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Morbidities and its Immediate Outcome in Newborns Born Through Mothers with Gestational Diabetes Mellitus

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ABSTRACT

Introduction: Gestational Diabetes mellitus is associated with significant risk of maternal and neonatal morbidity.

Objective: The objective of this study was to assess the different morbidities and their immediate outcome in newborns born to mother with gestational diabetes mellitus.

Methods: A descriptive cross sectional study was done among 349 inborn neonates born to mothers with gestational diabetes mellitus, at the Department of Pediatrics and Adolescent medicine, B.P. Koirala Institute of Health Sciences. Informed written consent and ethical approval was taken. The different socio demographic & clinical parameters of the mothers and neonates were taken. The data was analysed using relevant statistical tests.

Results: Out of the total 11977 deliveries, there were 431 (3.6%) deliveries of mothers with gestational diabetes mellitus. More than half of the neonates were male. The mean birth weight and gestational age of the neonates were 39±2 weeks and 3100 ± 570 gram respectively. Sixty four (18.3%) neonates had some form of morbidity. The three major morbidities in the neonates were small for gestational age (n=39, 11.2%), preterm birth (n=34, 9.7%) and neonatal hyperbilirubinemia (n=24, 6.9%). The incidence of macrosomia, hypoglycemia, hypocalcemia, polycythemia, cardiac defects and gross congenital anomalies were 21 (6%), 22 (6.3%), six (1.7%), one (0.3%), eight (2.3%) and two (0.6%) respectively. Similarly, 22 (6%) neonates needed admission, out of which 16 (4.6%) recovered and got discharged, while six (1.4%) expired.

Conclusions: The major morbidities associated with neonates born to mother with gestational diabetes mellitus were small for gestational age, prematurity, neonatal hyperbilirubinemia and hypoglycemia.

Keywords: Hypoglycemia; macrosomia; prematurity; small for gestational age.

INTRODUCTION

Gestational Diabetes Mellitus (GDM) is defined as any degree of impaired glucose tolerance with onset or first recognition during pregnancy.[1] GDM is one of the most common complications occurring in pregnancy and is associated with a significant risk of maternal and neonatal morbidity.[2] The rise in maternal blood glucose level results in fetal hyperinsulinemia which increases the fetal growth.[3] There is an increased risk of perinatal mortality and morbidity, including hyperbilirubinemia, macrosomia, small for gestation, birth trauma, and hypoglycemia in infants born to mothers with GDM.[4] An increased rate of stillbirths in untreated GDM have been observed in other studies as well.[4,5] The babies born to mother with GDM are at a risk of obesity and type 2 diabetes in adulthood. A better glycemic control in GDM could potentially decrease the risk of maternal/fetal complications, and also the risk of diabetes in adults.[6]

This study has focused on finding the morbidities in newborns and their immediate outcome. This will help in the early diagnosis, management, prevention of morbidities and complications, and prognostication of newborns born to mothers with

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GDM. The objective of this study was to assess the different morbidities and their immediate outcome in newborns born to mother with GDM.

METHODS

A descriptive cross-sectional study was done in the Neonatology division of Department of Pediatrics and Adolescent medicine at B.P. Koirala Institute of Health Sciences (BPKIHS), a tertiary care referral center in eastern Nepal over a period of one year (from 15th July 2020 to 15th July 2021). The sample size was calculated using the following:

This study considered 95% confidence Interval (C.I) and 80% power to estimate a sample size. The total number of deliveries last year at BPKIHS was 12,096. According to a study done by Kumari R et. al in New Delhi, 20.6% of newborns of mothers with GDM developed Hypoglycemia.[7]

Using one sample formula,

$$n_0 = \frac{Z^2pq}{L^2}$$

where,

P=Percentage or proportion
Z= 1.96 at 95% CI
p= 20.6
q=100-20.6 = 79.4
q=100-p
L=Permissible error
L= 10% of p=2.06

Sample size (n_0) = 1525

Based on previous medical records of BPKIHS, the number of cases of GDM has been reported 400 in 2018.

So, N=400

Corrected sample size,

$$n = \frac{n_0}{1+n_0/N}$$

Now corrected sample size: n=317
Adding 10% of non-responders
Final sample size n=317+10% of 317=349
Final sample size n=349

Convenience sampling technique was used. All inborn neonates born through mothers with Gestational Diabetes Mellitus, and whose parents consented to participate, were included in the study. However, neonates of mothers with: underlying infectious diseases, autoimmune diseases, pregnancy induced hypertension or chronic hypertension, history of teratogenic drugs intake, mothers who left against medical advice, outborn deliveries, and those not willing to take part in the study were excluded. Ethical clearance was obtained from Institutional Review Committee, BPKIHS (Ref number: 480/076/077-IRC; dated 14th July 2020).

Informed written consent was obtained from the parents in local language. All newborns born to mothers diagnosed with GDM were enrolled in the study. GDM was diagnosed based on the Carpenter and Coustan criteria. The threshold values used for blood glucose levels were 95mg/dL, 180mg/dL, 155mg/dL, and 140mg/dL at fasting, 1 hour, 2 hour and 3 hour after a 100 gram oral sugar load. The detailed socio demographic & clinical history of the mother and clinical and anthropometric parameters of the baby were taken and entered in a pre-designed proforma.

The anthropometric parameters were interpreted by looking at different growth charts. For preterm babies (defined as babies born before 37 weeks of gestation), Intergrowth 21 chart and for term babies (defined as babies born between 37 0/7 weeks of gestational age till 41 6/7weeks), World Health Organization (WHO) growth chart were taken for reference and accordingly the diagnosis of Large for Gestational Age (LGA; defined as birth weight above 90th percentile), Small for Gestational Age (SGA; defined as birth weight less than 10th percentile) and Appropriate for Gestational Age (AGA; defined as birth weight between 10th and 90th percentile) was made.[8] A thorough physical examination of the baby was done typically focussing on gross congenital anomalies (defined as presence of any visible life threatening birth defect).

All the newborns of diabetic mothers enrolled in this

study underwent blood sugar testing by glucose strip test at 0,1,3,6,12,24,36, 48 and 72 hours of life, as is being routinely done. Any alteration in the blood glucose diagnosed as hypoglycaemia (defined as a blood glucose level less than 45mg/dl, which could be symptomatic or asymptomatic. Symptomatic hypoglycemia was defined as a blood glucose level less than 45 mg/dl with clinical symptoms like lethargy, jitteriness, poor sucking or seizure; while asymptomatic hypoglycemia was defined as a blood glucose levels less than 45 mg/dl without any clinical symptoms) was treated as per the standard treatment guidelines. No alteration in the treatment protocol was made in this regard.

Those babies who were symptomatic; that is having poor feeding (ill sustained rooting/sucking), lethargy, abnormal body movement, fast breathing, grunting, yellowish discolouration of body were admitted and these babies were screened for hypocalcemia (defined as ionic serum calcium less than 1mmol/l in preterm neonates and less than 1.2mmol/l in term neonates), polycythemia (defined as venous hematocrit more than 65% or a venous hemoglobin concentration of more than 22 gm/dl), hypomagnesemia (defined as total magnesium ≤0.65 mmol/L (1.6 mg/dl)), hyperbilirubinemia (defined as yellowish discoloration of body along with altered total bilirubin levels for preterm and term babies according to bilirubin normogram) and congenital heart diseases (defined as **range of birth defects that affect the normal way the heart works)** respectively. Serum ionized calcium, serum magnesium and echocardiography of the babies were performed whenever there was clinical suspicion of hypocalcemia, hypomagnesaemia and congenital heart disease respectively. No deviation from the routine treatment protocol was made in this regard. The Outcome of the babies was defined as those requiring admission and those not requiring admission (sent to mother side). Further the outcome of those babies who required admission was classified as recovered (discharged) and not recovered (expired).

Data was entered in Microsoft Excel, and converted into Statistical Package for Social Sciences (SPSS 11.5) for statistical analysis. Descriptive statistics were used to analyze the data like mean, median and standard deviation (SD).Chi-square test was used for analysis of categorical data and association between the variables. Fisher's exact test and continuity correction was used as per the need of data. After analysis of data, the results were presented through tabulations and charts.

RESULTS

This study was conducted over a period of one year among 349 babies who were born to mothers with Gestational Diabetes Mellitus (GDM). Out of the total 11977deliveries in this hospital during this study period, the number of mothers with GDM who delivered was 431(3.6%). The mean age of the mothers was 27.7±4.6 years. There were 153 (44%) primigravida mothers, while the remaining 196 (56%) were multigravida. Serum glycosylated haemoglobin level (HbA1C) level could be done in only 30 mothers. Of those, in whom serum glycosylated haemoglobin level was done, the mean value (in %) was 5.6±0.8. The baseline characteristics of the mothers are shown in Table 1 below.

Only seven (2%) mothers had GDM related complications (nephropathy and neuropathy). None

Table 1: Baseline characteristics of mothers.

S.N.	Characters	Mean±SD
1.	Age of Mother(years)	27.7±4.6
2.	Gestational age(weeks)	39±2
3.	Weight(kg)	64.5±5.8
4.	Height(cm)	152.6±4.3
5.	BMI(Kg/m²)	27.8±2.9
6.	Period of Gestation at which GDM Detected(weeks)	23.1±5.3

had retinopathy. Twenty mothers (5.7%) had family history of diabetes while 33(2%) had hypothyroidism and were under medication.

Majority of the mothers (77.1%, n=269) were under diabetic diet only as a mode of treatment, while 33 (9.5%) mothers were taking oral hypoglycemic drugs. Eleven (3.2%) took insulin, while 36 (10.3%) were not under any medication or diabetic diet.

There were 192 (55%) male and 157 (45%) female neonates. The mean birth weight, head circumference and length of the neonates were 3100 ± 570 gm, 32.7 ± 1.2 cm and 46.9 ± 1.9 cm respectively. There were 289 (82.8%) neonates who were born appropriate for gestational age. Similarly, there were 297 (85.1%) term neonates. Spontaneous Vaginal Delivery (SVD), Lower Segment Caesarean Section (LSCS) and Vacuum Assisted Vaginal Delivery (VAVD) were the modes of delivery. The different baseline characteristics of the neonates are given in Table 2 below.

Sixty four (18.3%) neonates had some form of morbidity, while the remaining 285 (81.75%) had no morbidities, whatsoever. Factors like gender, mode of delivery and gestational age at diagnosis of GDM were compared with the occurrence of morbidity in the neonates. It was observed that the rate of morbidity was significantly higher in the male neonates as compared to female neonates. However, the mode of delivery and gestational age at diagnosis of GDM had a comparable rate of morbidity. The details are given in Table 3.

Table 2: Baseline characteristics of neonates.

Characteristics		Frequency, n (%)
Gender	Male	192(55)
	Female	157(45)
Mode of Delivery	SVD	184(52.7)
	LSCS	156(44.7)
	VAVD	9(2.6)
APGAR score	Normal	337(96.6)
	Abnormal	12(3.4)
Birth weight	<1 kg	1 (0.3)
	1-1.5 kg	3 (0.9)
	1.5-2.49 kg	39 (11.2)
	2.5-3.9 kg	285 (81.7)
	≥4 kg	21 (6)

Table 3: Comparison of different factors with occurrence of morbidity in babies.

Characteristics		Morbidity in baby		Total	p value
		Morbidity present	Morbidity absent		
Gender	Male	43 (12.3)	149 (42.7)	192 (55)	0.03*
	Female	21 (6)	136 (39)	157 (45)	
Mode of delivery	SVD	33 (9.5)	151 (43.3)	184(52.7)	0.94*
	LSCS	29 (8.3)	127 (36.4)	156(44.7)	
	VAVD	2 (0.6)	7 (2)	9(2.6)	
Gestational age at which GDM was diagnosed (weeks)	<20	8 (2.3)	53 (15.2)	61 (17.5)	0.24†
	20-25	30 (8.6)	152 (43.6)	182 (52.1)	
	26-30	22 (6.3)	67 (19.2)	89 (25.5)	
	>30	4 (1.1)	13 (3.7)	17 (4.9)	
Total		64 (18.3)	285 (81.7)		

*: chi square test; †: Fisher Exact test

The three major comorbidities seen in the neonates were SGA, preterm birth and Neonatal Hyperbilirubinemia (NNH). All neonates who developed NNH received phototherapy and none underwent Double Volume Exchange Transfusion (DVET) or developed Acute Bilirubin Encephalopathy (ABE). There were 21 (6%) neonates who were born large for gestational age. However, none of them developed shoulder dystocia or any forms of birth injury. Glucose monitoring was done in all neonates. Hypoglycemia was the major metabolic derangement seen. Out of 22 (6.3%) neonates who developed hypoglycemia, 16 (4.6%) had asymptomatic hypoglycemia, while six (1.7%) neonates were symptomatic and got admitted. The median (Inter quartile range) age at which hypoglycemia occurred was 12 hours (7.6, 24). Similarly, six (1.7%) neonates developed asymptomatic early onset hypocalcemia while three (0.9%) had hypomagnesemia. None of the neonates developed seizure or any neurological deficit secondary to metabolic derangements. Complete blood count was sent in the admitted neonates only. Majority (n=14, 4.6%) of the admitted neonates had a normal complete blood count result. Echocardiography was done in all the admitted neonates. Cardiac defects were seen in the echocardiography of eight (2.2%) neonates, who were admitted. Out of three (0.9%) neonates with Patent Ductus Arteriosus (PDA), two were preterm. One of those preterm expired due to cardiogenic shock. Similarly, gross congenital anomaly was seen in two neonates (0.6%), of which there was a case each of anencephaly and cleft lip and palate.

The details of the morbidities seen in the neonates are given in Table 4.

Only 28 (8%) neonates required some form of resuscitation (oronasal suction, tactile stimulation, bag and mask ventilation and bag and tube ventilation). Of the total enrolled neonates, 22(6%) required admission while the remaining 327 (93.7%)

Table 4: Comorbidities seen in neonates.

Comorbidity		Frequency, n (%)
Small for Gestational age		39(11.2)
Large for Gestational age		21(6)
Pre term		34(9.7)
Post term		18(5.2)
Respiratory Distress Syndrome		10(2.9)
Perinatal Asphyxia		7(2)
Neonatal Hyperbilirubinemia		24(6.9)
Sepsis		2(0.6)
Metabolic Complications	Hypoglycemia	22(6.3)
	Hypocalcemia	6(1.7)
	Hypomagnesemia	3(0.9)
Hematological abnormality	Anemia	1(0.3)
	Polycythemia	1(0.3)
	Thrombocytopenia	6(1.7)
Cardiac defect	Atrial Septal defect	3 (1)
	Ventricular Septal defect	2(0.6)
	Patent Ductus Arteriosus	3 (0.9)
Gross congenital anomaly	Anencephaly	1(0.3)
	Cleft lip and palate	1(0.3)

Table 5: Interventions needed during neonatal resuscitation.

Characteristics	Frequency, n (%)
Oronasal Suctioning	12 (3.5)
Bag and mask ventilation	10 (3)
Bag and tube ventilation	3 (1)
Tactile stimulation	3 (1)
Total	28 (8)

Table 6: Final outcome of admitted neonates.

Characteristics		Frequency, n (%)
Required admission		22 (6)
Indication for admission	Prematurity	11 (3.2%)
	Respiratory Distress Syndrome	10 (2.9%)
	Perinatal asphyxia	7 (2%)
	Hypoglycemia	6 (1.7%)
	NNH	3 (0.9%)
Discharged after recovery		16 (4.6)
Expired		6 (1.4%)
Cause of death	Anencephaly	1 (0.3)
	Sepsis	2 (0.6)
	Cardiogenic shock	1 (0.3)
	Respiratory Distress Syndrome	2 (0.6)

were sent mother side. The different interventions needed during neonatal resuscitation are mentioned in table 5 above.

Out of 22 (6%) neonates who were admitted, 16(4.6%) recovered and were discharged whereas six (1.4%) expired. The details of the outcome of the admitted neonates are given in Table 6 above.

DISCUSSION

Gestational diabetes mellitus (GDM) is associated with increased maternal, fetal, and neonatal risks and complications. The prevalence of GDM has been on an increasing trend, probably because of increasing rate of overweight and obesity.[9]

During the study period, the total number of hospital delivery was 11977, out of which 431 (3.6% of total deliveries) had GDM. Therefore, the hospital incidence of GDM pregnancy was seen to be 3.6%. This is similar to the findings of study done by Wasim Rafiq et al and Deorari AK et al.[10,11] The reason might be the similarity between the study population in these studies.

The incidence of macrosomia in this study was six percent. Similar were the findings made by Langer O et al, Mitanchez D et al and Nair VG et al.[12-14] However the incidence of macrosomia was found to be higher in the study done by Cordero L et al (36%).[15] The reason for the lower incidence of macrosomia in our study could be the treatment received by most of the mothers (89.7%) resulting in good glycemic control. In contrast, the reason for higher incidence of macrosomia in the latter study was that the study population had not received treatment.

The incidence of SGA in this study was 11.2%. This is dissimilar with the findings of study done by Barquiel B et al, in which a higher incidence (23.9%) of SGA was noted.[16] Also, Cordero L et al found that only two percent of babies in their study were

SGA.[15] The reason might be the racial differences and references of growth chart used.

Out of the total number of babies born to mothers with GDM, 9.7% were born preterm. Contrary to this finding Yogev Yet al and Wang C et al, in their studies found the incidence of preterm delivery in GDM mothers to be 0.7% and 2.7% respectively.[17,18] The discrepancy could be attributed to other factors causing preterm delivery like age at delivery, Body Mass Index (BMI) and presence of other comorbidities in mother.

In this study the incidence of gross congenital anomaly was 0.6%. This includes one case of anencephaly and one cleft lip and palate. However, Wasim Rafiq et al (3.12%) and Silverman BL et al (7%) observed a higher rate of detection of gross congenital anomaly.[10,19] This lower rate of gross congenital anomaly in our study could be attributed to lower sample size.

Hypoglycemia is a major problem in babies born to mothers with GDM. The incidence of hypoglycemia was 6.3% in our study. This is similar to the other studies done by Barquiel B et al (4.9%), Crowther CA et al (7%) and Voormolen DN et al (5%).[16,20,21] The routine testing of blood glucose in neonates might be the reason for the timely detection of hypoglycemia. Similarly, the incidence of hypocalcemia in this study was 1.7%.However, Barquiel B et al, in his study, found the incidence of hypocalcemia to be 0.4%.[16]

Out of total neonates born to mothers with GDM, 0.3% had polycythemia which was similar to the findings given by Barquiel B et al.[16] However, Deorari AK et al found a higher incidence of polycythemia (11%) in their study.[11] Likewise, the incidence of respiratory distress syndrome (RDS) in this study was found to be 2.9%, which is similar to the findings of Barquiel B et al (3.4%) and Persson M et al (1.8%).[16,22] However, in the study done by Wasim Rafiq et al, the incidence of RDS was higher, that is, 13%.[10] Nearly seven percent of the babies developed neonatal hyperbilirubinemia, in our study, which was similar to the findings of Crowther CA et al (9%).[20] In the present series, perinatal asphyxia was seen in two percent babies. Also, none of the babies had shoulder dystocia. The reason for not having a case of shoulder dystocia might be the lower incidence of macrosomia and instrumental deliveries. Similarly, neonatal sepsis was seen in only 0.6% of babies .Lower incidence of sepsis must be attributed to the study subjects being inborn and strict aseptic protocols followed during the time of delivery.

Cardiovascular anomaly was seen in 2.2% babies, which included ASD, VSD and PDA. Cordero L et al (3.37%) observed a similar incidence of cardiovascular anomaly in their studies.[15] However, Tabib A et al observed a higher incidence (8.8%) of cardiovascular anomaly in their study.[23] The reason for the higher incidence of detection of cardiovascular anomaly in the latter study might be the screening echocardiography done in all enrolled mothers with GDM.

The final outcome in this study was divided as those babies who required admission and those who did not. Six percent of babies required admission, out of which 4.6% recovered and got discharged while 1.4% expired. This was similar to the findings done by Wasim Rafiq et al.[10] However Odar E et al found a higher incidence of perinatal mortality (16.7%) in their study.[24]

Limitations of the study: Not all mothers in the study were booked. The mothers presented to the hospital at different gestational age. Serum HbA1C level could not be done in all mothers. Thus the degree of glycemic control over the past three months could not be ascertained. Similarly, the time of initiation of treatment in mothers with GDM was different. Therefore, the degree of glycemic control could not be compared with the occurrence of morbidities in the neonates.

CONCLUSIONS

Gestational Diabetes Mellitus is associated with significant neonatal morbidity. Small for gestational age, prematurity, neonatal hyperbilirubinemia and hypoglycemia were the leading morbidities observed in the study. A timely anticipation of these morbidities in neonates born to mothers with gestational diabetes mellitus is essential for the detection, treatment and prognostication of such morbidities.

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