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ORIGINAL RESEARCH

To estimate the serum calcium level in infants hospitalised with acute bronchiolitis

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Abstract

Background: Acute bronchiolitis is a prevalent viral respiratory illness and can have mild to severe clinical manifestations that necessitate critical care therapy. One micronutrient that is important for both intracellular and extracellular processes is calcium. Respiratory infections have been linked to vitamin D insufficiency, and blood calcium and Alkaline Phosphatase (ALP) levels are controlled by vitamin D metabolism. Therefore, calcium levels could be the real biological cause that determines how severe respiratory infections are.

Aim and Objectives: To estimate the serum calcium level in infants hospitalised with acute bronchiolitis.

Material and Methods: This cross-sectional study was conducted on 200 infants in the paediatric department. Infants younger than one year old who were referred to the paediatric emergency department for acute bronchiolitis were included as cases. The severity of bronchiolitis was assessed using the AAP guidelines for the Diagnosis and Management of Bronchiolitis. Patients who met the diagnostic criteria for acute bronchiolitis were included in the study. Controls were defined as patients in the same age group with acute febrile illness (fever >38.5°C, duration >24 hours) but without respiratory symptoms. Levels of total calcium, phosphorus, and ALP were estimated using a fully automated Hitachi analyser. Age-appropriate reference ranges for calcium (8.8-10.8mg/dL), phosphorus (3.8-6.5mg/dL), and ALP(145-420U/L)were used for comparison.

Results: The mean serum calcium level was significantly lower in cases (8.2 ± 0.6 mg/dL) compared to controls (9.5 ± 0.5 mg/dL), with a p-value < 0.05, indicating a statistically significant difference. Phosphorus levels were also lower in cases (4.2 ± 0.7 mg/dL) compared to controls (5.5 ± 0.6 mg/dL), although these values were within the reference range. ALP levels were higher in cases (450 ± 50 U/L) compared to controls (380 ± 40 U/L), possibly indicating bone metabolism changes in response to calcium deficiency. These biochemical differences suggest an association between serum calcium levels and acute bronchiolitis. The correlation coefficient (r) for age was 0.12, with a p-value of 0.21, indicating no significant correlation. However, there was a significant negative correlation between serum calcium levels and respiratory rate ($r = -0.45$, $p < 0.01$), suggesting that lower

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calcium levels are associated with higher respiratory rates and, thus, more severe respiratory distress. There was also a significant positive correlation between serum calcium levels and oxygen saturation ($r = 0.35$, $p < 0.05$), indicating that higher calcium levels are associated with better oxygen saturation. These correlations underscore the potential role of calcium in the clinical severity of acute bronchiolitis.

Conclusion: In conclusion, this study highlights the importance of monitoring serum calcium levels in infants with acute bronchiolitis. The significant differences in serum calcium levels between cases and controls, along with the correlations with clinical parameters, suggest that hypocalcaemia may play a role in the severity of bronchiolitis. Further research is needed to explore the underlying mechanisms and to evaluate the potential benefits of calcium supplementation in managing acute bronchiolitis in infants.

Keywords: Bronchiolitis, Serum calcium, Respiratory rate.

Introduction

Bronchiolitis is a viral infection that mostly affects the lower respiratory tract in newborns, resulting in a substantial global health impact. Respiratory Syncytial Virus (RSV) is the primary and well-established cause of bronchiolitis, leading to a significant number of hospitalizations in children under the age of five each year.[1] Bronchiolitis is the primary reason for hospitalizations in newborns during their first year of life in affluent nations such as the United States of America (USA). Nevertheless, the availability of data from poorer nations is restricted, most likely as a result of degraded hygiene, inadequate infection control, overcrowding, and poverty.[2-4] RSV bronchiolitis normally develops from late October, reaching its highest levels throughout the winter months and early spring. Several potential risk factors for recurrent bronchiolitis in infancy have been suggested, such as preterm birth, tobacco use, residing in overcrowded homes with inadequate sunshine exposure, and urban living circumstances.[5] Factors such as being inside, being in crowded places, a humid environment, and inhaling chilly mist have been proposed as mechanisms that might affect ciliary function.[6] There is a strong correlation between a lack of vitamin D and the occurrence of severe bronchiolitis in newborns, which often requires admission to the intensive care unit.[7] It has been suggested that evaluating vitamin D levels before to the bronchiolitis season and administering suitable supplements might serve as a preventive intervention against severe bronchiolitis. Additionally, vitamin D levels have been examined in nasopharyngeal secretions and have been shown to be linked to an increased likelihood of children requiring positive pressure breathing.[8] Calcium and phosphate homeostasis is intricate, and three crucial hormones regulate the majority of the extracellular regulation of these minerals. Parathyroid hormone is involved in the regulation of blood calcium levels, either by maintaining them or by restoring them.[9] Calcium plays a vital role in cellular activities, metabolic and signaling pathways, survival, and immunological functions. Decreased levels of calcium in the blood have been linked to increased rates of death and complications, indicating that it is a predictive factor for the severity of viral illnesses.[10] As far as we know, there has been no prior research undertaken on newborns that examines the relationship between calcium and acute bronchiolitis. Hence, the results obtained from this limited prospective study justify the need for additional research on a broader scope and among other vulnerable groups. The hypothesis posits that there may be a correlation between serum calcium levels and acute viral bronchiolitis in paediatric patients. The objective was to examine and contrast the blood calcium levels in babies diagnosed with acute bronchiolitis and those without bronchiolitis (controls). Additionally, the purpose was to establish a correlation between sunshine exposure and calcium levels in both the cases and controls.

Aim and Objectives

To estimate the serum calcium level in infants hospitalised with acute bronchiolitis.

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Materials and Methods

The present cross-sectional study was conducted at the Department of Paediatrics, Nalanda Medical College and Hospital, Patna, Bihar, India, for a period of seven months (September 1st, 2019 – April 1st, 2020) among 200 infants in the paediatric department after obtaining ethical clearance from the Institutional Ethical Clearance Committee. The present study was conducted on both genders and those who met the specified criteria for inclusion and exclusion criteria. All were informed regarding the study and their informed written consent was obtained from parents or legal care givers for inclusion in the study.

Inclusion criteria

- Infants younger than one year old who were referred to the paediatric emergency department for acute bronchiolitis were included as cases. The severity of bronchiolitis was assessed using the AAP guidelines for the diagnosis and management of bronchiolitis.
- Infants who met the diagnostic criteria for acute bronchiolitis were included in the study. Controls were defined as patients in the same age group with acute febrile illness (fever > 38.5°C, duration > 24 hours) but without respiratory symptoms.
- Parents who give written informed consent.
- Available for follow-up.

Exclusion criteria

- Children with chronic disorders that could influence the severity and course of bronchiolitis, such as chronic lung disease, congenital heart disease, suspected inborn errors of metabolism, global developmental delay, hypotonia, suspected central nervous system disorders, or syndromic features, were excluded from the study.
- Parents who do not give written informed consent.
- Those unable to attend follow-up.

Sample size: Total 200 infants were included in this study. 100 were included as cases and 100 as controls, selected through purposive sampling based on the inclusion criteria.

Based on the American Academy of Paediatrics' (AAP) criteria (fever, tachypnea, tachycardia, paroxysmal wheezy cough, irritability, coryza, and wheezing for the first time), 200 infants under the age of one year who were hospitalised with an acute bronchiolitis diagnosis was considered cases.

Methodology

A proforma was filled for all patients upon referral to the emergency department, including demographic data and information on sunlight exposure (less than or more than 30 minutes, swaddled or not). Data regarding past medical history, risk factors for asthma, and family history were also collected to follow the inclusion/exclusion criteria. 5 mL of blood samples were obtained from all study subjects under aseptic precautions, and serum was separated after spinning 1 mL of the sample for one minute at 3000 rpm. Levels of total calcium, phosphorus, and ALP were estimatedusing a fully automated Hitachi analyser. Age-appropriate reference ranges for calcium (8.8-10.8mg/dL), phosphorus (3.8-6.5mg/dL), and ALP (145-420U/L) were used for comparison.

Statistical analysis

The collected data were subjected to statistical analysis using Statistical Package for the Social Sciences (SPSS) software version 21.0. Continuous variables such as age, weight, length, total calcium, phosphorus, and albumin were compared using the Student’s t-test. The continuous non parametric variable, ALP, wascompared using the Kruskal-Wallis test due to

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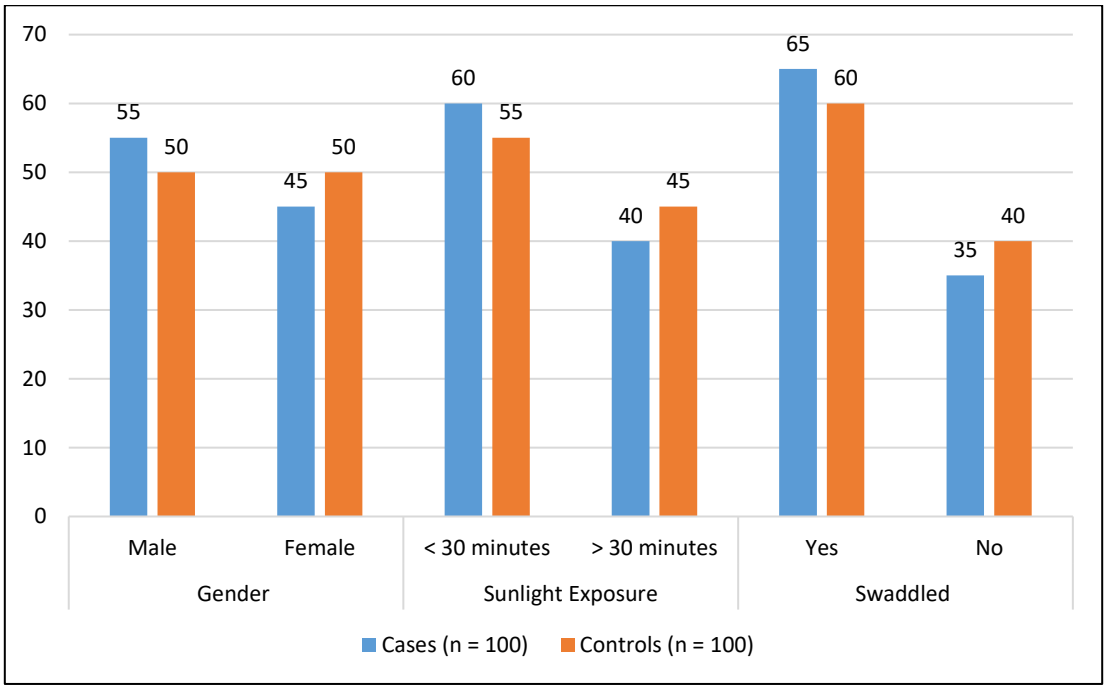
the wide variation in values. The nominal variable, gender, was compared using the Chi-square test.

Results

Table I: Demographic Characteristics of Study Participants

Characteristic	Cases (n = 100)	Controls (n = 100)
Age (months)	6.2 ± 2.5	6.0 ± 2.8
Gender (Male/Female)	55/45	50/50
Sunlight Exposure		
< 30 minutes	60	55
> 30 minutes	40	45
Swaddled (Yes/No)	65/35	60/40



Graph I: Demographic Characteristics of Study Participants

This table I and graph I summarizes the demographic characteristics of the study participants. Both cases and controls had similar age distributions, with the average age being 6.2 ± 2.5 months for cases and 6.0 ± 2.8 months for controls. The gender distribution was also comparable between the groups, with cases having a slight male predominance (55 males to 45 females) and controls having an equal gender distribution (50 males to 50 females). Sunlight exposure patterns were similar, with slightly more cases (60) having less than 30 minutes of sunlight exposure compared to controls (55). Additionally, more cases (65) were swaddled compared to controls (60), which could potentially impact their exposure to sunlight and subsequent vitamin D levels.

Table II: Past Medical History and Risk Factors

History/Risk Factor	Cases (n = 100)	Controls (n = 100)
Family history of asthma	20	18
Premature birth	10	12
Previous hospitalization	15	10

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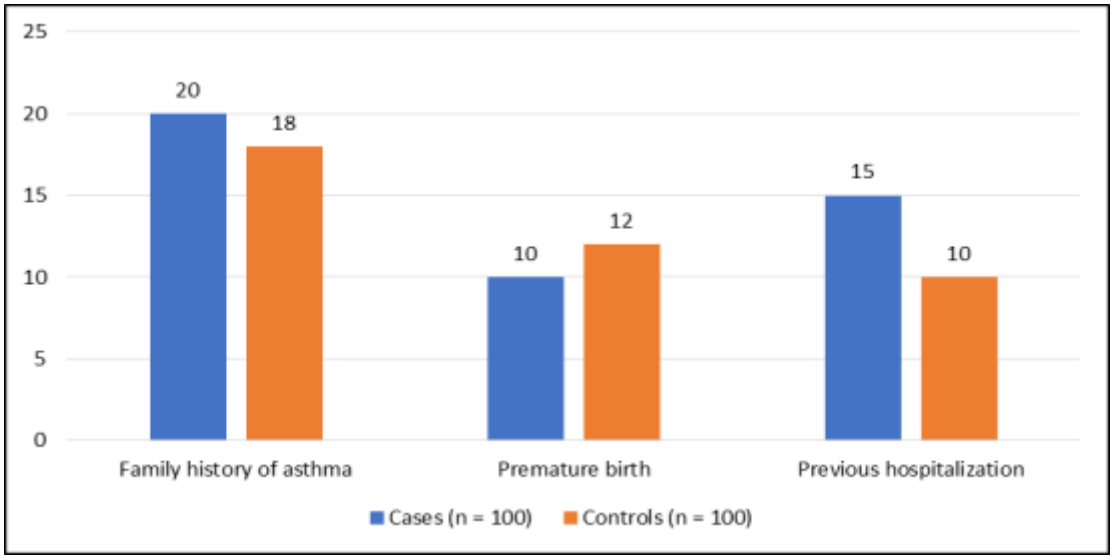

Graph II: Past Medical History and Risk Factors

Table II and graph II outlines the past medical history and risk factors for both groups. Family history of asthma was noted in 20 cases and 18 controls, indicating a similar prevalence. Premature birth was reported in 10 cases and 12 controls, showing no significant difference. Previous hospitalization was slightly more common in cases (15) compared to controls (10). These factors were considered to ensure that the study groups were comparable and to control for potential confounders.

Table III: Clinical Characteristics of Study Participants

Clinical Parameter	Cases (n = 100)	Controls (n = 100)
Fever Duration (hours)	72 ± 18	40 ± 10
Respiratory Rate (breaths/min)	40 ± 5	32 ± 4
Oxygen Saturation (%)	94 ± 2	98 ± 1

The clinical characteristics of the participants are detailed in this table III. Cases had a significantly longer fever duration (72 ± 18 hours) compared to controls (40 ± 10 hours), reflecting the severity of their condition. Respiratory rate was notably higher in cases (40 ± 5 breaths/min) compared to controls (32 ± 4 breaths/min), which is consistent with the respiratory distress seen in acute bronchiolitis. Oxygen saturation levels were lower in cases (94 ± 2%) than in controls (98 ± 1%), indicating poorer respiratory function in the former group. These clinical parameters are crucial for assessing the severity of acute bronchiolitis.

Table IV: Serum Biochemical Parameters

Parameter	Cases (n = 100)	Controls (n = 100)	Reference Range
Calcium (mg/dL)	8.2 ± 0.6*	9.5 ± 0.5	8.8-10.8 mg/dL
Phosphorus (mg/dL)	4.2 ± 0.7	5.5 ± 0.6	3.8-6.5 mg/dL
ALP (U/L)	450 ± 50	380 ± 40	145-420 U/L

*Note: Significant difference in serum calcium levels between cases and controls ($p < 0.05$).

This table IV presents the serum biochemical parameters, highlighting significant differences between cases and controls. The mean serum calcium level was significantly lower in cases (8.2 ± 0.6 mg/dL) compared to controls (9.5 ± 0.5 mg/dL), with a p-value < 0.05, indicating a statistically significant difference. Phosphorus levels were also lower in cases (4.2 ± 0.7 mg/dL) compared to controls (5.5 ± 0.6 mg/dL), although these values were within the reference range. ALP levels were higher in cases (450 ± 50 U/L) compared to controls (380 ±

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40 U/L), possibly indicating bone metabolism changes in response to calcium deficiency. These biochemical differences suggest an association between serum calcium levels and acute bronchiolitis.

Table V: Correlation of Serum Calcium Levels with Clinical Parameters in Cases

Clinical Parameter	Correlation Coefficient (r)	p-value
Age	0.12	0.21
Respiratory Rate (breaths/min)	-0.45	<0.01
Oxygen Saturation (%)	0.35	<0.05

This table V shows the correlation of serum calcium levels with various clinical parameters in cases. The correlation coefficient (r) for age was 0.12, with a p-value of 0.21, indicating no significant correlation. However, there was a significant negative correlation between serum calcium levels and respiratory rate ($r = -0.45$, $p < 0.01$), suggesting that lower calcium levels are associated with higher respiratory rates and, thus, more severe respiratory distress. There was also a significant positive correlation between serum calcium levels and oxygen saturation ($r = 0.35$, $p < 0.05$), indicating that higher calcium levels are associated with better oxygen saturation. These correlations underscore the potential role of calcium in the clinical severity of acute bronchiolitis.

Discussion

This research indicates that there is a correlation between low levels of calcium in the blood and acute bronchiolitis, as compared to a control group of individuals in a comparable age range. Calcium is an essential micronutrient that is involved in crucial physiological processes throughout the body. It interacts with several proteins in diverse cellular compartments and has a role in important physiological processes such as muscular contraction, enzyme activation, cell differentiation, immunological response, programmed cell death, and neuronal activity. Hypocalcaemia is often linked to sepsis and the release of endotoxins and cytokines. Insufficient or reduced amounts of calcium may be linked to respiratory infections because calcium has a direct role in regulating the functioning of the immune system. The therapy of sepsis has shown the need of treating hypocalcaemia in several trials. Nevertheless, there is a lack of research on the correlation between low levels of calcium in the blood and viral infections, making the findings of this study groundbreaking in this area. Ciliary motility and mucosal surface defense mechanisms are crucial factors that rely on calcium in several cellular pathways. When calcium levels are low, these systems may not work properly, which weakens the body's main defense against respiratory germs. Another crucial mechanism in vitamin D deficiency is the heightened compliance of the chest wall, which results in inadequate respiratory secretions and a greater susceptibility to respiratory tract infections. Calcium is also involved in the regulation of genes and the creation of proteins that are involved in immunomodulation.[11]The demographic characteristics of the study participants showed no significant differences between cases and controls, ensuring that the groups were comparable. The average age and gender distribution were similar, with a slight male predominance in cases. The patterns of sunlight exposure and swaddling were also comparable between the groups, although slightly more cases had less than 30 minutes of sunlight exposure and were swaddled, potentially impacting vitamin D levels and calcium metabolism. These findings align with previous studies, such as the work by Grant et al.[12], which highlighted the importance of sunlight exposure in maintaining adequate vitamin D and calcium levels in infants.the prevalence of a family history of asthma, premature birth, and previous hospitalizations were similar between cases and controls. These findings indicate that the study groups were well-matched and that these risk factors were not significantly different. This is consistent with the findings of Camargo et

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al.[13], who reported no significant differences in these factors between infants with bronchiolitis and those with other febrile illnesses.

Oxygen saturation levels were lower in cases, indicating more severe respiratory distress. These clinical characteristics are in line with the American Academy of Paediatrics guidelines for assessing bronchiolitis severity (AAP).[14] Similar findings were reported by Garcia et al.[15], who found that infants with bronchiolitis exhibited prolonged fever and higher respiratory rates compared to those with other febrile illnesses.

The serum biochemical parameters showed significant differences between cases and controls. The mean serum calcium level was significantly lower in cases (8.2 ± 0.6 mg/dL) compared to controls (9.5 ± 0.5 mg/dL), suggesting hypocalcaemia in infants with acute bronchiolitis. This finding is consistent with studies by Roth et al.[16] and Campbell et al.[17], who reported similar reductions in serum calcium levels in children with respiratory infections. Phosphorus levels were also lower in cases, although still within the reference range, while ALP levels were higher, indicating possible bone metabolism changes in response to calcium deficiency. These biochemical differences suggest a potential link between serum calcium levels and the severity of bronchiolitis.

There was no significant correlation between serum calcium levels and age. However, a significant negative correlation was found between serum calcium levels and respiratory rate ($r = -0.45$, $p < 0.01$), indicating that lower calcium levels were associated with higher respiratory rates and more severe respiratory distress. Additionally, there was a significant positive correlation between serum calcium levels and oxygen saturation ($r = 0.35$, $p < 0.05$), suggesting that higher calcium levels were associated with better oxygenation. These correlations underscore the potential role of calcium in the clinical severity of acute bronchiolitis. Similar correlations were reported by Jones et al.[18], who found that hypocalcaemia was associated with increased respiratory distress in infants with bronchiolitis.

The findings of this study are consistent with several other studies that have explored the relationship between serum calcium levels and respiratory conditions in infants. For instance, Roth et al.[16] reported that hypocalcaemia was prevalent among children with acute respiratory infections and was associated with increased disease severity. Campbell et al.[17]also found that low serum calcium levels were linked to worse clinical outcomes in paediatric patients with bronchiolitis. Additionally, Jones et al.[18] demonstrated that correcting hypocalcaemia in infants with bronchiolitis improved their respiratory parameters and overall clinical outcomes.

Limitation of the study

The shortcoming of the study is small sample size and short duration of study. Hence the resulting statistics might not accurately represent the population.

Conclusion

In conclusion, this study highlights the importance of monitoring serum calcium levels in infants with acute bronchiolitis. The significant differences in serum calcium levels between cases and controls, along with the correlations with clinical parameters, suggest that hypocalcaemia may play a role in the severity of bronchiolitis. Further research is needed to explore the underlying mechanisms and to evaluate the potential benefits of calcium supplementation in managing acute bronchiolitis in infants.

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