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ORIGINAL ARTICLE

Neonatal Outcome and Its Correlation with Hemoglobin A1c in Gestational Diabetes Mellitus

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ABSTRACT

Aim: To determine neonatal outcome in women with gestational diabetes mellitus (GDM) diagnosed using Diabetes in Pregnancy Study Group of India (DIPSI) recommended method.

Materials and methods: Out of 487 antenatal women, 52 were diagnosed with GDM using DIPSI test. All women were followed up until delivery and evaluated for neonatal outcome and managed accordingly. The appropriate statistical tests for various variables were applied by using Epi Info 7 software and evaluated at the level below than 5%.

Results: Apgar score of <6 at 5 minutes was found in 10 (20%) neonates of GDM mothers as compared with 18 (4.1%) in non-GDM group (p-value of 0.00001). Respiratory distress was present in 19 (38%) neonates in GDM group, while it was 48 (11.1%) in non-GDM group (p-value of 0.00002). Association of GDM and hyperbilirubinemia was nonsignificant in 2 (4%) neonates among GDM group, while it was 6 (1.4%) in non-GDM group. Hypoglycemia was 5 (10%) in GDM group, while 3 (0.7%) in non-GDM group (p-value of <0.0003). A total of 3 (6%) among GDM group had hypocalcemia, while 3 (0.7%) had hypocalcemia in non-GDM group (p-value of 0.02). The neonatal intensive care unit admissions were 29 (58%) in GDM group, while it was 96 (22.1%) neonates belonging to non-GDM group (p-value of 0.00001). No neonatal deaths were reported in GDM group, while there were 2 (0.5%) in non-GDM group. Anomalies were found in 6 (11.5%) in GDM group as compared with 5 (1.1%) in non-GDM (p-value of 0.00001). About 44.2% women with GDM had hemoglobin (Hb)A1c levels between 6 and 6.9%. Among GDM women, 4 (7.7%) had pregnancy losses as compared with 7 (1.6%) in non-GDM group.

Conclusion: The GDM is associated with significant fetal and neonatal morbidity; hence, preconceptional counseling, early diagnosis, and proper treatment are recommended.

Clinical significance: Preconceptional correction of HbA1c is also recommended based on risk of anomalies in fetus of GDM mother.

Keywords: Diabetes, Fetal outcomes, Gestational diabetes mellitus, Hemoglobin A1c, Neonatal outcomes, Pregnancy outcomes.

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INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance with onset or recognition during pregnancy,[1] which is associated with adverse maternal and fetal outcomes. The pregnancy of diabetic woman carries significantly greater risk for spontaneous abortion, preterm deliveries, unexplained stillbirth, congenital malformation, hydramnios, and perinatal morbidity and mortality. Neonates of diabetic mothers are at risk of developing respiratory distress syndrome (RDS), hypoglycemia, hypocalcemia, hyperbilirubinemia, polycythemia, cardiomyopathy, and certain birth defects. Diabetes may also affect long-term cognitive development in offsprings.[2]

The major congenital anomalies for fetus and infants of diabetic mothers are related to maternal hemoglobin (Hb)A1c values at 14 weeks gestation. Pregnant women with HbA1c of less than 7% have minimal risk of infants having congenital anomalies. If HbA1c values are between 7 and 8.5%, then risk of congenital malformation is 5%. The risk of congenital malformation rises to 22% if mothers had HbA1c values of more than 10%.[3] Women diagnosed to have GDM are also at increased risk of future diabetes, predominantly type II DM, as are their children. Timely action taken in screening all pregnant women for glucose intolerance, achieving euglycemia in them, and ensuring adequate nutrition may prevent in all probability the vicious cycle of transmitting glucose intolerance from one generation to another.[4]

Since very few data are available with regard to neonatal outcome of gestational diabetes from Maharashtra, the present study has been compiled to serve this purpose. It also determines correlation of HbA1c levels with adverse neonatal outcomes.

MATERIALS AND METHODS

The present study was carried out at a tertiary care hospital attached to the medical college in the Department of Obstetrics and Gynecology, between November 2013 and October 2015, after approval of the Institutional Ethics Committee. Totally, 487 antenatal women were screened for GDM. Inclusion criteria included all singleton pregnancies and those willing for regular antenatal checkup, while women who were known cases of DM or with multiple pregnancies or with history of pancreatitis and those not willing for any intervention were excluded. Demographic data of these women were noted. Detailed history and examination was done. Gestational age at first visit was noted. A thorough clinical and obstetrical examination was done. All antenatal patients screened were made to drink 75 gm glucose dissolved in 200 mL of water consumed over a period of 5 minutes, irrespective of whether she is in the fasting or nonfasting state and without regard to the time of the last meal. A venous blood sample was collected at 2 hours for estimating plasma glucose by glucose oxidase–peroxidase method at the central laboratory of the institute. All those women who had 2 hours postglucose blood sugar (PGBS) ≥140 mg/dL were classified as GDM, and who had <140 mg/dL were classified as non-GDM according to Diabetes in Pregnancy Study Group of India (DIPSI) criteria.

Apart from routine investigations, additional parameters that were monitored in patients with GDM were HbA1c, examination of fundus for evidence of retinopathy every month, serum creatinine levels for evidence of nephropathy, blood pressure, and estimation of microalbuminuria for evidence of pregnancy-induced hypertension. The patients with PGBS between 140 and 199 mg/dL were advised medical nutrition therapy (MNT) under supervision of dietician and continued for 2 weeks. If MNT failed to achieve control, i.e., fasting plasma glucose ~90 mg/dL and 2 hours postmeal glucose ~120 mg/dL, patients were admitted and insulin was initiated and physician opinion was taken. Those with initial PGBS ≥200 mg/dL were started on insulin along with MNT and were admitted for sugar monitoring. Appropriate maternal and fetal monitoring and management were done for GDM women. All antenatal, intrapartum, postpartum, and neonatal complications were noted and managed accordingly. The appropriate statistical tests for various variables were applied by using statistical analysis program of Epi Info 7 software and evaluated at the level below than 5%.

ETHICS

Ethical committee permission was taken.

RESULTS

Table 1 demonstrates distribution of neonates in the two groups according to birth weight. Among neonates of GDM women, 12 (23%) weighed <2.5 kg, 21 (40.3%) neonates weighed between 2.5 and 3 kg, 13 (25%) neonates weighed between 3.1 and 3.5 kg, and 6 (11.5%) neonates weighed >3.5 kg. Abortions were included in <2.5 kg group.

Macrosomia (>3.5 kg) was found to be significantly associated with GDM group, which had 6 (11.5%) as compared with non-GDM group in which 7 (1.6%) neonates had weight >3.5 kg. This was indicated by p-value of <0.00 (p-value <0.05).

Mean birth weight of neonates was 2.68 ± 0.48 kg. Mean birth weight of neonates of GDM mothers was 2.82 ± 0.81 kg and of non-GDM mothers was 2.66 ± 0.42 kg. The t-value is 2.329373. The p-value is 0.010124. The result is significant at $p < 0.05$.

Table 2 demonstrates neonatal complications in both the groups. Neonatal outcomes were noted in 484 women as 3 had aborted. Apgar score of <6 at 5 minutes was

Table 1: Distribution of neonates according to birth weight

	GDM (n = 52)		*Non-GDM (n = 435)*	
Birth weight (kg)	*Number*	*%*	*Number*	*%*
<2.5	12	23	104	23.9
2.5–3	21	40.3	265	60.9
3.1–3.5	13	25	59	13.5
>3.5	6	11.5	7	1.6
Total	52	100	435	100

Table 2: Neonatal complications among study population

	GDM (n = 50)*		*Non-GDM (n = 434*)*			
Neonatal complication	*Number*	*%*	*Number*	*%*	*Total n = 484**	*p-value*
Apgar at 5 minutes <6	10	20	18	4.1	28	0.00001
Respiratory distress	19	38	48	11.1	67	0.00002
Hyperbilirubinemia	2	4	6	1.4	8	>0.05
Hypoglycemia	5	10	3	0.7	8	0.0003
Hypocalcemia	3	6	3	0.7	6	0.02
NICU admission	29	58	96	22.1	125	0.00001
Early neonatal death	0	0	2	0.5	2	Not applicable

*Abortions excluded

found in 10 (20%) neonates of GDM mothers as compared with 18 (4.1%) in non-GDM group. This was found to be statistically significant with p-value of 0.00001 ($p < 0.05$).

Respiratory distress was present in 19 (38%) neonates in GDM group as compared with 48 (11.1%) in non-GDM group. This association of respiratory distress and GDM was found to be statistically significant as indicated by p-value of 0.00002 ($p < 0.05$).

Association of GDM and hyperbilirubinemia was found to be nonsignificant as 2 (4%) neonates among GDM group had hyperbilirubinemia as compared with 6 (1.4%) in non-GDM group; this was indicated by p-value of >0.05.

Hypoglycemia was found in 5 (10%) neonates of GDM mothers as compared with 3 (0.7%) neonates of non-GDM mothers. This association was found to be statistically significant with p-value of <0.0003 ($p > 0.05$); 3 (6%) women among GDM group had neonates who developed hypocalcemia as compared with 3 (0.7%) women in non-GDM group. This was found to be statistically significant with p-value of 0.02 ($p < 0.05$).

Number of neonates admitted to neonatal intensive care unit (NICU) were 29 (58%) in GDM group as compared with 96 (22.1%) neonates belonging to non-GDM group. Proportion of NICU admissions and its association with GDM group was found to be statistically significant with p-value of 0.00001 ($p < 0.05$).

Among GDM women, no neonatal deaths were reported, while in non-GDM group, 2 (0.5%) neonatal deaths were reported.

Distribution of the two groups according to frequency of congenital anomalies is demonstrated in Table 3. Among GDM group, 6 (11.5%) neonates were affected as compared with non-GDM with 5 (1.1%) affected neonates. Anomalies were significantly associated in GDM group as denoted by p-value of 0.00001 (p-value <0.05). Among fetuses of GDM woman, one was diagnosed with Budd–Chiari syndrome, one had spina bifida, and four had renal abnormalities, while among non-GDM women, one had single umbilical artery, one had cleft lip and palate, two had renal abnormalities, and one had undescended testes. None of the women were diagnosed with fetal cardiovascular anomaly in both the groups.

Table 3: Distribution of congenital anomalies among study population

Anomalies	*GDM n = 52 (%)*	*Non-GDM n = 435 (%)*	*Total n = 487 (%)*	*p-value*
Present	6 (11.5)	5 (1.1)	11 (2.2)	0.00001 S
Absent	46 (88.5)	430 (98.9)	476 (97.8)	

S: Significant

Table 4 depicts distribution of women with GDM according to their HbA1c levels. About 44.2% women with GDM had HbA1c levels between 6 and 6.9%. In the present study, mean HbA1c levels in GDM group were 6.26 ± 0.77%.

Out of 16 women with HbA1c levels <6%, 1 (6.2%) woman had intrauterine fetal demise, 1 (6.2%) woman had anomalous baby, and none had aborted, while out of 36 women with HbA1c levels ≥6%, 1 (2.8%) woman had intrauterine fetal demise, 5 (13.9%) women had anomalous babies, and 2 (5.5%) women had abortions.

Table 5 depicts fate of current pregnancy in both the groups. Among GDM women, 4 (7.7%) had pregnancy losses including 2 abortions and 2 intrauterine device (IUD) as compared with 7 (1.6%) in non-GDM group in which there was 1 abortion, 4 IUDs, and 2 neonatal deaths. It was found to be statistically significant in GDM group as depicted by p-value of <0.03 (p-value < 0.05).

Table 4: Distribution of women with GDM according to HbA1c levels at first visit and its effect on fetal outcome

HbA1c (%)	*Gestational age (weeks)*	*Total n = 52 (%)*	*Intrauterine death*	*Congenital anomalies*	*Abortion*
<6	<24	1	1	0	0
	≥24	15	0	1	0
6–6.9	<24	4	0	1	0
	≥24	19	1	2	0
7–7.9	<24	4	0	1	2
	≥24	9	0	1	0
>8		0	0	0	0
Total		52	2	6	2

Table 5: Fate of current pregnancy among study population

	GDM (n = 52)		*Non-GDM (n = 435)*		
Pregnancy outcome	*Number*	*%*	*Number*	*%*	*Total*
Healthy	48	92.3	428	98.4	476
Abortions	2	3.8	1	0.02	3
Intrauterine device	2	3.8	4	0.9	6
Early neonatal death	0	0	2	0.5	2

p-value <0.03

DISCUSSION

In the present study, no case of neonatal mortality was recorded in GDM women, but neonatal morbidities like respiratory distress, hypoglycemia, hypocalcemia, NICU admissions, congenital anomalies, and macrosomia were higher. Intrauterine demise in GDM women was observed in those who were diagnosed late. Raised HbA1c levels were associated with increased incidence of pregnancy losses and congenital anomalies.

As expected, prevalence of GDM is increasing substantially and so are its complications. The DIPSI method is a promising single-step procedure to diagnose GDM at an early stage and prevent its subsequent complications.

In our study, total 52 (10.7%) women were diagnosed as GDM out of 487 women.

In the present study, 20% neonates of GDM women had Apgar score of less than 6 at 5 minutes of birth. None of the studies mentioned about number of neonates with Apgar score at 5 minutes of birth.

The RDS was found in 38% of neonates in the present study, while 21.2% neonates had RDS in a study by Kalyani et al[5] and 5% in a study by Saxena et al.[6]

Hyperbilirubinemia was found in 7.1, 10.8, and 12.1% in studies by Johns et al,[7] Aburomman et al,[8] Kalra et al,[9] respectively, as compared with 4% in the present study.

Hypocalcemia was found in 7% in Saxena et al[6] study, while none developed hypocalcemia in a study by Johns et al.[7] In our study, 6% neonates developed hypocalcemia.

The NICU admission rates in our study were 58% as compared with the study by Kalyani et al[5]; it was 56% while in Kalra et al[9] 27.2% and Johns et al,[7] 12.1% had NICU admissions. The NICU admissions were significantly higher in GDM women as many of them were shifted to NICU only for observation and monitoring purpose.

In the present study, 10% neonates had hypoglycemia. None of the studies evaluated this entity.

None of the women had early neonatal death among GDM group. This might be because of vigilant intrapartum fetal monitoring and good neonatal care.

In our study, 2.2% anomalies were detected. About 11.5% fetuses of GDM women were affected as compared with 1.1% non-GDM women. Most common anomalies were those involving the renal system. Similar frequency for anomalies was found in a study by Saxena et al,[6] in which 5% total fetuses were affected and 10% of diabetic pregnancies had anatomical defects (cleft lip, cleft palate, foot drop, hip dislocation) or involved the cardiovascular (pericardial effusion) or nervous system (anencephaly, meningocele). In studies by Mahalakshmi et al[10] and Kushal et al,[11] there were 4.3 and 6.3% anomalies found in the GDM group.

Mean HbA1c level among GDM women in our study was 6.26 ± 0.77% at first visit. In a study by Mahalakshmi et al,[10] mean HbA1c of the 272 women was found to be 6.2% at first visit, which closely resembles our study. Aburomman et al[8] demonstrated that GDM mothers had mean HbA1c of 5.5% ± 1.8.

Also in our study, among 16 GDM women with HbA1c < 6%, 1 woman had IUD, 1 woman had anomalous baby, while none aborted. And those 36 GDM women with HbA1c ≥ 6%, 1 woman had IUD, 5 women had anomalous baby, and 2 women aborted spontaneously. Thus, uncontrolled glycemic levels can lead to adverse fetal outcome as demonstrated in our study. None of the studies mentioned relation of HbA1c levels with IUD anomalies or abortions.

In the present study, among GDM women, 4 (7.7%) had pregnancy losses including 2 abortions and 2 IUDs as compared with 7 (1.6%) in non-GDM group – 1 abortion, 4 IUD, and 2 neonatal deaths. None of the studies mention overall outcome of current pregnancy. The GDM women with IUD were diagnosed late in pregnancy. No case of neonatal death was found in GDM group, owing to vigilant antepartum, intrapartum monitoring, and good neonatal care.

CONCLUSION

In many cases, there has been a long interval between diagnosis of DM and pregnancy, so all women with DM should receive counseling at frequent intervals about pregnancy and the importance of planning. Women who plan their pregnancies have improved outcomes, with decreased rate of cesarean section, better glycemic control, and better neonatal Apgar scores.[12] Thus, preconception care, intensive regulation of maternal glucose metabolism, and fetal surveillance throughout pregnancy are critical.

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