

# Frequency of Hypocalcemia in Infants of Diabetic Mothers within 24 Hours of Life

NAGHAM NAWAZ AWAN<sup>1</sup>, SUMBAL ABBAS<sup>2</sup>, MARINA NAZ<sup>3</sup>, MADIHA JAMEEL<sup>4</sup>, SABIKA IFTIKHAR<sup>5</sup>

<sup>1</sup>FCPS Pediatrics, Fellow Neonatology Department Childrens Hospital Pakistan Institute of Medical Sciences, Islamabad

<sup>2</sup>FCPS Pediatrics, Fellow at Paeds Oncology Department Shukat Khanum Hospital and Research Centre, Lahore

<sup>3</sup>MBBS, FCPS (Paeds Medicine), Senior Registrar Paeds Medicine University of Lahore

<sup>4</sup>FCPS Pediatrics Fellow Pediatric Oncology Shuakat Khanum Memorial Cancer Hospital and Research Centre, Lahore

<sup>5</sup>FCPS Pediatrics Neonatology Fellow Pediatrics Department Hameed Latif Hospital Lahore

Correspondence to: Nagham Nawaz Awan, Email: [nagham\\_awan@hotmail.com](mailto:nagham_awan@hotmail.com), Cell: +92 333 2447441

## ABSTRACT

**Objective:** To find frequency of Hypocalcemia in infants of diabetic mothers within 24 hours of life.

**Study Design:** It was a cross-sectional study.

**Study Duration:** The study was conducted at paediatric department of Ittifaq hospital Lahore from April 12, 2018 till Oct 12, 2019.

**Material and Methods:** A total of 260 cases after getting approval of synopsis were taken from Neonatal ward after delivery from Ittifaq hospital Lahore. All neonates fulfilling / meeting inclusion criteria were assessed for hypocalcaemia. Their basic history like age (hours), gender, gestational age, birth weight and baseline calcium level were noted. Venous blood was taken for analysis of calcium level and hypocalcaemia was labeled as per operational definition.

**Results:** The mean age of infants was  $11.92 \pm 6.66$  hours with minimum and maximum age as 1 and 24 hours. There were 137(52.7%) male and 123(47.3%) female cases, with higher male to female ratio. The mean gestational age was  $39.48 \pm 1.68$  weeks with minimum and maximum gestational age as 37 and 42 weeks. The mean birth weight was  $3193.99 \pm 404.12$  g with minimum and maximum birth weight as 2500 and 3892 grams. A total of 67(25.8%) neonates had hypocalcaemia while 193(74.2%) neonates had normal calcium level.

**Practical implication:** This study was done to determine the frequency of neonatal hypocalcemia among infants with maternal hypocalcemia due to the lack of data, especially at the local level. If diagnosed early, they can begin treatment right away, which could reduce their mortality and morbidity in our region of the world.

**Conclusion:** Through the findings of this study, it is concluded that, almost a quarter i.e. 25.8% neonates had hypocalcaemia that is considerably high percentage. So, infants born to diabetic mothers should be screened for hypocalcaemia to minimize the risk of related complications like seizure and loss of consciousness etc.

**Keywords:** Pregnancy, diabetes mellitus, gestational diabetes mellitus, calcium level, hypocalcaemia

## INTRODUCTION

Diabetes mellitus, or sugar intolerance, is the most frequent metabolic disease associated with pregnancy complications. Pregnancy-related complications from diabetes mellitus affect about 1-4% of all pregnancies, 90% of which are Gestational Diabetes Mellitus (GDM).<sup>1</sup> Maternal and foetal health might be negatively impacted by the gestational diabetes mellitus (GDM), a common obstetrical issue.<sup>2</sup> Since the introduction of specialised maternal, foetal and neonatal care for those women who have diabetes and their offsprings, the morbidity and mortality rates for infants of diabetic mothers have decreased by roughly 30 times. Before that time, the combined foetal and neonatal rate of death had reached to 65%.<sup>3</sup> Preventing hypoglycemia, the most common metabolic condition in newborns, should begin as soon as feasible after birth.<sup>4</sup> Maternal hyperglycemia can potentially lead to hypocalcemia in newborns. Deficiencies in calcium metabolism are probably the result of a sluggish changeover from foetal to neonatal parathyroid regulation. Due to the large amount of calcium that crosses the placenta during pregnancy, the foetal parathyroids are dormant. Vitamin D and maternal parathyroid hormone do not transfer in adequate quantities across the placenta. Myocardial insufficiency (in the form of transitory hypertrophic subaortic stenosis), thrombosis of the renal veins, and small left colon syndrome are some of the other common causes of death.<sup>5</sup>

At birth, infants of diabetic mothers experience hyperinsulinism because of the elevated levels of glucose and other nutrients transferred across the placenta, which stimulates hyperplasia of the islets of Langerhans in the fetus and leads to increased insulin secretion as well as an elevated amount of C-peptide and free insulin in the cord blood.<sup>6</sup> Clamping the umbilical cord cuts off the newborn's source of glucose from the mother, and the newborn's blood glucose level may drop suddenly and rapidly due to the excess insulin in the first few hours after birth. Normal serum calcium levels naturally drop in the first 2 days after birth in healthy term infants.<sup>8,9</sup> Because of this, a healthy full-term infant's

calcium level begins to drop immediately after birth, and by 24 to 48 hours of life, it has dropped to a nadir of 7.5 to 8.5 mg/dl. Severe symptoms, such as seizures, can result from a serum calcium level at or below the hypocalcemia threshold in premature infants, infants of diabetic mothers, and infants with perinatal asphyxia. The incidence of hypocalcemia in newborns born to diabetes mothers varies widely, from 4% to as high as 50%, with an average incidence of 22%.<sup>10,11</sup>

A study reported frequency of Hypocalcaemia among neonates of diabetic mothers was 5.2%<sup>1</sup> while another study reported nine (21.4%) had hypocalcaemia.<sup>12</sup>

The rationale of this study is to find frequency of Hypocalcaemia in infants of diabetic mothers within 24 hours of life. No local data is published and studies form other part of the world shows variation in frequency of Hypocalcaemia in infants of diabetic mothers i.e. 5.2%- 21.4% (more than 4 times difference) 6. Through this study baseline data will help us to know frequency of Hypocalcaemia among neonates of diabetic mothers in our own population. If we find higher frequency then in future infants born to diabetic mothers can be screened for hypocalcaemia to minimize the risk of related complications like seizure and loss of consciousness etc. Also, the best possible care for these infants can be given for the condition's prevention, early detection, and treatment.

## MATERIALS AND METHODS

**Study Setting:** This study was carried out at paediatric department of Ittifaq hospital Lahore. **Study Duration:** Over 6 months from April 12, 2018 till Oct 12, 2019.

**Study Design:** Cross Sectional Study.

**Sample Size:** A total of 260 is calculated at 5% level of significance and 5% margin of error, and taking expected percentage of Hypocalcemia as 21.4%.<sup>6</sup>

**Sampling Technique:** Non-Probability consecutive sampling technique will be used.

**Inclusion Criteria:**

1. Patients of either gender aged 1st 24 hours of life

2. Infants of diabetic mother as per operational definition.
3. Gestational age at birth 37-42 weeks (on antenatal scan)
4. Birth weight 2500 – 4000 g

**Exclusion criteria:** All neonates was excluded if they

1. are receiving phototherapy (on clinical record)
2. had Apgar of less than 7 at 5 minutes of birth (on clinical record)
3. are suffering from neonatal asphyxia, severe respiratory distress and those receiving total calcium supplementation, parenteral nutrition, blood transfusion and intravenous fluids (on clinical record).

**Data Collection Procedure:** A total of 260 cases after getting approval of synopsis were taken from Neonatal ward after delivery from Ittifaq hospital Lahore. All neonates fulfilling / meeting inclusion criteria were assessed for hypocalcaemia after obtaining the parents' or attendees' informed consent. Their basic history like age (hours), gender, gestational age, birth weight and baseline calcium level were noted. Venous blood was taken for analysis of calcium level and hypocalcaemia was labeled as per operational definition. All data was collected by researcher herself on attached proforma..

**Data Analysis:** Using SPSS version 22, all information and data that were gathered were entered and analyzed. Mean ± SD was used quantitative data like age, gestational age and birth weight. Percentage and frequency was calculated for categorical data like gender and hypocalcaemia. Data was stratified for age (hours), gender, types of maternal diabetes (pre pregnancy or GDM) to report effect modifiers. After stratification, a Chi-square test was performed, and a p-value of less than 0.05 was considered significant.

## RESULTS

The mean age of infants was 11.92 ± 6.66 hours with minimum and maximum age as 1 and 24 hours. There were 145(55.8%) cases were 1-12 hours old and 115(44.2%) infants were 12-24 hours old. There were 137(52.7%) male and 123(47.3%) female cases, with higher male to female ratio. The mean gestational age was 39.48 ± 1.68 weeks with minimum and maximum gestational age as 37 and 42 weeks. The mean birth weight was 3193.99 ± 404.12 g with minimum and maximum birth weight as 2500 and 3892 grams. A total of 35(13.5%) mothers had pre pregnancy diabetes mellitus and 225(86.5%) mothers had Gestational diabetes mellitus. A total of 67(25.8%) neonates had hypocalcaemia while 193(74.2%) neonates had normal calcium level. When data was stratified for age, among 1-12 hours old neonates 39(26.9%) had hypocalcaemia and 106(73.1%) had normal calcium level. Among 12-24 hours old neonates, 28(24.3%) cases had hypocalcaemia and 87(75.7%) neonates had normal calcium level. The frequency of hypocalcaemia was statistically same in both age groups, p-value > 0.05. Among male cases 35(25.5%) had hypocalcaemia and 102(74.5%) cases had normal calcium levels. Among female cases, 32(26%) cases had hypocalcaemia and 91(74%) neonates had normal calcium levels. The frequency of hypocalcaemia was statistically same in both male and female cases, p-value > 0.05. Among females with pre pregnancy diabetes 7(20%) neonates had hypocalcaemia and 28(80%) cases had normal calcium levels. Among female with GDM, 60(26.7%) cases had hypocalcaemia and 165(73.3%) neonates had normal calcium levels. The frequency of hypocalcaemia was statistically same in both types of diabetes, p-value > 0.05.

Table 1: Descriptive statistics of age (hours), gestational age (weeks), birth weight (g)

Age (hours)	
Mean ± S.D	11.92±6.66
Range (Min-Max)	23.00 (1.00-24.00)
Gestational age (weeks)	
Mean ± S.D	39.48±1.68

Age (hours)	
Mean ± S.D	11.92±6.66
Range (Min-Max)	23.00 (1.00-24.00)
Gestational age (weeks)	
Range (Min-Max)	5 (37.00-42.00)
Birth weight (g)	
Mean ± S.D	3193.99±404.12
Range (Min-Max)	1392.00 (2500.00-3892.00)

Table 2: Percentages of age, gender, maternal diabetes and hypocalcaemia

Variables	Characteristics	Percentage%
Age	1-12 hours	145(55.77%)
	12-24 hours	115(44.23%)
Gender	Male	137(52.69%)
	Female	123(47.31%)
Maternal Diabetes	Pre Pregnancy	35(13.46%)
	GDM	225(86.54%)
Hypocalcaemia	Yes	67 (25.77%)
	No	193(74.23%)

Table 3: Comparison of in Hypocalcaemia in different Age groups (hours)

		Hypocalcaemia		Total	P-Value
		Yes	No		
Age groups (hours)	1-12 hours	39(26.9%)	106(73.1%)	145(100.0%)	0.641
	12-24 hours	28(24.3%)	87(75.7%)	115(100.0%)	
Total		67(25.8%)	193(74.2%)	260(100.0%)	

Table 4: Comparison of in Hypocalcaemia in different in male and female cases

		hypocalcaemia		Total	P-value
		Yes	No		
Gender	Male	35(25.5%)	102(74.5%)	137(100.0%)	0.931
	Female	32(26.0%)	91(74.0%)	123(100.0%)	
Total		67(25.8%)	193(74.2%)	260(100.0%)	

Table 5: Comparison of in Hypocalcaemia in types of maternal diabetes

		hypocalcaemia		Total	P-value
		Yes	No		
Types of maternal Diabetes	Pre pregnancy	7(20.0%)	28(80.0%)	35(100.0%)	0.402
	GDM	60(26.7%)	165(73.3%)	225(100.0%)	
Total		67(25.8%)	193(74.2%)	260(100.0%)	

## DISCUSSION

Diabetes Mellitus (DM) is one of the commonest found diseases globally with a prevalence of 2.8%. Almost 171 million individuals have been affected by DM in 2000 and incidence of diabetes was reported to be 7.1% in one study conducted in 2012. This incidence is increasing with time. The incidence of diabetes mellitus (DM) continues to rise, with a 7.1 percent yearly incidence in 2012. 13 As the obesity and type 2 diabetes epidemics continue the prevalence of gestational diabetes mellitus, which is diagnosed during pregnancy but is not obviously diabetes, is rising. One of the most prevalent health issues, it is brought on by an increase in insulin resistance and a failure of the pancreatic cells to secrete enough insulin to compensate. Insulin resistance and -cell dysfunction can be detected thanks to this metabolic stress test.<sup>14</sup> The prevalence of GDM is about 20% among all pregnant females.<sup>15</sup>

Our study included 137 male patients (52.7% of total), 123 female cases (47.3% of total), and had a greater male to female ratio. The mean gestational age was 39.48 ± 1.68 weeks with 37 and 42 weeks are the minimal and maximum gestational ages.

Mean birth weight was  $3193.99 \pm 404.12$  g with minimum and maximum birth weight as 2500 and 3892 grams. Another study reported almost similar findings i.e. 80 IDMs in all, 52.5% of whom were men and 47.5% of whom were women. The mean gestational age was 37.58 weeks (SD: 1.35). Most babies (73.8%) had birth weights of 2.5 to 3.99 kg.<sup>16</sup>

Bharti et al. conducted a study to determine the incidence of different complications in children born to diabetic mothers. 17 Out of 64 neonates, 19 (29.6%) were born to pregnant women with diabetes and 45 (70.3%) were born to women with gestational diabetes. We also found that A total of 35(13.5%) mothers had pre pregnancy diabetes mellitus and 225(86.5%) mothers had Gestational diabetes mellitus.

In current study a total of 67(25.8%) neonates had hypocalcaemia while 193(74.2%) neonates had normal calcium level. Alam et al.<sup>140</sup> conducted a similar study. They reported hypocalcemia in 15% 140. Toor et al. conducted a study a comparable study, hypocalcemia was documented in 10(12.5%).<sup>16</sup> Khan et al. reported that a total of 100 Type 2 diabetic mothers with age between 28 to 40 years, gestational age of 37-42 weeks assessed on dating scan presenting with multigravida and mutiparity were enrolled. They hypocalcemia as 20%.<sup>18</sup> In order to find out more about the health risks and outcomes for babies born to mothers with diabetes, Ashraf et al. undertook a study.<sup>19</sup> Forty-six infants were included in the study, with females making up 56.5% and males 43.5%. Birth weights ranged between 1 and 5.5 kg. The birth rate of infants without tachypnea was quite low. Hypoglycemia (73.9%), hyperbilirubinemia (52.2%) and hypocalcaemia (21.7%), were the most frequently observed metabolic complications. Mortality was 8.7% and mechanical ventilation was necessary for 6 patients.<sup>19</sup> Iqbal et al. conducted a study to determine the frequency of metabolic complications in infant of diabetic mother. Frequency of hypocalcaemia in infant of diabetic mother was recorded as 18.31%.<sup>20</sup> In current study the frequency of hypocalcemia is higher as reported in previous studies.

## CONCLUSION

Through the findings of this study, it is concluded that, almost a quarter i.e. 25.8% neonates had hypocalcaemia, that is considerably high percentage. So, infants born to diabetic mothers should be screened for hypocalcaemia to minimize the risk of related complications like seizure and loss of consciousness etc.

## REFERENCES

1. Rafiq W, Hussain SQ, Jan M, Najar BA. Clinical and metabolic profile of neonates of diabetic mothers. *Int J Contempor Pediatr.* 2017;2(2):114-8.

2. Fazel-Sarjoui Z, Khodayari Namin A, Kamali M, Khodayari Namin N, Tajik A. Complications in neonates of mothers with gestational diabetes mellitus receiving insulin therapy versus dietary regimen. *Int J Reproduct Biomed.* 2016;14(4):275-8.
3. Opara PI, Jaja T, Onubogu UC. Morbidity and mortality amongst infants of diabetic mothers admitted into a special care baby unit in Port Harcourt, Nigeria. *Italian J Pediatr.* 2019;36(1):1-6.
4. Mitanchez D, Zyzdorzcyk C, Simeoni U. What neonatal complications should the pediatrician be aware of in case of maternal gestational diabetes? *World J Diabetes.* 2015;6(5):734-43.
5. Abdul TC, Saldanha PR, Sahana K. High maternal HbA1c is associated with neonatal hypocalcemia. *J Evolution Med Dent Sci.* 2014;3(55):12531-7.
6. Merchant RH, Dalvi, R, Vidwans A. Infant of the diabetic mother. *Indian Paediatr* 2017; 27:373-9.
7. Mountain KR. The infant of the diabetic mother. *Bailliere's ClinObstetGynaecol* 2015;5: 413-441.
8. Aggarwal R, Upadhyay M, Deorari AK, Paul VK. Hypocalcemia in the newborn. *Ind J Pediatr.* 2021;68(10):973-5.
9. Khalesi N, Namirianian P, Samavati S, Farahani Z. The frequency of early and late hypocalcemia among hospitalized newborns in an iranian hospital. *Shiraz E-Med J.* 2015;16(6):547-55.
10. Rosenn B, Miodovnik M, Tsang R. Common clinical manifestations of maternal diabetes in newborn infants: implications for the practicing pediatrician. *Pediatr Ann.* 2018;25(4):215-22.
11. Tsang RC, Kleinman LI, Sutherland JM, Light IJ. Hypocalcemia in infants of diabetic mothers: studies in calcium, phosphorus, and magnesium metabolism and parathormone responsiveness. *J Pediatr.* 2019;80(3):384-95.
12. Sugawara D, Maruyama A, Imanishi T, Sugiyama Y, Ichihashi K. Complications in infants of diabetic mothers related to glycated albumin and hemoglobin levels during pregnancy. *Pediatr Neonatol.* 2016;57(6):496-500.
13. Geiss LS, Wang J, Cheng YJ, Thompson TJ, Barker L, Li Y, et al. Prevalence and incidence trends for diagnosed diabetes among adults aged 20 to 79 years, United States, 1980-2012. *J Am Med Assoc.* 2014;312(12):1218-26.
14. Coustan DR. Gestational diabetes mellitus. *Clinic Chem.* 2013;59(9):1310-21.
15. Afshari F, Abbasalizade F, Faraji M. Comparative evaluation of two treatment regimens, diet versus insulin, in gestational diabetes mellitus. *Europ J Experiment Biol.* 2013;3(4):71-6.
16. Toor KM, Wahid S, Azeem KJJolIM, College D. Frequency of metabolic complications in infants born to diabetic mothers at KRL Hospital, Islamabad. 2015;4(1):23-6.
17. Bharti P, Sharma Sijjoar. Frequency of various complications among hospitalized infants born to diabetic mothers. 2018;7(9):436-45.
18. Khan M, Malik KA, Bux KJ. profile of complications in infants born to diabetic mothers. 2016;22(2):787-93.
19. Ashraf S, Mushtaq SJ. Metabolic complications and outcome of infants born to diabetic mothers. 2018;34(7):39-42.
20. Iqbal W, Shamaoon M, Masood M, Butt MAJM. The frequency of metabolic complications in infant of a diabetic mother. 2017;34(3):435-42.