



Original Research Article

Comparison of Efficacy Between Nebulized 3% Solution in Bronchiolitis vs 7% Hypertonic Solution in Bronchiolitis

Article History:

Name of Author:

Akasha Bint E Athar¹, Emran Roshan², Abdul Rehman Akram³, Asma Arif⁴, Atikaa Rashid⁵, Areej Bajwa⁶

Affiliation: ^{1,3,5} MBBS, FCPS (Pediatrics), Post Graduate Resident PGR at Department of Pediatrics, Sughra Shafi Medical Complex (SSMC) / Sahara Medical College, Narowal

² MBBS, FCPS (Pediatrics), Professor & Head of Department of Pediatric Sughra Shafi Medical Complex (SSMC) / Sahara Medical College, Narowal

⁴ MBBS, FCPS (Pediatrics), Senior Registrar at Department of Pediatrics, Sughra Shafi Medical Complex (SSMC) / Sahara Medical College, Narowal

⁶ MBBS, FCPS (Pediatrics), House Officer at Department of Pediatrics, Sughra Shafi Medical Complex (SSMC) / Sahara Medical College, Narowal

Corresponding Author:

Dr. Akasha Bint E

Received: 12-11-2025

Revised: 25-11-2025

Accepted: 20-12-2025

Published: 30-12-2025

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-Noncommercial-Share Alike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Abstract: Background: Bronchiolitis is one of the most common causes of lower respiratory tract infection and hospitalization among infants and young children. Nebulized hypertonic saline has been used as an adjunctive therapy to improve mucociliary clearance and reduce airway edema; however, evidence regarding the optimal concentration remains inconsistent. **Objectives:** To compare the efficacy between Nebulized 3% solution and 7% hypertonic solution in children with bronchiolitis. **Study Design & Setting:** This study was conducted in the Department of Pediatrics, Sughra Shafi Medical Complex, Narowal from 1st February 2025 to 1st August 2025. **Methodology:** A total of 150 children aged 2–24 months with clinical diagnosis of bronchiolitis were enrolled using non-probability consecutive sampling and were allocated into two equal groups. Group A (n=75) received Nebulized 3% solution, while Group B (n=75) received 7% hypertonic solution along with standard supportive treatment. Baseline demographic and clinical characteristics were recorded. Efficacy was assessed using post-treatment clinical severity score, respiratory rate, oxygen saturation, and duration of hospital stay. Data were analyzed using SPSS version 26.0 and p-value ≤ 0.05 was considered statistically significant. **Results:** The mean age was 8.94 ± 4.12 months in Group A and 9.27 ± 4.35 months in Group B. Post-treatment respiratory rate was lower in Group B (41.88 ± 4.92 breaths/min) compared with Group A (45.12 ± 5.61 breaths/min) ($p=0.001$). Oxygen saturation improved to $96.22 \pm 1.28\%$ in Group B versus $95.08 \pm 1.47\%$ in Group A ($p<0.001$). Clinical severity score after treatment was lower in Group B (2.89 ± 0.98) than Group A (3.64 ± 1.12) ($p<0.001$). Mean hospital stay was shorter in Group B (3.68 ± 1.09 days) compared with Group A (4.52 ± 1.33 days) ($p<0.001$). Overall efficacy was observed in 84.0% of Group B and 66.7% of Group A patients ($p=0.014$). **Conclusion:** Nebulized 7% hypertonic solution demonstrated greater efficacy than Nebulized 3% solution in improving clinical outcomes and reducing hospital stay among children with bronchiolitis.

Keywords: Bronchiolitis, Efficacy, Hypertonic saline, Nebulization, Pediatrics, Respiratory distress.

INTRODUCTION

Bronchiolitis is an acute viral lower respiratory tract infection characterized by inflammation, edema, and obstruction of the small airways (bronchioles), predominantly affecting infants and young children below two years of age.¹ The disease is clinically recognized by symptoms of upper respiratory tract

infection followed by respiratory distress, wheezing, and impaired gas exchange. Because bronchiolitis mainly affects anatomically narrow pediatric airways, even minimal mucosal edema and increased secretions may produce significant airflow limitation and respiratory compromise.²

The etiology of bronchiolitis is predominantly viral,

with respiratory syncytial virus (RSV) identified as the most common causative agent. Other implicated pathogens include rhinovirus, human metapneumovirus, parainfluenza virus, influenza virus, adenovirus, and coronavirus species.^{3,4} Several risk factors have been associated with increased susceptibility and severity, including prematurity, low birth weight, younger age, lack of breastfeeding, overcrowded living conditions, exposure to environmental tobacco smoke, underlying cardiopulmonary disease, immunodeficiency states, and malnutrition.⁵ The pathophysiology of bronchiolitis involves viral invasion of bronchiolar epithelial cells, resulting in epithelial injury, inflammatory cell infiltration, edema of airway walls, mucus hypersecretion, and accumulation of cellular debris. These changes lead to narrowing and obstruction of small airways, causing air trapping, ventilation-perfusion mismatch, increased work of breathing, and impaired oxygen exchange. In severe cases, progressive respiratory compromise may culminate in hypoxemia and respiratory failure.^{6,7}

Current management of bronchiolitis is largely supportive and includes maintenance of hydration, oxygen supplementation when indicated, nasal suctioning, and monitoring of respiratory status. Pharmacological interventions such as bronchodilators, corticosteroids, and antibiotics have demonstrated inconsistent benefits and are not routinely recommended. Nebulized hypertonic saline has emerged as a therapeutic option because of its proposed ability to reduce airway edema, improve mucociliary clearance, and facilitate secretion removal.⁸ Among different concentrations, 3% hypertonic saline has been widely used in clinical practice and evaluated across multiple studies. More recently, 7% hypertonic saline has gained attention because of the possibility of enhanced osmotic action and greater improvement in airway clearance.^{9,10}

Previous studies evaluating 3% and 7% hypertonic saline have reported inconsistent findings regarding reduction in clinical severity scores, improvement in respiratory symptoms, and duration of hospital stay. Moreover, most available evidence originates from international populations with variable treatment protocols and patient characteristics, limiting direct applicability to local settings. In Pakistan, local comparative data evaluating the efficacy of nebulized 3% solution versus 7% hypertonic solution in bronchiolitis are scarce. Therefore, this study may provide indigenous evidence to support evidence-based selection of nebulized hypertonic saline concentration and contribute to optimizing management strategies for bronchiolitis in pediatric practice.

MATERIALS AND METHODS

This study was conducted in the Department

of Pediatrics of Sughra Shafi Medical Complex, Narowal Department of Pediatrics, Sughra Shafi Medical Complex, Narowal from 1st February 2025 to 1st August 2025 after approval from the Institutional Ethical Review Committee. A total of 150 patients diagnosed with bronchiolitis were included in the study using non-probability consecutive sampling technique. The sample size of 150 patients (75 patients in each group) was calculated by considering a 95% confidence level, 80% power of study, and anticipated difference in efficacy between nebulized 3% solution and 7% hypertonic solution reported in previous literature. The calculated sample size was further adjusted to achieve equal allocation and improve study precision.

Children aged 2 months to 24 months of either gender presenting with clinical diagnosis of bronchiolitis were included in the study. Bronchiolitis was diagnosed on the basis of first episode of wheezing associated with symptoms of viral upper respiratory tract infection including cough, rhinorrhea, tachypnea, respiratory distress, and chest findings suggestive of lower respiratory tract involvement. Patients with congenital heart disease, chronic lung disease, previous history of recurrent wheeze or bronchial asthma, severe malnutrition, immunodeficiency disorders, need for immediate mechanical ventilation, or known hypersensitivity to nebulization solutions were excluded from the study.

After obtaining informed written consent from parents or guardians, demographic details including age, gender, weight, duration of symptoms, and baseline clinical findings were recorded on a structured proforma. Patients were allocated into two equal groups using lottery method. Group A received nebulized 3% solution, while Group B received nebulized 7% hypertonic solution. Nebulization was administered according to departmental protocol at prescribed intervals during hospital stay in addition to standard supportive management including oxygen therapy, hydration, and nasal suctioning where indicated. Patients were monitored clinically throughout admission. Efficacy was assessed by improvement in bronchiolitis severity parameters including respiratory rate, oxygen saturation, wheezing, chest retractions, and overall clinical severity score after treatment. Duration of hospital stay and requirement for escalation of respiratory support were also documented where applicable.

All collected data were entered and analyzed using Statistical Package for Social Sciences (SPSS) version 26.0. Quantitative variables such as age, duration of symptoms, clinical severity score, and hospital stay were presented as mean $\pm$ standard deviation. Qualitative variables such as gender and efficacy were presented as frequency and percentage. Efficacy between both groups was compared using Chi-square

test, while independent sample t-test was applied for comparison of quantitative outcomes. Stratification was performed for age, gender, and baseline disease

severity to control effect modifiers. Post-stratification Chi-square test was applied and p-value ≤ 0.05 was considered statistically significant.

RESULTS

The study included a total of 150 patients, with 75 patients allocated to Group A (Neb 3% Solution) and 75 patients allocated to Group B (7% Hypertonic Solution). The mean age of patients in Group A was 8.94 ± 4.12 months, while in Group B it was 9.27 ± 4.35 months ($p=0.638$). In Group A, 52 (69.3%) patients were aged ≤ 12 months and 23 (30.7%) were aged >12 months, whereas Group B included 46 (61.3%) patients aged ≤ 12 months and 29 (38.7%) aged >12 months ($p=0.304$). Regarding gender distribution, males constituted 42 (56.0%) and females 33 (44.0%) in Group A, while Group B included 45 (60.0%) males and 30 (40.0%) females ($p=0.618$). The mean weight was 7.46 ± 1.88 kg in Group A and 7.61 ± 1.95 kg in Group B ($p=0.629$). The mean duration of symptoms was 3.82 ± 1.21 days in Group A and 3.94 ± 1.35 days in Group B ($p=0.571$), as given in Table 1.

Table 1: Baseline Demographic Characteristics of Study Participants (n=150)

Variable	Group A (Neb 3% Solution) n=75	Group B (7% Hypertonic Solution) n=75	p-value
Age (months)	8.94 ± 4.12	9.27 ± 4.35	0.638
≤12 months	52 (69.3%)	46 (61.3%)	0.304
>12 months	23 (30.7%)	29 (38.7%)	
Gender			
Male	42 (56.0%)	45 (60.0%)	0.618
Female	33 (44.0%)	30 (40.0%)	
Weight (kg)	7.46 ± 1.88	7.61 ± 1.95	0.629
Duration of symptoms (days)	3.82 ± 1.21	3.94 ± 1.35	0.571

Baseline clinical characteristics showed comparable findings between both treatment groups. The mean respiratory rate at presentation was 57.42 ± 6.83 breaths/min in Group A and 58.15 ± 6.21 breaths/min in Group B ($p=0.495$). Mean oxygen saturation was recorded as $91.28 \pm 2.14\%$ in Group A and $91.05 \pm 2.36\%$ in Group B ($p=0.532$). Similarly, the mean baseline clinical severity score was 6.92 ± 1.08 in Group A and 7.01 ± 1.16 in Group B ($p=0.624$), as given in Table 2.

Table 2: Baseline Clinical Characteristics of Bronchiolitis Patients (n=150)

Variable	Group A (Neb 3% Solution) n=75	Group B (7% Hypertonic Solution) n=75	p-value
Respiratory Rate (breaths/min)	57.42 ± 6.83	58.15 ± 6.21	0.495
Oxygen Saturation (%)	91.28 ± 2.14	91.05 ± 2.36	0.532
Clinical Severity Score	6.92 ± 1.08	7.01 ± 1.16	0.624

Post-treatment comparison demonstrated improvement in clinical outcomes in both groups. The mean respiratory rate after treatment was 45.12 ± 5.61 breaths/min in Group A and 41.88 ± 4.92 breaths/min in Group B ($p=0.001$). Mean oxygen saturation after treatment was $95.08 \pm 1.47\%$ in Group A and $96.22 \pm 1.28\%$ in Group B ($p<0.001$). The mean post-treatment clinical severity score was 3.64 ± 1.12 in Group A and 2.89 ± 0.98 in Group B ($p<0.001$). The mean duration of hospital stay was 4.52 ± 1.33 days in Group A compared to 3.68 ± 1.09 days in Group B ($p<0.001$), as given in Table 3.

Table 3: Comparison of Post-Treatment Clinical Outcomes Between Groups (n=150)

Variable	Group A (Neb 3% Solution) n=75	Group B (7% Hypertonic Solution) n=75	p-value
Respiratory Rate after treatment (breaths/min)	45.12 ± 5.61	41.88 ± 4.92	0.001
Oxygen Saturation after treatment	95.08 ± 1.47	96.22 ± 1.28	<0.001
Clinical Severity Score after treatment	3.64 ± 1.12	2.89 ± 0.98	<0.001
Hospital Stay (days), Mean $\pm$ SD	4.52 ± 1.33	3.68 ± 1.09	<0.001

Comparison of efficacy between the two groups revealed that efficacy was achieved in 50 (66.7%) patients in Group A and 63 (84.0%) patients in Group B. Ineffective response was observed in 25 (33.3%) patients receiving Neb 3% Solution and in 12 (16.0%) patients receiving 7% Hypertonic Solution. Overall, efficacy was observed in 113 (75.3%) patients with a statistically significant difference between groups ($p=0.014$), as given in Table 4.

Table 4: Comparison of Efficacy Between Both Groups (n=150)

Efficacy	Group A (Neb 3% Solution) n=75	Group B (7% Hypertonic Solution) n=75	Total	p-value
Effective	50 (66.7%)	63 (84.0%)	113 (75.3%)	0.014
Ineffective	25 (33.3%)	12 (16.0%)	37 (24.7%)	

Stratification analysis was performed with respect to age, gender, and baseline clinical severity score. Among patients aged ≤ 12 months, efficacy was observed in 34 (65.4%) patients in Group A and 44 (86.3%) patients in Group B ($p=0.015$), whereas among patients aged >12 months efficacy was reported in 16 (69.6%) and 19 (79.2%) patients respectively ($p=0.438$). According to gender, efficacy among males was observed in 29 (69.0%) patients in Group A and 38 (84.4%) patients in Group B ($p=0.088$), while among females efficacy was noted in 21 (63.6%) and 25 (83.3%) patients respectively ($p=0.072$). Regarding baseline clinical severity score, patients with score ≤ 7 showed efficacy in 31 (70.5%) cases in Group A and 39 (88.6%) cases in Group B ($p=0.034$), while among patients with score >7 , efficacy was observed in 19 (61.3%) and 24 (77.4%) patients respectively ($p=0.168$), as given in Table 5.

Table 5: Stratification of Efficacy with Respect to Age, Gender and Baseline Clinical Severity Score (n=150)

Variable	Group A Effective n (%)	Group B Effective n (%)	p-value
Age Group			
≤ 12 months (n=98)	34 (65.4%)	44 (86.3%)	0.015
>12 months (n=52)	16 (69.6%)	19 (79.2%)	0.438
Gender			
Male (n=87)	29 (69.0%)	38 (84.4%)	0.088
Female (n=63)	21 (63.6%)	25 (83.3%)	0.072
Baseline Clinical Severity Score			
Score ≤ 7 (n=88)	31 (70.5%)	39 (88.6%)	0.034
Score >7 (n=62)	19 (61.3%)	24 (77.4%)	0.168

DISCUSSION

The disease is characterized by inflammation, edema, and mucus accumulation within the bronchioles, leading to airway obstruction and respiratory distress. Management is primarily supportive; however, nebulized hypertonic saline has been increasingly used because of its potential to improve mucociliary clearance and reduce airway edema.¹¹ Among different concentrations, 3% hypertonic saline has been commonly used in routine practice, while 7% hypertonic saline has emerged as a possible alternative with greater osmotic effect.^{12,13} Therefore, comparative evaluation of nebulized 3% solution and 7% hypertonic solution remains clinically relevant in optimizing bronchiolitis management.

The present study compared the efficacy between Nebulized 3% solution and 7% hypertonic solution in children with bronchiolitis and demonstrated superior outcomes with 7% hypertonic solution across multiple clinical parameters. Baseline characteristics between both treatment groups remained comparable, with mean age of 8.94 ± 4.12 months in Group A and

9.27 ± 4.35 months in Group B ($p=0.638$), similar gender distribution ($p=0.618$), and comparable baseline respiratory rate (57.42 ± 6.83 vs 58.15 ± 6.21 breaths/min; $p=0.495$), oxygen saturation ($91.28 \pm 2.14\%$ vs $91.05 \pm 2.36\%$; $p=0.532$), and clinical severity score (6.92 ± 1.08 vs 7.01 ± 1.16 ; $p=0.624$). Following treatment, patients receiving 7% hypertonic solution achieved significantly lower respiratory rate (41.88 ± 4.92 vs 45.12 ± 5.61 breaths/min; $p=0.001$), higher oxygen saturation ($96.22 \pm 1.28\%$ vs $95.08 \pm 1.47\%$; $p<0.001$), lower clinical severity score (2.89 ± 0.98 vs 3.64 ± 1.12 ; $p<0.001$), shorter hospital stay (3.68 ± 1.09 vs 4.52 ± 1.33 days; $p<0.001$), and greater overall efficacy (84.0% vs 66.7%; $p=0.014$).

Our findings are consistent with the observations reported by Al-Ansari et al. (2010), who evaluated different concentrations of hypertonic saline and demonstrated progressively better outcomes with increasing saline concentration. Their study reported mean bronchiolitis severity score at 48 hours of 3.69 ± 1.09 with 5% saline, 4.00 ± 1.22 with 3% saline,

and 4.12 ± 1.11 with normal saline. Although our study compared 7% and 3% hypertonic solutions rather than normal saline, the lower post-treatment clinical severity score observed in the 7% group (2.89 ± 0.98) compared with the 3% group (3.64 ± 1.12) supports the concept that higher saline concentrations may provide greater clinical improvement through enhanced airway hydration and mucociliary clearance.¹⁴

The findings of Pandit et al. (2022) partially support our results. Their study comparing 3% hypertonic saline with normal saline plus salbutamol demonstrated improvement in oxygen saturation and clinical severity over time; however, between-group differences remained statistically non-significant. Mean duration of oxygen therapy was 33.6 ± 21.7 hours versus 36.8 ± 22.5 hours ($p > 0.05$), and mean hospital stay was 2.91 ± 1.54 versus 3.09 ± 1.85 days ($p > 0.05$). In contrast, our study observed statistically significant improvement in oxygen saturation ($96.22 \pm 1.28\%$ vs $95.08 \pm 1.47\%$; $p < 0.001$) and significantly reduced hospital stay (3.68 ± 1.09 vs 4.52 ± 1.33 days; $p < 0.001$). This difference may be attributed to direct comparison of two hypertonic saline concentrations rather than comparison against normal saline and bronchodilator therapy.¹⁵

Our results also align with Yu et al. (2022), who reported that nebulized 3% hypertonic saline significantly reduced hospital stay, improved clinical severity score, reduced oxygen requirement, and improved respiratory distress compared with normal saline. Similarly, in the present study both treatment groups demonstrated clinical improvement; however, patients treated with 7% hypertonic solution experienced superior outcomes, indicating that increasing saline concentration may further enhance therapeutic response beyond the benefits already demonstrated with 3% saline.¹⁶

The observations of Wu et al. (2014) are also comparable to our findings. Their randomized trial emphasized respiratory outcomes and length of hospital stay as principal endpoints and demonstrated favorable effects of hypertonic saline in infants with bronchiolitis. Our findings extend these observations by demonstrating that among hypertonic saline concentrations themselves, 7% solution was associated with shorter hospitalization and greater improvement in respiratory parameters.¹⁷ Similarly, Teunissen et al. (2014) compared 3%, 6%, and normal saline and evaluated length of hospital stay, supplemental oxygen requirement, and feeding support. Their findings suggested clinical benefits associated with hypertonic saline use. The present study further contributes to this evidence by evaluating an even higher concentration (7%) and demonstrating improved oxygen saturation and reduced hospitalization duration. The higher oxygen

saturation achieved in our 7% group ($96.22 \pm 1.28\%$) compared with the 3% group ($95.08 \pm 1.47\%$) may reflect enhanced osmotic action facilitating secretion clearance.¹⁸

Our findings were also comparable with Ngo et al. (2024), who conducted a randomized trial involving 140 infants and reported significantly lower clinical severity score (median 1 vs 2; $p < 0.001$) and reduced hospital stay (5 vs 7 days; $p < 0.001$) with nebulized hypertonic saline. Likewise, our study demonstrated significantly lower post-treatment clinical severity score (2.89 ± 0.98 vs 3.64 ± 1.12 ; $p < 0.001$) and reduced duration of hospitalization (3.68 ± 1.09 vs 4.52 ± 1.33 days; $p < 0.001$), supporting the beneficial role of hypertonic saline in improving clinical recovery.¹⁹ Among Pakistani studies, Omparkash et al. (2023) reported mean hospital stay of 61.7 ± 14.5 hours in the hypertonic saline group compared with 81.4 ± 18.2 hours in the normal saline plus salbutamol group and observed reduced oxygen therapy duration (13.5 ± 4.2 vs 23.8 ± 4.9 hours) with rapid recovery in 91.67% of patients.²⁰

Goheer et al. (2023) reported mean ages of 14.37 ± 4.31 months and 15.80 ± 4.15 months in study groups and observed significantly shorter hospital stay with hypertonic saline (3.533 vs 4.266 days; $p = 0.000$). Our population was relatively younger with mean ages below 10 months in both groups, yet the trend remained consistent, with significantly reduced hospital stay among patients receiving 7% hypertonic solution (3.68 ± 1.09 vs 4.52 ± 1.33 days; $p < 0.001$).²¹ Abid et al. (2024) demonstrated comparable baseline characteristics and reported significantly shorter hospital stay (45.92 ± 12.19 vs 75.53 ± 43.87 ; $p = 0.000$) and shorter duration of nebulization among oxygen-requiring patients (10.67 ± 7.91 vs 27.21 ± 26.20 ; $p = 0.03$), although clinical severity score remained non-significant (4.50 ± 2.88 vs 5.42 ± 2.88 ; $p = 0.921$). In contrast, our study showed statistically significant improvement in clinical severity score (2.89 ± 0.98 vs 3.64 ± 1.12 ; $p < 0.001$), suggesting that comparison of higher saline concentration may provide more measurable improvement in symptom severity.²²

The findings reported by Mazhar S et al. (2024) strongly support our results. Their study demonstrated significantly improved oxygen saturation at discharge ($98.3 \pm 0.60\%$ vs $97.6 \pm 0.91\%$; $p < 0.001$), progressive reduction in clinical severity score over time with values reaching 2.6 ± 0.59 versus 3.9 ± 0.66 at 48 hours ($p < 0.001$), and shorter oxygen therapy duration (16.2 ± 2.47 vs 23.3 ± 2.37 hours; $p < 0.001$). Comparable improvements were observed in our study, where oxygen saturation increased significantly and clinical severity score decreased substantially in the 7% group.

However, our findings contrast with Shahzad et al.

(2022), who reported statistically better outcomes with normal saline compared with hypertonic saline for change in clinical severity score and duration of hospital stay ($p=0.001$). In contrast, our results demonstrated superior efficacy of higher concentration hypertonic saline. Differences in patient selection, severity profile, treatment protocol, outcome definitions, and comparison groups may explain the variation in findings.²³

Study Limitations

This study was conducted at a single center, which may limit generalizability of findings to broader populations. Follow-up was restricted to the duration of hospital stay and long-term clinical outcomes were not assessed. Additionally, virological confirmation and evaluation of individual causative pathogens were not performed.

CONCLUSION

Nebulized 7% hypertonic solution demonstrated better efficacy compared with nebulized 3% solution in the management of bronchiolitis. Patients receiving 7% hypertonic solution showed greater improvement in clinical parameters and shorter hospital stay. These findings support consideration of 7% hypertonic solution as an effective therapeutic option in children with bronchiolitis.

Acknowledgement: We sincerely acknowledge the support and guidance of our mentors, colleagues, and the staff of the participating hospital for their valuable assistance throughout this study..

Conflict of Interest: No

Funding Disclosure: None

REFERENCES

1. Orzolek I, Ambrożej D, Makrinioti H, Zhu Z, Jartti T, Feleszko W. Severe bronchiolitis profiling as the first step towards prevention of asthma. *Allergologia et immunopathologia*. 2023 May 1;51(3):99-107.
2. Short R, Short C, Gawlik KS, Teall AM, Pittman O, Exacerbation A. Evidence-Based Assessment of the Lungs and Respiratory System. Evidence-Based Physical Examination: Best Practices for Health and Well-Being Assessment. 2024 Mar 26;247.
3. Hon KL, Leung AK, Wong AH, Dudi A, Leung KK. Respiratory syncytial virus is the most common causative agent of viral bronchiolitis in young children: an updated review. *Current pediatric reviews*. 2023 May 1;19(2):139-49.
4. Rodriguez-Fernandez R, González-Sánchez MI, Perez-Moreno J, González-Martínez F, de la Mata Navazo S, Mejias A, Ramilo O. Age and respiratory syncytial virus etiology in bronchiolitis clinical outcomes. *Journal of Allergy and Clinical Immunology: Global*. 2022 Aug 1;1(3):91-8.
5. Hunter PJ, Awoyemi T, Ayede AI, Chico RM, David AL, Dewey KG, Duggan CP, Gravett M, Prendergast AJ, Ramakrishnan U, Ashorn P. Biological and pathological mechanisms leading to the birth of a small vulnerable newborn. *The Lancet*. 2023 May 20;401(10389):1720-32.
6. Moretti C, Gizzi C, Barbara CS, Pozzi N, Midulla F, Cogo P. Severe Bronchiolitis as a Cause of ARDS in Early Childhood. Pathophysiology and Strategies to Minimize Lung Injury. *Medical Research Archives*. 2022 Jun 1;10(5).
7. Sadek As, Abd-Elghaffar Sk, Radad K, Hassanein K, Gamaleldin Ma, Hassan AK. Pathology and molecular detection of infectious bronchitis virus infection in broiler chickens. *Assiut Veterinary Medical Journal*. 2024 Jul 1;70(182):178-91.
8. De Luca D, Pezza L, Vivalda L, Di Nardo M, Lepainteur M, Baraldi E, Piastra M, Ricciardi W, Conti G, Gualano MR. Critical care of severe bronchiolitis during shortage of ICU resources. *EClinicalMedicine*. 2024 Mar 1;69.
9. Hourmant Y, Huard D, Latte DD, Bouras M, Asehnoune K, Pirrachio R, Roquilly A. Effect of continuous infusion of hypertonic saline solution on survival of patients with brain injury: a systematic review and meta-analysis. *Anaesthesia Critical Care & Pain Medicine*. 2023 Apr 1;42(2):101177.
10. Holden DN, Mucksavage JJ, Cokley JA, Kim KS, Tucker NL, Esordi MS, Cook AM. Hypertonic saline use in neurocritical care for treating cerebral edema: a review of optimal formulation, dosing, safety, administration and storage. *American Journal of Health-System Pharmacy*. 2023 Mar 15;80(6):331-42.
11. Aegerter H, Lambrecht BN. The pathology of asthma: what is obstructing our view?. *Annual Review of Pathology: Mechanisms of Disease*. 2023 Jan 24;18(1):387-409.
12. Safiejko K, Smereka J, Pruc M, Ladny JR, Jaguszewski MJ, Filipiak KJ, Yakubtsevich R, Szarpak L. Efficacy and safety of hypertonic saline solutions fluid resuscitation on hypovolemic shock: A systematic review and meta-analysis of randomized controlled trials. *Cardiology journal*. 2022;29(6):966-77.
13. Martínez-Sánchez FD, Gutierrez-Rosas LE, Barranco-Hernandez LH, Gonzalez-Alvarez G, Bastida-Castro LA, Rocha-Haro A, Barrientos-Cabrera G, Martínez-Cabrera CF, Balderas-Juarez J, Salinas-Ramirez MA, Hernandez-Castillo JL. Hyponatremia: Evolving diagnostics and emerging therapeutics in clinical practice. *World Journal of Nephrology*. 2026 Mar 25;15(1):115252.
14. Al-Ansari K, Sakran M, Davidson BL, El Sayyed R, Mahjoub H, Ibrahim K. Nebulized 5% or 3% hypertonic or 0.9% saline for treating acute bronchiolitis in infants. *The Journal of pediatrics*.

2010 Oct 1;157(4):630-4.

15. Pandit P, Hoque MA, Pandit H, Dhar SK, Mondal D, Ahmad F. Efficacy of nebulized hypertonic saline (3%) versus normal saline and salbutamol in treating acute bronchiolitis in a tertiary hospital: a randomized controlled trial. *Mymensingh medical journal: MMJ*. 2022 Apr 1;31(2):295-303.
16. Yu JF, Zhang Y, Liu ZB, Wang J, Bai LP. 3% nebulized hypertonic saline versus normal saline for infants with acute bronchiolitis: A systematic review and meta-analysis of randomized controlled trials. *Medicine*. 2022 Oct 28;101(43):e31270.
17. Wu S, Baker C, Lang ME, Schrager SM, Liley FF, Papa C, Mira V, Balkian A, Mason WH. Nebulized hypertonic saline for bronchiolitis: a randomized clinical trial. *JAMA pediatrics*. 2014 Jul;168(7):657-63.
18. Teunissen J, Hochs AH, Vaessen-Verberne A, Boehmer AL, Smeets CC, Brackel H, van Gent R, Wesseling J, Logtens-Stevens D, de Moor R, Rosias PP. The effect of 3% and 6% hypertonic saline in viral bronchiolitis: a randomised controlled trial. *European Respiratory Journal*. 2014 Sep 30;44(4):913-21.
19. Ngo QC, La QP, Le SH, Do Tran H, Le VV. The Efficacy of Nebulized 3% Hypertonic Saline for Acute Bronchiolitis in Infants: A Randomized Controlled Trial. *Brieflands*; 2025.
20. Omparkash Al, Laghari Tm, Sirichand Ma, Aslam M. Compare the Clinical Severity and Length of Hospital Stay in Children with Bronchiolitis Treated with the 3% Hypertonic Saline Nebulization Versus Normal Saline and Salbutamol. *Pakistan Journal of Medical & Health Sciences*. 2023;17(03):448-52
21. Goheer L, Ahmad AM, Nadeem MT, Haq ZU, Khattak SZ, Bashir J. Comparison of Hypertonic Saline and Salbutamol Nebulization in Children with Acute Bronchiolitis in a Tertiary Care Hospital. *Pakistan Pediatric Journal*. 2023;47(4):892-97.
22. Abid U, Afzal A, Zaman N, Farooq A, Yousaf S, Fazal S. Comparing Treatment with Nebulized 3% Hypertonic Saline Versus Nebulized 0.9% Saline In Patients With Acute Bronchiolitis: A Double-Blind Randomized Controlled Trial. *Journal of Rawalpindi Medical College*. 2024 Mar 28;28(1).
23. Shahzad MS, Khan S, Ahmad F, Qadir W, Bhatti ZI, ul Zaman MF. Comparison of hypertonic-saline vs normal-saline nebulization in children with bronchiolitis. *The Professional Medical Journal*. 2022 Jul 31;29(08):1213-7.