

Neonatal Morbidity among Infants of Diabetic Mothers in Sagamu: A 10-year Review

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Abstract

Background: Diabetes in pregnancy constitutes a high risk factor for increased maternal and perinatal morbidity and mortality. There is inadequate knowledge of the diabetic pregnancy and its impact on neonatal health in our environment, hence the need for more research. **Objective:** To describe the morbidity pattern among infants of diabetic mothers (IDMs). **Materials and Methods:** Hospital records of all neonates diagnosed as IDMs and admitted into the neonatal ward of a tertiary hospital in South-Western Nigeria over a 10-year period were reviewed. Relevant data were extracted and analyzed. **Results:** Twenty-four cases met inclusion criteria, with a slight male preponderance. Mean (standard deviation [SD]) gestational age was 38.1 (1.8) weeks while the mean (SD) birth weight was 3.9 (0.4) kg. Fifty-eight percent of the subjects were delivered by cesarean section. 12 (50%) babies were macrosomic while the most common morbidities among the subjects were hypoglycemia, neonatal jaundice, and birth asphyxia which were observed in 75%, 75%, and 33.3% of the study population, respectively. Less frequently observed conditions include prematurity, transient tachypnea of the newborn, neonatal sepsis, and birth injury. 2 (8.3%) babies presented with congenital malformation affecting the heart and central nervous system, respectively. There was only one case of mortality. **Conclusion:** IDMs are prone to macrosomia, hypoglycemia, neonatal jaundice, and birth asphyxia in our environment. Early antenatal screening of all pregnant women for diabetes mellitus is required and good glycemetic control of diabetic pregnancies should be the ultimate goal in order to minimize neonatal complications.

Key words: Infant of diabetic mother, macrosomia, neonatal hypoglycemia, neonatal morbidity

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INTRODUCTION

Diabetes mellitus is a disorder of glucose metabolism resulting from a deficiency of insulin action that has a myriad of physiologic as well as pathologic effects on homeostasis. When it affects a pregnant woman, it constitutes a high risk factor to the fetus in utero. Maternal diabetes is characterized by the increased transport of glucose and other nutrients from the mother to the fetus resulting in fetal overnutrition.¹ It also induces an alteration in lipid metabolism, leading to maternal and fetal hypertriglyceridemia and hypercholesterolemia.^{2,3}

Fetal hyperglycemia consequent upon maternal hyperglycemia stimulates pancreatic islet cells and induces fetal hyperinsulinemia.⁴ The combined effects of hyperglycemia and hyperinsulinemia in the fetus lead to both functional and structural abnormalities which include macrosomia, visceromegaly, polycythemia with hyperviscosity, and a variety

of congenital anomalies.⁵⁻⁷ Furthermore, there is additional risk of metabolic derangements in the immediate neonatal period including hypoglycemia and hypocalcemia.⁸

It has been pointed out that there is inadequate knowledge of gestational diabetes and its consequences in Africa underscoring the need for further research.⁹ Whether or not these complications and abnormalities occur at similar frequencies in the tropical climes with different dietary contents and habits, has not been well defined. Moreover, we are not aware of any previous study that has been conducted on infants of diabetic mothers (IDMs) in our local environment.

The present study was, therefore, undertaken to describe the spectrum of neonatal morbidity among IDMs managed at a tertiary hospital in the South-Western part of Nigeria.

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MATERIALS AND METHODS

The study was a retrospective review covering a 10-year period from January 2004 to December 2013. All IDMs admitted into the neonatal ward (NNW) of Olabisi Onabanjo University Teaching Hospital, Sagamu, during the study period were included in the study.

The hospital record of each of the subjects was reviewed in order to extract relevant data including biodata, birth weight, gestational age, place and mode of delivery, type of maternal diabetes, indication for admission, clinical problems identified and treated, duration of hospital stay, and outcome. Serum blood glucose <2.0 mmol/L defined neonatal hypoglycemia in this study.

All infants born to known diabetic mothers or mothers diagnosed with gestational diabetes would normally be admitted into the NNW for proper monitoring and clinical management. Diabetic pregnancy was suspected on the basis of prenatal glycosuria, and/or elevated fasting blood glucose, and confirmed by impaired oral glucose tolerance test and fetal weight assessment >95th percentile for gestational age, especially from the second trimester.

The unit protocol for the management of IDMs includes initial stabilization and nursing under the radiant warmer to ensure that body temperature is maintained within the normal range. Initial assessment/evaluation for the presence of any congenital anomaly and estimation of gestational age by using the date of mother's last menstrual period or Ballard scoring would be done. Immediate blood sugar estimation is carried out, followed by 2 hourly monitoring for the first 6–12 h and 4–6 hourly monitoring, thereafter till 3–4 consistent normoglycemic readings are obtained. Blood samples would also be obtained for other baseline investigations such as full blood count, serum electrolytes and urea, and serum calcium. Sepsis work-up is also carried out, where indicated.

Other aspects of the protocol include commencement of intravenous fluid infusion using 10% dextrose as the initial fluid for the first 24 h, followed by 7% dextrose/0.18N saline, and estimation of serum bilirubin (total and conjugated), where indicated. Further treatment of the infant would depend on clinical problems identified in the course of daily review as well as the results of laboratory investigations. Hypoglycemia and hypocalcemia are promptly corrected using standard methods, while unconjugated hyperbilirubinemia is managed with phototherapy. Exchange blood transfusion is carried out where indicated for severe jaundice. Neonatal sepsis is aggressively treated with antibiotics, starting with a combination of a second generation cephalosporin (cefuroxime) and an aminoglycoside, usually gentamicin, and subsequently tailored to the blood culture and sensitivity result. Preterm and very low birth weight infants would normally be nursed in an infant incubator. Exclusive breastfeeding is commenced as soon as the infant's clinical condition permits and there are no contraindications.

Data analysis was carried out by means of SPSS (SSPS Inc., Chicago) version 16.0 software program. Descriptive statistics,

including range, mean, standard deviation (SD), and percentages, was computed.

RESULTS

During the 10-year period of study, there were a total of 3451 admissions into the NNW. Of this number, there were 24 cases of IDMs making the prevalence rate 0.7% among neonatal admissions. Table I presents the distribution of the subjects according to gender, gestational age, and birth weight. Male to female ratio was 1.4: The birth weight of the subjects ranged from 3.0 kg to 4.6 kg with a mean (SD) of 3.9 (0.4) kg. Notably, there was no case of low birth weight (i.e. birth weight <2.5 kg) while 12 (50%) of them were macrosomic, weighing more than 4 kg at birth. Estimated gestational age at birth ranged from 34.0 to 42.7 weeks. Mean (SD) gestational age was 38.1 (1.8) weeks. 14 (58.3%) babies were products of cesarean section while 8 (33.3%) babies were products of spontaneous vertex delivery and the remaining 2 (8.3%) were delivered by vacuum extraction. Based on their birth weight relative to gestational age, it was observed that 16 (75.0%) babies were large for gestational age, while the remainders were appropriate for gestational age. None of them was small for gestational age. 15 (62.5%) of the subjects' mothers had gestational diabetes, while the remainder 9 (37.5%) had pregestational diabetes. Majority (91.7%) were inborn babies, while the remaining 2 (8.35%) were referred from private hospitals.

Table II presents the clinical features of the babies at the point of admission into the NNW. Most frequent clinical feature

Table I: Distribution of patients according to gender, gestational age, and birth weight

Gender	n (%)
Male	14 (58.3)
Female	10 (41.7)
Total	24 (100)
Gestational age (weeks)	
<37	4 (16.7)
37-42	17 (70.3)
>42	3 (12.5)
Birth weight (kg)	
<2.5	0 (0.0)
2.5-3.9	12 (50.0)
≥4.0	12 (50.0)

Table II: Clinical features of the subjects at the point of admission

Sign/symptom	n (%)
Respiratory distress	10 (41.7)
Poor suck	6 (25.0)
Jitteriness	4 (16.7)
Cyanosis	4 (16.7)
Jaundice	2 (8.3)
Seizure	1 (4.2)

observed was respiratory distress which was seen in 10 (41.7%) of the babies, followed by a poor suck observed in 6 (25.0%) babies. Other symptoms observed among the subjects were jitteriness, cyanosis, jaundice, and seizures as shown in Table II.

Table III depicts the hematologic profile of the subjects. Mean (SD) hematocrit was 49.5 (4.3%), while mean (SD) total leukocyte count was $11.9 (3.1) \times 10^9/L$. There was no case of anemia, that is, hematocrit $<40\%$. Similarly, none of the babies had polycythemia, that is, hematocrit $>65\%$. Mean (SD) platelet count was $230 \times 10^9/L$.

Analysis of the results of laboratory studies further revealed that neonatal hypoglycemia was a common clinical problem, affecting 18 (75%) of the babies. Out of these, 4 (16.7%) babies had only one episode of hypoglycemia, while 8 (33.3%) and 6 (25%) babies had two and three episodes, respectively. There was no case of persistent or intractable hypoglycemia.

As shown in Table IV, neonatal jaundice in the form of unconjugated hyperbilirubinemia was another commonly observed clinical problem among the subjects. 18 (75%) babies were affected. Of this number, 4 (22.2%) could be arbitrarily classified as mild jaundice with peak unconjugated serum bilirubin (USB) <9 mg/dl, while majority had moderate jaundice with peak USB ranging from 9 to 15 mg/dl. 2 (11.1%) had severe jaundice with USB >15 mg/dl. All the cases were effectively managed with phototherapy except one baby that required exchange blood transfusion. Overall, peak SB ranged from 3.3 to 23.2 mg/dl.

Table IV further shows that macrosomia and birth asphyxia were observed in 12 (50%) and 8 (33.3%) subjects, respectively. Other clinical problems observed include transient tachypnea of the newborn, prematurity, neonatal sepsis, ophthalmia

Parameter	Range	Mean (SD)
Hematocrit (%)	40-57	49.5 (5.4)
Total leukocyte count ($\times 10^9/L$)	7.5-13.2	11.9 (4.32)
Platelet count ($\times 10^9/L$)	120-440	230 (47)

SD: Standard deviation

Clinical problem	n (%)
Hypoglycemia	18 (75.0)
Hyperbilirubinemia	18 (75.0)
Macrosomia	12 (50.0)
Birth asphyxia	8 (33.3)
Prematurity	4 (16.7)
Transient tachypnea of the newborn	4 (16.7)
Neonatal sepsis	4 (16.7)
Ophthalmia neonatorum	4 (16.7)
Respiratory distress syndrome	2 (8.3)
Birth injury	2 (8.3)
Congenital anomaly	2 (8.3)

IDMs: Infants of diabetic mothers

neonatorum, birth injury, respiratory distress syndrome (RDS), and congenital anomaly. The cases of birth injury consisted of one case each of fractured humerus and brachial plexus injury. Of the two patients that had congenital anomaly, one had acyanotic congenital heart disease (ventricular septal defect), while the other presented with myelomeningocele in the lumbosacral part of the spine.

Duration of hospital stay for the subjects ranged from 0.3 to 12 days, with a mean (SD) of 6.9 (2.3) days and a median of 7 days. 21 (87.5%) responded well to treatment and were discharged home to be followed up at the clinic, while 2 (8.3%) babies were discharged against medical advice. One baby died on the 1st day of life of severe birth asphyxia and fractured humerus resulting in a mortality rate of 4.2%.

DISCUSSION

The observation that the majority of IDMs in the present study belonged to mothers with gestational diabetes conforms to the pattern described by earlier workers.¹⁰⁻¹² Similarly, the relatively high mean birth weight of 3.9 kg for the subjects compares well with the figures of 3.75 kg and 4.1 kg reported by Wokoma *et al.*¹³ and Opara *et al.*,¹² respectively, from other parts of Nigeria. It is, however, higher than 3.2 kg reported by workers from Bangladesh.¹¹ Whether or not the difference is due to racial factors could not be immediately ascertained and further research is required.

The present study also observed a high rate of delivery by cesarean section among the IDMs and this is in keeping with previous reports.^{11,12,14} One major reason for this is the propensity for these babies to be macrosomic,^{15,16} thereby causing relative cephalo-pelvic disproportion.¹⁰ For the same reason, vaginal delivery of such babies has been associated with the complication of shoulder dystocia and attendant risks of birth asphyxia and birth injury.^{6,15,17,18} Closely related to this observation, therefore, is the finding that macrosomia was diagnosed in exactly 50% of the babies in the present study. Previous workers have attributed the high incidence of macrosomia among IDMs to poor glycemic control in the pregnant diabetic. Persistent maternal hyperglycemia would cause fetal hyperglycemia which would lead to fetal hyperinsulinism. This would persistently stimulate anabolic metabolism in the fetus thereby leading to the formation of a big baby. Good metabolic control throughout pregnancy with judicious insulin therapy would prevent fetal macrosomia and promote fetal well-being.⁸

Opara *et al.*,¹² working in Port Harcourt, Nigeria had reported a higher figure of 61.7% for macrosomia among their IDMs. Many studies from outside Nigeria, on the other hand, reported much lower figures for macrosomia. These figures range from 15% to 25%.^{5,7,11} It appears, therefore, that IDMs born to Nigerian mothers are at a higher risk of developing macrosomia than others probably due to differences in the level of metabolic control. Macrosomia in IDMs has also been associated with polycythemia,^{6,19,20} but we observed no

case of overt polycythemia among the subjects of the present study even though mean hematocrit level was relatively high.

It was also observed that there were four preterm babies among the IDMs in the present study. It is, therefore, pertinent to mention that their size notwithstanding, this group of babies requires close observation and attention as they are equally prone to complications of prematurity such as neonatal jaundice, hypoglycemia, hypocalcemia, and increased susceptibility to sepsis.

Neonatal hypoglycemia emerged as one of the leading causes of morbidities among IDMs in the present study with many of them having multiple episodes in spite of early commencement of glucose infusion. This finding is in agreement with earlier reports.^{7,11,12} It has been attributed to neonatal hyperinsulinism consequent upon maternal hyperglycemia. Hence, Soler *et al.*⁸ suggested that normoglycemia should be encouraged on the day of delivery to minimize the incidence of neonatal hypoglycemia secondary to maternal hyperglycemia. Prolonged hypoglycemia carries the risk of permanent neuronal injury and subsequent mental retardation. It is, therefore, noteworthy to observe that none of the subjects of the present study suffered from prolonged hypoglycemia. Another major observation worthy of note was the high incidence of neonatal jaundice among the subjects. About 55% of them had unconjugated hyperbilirubinemia, a finding that is in conformity with earlier reports.^{6,8,12} The pathogenesis is uncertain but increased extramedullary hematopoiesis and increased hematocrit have been implicated as contributory factors.⁸

Previous reports have directed attention to the steady decline in the incidence of RDS among IDMs.^{21,22} This is further buttressed by the observation of only one case of RDS in our study spanning a 10-year period. This low incidence of RDS among IDMs has been attributed to the modern approach to the management of diabetic pregnancy with emphasis on optimal metabolic control and the judicious use of insulin. Moreover, it has been reported that RDS is not common in the African population due to early lung maturity.²³

There was no sufficient data to determine the incidence of hypocalcemia among the IDMs of the present study. However, other researchers have raised concern about a high incidence of hypocalcemia among IDMs, especially the ones whose mothers have type 1 diabetes.^{8,11,24} This is thought to be due to such factors as neonatal hyperphosphatemia and delayed pituitary gland response.

Another important observation in the present study has to do with the incidence of congenital anomaly among IDMs. Two of the subjects presented with this complication in the form of congenital heart defect and spina bifida, respectively. Several reports have highlighted an increased incidence of congenital malformations among IDMs.^{7,25} A variety of malformations involving different organs have been reported, but the more common ones include congenital heart defects, central nervous system deformities (spinal bifida, anencephaly, and

hydrocephalus), musculoskeletal deformities (e.g., caudal regression syndrome and polydactyly), ambiguous genitalia, and small left colon syndrome.^{6,26-28} The longer the duration of maternal diabetes, the higher is the risk of major congenital malformation.⁸ Apart from being an important cause of morbidity, major congenital anomalies are also a leading cause of perinatal mortality among IDMs.⁸ However, the only case of mortality in the present study was due to severe birth asphyxia and not congenital malformation.

Finally, the prevalence of diabetes mellitus in pregnancy has been known to show regional and racial variation. Previous workers have reported a low prevalence of diabetes mellitus in pregnancy among antenatal populations in Nigeria.^{13,29} This would therefore explain the relatively small number of IDMs observed over a 10-year period in the present study.

CONCLUSION

IDMs are at the risk of macrosomia, neonatal hypoglycemia, hyperbilirubinemia, birth asphyxia, congenital malformations, and sepsis in our environment. It is important to ensure that pregnant women are routinely screened for diabetes mellitus, and when detected, good glycemic control should be aimed at in order to minimize neonatal complications in the IDM.

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Conflicts of interest

There are no conflicts of interest.

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