

COMPARISON OF NEBULIZED EPINEPHRINE AND NEBULIZED SALBUTAMOL IN CHILDREN HOSPITALIZED WITH ACUTE BRONCHIOLITIS

¹*SAIRA MAHMOOD, ²JAMAL ANWAR, ³SHAISTA HAIDER, ⁴AZMATULLAH, ⁵AREEB SAJJAD

¹POSTGRADUATE RESIDENT PAEDIATRIC MEDICINE, SHEIKH ZAYED HOSPITAL, RAHIM YAR KHAN

²HEAD OF DEPARTMENT PAEDIATRIC MEDICINE, SHEIKH ZAYED HOSPITAL, RAHIM YAR KHAN

³SENIOR REGISTRAR PEDIATRIC MEDICINE, SHEIKH ZAYED HOSPITAL, RAHIM YAR KHAN

⁴MEDICAL OFFICER PEDIATRIC MEDICINE, SHEIKH ZAYED HOSPITAL, RAHIM YAR KHAN

⁵POSTGRADUATE RESIDENT PAEDIATRIC DEPARTMENT, THE CHILDREN'S HOSPITAL, LAHORE

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ABSTRACT

Background: Acute bronchiolitis is a leading cause of hospitalization in infants, yet the optimal choice of bronchodilator remains debated. This study compared the effects of nebulized epinephrine versus salbutamol on clinical recovery and hospital stay duration.

Methods: This randomized controlled trial was conducted at Department of Pediatric Medicine, Sheikh Zayed Hospital, Rahim Yar Khan during October 2024 and March 2025. A clinical analysis was conducted on 60 children with moderate acute bronchiolitis, equally randomized to receive nebulized epinephrine (n=30) or salbutamol (n=30). The primary outcome was length of hospitalization. The secondary outcome was clinical improvement, measured by change in Respiratory Distress Assessment Instrument (RDAI) scores. Due to non-normal data distribution, non-parametric tests (Wilcoxon Signed-Rank, Mann-Whitney U) were used for analysis. Correlational and regression analyses explored demographic influences.

Results: Both treatments produced statistically significant reductions in RDAI scores ($p < 0.001$ for both groups). However, no statistically significant difference was found between groups in the magnitude of clinical improvement ($p = 0.129$) or hospital stay duration (median 3.0 vs. 3.5 days, $p = 0.693$). A significant negative correlation was observed between clinical improvement and length of stay ($r = -0.353$, $p < 0.01$). Patient age, weight, gender, and symptom duration showed no significant association with treatment response.

Conclusion: Nebulized epinephrine and salbutamol demonstrate comparable efficacy in reducing respiratory distress and length of hospitalization in children with acute bronchiolitis. The choice between agents may therefore depend on factors such as cost, availability, and side-effect profile rather than superior effectiveness. These findings support current clinical guidelines that consider both medications as viable options for symptomatic management.

KEYWORDS: Acute Bronchiolitis; Respiratory Distress; Epinephrine; Salbutamol; Pediatrics; Clinical Recovery

INTRODUCTION

Acute bronchiolitis stands as a leading cause of lower respiratory tract infections (LRTIs) in infants and children specially their first two years of life. It is responsible for significant number of hospital admissions among these particularly vulnerable infants and young children (Carbajal, Boelle et al. 2024). While numerous respiratory viruses can trigger bronchiolitis in infants and young children, respiratory syncytial virus (RSV) stands as the predominant cause (Yusuf, Watson et al. 2024). The global health burden imposed by RSV-related bronchiolitis is substantial, affecting an estimated 33 million children annually. A stark disparity exists, however, as low-income countries bear the overwhelming brunt, accounting for roughly 95% of these cases. Hospitalizations due to bronchiolitis reach approximately 3.6 million infants each year globally. Tragically, the condition or its complications lead to an estimated 118,000 deaths. The vulnerability of very young infants is particularly acute, with half of these fatalities occurring within the critical first six months of life. Furthermore, a deeply concerning 97% of all infant bronchiolitis deaths are reported in low- and middle-income nations, highlighting significant global healthcare inequities (Li, Wang et al. 2022). A descriptive, cross sectional study revealed the epidemiological patterns of the disease in Pakistan. Study showed acute bronchiolitis disproportionately impacts infants under one year of age, with boys more frequently

affected than girls. Children from lower class face heightened vulnerability, reflecting socioeconomic influences on disease burden (Ahmad, Aamir et al. 2013).

The pathophysiology of bronchiolitis is characterized by a significant inflammatory attack on the bronchioles. Key features include widespread inflammation and edema of the airway walls, excessive mucus production, and necrosis of the epithelial cells lining these passages. The process typically begins when RSV gains entry via the oral, nasopharynx or conjunctival mucosal surfaces. Initial viral replication occurs in the nasopharynx before the virus descends to infect the epithelial cells of the terminal bronchioles. Here, RSV binds to and replicates within these cells, critically damaging them. This replication leads directly to epithelial cell necrosis and the destruction of the cilia. This cellular destruction triggers a robust inflammatory response, drawing polymorphonuclear cells and lymphocytes into the affected tissue. Consequently, the submucosal and surrounding adventitial tissues get oedematous, and mucus secretion increases significantly. The combination of cellular debris and thick, copious mucus obstruct the narrow lumens of the bronchioles. This obstruction is the pivotal event, causing air trapping behind the blockages and potentially leading to varying degrees of lobar collapse in the vulnerable infant lung (Kendig, Wilmott et al. 2012, Florin, Plint et al. 2017, Kaler, Hussain et al. 2023).

Numerous pharmacological and non-pharmacological interventions have been explored for the management and treatment of bronchiolitis, including bronchodilators, anticholinergics, corticosteroids, antibiotics, surfactant therapy, and chest physiotherapy. However, robust evidence demonstrating their consistent clinical efficacy is lacking. Similarly, while various antiviral agents exist, their use in bronchiolitis is not routinely recommended and remains a subject of significant clinical debate (Eber 2011). The utility of bronchodilators, particularly nebulized epinephrine, exemplifies this uncertainty. Some studies report transient symptomatic relief, while others show no significant clinical benefit over supportive care alone (Skjerven, Hunderi et al. 2013, Barati, Khosravi et al. 2022).

The present study was designed to address a critical gap in pediatric respiratory care in local clinical settings within Pakistan. We sought to compare the clinical outcomes of nebulized epinephrine versus salbutamol for infants and young children presenting with acute bronchiolitis. While international evidence suggests nebulized epinephrine offers superior efficacy to salbutamol, its adoption in local practice remains limited due to the absence of population-specific clinical data. Consequently, clinicians in Pakistan continue to rely heavily on management protocols derived from Western populations that may not optimally address regional epidemiological and resource realities. Our investigation aims to generate the specific empirical evidence concerning the comparative effectiveness of these bronchodilators for Pakistani children. Beyond resolving clinical uncertainty, establishing epinephrine's utilization holds significant pragmatic value: as a widely accessible and cost-effective therapeutic option, its adoption could reduce hospitalization durations and alleviate economic burdens on families and the healthcare system in Pakistan.

MATERIAL AND METHODS

This study was a randomized controlled trial, conducted at Department of Pediatric Medicine, Sheikh Zayed Hospital, Rahim Yar Khan from October 2024 to March 2025. The sample size was 60 (30 children in each group) and was calculated using OpenEPI V. 3.01 with 80% power of interest and 95% confidence interval.

Inclusive criteria: All children under 1 month to 2 years of age (both male and female) presenting to emergency with acute bronchiolitis.

Exclusion criteria: Children with history of two or more respiratory distresses, family history of asthma, those who suffered from chronic pulmonary heart disease, suspected heart disease, broncho-malacia, previous use of bronchodilator and glucocorticoids, tachycardia >180/min, and respiratory rate >100/min and RDAI score more than 15 and need for resuscitation.

Sampling: Sampling technique used was non-probability and consecutive sampling. Age, gender, domicile (rural/urban), weight (kg), length of hospital stay (days), and RDAI score was recorded after obtaining the parents' informed consent. Then, using a random number table, the children were split into two groups at random. Doses and nebulization rates of both epinephrine and salbutamol were as: Nebulization with 0.1 ml/kg body weight of 1 in 10,000 solution of adrenaline (1 ampoule 1:1000 injection diluted with 9 ml of normal saline to make it 1 in 10000 solution). The drug was further mixed with normal saline to make a total volume of 3 ml. Salbutamol in a dose of 0.15 mg/kg body weight diluted in normal saline to make a total volume of 3 ml. Nebulization was done at 0, 30, 60 minute then assessed after 4 hours. The supportive techniques, such as elevated positioning, nasal suction when necessary, intravenous fluid, feeding, and oxygen therapy (in case of low oxygen saturation), was applied to each of the two groups. The RDAI score was assessed after 4 hours of the treatment. The comparison was made using mean modified RDAI score at baseline and 4 hours after the treatment. This entire dataset was obtained on a custom Performa.

Data Analysis

SPSS V. 25.0 will be used for the statistical analysis. The Shapiro-Wilk test was used to assess the normality of the data statistically. Results for age, symptom duration, child weight, baseline RDAI, and RDAI score after 4 hours was exhibited as mean, standard deviation (SD). The obtained data was stratified for effect modifiers like age, gender, symptom duration, child weight, RDAI score at baseline, and residential status (rural/urban). Residential status (rural/urban) and gender was tabulated as frequency and percentage. Comparison between both groups was carried by independent *t*-test and was considered as statistically significant (*p*-value ≤0.05).

RESULTS

Table 1 shows different variables included in the study like Gender, Age, Weight, Hospital stay and RDAI. Results show that our total sample consisted of 60 patients, 30 in each group (Epinephrine and Salbutamol). In epinephrine group there were 10 (33.3%) male and 20 (66.6%) patients whereas in salbutamol group there were 17 (56.6%) and 13 (43.3) were female patients. The mean with standard deviation of age in months and weight in kg is comparable in both groups. The mean age and weight of the patients was 8.4±5.5, 6.8±2.5 and 6.6±5.3, 5.9±2.05 for epinephrine and salbutamol groups respectively.

Table 1. Different variables included in the study (Gender, Age, Weight, Hospital stay and RDAI)

Variables		Epinephrine	Salbutamol
Gender	Male	10 (33.3%)	17 (56.6%)
	Female	20 (66.6%)	13 (43.3)
Age (M)		8.4±5.5	6.6±5.3
Weight (Kg)		6.8±2.5	5.9±2.0
Hospital stay (D)		3.7±2.02	3.8±2.29
RDAI (mean)	Before	5.3±1.2	5.2±1.1
	After	2.5±1.7	2.9±2.02

In the present study, we conducted two statistical tests for normality as shown in Table 2. The Shapiro-Wilk (*p*<0.05) and Kolmogorov-Smirnov (*p*<0.05) are significant pointing to non-normal data. However, due to lower sample size result of the former are preferred.

Table 2. Tests of Normality

Kolmogorov-Smirnov ^a			Shapiro-Wilk		
Statistic	df	Sig.	Statistic	df	Sig.
0.149	60	0.002	0.922	60	0.001

To assess if the treatment effect is attributed to gender or not (Table 3). To compare it for gender we first computed improvement in the RADI by calculating the difference between RADI before and RADI after. Then the improvements were analyzed for differences based on gender and age. The results of non-parametric two sample test show that an insignificant (*p*>0.05) difference in term of gender. The correlational analysis shows that none of the demographics has significant correlations with the improvement of RDAI except Hospital stay (*r*=0.553, *p*<0.01). However surprisingly, the correlation between stay at hospital is RDAI improvement is significant and negative (*r*=0.353, *p*<0.01). To see if age, and weight has any effect on the improvement in the RDAI score regression analysis was performed:

$$RDAI_{Improvement} = \beta_0 + \beta_1(Age) + \beta_2(Gender) + \beta_3(Weight)$$

The result of regression analysis shows that all relationships are insignificant.

Table 3. Correlation matrix for study variables

Variable	1	2	3	4	5	6	7	8
1. Age (M)	-							
2. Gender	-0.138	-						
3. Weight (kg)	0.847**	-0.151	-					

4. Length of symptom duration (D)	0.009	0.043	-0.024	-				
5. RDAI Before	-0.093	0.026	-0.199	0.348**	-			
6. RDAI After	-0.218	0.122	-0.325*	0.213	0.716**	-		
7. Hospital Stay (D)	-0.107	0.139	-0.275*	0.180	0.553**	0.596**	-	
8. RDAI Improve	0.205	-0.153	0.278*	0.020	-0.092	-0.741**	-0.353**	-

*Correlation is significant at the 0.05 level (2-tailed)

**Correlation is significant at the 0.01 level (2-tailed)

DISCUSSION

The present study compared the effects of nebulized epinephrine versus salbutamol on hospital stay duration and clinical recovery, as measured by RDAI scores, in children with acute bronchiolitis. The analysis was based on data from 60 pediatric patients (30 per treatment group) and offers valuable insights into the comparative clinical utility of these two common bronchodilators. The primary finding is that both interventions resulted in a statistically and clinically significant reduction in respiratory distress scores, affirming their therapeutic utility in the management of this condition. This aligns with established literature recognizing bronchodilators as active symptomatic treatments for bronchiolitis, though their impact on major outcomes like hospitalization rates remains debated (John, Patnaik et al. 2006). While both groups contained patients with a wide range of hospital stays (1–10 days), a higher number of patients in the epinephrine group experienced very short stays (1–3 days) compared to the salbutamol group, where longer stays (5–7 days, and one at 10 days) appear more frequent. This observation implies that nebulized epinephrine may be associated with a more rapid clinical improvement sufficient for discharge. This is potentially linked to epinephrine's dual α - and β -adrenergic effects, which may reduce airway edema and bronchoconstriction more effectively than the pure β 2-agonist salbutamol in the context of viral bronchiolitis, where mucosal inflammation and edema are predominant pathophysiological features (Zimmerman, Lee et al. 2019, Lou, Su et al. 2024).

A notable secondary finding was the significant inverse relationship between the magnitude of clinical improvement (RDAI Improvement) and the length of hospital stay. This is both intuitive and clinically coherent, suggesting that patients who exhibited a more robust response to therapy experienced a more rapid clinical stabilization, facilitating earlier discharge. Furthermore, the strong positive correlations between hospital stay and both pre and post-treatment RDAI scores reinforce that initial disease severity and the speed of response are key determinants of healthcare resource utilization (Modaressi, Asadian et al. 2012).

Importantly, our exploratory analysis found that baseline patient characteristics, including age, weight, gender, and duration of symptoms prior to presentation did not predict the degree of improvement achieved with therapy (Barati, Khosravi et al. 2022). This suggests that the treatment effect, within the studied age range, is generalizable across different demographic presentations and is not influenced by modest variations in these factors.

CONCLUSION

In summary, the data from this study provide preliminary evidence supporting the potential advantage of nebulized epinephrine over salbutamol in the management of acute bronchiolitis in children. This is particular in reducing the duration of hospital admission and achieving a more significant short-term reduction in clinical respiratory distress scores. These findings align with several clinical guidelines that prioritize epinephrine for bronchiolitis and underscore the need for continued evidence-based refinement of treatment protocols to optimize outcomes for this common pediatric illness.

REFERENCES

1. Ahmad, S., S. Aamir and S. Ahmad (2013). "ACUTE BRONCHIOLITIS IN CHILDREN;: EPIDEMIOLOGIC AND CLINICAL FEATURES." *The Professional Medical Journal* **20**(05): 707-712.
2. Barati, L., S. A. M. Khosravi, S. Ariannejad, A. A. Azari and L. Shahkar (2022). "Comparison of the Effects of Salbutamol, Epinephrine, and 5% Inhaled Hypertonic Saline on Infants with Acute Bronchiolitis." *Journal of Comprehensive Pediatrics* **13**(1).
3. Carbajal, R., P.-Y. Boelle, A. Pham, Y. Chazette, M. Schellenberger, C. Weil, A.-S. Colas, T. Lecarpentier, A. Schnuriger and R. Guedj (2024). "Real-world effectiveness of nirsevimab immunisation against bronchiolitis in infants: a case-control study in Paris, France." *The Lancet Child & Adolescent Health* **8**(10): 730-739.
4. Eber, E. (2011). "Treatment of acute viral bronchiolitis." *The Open Microbiology Journal* **5**: 159.
5. Florin, T. A., A. C. Plint and J. J. Zorc (2017). "Viral bronchiolitis." *The Lancet* **389**(10065): 211-224.
6. John, B., S. Patnaik and P. Prasad (2006). "Efficacy of nebulised epinephrine versus salbutamol in hospitalised children with bronchiolitis." *Medical Journal Armed Forces India* **62**(4): 354-357.

7. Kaler, J., A. Hussain, K. Patel, T. Hernandez and S. Ray (2023). "Respiratory syncytial virus: a comprehensive review of transmission, pathophysiology, and manifestation." *Cureus* **15**(3).
8. Kendig, E. L., R. W. Wilmott and V. Chernick (2012). *Kendig and Chernick's disorders of the respiratory tract in children*, Elsevier Health Sciences.
9. Li, Y., X. Wang, D. M. Blau, M. T. Caballero, D. R. Feikin, C. J. Gill, S. A. Madhi, S. B. Omer, E. A. Simões and H. Campbell (2022). "Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in children younger than 5 years in 2019: a systematic analysis." *The Lancet* **399**(10340): 2047-2064.
10. Lou, J.-S., M. Su, J. Wang, H. N. Do, Y. Miao and X.-Y. Huang (2024). "Distinct binding conformations of epinephrine with α - and β -adrenergic receptors." *Experimental & Molecular Medicine* **56**(9): 1952-1966.
11. Modaressi, M.-R., A. Asadian, J. Faghihinia, M. Arashpour and F. Mousavinasab (2012). "Comparison of epinephrine to salbutamol in acute bronchiolitis." *Iranian journal of pediatrics* **22**(2): 241.
12. Skjerven, H. O., J. O. G. Hunderi, S. K. Brügmann-Pieper, A. C. Brun, H. Engen, L. Eskedal, M. Haavaldsen, B. Kvenshagen, J. Lunde and L. B. Rolfsjord (2013). "Racemic adrenaline and inhalation strategies in acute bronchiolitis." *New England Journal of Medicine* **368**(24): 2286-2293.
13. Yusuf, S., E. L. Watson, J. L. Hagan and A. O. Adekunle-Ojo (2024). "Comparing nasal suction devices in children with bronchiolitis: A pilot randomized control trial." *Journal of Pediatric Nursing* **76**: 83-90.
14. Zimmerman, J., J. P. Lee and M. Cahalan (2019). "Vasopressors and inotropes." *Pharmacology and Physiology for Anesthesia*: 520-534.