

**HIGH MATERNAL HbA1c IS ASSOCIATED WITH NEONATAL HYPOCALCEMIA**Abdul Tawab C. N<sup>1</sup>, Prakash R. M. Saldanha<sup>2</sup>, Sahana K. S<sup>3</sup>**HOW TO CITE THIS ARTICLE:**

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**ABSTRACT: INTRODUCTION:** Hypocalcemia occurs within the first 72 hours of birth in up to 50% of IDMs. The objective of the study was to compare the incidence of hypocalcemia in Infants of Pre-Gestational Diabetic & Gestational Diabetic mothers and to find the association of hypocalcemia and maternal diabetic control. **MATERIAL AND METHODS:** A tertiary care teaching hospital based prospective study over a period of 2 years. 40 Cases were included in the study 20 breast fed full term infants of Gestational diabetic mothers and 20 breastfed full term infants of Pre-Gestational diabetic mothers were enrolled in the study. Serum calcium of neonates in both groups was sent at 48 hours of life. Mean maternal HbA1c level was used to access maternal diabetic control. **OBSERVATION AND RESULTS:** Neonates of GDM showed statistically significant change in the serum calcium levels (Mean calcium level 9.055 mg/dl) and maternal HbA1c levels (mean HbA1c level 5.85%) an compared to neonates of PGDM (Mean calcium level 8.015 mg/dl, mean HbA1c level 6.75%) (p=0.0001). 7 out of 20 neonates (35 %) of Pre Gestational Diabetic mothers had hypocalcemia at 48 hour postnatal age and 3 out of 20 neonates (15%) of Gestational Diabetic mothers had hypocalcemia at 48 hour postnatal age. Incidence of hypocalcemia is more when diabetes is poorly controlled [HbA1C>6%] in both groups and it was statistically significant. **CONCLUSION:** Infants born to Pre-Gestational diabetic mothers are at a higher risk of developing hypocalcemia than infants of gestational diabetic mothers. Incidence of hypocalcemia can be predicted with diabetic control [maternal HbA1c levels]. Studies with larger sample size will give more definitive results on this issue.

**KEYWORDS:** Hypocalcemia, Infant of diabetic mother, Pre-Gestational diabetic mothers [PGDM], Gestational diabetes mellitus (GDM), HbA1c.

**INTRODUCTION:** Infants born to mothers with diabetes are at a greater risk for spontaneous abortion, stillbirth, congenital malformations, hypoglycemia, hypocalcemia and perinatal morbidity and mortality.<sup>1</sup> Hypocalcemia and hypomagnesemia occur within the first 72 hours of birth in up to 50% of IDMs.<sup>5</sup> Infants with respiratory distress or have been asphyxiated are at a higher risk of hypocalcemia. The exact mechanism of hypocalcemia is not known.

Abnormalities in calcium metabolism most likely represent a delayed transition from fetal to neonatal parathyroid control. In utero, the fetal parathyroids are relatively inactive because of the high transplacental flux of calcium. Maternal parathyroid hormone and vitamin D do not cross the placenta in significant amounts.

During neonatal transition, calcium delivery decreases. Low fetal parathyroid hormone levels at the end of gestation and persistently high levels of calcitonin and possible alterations in vitamin D metabolism may complicate neonatal calcium homeostasis.<sup>1,5</sup> These effects may occur for the first 24

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to 72 hours, which leaves the newborn vulnerable to early neonatal hypocalcemia<sup>1</sup>. The parathyroid hormone system becomes more reactive after 72 hours.

IDMs demonstrate a delay in this postnatal parathyroid hormone response, the pathophysiology of which is not well established. The signs and symptoms of neonatal hypocalcemia and hypomagnesemia are similar to those of hypoglycemia and include jitteriness, sweating, tachypnea, irritability, and seizures. They present at 24 to 72 hours, somewhat later than hypoglycemic symptom<sup>5</sup>. There are very limited published reports on incidence of hypocalcemia in Infants of Pre-Gestational & Gestational Diabetic mothers and the association of hypocalcemia and diabetic control. This study was planned to compare the occurrence of hypocalcemia in full term infants of Pre-Gestational & Gestational Diabetic mothers and to find the association of hypocalcemia and diabetic control.

**MATERIALS AND METHODS:** The study was performed in accordance with Declaration of Helsinki <sup>2</sup>. This was a tertiary care teaching hospital based, prospective study done in the Department of Pediatrics at Yenepoya Medical College hospital, Mangalore over a period of 2 years- from april 2012 to April 2014. 20 breastfed full term infants of Gestational diabetic mothers [GDM] and 20 full term Infants of Pre-Gestational diabetic mothers [PGDM]; in consecutively enrolled cohort of apparently healthy breast fed neonates were included in the study. Gestational diabetes mellitus (GDM) is defined by glucose intolerance of variable severity with onset of first recognition during pregnancy.

The glucose tolerance test was done between 24-28 weeks of pregnancy.

Pre Gestational diabetes mellitus (PGDM) is defined by glucose intolerance of variable severity before diagnosing pregnancy [Type 1 and Type 2 diabetes mellitus]. Neonates receiving phototherapy, neonates with Apgar of less than 7 at 5 minutes of birth, babies suffering from neonatal asphyxia, severe respiratory distress and those receiving total parenteral nutrition, calcium supplementation, intravenous fluids and blood transfusion were excluded from the study.

Information about the type of diabetes and control of diabetes (by HbA1c) was recorded from the maternal records. A mean of all HbA1c levels throughout pregnancy was used for comparison purposes. Serum calcium of neonates in both groups was sent at 48 hours of life. All babies are breastfed. Hypocalcemia is defined as calcium level less than 8.0mg/dl. Maternal HbA1c level more than 6% was considered as uncontrolled diabetes. Statistical analysis: The data obtained were analyzed using SPSS software version 17.0 for Windows (SPSS, Chicago, IL).

Numerical variables were compared between the two groups by using the independent unpaired t- test. P values of less than 0.05 were considered as statistically significant. The association between type of diabetes and the control of blood glucose within each group upon neonatal calcium levels was measured.

**OBSERVATION AND RESULTS:** A total of 40 neonates (n=20) breastfed full term infants of Gestational diabetic mothers and (n=20) breast fed full term infants of Pre-Gestational diabetic mothers were enrolled in the study. There was no significant difference in the sex (GDM, M: F12:8vs PGDM 9:11), and birth weight (mean birth weight, GDM 3.03Kg vs PGDM 3.43) of the studied groups.

Among the neonatal factors, birth weight, gestational age, APGAR score and Ballard score were not statistically different.

There was no statistical difference in the studied maternal parameters like, maternal age,

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parity, mode of delivery and maternal blood group.

3 out of 20 neonates (15%) of GDM and 7 of 20 neonates (35 %) of PGDM had hypocalcemia at 48 hour postnatal age.

It was observed that neonate of GDM showed statistically significant change in the serum calcium levels (Mean calcium level 9.055) and maternal HbA1c levels (mean HbA1c level 5.85) as compared to neonates of PGDM (Mean calcium level 8.015, mean HbA1c level 6.75) ( $p=0.0001$ ). Calcium values were lower in pre gestational diabetes and was statistically significant. The Maternal HbA1c values were higher in pre gestational diabetes and was statistically significant. {Table 1}.

	GROUP	N	Mean	Std. Deviation	t	df	Sig. (2-tailed)
SERUM CALCIUM AT 48HRS (mg/dl)	GESTATIONAL DIABETES	20	9.055	0.959427	4.208	30.236	<0.001
	PRE GESTATIONAL DIABETES	20	8.015	0.548946			
Maternal HbA1C (%)	GESTATIONAL DIABETES	20	5.85	0.489361	-5.002	38	<0.001
	PRE GESTATIONAL DIABETES	20	6.75	0.638666			

Table 1: COMPARISON OF THE TWO GROUP USING T TEST (INDEPENDANT)

THERE IS SIGNIFICANT HIGHER LEVELS OF SERUM CALCIUM IN GESTATIONAL DIABETES AND LOWER MATERNAL HbA1c IN GESTATIONAL DIABETES.

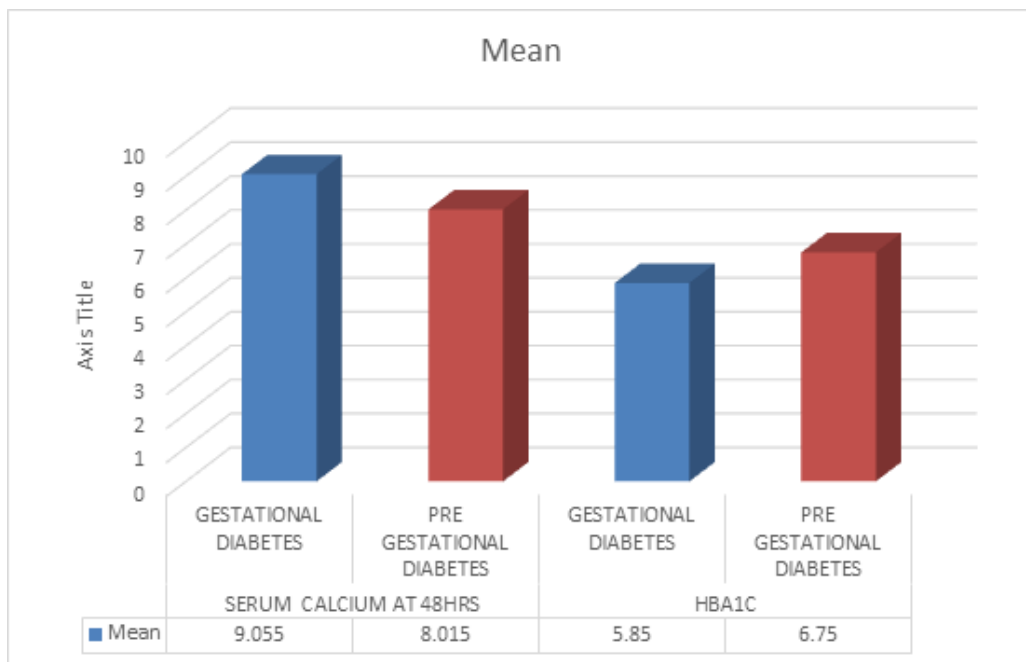
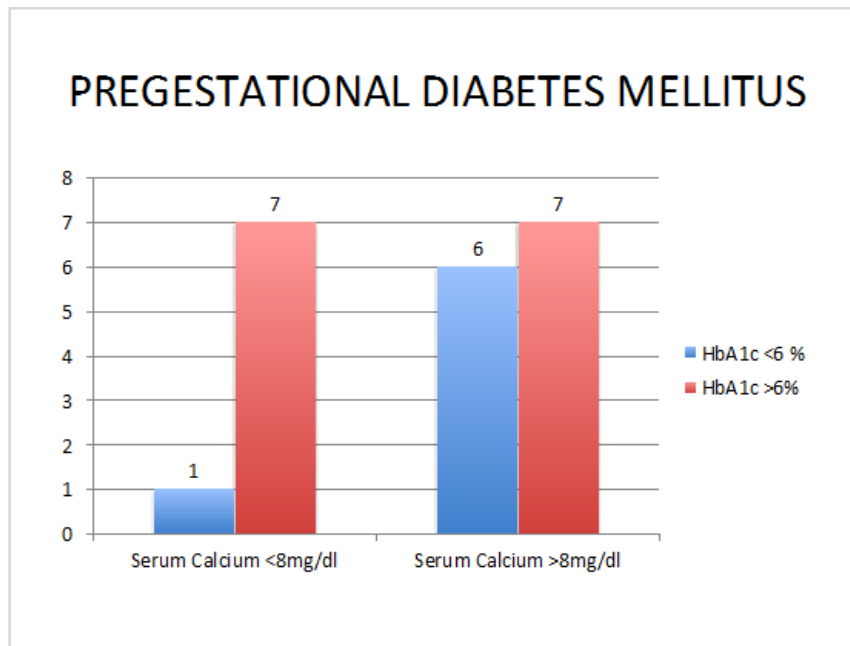


Figure 1

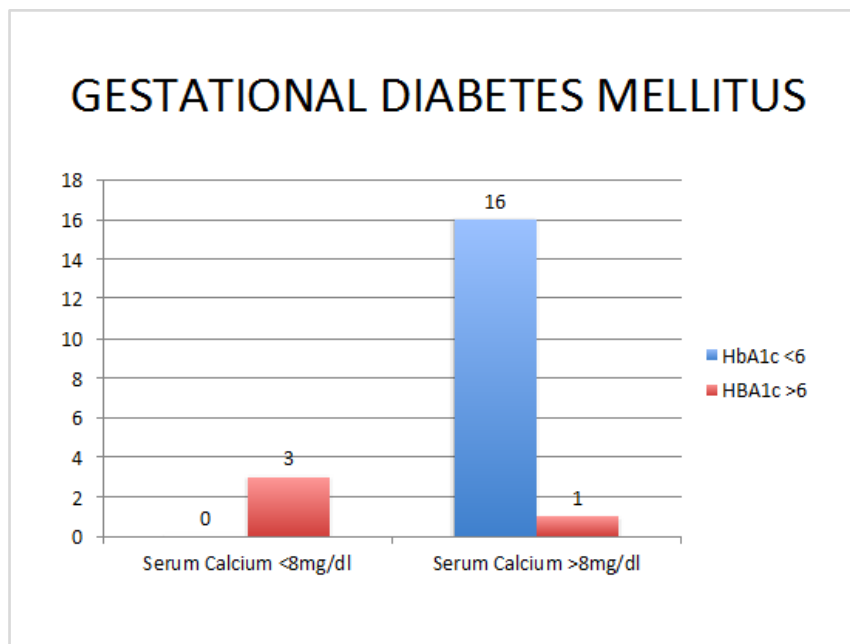
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On comparing the control of blood glucose within each group and it's association with hypocalcemia, [FIGURE 1, 2 AND TABLE 2]



**Figure 2**

Six out of seven neonates having hypocalcemia in Pre gestational diabetes group had poor diabetic control [HBA1c >6]. {figure 1}.



**Figure 3**

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All three neonates having hypocalcemia in Gestational diabetes mellitus group had poor diabetic control [HbA1c >6].{figure 2}

### COMPARISON OF THE CATEGORIES USING CHI SQUARE TEST:

#### Chi-Square Tests:

GROUP		Value	df	Asymp. Sig. (2-sided)
GESTATIONAL DIABETES	Pearson Chi-Square	14.118 <sup>a</sup>	1	<0.001
	N of Valid Cases	20		
PRE GESTATIONAL DIABETES	Pearson Chi-Square	4.615 <sup>c</sup>	1	.032
	N of Valid Cases	20		

a. 3 cells (75.0%) have expected count less than 5. The minimum expected count is .60.

c. 3 cells (75.0%) have expected count less than 5. The minimum expected count is 2.10.

Among infants of both groups, incidence of hypocalcemia is more when diabetes is poorly controlled [HbA1c >6].it is statistically significant

**DISCUSSION:** In this study, there was a statistically significant difference between fetal calcium levels and maternal HbA1c levels in IDMs of pre-gestational and gestational diabetics. HbA1c levels were significantly higher in infants of PGDM compared to infants GDM. Calcium values were significantly lower in infants of pre gestational diabetes.

There was also difference between the incidence of hypocalcemia in IDMs of pre-gestational and gestational diabetics [35% vs 15%].There was no serious clinical manifestations in hypocalcemic infants. All three infants who had mild symptoms like jitteriness and irritability was from Pre gestational diabetic mother group.

Among infants of both groups, incidence of hypocalcemia is more when HbA1c is more than 6%.

This study shows that Infants born to PGDM have a higher risk of developing hypocalcemia than infants of GDM and incidence of hypocalcemia is more when diabetes is poorly controlled.

In a similar study by Samrat U. Das and Pratibha Ankola, the incidence of clinical hypocalcemia at 24 hour of life is higher in infants born to women with PGDM compared to the neonates born to women with GDM and there was significant difference in maternal HbA1c levels (PGDM:GDM,7.2%:5.9%).<sup>3</sup>

But there was no significant difference in serum calcium levels at 24 hours of life (PGDM:GDM, 8.2 mg/dl ± 1.2: 8.6 mg/dl ± 1.0).Another study by Demarini, Mimoun, Tsang R et al infants in the strict diabetic control group had a significantly lower rate of hypocalcemia than infants in the customary control group.<sup>4</sup> Both these studies are in consistent with our results in association of neonatal hypocalcemia and maternal diabetic control.

The strengths of the study were that this was a consecutively enrolled prospective cohort study. Well-defined inclusion and exclusion criteria, study of single outcome variable i.e., calcium level at 48 hours make this study a simple but effective one. A small sample size of the studied patients was the major limitation. Serum magnesium levels and parathyroid hormone levels were not studied. Also only single serum calcium level values were studied.

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**CONCLUSION:** Infants born to PGDM are at a higher risk of developing hypocalcemia and can be predicted based on diabetic control with maternal HbA1c levels. Studies with larger sample size will give more definitive results on this issue.

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### AUTHORS:

1. Abdul Tawab C. N.
2. Prakash R. M. Saldanha
3. Sahana K. S.

### PARTICULARS OF CONTRIBUTORS:

1. Post Graduate Student, Department of Pediatrics, Yenepoya Medical College, Mangalore.
2. Professor and HOD, Department of Pediatrics, Yenepoya Medical College, Mangalore.
3. Associate Professor, Department of Pediatrics, Yenepoya Medical College, Mangalore.

### NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Abdul Tawab C. N,  
Department of Pediatrics,  
Yenepoya Medical College,  
Derlakatte, Mangalore-575018,  
Karnataka, India.  
Email: [abdultawab03@gmail.com](mailto:abdultawab03@gmail.com)

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