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Assessment of Serum N-Terminal PRO B type Natriuretic Peptide in Acute Bronchiolitis

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Abstract

Background: Acute bronchiolitis is one of the most common lower respiratory tract infections among infants and young children and is an important cause of hospitalization during early childhood. The clinical course varies from moderate respiratory illness to severe respiratory distress requiring prolonged hospitalization. Although clinical assessment remains the cornerstone for determining disease severity, an objective biomarker may facilitate early recognition of severe disease and assist in prognostication. N-terminal pro-B-type natriuretic peptide (NT-proBNP), a biomarker released in response to myocardial wall stress, has emerged as a potential marker of severity in respiratory illnesses.

Aim and Objectives: To assess serum NT-proBNP levels in children with acute bronchiolitis and determine their correlation with disease severity, clinical parameters, and duration of hospitalization.

Materials and Methods: This cross - sectional observational study was conducted in the Department of Paediatrics, National Institute of Medical Sciences and Research (NIMS) Hospital, Jaipur, Rajasthan. Thirty children aged 2 months to 2 years with clinically diagnosed acute bronchiolitis were included. The children actually enrolled had ages ranging from 2 to 12

months (mean 6.20 ± 3.478 months), a narrower span than the stated eligibility window. Clinical severity was assessed using respiratory rate, chest retractions, nasal flaring, wheezing, general condition, and other vital parameters. Serum NT-proBNP was estimated using a fully automated chemiluminescence analyzer. Statistical analysis was performed using SPSS version 27.0, with a p-value <0.05 considered statistically significant.

Results: Of the 30 children, 24 had moderate and 6 had severe bronchiolitis. Male predominance was observed, with 23 (76.7%) children being male. Children with severe bronchiolitis had a significantly higher mean respiratory rate than those with moderate disease (65.33 vs. 56.33/min; p<0.001). The mean duration of hospitalization was significantly longer in severe cases (12.00 ± 5.514 days) than in moderate cases (5.08 ± 0.974 days; p<0.001). Serum NT-proBNP levels were markedly elevated in severe bronchiolitis (3738.17 ± 3301.154 pg/mL) compared with moderate bronchiolitis (419.79 ± 237.195 pg/mL), with a statistically significant difference (p<0.001). NT-proBNP showed a strong positive correlation with duration of hospital stay (r=0.912, p<0.001) and a significant positive correlation with respiratory rate (r=0.614, p<0.001). A significant negative correlation was observed between NT-proBNP and oxygen saturation (r=-0.446, p=0.014).

Conclusion: Serum NT-proBNP levels were significantly elevated in children with severe acute bronchiolitis and demonstrated significant correlations with important indicators of clinical severity, particularly respiratory rate, oxygen saturation, and duration of hospitalization. These findings suggest that serum NT-proBNP may serve as a useful adjunctive biomarker for assessing disease severity and predicting clinical course in children with acute bronchiolitis.

Keywords: Acute bronchiolitis, NT – proBNP, Disease Severity, Infants, Respiratory Distress, Biomarker, Hospitalization.

Introduction

Acute bronchiolitis is one of the most common acute lower respiratory tract infections encountered during infancy and early childhood and represents an important cause of morbidity and hospitalization among children younger than two years of age[1, 2]. It is characterized by acute inflammation, edema, increased mucus production, and obstruction of the small airways, producing a clinical picture that commonly includes rhinorrhea, cough, tachypnea, wheezing, chest retractions, and varying degrees of respiratory distress[3,4].

Although the majority of affected children experience a self - limiting illness, a proportion develop severe respiratory compromise requiring hospitalization, oxygen supplementation, respiratory support, or intensive care [5]. Bronchiolitis primarily affects children below two years of age, with the highest incidence occurring during the first year of life[1,6]. Infants are particularly susceptible because of the relatively small caliber of their peripheral airways, immature respiratory and immune systems, increased airway resistance, and limited respiratory reserve[7]. Even a relatively small degree of mucosal edema and accumulation of secretions can therefore result in substantial airflow limitation and respiratory distress in young infants[7,8.] Respiratory syncytial virus (RSV) is the most frequently identified viral pathogen associated with acute bronchiolitis and accounts for a substantial proportion of cases worldwide [2,9]. However, several other respiratory viruses, including rhinovirus, human metapneumovirus, influenza virus, parainfluenza virus, adenovirus, and corona virus, may produce a similar clinical syndrome[9,10]. Viral infection of

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the respiratory epithelium results in epithelial injury, inflammation, edema, increased mucus secretion, and accumulation of cellular debris within the bronchioles. These pathological changes cause narrowing and obstruction of the small airways, leading to increased airway resistance, air trapping, ventilation-perfusion mismatch, hypoxemia, and increased work of breathing [3,11].

The clinical manifestations of acute bronchiolitis may vary considerably. The illness frequently begins with symptoms of an upper respiratory tract infection, such as rhinorrhea, nasal congestion, and mild fever, which are subsequently followed by cough, tachypnea, wheezing, and respiratory distress [4,12]. With increasing severity, infants may develop prominent intercostal and subcostal retractions, nasal flaring, reduced feeding, irritability, hypoxemia, exhaustion, and occasionally apnea[5,13].

Young age, prematurity, congenital heart disease, chronic lung disease, immunodeficiency, and underlying neuromuscular disorders have been recognized as important factors associated with an increased risk of severe disease [5,14,15].

Various clinical severity scores have also been developed to improve objectivity; however, considerable variability may occur between observers and between different scoring systems[15,16]. Nevertheless, oxygen saturation alone does not provide a complete assessment of the physiological consequences of respiratory distress. Similarly, respiratory rate and the degree of chest retraction can be influenced by factors such as fever, agitation, crying, hydration status, and the age of the child [15,17]. Consequently, there has been increasing interest in identifying objective laboratory biomarkers that may complement clinical assessment and assist in early recognition of children at greater risk of severe disease. The cardiovascular system may be significantly affected during severe respiratory illness. Increased work of breathing, hypoxemia, pulmonary vasoconstriction, and changes in pulmonary vascular resistance may increase right ventricular pressure and myocardial wall stress [18,19]. Severe bronchiolitis may therefore produce measurable cardiovascular effects even in children without pre-existing structural cardiac disease. Recognition of this cardiopulmonary interaction has generated interest in cardiac biomarkers as potential indicators of disease severity [19,20].

B-type natriuretic peptide (BNP) is a peptide hormone predominantly synthesized and released by ventricular myocardial cells in response to increased myocardial wall tension, pressure overload, and volume expansion [21]. Its precursor, pro-B-type natriuretic peptide (proBNP), is cleaved into biologically active BNP and an inactive amino-terminal fragment known as N-terminal pro-B-type natriuretic peptide (NT-proBNP) [21,22].

NT-proBNP has several characteristics that make it potentially useful as a laboratory biomarker. Compared with BNP, NT-proBNP has a relatively longer circulating half-life and greater stability in blood samples, facilitating its measurement in routine clinical laboratories [22,23]. Measurement of NT-proBNP is well established in the assessment of heart failure and ventricular dysfunction in adults, while its potential applications in pediatric cardiovascular and respiratory disorders have increasingly been investigated[23,24].

Therefore, age and the clinical setting must be considered while interpreting NT-proBNP concentrations in pediatric patients. Despite these physiological variations, markedly increased levels may

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indicate significant myocardial strain or cardiopulmonary stress [25].

In acute bronchiolitis, several mechanisms may potentially contribute to increased NT-proBNP concentrations. Airway obstruction and ventilation-perfusion mismatch may result in hypoxemia. Hypoxemia can induce pulmonary vasoconstriction and increase pulmonary arterial pressure, thereby increasing right ventricular afterload [18,26]. Previous studies have investigated natriuretic peptides in infants and children with respiratory illnesses and have suggested a relationship between elevated BNP or NT-proBNP concentrations and disease severity, cardiac involvement, pulmonary hypertension, or the need for intensive respiratory support [20,27,28]. These observations have raised the possibility that NT-proBNP could supplement conventional clinical assessment in children presenting with acute bronchiolitis [27].

The ability to identify severe bronchiolitis at an early stage is clinically important. Infants who initially appear relatively stable may subsequently develop increasing respiratory distress, feeding difficulty, hypoxemia, apnea, or respiratory failure [5,13,29].

An objective biomarker associated with disease severity could therefore potentially assist clinicians in risk stratification, closer monitoring, decisions regarding hospitalization, and anticipation of prolonged clinical illness. The relationship between NT-proBNP and routinely assessed physiological variables is also of particular interest. Respiratory rate is an important clinical indicator of respiratory distress, whereas oxygen saturation reflects the degree of impairment in oxygenation. Increasing respiratory rate and decreasing oxygen saturation generally indicate worsening respiratory compromise [4,15]. Demonstration of a positive correlation between NT-proBNP and respiratory rate and a negative correlation with oxygen saturation would provide physiological support for its role as a marker of bronchiolitis severity. Despite advances in understanding the pathophysiology and management of acute bronchiolitis, treatment remains predominantly supportive, and routine use of many pharmacological interventions is not recommended [4,30]. Therefore, accurate assessment, monitoring, maintenance of adequate oxygenation and hydration, and timely recognition of deterioration remain central to management. Biomarkers capable of complementing clinical examination could consequently have practical value, particularly in children in whom clinical severity assessment is difficult or equivocal.

However, NT-proBNP should not be considered a replacement for careful clinical assessment. Its potential value lies in its use as an adjunct to established clinical parameters. The combination of clinical examination, oxygen saturation, respiratory rate, severity indicators, and an objective biochemical marker may potentially provide a more comprehensive assessment of the physiological impact of acute bronchiolitis. There remains comparatively limited information regarding the role of NT-proBNP specifically in otherwise eligible infants and young children presenting with acute bronchiolitis, particularly regarding its relationship with clinical severity and hospitalization. Further evaluation of this association may help clarify whether serum NT-proBNP can serve as a practical biomarker for severity assessment in this common pediatric respiratory illness.

Therefore, the present study was undertaken to assess serum N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels in infants and young children with acute bronchiolitis and to analyze the correlation of serum NT-

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proBNP levels with the severity of the disease. The study also evaluates its relationship with relevant clinical parameters and the clinical course of affected children.

Materials and Methods

The present study was designed as a cross-sectional observational study to assess serum N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels in children with acute bronchiolitis and to evaluate their relationship with the severity of the disease. The study was conducted in the Department of Paediatrics, National Institute of Medical Sciences and Research (NIMS) Hospital, Jaipur, Rajasthan. Children presenting to the outpatient and inpatient services of the Department of Paediatrics with clinical features suggestive of acute bronchiolitis were screened for eligibility. The study was conducted over a period of 18 months, from 1 July 2024 to 31 December 2025**.**The study population consisted of children of either sex, aged 2 months to 2 years, presenting with acute bronchiolitis to the Department of Paediatrics, NIMS Hospital, Jaipur. The age of children actually enrolled in the study ranged from 2 to 12 months, with a mean age of 6.20 ± 3.478 months (Table 1), narrower than the stated eligibility window of 2 months to 2 years. A total of 30 children fulfilling the predefined eligibility criteria were included in the study.

Inclusion Criteria

1. Children of either sex presenting with acute bronchiolitis.
2. Age between 2 months and 2 years**.**
3. Children whose parents or legal guardians provided informed consent for participation in the study.

Note: Although the eligibility criteria permitted enrolment of children up to 2 years of age, all 30 children actually enrolled during the study period were aged between 2 and 12 months (mean 6.20 ± 3.478 months; Table 1).

Exclusion Criteria

Children with any of the following conditions were excluded:

1. Congenital abnormalities of the lungs.
2. Cardiac diseases.
3. Renal diseases.
4. Immunodeficiency disorders.

Ethical Considerations

Prior approval was obtained from the Institutional Ethics Committee before initiation of the study. The study was conducted in accordance with established ethical principles. Parents or legal guardians of eligible children were informed about the nature and purpose of the study in a language they could understand.

Written informed consent was obtained from the parent or legal guardian before enrollment. Confidentiality of patient information was maintained throughout the study.

Study Methodology

Children presenting to the outpatient or inpatient services with clinical features suggestive of acute bronchiolitis were screened according to the predefined inclusion and exclusion criteria. Eligible children were enrolled after obtaining informed consent from their parents or legal guardians. A detailed clinical history was obtained and a comprehensive physical examination was performed in every participant. Data were recorded using a pre-designed and pre-tested case record proforma**.** The proforma included demographic characteristics, relevant clinical history, physical examination findings, laboratory investigations, severity-related clinical parameters, and serum NT-proBNP levels. The diagnosis of acute bronchiolitis was

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established on clinical grounds. Each enrolled child underwent systematic assessment for clinical manifestations and severity of respiratory distress. Disease severity was assessed using standardized clinical parameters, particularly the degree of chest retractions, nasal flaring, characteristics of wheezing, respiratory rate, and general condition of the child.

Based on the clinical assessment used in the study, children were categorized according to the severity of acute bronchiolitis for subsequent comparison with serum NT-proBNP levels.

Severity was classified as moderate or severe using a structured clinical assessment adapted from standard pediatric bronchiolitis severity-scoring tools, incorporating respiratory rate, pattern of chest retractions, degree and persistence of nasal flaring, character of wheezing, and general clinical status of the child. Children with intercostal retractions alone, mild or absent nasal flaring, wheeze audible only on auscultation, and a generally consolable status with occasional crying were classified as having moderate bronchiolitis. Children with intercostal, subcostal, and supraclavicular retractions, moderately severe and intermittent nasal flaring, wheeze audible without a stethoscope during both inspiration and expiration, and a persistently distressed state with continuous crying were classified as having severe bronchiolitis (Tables 5–8).

Blood Sample Collection

Approximately 2 mL of venous blood was collected from each participant using standard venipuncture technique under strict aseptic precautions. Blood was collected into a plain vial and allowed to clot appropriately. The samples were subsequently centrifuged to separate serum. The separated serum was transported to the Biochemistry Laboratory of NIMS Hospital for estimation of NT-proBNP.

Standard precautions for collection, handling, transportation, and processing of biological specimens were followed throughout the study.

Estimation of Serum NT-proBNP

Serum N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels were measured using the MAGLUMI X3 fully automated chemiluminescence analyzer. The estimation was performed using the flash Chemiluminescent reaction method according to the manufacturer's instructions. Appropriate laboratory quality-control procedures were followed during analysis to maintain the accuracy, precision, and reproducibility of the test results. NT-proBNP concentrations were expressed in pg/mL.

Assessment of Disease Severity and NT-proBNP

After clinical assessment, serum NT-proBNP concentrations were compared according to the severity of acute bronchiolitis. The relationship of NT-proBNP with clinically relevant variables was also evaluated. This assessment was performed to determine whether increasing serum NT-proBNP concentrations were associated with greater clinical severity and a more prolonged clinical course.

Data Collection and Management

All demographic, clinical, laboratory, and hospitalization - related information was entered into the study proforma. The collected data were checked for completeness and consistency before statistical analysis.

Statistical Analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS), version 27.0.

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Result

The majority of patients belonged to the 5-10 months age group, accounting for 40% of the study population, followed by children aged below 5 months (36.67%). The 11-15 months age group constituted 23.33% of the cases. The mean age of the study population was 6.20±3.478 months with a median age of 5 months and anagerange of 2-12 months. This distribution indicates that acute bronchiolitis was more commonly observed in younger children, particularly those below 10 months of age, highlighting the vulnerability of this age group to the disease.

Table 1: Distribution of Age among study patients.

Age Group	No.	Percentage
<5	11	36.67%
5-10	12	40.00%
11-15	7	23.33%
Total	30	100.00%
Mean ± SD	6.20±3.478	
Median	5	
Range	2-12	

Table 2: Distribution of Gender among study patients

Gender	No.	Percentage
Male	23	76.7%
Female	7	23.3%
Total	30	100.0%

Table 2: depicts the gender distribution of the study participants. Out of 30 children, 23 (76.7%) were males, while 7 (23.3%) were females demonstrating a clear male predominance among cases of acute bronchiolitis. This finding suggests that male children were more frequently affected or presented more commonly to the hospital with acute bronchiolitis during the study period.

Table 3: Distribution of Place among study patients

Place	No.	Percentage
Rural	25	83.3%
Urban	5	16.7%
Total	30	100.0%

Table 3: illustrates the distribution of study patients based on place of residence. A large majority of children, 25 (83.3%), belonged to rural areas, whereas only 5 (16.7%) were from urban areas.

This finding indicates that acute bronchiol it is cases were predominantly observed among children from rural settings, which may be related to factors such as environmental exposure, socioeconomic conditions, limited access to healthcare facilities or delayed presentation to tertiary care centers.

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Table 4: Distribution of Presenting Symptoms among study patients.

Presenting Symptoms	No. (n=30)	Percentage
Fever	30	100%
Cough	30	100%
Fast breathing	30	100%
Poor feeding	7	23.3%

Table 4 depicts the distribution of presenting symptoms among children with acute bronchiolitis. All study participants (100%) presented with fever, cough and fast breathing indicating that these symptoms were universal clinical features in the study population. Poor feeding was observed in 7 children (23.3%), suggesting that feeding difficulty was present in nearly one-fourth of the cases and may reflect increased disease severity or respiratory distress. Overall, the findings highlight that acute bronchiolitis commonly presents with classical respiratory symptoms with systemic manifestations such as poor feeding occurring less frequently but indicating greater clinical compromise.

Table 5: Retractions in Children with the Severity of Bronchiolitis

Retractions	Classification		Total	□2	p-value
	Moderate	Severe			
Intercostal	24	0	24		
	100.0%	0.0%	80.0%		
Intercostal, subcostal, supraclavicular	0	6	6		
	0.0%	100.0%	20.0%		
Total	24	6	30		
	100.0%	100.0%	100.0%	30.00	<0.001

Table 5 shows the association between the pattern of chest retractions and the severity of bronchiolitis. Among children classified as having moderate bronchiolitis, all 24 patients (100%) exhibited intercostal retractions alone, while none showed involvement of additional muscle groups. In contrast, all children with severe bronchiolitis (100%) demonstrated intercostal, subcostal and supraclavicular retractions, indicating increased respiratory effort. The association between the type of retractions and disease severity was found to be statistically significant ($p < 0.001$). This finding suggests that the presence of multiple retractions involving accessory muscles is strongly associated with severe bronchiolitis and serves as an important clinical marker for disease severity assessment.

Table 6: Nasal flaring during inspiration in Children with the Severity of Bronchiolitis

Nasal flaring during inspiration	Classification		Total	□2	p-value
	Moderate	Severe			
	16	0	16		

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Mild and rarely	66.7%	0.0%	53.3%		
Moderately severe and intermittently	0	6	6		
	0.0%	100.0%	20.0%		
No	8	0	8		
	33.3%	0.0%	26.7%		
Total	24	6	30		
	100.0%	100.0%	100.0%	29.487	<0.001

Table 6: illustrates the relationship between nasal flaring during inspiration and the severity of acute bronchiolitis. Among children with moderate bronchiolitis, 16 patients (66.7%) exhibited mild and rare nasal flaring, while 8 patients (33.3%) showed no nasal flaring. In contrast, all children with severe bronchiolitis (100%) demonstrated moderately severe and intermittent nasal flaring and none had mild or absent nasal flaring. The association between nasal flaring severity and bronchiolitis severity was found to be statistically significant (p<0.001).These findings indicate that increasing severity and persistence of nasal flaring are strongly associated with severe bronchiolitis and reflect heightened respiratory distress.

Table 7: Wheezing in Children with the Severity of Bronchiolitis

Wheezing	Classification		Total	□2	p-value
	Moderate	Severe			
Heard in both	0	6	6		
Expiration and					
inspiration with	0.0%	100.0%	20.0%		
stethoscope				31.400	<0.001
Heard only with	24	0	24		
stethoscope	100.0%	0.0%	80.0%		
Total	24	6	30		
	100.0%	100.0%	100.0%		

Table 7 shows the distribution of wheezing patterns in relation to the severity of bronchiolitis. All children with moderate bronchiolitis (100%) had wheezing heard only with a stethoscope, suggesting less severe airway obstruction. In contrast, all children with severe bronchiolitis (100%) exhibited wheezing that was audible during both inspiration and expiration, even without a stethoscope. This association was found to be statistically significant (p<0.001). The findings demonstrate that the intensity and audibility of wheezing increase with disease severity and can be used as an important clinical indicator for identifying severe bronchiolitis.

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Table 8: General Condition of Children with the Severity of Bronchiolitis

General Condition	Classification		Total	□2	p-value
	Moderate	Severe			
Moderately uneasy with occasional crying	24	0	24	30.00	<0.001
	100.0%	0.0%	80.0%		
Very uneasy and crying continuously	0	6	6		
	0.0%	100.0%	20.0%		
Total	24	6	30		
	100.0%	100.0%	100.0%		

Table 8: demonstrates the association between the general clinical status of children and the severity of bronchiolitis. All children classified as having moderate bronchiolitis (100%) were observed to be moderately uneasy with occasional crying, indicating relatively preserved general condition despite respiratory symptoms. In contrast, all children with severe bronchiolitis (100%) were very uneasy and crying continuously, reflecting marked distress and poor general status. The association between general status and disease severity was found to be statistically significant (p<0.001). These findings suggest that worsening general condition, characterized by persistent irritability and continuous crying is a strong clinical indicator of severe bronchiolitis.

Table 9: Mean Vital Parameters in Children with the Severity of Bronchiolitis

Vital Parameters	Severity	N	Mean	Std. Deviation	t-value	p-value
Pulse Rate (/min)	Moderate	24	145.96	11.149	0.841	0.408
	Severe	6	150.33	12.501		
Temperature (ºF)	Moderate	24	100.125	.5735	0.491	0.627
	Severe	6	100.250	.4764		
SPO2(%)	Moderate	24	96.00	.885	2.022	0.053
	Severe	6	95.17	.983		
Respiratory Rate(/min)	Moderate	24	56.33	4.331	4.590	<0.001
	Severe	6	65.33	4.131		

Table 9 compares the mean pulse rate was slightly higher in children with severe bronchiolitis compared to those with moderate disease; however, this difference was not statistically significant(p=0.408). Similarly, mean body temperature showed no significant difference between the two groups(p=0.627). Oxygen Saturation (SpO_2) levels were lower in the severe group compared to the moderate group, approaching statistical significance (p = 0.053). In contrast, the mean respiratory rate was significantly higher in children with severe bronchiolitis compared to those with moderate disease (p <0.001).

These findings indicate that among vital parameters, respiratory rate was the most reliable marker distinguishing severe from moderate bronchiolitis, while

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pulse rate and temperatures Showed limited discriminatory value.

Table 10: Duration of hospital stay in hospitalized children with the severity of bronchiolitis

Hospital stay	Classification		Total	± 2	p-value
	Moderate	Severe			
≤7 days	24	0	24	30.000	<0.001
	100.0%	0.0%	80.0%		
>7 days	0	6	6		
	0.0%	100.0%	20.0%		
Total	24	6	30		
	100.0%	100.0%	100.0%		
Mean±SD	5.08±0.974	12.00±5.514			
Median	5	10.5			
Range	4-7	8-23			

Table 10 illustrates the relationship between the duration of hospital stay and the severity of bronchiolitis. All children with moderate bronchiolitis (100%) had a hospital stay of ≤7 days, whereas all children with severe bronchiolitis (100%) required hospitalization for more than 7 days. This association was found to be statistically significant ($p < 0.001$). The mean duration of hospital stay was 5.08 ± 0.974 days in the moderate group and 12.00 ± 5.514 days in the severe group. The median duration of stay was 5days for moderate cases and 10.5days for severe cases with a wider range observed in severe bronchiolitis (8-23 days). These findings indicate that disease severity was strongly associated with prolonged hospitalization, reflecting increased morbidity in children with severe bronchiolitis.

Table 11: Mean NT-PRO BNB level (pg/ml) in Children with the Severity of Bronchiolitis

Severity	N	Mean	Std. Deviation	t-value	p-value
Moderate	24	419.79	237.195	5.151	<0.001
Severe	6	3738.17	3301.154		

Table11: compares the mean serum NT-proBNP levels between children with moderate and severe bronchiolitis. Children with moderate bronchiolitis had a mean NT-proBNP level of 419.79 ± 237.195 pg/ml, whereas those with severe bronchiolitis exhibited markedly elevated levels with a mean of 3738.17±3301.154 pg/ml. The difference in NT-proBNPlevels between the two groups was found to be statistically significant ($p < 0.001$). This finding suggests a strong association between elevated NT-proBNP levels and increased severity of bronchiolitis, indicating that NT-proBNP may serve as a useful biomarker for assessing disease severity in affected children.

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Graph 1: Mean NT-PROBNB level (pg/ml) in Children with the Severity of Bronchiolitis

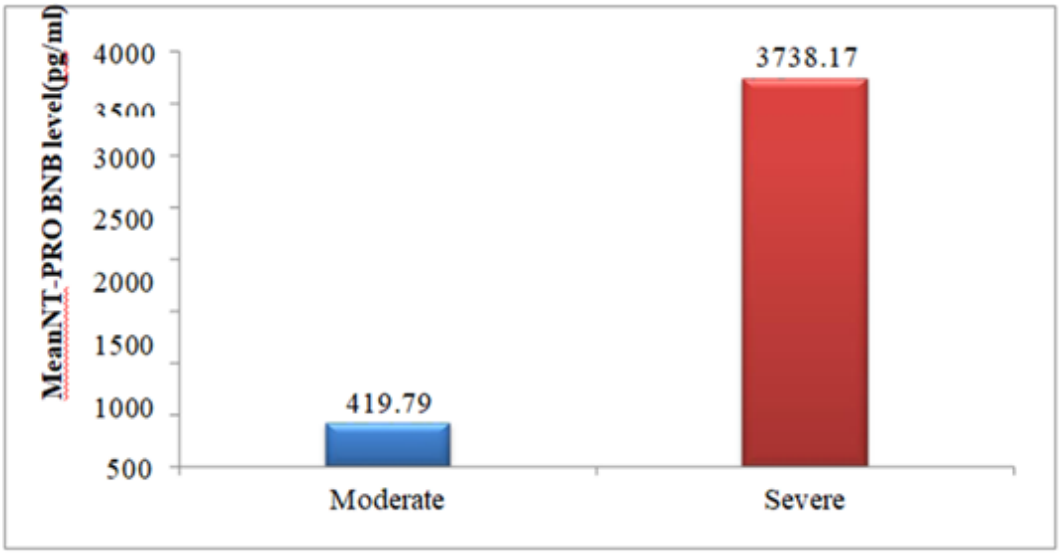

Table 12: Correlation between Hospital stay, Vital parameters and NT-PRO BNB level (pg/ml) in Children with acute Bronchiolitis.

	NT-PROBNB level (pg/ml)	
	r	p-value
Hospital Stay	0.912	<0.001
Pulse Rate(min)	0.377	0.040
Temperature (°F)	-0.099	0.603
SpO2(%)	-0.446	0.014
Respiratory Rate(min)	0.614	<0.001

Table12: shows the correlation between serum NT-proBNP levels and various clinical parameters in children with acute bronchiolitis. A strong positive correlation was observed between NT-proBNP level sand duration of hospital stay (r=0.912,p< 0.001), indicating that higher NT-proBNP levels were associated with longer hospitalization. A moderate positive correlation was also noted between NT-proBNP levels and pulserate (r=0.377,p=0.040),as well as respiratory rate (r=0.614, p< 0.001). Conversely, NT-proBNP levels showed a significant negative correlation with oxygen saturation (SpO_2) (r = -0.446, p = 0.014), suggesting that higher NT-proBNP levels were associated with lower oxygen saturation. No significant correlation was found between NT-proBNP levels and body temperature (p=0.603). Overall, these findings indicate that elevated NT-proBNP levels were closely associated with greater clinical severity and poorer outcomes in children with acute bronchiolitis.

Disease severity was significantly associated with the duration of hospitalization. All 24 children with moderate bronchiolitis had a hospital stay of ≤7 days, whereas all 6 children with severe bronchiolitis required hospitalization for >7 days (p<0.001). The mean duration of hospital stay was 5.08 ± 0.974 days in the moderate group compared with 12.00 ± 5.514 days in the severe group. The median duration of hospitalization was 5 days in moderate cases and 10.5 days in severe

cases, with respective ranges of 4–7 days and 8–23 days. Thus, severe bronchiolitis was associated with a substantially prolonged duration of hospitalization.

A marked difference was observed in serum NT-proBNP concentrations according to the severity of bronchiolitis. Children with moderate bronchiolitis had a mean serum NT-proBNP level of 419.79 ± 237.195 pg/mL, whereas children with severe bronchiolitis had a markedly higher mean level of 3738.17 ± 3301.154 pg/mL. This difference was highly statistically significant ($p<0.001$), demonstrating a strong association between elevated serum NT-proBNP concentrations and increasing severity of acute bronchiolitis.

Correlation analysis further demonstrated significant relationships between serum NT-proBNP and several clinical parameters. NT-proBNP showed a strong positive correlation with duration of hospital stay ($r=0.912$, $p<0.001$), indicating that increasing NT-proBNP concentrations were associated with prolonged hospitalization. A significant positive correlation was also observed with respiratory rate ($r=0.614$, $p<0.001$) and pulse rate ($r=0.377$, $p=0.040$). In contrast, serum NT-proBNP demonstrated a significant negative correlation with oxygen saturation (SpO_2) ($r=-0.446$, $p=0.014$), indicating that higher NT-proBNP concentrations were associated with lower oxygen saturation. No statistically significant correlation was observed between NT-proBNP and body temperature ($r=-0.099$, $p=0.603$).

Overall, the results demonstrated that serum NT-proBNP levels were substantially higher in children with severe acute bronchiolitis and were significantly associated with important indicators of clinical severity. Higher NT-proBNP concentrations were particularly associated with increased respiratory rate, lower oxygen saturation, and longer duration of hospitalization, supporting its potential role as an objective biomarker of disease severity in children with acute bronchiolitis.

Discussion

Acute bronchiolitis remains one of the most frequent causes of lower respiratory tract illness and hospitalization among infants and young children [1,2].

Although the diagnosis is predominantly clinical, considerable variation exists in disease severity, ranging from relatively uncomplicated respiratory illness to severe respiratory distress requiring prolonged hospitalization and respiratory support[3,4]. Accurate assessment of severity is therefore essential for appropriate monitoring, treatment, and prognostication. In recent years, increasing attention has been directed toward objective biomarkers that may complement clinical assessment. Among these, N-terminal pro-B-type natriuretic peptide (NT-proBNP) has emerged as a potential indicator of cardiopulmonary stress and disease severity[20-24].

The present cross-sectional observational study evaluated serum NT-proBNP levels in 30 children with acute bronchiolitis and assessed their relationship with disease severity and various clinical parameters. Of the 30 children, 24 (80%) had moderate bronchiolitis and 6 (20%) had severe bronchiolitis. The principal finding of the study was a marked elevation of serum NT-proBNP among children with severe disease. Mean NT-proBNP was 3738.17 ± 3301.154 pg/mL in severe bronchiolitis compared with 419.79 ± 237.195 pg/mL in moderate bronchiolitis, and this difference was highly statistically significant ($p<0.001$). Furthermore, NT-proBNP demonstrated significant correlations with duration of hospitalization, respiratory rate, oxygen saturation, and pulse rate. These observations support the potential

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utility of NT-proBNP as an adjunctive marker of disease severity in acute bronchiolitis.

Demographic Characteristics

The mean age of the children in the present study was 6.20 ± 3.478 months, with a median age of 5 months. The majority of cases occurred among younger infants, with 36.67% aged below 5 months and 40.00% aged between 5 and 10 months. Thus, more than three-fourths of the study population was below 10 months of age. This age distribution is consistent with the established epidemiology of acute bronchiolitis, which predominantly affects infants during the first year of life [1,2]. Florin et al.[1] emphasized that bronchiolitis is primarily a disease of young infants, while Meissner[2] similarly described the greatest burden of clinically significant bronchiolitis in early infancy. The increased vulnerability of younger infants may be explained by their relatively narrow peripheral airways, immature immune responses, increased airway resistance, and limited respiratory reserve[3,7].

The present study demonstrated a clear male predominance, with 23 (76.7%) males and 7 (23.3%) females. Male predominance has also been described in epidemiological studies of bronchiolitis and other viral lower respiratory tract infections[6,9]. The reason for this difference is likely multifactorial and may involve anatomical, developmental, immunological, and environmental factors. A majority of children in the present study, 25 (83.3%), belonged to rural areas, whereas only 5 (16.7%) were from urban areas. This distribution may reflect the population served by the study hospital rather than indicating an independent causal relationship between rural residence and bronchiolitis. Environmental exposures, socioeconomic circumstances, household crowding, access to healthcare, and patterns of referral may potentially influence presentation to a tertiary-care facility.

Clinical Presentation

Fever, cough, and fast breathing were present in all children included in the study, while poor feeding was documented in 23.3%. These findings are broadly compatible with the recognized clinical spectrum of acute bronchiolitis. Bronchiolitis typically begins with upper respiratory symptoms followed by cough, tachypnea, wheezing, and increased respiratory effort [3,4,12]. Poor feeding is particularly important in infants because respiratory distress may interfere with effective sucking and swallowing and can contribute to dehydration. Clinical guidelines emphasize assessment of feeding and hydration as an integral component of severity evaluation in bronchiolitis [4,5,12].

Clinical Severity of Bronchiolitis

Among the 30 children included in the present study, 24 (80%) were categorized as having moderate bronchiolitis and 6 (20%) as having severe bronchiolitis. Several individual clinical signs demonstrated highly significant relationships with severity. All children with moderate bronchiolitis demonstrated intercostal retractions alone, whereas all children with severe disease had intercostal, subcostal, and supraclavicular retractions. The association between the pattern of retractions and disease severity was highly significant ($p<0.001$). Retractions represent increased respiratory effort resulting from airway obstruction and reduced pulmonary compliance. As respiratory distress progresses, recruitment of additional accessory respiratory muscles becomes more prominent. Therefore, involvement of multiple sites of retraction is clinically consistent with increasing respiratory compromise [4,12,15].

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Nasal flaring also demonstrated a significant association with disease severity. Among children with moderate disease, 66.7% showed mild and occasional nasal flaring and 33.3% had no nasal flaring. In contrast, all children with severe bronchiolitis had moderately severe and intermittent nasal flaring ($p<0.001$). Nasal flaring is an established clinical manifestation of increased respiratory effort in infants and is commonly incorporated into clinical assessment of respiratory distress [15,16].

Wheezing patterns were similarly associated with severity. All children with moderate disease had wheezing heard only with a stethoscope, whereas all children with severe disease exhibited more prominent wheezing during both inspiration and expiration. The association was statistically significant ($p<0.001$). Viral injury to bronchiolar epithelium, mucosal edema, mucus accumulation, and cellular debris result in small-airway obstruction and produce the characteristic wheezing of bronchiolitis [3,11]. The general condition of the children also differed significantly between severity groups. Children with moderate bronchiolitis were moderately uneasy with occasional crying, whereas all children with severe bronchiolitis were very uneasy and crying continuously ($p<0.001$). These observations reinforce the importance of overall clinical appearance in severity assessment rather than relying on a single physiological parameter [4,5].

Vital Parameters and Disease Severity

Among the measured vital parameters, respiratory rate demonstrated the clearest relationship with disease severity. Mean respiratory rate was 56.33 ± 4.331/min among children with moderate bronchiolitis and increased to 65.33 ± 4.131/min among children with severe disease. This difference was highly statistically significant ($p<0.001$).

Tachypnea is an important manifestation of lower respiratory tract involvement and increased work of breathing. Current recommendations for bronchiolitis assessment emphasize respiratory rate together with retractions, oxygenation, feeding ability, and general condition [4,5,12]. The significantly higher respiratory rate observed in severe cases in the present study therefore supports its continued importance as a readily available clinical marker of severity Mean pulse rate was slightly higher in severe bronchiolitis (150.33 ± 12.501/min) compared with moderate disease (145.96 ± 11.149/min), although the difference was not statistically significant ($p=0.408$). Similarly, body temperature did not differ significantly between the groups ($p=0.627$). These findings suggest that pulse rate and temperature, when considered independently, had limited discriminatory value for differentiating moderate from severe bronchiolitis in the present study.

Mean oxygen saturation was lower in severe bronchiolitis (95.17 ± 0.983%) compared with moderate bronchiolitis (96.00 ± 0.885%). The difference approached but did not reach conventional statistical significance ($p=0.053$). Oxygen saturation is nevertheless an important component of bronchiolitis assessment and management [4,17]. Schuh et al.[17] demonstrated the substantial influence of pulse oximetry readings on hospitalization decisions in bronchiolitis, highlighting both its clinical importance and the need to interpret it within the complete clinical context.

Duration of Hospitalization

A strong relationship between disease severity and duration of hospitalization was observed. All children with moderate bronchiolitis had hospital stays of ≤7

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days, whereas all children with severe bronchiolitis remained hospitalized for >7 days (p<0.001).

The mean duration of hospital stay was 5.08 ± 0.974 days in moderate cases compared with 12.00 ± 5.514 days in severe cases. The median hospital stay was 5 days in moderate disease and 10.5 days in severe disease. These results demonstrate the greater clinical burden associated with severe bronchiolitis. Children with greater respiratory compromise generally require more intensive observation and supportive management and consequently may experience longer hospitalization [5,29]. The duration of hospital stay therefore represents a clinically meaningful outcome when evaluating potential prognostic biomarkers.

Serum NT-proBNP and Severity of Bronchiolitis

The most important finding of the present study was the strong association between serum NT-proBNP levels and severity of acute bronchiolitis. Mean serum NT-proBNP was 419.79 ± 237.195 pg/mL in moderate bronchiolitis**,** compared with 3738.17 ± 3301.154 pg/mL in severe bronchiolitis**.** This approximately nine-fold difference was highly statistically significant (p<0.001).

NT-proBNP is released following cleavage of proBNP and its circulating concentration increases in response to myocardial wall stress[21,22]. Although traditionally used in cardiovascular disease, increasing evidence suggests that natriuretic peptide concentrations may also increase during severe respiratory illnesses as a consequence of cardiopulmonary interactions [19,20].

The substantially increased NT-proBNP concentrations observed in children with severe bronchiolitis may be explained by several physiological mechanisms. Severe small-airway obstruction produces ventilation-perfusion mismatch and may lead to hypoxemia. Hypoxemia can induce pulmonary vasoconstriction and increase pulmonary vascular resistance, thereby increasing right ventricular after load and myocardial wall stress [18,19]. Increased work of breathing and changes in intrathoracic pressure may further affect ventricular loading conditions.

Rodriguez Gonzalez et al.[20] evaluated NT-proBNP in infants with respiratory syncytial virus infection and investigated its potential relationship with pulmonary hypertension. Their observations support the concept that increased NT-proBNP during significant respiratory illness may reflect cardiopulmonary stress rather than primary structural cardiac disease alone.

Similarly, Rodríguez-González et al.[27] reported an association between early elevation of NT-proBNP and severe bronchiolitis in infants. This is consistent with the present study, in which NT-proBNP concentrations were markedly higher in children categorized as having severe bronchiolitis. The interpretation of NT-proBNP in infants requires consideration of age because normal concentrations vary considerably throughout childhood, particularly during infancy[24,25]. Nir et al.[24] demonstrated age-dependent reference values for NT-proBNP in infants and children. Consequently, absolute NT-proBNP values should always be interpreted in relation to age and clinical circumstances. Nevertheless, the marked difference between the moderate and severe groups within the present study suggests a clinically meaningful association with disease severity.

Correlation Between NT-proBNP and Hospital Stay

One of the strongest findings of the study was the relationship between serum NT-proBNP and duration of hospitalization. A strong positive correlation was observed between NT-proBNP concentration and hospital stay **(**r=0.912, p<0.001**).**

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This indicates that children with higher serum NT-proBNP levels tended to remain hospitalized for longer periods. As prolonged hospitalization is generally associated with a more complicated or severe clinical course, this relationship further supports the potential prognostic significance of NT-proBNP.

The strength of this correlation is particularly noteworthy. It suggests that NT-proBNP may potentially provide information not only regarding severity at presentation but also regarding subsequent clinical course.

However, because the present study included only 30 participants, this relationship should be interpreted cautiously and validated in larger populations.

Correlation Between NT-proBNP and Respiratory Rate

Serum NT-proBNP demonstrated a significant positive correlation with respiratory rate **(**r=0.614, p<0.001**).** Thus, children with increasing NT - proBNP concentrations generally had higher respiratory rates.

This finding is physiologically plausible. Respiratory rate increases with greater airway obstruction, ventilation-perfusion abnormalities, and respiratory effort. More severe respiratory compromise may simultaneously produce greater cardiopulmonary stress and stimulate natriuretic peptide release[18-20].

The significant correlation between NT-proBNP and respiratory rate provides additional evidence that NT-proBNP concentrations reflect the physiological severity of bronchiolitis rather than representing an isolated biochemical abnormality.

Correlation Between NT-proBNP and Oxygen Saturation

An important inverse relationship was observed between NT-proBNP and oxygen saturation. Serum NT-proBNP demonstrated a significant negative correlation with SpO_2 (r=-0.446, p=0.014**).** Therefore, increasing NT-proBNP concentrations were associated with decreasing oxygen saturation.

Hypoxemia is an important manifestation of significant lower respiratory tract disease and may contribute to pulmonary vasoconstriction and increased right ventricular workload[18]. Consequently, the observed inverse relationship between NT-proBNP and oxygen saturation is biologically plausible. This finding also complements the positive relationship observed with respiratory rate. Taken together, higher NT-proBNP concentrations were associated with both increased respiratory effort and poorer oxygenation, strengthening the argument that NT-proBNP may reflect the overall cardiopulmonary burden of acute bronchiolitis.

Correlation with Pulse Rate and Temperature

A weaker but statistically significant positive correlation was observed between NT-proBNP and pulse rate **(**r=0.377, p=0.040). Tachycardia may accompany increased respiratory effort, fever, agitation, hypoxemia, or systemic physiological stress. The relatively modest correlation suggests that pulse rate alone is less closely associated with NT-proBNP than respiratory rate or duration of hospitalization.

No significant correlation was observed between NT-proBNP and body temperature **(**r=-0.099, p=0.603**).** This finding suggests that elevation of NT-proBNP in the study population was unlikely to simply reflect the degree of fever. Instead, its stronger relationships with respiratory rate, oxygen saturation, hospital stay, and overall severity suggest a closer association with cardiopulmonary stress.

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Clinical Significance of the Findings

The findings of the present study have potential clinical relevance because severity assessment in acute bronchiolitis continues to rely predominantly on clinical examination and pulse oximetry[4,5]. Although these methods are practical and essential, clinical assessment may be influenced by observer variation, particularly when evaluating respiratory effort, wheezing, and general condition[15,16]. An objective laboratory marker that correlates with established clinical indicators could therefore complement clinical assessment. The present study demonstrated that serum NT-proBNP was significantly elevated in severe bronchiolitis and correlated strongly with hospital stay, positively with respiratory rate, and negatively with oxygen saturation.

These findings suggest that NT-proBNP may potentially assist in identifying children who are likely to experience a more severe clinical course. A markedly elevated value in conjunction with tachypnea, increased retractions, worsening oxygenation, and poor general condition could alert clinicians to the need for closer monitoring and appropriate escalation of supportive care. However, NT-proBNP should not be interpreted as a standalone diagnostic or severity marker. Clinical assessment remains fundamental to bronchiolitis management[4,5].

NT-proBNP concentrations are influenced by age and may also be affected by cardiovascular, renal, and other physiological factors [21-25]. The exclusion of children with cardiac and renal diseases in the present study was therefore important in reducing potential confounding.

Furthermore, management of bronchiolitis remains predominantly supportive, with careful monitoring of respiratory status, maintenance of hydration, oxygen therapy when indicated, and appropriate respiratory support [4,5,30]. The potential role of NT-proBNP is therefore more appropriately considered as an adjunctive biomarker for severity assessment and prognostication rather than as a replacement for clinical evaluation.

Overall Interpretation

Overall, the present study demonstrated a consistent relationship between increasing clinical severity of acute bronchiolitis and serum NT-proBNP concentrations. Severe bronchiolitis was characterized by more extensive chest retractions, greater nasal flaring, more prominent wheezing, poorer general condition, significantly increased respiratory rate, and prolonged hospitalization. Importantly, these children also demonstrated markedly higher serum NT-proBNP concentrations. The strong positive correlation between NT-proBNP and hospital stay ($r=0.912$), significant positive correlation with respiratory rate ($r=0.614$), and significant negative correlation with oxygen saturation ($r=-0.446$) provide converging evidence supporting its relationship with disease severity. The findings are broadly consistent with the physiological basis of NT - proBNP release [21-24] and with previous investigations suggesting an association between NT - proBNP elevation and severe bronchiolitis or cardiopulmonary involvement in affected infants [20,27].

Therefore, serum NT-proBNP appears to be a promising adjunctive biomarker for assessing the severity of acute bronchiolitis in infants and young children. Nevertheless, given the relatively small sample size of the present study, larger prospective and multicentric studies are required to establish age-specific cut-off values, evaluate diagnostic and prognostic accuracy, and determine whether incorporation of NT-proBNP into routine clinical assessment provides additional benefit over established clinical severity parameters.

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Conclusion

The present study demonstrates that serum N-terminal pro-B-type natriuretic peptide (NT-proBNP) is significantly associated with the severity of acute bronchiolitis in infants and young children. Children with severe bronchiolitis had markedly higher mean serum NT-proBNP levels (3738.17 ± 3301.154 pg/mL) compared with those with moderate bronchiolitis (419.79 ± 237.195 pg/mL), with the difference being highly statistically significant ($p<0.001$). Serum NT-proBNP also showed a strong positive correlation with the duration of hospital stay and a significant positive correlation with respiratory rate, while a significant negative correlation was observed with oxygen saturation. Thus, increasing NT-proBNP levels were associated with greater respiratory compromise and prolonged hospitalization. The study therefore suggests that serum NT-proBNP may serve as a useful adjunctive biomarker for assessing disease severity and predicting the clinical course of children with acute bronchiolitis. Its use alongside conventional clinical parameters such as respiratory rate, oxygen saturation, chest retractions, nasal flaring, wheezing, and general condition may contribute to more objective assessment and early identification of children with severe disease. However, NT-proBNP should be considered an adjunct to, rather than a replacement for, careful clinical assessment. Further studies involving larger populations are required to validate these findings and establish appropriate age-specific cut-off values for predicting severe acute bronchiolitis.

Limitations

1. Small sample size of 30 children.
2. Single-center study, limiting generalizability.
3. Only a few patients had severe bronchiolitis.
4. Serial NT-proBNP levels were not measured.
5. Larger multicentric studies are required to validate the findings.

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