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Original Article

Birth Weight Pattern and Immediate Morbidities in 452 Neonates Born to Diabetic Mothers: A Tertiary Centre Perspective

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Abstract

Introduction: Neonates born to diabetic mothers continue to remain as high-risk neonates despite advanced care of gestational diabetes mellitus (GDM). Morbidities including macrosomia remain a significant problem. We aimed to study the birth weight pattern, incidence of hypoglycemia and immediate morbidities in neonates born to diabetic mothers.

Methods: Neonates born to diabetic mothers were prospectively studied over 18 months. The birth weight pattern, hypoglycemia, biochemical abnormalities, hyperbilirubinemia and other systemic morbidities were studied.

Results: Among 4654 live births, 516 (11%) neonates were born to diabetic mothers. After excluding 64, 452 neonates were further studied. Overall, 76.1% had normal birth weight. Large for gestational age (LGA) was found in 46 (10.2%). Small for gestational age (SGA) was found in 2.9%. Among 320 neonates born to GDM mothers on diet, 8 (2.5%) were SGA and 32 (10%) were LGA. Among 78 neonates born to GDM mothers on oral hypoglycemic agents, 2 (2.6%) were SGA and 12 (15.4%) were LGA. In 54 neonates born to GDM mothers on insulin, 3 (5.6%) were SGA and 2 (3.7%) were LGA. Overall, 21.7% had one or other morbidity. The overall incidence of hypoglycemia was 15.9%. Hyperbilirubinemia (34.5%) and congenital heart defects (31.8%) were the common morbidities. The other immediate morbidities included respiratory morbidities (9.7%), sepsis (3.8%), polycythemia (2%), birth injuries (1.7%) and perinatal asphyxia (0.9%).

Conclusion: About 10% of neonates born to diabetic mothers have macrosomia. Macrosomia was found more in neonates born to GDM mothers who were on oral glycemic agents than those on insulin. Glucose monitoring is needed in neonates of GDM mothers to detect hypoglycemia early.

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Introduction

Neonates born to diabetic mothers continue to remain as high-risk neonates despite reported improvement in neonatal outcome following treatment of gestational diabetes mellitus (GDM).[1-6] The WHO has predicted 35% increase in prevalence of diabetes between 1995 and 2025, of which Asian women display highest prevalence of GDM (17%).[2] Incidence of diabetes is reported in 4% in pregnancies with live births and 88% of these are complicated by GDM. GDM reported to occur in 3 – 12% of pregnancies in the USA.[3] It is estimated that about 4 million women are affected by GDM in India, at any point of time.[4] A community-based prospective

Indian program showed GDM prevalence of 13.9% (1679 / 12056).[5] The frequency across rural, semi-urban and urban areas was 9.9%, 13.8% and 17.8% respectively.

Morbidity among neonates born to diabetic mothers remains a significant problem.[7-12] The causes for fetal and neonatal sequelae of maternal diabetes are multifactorial. A recent WHO Global Survey on maternal and perinatal outcomes in 23 developing countries identified macrosomia as one of the main complications in neonates of mothers with GDM (0.5% to 15%).[7] These neonates are also at increased risk of hypocalcaemia, hypoglycaemia, hypomagnesaemia, hyperbilirubinemia, polycythemia, RDS, congenital malformations and hypertrophic cardiomyopathy.[13-17]

We aimed to study the birth weight pattern, incidence of hypoglycemia and immediate morbidities in neonates born to diabetic mothers.

Methods

Neonates born to diabetic mothers at Manipal Teaching Hospital, Mangalore, India were prospectively studied over 18 months (January 2017 to June 2018). Approval was obtained from Institution Ethics Committee prior to commencing the study. An informed consent was taken from the parents. Macrosomic neonates with known syndromes such as Beckwith-Wiedemann syndrome and multiple births were excluded. Diabetes in pregnant woman was classified as pre-gestational diabetes (PGDM) or GDM. PGDM was confirmed by history and past laboratory tests that existed before conception. PGDM was diagnosed if fasting plasma glucose ≥ 7.0 mmol / L (126 mg / dl). Mothers with HbA1c > 6.5% were considered as poor glycemic control and < 6.5% as good glycemic control. GDM was based on International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria, as follows: At any time in pregnancy if one or more of the following criteria are met: fasting plasma glucose ≥ 93 mg / dL (5.1 mmol / L); One hour plasma glucose ≥ 180 mg / dL (10.0 mmol / L) following a 75 g oral glucose load 2-hour plasma glucose ≥ 153 mg / dL (8.5 mmol / L) following a 75 g oral glucose load (OGTT).[14] OGTT was obtained at 24 - 28 weeks of gestation.[12] Demographic data, detailed antenatal history, blood glucose levels, results of OGTT, timing of diagnosis of diabetes, details of antenatal management of diabetes and neonatal details were obtained. Blood sample of neonates were noted with Glucometer (Accu Chek). Serum sodium, calcium, magnesium, Hb and packed cell volume (PCV) were carried out on second day of life. Abnormal laboratory parameters were followed up until normalized. Hypoglycemia was managed as per standard protocol. If hypoglycemia is documented, feed was given and GRBS repeated within one hour. If hypoglycemia persisted despite oral feeds, intravenous (IV) glucose with GIR at 6 mg / kg / min was administered and GRBS monitored further. In VLBW and preterm neonates < 34 weeks gestation, IV glucose was commenced from birth. If hypoglycemia still persisted then insulin level was obtained. Onset and progression of the jaundice was documented by visual and transcutaneous assessment. The need for phototherapy and its duration was noted. Findings of neonatal echocardiography were recorded. Weight of unclothed newborn within the first hour of life to the nearest of 5 g with electronic weighing machine was taken as birth weight (BW). Gestational age was determined by maternal last menstrual period (LMP) and / or antenatal ultrasonography (USG) and classified as preterm: gestational age < 37 completed weeks; term: gestational age of 37 to less than 42 completed weeks and post term: gestational age of ≥ 42 completed weeks. Neonates were classified as appropriate for gestational age (AGA) if birth weight was between 10th and 90th percentile for gestational age; small for gestational age (SGA) if birth weight was less than 10th percentile for gestational age and large for gestational age (LGA) if birth weight was above the 90th percentile for gestational age.

Hypoglycemia was defined as GRBS less than 45 mg / dL on day 1 of life and less than 50 mg / dL beyond 24 hours of life. If hypoglycemia detected, formal glucose by glucose oxidase method was obtained. Hypocalcemia was defined as total serum calcium concentration < 7 mg / dL or ionic calcium < 4 mg / dL. Corrcted calcium was considered if there was hypoalbuminemia. Hypomagnesemia was defined as serum magnesium < 1.6 mg / dL. Polycythemia was defined as venous hematocrit greater than 65%. Hyperbilirubinemia was defined as per AAP criteria.[15] Perinatal asphyxia was considered in a neonate who satisfied any of the following criteria: Apgar score of < 6 at 5 minutes or umbilical cord blood pH ≤ 7.0 or features suggestive of hypoxic encephalopathy (HIE). HIE was considered in the presence of the following features in an asphyxiated neonate: neurologic manifestations like hyper alertness, seizures, coma or tone abnormality along with other clinical features of Sarnat's stages 1, 2 or 3. RDS syndrome was considered if there is onset of tachypnea, chest retractions and grunt within six hours of birth with or without suggestive chest radiograph. Congenital heart defects were noted as detected by Echocardiography findings. Asymmetric septal hypertrophy was considered when echocardiographic measurement of interventricular septal thickness of 5 mm or more.

Results

Among 4654 live births, 516 (11%) neonates were born to diabetic mothers (Figure 1). Among 516 neonates born to GDM mothers, 64 were excluded and 452 neonates were studied further.

Neonatal characteristics like sex, birth weight, mode of delivery, AGA, SGA, LGA, maternal diet and therapy and various comorbidities noted in the neonates have been depicted in Tables 1 - 6.

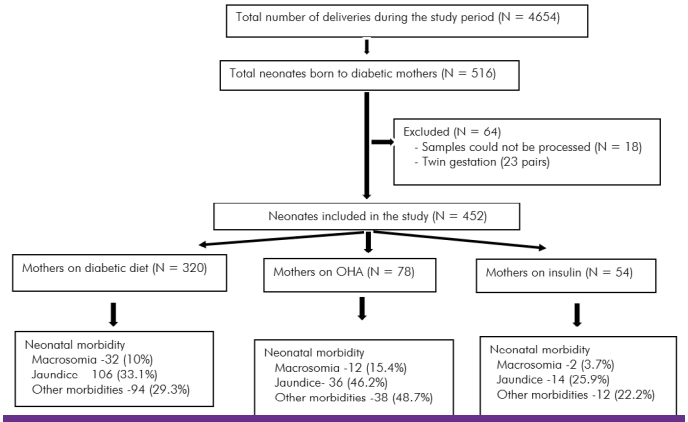

Fig 1: Study Flow Diagram

Table 1: Neonatal characteristics (N = 452)

Characteristics	N	%
Gender		
Male	242	53.5
Female	210	46.5
Gestational age		
Term	354	78.3
Preterm	98	21.7
Birth weight		
< 1000g	3	0.6
1000 - 1499g	13	2.9
1500 - 2499g	74	16.4
2500 - 3999g	344	76.1
≥ 4000g	18	4.0
AGA	393	86.9
LGA	46	10.2
SGA	13	2.9
Mode of delivery		
Normal vaginal delivery	138	30.5
Assisted vaginal delivery	11	2.4
Total LSCS	303	67.1
Elective LSCS	102	22.6
Emergency LSCS	201	44.5

AGA - Appropriate for gestational age, LGA - large for gestational age, SGA - Small for gestational age, LSCS - lower segment Caesarian section

Table 2: Distribution of birth weight of the neonates (N = 452)

Birth weight	Maternal treatment		
	Dietalone (N =320)	Oral hypo-glycemic agents (N = 78)	Insulin (N =54)
< 1000 g (N = 3)	2	0	1
1000 - 1499 g (N = 13)	7	3	3
1500 – 2499 g (N = 74)	50	11	13
2500 - 3499 g (N = 273)	200	40	33
3500 - 3999 g (N= 71)	49	19	3
≥ 4000 g (N = 18)	12	5	1

Table 3: Distribution of neonates based on AGA, LGA and SGA categories and maternal treatment for diabetes (N = 452)

Neonatal Categories	Maternal treatment		
	On diabetic diet (N = 320)	On OHA (N = 78)	On insulin (N = 54)
AGA (N = 393)	280	64	49
LGA (N = 46)	32 (10%)	12 (15.4%)	2 (3.7%)
SGA (N = 13)	8	2	3

Table 4: Morbidities in the neonates born to diabetic mothers (N = 452)

Morbidity	N	%
No morbidity	354	78.3
Hyperbilirubinemia	156	34.5
Congenital heart diseases	144	31.8
Hypoglycemia	72	15.9
Macrosomia	46	10.1
Respiratory morbidity	44	9.7
Sepsis	17	3.8
Polycythemia	9	2
Birth injuries	8	1.7
Birth asphyxia	4	0.9
Others	99	21.9

Table 5: Hypoglycemia in neonates born to diabetic mothers (N = 452)

Glucose abnormality	Maternal treatment		
	On Diabetic diet (N = 320)	On OHA (N = 78)	On insulin (N = 54)
No hypoglycemia (N = 380)	268	70	42
Hypoglycemia (N = 72)	52	8	12
Asymptomatic hypoglycemia (N = 58)	42	7	9
Symptomatic hypoglycemia (N = 14)	10 (3.1%)	1 (1.3%)	3 (5.6%)

Table 6: Biochemical, hematological abnormalities, respiratory and cardiac morbidities (N = 452)

Morbidity	N	%
Hyperbilirubinemia	156	34.5
Hypoglycemia	72	15.9
Hypocalcemia	21	4.6
Hypomagnesemia	13	2.8
Polycythemia	9	2
Respiratory morbidities		
Respiratory distress syndrome (RDS)	35	7.7
Transient tachypnea of newborn (TTNB)	6	1.2
Meconium aspiration syndrome	3	0.6
Cardiac morbidities		
ASD	81	17.9
PDA	21	4.7
VSD	14	3
ASD + PDA	17	3.8
ASD + VSD	6	1.3
Septal hypertrophy	4	0.9
TGA	1	0.2

ASD, atrial septal defect; PDA, patent ductus arteriosus; VSD, ventricular septal defect; TGA, transposition of great arteries.

Discussion

In the present study, a large number of neonates born to diabetic mothers were studied prospectively. Macrosomia, hypoglycaemia hyperbilirubinemia and congenital heart defects were observed as immediate morbidities. Of 4654 live births during study period, 516 (11%) neonates were born to diabetic mothers. This 11% prevalence of diabetes among pregnant mothers is lower compared to other Indian (13.9%) and Asian countries' (17%) estimates.[2,5] It matches with reports from USA (3 - 12%).[3] This variation could be due to the hospital based nature of present study. Among pregnant diabetic mothers, GDM shares large percentage.[18-24] GDM and PGDM mothers in the present study constituted 419 (92.7%) and 33 (7.3%) respectively. Prabhavathi et al reported GDM and PGDM in 105 (87.5%) and 15 (12.5%) respectively (N = 120).[21] The caesarean delivery rate of 67.1% in the present study is because of the hospital being the tertiary care centre. Other studies reported much higher rates of Caesarean section, 80.8% and 83%.[18, 22]

Male neonates constituted 242 (53.5%) with male to female ratio of 1.15:1. Male to female ratio of 1.5:1 has been reported in other studies.[21,22] Preterm constituted 21.7% in the present study. A study from USA[25] found preterm contributing 36%. In contrast, lower preterm percentage (15%) reported in an Indian study.[21]

Mean birth weight of the neonates in the present study was 2950 ± 655 g. Devi et al (N = 198) found mean birth weight of 2932 ± 820 g with most of the neonates (38.4%) weighed between 2500 to 3500 g.[22] Diabetes in mother despite treatment leads to LGA neonates. A USA study[25] involving 530 neonates found LGA in 36%, whereas the present study found LGA in 10.2%. When mothers' treatment is considered, LGA neonates were least in mothers receiving insulin than oral hypoglycemic agents (3.7% vs. 15.4%). Low percentage of SGA of 2.9% matches with other studies.[21,25]

In this study, 21.7% had one or other morbidity. Common morbidities were hyperbilirubinemia (34.5%), hypoglycemia (15.9%) and macrosomia (10.2%). Hyperbilirubinemia in neonates of diabetic mothers is much higher compared to neonates in general population (about 16.5 per 1000 live births). Opara et al reported hyperbilirubinemia (57.4%) as commonest morbidity.[18] Devi et al (N = 198) reported hyperbilirubinemia in 24.2% neonates born to diabetic mothers.[22] Thomas N et al (N = 278) observed lower rate of hyperbilirubinemia (in 28 of 278 neonates; 10.1%).[19] Macrosomia is a risk factor for adverse delivery outcomes. Reported macrosomia among infants of diabetic mothers ranges from 0.5% to 15%.[7] Macrosomia was observed in 46 neonates (10.2%) in the present study and eight of them had hypoglycemia. Two Indian studies reported macrosomia in

3.2% (N = 278) and 20% (N = 120).[19,21] Macrosomia may also cause difficult delivery and birth injuries. In the present study, eight neonates (1.7%) had various birth injuries. Two neonates had Erb's palsy with clavicular fracture, both were delivered by vaginal route. Similar birth injuries were reported in other studies with rate ranging from 1% to 4.3 %.[18,19,21]

In the present study, hypoglycaemia was observed in 72 (15.9%) neonates. Among them 14 (3%) were symptomatic. Five neonates with hypoglycaemia had seizures. Reported incidence of hypoglycemia among neonates of diabetic mothers range from 9%-28%.[19,21,25] Taken together, these findings stress the need for glucose monitoring because neonatal hypoglycaemia may lead to long term consequences.[26,27] Hypocalcemia (4.6%), hypomagnesemia (2.8 %) and polycythemia (2%) occurring in small percentage of neonates of diabetic mothers match the reports mentioned in the literature.[19,25]

Systemic morbidities and congenital defects are significant problems in neonates of diabetic mothers.[18,25-30] A study from USA on 4180 pregnant mothers complicated by diabetes found that the most commonly affected organ systems in neonates were the cardiac (37.6%), musculoskeletal (14.7%), and central nervous systems (9.8%) and anomalies involving multiple organ systems (16%).[29] In the present study, 9.7% had respiratory morbidity with RDS having the major share. Opara et al reported respiratory morbidity in 34% neonates.[18]

Cardiac anomalies were found in 31.8% of neonates born to diabetic mothers with atrial septal defect being the commonest defect. Echocardiographic study of 100 neonates of diabetic mothers in Saudi Arabia reported patent ductus arteriosus (PDA; 70%), patent foramen ovale (68%), atrial septal defect (5%), small muscular ventricular septal defect (4%), mitral valve prolapse (2%), and pulmonary stenosis (1%).[28] Further, interventricular septal hypertrophy was found in 38% of cases. Another study form Iran using fetal echocardiography found that 8.8% fetuses of diabetic mothers having cardiac malformations with hypertrophic cardiomyopathy as the most common cardiac malformation (40% of malformations).[30] Sepsis observed in 3.8% of present study population agrees with reported sepsis rate of 2.5% to 15.1% mentioned in the literature.[19,22] Adequate glycemic control before and during pregnancy is crucial in improving neonatal outcome.[6,29]

The limitations of the study include not gathering the information on maternal antenatal glycemic control. Hence we could not establish the relationship of neonatal morbidities with various modes of antenatal management of diabetic mothers.

Conclusion

Large number of neonates born to diabetic mothers have normal birth weight and mostly belong to AGA category. Macrosomia among neonates continues to exist despite advances in antenatal care. As asymptomatic and symptomatic hypoglycemia among these neonates continues to occur, glucose monitoring is needed in the initial days of life. Hyperbilirubinemia, congenital heart disease, respiratory abnormalities, polycythemia, birth injuries and birth asphyxia needs be identified in these neonates and treated appropriately.

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Conflicts of Interest None

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