Original Research Article

Study of maternal, fetal and neonatal outcomes in patients with gestational diabetes mellitus in a tertiary care hospital

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ABSTRACT

Background: GDM is defined as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy. Women with gestational diabetes are characterized by a relatively diminished insulin secretion and pregnancy induced insulin resistance primarily present in the skeletal muscle tissue. Normal pregnancy is a diabetogenic state characterized by exaggerated rate and amount of insulin release, associated with decreased sensitivity to insulin at cellular levels. The objective of the study was to study the maternal, the fetal and the neonatal outcomes of treated patients of GDM in present study.

Methods: It was a hospital based clinical study. 1000 patients were enrolled between 24-28 weeks of gestation and DIPSI test was performed. Diagnosis of GDM was done using DIPSI criteria. 80 patients were diagnosed with GDM and followed till delivery to study the maternal, fetal and neonatal outcome.

Results: Elderly patients, patients with previous history of GDM, patients with family history of diabetes, patients with high BMI and patients with polyhydramnios are at high risk for GDM.

Conclusions: Hypertensive disorders and preterm birth are known to be higher with GDM are similar to the non-GDM group suggesting that early diagnosis and prompt treatment and maintaining strict glycemic control by patient may be beneficial. GDM can be managed well on MNT and lifestyle modifications, only few patients required insulin therapy. In spite of appropriate glycemic control, the incidence of macrosomia found to be high in GDM group. Sudden unexplained stillbirth can occur in spite of strict glycemic control. Neonatal complications have occurred despite well glycemic control.

Keywords: DIPSI, GDM, MNT, Macrosomia, Stillbirth

INTRODUCTION

Diabetes mellitus is a group of metabolic disorders characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both.[1] It is defined as carbohydrate intolerance of variable severity with an onset or first recognition during pregnancy.[2] Women with gestational diabetes are characterized by a relatively diminished insulin secretion and pregnancy induced insulin resistance primarily present in the skeletal muscle tissue. Normal pregnancy is a diabetogenic state characterized by exaggerated rate and amount of insulin release, associated with decreased sensitivity to insulin at cellular levels. Many of the changes are results of the progressive rise in the levels of estrogen, progesterone, human placental lactogen, cortisol and prolactin as pregnancy advances. Many of these hormones are insulin antagonists, causing insulin resistance in the mother and cause abnormal glucose tolerance in some women rendering them to develop gestational diabetes.[3] During early pregnancy, glucose crosses the placenta to the fetus by facilitated diffusion resulting in the decrease in fasting

blood glucose to 50-65 mg%. As pregnancy progresses 3 factors are responsible for causing post prandial hyperglycemia: insulin antagonists such as estrogen, progesterone and human placental lactogen. There is 3-fold rise in serum cortisol and human placenta contains enzymes (eg. insulinase) that increase the degradations by potentiating the secretion of insulin, but in GDM the pancrease fail to respond adequately.[4] GDM is associated with increased fetomaternal morbidity as well as long term complications in mother and babies. American college of obstetricians and gynecologists (ACOG) on contrary advocates selective screening for patients with high risk factors such as history of previous GDM, strong family history of diabetes, member of an ethnic group with high prevalence of GDM, maternal age more than 25 years, obesity, persistent glycosuria, macrosomia (birth weight >4gm,)polycystic ovarian syndrome, spontaneous abortions and unexplained still births.[5] Maternal complications are increased incidence of asymptomatic bacteriuria, urinary tract infections, increased incidence of pre ecclamsia,10% risk of polyhydramnios which may increase the incidence of preterm labour, placental abruption and postpartum hemorrhage. Risk of developing diabetes mellitus and the complications in fetus are macrosomia, which will increase risk of operative delivery and shoulder dystocia, increase incidence of hypoglycemia, hypocalcemia, congenital malformations, polycythemia, hyperbilirubinemia, respiratory distress syndrome, and long term complications are obesity, development of type 2 diabetes mellitus during childhood, impaired motor functions and higher rates of in attention and hyper activity.[6] Several studies have shown that 50% GDM developed diabetes mellitus within 10-20 years of index pregnancy. Furthermore, there were reported increased incidence of hypertension, hyperlipedimia, proteinuria, abnormal ECG and higher morbidity and mortality.

The incidence of juvenile diabetes mellitus in offspring is 20 times more than in the controlled population. Attempts to detect unrecognized diabetes in pregnancy should be practiced in antenatal clinics which are justified by the increased risk of maternal, perinatal and neonatal morbidity mortality among women with abnormal OGTT in pregnancy.

METHODS

It was a hospital based study. 1000 pregnant women in second trimester between 24-28 weeks of gestational age attending antenatal clinic of tertiary care center in a time period of one year (September 2015 to December 2016) were enrolled in this study after providing informed consent. Diagnosis of GDM was done using DIPSI criteria. A detailed assessment of patient was performed including history (any family history of diabetes, history of previous pregnancies and socioeconomic status etc.), general examination and obstetric examination. Routine investigations during antenatal visits were done. Informed consent to participation was taken during initial assessment. A standard proforma was used to record the data of tests performed, detailed clinical assessment of patients, including history and examination findings, investigations including the test results.

Diabetes in Pregnancy Study Group India (DIPSI) diagnostic criterion of 2-h plasma glucose ≥7.8 mmol/L with 75 gm oral glucose load is a modified version of WHO criterion, in that the WHO procedure requires women to be in the fasting state, whereas DIPSI procedure was performed in the fasting/ non-fasting state irrespective of last meal timing. Diagnosis of GDM according to DIPSI criteria is as follows.[7]

Inclusion criteria

- All consenting pregnant women in second trimester between 24-28 weeks
- Pregnant women of any parity
- Singleton pregnancy.

Exclusion criteria

- Pre-gestational diabetes
- Chronic renal/ cardiac/ hepatic/ respiratory diseases
- Taking drugs that alter glucose metabolism
- Women who refuse to participate.

Table 1: DIPSI criteria.

Interpretation of OGTT	2-hour venous blood sugar (mg/dl)
Normal	<140
Gestational diabetes mellitus	140-199
Overt diabetes	≥200

RESULTS

Out of the 1000 women screened 80 women were diagnosed as GDM using DIPSI criteria. Maternal, fetal and neonatal outcomes compared in women with GDM and those without GDM.

Table 2: Co-relation of advanced maternal age with GDM.

		GDM		Total
		Yes	No	
Elderly gravida (≥35 years)	Yes	7 (26.92%)	19 (73.08%)	26 (2.6%)
	No	73 (7.49%)	901 (92.51%)	974 (97.4%)
Total		80 (8%)	920 (92%)	1000 (100%)

From Table 2 there were total 26 elderly (≥35 years) pregnant woman of which 7 (26.92%) were diagnosed with gestational diabetes mellitus and 19 (73.08%) were having non-GDM. For Table 2 Pearson's chi-square value is 12.99, df is 1 and P value is 0.0003, which is

statistically significant and implies positive co-relation of advanced maternal age with gestational diabetes mellitus.

Table 3: Incidence of GDM in different BMI groups at first registration.

| BMI (kg/m2) | GDM | | Total |
	Yes	No	
High (> 30)	9 (64.29%)	5 (35.71%)	14 (1.4%)
Low (< 19)	1 (0.78%)	128 (99.22%)	129 (12.9%)
Normal (19-29.99)	70 (8.17%)	787 (91.83%)	857 (85.7%)
Total	80 (8%)	920 (92%)	1000 (100%)

From Table 3, incidence of gestational diabetes mellitus in high body mass index group (>30) was 64.29% whereas in normal body mass index group (19-29.99) is 8.17%. In low Body mass index (<19) incidence of gestational diabetes mellitus was 0.78%. For Table 3 chi-square value is 69.44, df is 2 and P value is <0.0001. Which signifies positive co-relation of high body mass index with incidence of gestational diabetes mellitus.

Table 4: Co-relation of gravidity with GDM.

| | | GDM | | Total |
		Yes	No	
Gravidity	Primigravida	6 (7.5%)	174 (18.91%)	180 (18%)
	G2 and above	74 (92.5%)	746 (81.09%)	820 (82%)
Total		80 (8%)	920 (92%)	1000 (100%)

From Table 4 the incidence of GDM in primigravida was 6 (7.5%) and in multigravida it was 74 (92.5%). For

Table 4 Pearson's chi-square value is 5.74, df is 1 and P value is 0.016, which implies positive co-relation between multigravida and GDM.

Table 5: Co-relation between previous history of GDM and GDM.

| | | GDM | | Total |
		Yes	No	
Previous history of GDM	Yes	18 (22.5%)	9 (0.98%)	27 (2.7%)
	No	62 (77.5%)	911 (99.02%)	973 (97.3%)
Total		80 (8%)	920 (92%)	1000 (100%)

Table 5 shows that there were total 27 patients with previous history of GDM of which 18 (22.5%) developed GDM in this pregnancy and only 9 (0.98%) were non GDM.

Out of 973 patients with no previous history of GDM only 62 (77.50%) developed GDM and 911 (99.02%) were non GDM. For Table 5 Pearson's chi-square value is 121.7, df is 1 and P value is <0.0001. Which signifies positive co-relation between previous history of GDM and GDM.

Table 6: Co-relation between family history of diabetes and GDM.

| | | GDM | | Total |
		Yes	No	
Family history of diabetes	Yes	34 (42.5%)	78 (8.48%)	112 (11.2%)
	No	46 (57.5%)	842 (91.52%)	888 (88.8%)
Total		80 (8%)	920 (92%)	1000 (100%)

Table 6 shows that in our study out of 80 patients with GDM, 34 (42.5%) had family history of diabetes in first degree relative while 46 (57.5%) had no family history of diabetes. Also, out of 920 patients with non GDM only 78 (8.48%) had family history of diabetes and 842 (91.52%) had no family history of diabetes mellitus.

For Table 6 Pearson's chi-square value is 82.27, df is 1 and P value is <0.0001. Which shows strong association between family history of diabetes and GDM.

Table 7: Distribution of obstetric and medical risk factors.

Obstetric and medical risk factors	Number	%
Previous LSCS	117	11.70
Pre-eclampsia	109	10.90
Anaemia	109	10.90
GDM	80	8.00
Elderly gravida	26	2.60
Hypothyroidism	20	2.00
PROM	12	1.20
Polyhydramnios	22	2.20
Oligohydramnios	3	0.30
Abruption	1	0.10

In study sample of 1000 participants obstetric and medical risk factors like previous LSCS, pre-eclampsia, anaemia and gestational diabetes mellitus were important factors having occurrence rate of 11.70%, 10.90%, 10.90% and 8.00%. Whereas elderly gravida, hypothyroidism, PROM, polyhydramnios, oligohydramnios and abruption factors constituted about 2.60%, 2.00%, 1.20%, 2.20%, 0.30% and 0.10% respectively in sample.

Table 8: Co-relation of pre-eclampsia with gestational diabetes mellitus.

		GDM		Total
		Yes	No	
Pre-eclampsia	Yes	9 (11.25%)	100 (10.87%)	109 (10.9%)
	No	71 (88.75%	820 (89.13%)	891 (89.1%)
Total		80 (8%)	920 (92%)	1000 (100%)

From Table 8, incidence of pre-eclampsia was almost same in gestational diabetes mellitus (11.25%) and non-gestational diabetes mellitus group (10.87%). For Table 8 Pearson's chi-square value is 0.01, df is 1 and P value is 0.92. Which is statistically non-significant and implies there is no co-relation between gestational diabetes mellitus and occurrence of pre-eclampsia.

Table 9: Co-relation of GDM and polyhydramnios.

Amniotic fluid index	GDM		Total
	Yes	No	
Polyhydramnios (>20 cm)	6 (7.5%)	16 (1.74%)	22 (2.2%)
Normal (5-19.9 cm)	74 (92.5%)	901 (97.94%)	975 (97.5%)
Oligohydramnios (<5 cm)	0	3 (0.33%)	3 (0.3%)
Total	80 (8%)	920 (82%)	1000 (100%)

For study purpose, we have defined polyhydramnios as amniotic fluid index (AFI) more than 20 cm and oligohydramnios as amniotic fluid index less than 5 cm. From Table 9, in patients with gestational diabetes mellitus polyhydramnios was found in 6 (7.5%) cases and normal AFI in 74 (92.5%) cases. Whereas in non-gestational diabetes mellitus group polyhydramnios was found in 16 (1.74%) cases, oligohydramnios in 3 (0.33%) cases and normal AFI in 901 (97.94%) cases. For Table 9 chi-square value is 11.59, df is 2 and P value is 0.003 which suggests association of polyhydramnios with gestational diabetes mellitus.

Table 10: Comparison of fetal anomaly in GDM and non-GDM group.

Fetal anomaly	GDM		Total
	Yes	No	
Yes	3 (3.75%)	25 (2.72%)	28 (2.8%)
No	77 (96.25%)	895 (97.28%)	972 (97.2%)
Total	80 (8%)	920 (92%)	1000 (100%)

From Table 10, incidence of congenital anomalies was almost same in gestational diabetes mellitus (3.75%) and non-gestational diabetes mellitus group (2.72%). For Table 10 Pearson's chi-square value is 0.29, df is 1 and P value is 0.59. Which is statistically non-significant and implies there is no co-relation between gestational diabetes mellitus and congenital anomalies.

From Table 11, incidence of macrosomia in gestational diabetes mellitus was 42.50% whereas it was quite low for non-gestational diabetes mellitus i.e. 8.70%. Whereas normal and low weight babies were relatively higher in non-gestational diabetes mellitus cases (80% and 11.30% respectively) than in case of gestational diabetes mellitus cases (52.50% and 5% respectively).

Table 11: Co-relation of birth weight in GDM and non-GDM.

Birth Weight	GDM		Total
	Yes	No	
Macrosomia (≥3.5 kg)	34 (42.5%)	80 (8.70%)	114 (11.4%)
Normal (2.4-3.5 kg)	42 (52.5%)	736 (80.0%)	778 (77.8%)
Low (≤2.4 kg)	4 (5.0%)	104 (11.30%)	108 (10.8%)
Total	80 (8%)	920 (92%)	1000 (100%)

For Table 11 chi-square value is 83.64, df is 2 and P value is <0.0001 which suggests there is strong co-relation between macrosomia and gestational diabetes mellitus.

Table 12: Treatment given in GDM.

Mode of treatment	MNT+ lifestyle modification +SMBG	MNT + lifestyle modification +SMBG +insulin	Total
No. of patients	67	13	80
%	83.75	16.25	100

Out of 80 patients 67 (83.75%) were controlled on MNT and lifestyle modification and 13 (16.25%) patients additionally required insulin therapy.

Table 13: Comparison of gestational age at delivery in GDM and non-GDM.

Gestational age at delivery	GDM		Total
	Yes	No	
Term	67 (83.75%)	758 (82.39%)	825 (82.5%)
Preterm	13 (16.25%)	162 (17.61%)	175 (17.5%)
Total	80 (8%)	920 (92%)	1000 (100%)

From Table 13, incidence preterm delivery was almost same in gestational diabetes mellitus (16.25%) and non-gestational diabetes mellitus group (17.61%). The incidence of term delivery was (83.75%) in GDM and (82.39%) in non GDM group.

For Table 13 Pearson's chi-square value is 0.02, df is 1 and P value is 0.8875. Which is statistically non-significant and implies there no is co-relation between gestational diabetes mellitus and gestational age at delivery. From Table 14, incidences of caesarean, instrumental and normal deliveries in patients with gestational diabetes mellitus cases were 23.75%, 3.75% and 72.50 % respectively whereas in non-gestational diabetes mellitus cases it stood for 26.85%, 2.61% and 70.54% respectively, which were approximately equal in both GDM and non-GDM cases.

Table 14: Co-relation of type of delivery with GDM and non-GDM.

Type of delivery	GDM		Total
	Yes	No	
Caesarean	19 (23.75%)	247 (26.85%)	266 (26.6%)
Instrumental	3 (3.75%)	24 (2.61%)	27 (2.7%)
Normal	58 (72.5%)	649 (70.54%)	707 (70.7%)
Total	80 (8%)	920 (92%)	1000 (100%)

For Table 14 chi-square value is 0.66, df is 2 and P value is 0.7189 which suggests there is no co-relation of type of delivery with gestational diabetes mellitus.

Neonatal complications like hyperbilirubinemia (12.5%), hypoglycemia (10%), RDS (5%), still birth (2.5%) and sepsis (3.75%) (table 22) in gestational diabetes mellitus were collectively 33.75% whereas they stood at 4.78% (Table 15) for non-gestational diabetes mellitus group.

Table 15: Neonatal complications in GDM and non-GDM.

Neonatal complications	GDM		Total
	Yes	No	
Yes	27 (33.75%)	44 (4.78%)	71 (7.1%)
No	53 (66.25%)	876 (95.22%)	929 (92.9%)
Total	80 (8%)	920 (92%)	1000 (100%)

For Table 16 Pearson's chi-square value is 89.29, df is 1 and P value is <0.0001 which implies very strong co-relation of gestational diabetes mellitus with incidence of neonatal complications.

Table 16: Incidence of neonatal complications in GDM cases.

Neonatal complications	Number	%
Hyperbilirubinemia	10	12.5
Hypoglycemia	8	10
RDS	4	5
Sepsis	3	3.75
Still Birth	2	2.5
Total	27	33.75

DISCUSSION

Risk factors for GDM

Compared with women of normal OGTT, women with GDM were older. The mean age in GDM group was 26.625±4.309 years while in non-GDM group it was 25.269±3.505 years. Similar study from south India showed age more than 25 years as a risk factor for GDM.[8]

Several studies revealed that obesity is significant risk factor for GDM. Obesity or overweight at the start of pregnancy predisposes to GDM. In present study, we had 64.29% obese (BMI>30kg/m²) cases were having GDM, which was 67% (BMI>25kg/m²) in study done by Kalra P et al. (Jodhpur, Rajasthan) and was 27.5% (BMI>25kg/m²) in study done by Wahi P et al. (Jammu and Kashmir). The positive correlation of obesity with GDM was also shown by studies like Nilofer AR et al as 88.89%, by Das et al as 25%.[9,10]

In present study 92.5% cases of GDM were multigravida (gravida 2 and above), whereas in study done by Rajput M. et al it was 18.2%, while in study done by Seshiah et al it was 25.8%, these both studies considered multigravida as gravida 4 and above.[11,12] It suggests significant correlation between multigravidity and GDM.

In current study, there were 22.5% cases of GDM having previous history of GDM, while in study done by Seshiah et al about 50% patients were having previous history of GDM.[13] In this study, there were 42.5% cases of GDM having family history of diabetes in first degree relatives, while in study done by Bhat M. et al it was 37.3%.[14] In study done by Wahi P et al it was 24.19%, whereas in study done by Seshiah et al it was 32.3%. In study done by Sivakumar V et al it was 64.86% while in study done by Rajput M. et al it was 18.14%.[15,8,16,11] Thus, family history of diabetes is significant risk factor associated with development of GDM.

Incidence of obstetric complications in GDM cases

In this study hypertensive disorders in pregnancy like pre-eclampsia was found in 9 (11.25%) cases, PROM in 1 (1.25%) case, preterm labour in 13 (16.25%) cases and LSCS was done in 19 (23.75%) cases. In present study, all the obstetric complications associated with GDM were

on lower side. This may be due to early diagnosis and prompt treatment of GDM with patient education, medical nutrition therapy, lifestyle modification and appropriate glycemic control by insulin therapy wherever necessary. In Kalra P et al study, the rate of hypertensive disorders of pregnancy, antepartum haemorrhage and LSCS were high. In present study, we studied type of delivery in GDM patients. Amongst 80 patients with GDM, 19 (23.75%) patients were delivered by caesarean section, 58 (72.5%) patients. were delivered vaginally and 3 (3.75%) patients had instrumental delivery. In present study rate of LSCS was 23.75% and the most common indication of LSCS was meconium stained liquor (31.58%); non-progress of labour (15.79%); CPD, macrosomia, previous LSCS (10.53% each); breech etc. In present study number of term deliveries in GDM patients were 67 (83.75%), while 13 (16.25%) GDM patients had preterm delivery.

Table 17: Comparison of incidences of obstetric complications in GDM cases in various studies in India.

Study	Hypertensive disorders in pregnancy	Antepartum haemorrhage	PROM	Preterm	LSCS
Present study	9 (11.25%)	-	1 (1.25%)	13 (16.25%)	19 (23.75%)
Kalra P et al.	9 (27%)	7 (21%)	6 (18.1%)	-	26 (76%)
Wahi P et al.	4 (6.4%)	2 (2.7%)	-	13 (20.1%)	14 (22.5%)

Fetal outcomes in various studies

In our study when we compared the birth weight of babies in patients with GDM, 34 (42.5%) patients had macrosomic baby (≥3.5 kg), 42 (52.5%) patients had normal weight babies (2.4-3.5 kg), whereas 4 (5%) patients had low birth weight babies (≤2.4 kg) and all these 4 babies were preterm (<37 weeks). None of the babies had extremely low birth weight (<1 kg).

In present study, there were 2 (2.5%) full term unexplained intrauterine fetal demise (stillbirth). Both patients were on medical nutritional therapy and advised lifestyle modifications. Both patients had good glycemic control. Fetal demise may be due to extramedullary hematopoiesis due to chronic hypoxia and electrolyte imbalance. Whereas in study done by Priyanka Kalra, et al. still birth was 3 (9.09%) and in study done by Wahi P, et al stillbirth was 3 (4.84%) cases.

Table 18: Comparison of fetal outcomes in various studies in India.

Study	Still birth	Macro-somia	Hypoglycemia	Hyperbilirubinemia	Shoulder Dystocia	NICU admission
Present study	2 (2.5%)	34 (42.5%)	8 (10%)	10 (12.5%)	-	17 (21.25%)
Kalra P et al.	3 (9.09%)	6 (18%)	3 (9.05%)	6 (10.12%)	7 (10%)	9 (27.2%)
Wahi P et al.	3 (4.84%)	7 (11%)	-	-	1 (3%)	-

Out of 143 babies born 17 (21.25%) babies were admitted in NICU. Most common reason for Macrosomic babies were high 34 (42.5%) in present study, whereas 6 (18%) in study done by Priyanka Kalra, et al. and 7 (11%) in study done by Wahi P., et al There were 8 (10%) babies of neonatal hypoglycemia in present study, while there were 3 (9.05%) babies in study done by Priyanka Kalra, et al.

There were 10 (12.5%) babies of neonatal hyperbilirubinemia in our study, while there were 6 (10.12%) babies in study done by Priyanka Kalra, et al. There was no case of shoulder dystocia in our present study as was seen in 7 (10%) cases in study done by Kalra P et al. and 1(3%) case in study done by Wahi P, et al.

CONCLUSION

Study found that elderly patients, patients with previous history of GDM, patients with family history of diabetes, patients with high BMI and patients with polyhydramnios are at high risk for GDM. In study, obstetric complications like hypertensive disorders and preterm birth are known to be higher with GDM are similar to the non-GDM group suggesting that early diagnosis and prompt treatment and maintaining strict glycemic control by participant may be beneficial. GDM can be managed well on MNT and lifestyle modifications, only few patients required insulin therapy. In spite of appropriate glycemic control, the incidence of macrosomia is found to be high in GDM group. Sudden unexplained stillbirth can occur in spite of strict glycemic control. Neonatal

complications have occurred despite well glycemic control.

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