

# "Metabolic and hematological abnormalities in infants of diabetic mothers in the neonatal period"

KEYWORDS	Infants of diabetic mothers; Diabetes in pregnancy; glycemic control; complications in IDMs.	
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ABSTRACT BACKGROUND: The present study aims to study the metabolic and hematological profile in infants of diabetic mothers in the neonatal period.

**METHODOLOGY:** 50 neonates born to diabetic mothers were enrolled in the study. Gestational age, birth weight, relevant perinatal history and examination findings were recorded. Blood samples were collected to perform relevant biochemical tests and managed as per unit protocol. Echocardiography and ultrasound abdomen was done routinely in all neonates.

**RESULTS:** Hyperbilirubinemia (26/50-52%) and hypoglycemia (21/50-42%) were the most common hematologic and metabolic abnormality respectively seen in IDMs. Hypoglycemia was usually asymptomatic, occurred with in first 3 hours of life ( $P<0.000^{**}$ ) and responded to enteral feeds. Polycythemia was seen in 18% (9/50) and hypocalcemia in 12% (6/50) of neonates. Congenital malformations were seen in 24 %( 12/50) of neonates, of which most of them had congenital heart disease. 6% (3/50) of the babies had suffered birth injuries. There was no significant statistical difference in the incidence of complications among infants born to women with pregestational and gestational diabetes. Complications like macrosomia, hypocalcemia, polycythemia, hyperbilirubinemia, hypoglycemia, congenital anomalies were seen most commonly in women with suboptimal glycemic control.

**CONCLUSION:**Hypoglycemia and hyperbilirubinemia remain the most common biochemical and hematological abnormality respectively. Infants of diabetic mother are high risk neonates requiring intensive monitoring but their blood glucose measurements may be limited to initial 3 hours minimising trauma and expense. There are no significant differences in neonatal morbidity profiles of IDMs born to pregestational and gestational diabetic mothers if under optimal glycemic control.

### INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder due to either insulin deficiency (relative or absolute) or due to peripheral tissue resistance to the action of insulin [1]. Women are separated into those who were known to have diabetes before pregnancy as pregestational (PGDM) or overt, and those diagnosed during pregnancy as gestational (GDM) [2]. World Health Organization (WHO) has predicted that between 1995 and 2025, there will be a 35% increase in the world wide prevalence of diabetes [3]. Moreover, women born in Asian countries display the highest prevalence of GDM, with up to 17% of women likely to develop GDM in comparison to 4% of European and white American women. Currently, 3% to 8% of pregnancies are complicated by abnormal glycemic control. Of these, 80% are caused by gestational diabetes mellitus as opposed to pregestational diabetes mellitus [4]. The IDMs are at an increased risk for peri-conceptional, fetal, neonatal and long term morbidities. Short-term neonatal complications, such as hypoglycemia, RDS, hypocalcemia, hypomagnesemia, hyperbilirubinemia, polycythemia, are related mainly to fetal hyperinsulinemia, hypoxemia, and prematurity. Long-range complications include an increased rate of childhood and adolescent obesity, impaired glucose tolerance or diabetes mellitus, and subtle neuropsychological dysfunctions [10]. The causes of the fetal and neonatal sequelae of maternal diabetes are likely multifactorial; however, many of the perinatal complications can be traced to the effect of maternal glycemic control on the fetus and can be prevented or at least reduced through meticulous prenatal and intrapartum care.

The present study focuses on the metabolic and hematological profile in IDMs.

#### METHOD:

After obtaining institutional ethical committee clearance, the study was undertaken in 50 neonates born to diabetic mothers who were admitted to the neonatal intensive care unit (NICU), ASRAM, ELURU. This followed the attainment of written informed consent. Still born babies and abortions of diabetic mothers were excluded. It was a hospital based prospective study conducted during the study period

of one and half years i.e., from November 2014 to April 2016. Diabetic status and treatment was abstracted from the antenatal records. The glycemic status of the diabetic mothers was ascertained based on the serial estimation of fasting and postprandial glucose levels. Each patient's fasting and 2 hour postprandial blood glucose values were averaged, yielding one mean value per patient. Blood glucose control was defined according to American College of Obstetricians and Gynecologists guidelines: a mean fasting value of < 95 mg/dl or mean 2 hour postprandial value of <120mg/dl. Two groups were identified: women with blood glucose averages within the recommended guidelines (blood glucose controlled or optimal control) and women with blood glucose averages higher than the recommended guidelines (blood glucose not controlled or suboptimal control). Other associated Obstetrical and medical problems were noted. Babies born to diabetic mothers were evaluated immediately after birth .Those requiring resuscitation was resuscitated according to National Neonatal Forum Protocol for new born resuscitation. Birth asphyxia was defined as an Apgar score of≤6 at 5 minutes. The baby was shifted to the NICU and its blood glucose levels monitored at regular intervals (1, 2, 3, 6, 12, 24, 36 and 48hrs) for first 48 hours [6] of life by the standard heal prick using glucometric reagent strip method with the same glucometer for uniformity. At admission, weight was recorded using digital weighing scale (to nearest 10gms). The babies were grouped as SGA, AGA or LGA depending on the birth weight and gestational age according to growth chart .Data regarding detailed examination of the new born was collected in a predesigned proforma. Congenital anomalies were identified clinically. In the nursery, supportive care was given while a continuous evaluation of the infant is made. Hypoglycemia was defined as a blood glucose level less than or equal 40 mg/dl in any infant, regardless of gestational age and whether symptomatic or not [6]. IV dextrose was administered only if the baby was symptomatic or unable to take orally or if blood glucose levels were <20mg/dl. Hematocrit levels are checked at 1 and 24 hours. Polycythemia was defined as venous hematocrit (PCV) of more than 65% [6]. Calcium levels are checked if the infant appears jittery or is sick for any reason. Hypocalcemia was defined as total serum calcium less than 7mg/dl and hypomagnesemia as serum magnesium level of less than

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1.7mg/dl [6] .S.Bilirubin estimation was done in the biochemical laboratory if the neonate had clinical jaundice and repeated if necessary. Chest x-ray and arterial blood gas analysis was done if baby had significant respiratory distress and 2D-echocardiography was done if cardiac disease was suspected by the pediatrician. Other investigations like Serum electrolytes, indirect ophthalmoscopy for ROP, neurosonogram, sepsis screen, and USG Abdomen were done if relevant. The baby was treated as per standard NICU guidelines of the hospital and shifted to mothers' side when stable.

**Statistical Methods:** Descriptive statistical analysis was carried out in the present study. Chi square/Fisher exact test was used to find the significance of study parameters on categorical scale between two or more groups. The data was analysed using SPSS software and results obtained.

RESULTS: Of the 60 neonates born to diabetic mothers, 10 neonates were excluded - 3 neonates were stillborn and remaining 7 neonates were excluded because of lack of proper data and remaining 50 were analyzed. Majority of the infants (40/50-80%) were born to GDM mothers and 20 %( 10/50) were born to pregestational DM mothers.60% (30/50) of mothers of the study sample had suboptimal glycemic control during pregnancy. Suboptimal glycemic control was seen in 70% (7/10) mothers with Pregestational diabetes and 57.5% (23/40) with Gestational diabetes. Pregnancy induced hypertension (15/50-30%) was the most common complication observed in the mothers of the study sample followed by Polyhydramnios (9/50-18%) Majority of the infants (33/50-66%) were delivered by cesarean section. 46% (23/50) of IDMs were preterm and 54% (27/50) were term. Out of 50 infants included in the study, 27 (54%) were males and 23 (46%) were females. The mean birth weight was 2.92 + 0.65 Kg and majority of them were born appropriate for gestational age (35/50-70%). In the present study, birth injuries occurred in 3/50(6%) IDMs. Erb's palsy 2/50 (4%) was the commonest, followed by clavicle fracture in 1/50(2%) of IDMs.

Table 1: Distribution of metabolic abnormalities and diabetic status

Diabetic status	Hypoglycemia	Hypocalcemia
GDM (n=40)	17 (42.5%)	4 (10%)
PGDM (n=10)	4 (40%)	2 (20%)
P value	1	0.58

Hypoglycemia (21/50-42%) was the most common metabolic abnormality, followed by hypocalcemia in (6/50-12%). Hypoglycemia was seen in neonates born to 40% (4/10) of PGDM and 42.5 %(17/40) of GDM mothers. Hypocalcemia was observed in 4/40 (10%) neonates born to GDMs and 2/10 (20%) neonates of PGDMs. There were no cases of hypomagnesemia in the present study.

Table 2: Distribution of hematological abnormalities and diabetic status

Diabetic status	Polycythemia	Hyperbilirubinemia
GDM (n=40)	6 (15%)	22 (55%)
PGDM (n=10)	3 (30%)	4 (40%)
P value	0.358	0.489

Hyperbilirubinemia (26/50-52%) was the most common hematologic abnormality, followed by polycythemia (9/6-18%). Hyperbilirubinemia requiring phototherapy was the commonest complication observed in IDMs of both pregestational 4(40%) and gestational 22 (55%) diabetes .Polycythemia was observed in 6 (15%) neonates born to GDMs and 3 (30%) neonates of PGDMs.

There was no significant statistical difference in the incidence of metabolic and hematological complications between the two groups.

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Table 3: Distribution of metabolic abnormalities and its relation
to maternal glycemic control

DM	Hypoglycemia	Hypocalcemia
Optimal control(n=20)	7 (35%)	1 (5%)
Sub optimal control(n=30)	14 (46.66%)	5 (16.66%)
P value	0.56	0.38

Hypoglycemia and hypocalcemia were found in most of the infants born to mothers with suboptimal glycemic control. There were no cases of hypomagnesemia in the present study.

Table	4: Distribution	of hematological	abnormalities	and	its
relatio	on to maternal g	ycemic control.			

DM	Polycythemia	Hyperbilirubinemia
Optimal control (n=20)	2 (10%)	6 (30%)
Sub optimal control(n=30)	7 (23.33%)	20 (66.66%)
P value	0.28	0.02*

Hyperbilirubinemia and polycythemia were found in most of the infants born to mothers with suboptimal glycemic control, this observation was statistically significant.

#### Table 5: Post natal age in hours and incidence of hypoglycemia

Hypoglycemia	<6hrs	6-24hrs	24-48hrs
Present	21 (42%)	4 (8%)	3 (6%)
Absent	29 (58%)	46 (92%)	47 (94%)
Total	50	50	50

Hypoglycemia was most commonly observed in IDM in less than 6 hrs.(42%) of postnatal age where as it was less common at 6-24 hrs. (8%) and 24-48 hrs. (6%) of postnatal age. P <0.000\*\* [chi square=27]. This observation was highly statistically significant.

The occurrence of renal anomalies was more in infants 2/10(20%) of pregestational diabetes when compared to infants 1/40(2.5%) of gestational diabetic mothers. Cardiovascular anomalies were seen in 2 (20%) pregestational and 7 (17.5%) gestational diabetic mothers. Cardiovascular (8/30-26.66%) and renal anomalies (2/30-6.66%) were found in most of the infants born to mothers with suboptimal glycemic control. Renal anomalies: Out of 3 babies 2 had antenatal hydronephrosis and 1 had multiple simple cysts in left kidney. Hairy pinna was observed in 20 (40%), and polydactyly in 1 (2%) of IDMs.

There were no cases of neonatal mortality in the present study.

#### **DISCUSSION:**

Diabetes has long been associated with maternal and perinatal morbidity and mortality. In the present study, total number of IDMs was 50. Among them majority 40 (80%) were born to GDM mothers and rest 10 (20%) were born to PGDM mothers. Similar observation was reported in the studies done previously [8, 12]. In the present study, optimal glycemic control was observed in 17 (42.5%) GDM mothers and 3 (30%) in PGDM mothers.

Majority of the newborns amounting to 66% of total were born by LSCS (66%)-most of which (34%) were emergency and 32% were elective. All the emergency sections were indicated because of fetal distress. 34% of newborns were born by NVD. Similar observations were reported in the studies done previously [9, 13].

In the present study, majority of the IDMs were born appropriate for gestational age both in GDM and overt DM group. Similar observation was made in Nili Firouzeh et al [8] study. In the present study, the mean birth weight of IDMs was 2.92 + 0.65 Kg. Similar observations were reported in the studies done previously [8, 16].

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Estimates of the incidence of hypoglycemia in neonates vary with the definition of hypoglycemia used, the population of interest, and neonatal feeding patterns. A clinically useful threshold for neonatal hypoglycemia has not been determined [14]. This may account for wide range seen in various studies. Hypoglycemia was recorded in 42% and hypocalcemia in 12% of the neonates in the Present study which is comparable to Ranade et al [13] study. Hypoglycemia was most commonly observed in IDM in less than 6 hrs (42%) of postnatal age where as it was less common at 6-24 hrs (8%) and 24-48 hrs (6%) of postnatal age. **P** < **0.000**\*\*. This observation was highly statistically significant. It assumes more importance as a recent study[7] demonstrated that repeated heel sticks used to determine blood glucose levels in these infants resulted in more intense responses to subsequent painful procedures than that in other infants, which is better avoided.

Hyperbilirubinemia requiring phototherapy was observed in 52% of neonates in the present study Sudarshan et al[9] reported a similar high incidence of hyperbilirubinemia. This may be one of the most important factors in prolonging the stay in NICU, thereby exposing the infant to other hazards like sepsis. Polycythemia was observed in 18% of neonates in the present study, which was comparable to Alam et al [11] study

There were no significant statistical differences between pregestational and gestational IDMs with respect to birth weight, metabolic and hematological abnormalities if under optimal glycemic control.

In the present study, birth injuries occurred in 3(6%) IDMs. Erb's palsy 2 (4%) was the commonest, followed by clavicle fracture in 1(2%) of IDMs. All the infants who had birth injuries were born to GDM mothers and were delivered vaginally. The relatively less number of instrumental and high risk vaginal deliveries may be one of the primary contributors toward the less noted incidence of birth trauma. In the present study, there were overall 12 (24%) congenital malformations detected at birth. In the present study Congenital heart disease was observed in 9 (18%) neonates born to diabetic mothers when compared to 4 (1.5%) neonates in Deorari et al [5] study, 6(1.1%) neonates in Cordero et al[15] study, 4(10%) neonates born to diabetic mothers in Alam et al[11] study. The high rate of congenital cardiac anomalies in the present study probably relates to the ready availability of 2D-echocardigraphy to screen high risk neonates and the same utilized by the pediatricians.

Renal anomalies were observed in 3(6%) neonates born to diabetic mothers in the present study when compared to Cordero et al[15] study in which renal anomalies were observed in 3(1.1%) neonates born to diabetic mothers.

There were no cases of neonatal mortality in the present study.

#### CONCLUSION

In spite of intensive management of maternal diabetes, the infants of diabetic mother continue to be a high-risk population. Among the pregnancies complicated by diabetes, GDM continues to have a major contribution. Hypoglycemia remains the most common biochemical abnormality followed by, hyperbilirubinemia, polycythemia and hypocalcemia. Hypoglycemia continues to be a significant cause of morbidity in these babies. It tends to be asymptomatic or with subtle signs and seen only in early postnatal life within 3 hrs. Most often it could be managed by enteral feeds. Repeated estimations of blood glucose may be unnecessary after 3 hrs. as recurrent or late episodes of hypoglycemia are unlikely. The major congenital anomalies were cardiac, occurring in as high as 18% of the subjects which suggests a necessity for a thorough cardiac examination supplemented by 2D-echo if required, in all these infants. There are no significant differences in neonatal morbidity profiles of IDMs born to pregestational and gestational diabetic mothers if under optimal glycemic control. Hence, both the infant

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groups may be managed alike. IDMs may not require prolonged stay in NICU, especially if asymptomatic. Therefore, optimal care of infants of diabetic mothers is based on prevention, early recognition, and/or treatment of neonatal morbidities. It begins right from conception and continues through the infantile period and beyond, with the team work of the obstetrician and the pediatrician.

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