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Prevalence of Hypocalcemia in Infants of Mothers with Gestational Diabetes

Nida Sarwar, Khurram Fayyaz, Imrana Ata, Sehar Aslam, Hajra Begum, Khubaib Ahmed

ABSTRACT

Objective: To evaluate the prevalence of newborn hypocalcemia among infants of mothers with gestational diabetes.

Study Design & Setting: This cross-sectional study was conducted at PNS Shifa Hospital, Karachi, from November 2023 to March 2024

Methodology: Each mother's fasting blood sugar level was evaluated by drawing 5 ml of blood. At 24 hours after delivery, sterile blood samples (2 cc) were taken to determine the neonate's calcium level; a serum calcium level below 7 mg/dl was regarded as hypocalcemia. All information was gathered using a research template that was created in-house. Serum calcium was measured using the Arsenazo III method, and serum albumin was assessed using the bromocresol green (BCG) method.

Results: The mean ± S.D. of the maternal age of the study participants was 26.83 ± 3.87 years. The mean ± S.D. of the gestational age of the study participants was 37.35 ± 0.86 weeks. The mean ± S.D. of fasting glucose levels of the study participants was 104.5 ± 15.1 mg/dl. A total of 27.5% of infants born to mothers with gestational diabetes had hypocalcemia. Infants' median Apgar scores at 1 and 5 minutes were 6 and 9, respectively. The prevalence of hypocalcemia in newborns was highest among mothers aged 21–30, though this difference was not statistically significant (p = 0.139).

Conclusion: The results showed that 27.5% of infants born to mothers with gestational diabetes had hypocalcemia. Maternal age did not have a statistically significant association with hypocalcemia in newborns.

Keywords: Hypocalcemia, Infants, Gestational Diabetes, Maternal Hyperglycemia

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INTRODUCTION:

Pregnancy-related mortality and morbidity have long been associated with diabetes in mothers.[1] The impact of maternal diabetes extends beyond pregnancy itself, influencing both prenatal and postnatal health outcomes for the infant. A significant concern in this context is the exposure of the developing fetus to maternal hyperglycemia, which is a critical factor contributing to a range of prenatal, natal, and postnatal complications. Insufficient metabolic control in the mother exacerbates these issues, leading to various disorders that can affect the child's development and health outcomes.[1,2,3]

The spectrum of complications arising from maternal diabetes is broad, and among these, metabolic and hematological complications are particularly concerning. Infants born to mothers with diabetes are at an increased risk of developing conditions such as hyperbilirubinemia and polycythemia.[4] These conditions can have serious consequences for the newborn, necessitating careful monitoring and management from birth. Moreover, infants with a familial history of hypomagnesemia are particularly vulnerable to developing hypocalcemia, a condition that is closely linked to birth asphyxia.[5]

Hypocalcemia, characterized by abnormally low levels of calcium in the blood, is a frequent issue in newborns, especially those born to diabetic mothers. Normal blood calcium levels naturally decline in the first 48 hours after birth in healthy term infants. Typically, this drop in calcium levels reaches its lowest point, or trough, between 7.5 to 8.5 mg/dl within the first two days of life.[5] However, in certain

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cases, this decline can lead to significant health concerns. The most severe form of hypocalcemia can cause symptoms such as seizures, which are particularly common in premature newborns, babies born to mothers with diabetes, and infants who have experienced perinatal asphyxia.[6]

The incidence of hypocalcemia in infants born to diabetic mothers varies widely, with studies reporting rates ranging from 4% to as high as 50%, and an average incidence of around 22.7%. This wide variation highlights the need for further research to understand the factors contributing to this condition better. Hypocalcemia in these infants can be attributed to several factors, including premature delivery, birth asphyxia, low maternal calcium intake, high maternal calcium excretion rates, low neonatal parathyroid hormone (PTH) production, inadequate calcium intake, and poor calcium absorption. Among these, hypomagnesemia in both the mother and the child, resulting from increased maternal urinary excretion of magnesium during pregnancy, has been identified as a prevalent cause.[7,8]

One of the mechanisms by which maternal diabetes influences neonatal calcium levels involves the transfer of maternal calcium to the fetus through the placenta. In cases where the mother has hyperparathyroidism, this increased maternal calcium can inhibit fetal PTH synthesis, leading to a decreased PTH response after birth, which in turn contributes to hypocalcemia.[7] Furthermore, hypomagnesemia in the newborn can induce functional hypoparathyroidism, further exacerbating the hypocalcemia.[8]

Hypocalcemia is a common metabolic disorder in infants and young children, and its management remains a topic of ongoing debate in the medical community. While there is general agreement on the need to treat symptomatic hypocalcemia promptly, the appropriate calcium levels at which to initiate treatment and the best approach to managing asymptomatic cases are still under discussion.[8] The symptoms of neonatal hypocalcemia and hypomagnesemia often resemble those of hypoglycemia and can include jitteriness, tachypnea, sweating, convulsions, and irritability.[9]

The increasing recognition of the long-term effects of maternal diabetes on offspring has led to a growing awareness among obstetricians and neonatologists of the need to understand these complications better. Gestational diabetes mellitus (GDM) has been linked not only to impaired glucose tolerance during pregnancy but also to a higher incidence of perinatal complications, including neonatal hypocalcemia.[10] Despite the acknowledgment of these associations, there is a critical gap in the medical literature concerning the precise prevalence and mechanisms underlying neonatal hypocalcemia in the context of maternal diabetes, particularly on a regional basis.

This study is motivated by the need to address this gap by providing a comprehensive analysis of the prevalence, causes, and potential implications of hypocalcemia in newborns of diabetic mothers. Understanding the scope and nature of this issue is essential for developing targeted interventions and clinical guidelines that can improve neonatal outcomes and reduce the burden of hypocalcemia in this vulnerable population. Consequently, this research aims not only to quantify the prevalence of neonatal hypocalcemia in the context of maternal hyperglycemia but also to explore the contributing factors and possible preventive measures that could mitigate this significant health challenge. By doing so, this study seeks to contribute valuable insights that could enhance clinical practices and ultimately improve the health and well-being of infants born to mothers with diabetes.[8]

METHODOLOGY:

After receiving ethical approval from the institutional review board, this cross-sectional study was conducted at PNS Shifa Hospital, Karachi (ERC/2023/PED/57) over a five-month period from November 2023 to March 2024. The primary aim of the study was to evaluate the prevalence of neonatal hypocalcemia in infants born to mothers with gestational diabetes. Given the importance of this research and the need for robust data, the sample size calculation was a crucial step in the study design. The sample size was determined using the OpenEpi calculator, which is widely used in epidemiological studies for accurate sample size estimations.

The calculation was based on an anticipated prevalence rate of neonatal hypocalcemia in infants born to mothers with gestational diabetes, derived from previous studies. With a confidence level of 95%, a margin of error of 5%, and the estimated prevalence rate, the minimum required sample size was determined to be 70 subjects. However, to enhance the reliability of the findings and considering the available resources and time frame, the sample size was increased to 80 subjects. This slight increase was deemed sufficient to ensure that the study would have adequate statistical power to detect significant differences or associations.

The study employed a non-probability consecutive sampling technique, selecting all eligible patients who met the inclusion criteria during the study period. The inclusion criteria were specifically designed to focus on mothers aged 18 years and older diagnosed with gestational diabetes who had undergone any mode of delivery. Patients under the age of 18 or those with additional complications, such as autoimmune diseases, hypertension, or multiple pregnancies, were excluded from the study. This careful selection process ensured that the sample was as homogeneous as possible, minimizing confounding variables and increasing the study's internal validity.

Upon delivery, detailed records were made of each infant's Apgar scores at 1 minute, 5 minutes, and, if necessary, at later intervals. These scores provided a quick assessment of the newborn's health and helped identify infants who required further medical attention. Simultaneously, each mother's

diabetes status and treatment compliance were documented to establish any correlations between maternal diabetes control and neonatal outcomes. Information regarding the mothers' HbA1c levels and fasting blood glucose was also recorded as part of the evaluation of maternal hyperglycemia.

Immediately after the umbilical cord was clamped and cut, 2 mL of blood was collected from the newborn in a sterile container for calcium and albumin analysis. This step was crucial in diagnosing hypocalcemia and understanding its prevalence in the study population. All newborns underwent a thorough examination for major congenital defects at birth, and those with significant anomalies were excluded from further analysis to avoid skewing the results.

The gestational age of each infant was carefully estimated using the mother's reported due date, with further verification using the New Ballard Scoring System within a two-week margin of error. Birth weights were measured using an electronic scale and recorded to the nearest 10 grams. These weights were then plotted on percentile charts according to gestational age to assess growth standards.

Infants requiring admission to the neonatal intensive care unit (NICU) based on specific criteria, such as a birth weight under 2000 grams, an Apgar score of less than 7 at 5 minutes, or signs of respiratory distress, were immediately transferred to the NICU. These infants were started on intravenous fluids with calcium supplementation at the standard rate of 4 ml/kg/day. Healthy infants, on the other hand, were placed with their mothers and breastfed on demand, supporting natural feeding practices and promoting maternal-infant bonding.

During the first two to four days of life, each newborn's length was measured using an infant meter and compared to percentile charts for gestational age. At 48 hours of life, another 2 mL blood sample was collected from each newborn in a sterile container for repeat calcium and albumin testing. This allowed for the monitoring of changes in serum calcium levels and the early detection of hypocalcemia. Serum calcium was measured using the Arsenazo III method, known for its precision, and serum albumin was assessed using the bromocresol green (BCG) method, which is a standard procedure in clinical chemistry.

All data collected were meticulously entered into a custom-designed research template to ensure consistency and accuracy. Statistical analysis was performed using SPSS version 26, enabling a comprehensive examination of the data to identify significant trends and associations related to neonatal hypocalcemia in infants born to mothers with gestational diabetes. This methodological rigor ensured that the study's findings would be both reliable and valuable for guiding future research and clinical practice.

RESULTS

A total of 80 pregnant women who fulfilled the inclusion criteria were included in the present study. Table 1 shows the clinical and demographic parameters of the study participants. Mean±S. D of the maternal age of the study participants was 26.83±3.87 years. Mean±S. D of the gestational age of the study participants was 37.35±0.86 weeks. Mean±S. D of fasting glucose level of the study participants was 104.5±15.1 mg/dl. 73.7% of the participants in the present study had Primiparous parity and majority of the participant's mode of delivery was normal vaginal delivery (66.3%). 27.5% infants had hypocalcemia to all the diabetic mothers enrolled in the study (Figure 1). Infants' median Apgar scores at 1 and 5 minutes were 6 and 9, respectively (Figure 2). The prevalence of hypocalcemia in newborns was highest among mothers aged 21–30, although this difference was not statistically significant (p=01.39). The prevalence of hypocalcemia in newborns was highest among gestational age 37-39, although this difference was not statistically significant (p=0.991) (Table 2).

DISCUSSION:

Gestational diabetes mellitus (GDM) is a form of glucose intolerance that occurs during pregnancy, posing significant risks to both mother and infant. The impact of GDM on neonatal outcomes has been a topic of growing concern, particularly as the global prevalence of diabetes continues to rise. This study aimed to evaluate the prevalence of newborn hypocalcemia among 80 diabetic mothers, with

Table 1: Cinical and demographic parameters of the study participants

Parameters		Statistics
Mother age		26.83±3.87
Gestational Age		37.35±0.86
Fasting glucose		104.5±15.1
Parity	Primiparous	59 (73.7%)
	Multiparous	21 (26.3%)
Mode of delivery	Normal	53 (66.3%)
	C-section	27 (33.7%)
Infant gender	Male	35 (43.7%)
	Female	45 (56.3%)

Figure 1: Frequency of Hypcalecemia in infants born to diabetic mother

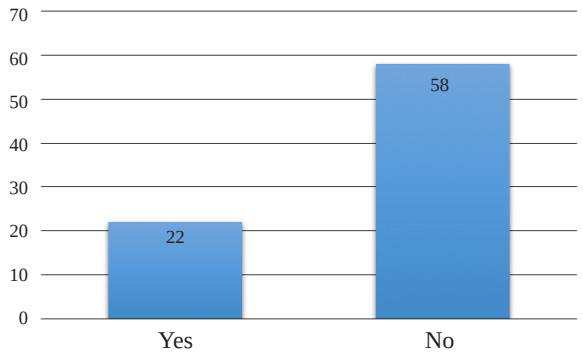

Figure 2: Apgar score of the newborns

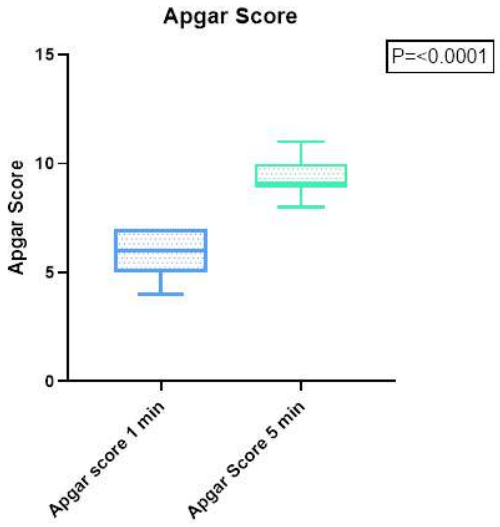

Table 2: Neonatal hypocalcemia as per maternal age and

Parameters		Hypocalcemia		P Value
		Yes	No	
Maternal age	<20	2	1	1.39
	21-30	13	51	
	<30	7	6	
Gestational Age	<36 weeks	4	9	0.991
	37-39 weeks	14	43	
	>40 weeks	4	6	

the goal of shedding light on the potential risks associated with maternal diabetes and informing clinical practices aimed at mitigating these risks.

The mothers in this study had an average gestational age of 37.35±0.86 weeks and were on average 26.83±3.87 years old. These demographic characteristics are consistent with those reported in similar studies, though there are some variations. For instance, previous studies have reported an average gestational age of 37.58±1.35 weeks, with 81.25% of births occurring between 37 and 39 weeks.[11] The slight difference in gestational age between studies could be attributed to differences in study populations, healthcare practices, and the criteria used to diagnose and manage GDM.

The age of the mothers in this study was slightly younger on average compared to some other studies. For example, one study found the average age of women with diabetes in the untreated IGT group to be 32.5±5.0 years, which is higher than the average age in the present study.[12] This discrepancy might be due to differences in the populations being studied or variations in the age distribution of diabetic pregnancies in different regions. Additionally, other studies have found that the majority of diabetic mothers were between 31 and 35 years of age.[13] These variations in maternal age could potentially influence the outcomes of pregnancies complicated by diabetes, as age is a known risk factor for both GDM and adverse neonatal outcomes.

The mode of delivery and neonatal outcomes also showed variation across studies. In this study, 26.3% of mothers had multiple pregnancies, 33.7% of births involved cesarean sections, and 56.3% of the neonates were female. These findings are somewhat consistent with other research, though differences in cesarean section rates and gender distribution are noted. For instance, one study found that 52.5% of infants born to diabetic mothers were male, while another study reported a gender distribution of 64% male and 36% female.[11,14] These differences could be attributed to variations in population demographics, the criteria used for diagnosing GDM, and the management practices during pregnancy, which differ across different healthcare settings.[14]

The variation in cesarean section rates is particularly interesting, as the decision for cesarean delivery in diabetic pregnancies can be influenced by several factors, including fetal macrosomia, poor glycemic control, and the presence of obstetric complications. The higher rate of cesarean sections in some studies may reflect more aggressive management strategies aimed at preventing complications associated with difficult vaginal deliveries in diabetic women. However, cesarean sections themselves carry risks for both mother and infant, including the potential for respiratory distress in the newborn, which underscores the need for careful decision-making in these cases.[14,15]

In terms of hypocalcemia, 27.5% of the infants in this study were affected, a prevalence that aligns with some previous studies.[15] However, other research reported lower incidences, while still others have shown higher frequencies of neonatal hypocalcemia, especially among infants of mothers with pregestational diabetes.[16,17] The relatively high prevalence observed in this study highlights the potential vulnerability of infants born to diabetic mothers to calcium metabolism disorders. This finding is particularly concerning given the critical role of calcium in various physiological processes, including neuromuscular function and bone development.[17]

The inconsistencies in the reported prevalence of neonatal hypocalcemia across studies could be due to several factors, including differences in sample sizes, study designs, or selection criteria. Additionally, variations in the management of GDM, such as differences in glucose control strategies and the timing of delivery, might also contribute to these discrepancies. For instance, stricter glycemic control during pregnancy might reduce the risk of neonatal hypocalcemia, whereas poorly controlled diabetes could exacerbate the condition. Some studies suggest that maternal and fetal hypomagnesemia contribute to transient neonatal hypocalcemia, particularly in infants born to women with pregestational, insulin-dependent diabetes.[16,17] This link

between hypomagnesemia and hypocalcemia is supported by the fact that magnesium plays a crucial role in the regulation of parathyroid hormone (PTH) secretion, which in turn regulates calcium homeostasis.

The severity of maternal diabetes has been linked to the degree of neonatal hypocalcemia, with a noted inverse relationship between neonatal calcium levels and maternal HbA1c concentrations.[18] This suggests that poor glycemic control during pregnancy may exacerbate the risk of hypocalcemia in newborns. Elevated HbA1c levels in mothers indicate chronic hyperglycemia, which could lead to various metabolic disturbances in the fetus, including impaired calcium metabolism.[19] Furthermore, maternal hyperglycemia can lead to fetal hyperinsulinemia, which has been associated with decreased calcium levels in the neonate.[20]

This study's findings emphasize the need for heightened clinical awareness and proactive management strategies to address the risk of hypocalcemia in infants born to mothers with GDM. The identification of risk factors such as maternal hypomagnesemia and poor glycemic control could allow for targeted interventions, such as magnesium supplementation or more rigorous monitoring of blood glucose levels during pregnancy. Additionally, early identification and treatment of hypocalcemia in newborns could prevent complications such as seizures, cardiac arrhythmias, and long-term developmental issues.

The strengths of this study include its focused examination of the prevalence of newborn hypocalcemia in diabetic mothers, providing crucial insights into a relatively underexplored area of neonatal health. The comparison with other studies and the use of a well-defined diabetic mother cohort add value to the findings. However, limitations exist, such as the relatively small sample size and the study's cross-sectional design, which may limit the generalizability of the results. The cross-sectional nature of the study precludes any conclusions about the long-term outcomes of hypocalcemia in these infants. Additionally, the study did not account for the potential influence of other factors, such as maternal nutritional status or genetic predispositions, which could also affect calcium levels in the newborn. These limitations underscore the need for further research in this area.

The scope for future research is vast. Future studies could expand on this work by including larger and more diverse populations to enhance the generalizability of the findings. Longitudinal studies could provide more definitive information on the progression of hypocalcemia in newborns of diabetic mothers and its long-term effects. For example, tracking these infants over time could help determine whether early hypocalcemia leads to developmental delays or other health issues later in life. Additionally, exploring the impact of various factors, such as different types and severities of maternal diabetes, dietary influences, and genetic predispositions, could provide deeper insights into the mechanisms behind neonatal hypocalcemia.

Further research could also explore the effectiveness of different prevention and treatment strategies. For instance, studies could examine whether early calcium supplementation or tighter glycemic control during pregnancy can reduce the incidence of neonatal hypocalcemia. Additionally, the role of magnesium supplementation in preventing hypocalcemia in infants of diabetic mothers warrants further investigation, given the potential link between maternal hypomagnesemia and neonatal hypocalcemia.

In conclusion, while this study provides important insights into the prevalence of hypocalcemia among newborns of diabetic mothers, it also highlights the complexity of this condition and the need for further research to fully understand its causes and consequences. Addressing this knowledge gap is crucial for developing effective interventions that can improve the health and well-being of infants born to mothers with diabetes. The findings underscore the importance of comprehensive prenatal care that includes close monitoring and management of maternal diabetes to prevent adverse neonatal outcomes, including hypocalcemia.

CONCLUSION:

In conclusion, this study indicates that a significant proportion, 27.5%, of infants born to diabetic mothers are affected by hypocalcemia, highlighting a clear association with maternal diabetes. While the study offers valuable insights, it underscores the necessity for broader research to fully understand and address this health issue. Future investigations should aim for larger sample sizes and a wider range of demographic settings to validate these findings and explore comprehensive preventive and treatment strategies for hypocalcemia in newborns of diabetic mothers.

Authors Contribution:
Nida Sarwar: Conception of Study, Data Collection, Drafting
Khurram Fayyaz: Design of Study Supervision of work
Imrana Ata: Data Collection, Drafting, Analysis of results
Sehar Aslam: Data Collection. Drafting
Hajra Begum: Data Collection, Drafting
Khubaib Ahmed: Data Collection, Drafting

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