

Original Research Article

An observational study of clinical profile of infants born to pregestational and gestational diabetic mothers

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ABSTRACT

Background: Diabetes has now become a global pandemic because of sedentary lifestyle, urbanization, and increasing incidence of obesity and the prevalence is on the rise in developing nations like India. The objective of this study was to study the clinical profile and complications of neonates born to established diabetic mothers and gestational diabetic mothers on insulin.

Methods: Over a period of one year, all consecutive live born neonates born to diabetic mothers, both gestational and pregestational (known/established diabetic), on insulin were included in the study.

Results: The incidence of hypoglycemia in IPGDM was 2-fold higher (55%) than 25% in IGDM (25%) which was statistically significant ($p = 0.009$). Congenital anomalies were seen more in IPGDM (41.9%) compared to 18.2% in IGDM which was statistically significant ($p=0.02$).

Conclusions: Congenital anomalies mostly involving cardiovascular, renal system were seen significantly more in newborns born to mothers with established diabetes compared to infants of gestational diabetic mothers. Hypoglycemia was the most common complication followed by hypocalcemia and hyperbilirubinemia.

Keywords: IDM, Gestational diabetes, Hypoglycaemia, Macrosomia

INTRODUCTION

Diabetes has now become a global pandemic because of sedentary lifestyle, urbanization, and increasing incidence of obesity and the prevalence is on the rise in developing nations like India. As the incidence of diabetes is rising in epidemic proportions, more women of childbearing age are at increased risk of diabetes during pregnancy. The prevalence of gestational diabetes in India is currently estimated to be around 16-18%.¹

Diabetes in pregnancy (type 1, type 2 or gestational) leads to increased risk for adverse pregnancy outcomes with long term complications in the baby including

abnormalities of growth, alterations in glucose and calcium levels, hematologic and cardiorespiratory problems and congenital anomalies. Diabetic mothers have a high incidence polyhydramnios, preeclampsia, pyelonephritis, preterm labour and chronic hypertension.

Insulin has been the primary mode of therapy for diabetes complicating pregnancy for many decades. Some of the adverse effects of pregnancy can be prevented by preconception counselling, careful planning of mode and time of delivery, better glycaemic control, early screening for fetal abnormalities and good neonatal care. Recent advances in the management of women suffering from diabetes mellitus have decreased maternal and neonatal

mortality but at the same time there has been an increased incidence of diabetic pregnancies.²

The incidence of congenital malformations is dependent upon periconceptional glucose levels and many cases with unrecognized diabetes enter prenatal care beyond the organogenesis period. Many of the perinatal complications are due to effect of maternal glycaemic control especially in last trimester on the foetus.

In the background of very few Indian studies comparing clinical profile and outcome of neonates born to mothers with gestational diabetes and established diabetes, this study was undertaken to evaluate the problems and immediate outcome of infants of diabetic mothers admitted in our neonatal unit and to compare the clinical profile between the two groups.

The aims and objectives of this study were to study the clinical profile and complications of neonates born to established diabetic mothers on insulin and gestational diabetic mothers on insulin and to compare the outcome between the two groups and to determine the immediate outcome in new-borns born to diabetic mothers.

METHODS

The present study was a hospital based prospective study conducted in the Institute of Child Health and Research Centre, Government Rajaji Hospital, Madurai for a period of one year (September 2013 to August 2014)

Inclusion criteria

All consecutive live born neonates born to diabetic mothers both gestational and pregestational (known/established diabetic), on insulin, at Government Rajaji hospital and admitted in neonatal unit from September 2013 to August 2014

Exclusion criteria

- Diabetic mothers on oral hypoglycemic therapy or diet control
- Diabetic mothers with coexisting pregnancy induced hypertension
- Infants of diabetic mothers admitted after 24 hours of delivery (as referred case from other hospitals).

After taking informed written consent from the parent or guardian, the relevant information from history, physical examination and investigation were recorded in a predesigned proforma. Women are separated into those who were known to have diabetes before pregnancy-pregestational or established, and those diagnosed during pregnancy-gestational.

The diagnosis of gestational diabetes was by oral glucose tolerance test with criteria as laid out by Carpenter and Couston: which was done if glucose challenge test cut off

is 140 mg/dl or higher. Glycemic control of diabetes in the third trimester (by taking average of third trimester random blood sugar values), family history of diabetes and antenatal ultrasound findings were recorded in maternal history. Optimal control is defined as fasting blood sugar <95 mg/dl and 2-hour postprandial value <120 mg/dl.³

Mode of delivery, APGAR score, baby weight (using digital weighing scale) was recorded. Baby was resuscitated as per National neonatology forum protocol 2010. Birth asphyxia was diagnosed if APGAR score <7 at 1 minute (WHO guidelines). Birth weight of babies was recorded and plotted against their gestational age and classified accordingly as large, small or appropriate for gestational age. Small for gestational age (SGA) describes a neonate whose birth weight is less than 10th percentile for gestational age.

Macrosomia was defined as birth weight more than 90th percentile.¹ Babies born before 37 completed weeks were classified as preterm and 42 weeks or more as post-term. A subgroup of infants born at 34 to 36 weeks was categorized as late preterm and those born between 37 to 41 6/7 weeks as term baby.¹ Gestational age assessment was confirmed by the new Ballard score.

A screening physical examination for the presence of major and minor congenital anomalies, birth injuries and general systemic examination was performed.

Blood glucose levels were checked at 2, 6, 12, 24, 48, and 72 hours by gluco-stix (capillary blood glucose). Working definition for hypoglycaemia was blood glucose level of less than 40 mg/dL.⁴ All babies were started on oral feeds or intravenous infusion soon after birth. Blood glucose <20 mg/dl or two consecutive values <40 mg/dl necessitates intravenous glucose infusion.

Serum calcium levels are measured if baby is symptomatic with jitteriness or is sick for any reason.¹ Hypocalcemia is defined as total serum calcium level less than 7 mg/dl.⁴ Hemoglobin and hematocrit were looked for in capillary blood sample at 24 hours. Polycythemia is defined as venous hematocrit more than 65% or a venous hemoglobin concentration in excess of 22.0 g/dL.¹

Serum bilirubin was taken at the onset of clinical jaundice and phototherapy given as per AAP charts.⁵ Chest X ray and ECG were taken if respiratory distress was persistent and/or cardiac anomaly was suspected. Screening echocardiogram was done by a cardiologist in all cases. Ultrasound abdomen was done if anomalies were detected in antenatal ultrasound or if external markers like single umbilical artery, preauricular tag were present. Among other investigations sepsis screening, blood culture, plain X ray lumbosacral spine, cranial USG, CT brain or EEG were done for clinically indicated cases. All clinical details were recorded in a printed proforma.

The clinical profile was then compared between the two sub groups-Infant of pregestational/established diabetic mother (IPGDM) and Infant of gestational diabetic mother (IGDM).

RESULTS

The present study is a hospital based prospective study to know the occurrence of metabolic, hematological abnormalities, congenital anomalies in infant of diabetic mothers and to compare the clinical profile and determine immediate outcome in infants born to gestational diabetic and known diabetic mothers with both groups on insulin treatment.

There were around 10,200 babies born in the study period from September 2013 to August 2014. Of which 127 were born to diabetic mothers with prevalence of diabetes as 1.24%. After excluding cases where the mother was managed by diet or oral hypoglycemic therapy and mothers with comorbid conditions, 75 neonates were studied of which 31 were born to known diabetic mothers and 44 to gestational diabetic mothers. 14.7% mothers had family history of diabetes.

Majority of mothers had gestational diabetes (58.7%) as against 41.3% with known diabetes. Based on average of random blood sugar values antenatally in the 3rd trimester due to non-availability of HbA1C in our setting and high cost, almost equal proportion of mothers belonged to good and poor control group each (~50%). Most of neonates were delivered by lower segment caesarean section (LSCS), 57.3%. Majority of new-borns were females (52%). Majority of neonates were born term (81.3%) and 17.3% were preterms. Majority of the neonates had birth weight in the range of 3-3.49 kg. Around 6.7% babies had birth weight ≥4 kg. Mean birth weight of neonates studied were 2.898±0.7641 kg.

Table 1: Distribution of neonates according to gestational age.

Gestational age	Frequency	Percentage
Term	61	81.3
Post-dated	1	1.3
Preterm	13	17.3
Total	75	100

Table 2: Distribution of neonates according to birth weight.

Birth weight (kg)	Frequency	Percentage
<2	7	9.3
2-2.49	8	10.7
2.5-2.99	19	25.3
3-3.49	24	32
3.5-3.99	12	16
≥4	5	6.7
Total	75	100

Majority of babies were appropriate for gestational age (AGA) 68% and 20% were large for gestational age. 12% were SGA. 12% neonates were asphyxiated. But all had good neurological outcome at discharge.

Table 3: Distribution of congenital anomalies in neonates.

Anomalies	Frequency	Percentage
CVS	16	21.33
CNS	1	1.3
Renal	2	2.67
Skeletal	2	2.67
GIT	1	1.3

Overall, 21 IDMs (28%) had congenital anomalies detected on screening examination or investigations done postnatally-echocardiogram or ultrasound. Most of the anomalies belonged to cardiovascular system (21.33%) followed by renal anomalies. Of skeletal anomalies-one baby had short lower limbs. X ray pelvis showed absent lower sacral vertebrae. One baby had anorectal malformation-imperforate anus. One baby had occipital encephalocele whose antenatal ultrasound was suggestive of Arnold Chiari III malformation. The most common congenital heart disease was ostiumsecondum ASD (29.41%).

Of all the complications, hypoglycaemia was the most common in 28 cases (37.3%). 50% of them were symptomatic with 4 of them requiring glucose infusion. Others were managed with oral feeds and maintenance fluids. Hypocalcaemia was seen in 24.7% of cases. 5 babies had jitteriness. Repeat values before discharge were normal.

Hyperbilirubinemia was the most common haematological problem (22.7%). Phototherapy given for required cases. Polycythaemia was seen in 13.3% cases. All were asymptomatic, managed conservatively. Repeat values were normal.

Overall mortality rate was 4%. Two were preterm infants with respiratory distress syndrome and pulmonary haemorrhage. One infant had culture positive sepsis (*Klebsiella*). The mean maternal age was 27.55±4.322. Mean birth weight of babies studied was 2.898±0.7641 kg. The mean duration of hospital stay was 6.29±4.940 days.

Poor glycaemic control was seen more in known diabetic mothers (58.1%) compared to GDM (41.9%). But was not statistically significant (p = 0.204).

Congenital anomalies were seen more in IPGDM (41.9%) compared to 18.2% in IGDM which was statistically significant (p = 0.02). Majority were cardiovascular anomalies which were equally distributed in both the groups. Rest of anomalies in renal (2 cases),

gastrointestinal (1 case) and skeletal (2 cases) were seen in neonates born to established diabetic mother.

Table 4: Distribution of cardiac problems.

ECHO	Frequency	Percentage
Bilateral ventricular hypertrophy	1	5.88
Complete AV canal defect	1	5.88
Mild septal hypertrophy	1	5.88
ASD	5	29.41
ASD, PDA	2	11.76
PDA	2	11.76
Severe PHT	1	5.88
VSD	3	17.64

Table 5: Distribution of hematological problems in IDMs.

Hematological complications	Frequency	Percentage
Polycythemia	10	13.3
Hyperbilirubinemia	17	22.7

Table 6: Immediate outcome of IDM.

Outcome at discharge	Frequency	Percentage
Alive	72	96
Expired	3	4
Total	75	100

Table 7: Distribution of glycaemic control in 3rd trimester in the two study groups.

Glycaemic control	Type of diabetes	
	GDM (n=44)	Established diabetes (n=31)
Good	25 (56.8)	13 (41.9)
Poor	19 (43.2)	18 (58.1)
P-value	0.204	

Table 8: Frequency of congenital anomalies in IDM with type of diabetes in mother.

Congenital anomalies	Diabetes type in mother	
	GDM (n=44)	Established diabetes (n=31)
Yes	8 (18.2)	13 (41.9)
No	36 (81.8)	18 (58.1)
P-value	0.024	

Anorectal malformation was surgically operated. A case with polydactyly was found to have ventricular septal defect in echo. Another baby with suspected caudal regression syndrome is under follow-up at neonatology and orthopaedic clinic. A preterm baby born to a mother with known diabetes, had occipital encephalocele, unruptured.

The incidence of hypoglycaemia in IPGDM was 2-fold higher (55%) than 25% in IGDM (25%) which was statistically significant (p = 0.009). Most of the infants manifested hypoglycaemia in the first 6 hours of life, with only 4/28 with hypoglycaemia (14.3%) requiring glucose infusion which could be tapered and stopped for three babies over 4-5 days. Only one baby required infusion up to 12 mg/kg/mt which had to be maintained for 3 days before it could be tapered and stopped over total period of 7 days. Others had glucose level corrected with feeding and/ maintenance fluids.

Table 9: Distribution of metabolic complications between the 2 groups.

Metabolic complications	Type of diabetes in mother		P-value
	GDM (n = 44)	Established diabetic (n = 31)	
Hypoglycemia	11 (25)	17 (54.8)	0.009
Hypocalcemia	7 (16.3)	11 (36.7)	0.047

Hypocalcaemia was more in IPGDM (36.7%) as against 16% in IGDM which was marginally significant (p = 0.047). They were managed with calcium gluconate 8 ml/kg/day added to IV fluids for 48 hours followed by 4 ml/kg/day over next 24 hours. Neonates on oral feeds were given oral calcium.

All the 3 deaths were IPGDM. All neonates born to gestational diabetic mother survived.

Majority of new-borns were appropriate for gestational age (AGA) associated with good control of diabetes. However poor glycaemic control was associated with LGA (32.4%) and SGA (18.9%) as against 7.9% and 5.3% respectively in the good control group which was statistically significant (p = 0.002).

Hypoglycaemia and hypocalcaemia were statistically significant in IDMs born to mothers with poorly controlled diabetes in the 3rd trimester (p <0.001). Hyperbilirubinemia was statistically significant in the poorly controlled diabetic group (p = 0.01). Polycythaemia was seen more in IPGDM but not statistically significant (p = 0.191).

DISCUSSION

The prevalence of diabetes is influenced by genetic, ethnic and socioeconomic factors. The World Health Organisation (WHO) has projected that prevalence is increasing in epidemic proportions especially in developing nations. India has the highest number of people with diabetes in this world with prevalence of gestational diabetic mothers around 16-18%. In Western world, the prevalence of GDM is 2-3%. This high number may be due to ethnic factor.

In the present study, the prevalence of total diabetes during pregnancy was 1.24% and GDM was 0.87%, which was similar to the study undertaken by Ramachandran A et al, to know the prevalence of diabetes in pregnant women a study from south India, which reported prevalence of total diabetes and GDM as 1.19% and 0.56%, respectively.

This present study with a total of 75 cases had 58.7% in GDM group and 41.3% in established group which is comparable to Ranade et al study-an analysis of 50 cases in 1989 with a positive family history in 20% cases.⁵ Family history of diabetes was seen in 14.7% in the present study, which was lower surprisingly, considering the increasing rates of type 2 diabetes in our country. This could be attributed to ignorance of the mother/attender or unrecognized cases in the family.

Though HbA1C has been recognized as the best tool to assess the glycaemic status of antenatal mother, with non-availability and high cost of this test, average of antenatal blood sugar values in the 3rd trimester was taken to assess the overall glycaemic control. Accordingly, inadequate control was seen in 37 (49.3% cases) and more in established diabetic mothers (58.1%) compared to 41.9% in infant of gestational diabetic mother (IGDM). This may be attributed to the fact that insulin resistance in type 2 diabetes is even more exacerbated in pregnancy requiring increase in insulin dosage. Poor compliance due to economic problems and irregular antenatal check-ups is another possible factor.

Most of IDM's were delivered by LSCS (57.3%) comparable to Farooq MU et al (59%) and Ranade et al study (58%) with more rates in GDM group (63.6%) as against 48.4% in established diabetic group which was not statistically significant.⁶

Fairly equal distribution of males (48%) and females (52%) in present study.

Most of babies born were term (81.3%) with 17.3% cases preterms. Lower incidence of preterms compared to other studies 26% in Mahmood et al and Ranade et al (36%) may be due to exclusion of mothers with comorbidities like hypertension in the present study.⁷

Majority of IDM's were born appropriate for gestational age with incidence of macrosomia in 20% which is comparable to Firouzeh N et al study conducted in Iran comparing morbidities between infants of pregestational and gestational diabetic women (24.3%) and Deodari et al study (20%).⁸

Mean birth weight was 2.898 ± 0.7641 comparable to Mahmood CB et al and Mohsin F et al study.

In the present study, birth injuries occurred in 2 (2.7%) IDMs. Both were born to known diabetic mothers. 12% of infants were asphyxiated but had no seizures and were

in normal neurological condition at discharge, the incidence being lower compared to 23% in Mahmood CB et al study.

The incidence of congenital anomalies in this study was 28% which was higher in comparison to other studies Deorari et al, Delhi reporting 4% and Mahmood CB et al 5%. The overall incidence is reported in literature as 6-9%. Greater number in this study could be due to routine screening of all neonates with echocardiogram and ultrasonogram in indicated cases and secondly greater number of ASD in cardiovascular malformations.

When distribution of congenital anomalies was compared between the two groups, incidence was more in newborns born to mothers with established diabetes with 13/31 cases accounting to 41.9%. Poor glycaemic control in periconceptional stage in overtly diabetic group may be the cause for higher incidence of congenital anomalies, in this study which was statistically significant. Higher incidence of anomalies seen in IPGDM in comparison to IGDM is similar to studies by Deodari et al and Akhlaghi et al.⁹

37.3% cases in present study were hypoglycemic which was slightly more comparable to other studies, may be due to meticulous screening of hypoglycaemia. Secondly high-risk groups for hypoglycaemia: preterm~17% SGA~12%, LGA~20% are present in this study. Third reason is due to suboptimal control of diabetes in 3rd trimester in over half of mothers.

24.7% cases were hypocalcemic, comparable to study conducted by Mahmood et al (19%). High incidence similar to literature~20% due to same reason as hypoglycaemia.

10 cases (13.3%) were, more in present study in comparison to Deodari et al study (2%) and Firouzeh N et al (4%), probably due to presence of SGA and IUGR babies. Lower compared to Mahmood et al study (19.23%).

22.7% had hyperbilirubinemia higher compared to 8% in Deodari et al study probably due to coexisting ABO incompatibility in some of the babies.

The incidence of hypoglycaemia and hypocalcemia were found to be significantly higher in IPGDM (54.8% and 36.7% respectively) in comparison to IGDM (25% and 16.3% respectively) which is comparable to Mahmood C B et al and Firouzeh N et al. This can be attributed to the fact that there is a higher proportion of women in established diabetic group with inadequately controlled glycemic levels in the 3rd trimester. Secondly due to higher percentage of SGA's, LGA's and preterm in IPGDM. Comparison of incidence of hypoglycaemia between the two groups was found to be statistically significant and hypocalcemia-marginally significant. The incidence of hyperbilirubinemia and polycythemia in this

study were more in IPGDM in comparison to IGDM (29% versus 18.2%) and (16.1% versus 11.4%) respectively comparable to studies by Deodari et al and Firouzeh N et al; which was not statistically significant.

3/75 cases died, all were IPGDM. 2 were preterms with RDS, one baby had proven sepsis. Overall mortality of 4% was comparable to other studies.

Limitations of this study were

- HbA1C estimation could not be done in mothers in view of non-availability of the investigation in our hospital setting, high cost and poor affordability of the patient. So average of three random blood sugar values in the 3rd trimester was taken as a rough estimate of the glycaemic status in mothers.
- Maternal factors like pre-pregnancy weight/Body mass index(BMI) social, economic factors and educational status of mothers, adherence of treatment was not considered in the study.

CONCLUSION

Congenital anomalies mostly involving cardiovascular, renal system were seen significantly more in newborns born to mothers with established diabetes compared to infants of gestational diabetic mothers.

Hypoglycemia was the most common complication followed by hypocalcemia and hyperbilirubinemia.

The incidence of hypoglycaemia and hypocalcemia were significantly more in newborns born to mothers with established diabetes compared to infants of gestational diabetic mothers. There was no statistically significant difference in the incidence of macrosomia between the two groups

There was no statistically significant difference in the incidence of polycythemia and hyperbilirubinemia between the two groups. Hyperglycemia in 3rd trimester in pre-existing/gestational diabetes is significantly associated with macrosomia and morbidities like hypoglycaemia, hypocalcaemia and hyperbilirubinemia.

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