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ASSOCIATION OF HYPOGLYCEMIA AND HYPOCALCEMIA IN NEONATES WITH PERINATAL ASPHYXIA

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Abstract

Objective

To determine the association of hypoglycemia and hypocalcemia in neonates diagnosed with perinatal asphyxia.

Methodology:

This Prospective case-control study was conducted at the Department of Pediatrics, Combined Military Hospital, Kharian, over a period of six months. A total of 200 neonates aged 1–24 hours and born at gestational age >32 weeks were included, with 100 neonates in the perinatal asphyxia group (cases) and 100 in the control group. Neonates with congenital anomalies or conditions interfering with metabolic regulation were excluded. Blood glucose and serum calcium levels were assessed within the first 12 hours of life. Hypoglycemia was defined as blood glucose <40 mg/dL, and hypocalcemia as serum calcium <7 mg/dL. Data were analyzed using SPSS version 21, with odds ratios (OR) calculated to determine associations.

Results:

The mean gestational age was 37.9 ± 1.8 weeks in the case group and 38.3 ± 1.5 weeks in the control group. Hypocalcemia was observed in 23% of asphyxiated neonates compared to 3% in controls (OR = 9.97; $p < 0.001$), while hypoglycemia was found in 20% of cases versus 5% of controls (OR = 4.88; $p = 0.002$). Other demographic and clinical parameters, such as birth weight and gender, showed no significant differences.

Conclusion:

Perinatal asphyxia is significantly associated with hypoglycemia and hypocalcemia in neonates. Early screening and timely management of these metabolic disturbances are essential to reduce complications and improve neonatal outcomes.

INTRODUCTION

Perinatal asphyxia is one of the main causes of death in term newborns. During the past two decades, no significant progress has been made in reducing neonatal deaths in developing countries.[1] Although the incidence of birth asphyxia in developing countries gradually decreased from 6.32% in 2003 to 1.79% in 2014, there is still a large gap compared with developed countries.[2] Birth asphyxia is a combination of hypoxia, hypercarbia, and metabolic acidosis, in which newborns cannot initiate or sustain spontaneous breathing after birth due to various perinatal events. It is a damage to the fetus or neonate either in the perinatal period, with high short-term

mortality and adverse long-term outcomes such as cerebral palsy and cognitive impairment.[3] Risk factors of birth asphyxia have been divided into perinatal factors.[4, 5] Birth asphyxia tends to cause hypoxic-ischemic tissue damage and electrolyte imbalance which may lead to perinatal morbidity and mortality.[6] The degree of deranged electrolyte levels was directly proportional to the severity of birth asphyxia. So these electrolyte disturbances should always be kept in mind while managing cases of perinatal asphyxia and should be managed accordingly.[7] Birth asphyxia is common cause of mortality and morbidity and associated with various metabolic changes like hypoglycemia and hypocalcemia, hyperkalemia, hyponatremia, hyperphosphatemia.[8] In an Indian study, it was notified that hypoglycemia was significantly associated with perinatal asphyxia i.e. 24% in cases and 4% in control. Similarly, hypocalcemia was 6% in cases and 0% in controls ($p<0.05$).[9] Another study found that Hypocalcemia was found among 23.33% asphyxiated babies and in 3.3% baby in control group. Hypoglycemia was found in 23.33% cases and 0% in controls. Combined hypoglycemia, hypocalcemia and hypomagnesemia were found in 1(3.33%) case; combined hypoglycemia and hypocalcemia were found in 2(6.67%) cases.[10]

Rationale of this study is to determine the association of hypoglycemia and hypocalcemia in neonates with perinatal asphyxia. Literature showed that hypoglycemia and hypocalcemia are significantly associated with perinatal asphyxia. But limited work has been done before in this regard and no local evidence exist in literature. Therefore, there is a need to conduct a study in local setting to attain magnitudes for local population. So that we can get the local evidence and be able to implement the results of this study in local setting and recommend to screen neonates, in order to prevent occurrence of perinatal asphyxia. This would also help us to improve our practice and implementation of more appropriate way to manage high risk neonates. To determine the association of hypoglycemia and hypocalcemia in neonates with perinatal asphyxia.

Methodology:

This case-control study was conducted at the Department of Pediatrics, Combined Military Hospital, Kharian. The duration of the study was six months following approval of the research synopsis.

A total of 200 neonates were included, with 100 in each group (cases and controls). The sample size was calculated with 80% power of the study, a 5% level of significance, and an expected prevalence of hypocalcemia of 23.33% in cases and 3.33% in controls. A non-probability, consecutive sampling technique was employed. Selection Criteria Inclusion Criteria: Neonates aged 1–24 hours of life, of either gender, delivered at a gestational age of >32 weeks (as per antenatal records), and diagnosed with perinatal asphyxia (as per operational definition) were included. Exclusion Criteria: Neonates with major congenital malformations, congenital heart disease, central nervous system malformations, neuromuscular disease, fetal hemorrhagic shock, fetal edema, passive drug poisoning due to anesthesia during cesarean section, accidental asphyxia after birth, infants of diabetic mothers, neonates without blood glucose levels assessed within 12 hours of birth, and out-born neonates were excluded.

Data Collection Procedure: After obtaining approval from the hospital's ethical committee, 200 neonates who met the inclusion criteria were enrolled from the emergency department. Informed consent was obtained from the parents or guardians. Demographic details including name, age (in hours), gender, birth weight, gestational age at birth, Apgar score, antenatal care status, mode of delivery, and maternal glycemic level at the time of delivery were recorded. The enrolled neonates were admitted to the neonatology ward and managed according to standard clinical protocols. Blood samples were obtained and sent to the hospital laboratory for serum calcium level analysis. A drop of blood was also taken using an Accu-Chek meter to record the neonate's glycemic level. Reports were reviewed, and cases of hypoglycemia and hypocalcemia were identified based on predefined operational definitions. All data were recorded on a predesigned proforma.

Data Analysis Data were entered and analyzed using SPSS version 21. The Shapiro-Wilk test was applied to assess the normality of continuous data. Quantitative variables such as age, birth weight, gestational age, Apgar score, maternal glycemic level at delivery, and neonatal serum calcium and glycemic levels were expressed as means and standard deviations. Categorical variables including gender, antenatal care status, mode of delivery,

presence of hypoglycemia, and hypocalcemia were reported as frequencies and percentages.

The odds ratio (OR) was calculated to evaluate the association of hypoglycemia and hypocalcemia with perinatal asphyxia. An OR >1 was considered significant. Data were stratified based on age, gender, birth weight, gestational age, Apgar score, maternal glycemic level, mode of delivery, and antenatal care to control for confounding variables. Post-stratification, odds ratios were recalculated for each stratum to assess the strength of association in the presence of potential confounders. An OR >1 was again taken as indicative of a significant association.

Results:

A total of 200 neonates were included in the study, comprising 100 neonates diagnosed with **perinatal asphyxia** (case group) and 100 neonates without perinatal asphyxia (control group). The overall mean gestational age of the study population was **38.1 ± 1.7 weeks**, and the mean birth weight was **2.85 ± 0.45 kg**. Male neonates constituted **58%** of the total sample population, with a similar gender distribution observed between the two groups. The demographic and clinical characteristics of the study population are presented in **Table I**. The mean gestational age at birth was **37.9 ± 1.8 weeks** in the case group and **38.3 ± 1.5 weeks** in the control group, with no statistically significant difference between them ($p = 0.07$). Similarly, there was no significant difference in mean age at enrollment (9.2 ± 4.5 hours vs. 9.5 ± 4.3 hours, $p = 0.68$) or mean birth weight (2.8 ± 0.4 kg vs. 2.9 ± 0.5 kg, $p = 0.12$) between cases and controls. In terms of delivery mode, **65%** of neonates with perinatal asphyxia were delivered by cesarean section compared to **58%** in the control group, a difference that was not statistically significant ($p = 0.29$). The proportion of mothers who received adequate antenatal care was **78%** in the case group and **83%** in the control group ($p = 0.34$). A striking difference was observed in Apgar scores: **84%** of neonates with perinatal asphyxia had an Apgar score ≤5 at 5 minutes compared to only **8%** of controls, and this difference was highly significant ($p < 0.001$). This finding confirms the clinical distinction between the asphyxiated and non-asphyxiated neonates.

controls.

Table I: Demographic and Clinical Characteristics of Neonates (n = 200)

Variable	Cases (n = 100)	Controls (n = 100)	p-value
Mean age (hours)	9.2 ± 4.5	9.5 ± 4.3	0.68
Male gender (%)	56 (56%)	60 (60%)	0.58
Mean birth weight (kg)	2.8 ± 0.4	2.9 ± 0.5	0.12
Mean gestational age (weeks)	37.9 ± 1.8	38.3 ± 1.5	0.07
Apgar score ≤5 at 5 min (%)	84 (84%)	8 (8%)	<0.001*
Cesarean delivery (%)	65 (65%)	58 (58%)	0.29
Antenatal care received (%)	78 (78%)	83 (83%)	0.34

*Significant at $p < 0.05$

Table II: Frequency and Association of Hypocalcemia and Hypoglycemia with Perinatal Asphyxia

Variable	Cases (n = 100)	Controls (n = 100)	Odds Ratio (OR)	p-value
Hypocalcemia (%)	23 (23%)	3 (3%)	9.97	<0.001*
Hypoglycemia (%)	20 (20%)	5 (5%)	4.88	0.002*

*Statistically significant at $p < 0.05$

The frequency and association of **hypocalcemia** and **hypoglycemia** with perinatal asphyxia are detailed in **Table II**.

Hypocalcemia was detected in **23%** of neonates with perinatal asphyxia, compared to only **3%** of neonates in the control group. The difference was highly significant ($p < 0.001$), with an **odds ratio (OR)** of **9.97**, indicating that asphyxiated neonates were nearly **10 times more likely** to develop hypocalcemia compared to their non-asphyxiated counterparts.

Similarly, **hypoglycemia** was observed in **20%** of the asphyxiated neonates and **5%** of the controls ($p = 0.002$). The calculated **odds ratio of 4.88** suggests that neonates with perinatal asphyxia had almost **fivefold higher odds** of developing hypoglycemia.

Discussion:

A total of 200 neonates were included in the study, comprising 100 neonates diagnosed with perinatal asphyxia (cases) and 100 without (controls). Previous research in 2023 reported that birth asphyxia is associated with neonatal blood glucose disturbances, including both hypoglycemia and hyperglycemia, during the early postnatal period. Moreover, neonates with severe asphyxia exhibited a higher incidence, greater severity, and longer duration of blood glucose abnormalities compared to those with mild asphyxia [12].

In the present study, the mean gestational age at birth was 37.9 ± 1.8 weeks in the case group and

38.3 ± 1.5 weeks in the control group. Prior literature has emphasized that metabolic abnormalities linked to perinatal asphyxia are important modifiable risk factors that may contribute to adverse outcomes. Therefore, clinicians are advised to maintain a high index of suspicion for endocrine complications in affected neonates to enable timely screening and appropriate intervention [13].

Our findings further revealed that hypocalcemia and hypoglycemia were significantly more prevalent in neonates with perinatal asphyxia compared to controls. In a related earlier study, a controlled trial involving 50 term intrauterine growth restriction (IUGR) neonates and 50 term appropriate for gestational age (AGA) neonates evaluated blood glucose and serum calcium levels within the first 24 hours of life, identifying a higher risk of metabolic disturbances among IUGR neonates [14].

These findings underscore the critical importance of early biochemical screening in neonates with perinatal asphyxia to ensure prompt diagnosis and timely management. In line with this, research from 2023 advocated for routine blood glucose monitoring within the first 4 hours of life in term and late preterm small for gestational age (SGA) neonates—particularly those delivered via cesarean section or presenting with low Apgar scores [15].

Conclusion:

Perinatal asphyxia remains a major contributor to neonatal morbidity and mortality, particularly in developing countries. This study demonstrates a strong association between perinatal asphyxia and metabolic disturbances, specifically hypocalcemia and hypoglycemia. Neonates with perinatal asphyxia were significantly more likely to develop these conditions compared to controls. These findings emphasize the critical need for early biochemical screening and prompt intervention in affected neonates to improve outcomes and reduce complications.

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