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Research Article

ADVERSE PREGNANCY OUTCOMES IN GESTATIONAL DIABETES MELLITUS - STUDY IN AN APEX HOSPITAL

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ABSTRACT
Diabetes is the most common medical complication of pregnancy (3 to 5% of all pregnancies). The aim of the present study was to evaluate maternal and fetal risks associated with gestational diabetes mellitus, so that we can reduce those risks by early diagnosis and active intervention. This was a retrospective case control study conducted in the Department of Gynecology and Obstetrics, Medical College and Hospital, Kolkata. 200 pregnant women with GDM were taken as cases and matched for age, parity and body mass index with 200 non diabetic pregnant women who acted as controls. Both the groups were compared on the basis of some maternal and fetal and neonatal complications. Maternal complications taken into account were pre-eclampsia, preterm delivery; induction of labour ,caesarean section; and foetal and neonatal complications taken into account were macrosomia, shoulder dystocia, admission to the neonatal intensive care unit (NICU), Apgar score <7 at 5 minutes, respiratory distress syndrome (RDS), neonatal hypoglycaemia, hyperbilirubinaemia, need for phototherapy, congenital anomalies and perinatal mortality. Two-proportion z-test, pooled for $H_0: p_1 = p_2$ was used to derive z value, from which p value was calculated (CI 95%). p‹ 0.05 was considered as statistically significant. The incidence of preeclampsia, preterm delivery and occurrence of cesarean delivery were more in GDM group and the association was extremely significant. The incidence of labour induction was also more in this group. Macrosomia, NICU admission, RDS and neonatal hypoglycaemia were significantly more in GDM group. (p< 0.0001). Evidence suggests that early diagnosis and strict control of blood sugar levels throughout the pregnancy can significantly reduce complications associated with gestational diabetes. A multicenter, randomized controlled trial, based on universally accepted criteria for GDM screening test, standardized diagnostic OGTT and management of all patients with GDM versus the standard obstetric management of the control is warranted.

Key Words: *Diabetes Mellitus, Gestational, Maternal and Fetal Outcome*

INTRODUCTION
Diabetes is the most common medical complication of pregnancy. 3 to 5% of all pregnancies are complicated by diabetes. Approximately 0.2% to 0.5% of all pregnancies occur in women with pre-existing diagnosis of type 1 diabetes mellitus (Garner *et al.,* 1995) and a similar number has pre-existing type 2 diabetes mellitus (Feig *et al.,* 2002). An additional 1% to 6% of women will develop sufficient hyperglycemia during pregnancy to meet the criteria for diagnosis of gestational diabetes mellitus (GDM) (Brody *et al.,* 2003) which is defined as carbohydrate intolerance resulting in hyperglycemia of variable severity with onset or first recognition during pregnancy, whether or not insulin is used and regardless of whether diabetes persists after pregnancy. (Report of the Expert Committee on the Diagnosis and classification of Diabetes Mellitus, 2003). Patients with gestational diabetes not only have an increased incidence of caesarean section, preeclampsia, macrosomia and need for neonatal phototherapy (Sermer *et al.,* 1995), the cumulative incidence of type 2 diabetes mellitus increases markedly in the first 5 years after delivery and appears to plateau after 10 years (Kim *et al.,* 2002).

The aim of the present study was to evaluate maternal and fetal risks associated with gestational diabetes mellitus, so that we can reduce those risks by early diagnosis and active intervention.

MATERIALS AND METHODS

This was a retrospective case control study conducted in the Department of Gynecology and Obstetrics, Medical College and Hospital, Kolkata. Data was collected from the bed head tickets (BHT) of the patients admitted to the hospital from January 2007 to December 2007. 200 pregnant women with GDM were taken as cases and matched for age, parity and body mass index with 200 non diabetic pregnant women who acted as controls. WHO recommended 75-g 2-hour oral glucose tolerance test was used to diagnose GDM. Patients with multiple pregnancies and abnormal presentation of the foetus were excluded from the study.

The GDM patients were treated with either diet alone or with additional insulin in some patients who required better control of their blood sugar levels.

Both the groups were compared on the basis of four maternal and ten foetal and neonatal complications. The maternal complications taken into account were preeclampsia (Zamorski *et al.,* 2001), preterm delivery (delivery before 37 completed weeks) , induction of labour and delivery by caesarean section (Table 2) and foetal and neonatal complications considered were macrosomia (birth weight › 4000gm) Boyd *et al.,* 1983), shoulder dystocia, NICU admission, Apgar ‹ 7 at 5 minutes after birth ,respiratory distress syndrome, neonatal hypoglycaemia (‹ 2.5 mmol/l) (Flores-le Roux *et al.,* 2012), neonatal hyperbilirubinaemia (> 85 umol/l) , need for phototherapy, congenital anomaly and perinatal mortality (stillbirth, from 28 weeks of gestation to the end of the neonatal period of 4 weeks after birth). (Table 3).

Two-proportion z-test, pooled for $H_0: p_1 = p_2$ was used to derive z value, from which p value was calculated (CI 95%). p‹ 0.05 was considered as statistically significant.

RESULTS

On the basis of age, parity and body mass index (BMI) both GDM and non GDM groups were comparable (Table 1).

Table 1: Age, gravidity and BMI distribution in GDM and non GDM groups

Age (Years)	**GDM**	**Non GDM**
≤20	43 (21.50%)	44 (22.00%)
>20-25	48 (24.00%)	51 (25.50%)
>25-30	87 (43.50%)	81 (40.50%)
>30-35	18 (09.00%)	16 (08.00%)
>35	04 (02.00%)	08 (04.00%)
Total	200	200
Gravida	**GDM**	**Non GDM**
1	174 (87.00%)	177 (88.50%)
2	019 (09.50%)	017 (08.50%)
≥3	007 (03.50%)	006 (03.00%)
Total	200	200
BMI	**GDM**	**Non GDM**
‹18.5 (Underweight)	010 (05.00%)	12(06%)
18.5-24.99 (Normal)	102 (51.00%)	98(49%)
25-29.99 (Overweight)	079 (39.50%)	80(40%)
≥30 (Obese)	009 (04.50%)	10(05%)
Total	200	200

Values are given as number (percentage)

The incidence of preeclampsia, preterm delivery and occurrence of cesarean delivery were more in GDM group and the association was extremely significant (p ‹ 0.0001, 0.0002 and ‹ 0.0001 respectively). The

incidence of labour induction was also statistically significantly more in GDM group (p= 0.0108). (Table 2)

Table 2: Frequency of maternal complications in GDM and non GDM groups

Maternal Complications	GDM	Non GDM	P
	N=200	N=200	
Preeclampsia	142 (71.0%)	45 (22.5%)	<0.0001
Preterm Delivery	064 (32.0%)	32 (16.0%)	0.0002
Induction of Labour	080 (40.0%)	56 (28.0%)	0.0108
Caesarean Section	101 (50.5%)	25 (12.5%)	<0.0001

Values are given as number (percentage)

Among 142 preeclamptic patients of GDM group 3 suffered from HELLP syndrome. Among 101 cesarean section in GDM group 71 were elective for cephalopelvic disproportion (56 cases), previous cesarean section (9 cases) and uncontrolled hypertension (6 cases) and rest were emergency for obstructed labour (8 cases), fetal distress (14), prolonged labour (6), and major degree placenta previa (2). Among 99 mothers who had vaginal delivery in GDM group, 4 had low forceps delivery for borderline cephalopelvic disproportion.

Macrosomia, NICU admission, RDS and neonatal hypoglycaemia were significantly more in GDM group (p ‹ 0.0001) , however shoulder dystocia, Apgar score ‹ 7, neonatal hyperbilirubinaemia, need for phototherapy, congenital anomaly and perinatal mortality were not significantly different between two groups (p› 0.05) (Table 3).

Table 3: Frequency of fetal and neonatal complications in GDM and nonGDM groups

Fatal and Neonatal Complications	GDM	Non GDM	P
	N=200	N=200	
Macrosomia	070 (35.0%)	14 (07.0%)	<0.0001
Shoulder Dystocia	006 (03.0%)	01 (00.5%)	0.0564
NICU Admission	064 (32.0%)	20 (10.0%)	<0.0001
Apgar ‹ 7	031 (15.5%)	25 (12.5%)	0.3914
RDS	055 (27.5%)	15 (07.5%)	<0.0001
Neonatal Hypoglycaemia	112 (56.0%)	11 (05.5%)	<0.0001
Neonatal Hyperbilirubinaemia	052 (26.0%)	57 (28.5%)	0.5823
Need for Phototherapy	046 (23.0%)	41 (20.5%)	0.5419
Congenital Anomaly	003 (01.5%)	01 (00.5%)	0.1527
Perinatal Mortality	006 (03.0%)	02 (01.0%)	0.1527

Values are given as number (percentage)

Among three babies with congenital anomalies in GDM group two had anencephaly and one had anal atresia, one from non GDM group had gastroschisis.

Causes of perinatal deaths in GDM group were prematurity (4 cases) and anencephaly (2 cases), and those in non GDM group were cord around neck (1 case) and gastroschisis (1 case).

DISCUSSION

Different studies have been conducted to find out the association between GDM and adverse pregnancy outcomes. Grasim (2012) in his study performed in Saudi Arabia has found that patients with GDM had a significantly higher incidence of pre-eclampsia ($p<0.0001$); preterm delivery ($p=0.0226$); induction of labour ($p<0.0001$); cesarean section ($p=0.0019$); higher mean birth weight ($p<0.0001$) of babies; large for gestational age infants ($p=0.0011$); macrosomia ($p=0.0186$); and admission to the neonatal intensive care unit ($p=0.0003$), compared with the control group. These findings were similar with those of ours. Apgar score <7 at 5 minutes, hyperbilirubinaemia and the need for phototherapy were similar in both groups of patients like us. However he has found no differences in the incidence of respiratory distress syndrome and neonatal hypoglycaemia which was different from our findings. Congenital anomalies and perinatal mortality rates, like our study, were not significantly different in the two groups. He concluded that even the mild form of GDM seems to have significant consequences for women and their off springs and is recommended to be aggressively treated.

In HAPO study (HAPO Study Cooperative Research Group, 2008) among 23,316 participants adjusted odds ratios were calculated for adverse pregnancy outcomes associated with an increase in the fasting plasma glucose level of 1 SD (6.9 mg per decilitre [0.4 mmol per litre]), an increase in the 1-hour plasma glucose level of 1 SD (30.9 mg per decilitre [1.7 mmol per litre]), and an increase in the 2-hour plasma glucose level of 1 SD (23.5 mg per decilitre [1.3 mmol per litre]). For birth weight above the 90th percentile, the odds ratios were 1.38 (95% confidence interval [CI], 1.32 to 1.44), 1.46 (1.39 to 1.53), and 1.38 (1.32 to 1.44), respectively; for cord-blood serum C-peptide level above the 90th percentile, 1.55 (95% CI, 1.47 to 1.64), 1.46 (1.38 to 1.54), and 1.37 (1.30 to 1.44); for primary caesarean delivery, 1.11 (95% CI, 1.06 to 1.15), 1.10 (1.06 to 1.15), and 1.08 (1.03 to 1.12); and for neonatal hypoglycaemia, 1.08 (95% CI, 0.98 to 1.19), 1.13 (1.03 to 1.26), and 1.10 (1.00 to 1.12). There were no obvious thresholds at which risks increased. Significant associations were also observed for preterm delivery, shoulder dystocia or birth injury, need for intensive neonatal care, hyperbilirubinaemia, and preeclampsia, although these tended to be weaker. Unlike them, we have found no differences in the incidence of shoulder dystocia and hyperbilirubinaemia between two groups. The differences between the occurrence of preeclampsia and preterm delivery in our study were extremely significant unlike them.

In a study by Riskin-Mashiah *et al.*, (2009) too, higher first trimester fasting hyperglycemia was strongly associated with large-for-gestational-age (LGA) neonates and/or macrosomia, and primary cesarean section.

Interestingly, Szymańska *et al.*, (2008) in their study have found that highest prevalence of large for gestational age (LGA) infants was noted in the group in whom GDM was diagnosed in first trimester and between 28 and 32 weeks of pregnancy. They compared these women and the results of the diagnostic tests with the group of standard time of GDM diagnosis (24-28 week of pregnancy) and the only difference was the late diagnosis.

Casey *et al.*, (1997) have found that hypertension (17 versus 12%), cesarean delivery (30 versus 17%), and shoulder dystocia (3 versus 1%) were significantly increased (all $P < .001$) in women with GDM compared with the general obstetric population. Infants born to women with class A1 gestational diabetes were significantly larger (mean birth weight 3581 +/- 616 versus 3290 +/- 546 g, $P < .001$), and this accounted for the increased incidence of dystocia.

CONCLUSION

In many studies, GDM has been proved to be associated with increased incidence of adverse maternal, foetal and neonatal outcomes. Our study also showed similar findings. Evidence suggests that early diagnosis and strict control of blood sugar levels throughout the pregnancy can significantly reduce those complications. A multicenter, randomized controlled trial, based on universally accepted criteria for GDM screening test, standardized diagnostic OGTT and management of all patients with GDM versus the standard obstetric management of the control is warranted

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