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Original Research Article

Prospective Study of Perinatal Outcomes in Infants of Diabetic Mothers

Abhinay Bhaskar Darwade[1], Parikshit Pundalik Deore[2], Avinash Dinkar Saindane[3]

[1]Assistant Professor, Pediatric Department, ACPM Medical College, Dhule
[2]Assistant Professor, Acpm Medical College, Sakri Road, Dhule
[3]Senior Resident Pediatric, ACPM Medical College, Dhule

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Corresponding author: Dr Abhinay Bhaskar Darwade
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Abstract

This prospective study aimed to investigate the incidence of perinatal complications in infants of diabetic mothers and the impact of maternal glycemic control on neonatal outcomes at Deenanath Mangeshkar Hospital, Pune, from April 2011 to April 2012.

Out of 1074 deliveries during the study period, 118 involved pregnancies with diabetes, resulting in a gestational diabetes incidence of 9.4%. Among the 130 live born infants of diabetic mothers studied, there were no reported mortalities. Approximately 13.07% of the mothers had pregestational diabetes, while the rest had gestational diabetes. Vaginal delivery occurred in 40.7% of cases, with assistance provided in 35% of these deliveries. Cesarean sections were performed in 59.2% of cases. Full-term deliveries were observed in 73.07% of cases, and 26.92% were preterm. The incidence of low birth weight was 20%, while rates of large for gestational age, appropriate for gestational age, and small for gestational age were 32.23%, 63.63%, and 4.13% respectively, based on Indian growth curves. Neonatal complications, excluding preterm and large/small for gestational age infants, were present in 67% of cases, with hypoglycemia being the most common (48.46%). Hypoglycemia was more prevalent in the pregestational diabetes mellitus group compared to the gestational diabetes mellitus group. Hyperbilirubinemia and hypocalcemia were also frequently observed. Major malformations were found in 17% of cases, predominantly cardiac malformations, with atrial septal defects being the most common structural heart disease.

The study highlights the significance of implementing meticulous, protocol-based care for infants born to diabetic mothers.

Keywords: Infants of Diabetic Mothers, Perinatal Complications, Maternal Glycemic Control, Neonatal Outcomes, Gestational Diabetes.

Introduction

Infants born to mothers with diabetes are at a higher risk of experiencing spontaneous abortion, stillbirth, congenital malformations, and perinatal morbidity and mortality. Before specialized maternal and neonatal care was developed, fetal and neonatal mortality rates were very high. However, over the past three decades, efforts have been made to improve the outcomes of diabetic pregnancies, aiming to achieve

results comparable to those of non-diabetic pregnancies. [1]

Advancements in maternal and fetal care have significantly improved the prospects for infants of diabetic mothers (IDM). [2,3] Proper prenatal care has led to a dramatic improvement in the outcomes of infants born to diabetic mothers. [4,5] Currently, 3% to 10% of pregnancies face challenges with glycemic control, with the majority being cases of gestational diabetes mellitus rather than pregestational diabetes mellitus. [6] It is expected that the number of pregnancies complicated by diabetes will increase in the next decade as the current significantly overweight pediatric population enters their child-bearing years. [7]

Recent national and international studies have highlighted the notable neonatal morbidity in IDM, which persists despite improved maternal care. In this prospective study, we have examined the perinatal outcomes of infants born to diabetic mothers.

Objectives

1 To investigate the incidence of perinatal complications in infants born to mothers with diabetes.

2 To examine how maternal glycemic control influences the neonatal outcomes of infants born to diabetic mothers.

3 To assess the appropriateness of the blood sugar level (BSL) monitoring protocol employed in the research.

4 To determine whether outcomes are influenced by the type of gestational diabetes and the obstetric management employed.

Materials and Methods

This prospective study was conducted at Deenanath Mangeshkar Hospital in Pune over a 12-month period from April 2011 to April 2012. The sample size consisted of 130 cases, including all infants born to diabetic mothers, irrespective of their gestational age at birth.

The study employed a prospective design and focused on analyzing data from infants born to diabetic mothers who received care at Deenanath Mangeshkar Hospital.

The study aimed to assess the following outcome variables: hypoglycemia, hypocalcemia, hyperbilirubinemia, and major congenital malformations. The predictor variables of interest included the type of diabetes (pregestational vs. gestational), mode of delivery (cesarean section vs. vaginal), and birth weight for gestational age.

Additionally, the study included subgroup analyses such as comparing birth weight for gestational age using international and Indian standards, examining maternal profile and neonatal complications in babies born large for gestational age (LGA) with insulin treatment, studying outcomes in the pregestational diabetes mellitus (PGDM) group, and comparing outcomes between insulin-treated and non-insulin-treated groups. [8] The data collection process involved the Neonatal Intensive Care Unit (NICU) and newborn nursery, with thorough assessments at birth, feeding protocols, clinical observation and monitoring, and specific investigations based on clinical suspicion. [9]

The investigation protocols included monitoring blood sugar levels, conducting complete blood counts and bilirubin assessments, and checking calcium and magnesium levels when symptomatic. Additional investigations such as 2D echocardiograms and cardiac enzyme measurements were performed when specifically indicated. The statistical analysis involved examining the associations between maternal and perinatal factors and outcome variables related to neonatal morbidity. The Chi-square test was used to calculate p-

values, with values less than 0.05 considered statistically significant and values less than 0.001 considered highly significant.

Results

There were a total of 1074 deliveries during the study period. Out of which, 118 were in pregnancies with diabetes (gestational and pregestational diabetes mellitus). The overall incidence of diabetes in pregnancy (gestational and pregestational) in our institute was 10.98%, whereas that of gestational diabetes alone was 9.40%. 3 (2.5%) of these resulted in stillbirths.

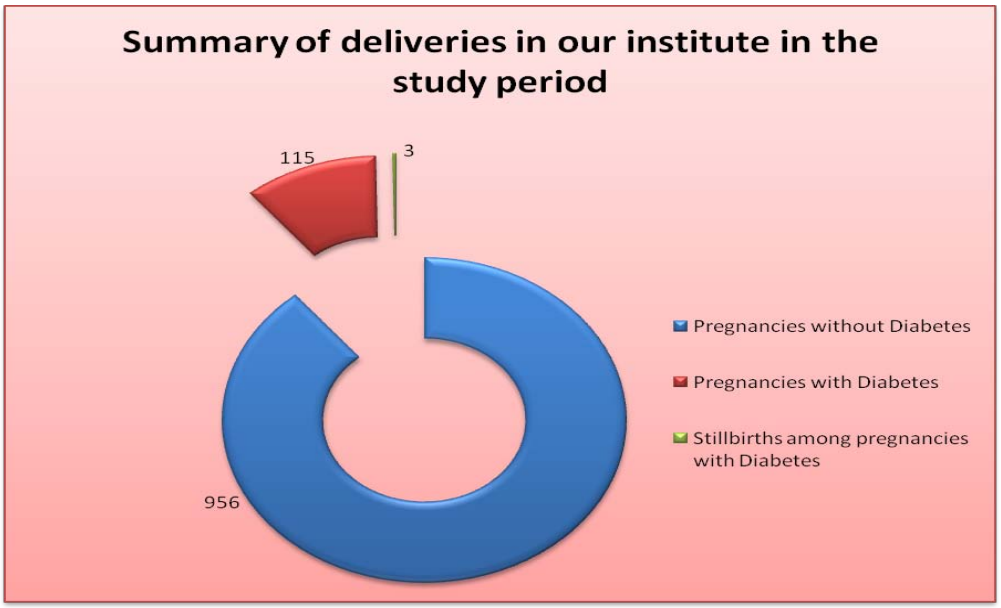

Figure 1: Summary of deliveries in our institute in the study period

A total of 130 infants of diabetic mothers were studied. 115 of these were born in our institute. The remaining 15 IDM babies were referred to our institute from other hospitals for further care. The main reason of referral included preterm care, respiratory distress, besides monitoring for hypoglycemia and other complications.

There was no mortality after an average period of observation of 6 days. The period of observation after birth ranged from 5 days to 2 months.

A total of 32 (26.1%) of the 130, were managed in the newborn nursery. 3 of these were later transferred to the NICU for symptomatic hypoglycemia. Babies born to mothers on insulin were admitted to the NICU irrespective of other risk factors. Other factors necessitating NICU admission were need of intensive resuscitation at birth (6 cases), preterm care (35 cases), and LBW care (19 cases).

Table 1: Maternal and neonatal demographics

Mean age of mothers in GDM group	30.3 years
Mean age of mothers in PGDM group	31 years
Mean gestational age at birth	37 weeks
Mean birth weight	2.94g

Maternal Demographics:

A total of 17 (13.07%) mothers had pregestational diabetes. The mean duration of pre pregnancy diabetes was 16 years. This group included Juvenile diabetes in addition to Type II diabetes. All were being managed with insulin. 31 mothers had family history of diabetes: 22% of GDM group and 35% of PGDM group.

Of the GDM group, most mothers were diagnosed in the third trimester of pregnancy. Of those who developed gestational diabetes, 47 (41.5%) were diagnosed in the second trimester, and 62 (54.86%) were diagnosed in the third trimester, whereas only 4 (3.5%) were diagnosed in the first trimester.

HbA_{1C} done at the time of diagnosis of was on an average 5.9 gm% in the GDM group and 6.5 gm% in PGDM group during pregnancy. Poor control with HbA_{1C} of 9.8 gm% was seen in 1 PGDM case. It is of note, that the infant born to this mother was full term SGA, required resuscitation at birth and was the only case of lumbar meningomyelocele in our study.

Out of the 17 cases of PGDM, only 3 mothers had duration of diabetes.

>10 yrs and HBA_{1C} > 7.5 gm %. Babies born to these 3 mothers had symptomatic hypoglycemia with BSL < 30mg/dl. Major malformations like congenital heart disease with congestive cardiac failure and meningomyelocele were also seen in these infants.

Most mothers 45 (39.82%) were managed on insulin, whereas 16 (14.15%) were managed on oral hypoglycemic agents. The remaining 46% were managed on diet alone. A total of 69 (53%) mothers were primigravida. 13 (10%) of the multigravida had bad obstetric history.

MODE OF DELIVERY:

There was vaginal delivery in 53 (40.7%) cases. Of which 35% were assisted.

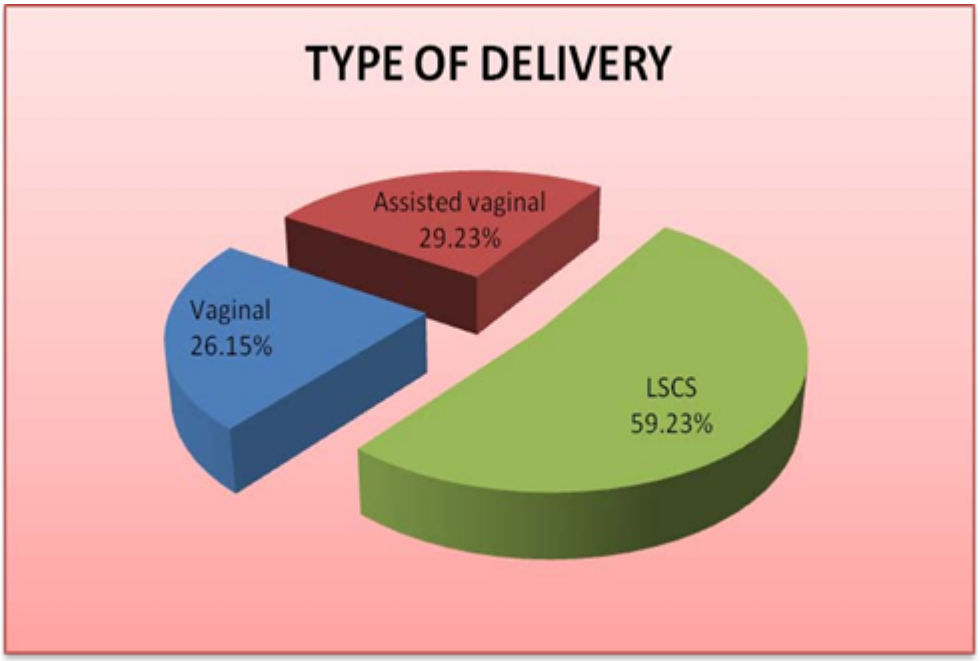

Figure 2: Mode of delivery

LSCS was done in 77 (59.2%) of total cases. 58% of all LSCS were emergency LSCS. The commonest indications for emergency LSCS were fetal 14 (30.43%) (Meconium-stained

amniotic fluid, loop of cord around neck, breech and footling presentation). Maternal indications were 25 (54.34%) (PIH, pre-eclampsia) and combined fetal as well as maternal 4 (8.69%) preterm prolonged rupture of membranes, failed instrumental delivery, polyhydramnios and deep transverse arrest.) Elective LSCS was performed for causes such as twins, previous LSCS, breech, CPD or HIV seropositivity in mother.

I. Neonatal Demographics:

Gestational Age At Birth:

Gestational age > 37 weeks at birth (full term deliveries) was seen in 95 (73.07%). Rests 26.92% were born preterm.

Table 2: Mean birth weight

Mean birth weight in term delivery	3.14 kg
Mean birth weight in preterm delivery	2.41 kg

The incidence of low birth weight (birth weight < 2.5 kg) was 20% (26 of 130) cases.

Weight For Gestational Age:

This study used 2 different standards to classify birth weight with respect to gestational age. First was intrauterine growth curves generated by using data on 3,91,681 infants aged 22-42 weeks at birth. This American study was published in 2010. [10]

Using these growth curves we found SGA (<10^{th} percentile) 12 (9.2%) cases, AGA (10-90^{th} percentile for gestational age) in 103 (79.23%) cases and LGA in15 (11.53 %).

Indian data for birth weight at various gestational ages was presented by Matthews Matthai et al in 1996. As the mean weight of Indian babies was significantly lower than those of the American growth curves, we reclassified babies as SGA, AGA and LGA as birth weight < 10^{th} percentile, between 10th and 90^{th}, and > 90^{th} percentile respectively. [11-14]

As birth weight data less than 33 weeks has not been studied, we could reclassify 121 out of the 130 babies. We found that birth weight > 90^{th} percentile was seen in 39 (32.23%) and < 10^{th} percentile were 5 (4.13%).

Table 3: Comparison between birth weight for gestational age by Indian and American growth curves.

	Indian data	American charts
LGA	32.23 %	11.5 %
AGA	63.63%	79.2 %
SGA	4.13 %	9.2 %

Figure 3: Comparison between birth weight for gestational age by Indian and American growth curves.

Table 4: Comparison between outcomes in terms of LGA in the insulin treated vs. Diet alone group.

Maternal treatment group (total =114)	LGA cases	AGA+SGA cases
Mothers on diet alone (52)	13	39
Mothers on diet and Insulin (62)	22	40
P value=0.22		

Neonatal Complications:

Overview:

Complications (excluding preterm and LGA/SGA) were seen in 88 (67%) of cases.

Table 5: Neonatal morbidity

Complication	No. of cases	Percentage (%)
Hypoglycemia	63	48
Hyperbilirubinemia	54	41.5
Hypocalcemia	18	13.8
Hypomagnesemia	9	6.9
Polycythemia	8	6.15
Cardiac dysfunction	13	10
RDS	3	2.3
Major Malformations	23	17.69

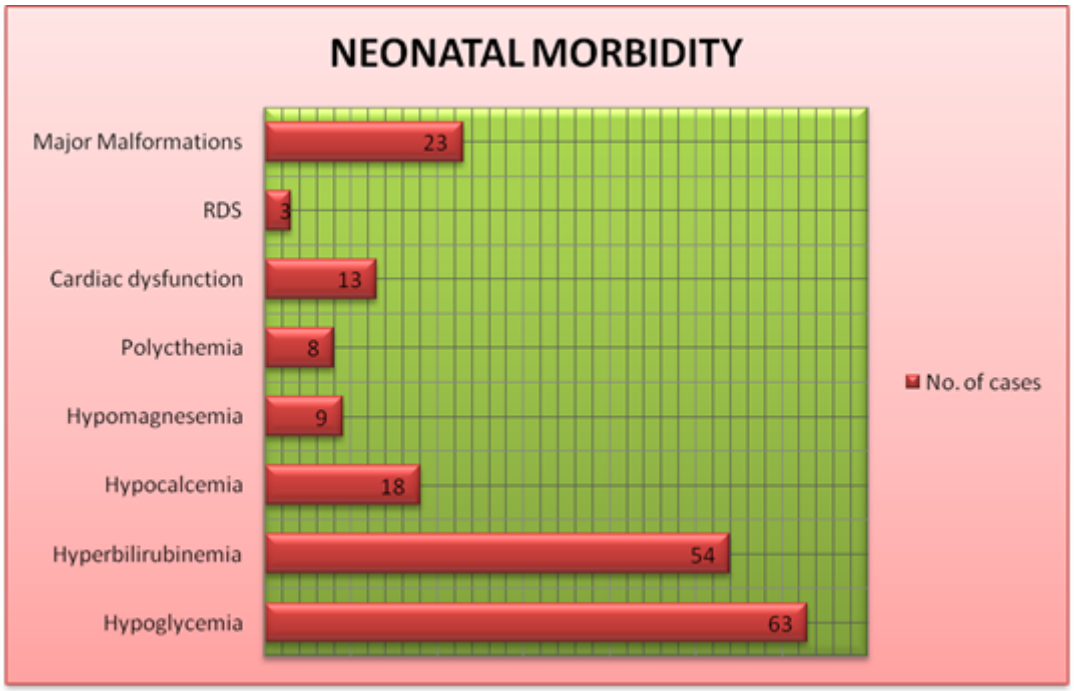

Figure 4: Neonatal morbidity

Hypoglycemia was the commonest neonatal complication, followed by hyperbilirubinemia and hypocalcemia. Major malformations were seen in 23 (17.6%) cases. Congenital heart disease was the commonest major malformation. Hairy pinna was seen in 15 (11.5%) cases.

Of other neonatal complications, need for intensive resuscitation was studied. Need for intensive resuscitation was seen in 15 (13.27%) of the GDM group and 4 (23.5 %) of the PGDM group. Though neonatal resuscitation was required more often in babies of PGDM mothers, we could not demonstrate any statistical significance (p value 0.26).

Metabolic Complications: Hypoglycemia:

Hypoglycemia was seen in 48.46% infants. 15 (88.23%) newborns of the PGDM group and 48 (42.48%) of those of the GDM group developed hypoglycemia. This association was statistically significant with a p value of 0.0004.

Relation of hypoglycemia in babies managed in newborn nursery vs. those admitted to NICU

Hypoglycemia was uncommon in babies admitted to newborn nursery after birth (6.8 % of all nursery admissions), as compared to those admitted in the NICU with a p value of 0.000001.

Timing of occurrence of hypoglycemia

Total no of hypoglycemia cases: n = 63. A total of 59 out of 63 cases (93.65%) of hypoglycemia occurred in the 1st 6 hours of life. Onset of hypoglycemia was most common in the first six hours of life. Of these 59 cases, only 7 cases (11.86%) had HBA_{1C} level > 7.5 gm%

Table 6: Time of onset of hypoglycemia

Hypoglycemia at	Cases
1st hr	40
2nd hr	13
3rd hr	7
4th hr	2
6th hr	6
8th hr	2
12nd hr	1
>12th hr	1
>36th hr	0

Babies who developed hypoglycemia were more commonly delivered by LSCS. The p value of this association is 0.01 and is thus statistically significant.

Table 7: Relation between occurrence hypoglycemia and LGA

Birth weight for gestational age	Hypoglycemia present	Hypoglycemia absent
LGA babies	19 (48.71%)	20 (51.28%)
AGA + SGA babies	44(48.35%)	47(51.64%)
P value=0.96 total cases= 130		

There was no co-relation between frequency of hypoglycemia in the LGA group (48.7%) and the non-LGA group (48.3%) p value 0.96. Babies who developed hypoglycemia, were more commonly born by LSCS. This association was statistically significant with a p value of 0.01.

Relation between occurrence hypoglycemia and delivery by LSCS

In the current study the proportion of hypoglycemia in infants of the insulin treated group was higher (58 %) than the group treated with OHA (43.75%), but this association was not statistically significant (p value= 0.3).

Management Of Hypoglycemia:

A total of 15(23.80%) were managed on feeds alone, 27(42.85%) required intravenous, dextrose in addition to oral feeds 21(33.33%) required intravenous dextrose bolus.

HYPERBILIRUBINEMIA:

Hyperbilirubinemia was seen in 54 (41.5%) of infants. Though hyperbilirubinemia was more commonly seen in the PGDM group (58.82%) as compared to the GDM group, we could not demonstrate any statistical significance in this association (p value 0.12).

Hypocalcemia: Hypocalcemia was seen in 18 (13.8%) of infants.

Hypocalcemia in GDM group vs. PGDM group

In our study hypocalcemia was strongly associated with babies of PGDM (29.44%) with a p value of 0.046 which was statistically significant.

Hypomagnesemia: Hypomagnesemia was seen in 9 (6.9%) of infants.

Systemic Complication:

a) **Respiratory System:** TTN was seen in 5 (3.8%) cases. RDS requiring surfactant occurred in 3(2.3%). Respiratory distress secondary to all causes was seen in 25 (19.2%).

b) **Cardiovascular System:** Myocardial dysfunction on 2 D ECHO was seen in 13 (10%) cases. 6 of these 13 babies did not have structural heart disease. 6 cases were associated with ventricular septal hypertrophy with or without other structural heart disease. Though cardiac dysfunction was more often (11.76%) seen in babies of PGDM we could not demonstrate any statistical significance (p value 0.79). Five out of six infants with interventricular septal hypertrophy were LGA. This association is statistically significant (p value-0.006).

Table 8: Association of LGA and Interventricular septal hypertrophy

IVH	No. of LGA	AGA+SGA
Present	5 (83.33%)	1 (16.66%)
Absent	34 (29.56%)	81 (70.43%)
P value=0.006 total cases=121		

(Classification using data of 121 infants using Indian charts)

c) **Major Malformations:**

Cardiac malformations were the commonest, seen in 18(13.84%) of all IDM. It constituted 78.26% of all major malformations. ASD was the most common structural heart disease seen in 72.22%cases. ASD was found alone or in combination with other structural defects. Other common lesions were VSD and PDA. Rare findings were 1 case each of aortic regurgitation and pulmonary stenosis. Though CHD was more commonly found in babies of PGDM (23.52%), we could not demonstrate any statistical significance.

Predictors Of Neonatal Morbidity:

Table 9: Comparison between GDM and PGDM

Variables	PGDM N=17 N (%)	GDM N=113 N (%)	Total (%)	OR (PGDM/ GDM)	Chi-square	95% CI	P value
Hypoglycemia	15 (88.2%)	48 (42.4%)	63 (48.4%)	10.15	12.38	2.2-46.52	**0.0004**
Hyperbilirubinemia	10 (58.8%)	44 (38.93%)	54 (41.5%)	2.24	2.40	0.79-6.3	0.12
Hypocalcemia	5 (29.4%)	13 (11.5%)	18 (13.8%)	3.20	3.97	0.97-10.56	**0.046**
Hypomagnesemia	0	9 (7.9%)	9 (6.9%)	-	1.4	-	0.2
Polycythemia	1 (5.8%)	7 (6.1%)	8 (6.1%)	0.94	0.24	0.1-8.2	0.62
Cardiac dysfunction	2 (11.7%)	11 (9.7%)	13 (10%)	1.23	0.03	0.24-6.13	0.86
Major malformations	6 (35.2%)	17 (15.0%)	23 (17.6%)	3.08	4.16	1-9.44	**0.041**
LGA by AAP	2 (11.7%)	13 (11.5%)	15 (11.5%)	1.0256	0.14	0.2-5	0.7
LGA by Indian	6 (35.2%)	33 (29.2%)	39 (30%)	1.32	0.26	0.45-3.86	0.6

SGA	2 (11.7%)	10 (8.8%)	12 (9.2%)	1.37	0.003	0.27-6.88	0.95
Prematurity	5 (29.4%)	30 (26.5%)	35 (26.92%)	1.15	0.06	0.37-3.54	0.80
Resuscitation required	4 (23.5%)	15 (13.2%)	19 (14.6%)	2.01	0.55	0.5-6.98	0.45

Discussion

The prevalence of gestational diabetes varies in different studies. In an Indian study conducted in Jammu in 2011, the prevalence was reported as 6.94%. Other international studies have reported a prevalence of 2-6%.

A total of 130 babies born to diabetic mothers were included in the study. One baby was discharged against medical advice and lost to follow-up. The average observation period was 6 days, and no deaths occurred after a minimum follow-up of 3 days.

The stillbirth rate in our study was 2.5%, which is similar to findings from other studies. Out of 130 babies, 115 were born in our institution, while 15 were delivered elsewhere and referred to our institution for further care. Reasons for referral included preterm care, respiratory distress, monitoring for hypoglycemia, and other complications. [12,13-15]

Out of the 130 babies, 33 were managed in the newborn nursery. Infants born to mothers on oral hypoglycemic agents or those on diet control alone with no other major risk factors were also managed in the newborn nursery. Three of these babies were later transferred to the Neonatal Intensive Care Unit (NICU) due to severe hypoglycemia. In a previous study, 17.6% of babies admitted for routine care were subsequently transferred to the NICU for treatment of hypoglycemia, respiratory distress syndrome (RDS), or both. [16-18]

Babies born to mothers on insulin were admitted to the NICU, regardless of other risk factors. Other factors that necessitated NICU admission were the need for intensive resuscitation at birth (4 cases), preterm care (35 cases), and low birth weight (10 cases). A study found a significantly higher rate of admission to the NICU for infants of gestational diabetic mothers compared to babies of non-diabetic mothers (21.7% versus 7.8%). [19-22]

In our study, 17 mothers (13.07%) had pregestational diabetes. In another study of 466 diabetic patients, 28% had pre-existing clinical diabetes requiring insulin treatment during pregnancy, while 72% had gestational diabetes. The average duration of pre-pregnancy diabetes in our study was 16 years, and all these cases were managed with insulin. This group included cases of both juvenile diabetes and Type II diabetes. A study conducted in Scotland in 2003 examined the outcomes of pregnancies in women with Type 1 Diabetes. Out of 273 pregnancies, 40 ended in miscarriage, 20 in abortion, and 213 in delivery. [20-22]

A positive family history of diabetes was reported in 24.19% of mothers with gestational diabetes in a study by Vahi et al. In our study, 24 out of 113 (21%) mothers with gestational diabetes had a positive family history of diabetes. [23]

Among the gestational diabetes mellitus (GDM) group, most mothers were diagnosed in the third trimester of pregnancy. Of those who developed gestational diabetes, 47 were diagnosed in the second trimester, and 62 were diagnosed in the third trimester, while only 4 were diagnosed in the first trimester. The average HbA1C levels at the time of diagnosis were 5.9 gm% in the GDM group and 6.5 gm% in the pregestational diabetes mellitus (PGDM) group during pregnancy.

One case of PGDM had poor control with a high HbA1C level of 9.8 gm%, and this infant experienced several complications. The majority of mothers (39.82%) were managed with insulin, while a smaller percentage (14.15%) were managed with oral hypoglycemic agents. [24-26]

The overall incidence of diabetes in pregnancy (gestational and pregestational) in our institute is 10.98%, whereas that of gestational diabetes alone is 9.40%. 3 (2.5%) of these resulted in stillbirths.130 infants born to diabetic mothers were prospectively studied during the study period. A total of 17 (13.07%) mothers had pregestational diabetes.

All were being managed with insulin. Of the GDM group, most mothers (54.86%) were diagnosed in the third trimester of pregnancy. Again, most mothers (46%) were managed on diet alone, 39.82% were managed on insulin and only 14.15% were managed on oral hypoglycemic agents. [27-31]

Conclusion

Institutional policy regarding care of an infant of diabetic mother should be evidence based, and meticulously practiced. Appropriate training of medical and nursing staff should be routinely done, to implement optimum care.

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