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CLINICAL EPIDEMIOLOGICAL CHARACTERISTICS, SOME FACTORS RELATED TO SEVERITY AND EFFICACY OF SODIUMCLORID 3% IN TREATMENT OF BRONCHIOLITIS IN CHILDREN AT BACH MAI HOSPITAL

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ABSTRACT OF PhD THESIS

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LIST OF DISCLOSED SCIENTIFIC WORKS

RELATED TO THE THESIS

1. Nguyen Thuy Giang, Nguyen Tien Dung, Nguyen Huu Hieu (2019). Clinical characteristics of acute bronchiolitis in children under 2 years old. Journal of clinicalmmedicine. No.112 (11-2019), pages 85-91.

2. **Nguyen Thuy Giang**, Nguyen Ngoc Sang, Kieu Phuong Thuy, Tran Van Ban (2023). Factors affecting the severity of acute bronchiolitis in children. Journal of Vietnamese Medicine. Volume 524 (No. 2) pages 188-192.

3. **Nguyen Thuy Giang**, Nguyen Tien Dung, Nguyen Huu Hieu, Tran Van Ban (2023). Efficacy of aerosol sodium chloride 3% in the treatment of acute bronchiolitis in children under 2 years old at Bach Mai hospital. Journal of Vietnamese Medicine. Episode 542 (No. 2). pages 63-68.

INTRODUCTION

Acute bronchiolitis is a common respiratory disease and is the leading cause of hospitalization in children under 2 years of age. The main cause of the disease is the Respiratory Syncytial Virus (RSV), Rhinovirus, Adenoviruses and type 3 parainfluenza virus. When suffering from acute bronchiolitis, the child's respiratory failure increases, characterized by rapid breathing, respiratory muscle contractions and wheezing. The main cause in the pathogenesis of bronchiolitis is airway edema and formation of mucus plugs that block bronchiolar branches. When airway obstruction occurs, there is a risk of reduced alveolar ventilation due to partial obstruction of airflow. When complete obstruction leads to lung collapse, especially when breathing high concentrations of oxygen. Currently, bronchiolitis has no specific treatment, but symptomatic treatment: supportive care, ensuring gas exchange, fluid intake and nutrition for the patient.

There are many factors that affect the severity of the disease. Some risk factors such as: age of disease, gestational age, birth weight, congenital abnormalities. Some reasons such as living environment, mother smoking during pregnancy, passive smoking in the family, family with siblings at kindergarten age, poor family economic conditions, etc.

The effect of reducing inflammation and increasing clearance of secretions from the airways reduces the risk of atelectasis and increases the efficiency of gas exchange. Hypertonic sodium chloride 3% aerosol has the effect of reducing the risk of mucus plug formation in the bronchioles, increasing the ability of the cilia to push mucus out of the respiratory tract. Hypertonic sodium chloride has recently been studied as part of a treatment regimen for acute bronchiolitis in young children.

In the world, there have been studies on the use of nebulized hypertonic saline in the treatment of acute bronchiolitis in children. Various concentrations of hypertonic saline have been studied and applied such as 3%, 5%, 6%, 7%. Nebulized saline can be used alone or in combination with other bronchodilators such as salbutamol, terbutaline, or adrenaline. The results of many studies show that 3% sodium chloride aerosol can significantly reduce the length of hospital stay and improve the severity of acute bronchiolitis patients. Sodium chloride 3% nebulizer has the lowest hypertonic concentration but has the ability to significantly reduce the length of hospital stay and improve the severity of patients with

acute bronchiolitis. The method is considered safe due to the low rate of adverse effects.

In Vietnam, 3% sodium chloride aerosol in the treatment of acute bronchiolitis has been researched and applied clinically by some authors, but the results obtained are not consistent. The clinical epidemiological characteristics of acute bronchiolitis are different depending on each country and locality. What are the clinical epidemiological characteristics of acute bronchiolitis in the Pediatric Department of Bach Mai Hospital? What are the factors related to the severity of acute bronchiolitis and is 3% sodium chloride effective in treating it? Whether or not acute bronchiolitis is present in children are questions that need answers. Therefore, we conducted this study with the following three objectives:

1. To describe some clinical epidemiological characteristics of acute bronchiolitis in children under 2 years old at the Pediatrics Department of Bach Mai hospital from 2017 to 2019.

2. To describe some factors related to the severity of acute bronchiolitis.

3. To evaluate the effectiveness of aerosol Sodium chloride 3% in the treatment of acute bronchiolitis.

NEW CONTRIBUTIONS OF THE THESIS

The thesis adds clinical epidemiological characteristics, risk factors for severity, and effectiveness of treatment with 3% sodium chloride aerosol in children with acute bronchiolitis to the general medical literature. The thesis also contributes to the diagnosis, treatment and prognosis of acute bronchiolitis, a common emergency disease in children, specifically:

1. Regarding clinical epidemiological characteristics

The disease is common in boys (66.89%) and at the age of 6 to 12 months. Patients are hospitalized all year round but most often in May, June and July.

The main clinical symptoms are wheezing (100%), rapid breathing (100%), chest indrawing (90.7%), and fever (64.9%). Severity according to Modified Cincinnati bronchiolitis score (MCBS score) is 21.1%, average (78.9%). Paraclinical: Plain chest X-ray shows air congestion (70.97%). In addition to RSV (28.57%), we also encountered Rhinovirus (27.66%), Adenovirus (11.79%).

2. Regarding risk factors for the severity of acute bronchiolitis:

- Children living with smokers
- Children whose gestational age at birth is less than 34 weeks
- Children with birth weight less than 2500g

3. About the results of treatment with 3% sodium chloride aerosol

- Symptoms of wheezing, chest indrawing, and whistling rales were all improved in the intervention group compared to the control group and were significantly better in the group of seriously ill patients.

- MCBS score, breathing frequency, SpO2, and heart rate in the intervention group were also improved better than the control group and significantly better in the severe patient group.

STRUCTURE OF THE THESIS

The main part of the thesis is 129 pages long, including the following parts: Introduction: 2 pages; Chapter 1 - Overview: 36 pages; Chapter 2 - Research objects and methods: 19 pages; Chapter 3 - Research results: 35 pages; Chapter 4 - Discussion: 32 pages; Conclusion: 2 pages; Recommended: 1 page; The thesis has 108 references, including 14 Vietnamese documents and 94 English documents. The thesis has 49 tables, 21 figures, 1 diagram.

Chapter 1
LITERATURE REVIEW

1.1 Acute bronchiolitis overview

Bronchiolitis is an acute inflammatory disease of small bronchi, less than 2mm in diameter, also known as bronchioles.

Bronchiolitis is a lower respiratory tract disease that occurs commonly in children under 2 years of age, especially children aged 3-6 months. Bronchiolitis can cause epidemics, especially in the middle of winter and early spring (when the weather changes). The disease usually appears after a respiratory viral infection causing symptoms of sneezing, runny nose, and low-grade fever.

Bronchiolitis occurs when the bronchioles become damaged, swollen, and inflamed, creating mucus that blocks the airways. The disease is characterized by clinical symptoms: cough, wheezing, rapid breathing and may be accompanied by chest indrawing, respiratory muscle contraction, cyanosis... Caused by respiratory viruses, common disease children under 24 months of age.

1.2 Pathogenesis

Bronchiolitis is an acute inflammatory lesion in the bronchioles less than 2mm in diameter. The virus penetrates the cells of the respiratory tract mucosa causing direct destruction and inflammatory response.

Necrosis of the respiratory mucosa is one of the earliest changes and occurs within 24 hours of infection.

Lesions in the bronchioles and the resulting interaction between inflammation and mesenchymal cells can lead to diverse pathophysiological changes and clinical syndromes.

The immune response also plays a vital role in the pathogenesis of bronchiolitis and clinical severity. IgE-expressed type 1 allergic reactions cause clinically significant symptoms of bronchiolitis. In addition, chemical mediators such as cytokines and chemokines (IL-4, IL-8, IL-33) were also found to be highly concentrated in the airways of patients with bronchiolitis.

Acute bronchiolitis is characterized by obstruction of the bronchioles by debris of necrotic epithelial cells. Along with the increased mucus secretion of the submucosal glands, it creates a mucus plug that blocks the damaged bronchioles and infiltrates inflammatory cells.

These mucus plugs cause three types of blockages:

- Obstruction in exhalation: Air can still enter the alveoli during inhalation, but it is blocked when exhaling, causing the alveolar region to become increasingly swollen, compressing the adjacent alveoli.

- Inspiratory type of obstruction deflates the alveoli below.

- Type of obstruction during exhalation and inspiration: Causes atelectasis, usually diffuse lesions on both sides of the lungs but unevenly in each part of the lung, creating areas of air stasis, areas of atelectasis and normal areas.

In the areas of air stasis and atelectasis, there will be perfusion disturbances leading to hypoxia. Over-distended alveoli can rupture causing gas in the lung parenchyma or pneumothorax.

Obstruction of air circulation forces the patient to breathe faster and more forcefully, causing chest indrawing, which can cause respiratory arrest in neonates, and is clinically common in severe forms. Contraction of smooth muscles is transient and does not play a significant role in the respiratory failure pathogenesis of bronchiolitis.

1.3 Diagnose

Diagnosis confirmed

Diagnosis of bronchiolitis is based on clinical features and epidemiological factors. Subclinical results are meaningful in supporting the diagnosis.

Diagnosis of acute bronchiolitis includes:

1. Age < 2 years old.

2. Epidemiological factors: exposure to RSV, having epidemics in the community, common in winter and spring.

3. Clinical: Onset by upper respiratory tract inflammation syndrome (sneezing, runny nose, stuffy nose), full-blown with typical respiratory symptoms: cough, diffuse wheezing, shortness of breath (breathing). rapid, thoracic indrawing). Pulmonary examination revealed many whistling rales, snoring rales, possibly moist rales.

1.4. Treatment of acute bronchiolitis with aerosol Natrichloride 3%

Hypertonic saline increases clearance of ciliated mucosa in normal patients, patients with asthma, bronchiectasis, cystic fibrosis, and sinus disease. Similar benefits are expected in young children with acute bronchiolitis on the following grounds:

Hypertonic salts create an osmotic flow of water into the mucus layer → diluting the mucus layer.

Hypertonic salts break ionic bonds in mucus → reduce mucus viscosity and elasticity.

Hypertonic salts stimulate the activity of cilia, which transduces the mucosa via prostaglandin E_2.

In addition, by reabsorption of water from the mucosa and submucosa, hypertonic saline could theoretically reduce airway wall edema in children with acute bronchiolitis. Hypertonic saline aerosol can also produce sputum and stimulate coughing, thereby helping to expel sputum from the bronchi, reducing airway obstruction, and rehydrating the airway surface in children with bronchiolitis. However, these changes are inferred from the benefit of hypertonic saline in cystic fibrosis and may not be true for acute bronchiolitis due to different pathophysiological processes.

Recently, nebulized hypertonic sodium chloride has been introduced in the treatment of bronchiolitis. In these studies, several types of hypertonic saline were used: 3%, 5%, 7%, of which 3% was used the most. Sodium chloride 3% nebulizer can be used alone or in combination with other bronchodilators (salbutamol, terbutaline) or adrenaline. Most recent randomized trials have shown that nebulized 3% saline is the lowest hypertonic saline yet can significantly reduce hospital stay and improve the severity of patients with inflammatory bowel disease. acute bronchiolitis compared with sodium chloride 0.9%. Even when used alone, nebulized 3% hypertonic saline is considered safe due to the low rate of side effects.

1.5 Studies in the world and Vietnam

A meta-analysis performed by Maguire et al in 2015 of 15 trials and 1922 patients showed that the use of hypertonic saline reduced the length of hospital stay by an average of 0.36 days. The authors believe that hypertonic saline solutions have a positive effect in the treatment of bronchiolitis in children.

According to a meta-analysis by Zhang L, Mendoza-Sassi RA, Wainwright C, Klassen TP, published in 2015, evaluated 24 intervention studies involving 3209 patients. The results of the study showed that infants receiving hypertonic saline had a significant difference in hospital stay, with a mean reduction of 0.45 days (95% CI -0.82 to -0 .08; p = 0.01) compared with those who received 0.9% saline or routine care. In seven trials, hypertonic saline reduced the risk of hospitalization by 20% (relative risk ratio = 0.8; 95% CI 0.67 - 0.96) compared with 0.9% saline.

In Vietnam, research by Nguyen Ngoc Phuc and Phan Huu Nguyet Diem at Children's Hospital 1 in the treatment of moderate bronchiolitis in children 3-12 months old was treated with superior saline aerosol. Three percent diuretic combined with salbutamol; this may indirectly reduce hospital stay. In addition, 3% hypertonic saline nebulization is a safe measure even when used alone without additional bronchodilators.

Chapter 2
RESEARCH SUBJECTS AND METHODS

2.1 Research subjects

Children are diagnosed with acute BRONCHIOLITIS, treated at the pediatric department of Bach Mai Hospital.

2.1.1 Criteria for inclusion in the study

According to the new clinical practice guidelines for the diagnosis and treatment of bronchiolitis by the American Academy of Pediatrics (AAP) (2014), the diagnosis of bronchiolitis is accepted as a clinical diagnosis, based on medical inquiry and examination as follows:

- Signs of acute upper respiratory tract infection such as cough, sneezing, runny nose, stuffy nose, fever or not.
- Wheezing

- Progression in 24 - 48 hours may lead to dyspnea: tachypnea, chest indrawing, intercostal muscle contraction, nasal bulge or even cyanosis, decreased oxygen saturation in the blood. Auscultation of the lungs shows whistling rales, snoring rales, and possibly moist rales.

- Age: under 2 years old

2.1.2 Exclusion criteria

Excluded from the study the following cases:

- Wheezing due to other specified causes: bronchial asthma, extraneous object in the airway, soft laryngeal cartilage, whooping cough, external compression such as lymph nodes, gastroesophageal reflux ...

- Having one of the comorbidities such as: chronic lung disease, congenital heart disease, congenital encephalopathy, neuromuscular disease, etc.

- All children whose parents refused to participate in the study.

2.1.3 Time and place of research

**** Research time***

The study was conducted from January 2017 to December 2019

**** Research location***

The study was conducted at the Department of Pediatrics - Bach Mai Hospital.

2.2 Methodology

2.2.1 Research design

Cross-sectional study and clinical randomized controlled trial.

2.2.2 Sample size

The general formula for estimating sample size is:

$$n = \frac{(z_{\alpha/2} + z_b)^2}{(ES)^2}$$

According to the study of author Gaëlle Beal and his co-workers, the study compared the effectiveness of the aerosol group with 3% sodium chloride and 0.9 sodium chloride.

$$n = \frac{2 \times C}{(ES)^2} \quad \leftrightarrow \quad n = \frac{2 \times 13{,}33}{0{,}43^2} = 144{,}2$$

Thus, in our study, sample size n1, n2 ≥ 145.

Patients were randomly divided into two groups:

+ Group 1: Treating bronchiolitis according to the routine protocol (aspirating sputum, breathing oxygen ...) and nebulizing Sodium chloride 3% 3 times/day.

+ Group 2: Treating bronchiolitis according to the routine protocol (aspirating sputum, breathing oxygen ...) and nebulizing Sodium chloride 0.9% 3 times/day.

2.2.3 Research content

2.2.3.1 Research variables and indicators

- Epidemiological parameters

Age (months): age of disease; Gender (male, female); Weight (kg); Gestational age (weeks): full term, preterm; Birth weight (kg); Way of birth: Normal birth, surgery; Living with school-age siblings; Living in the same house as someone who smokes.

Clinical symptoms at admission:

Body temperature at admission: Fever (body temperature > 37.5 degrees C), no fever (body temperature < 37.5 degrees C).

Measure oxygen saturation, heart rate measured by monitoring.

Symptoms: cough, wheezing, wheezing, runny nose.

Fast breathing (Rapid breathing compared to age: ≥ 60 times/minute (<2 months), ≥ 50 times/minute (2-12 months), ≥ 40 times/minute (12 months - 5 years old).

Chest concavity

Listen to the lungs:

Ventilation at entry: Normal, reduced in one area, reduced in many areas.

Pulmonary rales: whistling rales, moist rales, explosive rales.

Subclinical symptoms:

Total blood cell analysis, CRP concentration

X-ray of the chest straight

Bacterial culture of nasopharyngeal fluid and evaluated for RSV, Adenovirus, Rhinovirus using PCR technique.

Assess the correlation of risk factors with severity

The correlation analysis of children living with smokers is with severity.

Analyze the correlation between children living with siblings of school age with severity.

Correlation of birth pattern with severity.

Correlation analysis of gestational age with severity

Correlation analysis of birth weight with severity.

Correlation analysis of RSV, Rhinovirus and Adenovirus infection with severity.

Evaluation of the therapeutic effect of aerosol Sodium chloride 3%

Evaluation of the change of clinical symptoms in two study groups and evaluate symptom changes in severe bronchiolitis group:

Chest indrawing; Degree of wheezing; Lung rales; Breathing frequency; Heart rate; SpO2; MCBS score; Number of days in hospital for treatment.

2.2.3.2 Conduct research

Patients < 2 years old, diagnosed with acute bronchiolitis, hospitalized for treatment.

Ask medical history, medical history, clinical examination, and record information in the research medical record according to the form.

- Research group: Treat bronchiolitis according to the usual regimen (sputum aspiration, oxygen ventilation, fluid replacement, fever reduction...) and receive 3% Sodium chloride nebulized 3 times/day, 4ml/time.

- Control Group: Treatment of bronchiolitis according to the usual regimen (sputum aspiration, oxygen ventilation, fluid replacement, fever reduction, etc.) and aerosolized Sodium chloride 0.9% 3 times/day, 4 ml/time.

Perform aerosolization according to the protocol:

Step 1:

Prepare pediatric patients: Instruct the child's parents on how to hold the child and monitor during the aerosolization process. Remove sputum, drool if any.

Prepare aerosol equipment: plug in the nebulizer, try the aerosol mask, select the aerosol mode.

Prepare aerosol drugs: Sodium chloride 0.9%, Sodium chloride 3%.

Prepare other drugs: bronchodilators, emergency drugs.

Step 2:

Conduct aerosolization through the mask for children.

Monitor during aerosolization.

Adjust your posture accordingly during aerosolization.

Step 3:

End aerosol.

Clean up tools.

Absorb sputum if present.

Reassess the child's condition, follow up in the ward.

Evaluation of complications, complications, and undesirable effects during treatment.

*** Definitions used in research**

Table 2.6: MCBS scoreboard

Index	0 Point	1 Point	2 Points
Breathing frequency according to age at rest (*)	Normal	Fast	
Use accessory muscles of ventilation	No pulling	Average pulling	Heavy pulling
Breathe exchange (listen)	Normal	Reduce an area	Reduce multiple areas
Wheezing	No/Exhale at the end	Exhaling all time	Both inhale and exhale
Total score	Max = 7 points		

(*): Rapid breathing rate: ≥ 60 times/minute (< 2 months old); ≥ 50 times/minute (2 months - 1 year old); ≥ 40 times/minute (1-2 years old)

Based on the Modified Cincinnati Bronchiolitis Score (MCBS), it is possible to classify the severity of pediatric bronchiolitis when admitted to the hospital into three levels:

Minor: 0-2 points | Average: 3 - 5 points | Severe: 6 -7 points

2.2.4 Data analysis

The data were collected and processed using SPSS 22.0 software.

2.2.5 Control bias

Medical record samples and questionnaires were consulted with experts.

Learn from previous studies and complete the questionnaire before conducting the research.

2.2.6 Ethical aspects

The research topic strictly complies with research ethics in Medicine. The project has been approved by the Research Council of Hai Phong University of Medicine and Pharmacy, Department of Pediatrics - Bach Mai Hospital. Informed consent was obtained from the parents and guardians of the research subjects, they are explained, consulted, and commit to voluntarily participating in the research, and patient information is guaranteed to be kept confidential.

Chapter 3
RESEARCH RESULTS

3.1 Clinical epidemiological features

3.1.1 Epidemiological characteristics of the study group

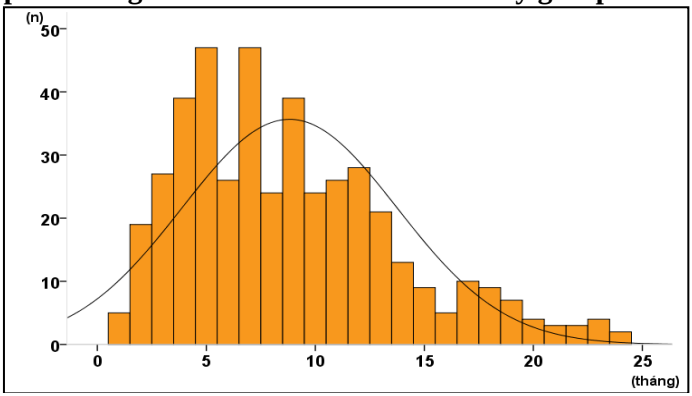

Figure 3.1: Age distribution in the study

Figure 3.1 showed that the age distribution in the study was found to be from 2 months old to 13 months old. The distribution rate in the group of children over 13 months is lower.

* The rate of moderate malnutrition in our study was 6.12% and severe malnutrition was 1.58%.

* The number of children hospitalized is highest in May, June, and July.

* The proportion of male patients in the study was 66.89% (295 children) more than female children (33.11% - 146 children).

3.1.2 Clinical features at admission

*** Symptoms at admission:** fever 64.9%, chest indrawing 90.7%; lung auscultation: 100% whistling rales and 55.55% moist rales.

*** Wheezing**

Table 3.1: Symptoms of wheezing at hospital admission

Symptoms of wheezing	Number of patients	Percentage
Exhale at the end	4	0.9
Exhale all time	44	10.0
Both time	393	89.1
Total	441	100

Table 3.1 showed that the highest rate of wheezing symptoms at hospital admission was heard in both periods with the rate of 89.1%.

*** Symptoms at admission:** fever 64.9%, chest indrawing 90.7%; lung auscultation: 100% whistling rales and 55.55% moist rales.

*** History at birth**

Table 3.2: Birth characteristics of the study group

The danger elements		Number of patients	Percentage
Gestational age	≤ 35 weeks	20	4.53
	> 35 weeks	421	95.47
The way to give birth	Surgery	158	35.83
	Normal birth	283	64.17
Weight at birth	≤ 2500g	31	7.03
	> 2500g	410	92.97

Table 3.2 showed that analysis of risk factors identified as preterm gestational age, cesarean section, weight less than 2500g in the study showed that the factor of cesarean section accounted for 35.83% was the highest and gestational age ≤ 35 weeks was the lowest with 4.53%.

3.1.4 The investigation results

Chest X-ray showed air congestion in 313 (70.97%), bronchial enhancement in 292 (66.21%).

PCR of nasopharyngeal fluid showed the percentage of RSV 106/358 (29.6%), Adenovirus 42/358 (11.73%), Rhinovirus 113/358 (31.56%)

3.2 Risk factors for severity of acute bronchiolitis

3.2.1 Children living with smokers

Table 3.3: The risk of children living with smokers affects the severity of bronchiolitis

Living with smokers	Severe acute bronchiolitis		Moderate acute bronchiolitis		OR (95%CI)	p
	n	%	n	%		
Yes	48	38.4	77	21.1	3.85 (2.38 – 6.23)	<0.05
No	45	14.2	271	77.9		
Total	93		348			

Table 3.3 showed that the group of children living with smokers had a severe rate of 38.4% higher than the group without a smoker with a severe rate of 13.9% ($p<0.05$). The analysis showed that the smoking group had a higher severity than the non-smoker group with a calculated OR of 3.85 (2.38 – 6.23).

3.2.2 The way to give birth

Table 3.4: Risks of birth method

Birth method	Severe acute bronchiolitis		Moderate acute bronchiolitis		OR (95%CI)	p
	n	%	n	%		
C-Section	35	21.7	126	78.3	1.049 (0.72-1.52)	> 0.05
Normal birth	58	20.7	222	79.3		
Total	93		348			

Table 3.4 showed that children born by cesarean section have a severe MCBS score of 21.7% and children born vaginally are 20.7%. The difference in severity rate of the 2 groups is not statistically significant with p>0.05.

The group of children born by cesarean section had the same rate of severe bronchiolitis as the group born vaginally with an OR of 1.049 (0.72-1.52).

3.2.3 Gestational age at birth

Table 3.5: Risk factors for gestational age at birth

Gestational age	Severe acute bronchiolitis		Moderate acute bronchiolitis		OR (95% CI)	p
	n	%	n	%		
≤ 34 weeks	9	45.0	11	55.0	3.28 (1.318 – 8.177	<0.05
> 34 weeks	84	19.95	337	80.05		
Total	93		348			

Table 3.5 showed that the group of preterm infants in the study had a MCBS severity rate of 50% higher than the full-term group of 19.95%. The difference is statistically significant with p < 0.05.

Assess the correlation between the group of children with gestational age ≤ 34 weeks whose severity is 3.28 times higher than the group of children with gestational age > 34 weeks.

3.2.4 Weight at birth

Table 3.6: Correlation of birth weight with MCBS score

Weight at birth	Severe acute bronchiolitis		Moderate acute bronchiolitis		OR (95% CI)	p
	n	%	n	%		
≤ 2500g	12	33.3	24	66.7	3.375 (2.14 – 5.32)	<0.05
> 2500g	81	14.07	324	85.93		
Total	93		348			

Table 3.6 showed that the group of children with birth weight ≤ 2500g had a severity level according to MCBS of 33.3% higher than the group with birth weight > 2500g with a rate of 14.07%. The difference is statistically significant with $p < 0.05$.

Analyzing the correlation between birth weight ≤ 2500g, the severity is 3.375 times higher than the group of children with birth weight > 2500g.

3.2.5 Correlation with virus infection

**** RSV***

Table 3.7: RSV infection

RSV	Severe acute bronchiolitis		Moderate acute bronchiolitis		OR (95%CI)	p
	n	%	n	%		
Positive	29	23,0	97	77	1,13 (0,769 – 1,668)	> 0,05
Negative	64	20,3	251	79,7		
Total	93	100	348	100		

Table 3.7 showed that RSV-positive patients had a severe rate of 23.0%, higher than the RSV-negative group (20.3%). However, the difference is not statistically significant with $p>0.05$. Analysis showed that children infected with RSV were 1.13 times more likely to have severe bronchiolitis than children without RSV infection.

**** Rhino virus***

Table 3.8: Rhino infection rate with severity

Rhino	Severe acute bronchiolitis		Moderate acute bronchiolitis		OR (95%CI)	p
	n	%	n	%		
Positive	33	27.05	89	72.95	1.60 (0.982 – 2.608)	< 0.05
Negative	60	18.81	259	81.19		
Total	93	100	348	100		

Table 3.8 showed that Rhino-positive patients had a severe rate of 27.0%, higher than the Rhino-negative group (18.8%). The difference was statistically significant with $p<0.05$.

Analysis shows that Rhino-infected pediatric patients are 1.6 times more likely to have severe bronchiolitis than Rhino-negative group.

3.3 Efficacy of sodium chloride 3% aerosol solution in the treatment

3.3.1 General characteristics of the two groups at hospital admission

*** Features of the patient**

Table 3.9: Features about age, gender, and weight of the two groups

Features		Intervention Group (n=276)	Control group (n=165)	p
Age (month)	$\overline{X} \pm SD$	8.68 ± 4.98	9.04 ± 4.85	> 0.05
	Min - max	1 - 24	1 - 23	
Weight (kg)	$\overline{X} \pm SD$	8.36 ± 2.02	8.38 ± 1.94	> 0.05
	Min - max	3.8 - 15	1 - 15	
Gender	Male	189 (68.5%)	106 (64.2%)	>0.05
	Female	87 (31.5%)	59 (35.8%)	>0.05

Table 3.9 showed that both groups were similar in age, gender, and weight.

*** MCBS scores at hospital admission of two groups**

Table 3.10: Distribution of MCBS scores at admission

MCBS Score	Intervention Group		Control group		p
	n	%	n	%	
3	29	10.5	19	11.5	> 0.05
4	113	40.9	72	43.6	> 0.05
5	77	27.9	49	24.2	> 0.05
6	50	18.1	27	16.4	> 0.05
7	7	2.5	7	4.2	> 0.05
Total	276	100	165	100	

Table 3.10 showed that the distribution of MCBS scores in the study was most common at 4 points in the study group of 113 children (40.9%) and 72 children in the control group (43.6%). There was no difference between the two study groups in the distribution of MCBS scores with p>0.05.

3.3.2 Changes in symptoms during treatment

*** Change in MCBS score in treatment**

Table 3.11: Change in MCBS score in treatment

Time		Intervention Group (n=276)	Control group (n=165)	p
At the admission	$\overline{X} \pm SD$ (Min–Max)	4.62 ± 0.98 (3 – 7)	4.58 ± 1.03 (3 – 7)	>0.05
Day 1	$\overline{X} \pm SD$ (Min–Max)	2.32 ± 0.98 (0 – 6)	2.46 ± 0.98 (1 – 06)	>0.05
Day 3	$\overline{X} \pm SD$ (Min–Max)	1.40 ± 0.67 (0 – 3)	1.55 ± 0.77 (0 – 4)	>0.05
		$p_{NC1} < 0.05$	$p_C < 0.05$	

Table 3.11 showed that MCBS scores of the two groups were highest at admission and decreased gradually with treatment days. On the 3rd day of treatment, the mean MCBS score of both groups was low with the mean level of the NC group of 1.40 ± 0.67 lower than that of the Control group of 1.55 ± 0.77. (p>0.05).

* Wheezing symptoms decreased after days of treatment in both the intervention group and the control group, but there was no difference between the two groups.

* Symptoms of chest indentation decreased better in the intervention group after 3 days of treatment, whistling rales in the intervention group also decreased better after 2 days of treatment.

3.3.3 Change in severe patients according to MCBS of two groups

* Change in wheezing symptoms

Table 3.12: Wheezing symptoms in severe patients

Treatment day	Intervention Group		Control group		p
	n	%	n	%	
At the admission	59	100	34	100	> 0.05
Day 2	28	47.45	26	76.47	**< 0.05**
Day 3	11	18.6	13	38.23	**< 0.05**

Table 3.12 showed that the improvement in wheezing symptoms of the intervention group was 0.9% better than the saline nebulization group for 2 days or more after treatment. The difference is statistically significant with $p < 0.05$.

* Symptoms of chest indentation, wheezing, breathing rate, heart rate, and SpO2 all improved better in the intervention group after 1 day of treatment.

*** MCBS Score**

Table 3.13: Change of MCBS in severe patients

Treatment day		Intervention Group (n=59)	Control group (n=34)	p
At the admission	$\overline{X} \pm SD$ (Min–Max)	6.12 ± 0.32 (6 – 7)	6.21 ± 0.41 (6 – 7)	>0.05
Day 2	$\overline{X} \pm SD$ (Min–Max)	3.75 ± 1.32 (1 – 6)	4.1 ± 1.19 (2 – 6)	**<0.05**
Day 3	$\overline{X} \pm SD$ (Min–Max)	2.84 ± 1.15 (1 – 5)	3.32 ± 1.22 (1 – 6)	**<0.05**
		$p_{NC1} < 0.05$	$p_C < 0.05$	

Table 3.13 showed that both groups in the study had MCBS scores gradually decreased with each day of treatment. In particular, the MCBS scores after 2 and 3 days of treatment of both groups in the study were lower than when entering the hospital. The difference is statistically significant with $p < 0.05$.

Chapter 4
DISCUSSION

4.1 Clinical epidemiological characteristics

4.1.1 Epidemiological features

*** Age**

During the period from January 2017 to December 2019, there were 441 children aged 1-24 months admitted to the Pediatric Department of Bach Mai Hospital who met the criteria for inclusion in the study. From table 3.1, it shows that the age group from 6 months to 13 months has the highest frequency. Analysis from the histogram shows that the parabolic peak occurs from the 4 month to 9 month age. The age group over 13 months was found to be significantly less than the age group from 4 months to 9 months. The results of our study are consistent with the pathology of acute bronchiolitis and are relatively similar to those reported by other authors in Vietnam and abroad.

In the study, author Nguyen Ngoc Phuc on the characteristics of moderate bronchiolitis was treated with 3% saline nebulizer. The age selected by the author is from 3 to 12 months old with an average age of 6.4 ± 2.5 months. Author Mr. Huy Thanh conducting a study on bronchiolitis at Children's Hospital 2 also selected 559 children aged 1 month to 2 years old. The author's research results also showed that the rate of children under 12 months old accounted for 86.4%. Research by Bui Binh Bao Son shows that the age under 12 months with bronchiolitis is 80.16%.

*** Number of patients hospitalized by month**

From the results of Figure 3.2 in our study, the number of hospitalized children diagnosed with bronchiolitis was highest in May with 75 children. In the study, the summer months of May, June, and July had the highest number of children hospitalized. RSV infections are often scattered throughout the year, increasing in the rainy season months from April to October, so depending on geographical location, climate each year as well as location, there are differences between regions.

In the study of Pham Thi Minh Hong, the number of children admitted to hospital in August was the highest, accounting for 12.08%, in September and October was 10.71% and 10.25% respectively. According to author Dang Thi Kim Huyen, October has the highest rate of hospitalized children with bronchiolitis. In the author's research, August, September, October, and November are the months with the highest rate. highest enrollment. Author Nguyen Ngoc Sang, author of statistics from 377 children with bronchiolitis, showed that the highest hospitalization rate was in March. The author's

research shows that the rate of children with bronchiolitis tends to increase more in winter and spring.

4.1.2 Features of symptoms at hospital admission

*** Features of wheezing symptoms at hospital admission**

According to the results of our study, the highest rate of wheezing symptoms at hospital admission was heard in both phases with the rate of 89.1%.

Author Nguyen Ngoc Phuc and his colleagues researched bronchiolitis and showed that wheezing symptoms in the study were 100%. In Dang Thi Kim Huyen's study, the rate of wheezing symptoms was 90.75%. In Thach Le Tin's study, wheezing symptoms were the reason for 29.88% of children being hospitalized. According to author Do Ngoc Thanh, VTPQ is the cause of wheezing symptoms in children from 2 months to 15 years old with a frequency of 36.8%.

The combination of clinical and paraclinical symptoms such as alveolar gas retention on radiographs is always consistent with the pathogenesis and pathophysiology of acute bronchiolitis.

4.1.3 Severity according to MCBS score

From the results of the study, we found that the distribution of MCBS scores in the study was most common at 4 points with a rate of 40.9% in the CT group and 43.6% in the control group.

The severity distribution in the study group and the control group was 20.6%. There was no difference between the two groups in the MCBS severity classification with $p>0.05$.

The results of our study are similar to those of the author Nguyen Ngoc Sang. In the author's study, the rate of children with severe diseases under 6 months old was 18%; the rate of children with severe bronchiolitis decreased gradually with age. in which group of 18 to 24 months old, there were no children with severe bronchiolitis according to MCBS score.

Nguyen Ngoc Phuc's study on 98 children with bronchiolitis and bronchiolitis treated with nebulized hypertonic saline 3% and salbutamol also used the MCBS score (improved Cincinnati score) to evaluate the effectiveness. In the author's research. Treatment with nebulized hypertonic saline and salbutamol improved MCBS scores. The median MCBS score decreased gradually from admission (median = 3) to day 3 (median = 0) after nebulizing 3% sodium chloride and remained at 0 until day 5.

In the world, multiple scorecards are used to assess the severity of children's acute bronchiolitis at admission. Susan Wu et al used the

Respiratory Distress Assessment Instrument (RDAI) score in the author's transcript. The criteria evaluated were related to auscultation and the degree of contractility of the respiratory muscles. In some studies, such as that of author Gaëlle Beal. Author Zhi - Yong Wang used the main score of severity, which is CSS (Wang clinical severity score). Jun Kubota used the GRSS and Wang scores to assess the severity of bronchiolitis and respiratory support measures on admission.

4.2 Some risk factors for the severity of acute bronchiolitis

4.2.1 Living with smokers

According to research results, the group of children who lived with a smoker had a severe rate of 38.4%, higher than the group who did not live with a smoker with a severe rate of 13.9%. The difference is statistically significant with $p < 0.05$. The analysis showed that the group living with a smoker had a severity level 3.85 times higher than the group not living with a smoker with an OR of 3.85 (2.38 – 6.23).

Many authors, when analyzing the factors that cause bronchiolitis and the risk of severe bronchiolitis, show that living with a smoker is a risk factor for children. In Susan Wu's study, the tobacco exposure rate of the two research groups was 9.1% in the NS group and 13.5% in the HS group, respectively. In the study of Pedro Flores, the drug exposure rate was 21.2% in the HS group and 17.1% in the NS group. Simran Grewal also found in the group of students, the rate of exposure to tobacco was 34.8%.

4.2.2 Correlation of gestational age with MCBS score

Premature newborns in the study had a severity rate according to MCBS of 45%, higher than the full-term newborn group of 19.95%. The difference is statistically significant with $p < 0.05$. Evaluate the correlation between gestational age and severity with OR of 3.28 (1.318 – 8.177).

Marcello Lanari conducted a study with the aim of evaluating the risk factors for hospitalization during the first year of life in children born at different gestational ages in Italy. The author selected a group of infants aged 33-34 weeks gestational age matched for sex and age with two groups of infants born at 35-37 weeks gestation and one group born when gestational age > 37 during pregnancy. three years (2009-2012). The results of the study included 2314 infants. of which 2210 (95.5 %) were followed for one year and included in the analysis; 120 (5.4 %) were hospitalized during the first year of life for bronchiolitis. Babies born between the ages of 33-34 weeks had a higher rate of hospitalization than the other two groups.

4.2.3 Correlation of birth weight with MCBS

According to the results, the birth weight characteristics of the two groups were different, but the difference was not statistically significant with p>0.05.

According to the results of the correlation between neonatal history and MCBS score, the group of children with birth weight ≤ 2500g, the severity according to MCBS was 33.3% higher than that of the group with birth weight > 2500g with the rate of 14.07%. The difference was statistically significant with p<0.05. Analysis of the correlation between birth weight and severity ratio according to MCBS score showed that the OR was 3.375 (2.14 – 5.32).

Author Thach Le Tin statistics of children's history of bronchiolitis, 7.29% of children weighing less than 2500g at birth. The rate of risk factors for bronchiolitis requiring hospitalization, factors <3 months of age, ranked first with the rate of 90.83%. Birth weight factor < 2500g ranked second with 26.66%.

In the research of the author Nguyen Ngoc Phuc and Phan Huu Nguyet Diem. The rate of children with bronchiolitis with birth weight below 2500g, accounted for 12.2%.

4.2.4 Correlation with RSV virus

*** Rhinovirus correlation with severity**

From the results of the study, we found that Rhinovirus infection has an increased risk of severity with OR=1.60. in which the Rhinovirus group had a risk of severe bronchiolitis 27.05% significantly higher than the group without Rhinovirus infection with a severe rate of 18.81%.

According to author Jonathan M. Mansbach statistics comparing RSV with RV showed. The rate of ICU stay of the RV infected group was the highest with 25% compared with 15% RSV infection and 18% RSV/RV superinfection.

4.3 Effect of aerosol Sodium chloride solution

4.3.1 Changes in the general research group

Symptoms of chest indrawing decreased better in the intervention group after 3 days of treatment, whistling rales in the intervention group also decreased better after 2 days of treatment.

The MCBS scores of the two groups were highest at admission and gradually decreased with the day of treatment. However, there was no difference between the two study groups.

4.3.2 Change in MCBS score in treatment

Symptoms of chest indrawing, whistling rales, breathing rate, heart rate, and SpO2 all improved better in the intervention group from 1 day after treatment.

The MCBS scores of the two groups were highest at admission and gradually decreased with the day of treatment. After 3 days of treatment, the average MCBS levels of both groups were low, the intervention group's average level was 2.84 ± 1.15, lower than the control group's 3.31 ± 1.22.

4.3.3. Hypertonic saline aerosol efficiency

Evaluation of the effectiveness of aerosol hypertonic sodium chloride in the treatment of acute bronchiolitis in children shows mixed results. Author Paula Heikkilä performed a meta-analysis that synthesized results from 18 studies on the evaluation of the effectiveness of nebulized hypertonic saline on 2102 children. In the results described in Table 2 in the author's research analysis, there are two studies using 7% saline. One study compared 6% and 3% salt concentrations. Two studies used 5% saline and most of the studies used 3% hypertonic saline. In the study results, there were differences in the length of hospital stay between studies. Many results show that nebulization of hypertonic saline reduces the length of hospital stay.

Zhang's most recent Cochrane review related to this topic concluded that hospitalized patients treated with aerosolized HS had statistically significantly shorter LOS than patients who received nebulizer alone. 0.9% normal saline (NS) or standard care only. According to author Heikkilä (2018) et al., aerosol HS also offers limited clinical benefit compared with NS but the heterogeneity between studies is significant. Similarly, a more recent RCT by Morikawa did not detect a difference in LOS between HS and NS. According to the author Nguyen Ngoc Phuc, the results of the treatment of VTP in combination with the ACE inhibitor Sodium chloride 3% and Salbutamol Clinical symptoms improved after 3 days of nebulizing hypertonic saline 3% Sodium chloride and Salbutamol.

CONCLUSION

Through the above research and discussion results, we would like to conclude that:

1. Clinical epidemiological characteristics of children with bronchiolitis

The disease is common in boys (66.89%) and at the age of 6 months to 12 months, the highest number of hospitalized children is from May to July.

Main clinical symptoms: wheezing (100%), rapid breathing (100%), chest indentation (90.7%), fever (64.9%). Severity according to MCBS score is 21.1%, average (78.9%). Paraclinical: Plain chest X-ray shows air congestion (70.97%). In addition to RSV (28.57%), there are also Rhinovirus (27.66%), Adenovirus (11.79%).

2. Factors affecting the severity of bronchiolitis

- Children who live with smokers are 3.85 times more likely to have severe bronchiolitis than children who do not live with smokers.

- The group of children with gestational age at birth <34 weeks is 3.28 times more likely to have severe bronchiolitis than the group of children with gestational age > 34 weeks.

- The group of children with birth weight ≤ 2500g is 3,375 times more likely to have severe bronchiolitis than the group of children with birth weight > 2500g.

3. Results of 3% hypertonic saline nebulization treatment

On the 3rd day of treatment: Wheezing symptoms in the intervention group were 21.7% lower than in the control group 24.5% . The rate of thoracic indentation in the intervention group was 2.89% and the control group was 3.6% ($p<0.05$). Symptoms of whistling rales (67.03%) in the intervention group were lower than in the control group (71.5%).

Severe pediatric patients according to the MCBS scale after 2 and 3 days of treatment:

- Wheezing symptoms decreased more clearly in the intervention group (47.45% and 18.6%) compared to the control group (76.47% and 38.23%), chest indrawing symptoms in the intervention group (20.33% and 3.3%) decreased compared to the control group (32.35% and 17.6%), wheezing symptoms in the intervention group (38.9% and 10.1%) were lower than with the control group (52.94% and 29.4%). MCBS score, breathing

frequency, SpO2, and heart rate in the intervention group also improved better than the control group.

RECOMMENDATIONS

From the research results, we make the following recommendations:

- When approaching a child < 24 months with fever, tachypnea, wheezing, and chest indrawing, they should be hospitalized to obtain a definitive diagnosis and immediate treatment.

- Cases of premature infants, low birth weight infants, and children living in the same house with preschool-aged siblings need to be closely monitored when the child has acute bronchiolitis. Children should not live with people who smoke.

- Hypertonic saline 3% nebulization should be applied to children with severe and moderate acute bronchiolitis, especially children with severe severity according to the MCBS score scale.

- Further studies are needed to verify the effectiveness of 3% hypertonic saline nebulization in children with severe bronchiolitis with a larger sample size and in many different centers.