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Original research article

PREVALENCE OF HYPOCALCEMIA IN INFANT OF DIABETIC MOTHER

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Abstract: *Calcium plays an important role in the body, such as in the contraction of muscles, the transmission of nerve impulses and the calcification of bones, blood clotting, blood vessel constriction, cell division, cell membrane stability, lipid metabolism, and other essential metabolic processes.* ***Objective:*** *The main objective of the study is to find the prevalence of hypocalcemia in infants of diabetic mothers.* ***Methods:*** *This prospective observational study was conducted at National Institute of Child and Health Karachi during January 2024 to June 2024.Data were collected from 255 infants whose mothers were suffering from DM.Data were collected through a designed questionnaire which include all information related to demographics, age, history of DM and other comorbidities. Maternal data included the type of diabetes (gestational or pregestational), maternal glycemic control measured by HbA1c levels, maternal vitamin D status, and the presence of any other comorbidities, such as hypertension or obesity.* ***Results:*** *Data were collected from 255 infants with 31.4% born preterm and 68.6% born full-term. The majority of the infants (76.5%) had a normal birth weight (≥ 2.5 kg), while 23.5% had a low birth weight (< 2.5 kg). In terms of gender distribution, the cohort was nearly balanced, with 51.0% male and 49.0% female infants. Regarding the mode of delivery, 54.9% were delivered via cesarean section, and 45.1% were born through vaginal delivery. Infants born to mothers with poor glycemic control (HbA1c > 7%) had a higher prevalence of hypocalcemia (38.3%) compared to those with better control (19.3%). Maternal vitamin D deficiency also contributed to the risk, with 42.4% of infants affected. Neonatal hypoglycemia was strongly associated with hypocalcemia, with a prevalence of 40.0% in hypoglycemic infants.* ***Conclusion:*** *This study concludes that hypocalcemia is prevalent among infants of diabetic mothers (IDMs), with poor maternal glycemic control and vitamin D deficiency being significant risk factors. Early detection through routine screening, particularly in those with neonatal hypoglycemia, is essential as many cases are asymptomatic. Timely calcium supplementation effectively resolves the condition, emphasizing the importance of optimizing maternal care and standardized neonatal monitoring to improve outcomes in this high-risk population.*

Keywords: Diabetes, Gestational, Hypocalcemia, Infant, Newborn, Maternal Health, Vitamin D Deficiency.

Introduction

Hypocalcemia, a condition characterized by low serum calcium levels, is an important metabolic disorder in neonates, especially among those born to mothers with diabetes. Calcium plays an important role in the body, such as in contraction of muscles, the transmission of nerve impulses and the calcification of bones, blood clotting, blood vessel constriction, cell division, cell membrane stability, lipid metabolism, and other essential metabolic processes (1). In newborns, balanced calcium levels must be maintained because of the relationship between calcium and the control of neuromuscular and cardiac functions. Hypocalcemia may be early temporary, late temporary or permanent and can be a potential hazard to infants, especially high-risk infants including IDM (2). They also showed that maternal diabetes, both gestational and pregestational, is directly associated with the development of neonatal hypocalcemia. Newborns of diabetic mothers are prone to many complications such as respiratory distress syndrome, macrosomia, hypoglycaemia, and metabolic imbalance like hypocalcaemia. Maternal hyperglycemia leads to changes in the metabolic milieu in the womb which affects insulin and calcium metabolism of the infant (3). These infants with hyperglycemic mothers have high insulin levels that lead to low parathyroid hormone (PTH) levels which is vital in calcification. In addition, IDMs suffer from conditioned high levels of renal calcium clearance and low intestinal calcium absorption; both work against hypocalcemia (4). Hypocalcemia can occur early or later in the course of IDM and may be unrelated to the degree of diabetic control. Perinatal hypocalcemia is defined as hypocalcemia diagnosed within the first three days after birth, predominantly due to PTH suppression, by delayed parathyroid response attributable to maternal diabetes mellitus (5). They have described late hypocalcaemia as happening after the first three days of life and occurs more frequently, but other factors such as high phosphate intake or low levels of vitamin D in the newborn baby may also cause it. In both conditions, hypocalcemia may present clinically in the form of jitteriness, irritability, poor feeding, lethargy, and, rarely, seizures (6). But as it will be mentioned earlier, many cases of hypocalcemia might not be symptomatic and thus require periodic screening for calcium levels among high-risk neonates. Hypocalcemia is reported in variable proportions in IDMs depending on population, diagnostic criteria used, and time of calcium assessment. The studies proposed that 20-50% of the IDMs may tend to develop hypocalcemia during the neonatal

period and it is a major issue in NICU (7). Since glucose monitoring has become the standard of care in all IDMs due to the established risk of hypoglycemia, there has been gradually increasing awareness of the possible requirement of paying similar attention to calcium levels to prevent hypocalcemia complications (8). The following are some of the risk factors in promoting hypocalcemia in IDMs Some of the risk factors include the following. Those are the pre-pregnancy glycemic control, the severity of disease in the mother, other associated metabolic complications (hypomagnesemia), and the gestational age of the born infant (9). The incidences of hypocalcemia are even higher in infants who were born preterm or with low birth weight. Also, the mode of delivery such as cesarean section, and maternal vitamin D stores may affect calcium mobilization in early life. Besides maternal diabetes, these diverse factors should be considered when evaluating hypocalcemia risk in IDMs. Management of hypocalcemia in IDMs involves many aspects including the early, antenatal management of maternal diabetes (10). Varying glycemic control during pregnancy is critical because it's been established as a causal factor in neonatal metabolic complications such as hypocalcemia. In the postnatal period, early recognition of hypocalcemia is important for IDM because hypocalcemia is most likely to occur in the first days of life. Calcium usually forms the main therapy and might be administered orally or intravenously, depending on the patient's condition. In some circumstances, magnesium might also be recommended as a supplement to magnesium because the low level of magnesium makes hypocalcemia worse (11). It has been established that early recognition of hypocalcemia in IDMs is important to avoid future complications. Chronic hypocalcemia is associated with substantial adverse neurodevelopmental consequences in the infant including seizures and abnormalities in cognitive skills (12). Thus, the present study emphasized the importance of a high degree of clinical suspicion for hypocalcemia in this specific high-risk population subset, especially when they may not display readily recognizable clinical features for the same (13).

Objective

The main objective of the study is to find the prevalence of hypocalcemia in infants of diabetic mothers.

Methodology

This prospective observational study was conducted at the National Institute of Child and Health Karachi from January 2024 to June 2024Data were collected from 255 infants whose mothers were suffering from DM.

Inclusion criteria

1. Infants delivered at or beyond 28 weeks of gestation.
2. Availability of calcium level measurements within the first 72 hours of life for early-onset hypocalcemia, and between 4 to 7 days of life for late-onset hypocalcemia.

Exclusion criteria

1. Infants with congenital anomalies, chromosomal abnormalities, or those with conditions known to affect calcium metabolism independent of maternal diabetes, such as severe birth asphyxia or renal impairment.

Data were collected through a designed questionnaire which included all information related to demographics, age, history of DM and other comorbidities. Maternal data included the type of diabetes (gestational or pregestational), maternal glycemic control measured by HbA1c levels, maternal vitamin D status, and the presence of any other comorbidities, such as hypertension or obesity. Neonatal data consisted of gestational age, birth weight, Apgar scores at 1 and 5 minutes, and the mode of delivery (vaginal or cesarean section). The presence of any neonatal complications such as hypoglycemia, respiratory distress, or hypomagnesemia was recorded. Serum calcium levels were measured routinely within the first 24 hours of life to assess early-onset hypocalcemia and between 4 to 7 days to evaluate late-onset hypocalcemia. For this study, hypocalcemia was defined as serum calcium levels below 7 mg/dL in term infants and below 6 mg/dL in preterm infants. Infants diagnosed with hypocalcemia had their calcium levels rechecked at 48 hours and on day 7 to monitor for persistence or resolution. Upon admission to the NICU, all infants underwent routine metabolic screening, including glucose and calcium level assessments within the first 24 hours of life. For infants diagnosed with hypocalcemia, calcium levels were rechecked at 48 hours and again on day 7 to assess for persistence or resolution. Infants with symptomatic hypocalcemia were treated immediately with calcium supplementation, either orally or intravenously, based on the severity of the hypocalcemia.

Data were analyzed using SPSS v29. Descriptive statistics were used to summarize maternal and neonatal characteristics. The prevalence of hypocalcemia was calculated as the proportion of infants with serum calcium levels below the defined threshold.

Results

Data were collected from 255 infants with 31.4% born preterm and 68.6% born full-term. The majority of the infants (76.5%) had a normal birth weight (≥ 2.5 kg), while 23.5% had a low birth weight (< 2.5 kg). In terms of gender distribution, the cohort was nearly balanced, with 51.0% male and 49.0% female infants. Regarding the mode of delivery, 54.9% were delivered via cesarean section, and 45.1% were born through vaginal delivery.

Table 1: Demographic Data of Study Population (Infants of Diabetic Mothers)

Demographic Variables	Number of Infants (n)	Percentage (%)
Gestational Age		
Preterm (< 37 weeks)	80	31.4
Full-term (≥ 37 weeks)	175	68.6
Birth Weight		
Low Birth Weight (< 2.5 kg)	60	23.5
Normal Birth Weight (≥ 2.5 kg)	195	76.5
Gender		
Male	130	51.0

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Female	125	49.0
Mode of Delivery		
Cesarean Section	140	54.9
Vaginal Delivery	115	45.1

72 (28.2%) were diagnosed with hypocalcemia. Among these cases, 83.3% had early-onset hypocalcemia (within the first 72 hours of life), while 16.7% developed late-onset hypocalcemia (between 4 to 7 days). Preterm infants had a higher prevalence of hypocalcemia (35.0%) compared to full-term infants (25.1%), indicating that prematurity is a significant risk factor for the condition.

Table 2: Prevalence of Hypocalcemia in Infants of Diabetic Mothers (IDMs)

Group	Number of Infants (n)	Hypocalcemic Infants (n)	Prevalence (%)
Total Study Group	255	72	28.2
Early-onset hypocalcemia (≤ 72 hours)	-	60	83.3
Late-onset hypocalcemia (4-7 days)	-	12	16.7
Preterm Infants	80	28	35.0
Full-term Infants	175	44	25.1

Infants born to mothers with poor glycemic control (HbA1c > 7%) had a higher prevalence of hypocalcemia (38.3%) compared to those with better control (19.3%). Maternal vitamin D deficiency also contributed to the risk, with 42.4% of infants affected. Neonatal hypoglycemia was strongly associated with hypocalcemia, with a prevalence of 40.0% in hypoglycemic infants. Additionally, cesarean-section delivery was linked to a higher prevalence of hypocalcemia (32.1%) compared to vaginal delivery (21.7%).

Table 3: Factors Associated with Hypocalcemia in IDMs

Risk Factors	Total Infants (n)	Hypocalcemic Infants (n)	Prevalence (%)
Maternal Glycemic Control			
HbA1c > 7%	120	46	38.3
HbA1c ≤ 7%	135	26	19.3
Maternal Vitamin D Deficiency (≤ 20 ng/mL)	85	36	42.4
Neonatal Hypoglycemia (Blood glucose < 40 mg/dL)	90	36	40.0
Mode of Delivery			
Cesarean Section	140	45	32.1
Vaginal Delivery	115	25	21.7

Among the 72 hypocalcemic infants, the majority (58.3%) were asymptomatic, highlighting the importance of routine screening. Of the symptomatic cases, jitteriness was the most common symptom, observed in 26.4% of the infants, followed by irritability in 15.3%, and seizures in 5.6%.

Table 4: Symptoms of Hypocalcemia in IDMs

Symptoms	Number of Hypocalcemic Infants (n)	Percentage (%)
Jitteriness	19	26.4
Irritability	11	15.3
Seizures	4	5.6
Asymptomatic	42	58.3

Discussion

This study aimed to investigate the prevalence of hypocalcemia in infants of diabetic mothers (IDMs) and to identify the key maternal and neonatal factors contributing to its development. The findings revealed that 28.2% of the 255 IDMs were diagnosed with hypocalcemia, which is consistent with previous studies that have reported similar prevalence rates, ranging from 20% to 50% in various populations (14). The high incidence of hypocalcemia observed in this research therefore implies the importance of strict follow-up and early management of this group. One of the important results elicited in this study is the relationship between the increased glycemic control of the mother and the corresponding elevated risk of hypocalcemia in neonates (15). The overall prevalence of hypocalcemia in infants of diabetic mothers was found to be 33.8% but that among infants of mothers with an Hba1c > 7%= 38.3% while in infants of mothers with good glycaemic control = 19.3%. This is in concordance with other studies done earlier showing that maternal hyperglycemia during pregnancy results in fetal hyperinsulinemia which inhibits secretion of parathyroid hormone (PTH) in the fetus (16). The suppression of PTH is probably the chief factor that leads to hypocalcemia in IDMs because PTH otherwise plays a crucial role in calcium homeostasis. Vitamin D is important for calcium absorption in the human body and for

the structuring of the skeleton, and lacking vitamin D in pregnant women results in impaired calcium metabolism in infants. Hence, this study recommends that pregnant women, particularly those with diabetes, be routinely screened and treated for vitamin D deficiency to optimize neonatal outcomes (17). The results also illustrate that there was a significant correlation between neonatal factors especially hypoglycemia and hypocalcemia (18). Hypocalcemia was significantly more frequent at 40.0% among the neonates with hypoglycemia within the first 24 hours as opposed to 18.0% among the neonates who did not have hypoglycaemia (19). In doing so, hypocalcemia and hypoglycemia are related, because both stem from similar metabolic roots, many of which are originating from insulin regulatory disorders found in IDMs. Low blood glucose levels are more likely to precipitate other metabolic complications in the neonate such as hypocalcemia. This implies that whenever a neonate has been diagnosed with hypoglycemia, other related conditions such as hypocalcemia should also be sought to enhance the management. Another implication derived from the mode of delivery became related to the prevalence of hypocalcemia (20). The studies also explained that it is not clear how this association occurred but maybe through stress response in neonates that results from cesarean section delivery and affects calcium metabolism. More studies are required to examine whether there are commercially significant differences between neonates born by Caesarean section and those born by vaginal delivery on calcium metabolism.

Conclusion

This study highlights the significant prevalence of hypocalcemia in infants of diabetic mothers (IDMs), with 28.2% of the cohort affected. Maternal glycemic control and vitamin D deficiency were identified as key maternal risk factors, with poor glycemic control (HbA1c > 7%) being strongly associated with higher rates of hypocalcemia. This study concludes that hypocalcemia is prevalent among infants of diabetic mothers (IDMs), with poor maternal glycemic control and vitamin D deficiency being significant risk factors. Early detection through routine screening, particularly in those with neonatal hypoglycemia, is essential as many cases are asymptomatic. Timely calcium supplementation effectively resolves the condition, emphasizing the importance of optimizing maternal care and standardized neonatal monitoring to improve outcomes in this high-risk population.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.
Ethics approval and consent to participate.
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Conflict of interest

The authors declared an absence of conflict of interest.

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References

1. Vuralli D. Clinical approach to hypocalcemia in newborn period and infancy: who should be treated? International journal of paediatrics. 2019;2019(1):4318075.
2. Rafiq W, Hussain SQ, Jan M, Najar BA. Clinical and metabolic profile of neonates of diabetic mothers. Int J Contemp Pediatr. 2015;2(2):114-8.
3. Fazel-Sarjoui Z, Namin AK, Kamali M, Namin NK, Tajik A. Complications in neonates of mothers with gestational diabetes mellitus receiving insulin therapy versus dietary regimen. International Journal of Reproductive BioMedicine. 2016;14(4):275.
4. 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 journal of paediatrics. 2010;36:1-6.
5. Mitanchez D, Yzydorczyk C, Simeoni U. What neonatal complications should the paediatrician be aware of in case of maternal gestational diabetes? World journal of diabetes. 2015;6(5):734.
6. Abdul TC, Saldanha PR, Sahana K. High maternal HbA1c is associated with neonatal hypocalcemia. Journal of Evolution of Medical and Dental Sciences. 2014;3(55):12531-7.
7. Merchant R, Dalvi R, Vidwans A. Infant of the diabetic mother. 1990.
8. Mahmood CB, Kayes MI. Problems and immediate outcome of infants of diabetic mothers. Journal of Bangladesh College of Physicians & Surgeons. 2008;26(2):67.
9. Awan NN, Abbas S, Naz M, Jameel M, Iftikhar S. Frequency of Hypocalcemia in Infants of Diabetic Mothers within 24 Hours of Life. Pakistan Journal of Medical & Health Sciences. 2023;17(02):586-.
10. Khalesi N, Namiranian P, Samavati S, Farahani Z. The frequency of early and late hypocalcemia among hospitalized newborns in an iranian hospital. Shiraz E-Medical Journal. 2015;16(6).
11. Rosenn B, Miodovnik M, Tsang R. Common clinical manifestations of maternal diabetes in newborn infants: implications for the practicing pediatrician. Pediatric annals. 1996;25(4):215-22.
12. Tsang RC, Kleinman LI, Sutherland JM, Light IJ. Hypocalcemia in infants of diabetic mothers: studies in calcium, phosphorus, and magnesium metabolism and parathormone responsiveness. The Journal of pediatrics. 1972;80(3):384-95.
13. 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. Pediatrics & Neonatology. 2016;57(6):496-500.
14. 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. Jama. 2014;312(12):1218-26.
15. Afshari F, Abbasalizade F, Faraji M. Comparative evaluation of two treatment regimens, diet versus insulin, in gestational diabetes mellitus. European Journal of Experimental Biology. 2013;3(4):71-6.
16. Toor KM, Wahid S, Azeem K. Frequency of Metabolic Complications in Infants Born to Diabetic Mothers at KRL Hospital, Islamabad. Journal of Islamabad Medical & Dental College. 2015;4(1):23-6.
17. Kumar S, Bhatla N, Sharma KA, Agarwal R, Verma A, Perumal V, et al. SCOPE: Surveillance of COVID-19 in pregnancy-results of a multicentric ambispective case-control study on clinical presentation and maternal outcomes in India between April to November 2020. PLoS One. 2023;18(3):e0272381.
18. Khan M, Malik KA, Bux K. PROFILE OF COMPLICATIONS IN INFANTS BORN TO DIABETIC MOTHERS. Medical Channel. 2016;22(2).
19. Ashraf S, Mushtaq S. Metabolic Complications and Outcome of Infants Born to Diabetic Mothers. Journal of Rawalpindi Medical College. 2018;22(1).
20. Iqbal W, Shamaoon M, Masood M, Butt MA. The frequency of metabolic complications in infant of a diabetic mother. Annals of Punjab Medical College. 2018;12(1):16-9.

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