ORIGINAL RESEARCH

Assessment of serum calcium level among hospitalised infants with acute bronchiolitis

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ABSTRACT

Background: Bronchiolitis, a viral illness affecting the lower respiratory tract, is prevalent among infants and contributes to a substantial global health burden. The present study was conducted to assess serum calcium level among hospitalised infants with acute bronchiolitis.

Materials & Methods: 110 infants with acute bronchiolitis of both genders were put in group I and equal number of healthy controls in group II. Features such as coryza, fever, tachypnoea, tachycardia, paroxysmal wheezy cough, and irritability were recorded. 5 ml of blood samples were collected for estimation of total serum calcium, phosphorus, and ALP using a fully automated Hitachi analyser.

Results: The mean age of infants in Group I was 4.5 ± 2.1 months, which was slightly higher than that of Group II, with a mean of 3.2 ± 1.9 months. This difference was marginally significant (p = 0.05), indicating that infants with bronchiolitis in this study tended to be slightly older. The mean weight of infants in Group I was 5.9 ± 1.4 kg, compared to 5.3 ± 1.2 kg in Group II. However, this difference was not statistically significant (p = 0.72), suggesting comparable nutritional status between the groups. Similarly, the average length in Group I was 58.4 ± 3.6 cm, slightly less than 60.2 ± 3.9 cm observed in Group II, but the difference did not reach statistical significance (p = 0.13). The mean calcium level was 8.2±3.1 mg/dL in group I and 9.4±2.5 mg/dL in group II. The mean phosphorus level was 5.3±1.8 mg/dL in group I and 5.7±2.5 mg/dL in group II. The mean alkaline phosphatase level was 364.2±16.3 U/L in group I and 340.7±14.2 U/L in group II. The difference was significant (P< 0.05). Rickets were seen in 11 in group I and 4 in group II. The difference was significant (P< 0.05).

Conclusion: An association was found by the authors between calcium levels and acute bronchiolitis. The results indicate that low serum calcium levels could be a risk factor for acute bronchiolitis. Additionally, the study found a higher prevalence of rickets among these patients, underscoring the importance of proper sunlight exposure and sufficient supplementation.

Keywords: Alkaline phosphatase, Bronchiolitis, Vitamin D

INTRODUCTION

Bronchiolitis, a viral illness affecting the lower respiratory tract, is prevalent among infants and contributes to a substantial global health burden. The Respiratory Syncytial Virus (RSV) is the most confirmed cause of bronchiolitis, leading to numerous hospitalizations in children under five each year.[1]

Electrolyte and metabolic disturbances, including abnormalities in serum calcium levels, have been increasingly recognised in acutely ill paediatric patients. Hypocalcaemia,

defined as a total serum calcium level below the age-specific reference range, can lead to neuromuscular irritability, seizures, and cardiac dysfunction (Cooper & Gittoes, 2008).[2]

RSV bronchiolitis usually starts in late October, with peak occurrences in winter and early spring. It has been suggested that several risk factors contribute to the occurrence of frequent bronchiolitis in infancy, such as prematurity, second hand smoke exposure, residing in overcrowded homes with inadequate sunlight, and urban environmental conditions. It has been proposed that factors like remaining indoors, crowding, humidity, and the inhalation of cold mist can lead to reduced ciliary function.[3]

There is a strong association between vitamin D deficiency and severe bronchiolitis in infants, as well as their need for intensive care unit admission. It has been suggested that evaluating vitamin D levels prior to the bronchiolitis season and administering suitable supplementation could serve as a protective strategy against severe bronchiolitis.[4] Also, levels of vitamin D in nasopharyngeal secretions have been assessed and found to correlate with an increased risk of positive pressure ventilation in children. The homeostasis of calcium and phosphate is intricate, with three key hormones regulating the majority of the extracellular management of these minerals.[5] Parathyroid hormone is involved in the maintenance or restoration of serum calcium levels. Calcium is essential for cellular processes, metabolic and signaling pathways, survival, and immune functions. Due to its association with increased mortality and complications, low serum calcium levels serve as a prognostic factor for the severity of viral diseases.[6]

Aim and Objectives

Aim

To assess the association between acute bronchiolitis in infants and biochemical parameters, particularly calcium levels, and to evaluate the prevalence of rickets among affected infants compared to healthy febrile controls.

Objectives

1. To compare serum calcium, phosphorus, and alkaline phosphatase levels in infants with acute bronchiolitis versus healthy febrile controls without respiratory symptoms.
2. To evaluate the prevalence of clinical or radiological rickets in infants diagnosed with acute bronchiolitis compared to controls.
3. To assess demographic comparability between study groups to ensure valid biochemical and clinical comparisons.

Materials and Methods

Study Design: This was a cross-sectional observational study conducted to evaluate serum calcium levels among infants diagnosed with acute bronchiolitis.

Study Population

A total of 110 infants (both males and females) presenting with acute bronchiolitis were enrolled as the case group (Group I). An equal number of healthy age-matched controls (Group II) without respiratory symptoms but with febrile illness were also included. Written informed consent was obtained from the parents or legal guardians of all participants.

Study Setting and Duration: The study was carried out in the Department of Pediatrics, Anugrah Narayan Magadh Medical College & Hospital, Gaya, Bihar, India. Data collection took place over a period of two years, from October 2019 to August 2021.

Ethical Considerations: The study received approval from the Institutional Ethical Committee. Informed written consent was obtained from the parents or caregivers of all participating infants prior to inclusion.

Inclusion Criteria

- Infants under one year of age referred to the pediatric emergency unit with clinical signs of acute bronchiolitis were eligible for the study.
- Diagnosis and severity assessment followed the American Academy of Pediatrics (AAP) guidelines for bronchiolitis.
- Controls were infants in the same age group presenting with febrile illness (temperature >38.5°C for over 24 hours) but lacking any respiratory complaints.

Exclusion Criteria

- Infants with chronic or congenital conditions potentially affecting bronchiolitis progression or calcium metabolism were excluded.
- This included those with chronic lung disease, congenital heart defects, suspected inborn errors of metabolism, global developmental delay, hypotonia, neurological disorders, or recognizable syndromic features.

Study Procedure

Upon emergency department referral, demographic details including name, age, sex, and medical history were recorded in a structured proforma. Data on sunlight exposure (duration and swaddling), prior illnesses, asthma risk factors, and family history were also documented.

Clinical features such as nasal discharge, fever, rapid breathing, increased heart rate, paroxysmal wheezy cough, and irritability were assessed. Blood samples (5 mL) were collected under sterile conditions from each subject. One millilitre of blood was centrifuged at 3000 rpm for one minute to obtain serum. Serum total calcium, phosphorus, and alkaline phosphatase (ALP) levels were estimated using a fully automated Hitachi analyser. Reference ranges used for infants were (Behrman RE)[7]:

- Calcium: 8.8–10.8 mg/dL
- Phosphorus: 3.8–6.5 mg/dL
- ALP: 145–420 U/L

Study Groups

- **Group I (Cases):** Comprised 55 infants (both sexes) under 1 year of age who were hospitalized with a clinical diagnosis of acute bronchiolitis, based on the American Academy of Pediatrics (AAP) criteria for diagnosis and severity assessment.
- **Group II (Controls):** Included 55 age-matched healthy infants who presented with acute febrile illness (temperature >38.5°C lasting more than 24 hours) but without any respiratory symptoms. These children served as controls to compare serum biochemical parameters.

Outcome Measures

The primary outcome was the comparison of serum calcium levels between infants with bronchiolitis and healthy controls. Secondary outcomes included measurements of serum phosphorus and ALP levels, and their correlation with clinical features.

Statistical Analysis

Data analysis was performed using SPSS version 21.0. Continuous variables such as age, weight, height, calcium, phosphorus, and albumin were compared using the Student's t-test. As ALP values exhibited high variability, they were analysed using the Kruskal-Wallis test. Categorical variables such as gender were compared using the Chi-square test. A p-value less than 0.05 were considered statistically significant.

RESULTS

Table 1: Demographic characteristics of the participants

Parameter	Group I (Cases), n=55, (Mean ± SD)	Group II (Controls), n=55, (Mean ± SD)	P-value
Age (months)	4.5 ± 2.1	3.2 ± 1.9	0.05
Weight (kg)	5.9 ± 1.4	5.3 ± 1.2	0.72
Length (cm)	58.4 ± 3.6	60.2 ± 3.9	0.13

Table 1 shows that the demographic characteristics of the two study groups—Group I (infants with acute bronchiolitis) and Group II (healthy febrile controls without respiratory symptoms)—were compared to assess baseline similarities. The mean age of infants in Group I was 4.5 ± 2.1 months, which was slightly higher than that of Group II, with a mean of 3.2 ± 1.9 months. This difference was marginally significant (p = 0.05), indicating that infants with bronchiolitis in this study tended to be slightly older. The mean weight of infants in Group I was 5.9 ± 1.4 kg, compared to 5.3 ± 1.2 kg in Group II. However, this difference was not statistically significant (p = 0.72), suggesting comparable nutritional status between the groups. Similarly, the average length in Group I was 58.4 ± 3.6 cm, slightly less than 60.2 ± 3.9 cm observed in Group II, but the difference did not reach statistical significance (p = 0.13). These findings indicate that apart from age, the two groups were demographically well-matched, which strengthens the reliability of further comparisons in biochemical parameters such as serum calcium.

Table 2: Comparison of biochemical parameters

Biochemical parameters	Group I (n=55)	Group II (n=55)	P value
Calcium (mg/dL)	8.2±3.1	9.4±2.5	0.01
Phosphorus (mg/dL)	5.3±1.8	5.7±2.5	0.72
Alkaline phosphatase (U/L)	364.2±16.3	340.7±14.2	0.26

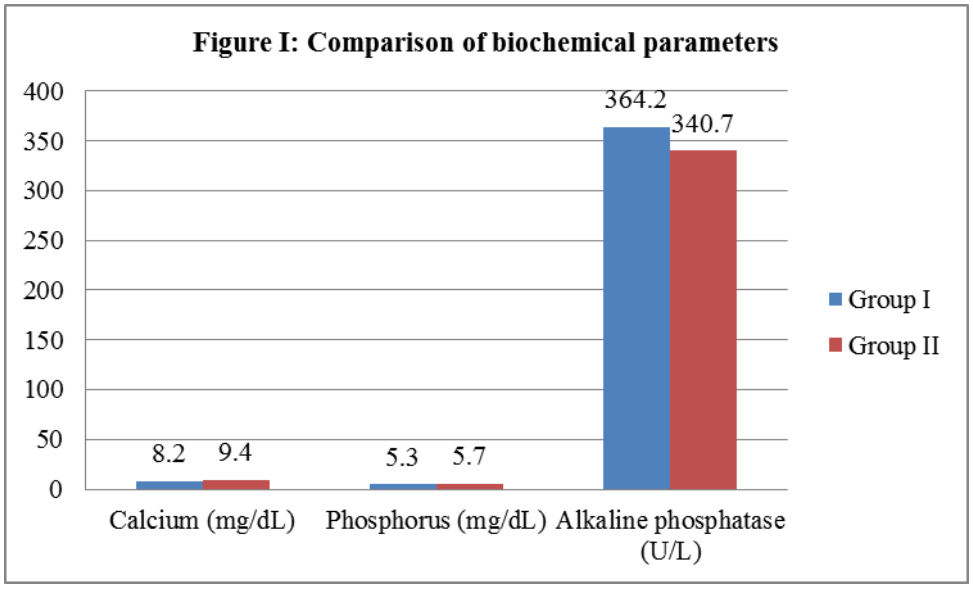

Table 2, figure I, shows that the comparison of biochemical parameters between infants with acute bronchiolitis (Group I) and healthy febrile controls (Group II) revealed a statistically significant reduction in serum calcium levels among the bronchiolitis group. The mean calcium level in Group I was **8.2 ± 3.1 mg/dL**, compared to **9.4 ± 2.5 mg/dL** in Group II (**p = 0.01**), indicating that hypocalcemia is more prevalent in infants during an episode of acute bronchiolitis. This finding may be attributed to factors such as reduced oral intake, systemic inflammation, or altered calcium metabolism during illness. In contrast, the mean serum phosphorus levels were **5.3 ± 1.8 mg/dL** in Group I and **5.7 ± 2.5 mg/dL** in Group II, with no significant difference (**p = 0.72**). This suggests that phosphorus homeostasis is not markedly affected in the acute phase of bronchiolitis. Similarly, the mean alkaline phosphatase (ALP) levels were slightly elevated in bronchiolitis cases (**364.2 ± 16.3 U/L**) compared to controls (**340.7 ± 14.2 U/L**), but this difference was not statistically significant (**p = 0.26**), indicating that ALP fluctuations may not be directly linked to the presence of bronchiolitis in otherwise healthy infants.

Table 3: Prevalence of rickets

Groups	Prevalence	P value
Group I (n=55)	11	0.01
Group II (n=55)	4	

Table 3 shows that in Group I (bronchiolitis patients**)**, 11 infants were found to have rickets, while in Group II (healthy febrile controls), only 4 infants had rickets. The p-value of 0.01 indicates that the difference in the prevalence of rickets between the two groups is statistically significant. This suggests that infants with acute bronchiolitis are at a higher risk for developing rickets compared to healthy infants with febrile illness but without respiratory symptoms.

DISCUSSION

Calcium is a micronutrient involved in essential reactions across the body. It engages with multiple proteins across various cellular compartments and plays a role in key bodily systems, including muscle contraction, enzyme activation, cell differentiation, immune response, programmed cell death, and neuronal activity.[8] It is known that hypocalcaemia is linked to sepsis and the release of endotoxins and cytokines.[9,10] In the context of bronchiolitis, factors such as poor feeding, vomiting, respiratory distress, and systemic inflammatory response may contribute to electrolyte imbalances, including disturbances in calcium homeostasis (Leung et al., 2005).[11] Calcium plays a crucial physiological role in multiple systems, including neuromuscular activity and respiratory muscle function. Studies suggest that hypocalcaemia may impair diaphragmatic contractility, potentially worsening respiratory distress in infants with bronchiolitis (Peacock et al., 2005).[12] However,

despite the potential impact of calcium imbalance on respiratory outcomes, serum calcium levels are not routinely assessed in all infants with bronchiolitis, and current literature on this association remains sparse.

The present study was conducted to assess serum calcium level among hospitalised infants with acute bronchiolitis.

We found that the mean age in Group I was 4.5 ± 2.1 months, slightly higher than 3.2 ± 1.9 months in Group II (p = 0.05). This finding aligns with previous literature indicating that bronchiolitis commonly affects younger infants, particularly under 6 months of age, with peak incidence between 2 and 6 months due to smaller airways and immature immune responses (Meissner, 2016; Hall et al., 2009).[13,14] The slightly higher mean age in the bronchiolitis group might reflect a delay in hospital presentation or referral patterns specific to the study setting.

No significant differences were observed in weight (5.9 ± 1.4 kg vs. 5.3 ± 1.2 kg; p = 0.72) or length (58.4 ± 3.6 cm vs. 60.2 ± 3.9 cm; p = 0.13) between the groups. This suggests that nutritional status, which could influence biochemical markers like calcium, was similar in both groups, thereby reducing potential confounding effects. Previous studies have emphasized the role of adequate nutrition and growth parameters in maintaining physiological calcium homeostasis in infants (Kovacs, 2014).[15]

Gupta et al.[12] compared serum calcium levels in infants with acute bronchiolitis and controls. A total of 223 infants (<1 year of age) hospitalised with a diagnosis of acute bronchiolitis, presenting with the first episode of wheeze based on American Academy of Paediatrics (AAP) criteria (including coryza, fever, tachypnoea, tachycardia, paroxysmal wheezy cough, and irritability). An equal number of age-matched controls (n=223), admitted for non- respiratory illnesses, were included. The study included 223 patients in both the case and control groups. In the control group, there were 76.58% males and 23.42% females, while in the cases, there were 81.53% males and 18.47% females. The mean age of cases was 5.78±3.45 months, and controls were 4.77±2.83 months, with a mean difference of 1.01 (95% CI, 0.42-1.59). The mean calcium levels were 9.00±1.43 mg/dL and 8.71±1.51 mg/dL in controls and cases, respectively, with a mean difference of 0.29 (95% CI0.02 to 0.56), which was statistically significant (p-value=0.037). There was no significant difference in phosphorus and ALP levels between the two groups.

The mean calcium level in bronchiolitis cases was 8.2 ± 3.1 mg/dL, while that of the control group was 9.4 ± 2.5 mg/dL, with a statistically significant difference (p = 0.01). This finding aligns with previous research suggesting that hypocalcemia may be a common metabolic disturbance in infants suffering from acute lower respiratory tract infections, including bronchiolitis.

Lower calcium levels during acute illness may result from several factors such as reduced dietary intake due to feeding difficulties, increased urinary calcium excretion, and alterations in parathyroid hormone function or vitamin D metabolism induced by systemic inflammation (Chen et al., 2019).[16] Moreover, proinflammatory cytokines released during respiratory infections can interfere with calcium homeostasis, further contributing to hypocalcemia (Singh et al., 2016).[17]

In contrast, the mean serum phosphorus levels in the two groups (5.3 ± 1.8 mg/dL in bronchiolitis cases vs. 5.7 ± 2.5 mg/dL in controls) did not differ significantly (p = 0.72). This observation is consistent with findings from earlier pediatric studies indicating that phosphorus levels generally remain stable during acute infections in the absence of significant renal or gastrointestinal pathology (Aggarwal et al., 2017).[18]

Alkaline phosphatase (ALP) levels were marginally higher in bronchiolitis patients (364.2 ± 16.3 U/L) compared to controls (340.7 ± 14.2 U/L), but this difference was not statistically significant (**p = 0.26**). Since ALP is predominantly associated with bone growth and turnover in infants, its levels tend to vary with age and growth rate rather than acute respiratory illness. However, mild elevations may be attributed to stress-related bone metabolism or non-specific hepatic responses to infection (Bishop et al., 2014).[19] Golan-Tripto I et al.[20] evaluated serum 25(OH) vitamin D levels in infants and toddlers with acute bronchiolitis, compared to subjects with non-respiratory febrile illness. One hundred twenty-seven patients aged < 24 months were recruited; 80 diagnosed with acute bronchiolitis and 47 patients with non-respiratory febrile illnesses. Both groups had similar demographics aside from age (median [IQR] 5 [3-9] vs. 9 [5-16] months in the bronchiolitis group compared to control group (p = 0.002)). Serum 25(OH) vitamin D levels were

significantly lower in the bronchiolitis group; median [IQR] 28[18-52] vs. 50[25-79] nmol/L, respectively, (p = 0.005). Deficient vitamin D levels (< 50 nmol/L) was found more frequently in the bronchiolitis group than controls; 73% vs. 51% (p = 0.028). Multivariate logistic regression showed vitamin D deficiency was more probable in bronchiolitis patients; OR [95% CI] 3.139[1.369-7.195]. No correlation was found between serum vitamin D levels and bronchiolitis severity, which was assessed via Modified Tal Score and by length of hospital stay.

The findings of this study reveal a significantly higher prevalence of rickets in infants with acute bronchiolitis (Group I) compared to healthy febrile controls (Group II), with 11 cases in the bronchiolitis group versus 4 in the control group (**p = 0.01**). This suggests that **vitamin D deficiency** may be more prevalent in infants hospitalized with respiratory infections, particularly bronchiolitis. Vitamin D plays a crucial role in calcium and phosphorus metabolism, and its deficiency can lead to rickets, particularly in infants with limited sunlight exposure and poor nutritional intake during illness. Respiratory infections like bronchiolitis can further exacerbate this deficiency by reducing feeding and outdoor activity, which are essential for adequate vitamin D synthesis (Holick, 2007).[21] Additionally, inflammatory cytokines released during infection may interfere with vitamin D metabolism, increasing the risk of rickets (Zhao et al., 2014).[22]

LIMITATIONS OF THE STUDY

- Small sample size (n = 110), which may limit the generalizability of the findings.
- Cross-sectional design limits the ability to establish a causal relationship between hypocalcemia/rickets and bronchiolitis.
- Lack of vitamin D level estimation, which would have provided direct biochemical evidence of deficiency contributing to rickets and hypocalcemia.
- Single-center study, which may not reflect wider population differences.
- Nutritional history and sunlight exposure were not evaluated, both of which are significant factors influencing calcium and vitamin D status.

CONCLUSION

The current study highlights a significant association between acute bronchiolitis in infants and lower serum calcium levels, suggesting a potential role of hypocalcemia in the pathophysiology or clinical course of the illness. While phosphorus and alkaline phosphatase levels did not differ significantly between cases and controls, the increased prevalence of rickets among bronchiolitis patients further emphasizes the need for early evaluation of vitamin D and calcium status in these infants. Routine monitoring of biochemical parameters in hospitalized infants with bronchiolitis may aid in timely intervention and improved clinical outcomes.

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