International Journal of Contemporary Pediatrics
Bhavya SO et al. Int J Contemp Pediatr. 2019 May;6(3):1325-1329
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20192037

Original Research Article

Early predictors of early onset neonatal hypocalcaemia in infants of diabetic mother

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Received: 12 March 2019
Accepted: 04 April 2019

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ABSTRACT

Background: The objective of this study was the magnitude of hypocalcemia and to assess the predictors for early onset neonatal hypocalcemia in infants of diabetic mother.
Methods: Total 100 infants of diabetic mother were followed for development of hypocalcaemia. weight length, gestational age, Apgar score, cord calcium was correlated for serum calcium at 48 hours of life.
Results: In present study 91% babies were term and 9% babies were preterm, the incidence of hypocalcemia was high in preterm babies i.e.22% when compared to term babies i.e. 4.3% was not significant and incidence of hypocalcemia was high in babies with Apgar <7 at 1 min (27.27%) was significant statistically. The association of hypocalcemia with cord calcium is not significant statistically.
Conclusions: The incidence of hypocalcaemia is more among preterm babies and babies with risk factors, so these babies need close monitoring for hypocalcaemia. No need of regular monitoring of calcium for healthy term babies unless they are symptomatic.

Keywords: Apgar score, Gestational age, Hypocalcaemia, Infant of diabetic mother

INTRODUCTION

Diabetes complicating pregnancy is seen in 3-5% of pregnancies, gestational diabetes is the most common and it constitutes 90% of diabetic pregnancies.[1] Infants of diabetic mothers (IDM) are at risk for immediate complications like perinatal asphyxia, hypoglycemia, hypocalcemia, hypomagnesemia, polycythemia, respiratory distress syndrome, congestive cardiac failure and later in life are also prone for childhood obesity and impaired intellectual development.[2]

After birth healthy term babies undergo a physiological decline in serum calcium level in first 2 days of life. Thus calcium level starts decreasing after delivery and reaches a nadir of 7.5-8.5 mg/dl in healthy term babies by 24-48 hours of life.[67] In preterm babies, infants of diabetic mothers and infants with perinatal asphyxia, this nadir of serum calcium may reach hypocalcemia levels and cause severe symptoms like seizures.[6,7] In infants of diabetic mother, incidence of hypocalcemia ranges from 4% to high as 50% with an average incidence of 22%.[8-12]

Hypocalcemia in a neonate is defined as

- Total serum Ca <8 mg / dl (2 mmol/L) or ionized Ca <4.4 (1.1 mmol /L), in term and preterm weight >1500 gm (gram),

- Total serum Ca <7.5 mg/dl (1.87 mmol/L) in preterm with <1500gm weight.[14]

Functional hypoparathyroidism in IDM is the main cause of hypocalcemia and is due to

- In diabetic mothers, magnesium is also lost in the urine due to glycosuria, which leads to maternal and then fetal hypomagnesemia.[3,13]
- The insulin dependent diabetic women fail to demonstrate the progressive increase in parathyroid hormone concentration and results in lower levels of PTH from mid gestation onwards.[3]
- Presence of some permeable substances capable of suppressing both maternal and fetal parathyroid hormone.[3]

Other reasons for hypocalcemia in IDM are

- Hypercalcitoninemia.[9]
- Vit D antagonism at the intestinal level due to increased cortisol.[9]
- Hyperphosphatemia due to tissue catabolism.[9]
- High concentrations of thyrocalcitonin (TCT).[16]

Both birth asphyxia and preterm deliveries are more common in IDM and even after reducing the incidence of asphyxia and prematurity, early neonatal hypocalcemia is still high in infants of diabetic mothers with advanced diabetes.[13]

The direct correlation between cord serum calcium and the nadir of postnatal calcium concentration at 24 hours of life has been described in normal neonates, so the best predictor of neonatal hypocalcemia in IDMs may be low cord serum calcium concentration. Authors have planned this study to assess the predictors for early onset neonatal hypocalcemia in IDM using the factors like cord calcium, gestational age, Apgar score, weight and length in centile in Indian babies.

The objective of this study was

Primary aim

- To study the magnitude of hypocalcemia in infants of diabetic mother in a tertiary center.

Secondary aim

- To assess the predictors for early onset neonatal hypocalcemia in infants of diabetic mother using cord calcium, gestational age, weight centile and length centile and apgar score.

METHODS

About 100 infants of diabetic mothers delivered in Bangalore Baptist hospital, Bengaluru, Karnataka, India during study period were included in the study, after obtaining the informed consent from the parents. Basic data of diabetic mothers admitted for delivery were recorded and after birth baby's Apgar score at 1 min, 5 min and later if indicated were noted. Two ml of blood from the umbilical cord was collected in plain container, after clamping and cutting the cord and sent for calcium and albumin estimation. Baby was examined for any obvious congenital anomalies and were excluded. Gestational age of baby was assessed by last menstrual period and was confirmed±2 weeks by New Ballard scoring. Weight of the newborn was recorded on an electronic weighing scale at birth and birth weight was recorded in grams to the nearest 10 grams and plotted on percentile charts according to the gestational age. Babies with a criterion for neonatal intensive care unit (NICU) admission (preterm <36 weeks, birth weight <2000-gram, Apgar score <7 at 5 min and respiratory distress) were shifted to NICU and started on intravenous fluid with calcium as per existing protocol i.e. 4ml/kg/day. Healthy babies were shifted to the mother's side and babies were given breast feeding on demand. Length of the baby was measured with infant meter within 24-48 hours of birth and plotted on percentile charts according to the gestational age.

Baby was monitored for symptoms of hypocalcemia and 2 ml blood was collected at 48 hours of life in plain container and sent for calcium and albumin estimation.

Serum calcium was measured by Arsenazo 3 and S. albumin by BCG (bromocresol green) method. Corrected calcium calculated for both calcium values using following formula i.e. total Ca decreased by 0.8 mg/dl for 1 gm/dl decreased in S albumin (reference value: S. albumin for cord blood is taken at 4 and at 48 hours is 3.5 gm/dl). Babies corrected calcium as not at 48 hours was correlated with corrected cord calcium levels, Apgar score, gestational age, weight and length percentile. Babies found to have asymptomatic hypocalcemia were treated with oral calcium for 3 days with Syp. Osteocalcium 80 mg/ kg/ day in 4 divided doses.

Inclusion criteria

- Total 100 Infants of diabetic mothers born in Bangalore Baptist Hospital, Bengaluru, Karnataka, India.

Exclusion criteria

- Infants born with major congenital anomalies to diabetic mothers,
- Those who do not wish to participate in the study.

Statistical analysis

The data collected was tabulated in an excel sheet and analyzed. A statistical association between hypocalcemia at 48 hours. of life and early predictors was assessed by

chi square test, univariate analysis. As tables contained values less than 5, fisher exact p value was calculated and p value <0.05 was considered as significant.

RESULTS

In present study 91% babies were term and 9% babies were preterm, there was no SGA baby and 13% were large for gestational age.11% babies had length <10th centile and 3% babies with length >90th centile. 11% of babies had Apgar <7 at 1 min and 2% babies had Apgar <7 at 5 min. Total male babies were 64% and female were 36%.

Table 1: Demographic data of the babies.

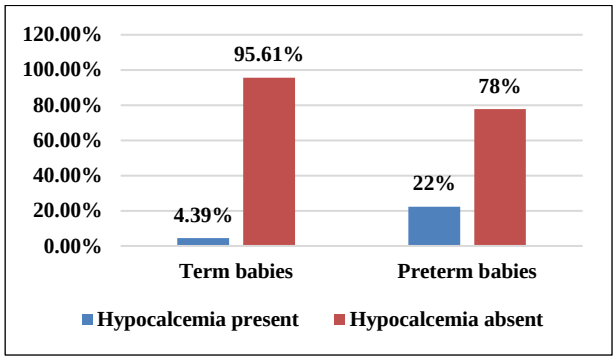
Demographic data of babies		Male {No. (percentage)}	Female {No (percentage)}	Total No.
Gestation age-term		59 (64.83)	32 (35.17)	91 (91)
Preterm		5 (55.55)	4 (44.45)	9 (9)
Weight-(centile)				
10-25th		10 (71.4)	4 (28.6)	14 (14)
25-50th		15 (48.38)	16 (51.61)	31 (31)
50-75th		14 (63.63)	8 (36.37)	22 (22)
75-90th		14 (70)	6 (30)	20 (20)
>90th		11 (84.6)	2 (15.4)	13 (13)
Length-(centile)				
<10th		7 (63.63)	4 (36.37)	11 (11)
10-25th		19 (70.37)	8 (29.63)	27 (27)
25-50th		21 (60)	14 (40)	35 (35)
50-75th		7 (63.63)	4 (36.37)	11 (11)
75-90th		9 (69.23)	4 (30.77)	13 (13)
>90th		1 (33.33)	2 (66.67)	3 (3)
Apgar score 1 min	<7	8 (72.72)	3 (27.28)	11 (11)
	>7	56 (62.92)	33 (37.08)	89 (89)
Apgar score 5 min	<7	1 (50)	1 (50)	2 (2)
	>7	63 (64.28)	35 (35.72)	98 (98)

The incidence of hypocalcemia was high in preterm babies i.e. 22% when compared to term babies i.e. 4.3%, but it was not significant statistically and can be attributed to low number of preterm babies in present study (Figure 1). The association of hypocalcemia with 1 min Apgar score was statistically significant. and incidence of hypocalcemia was high in babies with Apgar <7 at 1 min i.e.- 27.27% (Figure 2). The association of hypocalcaemia with cord calcium is not significant statistically. No babies with cord calcium <10 mg/dl were found to be hypocalcemic at 48 hrs ((Figure 3).

Table 2: Comparison between hypocalcemia and normal babies on selected parameters.

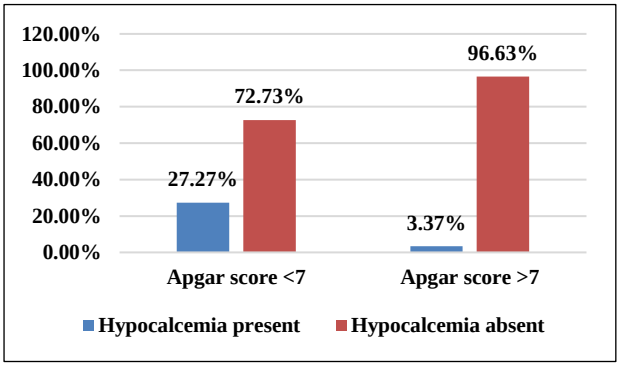
Variables	Mean (hypocalcemia babies)	Range (hypocalcemia babies)	Mean (non-hypocalcemia babies)	Range (non-hypocalcemia babies)	P value
Birth weight (gm)	2581±580.9	1520-3180	3061±497.2	1200-4300	0.025*
Birth length (cm)	44.75±3.28	39.5-48	46.84±2.70	39-52	0.07
Apgar score at 1 min	6.5±1.76	4-8	7.68±0.87	4-8	0.003*
Apgar score at 5 min	8.3±1.21	6-9	8.79±0.54	6-9	0.065
Cord Ca (mg/dl)	10.83±0.48	10.32-11.68	10.62±0.52	9.26-11.82	0.34
Maternal age (year)	28.33±3.83	24-35	28.38±3.60	21-38	0.97
Duration of diabetes in mother (months)	5.83±6.24	1-18	6.76±19.88	1-18	0.90

Z test is used to compare the mean between the 2 groups; *- significance; Among the variables, birth weight and APGAR score at 1 min were found to be statistically significant (p <0.05).



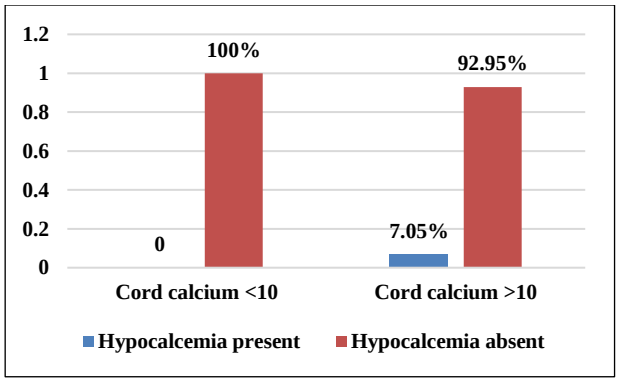
Fishers exact p value: 0.090

Figure 1: Association of hypocalcemia with gestation age.



Fishers exact p value: 0.017

Figure 2: Association of hypocalcemia with 1 min Apgar score.



Fishers exact p value: 0.09

Figure 3: Association of hypocalcemia with cord calcium.

DISCUSSION

The incidence of hypocalcemia in present study was 6%, it was in comparison with Yaseen HA et al, where incidence of hypocalcemia was 4%.[20] In present study there was no significant association of hypocalcemia and cord calcium (Figure 3). This was contradictory to Mimouna F et al, where there was significant association of hypocalcemia and cord calcium and it was predictor of hypocalcemia, and the incidence of hypocalcemia was 51%, it could be due to 50% mothers were in class D of white classification in the study but all our mother were well controlled in their diabetes, this could be due to better control of sugars during pregnancy and different group of population.[4] In Alam M et al, study, incidence of hypocalcemia seen in 15% and mortality was noticed in 7.5%.[21] In Demarini S et al, showed incidence of hypocalcemia in babies born mother in strict control group was significantly low as compared to customary control.[5] In preterm incidence of hypocalcemia was 22% (Figure 1) and in babies with Apgar <7 at 1 min was 27.27% (Figure 2) this result was in comparison with Salle B et al, study.[15] So, hypocalcemia in IDM was mainly related to prematurity and asphyxia. IDM per se was not a risk factor for hypocalcemia without any risk factors. In present study there was no significant correlation between hypocalcemia and gestation age (Figure 1), this was in contradictory to study conducted by Mimouni F et al, and Demarini S et al, where there was significant correlation between hypocalcaemia and gestational age, this can be explained due to the fact that we had small number of babies with gestational age <37 weeks. i.e. 9 and also preterm babies who needed NICU care were started on intravenous calcium due to ethical reasons.[4,5] Out of 11 babies depressed at birth i.e. Apgar <7 at 1 min 3 babies (27.27%) were found to have hypocalcemia. In the 2 babies who had low Apgar <7 at 5min, 1 baby was found to be hypocalcemic (50%). In present study there was a significant correlation between hypocalcemia in IDM and 1 min Apgar score (P=-0.017) (Figure 2), this was in agreement with study conducted by Mimouni F et al.[4]

The incidence of hypocalcemia in length <25th centile was 9.37% and the incidence in babies with length >25th centile was 4.4%, but it was not significant statistically. No babies were found to be hypocalcemia with length >75th centile (Table1).

In present study incidence LGA-13%, AGA-87% (Table 1), in comparison with Yaseen HA et al, study where incidence of SGA- 2%, LGA- 30%. In Nagy HK et al, study LGA- 25%, in Leandro et al, study 36% were LGA, 62% were AGA and only 2% were SGA. Alam M et al, 16 45% were LGA, 50% were AGA and 5% were SGA (Table 1).

Limitations of the study of this study were based on S. calcium was estimated at only 48 hours of life and not at 24 hours and 72 hours of life hence the exact estimation of hypocalcemia burden may not be accurate. The babies with risk factors requiring NICU care were started on intravenous fluid containing calcium as per the existing protocol. This could not be avoided due to ethical reasons. Hence actual incidence of hypocalcemia in this

group of infants would be higher. Larger sample size is needed to determine the predictors for hypocalcemia. Maternal and baby's vitamin D and parathyroid hormone levels which play an important role in calcium metabolism were not done

CONCLUSION

The incidence of hypocalcaemia in healthy babies of diabetic mothers is 2.29% and in those babies with additional risk factors is 30.77%, hence these babies should be monitored closely for hypocalcaemia even if asymptomatic. The incidence of hypocalcaemia in IDM was more in preterm babies and babies with risk factors like perinatal asphyxia-27.27% and, twins-25% in spite of being on intravenous calcium infusion as per the existing protocol. Hence these babies need to be closely monitored. None of the babies who had hypocalcaemia in present study were symptomatic, hence monitoring S. calcium for symptomatic babies alone may not detect magnitude of hypocalcaemia cord calcium is not a predictor for early onset neonatal hypocalcaemia in IDM.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Bhavya SO, Ranitha R. Early predictors of early onset neonatal hypocalcaemia in infants of diabetic mother. Int J Contemp Pediatr 2019;6:1325-9.