other race/ethnic groups, it is possible that the current screening method for diagnosing GDM, a 50-g post challenge test, may favor diagnosis among Asians across BMI categories (which could have been lower if fasting blood sugar level is included as a criteria).<sup>[1]</sup>

In addition to higher risk of perinatal morbidity, the offspring of mothers with GDM face increased risk of childhood obesity and early onset of type 2 diabetes mellitus. GDM is a condition that can be effectively controlled, thereby decreasing the associated risks, and eventually leading to the delivery of healthy infants.

Uttar Pradesh is the largest state in India with a population of 230 million and expectedly 4.5 million pregnancies every year. Added to this, is the fact that this state has one of the highest maternal mortality rate of 359 per lakh, just second to Assam at 390 – national average being 212!<sup>[7]</sup> Side by side, infant mortality rate too in Uttar Pradesh is one of the highest in the country. Infant mortality rates (IMR) is defined as the number of deaths of children less than one year of age per 1,000 live births. It is 53 for Uttar Pradesh, against national average of 42 – just as the fourth ranker following behind the first three rankers viz. Madhya Pradesh (56), Assam (55) and Orissa (53)!<sup>[8]</sup> The MMR and IMR might be having its causation, at least partially, in the GDM. Thus, appropriate management of GDM will improve both maternal and perinatal outcomes too.<sup>[5]</sup>

Primary objective of this study was to determine the prevalence of GDM and evaluate the maternal and fetal outcome in and around Kanpur. Thus, this study was undertaken to know the extent of burden on the healthcare, before scope of intervention could be defined.

## Materials and Methods

A prospective study from September, 2012 to October, 2014 was done at 198 healthcare facilities in antenatal mothers and 24,656 mothers were screened in their 24<sup>th</sup> to 28<sup>th</sup> weeks of pregnancy by impaired oral glucose

tolerance test (OGTT), as per guidelines of Diabetes in Pregnancy Study Group India (DIPSI) and Federation of Obstetric and Gynecological Societies of India (FOGSI).

DIPSI has prescribed a single test procedure to diagnose GDM in the community and it measures only 2 hours post-glucose (75 gm) > 140mg/ dl by GOD-POD method to screen positive for GDM.<sup>[9]</sup>

This cascading effect is advantageous as this would not result in false-positive diagnosis of GDM. This single-step procedure has been approved by Ministry of Health, Government of India and also recommended by WHO. Advantages of the DIPSI procedure are<sup>[9]</sup>:

- Pregnant women need not be fasting
- Causes least disturbance in a pregnant woman's routine activities
- Serves as both screening and diagnostic procedure.

Performa Accu check Glucometer from Roche were used and 75 gm Glucose Packets were prepared at our own center and distributed along with glucometers and strips, lancets, glass, spoon etc to all 198 Reporting health facilities.

Out of these 198 – 139 were in private hospitals and 59 in government health facilities including CHCs (Community Health center), PHCs (Primary health Center), UHP (Urban health Post), D-type center, UFWCs (Urban family Welfare Centres), District hospitals and other 4 major hospitals in Public sector.

Criteria for exclusion from the study were as follows:

- unwilling to participate in the study
- twin pregnancy/ abnormal lie or other known complications
- known cases of diabetes even before conception
- un-accessible in the given period of 24<sup>th</sup> to 28<sup>th</sup> week of gestation.

## Results

First of all, demographic profile of the GDM and non-GDM patients like age, BMI, nationality, parity, family history of diabetes, blood pressure and OGTT results were noted.

During the total study period of September, 2012 to September, 2014, > 55,000 women were supposed to be registered for pregnancy on 198 health centers in and around Kanpur, Uttar Pradesh, India.

**Table-1: Perinatal mortality in GDM versus non-GDM in pregnancy**

	GDM (N=856)	Rate	Non GDM (N=900)	Rate	P value	RR	OR
Still births	24	2.8%	12	1.33%	<0.0418	2.103	2.13 (1.06-4.29)
Neonatal deaths	28	3.2%	5	0.55%	<0.0001	5.888	6.05 (2.32-15.75)
Total Perinatal deaths	52	6.1%	17	1.9%	<0.0001	3.216	3.36 (1.92-5.85)

**Table-2: Maternal and Foetal outcome in GDM versus non-GDM mothers**

	GDM (N=856)	Non-GDM (N=900)	P Value	OR
Stillbirths	24 (2.80%)	12 (1.33%)	0.0449	2.13 (1.06-4.29)
Neonatal Deaths	28 (3.27%)	5 (0.55%)	0.0001	6.05 (2.32-15.75)
Perinatal Deaths	52 (6.07%)	17 (1.88%)	0.0001	3.36 (1.92-5.85)
Congenital Malformation	16 (1.87%)	2 (0.22%)	0.0005	8.55 (1.96-37.32)
Caesarean Section	445 (51.99%)	369 (41.00%)	0.0001	1.45 (1.2-1.75)
PBU care	82 (9.58%)	10 (1.11%)	0.0001	9.43 (4.85-18.31)
LGA	11 (1.29%)	1 (0.11%)	0.0027	11.7 (1.51-90.9)
LBW	302 (35.28%)	140 (15.55%)	0.0001	2.94 (2.18-3.96)
Preeclampsia	44 (5.14%)	27 (3.00%)	0.0290	1.75 (1.07-2.86)
Jaundice	29 (3.39%)	7 (0.77%)	0.0001	4.47 (1.95-10.27)

**Table-3: Perinatal Mortality as a function of Blood Sugar Value and its comparison with history of Previous Foetal loss**

Blood sugar value OGTT	Perinatal Mortality		P Value
	Present	Previous	
100-119 (n=283)	7 (3%)	7 (2.4%)	0.85
120-139 (n=317)	4 (1.26%)	12 (3.8%)	0.07
140-159 (n=445)	20 (4.5%)	111 (25%)	0.0001
160-179 (n=162)	11 (6.7%)	32 (20%)	0.0008
180-199 (n=95)	8 (8.4%)	15 (15.5%)	0.20
200->200 (n=154)	13 (8.4%)	21 (13.5%)	0.21

**Table-4: Maternal and Foetal outcome in GDM versus non-GDM & Its Relationship with History of Previous birth complications**

	GDM (N=856)	Previous Foetal Loss	P Value	Non-GDM (N=900)	Previous Foetal loss	P value
Stillbirths	24 (2.8%)	190 (22.2%)	0.0001	12 (1.33%)	32 (3.6%)	0.0038
Neonatal Deaths	28 (3.27%)	18 (2.1%)	0.6005	5 (0.55%)	3 (0.33%)	0.7364
Perinatal Deaths	52 (6.1%)	126 (14.72%)	0.0001	17 (1.8%)	36 (4%)	0.0094
Congenital Malformation	16 (1.9%)	4 (0.47%)	0.11	2 (0.22%)	2 (0.22%)	0.6104
Caesarean Section	445 (52%)	0	0	369 (41%)	0	0
PBU care	82 (9.6%)	0	0	10 (1.1%)	0	0
LGA	11 (1.3%)	0	0	1 (0.1)	0	0
LBW	302 (35%)	0	0	140 (15.5%)	0	0
Preeclampsia	44 (5.1%)	0	0	27 (3%)	0	0
Jaundice	29 (3.4%)	0	0	7 (0.77%)	0	0

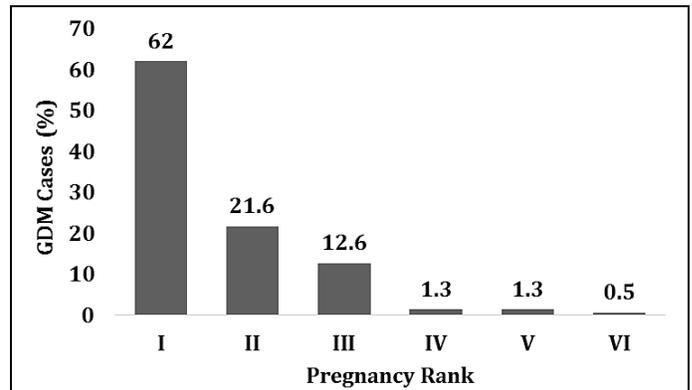


Figure-1: Pregnancy rank versus GDM cases

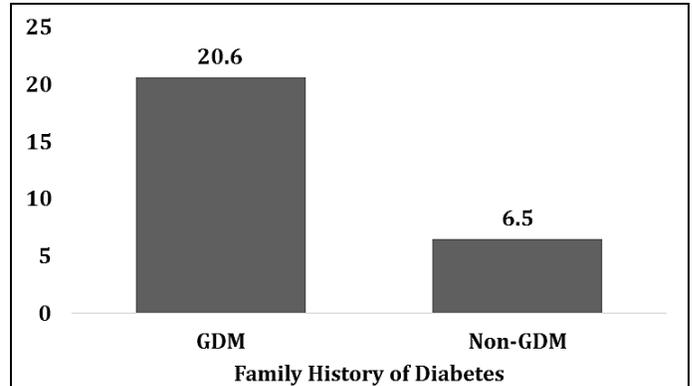


Figure-2: Family History of diabetes in GDM and non-GDM pregnancies

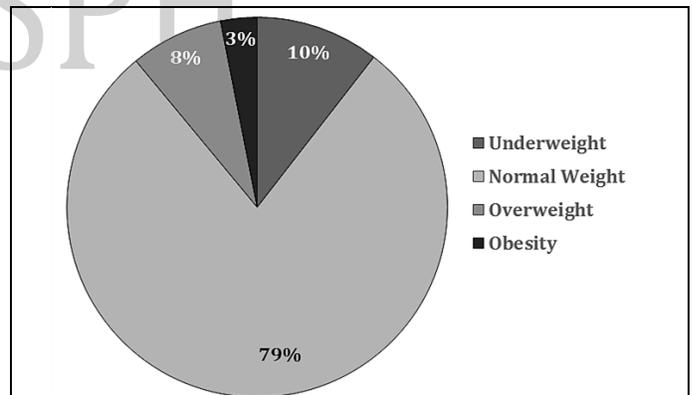


Figure-3: BMI in GDM versus non-GDM pregnancies

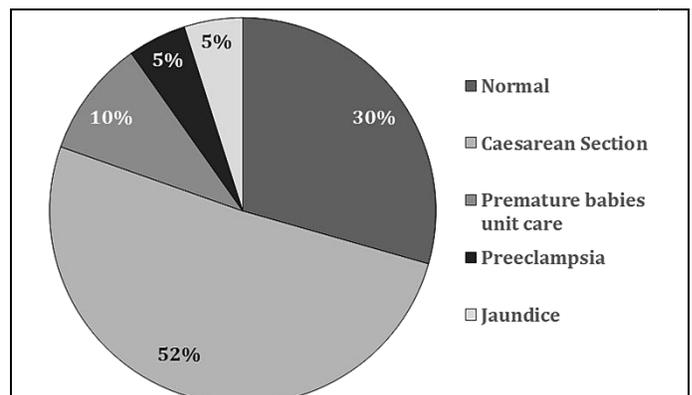


Figure-4: Feto-maternal outcome data

By the end of the year of study in September, 2013 – 18,556 pregnancies were personally screened in this study with confirmed 2,517 cases of GDM (a prevalence of 13.6%).

It was found that > 94% pregnant women in Uttar Pradesh do not know about GDM. Yet, more than 70% reporting women in Uttar Pradesh now receive at least one antenatal Care, and out of these reporting women, 67% deliveries are institutional deliveries.

Out of 24, 656 pregnancies screened by December, 2013 – 3,561 were screened positive on OGTT (as per DIPSI guideline) – thus the recent most prevalence of GDM was found to be 14.42%. After application of exclusion criteria, 856 patients were finally followed – for whom, age and BMI matched 900 controls were also selected for parallel comparative assessment.

Stillbirth, Perinatal & neonatal mortality were respectively 2, 3.3 & 6 times higher in GDM, compared to non-GDM. Most of the GDM positive cases were observed in the very first pregnancy i.e. primigravida cases (62%). Congenital Malformation was 8 times higher in GDM Women compared to Non-GDM. Low Birth Weight (LBW) was 35% in GDM Compare to 16% in Non GDM, which was significantly different – showing an increased relative risk for LBW in GDM. It's notable that LBW is a major cause of neonatal death and contributes in infant mortality rate and may be a confounding factor in calculation of isolated association.

Malformation in women with GDM is significantly higher compare with Non GDM case. GDM positive cases had 20.6% positive family history of diabetes. Mean blood pressure did not differ significantly in pregnant women with or without GDM. Among those who were diagnosed with GDM, rates of perinatal mortality, still births, neonatal deaths, congenital malformation, large for gestational age (LGA), cesarean section, post birth unit (PBU) care, jaundice were significantly higher compare to those without gestational diabetes.

Event of maternal mortality, Low birth weight and pregnancy induced hypertension (PIH) were not statistically significantly different, although PIH was 5.1% in gestational diabetes group and 3% in Non GDM group.

Perinatal mortality increased with Increase in Blood Sugar (OGTT) value and Perinatal mortality reduced

significantly in Intervention with Diet and exercise compare with history of perinatal mortality.

Though, non-pharmacological preventative therapy may not always be possible because of age, presence of various diabetic complications (hypertension, heart disease, retinopathy), and comorbid conditions (osteoarthritis, obesity).<sup>[10]</sup>

It was also found in our study that out of 16 stillbirths, 7 had pre-gestational diabetes and blood sugar OGTT value was > 200 mg %, while remaining 9 had blood sugar between 140 mg% to 200 mg%. Congenital malformation was significant cause of perinatal mortality. One maternal death was observed in GDM and Non GDM group each.

## Discussion

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with the onset or first recognition during pregnancy with or without remission after the end of pregnancy.<sup>[11]</sup> Compared to European women, the prevalence of gestational diabetes has increased 11-fold in women from the Indian subcontinent.<sup>[11]</sup>

Appropriate diagnosis and management of GDM can improve maternal and perinatal outcome. Many studies have been done in various parts of India on gestational diabetes, like Seshiah et al. in Chennai, Wahi et al. in Jammu, and Gajjar in Baroda, Gujarat.<sup>[12-14]</sup>

Perinatal outcomes associated with poor glycemic control in mothers are associated with as high as 42.9% mortality.<sup>[15]</sup> In our study it was found to be as low as 6.1%, which might be due to strict follow up and awareness programs running in parallel and all complicated cases excluded right in the beginning.

In another study conducted in the nearby state of Rajasthan, the prevalence of GDM was 6.6 % compared to our 14.42%, which might be due to different criteria of screening added by cultural and geographical differences.<sup>[11]</sup>

But more intuitively, the difference of this vastness is vested in single abnormal value approach as it is used in this study as per DIPSI guidelines, compared to the 3 values of OGTT. The difference is clearly elicited by such variation of the criteria as seen in a study form Haryana.<sup>[16]</sup>

While this study reports 10.87% GDM prevalence based on single abnormal value, the prevalence goes down to 7.1%, if all the three values are required to be abnormal. [16] Even a study from Japan agrees that new adaptation of criteria with a single aberrant value (mostly 2 hour post prandial), the prevalence estimates are expected to rise nearly 4 fold!<sup>[17]</sup>

Compared to the 1999 criteria of FPG  $\geq 126$  mg/dL and/or 2hPG  $\geq 140$  mg/dL, a recent 2013 criteria recommends a 75-g oral glucose tolerance test (OGTT) cut-off as follows<sup>[18]</sup>:

- fasting plasma glucose (FPG)  $\geq 92$  mg/dL,
- 1-hour plasma glucose (1hPG)  $\geq 180$  mg/dL,
- and 2-hour plasma glucose (2hPG)  $\geq 153$  mg/dL.

Thus this new criteria has a lower cut-off for FPG, higher cut-off for 2hPG, and also the addition of 1hPG values. If the criteria of 2 hours postprandial glucose level have been used, the prevalence of GDM in our study would have gone much lower.

Moreover, a study in Illawara region showed that Indian were worst hit with 11.9% prevalence rate<sup>[19]</sup> which rose to 16.7% in another study.<sup>[20]</sup> For preventive purposes, such an over-diagnosis by single abnormal value can be more welcome.

Positive family history for diabetes was seen in 20.6% GDM cases compared to just 6.5% non-GDM cases. The outcome is comparable to a study in which 31.7% of women with GDM had a positive family history of diabetes, compared with 12.8% in normal women.<sup>[5]</sup>

Pregnancy related complications were more common in GDM compared to non-GDM cases as seen in perinatal death (neonatal death as well as stillbirth), congenital malformation, caesarean section, PBU (intensive care) admissions, macrosomia, low birth weight, pre-eclampsia and jaundice incidences.

This outcome is comparable to many other studies. For example, in a study, women with GDM were more likely to develop pregnancy-induced hypertension, pre-eclampsia, antepartum hemorrhage, preterm labor, and caesarean delivery than those without GDM.<sup>[5]</sup>

Infants born to women with GDM in this study were at increased risk of being born preterm and were also significantly more likely to be macrosomic and birth trauma was significantly higher in offspring of GDM mothers.<sup>[5]</sup>

In yet another study, for the gestational diabetes mellitus group, adjusted odds ratios for hypertensive disorders during pregnancy, induction of labor and emergency caesarean section were 2.7, 3.1 and 2.5 respectively. For Apgar score  $< 7$  at 5 min, need for neonatal intensive care  $> 1$  day and large-for-gestational age infant adjusted odds ratio was 9.6, 5.2 and 2.5 respectively.<sup>[21]</sup>

In a study comparable to ours, Women with a diagnosis of GDM had significantly higher levels of emergency caesarean section (odds ratio 1.75), their infants had significantly higher levels of neonatal unit admission (odds ratio 3.14) and costs of care were 34% greater than in women without GDM. Other variables that significantly increased costs were weight, age, primiparity, and premature delivery.<sup>[22]</sup>

The strategy that has the greatest likelihood of being cost-effective is dependent on the risk of gestational diabetes mellitus (GDM) for each individual woman. When GDM risk is less than 1% then the no screening/treatment strategy is cost-effective.<sup>[23]</sup>

Where risk is between 1.0% and 4.2% fasting plasma glucose followed by OGTT is most likely to be cost-effective; and where risk is greater than 4.2%, universal OGTT is most likely to be cost-effective. However, acceptability of the test alters the most cost-effective strategy.<sup>[23]</sup>

## Conclusion

Incidence of GDM in the studied Indian population is 14.42% which relies on DIPSI recommendation – based on other screening criteria, this value varies considerably. Moreover, confusion concerning ‘an efficiently predictive screening criteria’ still remains an issue. The outcome of pregnancy, in terms of mother as well as baby, is expectedly far worse with GDM. Awareness concerning GDM and its possible morbid outcomes among mothers is very low (6%) and can be a target area to improve the outcome.

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