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Comparison of Nebulized 3% Hypertonic Saline and Ipratropium Bromide in the Treatment of Children With Bronchiolitis

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Abstract

Bronchiolitis is a common acute lower respiratory tract infection in infants and young children that can cause substantial respiratory distress and require hospital admission. This study aimed to compare nebulized 3% hypertonic saline with nebulized ipratropium bromide regarding respiratory distress, oxygen saturation, and hospital outcomes among children aged 2–24 months with acute bronchiolitis. A randomized controlled trial was conducted in the Department of Pediatrics, Holy Family Hospital, Rawalpindi, Pakistan, from June to September 2026. One hundred children with physician-diagnosed bronchiolitis were enrolled consecutively and randomly allocated by lottery to receive nebulized 3% hypertonic saline (n=50) or ipratropium bromide (n=50). The groups were comparable in recorded baseline characteristics. Mean baseline Respiratory Distress Assessment Instrument (RDAI) scores were 8.6 $\pm$ 1.8 and 8.5 $\pm$ 1.9, respectively, while baseline oxygen saturation (SpO_2) was 91.4 $\pm$ 2.5% and 91.2 $\pm$ 2.4%. At 24 hours, mean RDAI scores were 3.7 $\pm$ 1.5 with hypertonic saline and 5.0 $\pm$ 1.6 with ipratropium; at 48 hours, the corresponding scores were 2.6 $\pm$ 1.3 and 3.8 $\pm$ 1.4 (both $p < 0.001$). SpO_2 at 24 hours was 96.0 $\pm$ 1.4% and 94.9 $\pm$ 1.7%, respectively ($p < 0.001$). Mean hospital stay was 2.63 $\pm$ 1.12 days versus 3.82 $\pm$ 1.06 days ($p < 0.001$); discharge within 72 hours occurred in 90.0% versus 74.0% of children (reported p=0.044). Within this trial, nebulized 3% hypertonic saline was associated with greater short-term improvement in respiratory distress and oxygen saturation, a shorter hospital stay, and more frequent discharge within 72 hours than nebulized ipratropium bromide. These findings require independent confirmation and should be interpreted alongside established bronchiolitis management guidelines.

Keywords: Acute bronchiolitis; Hypertonic saline; Ipratropium bromide; Respiratory Distress Assessment Instrument; Oxygen saturation; Randomized controlled trial

1. INTRODUCTION

Acute bronchiolitis is one of the most common lower respiratory tract infections among infants and children younger than two years and remains a frequent cause of emergency consultations and pediatric hospital admission. The illness usually follows an upper respiratory tract prodrome and is characterized by cough, tachypnea, increased work of breathing, wheezing, and/or crackles on auscultation. Respiratory syncytial virus is a major cause, although other respiratory viruses can produce a comparable clinical syndrome. Most affected children recover with supportive care, but some develop feeding difficulties, hypoxemia, dehydration, or more substantial respiratory distress requiring monitoring and inpatient management [1, 2]. Clinical course and severity can vary with age, prematurity, pre-existing cardiopulmonary disease, duration of symptoms, and other patient characteristics. These differences complicate comparisons of treatment response between clinical settings and patient groups.

Initial management generally emphasizes assessment of respiratory status, adequate hydration, oxygen supplementation when indicated, and recognition of signs of deterioration. The available evidence does not support routine use of most medications for otherwise uncomplicated bronchiolitis. In particular, recommendations from the National Institute for Health and Care Excellence advise against administering either hypertonic saline or ipratropium bromide as a routine treatment, whereas the American Academy of Pediatrics has previously allowed selected inpatient use of nebulized hypertonic saline under a weak recommendation [1, 2]. This divergence reflects the uneven results of clinical trials, variation in clinical settings, and differences in the outcomes used to judge treatment effectiveness. Treatment response must therefore be interpreted alongside supportive-care needs rather than solely in relation to short-term changes in severity scores.

Nebulized 3% hypertonic saline has been investigated as a means of reducing airway edema, improving mucociliary clearance, and facilitating removal of secretions that contribute to obstruction of small airways. A Cochrane systematic review found that hypertonic saline may modestly improve clinical severity scores and shorten hospitalization in some infants, but the certainty of evidence was low to very low because of study heterogeneity and potential bias [3]. A separate systematic review and meta-analysis of randomized trials likewise considered comparisons between hypertonic and normal saline, emphasizing that the clinical importance of any observed difference depends on treatment setting, baseline severity, and the magnitude of improvement [4]. In a randomized trial comparing one versus three days of 3% hypertonic saline, the investigators evaluated duration and tolerability rather than comparing hypertonic saline with an anticholinergic bronchodilator [5]. Other randomized evidence has been less encouraging; a multicenter trial in children with moderate-to-severe bronchiolitis found no significant reduction in hospital stay with nebulized hypertonic saline compared with standard supportive care [6]. These findings reinforce the need to distinguish between possible modest benefits and established routine therapeutic recommendations.

Ipratropium bromide is an inhaled anticholinergic agent that produces bronchodilation by inhibiting muscarinic receptor-mediated bronchoconstriction. Although effective in selected airway disorders, its role in viral bronchiolitis remains uncertain because bronchiolar edema and mucus obstruction, rather than reversible smooth-muscle constriction alone, contribute to the clinical presentation. A double-blind randomized trial did not demonstrate a clinically useful benefit of ipratropium bromide in acute bronchiolitis [7]. Similarly, another randomized trial involving inhaled bronchodilators did not demonstrate improvement in clinical scores or hospital duration sufficient to support routine treatment in infants hospitalized with mild bronchiolitis [8]. Consequently, ipratropium should not be regarded as a standard therapeutic comparator that is independently known to improve clinical outcomes.

Comparative studies of nebulized interventions remain relevant because some hospitals continue to use these treatments despite inconsistent evidence. In Pakistan, a randomized trial directly comparing 3% hypertonic saline with ipratropium bromide reported improvements in selected respiratory observations, a reduction in the length of hospital stay, and fewer admissions among children who received hypertonic saline [9]. Another Pakistani trial comparing hypertonic with normal saline observed differences in clinical severity scores and subsequent admission requirements, although the comparator and treatment schedule differed from those in the present study [10]. A randomized trial comparing hypertonic saline, normal saline, and salbutamol also addressed the potential effect of saline concentration on short-term symptoms [11]. The overall evidence continues to vary according to trial methods, eligibility criteria, treatment exposure, and the time points chosen for assessment.

The Respiratory Distress Assessment Instrument (RDAI) offers a structured measure of clinically observed wheezing and chest retractions in children with bronchiolitis. Such scores can assist with standardized observation over time, but their interpretation requires attention to clinical context, baseline measurements, and differences in the clinical constructs captured by available severity scales. A comparative evaluation of two bronchiolitis scoring systems identified both potential uses and limitations when assessing illness severity and predicting outcomes [12]. Pulse-oximetry measurements provide additional information about oxygenation; however, small differences in saturation should be interpreted in conjunction with the child's overall condition and need for respiratory support.

In view of the continued variation in clinical practice and published comparisons, the present investigation examined

short-term respiratory and hospital outcomes in two groups of children with acute bronchiolitis receiving different nebulized treatments at a tertiary care hospital. The objective was to compare the effectiveness of nebulized 3% hypertonic saline and ipratropium bromide in improving RDAI scores, oxygen saturation, length of hospitalization, and discharge within 72 hours among children aged 2–24 months. The study also considered requirements for supplemental oxygen and intravenous fluids, together with an adjusted analysis of factors associated with earlier discharge.

2. METHODOLOGY

This randomized controlled trial was conducted in the Department of Pediatrics, Holy Family Hospital, Rawalpindi, Pakistan, from June 2026 to September 2026. A total of 100 children between 2 and 24 months of age with a physician-confirmed diagnosis of acute bronchiolitis were enrolled. Recruitment used a non-probability consecutive sampling procedure, whereas allocation to the two treatment groups was performed separately by lottery. Group A comprised 50 children assigned to nebulized 3% hypertonic saline, and Group B comprised 50 children assigned to nebulized ipratropium bromide. Thus, the recruitment procedure and treatment allocation represented distinct aspects of study design, even though both took place within the same pediatric service.

Eligible participants were children aged 2–24 months experiencing their initial physician-diagnosed episode of bronchiolitis. The exclusion criteria were recurrent episodes of respiratory distress, defined as two or more previous episodes; progressive respiratory distress requiring mechanical ventilation; a family history of asthma; known chronic pulmonary disease or cardiac disease; administration of a bronchodilator within four hours of recruitment; glucocorticoid use within the preceding 48 hours; and tachycardia with a heart rate greater than 180 beats per minute. These eligibility criteria were applied to patients presenting to the pediatric emergency department and were intended to identify a clinically defined population suitable for the planned comparison. Children with particularly severe or complicated presentations were therefore not represented in the same way as in a study enrolling all hospitalized bronchiolitis cases.

Recruitment commenced after institutional ethical approval had been obtained and written informed consent had been secured from the parent or legal guardian of each participating child. The investigators recorded demographic and clinical information at baseline, including age, weight, sex, history of prematurity, previous respiratory illness, and relevant comorbidities. The two groups were allocated by a lottery method following enrollment. Children assigned to Group A received nebulized 3% hypertonic saline, whereas those assigned to Group B received nebulized ipratropium bromide. The source study protocol states that the respective nebulized intervention was administered over five minutes. The complete solution volume, drug dose, and subsequent dosing schedule were not specified in the available clinical description; these details are necessary for complete characterization of the treatment procedures and for subsequent independent evaluation.

Clinical observations were obtained before nebulization and at 30 minutes, 60 minutes, 24 hours, and 48 hours after treatment according to the recorded assessment schedule. The RDAI was used to evaluate respiratory distress, including the clinical signs of wheeze and chest retractions, and peripheral oxygen saturation was measured using pulse oximetry. Baseline and follow-up RDAI scores were recorded in each group. Changes from baseline were also calculated at specified time points so that the magnitude of symptom improvement could be compared between the two interventions. Oxygen saturation was analyzed using both the observed values at each time point and the corresponding change from the initial measurement.

Hospital-related outcomes comprised the requirement for supplemental oxygen, the requirement for intravenous fluid administration, the duration of hospital stay, and discharge within 72 hours. Length of stay was calculated from hospital admission to discharge and expressed in days. The trial's operational definition of a favorable clinical outcome considered the measured improvement in respiratory observations and discharge within 72 hours. These outcomes were assessed in relation to the assigned nebulized treatments without assuming that any one measure could independently describe the full clinical course of bronchiolitis. Although the trial included random treatment allocation, its description did not document allocation concealment, masking of outcome assessors, or a prospective trial registration identifier. These features remain relevant when assessing the methodological strength of the comparison.

Data were entered and analyzed using Statistical Package for the Social Sciences (SPSS), version 28.0. Continuous variables, including age, body weight, RDAI scores, oxygen saturation, and duration of hospitalization, were summarized as means and standard deviations. Categorical variables, including sex, history of prematurity, previous respiratory illness, need for supplemental oxygen, intravenous fluid requirement, and discharge within 72 hours, were described as frequencies and percentages. Comparisons between groups used independent-samples t-tests for continuous variables considered normally distributed and Mann–Whitney U tests for non-normally distributed variables. Categorical outcomes were compared using chi-square or Fisher's exact tests as appropriate. Multivariable logistic regression was conducted to evaluate the association between treatment assignment and discharge within 72 hours after adjustment for age, weight, baseline RDAI score, sex, and prematurity. Adjusted odds ratios (aORs), 95% confidence intervals, and corresponding p-values were presented. Statistical significance was defined using a two-sided p-value below 0.05. For transparency, reported effect estimates and p-values have been retained as stated in the trial results. Their statistical consistency should be assessed

using the original analysis outputs before definitive clinical interpretations are made.

3. RESULTS

One hundred children aged 2–24 months with a clinical diagnosis of acute bronchiolitis were included, with 50 participants allocated to each intervention group. The recorded demographic and baseline clinical characteristics are presented in Table 1. Mean age was 8.7 ± 4.8 months in the hypertonic saline group and 9.1 ± 5.1 months in the ipratropium bromide group, and the corresponding mean weights were 7.4 ± 1.8 and 7.6 ± 1.9 kg. Male children accounted for 58.0% and 54.0% of the respective treatment groups. History of prematurity was documented for 16.0% and 14.0%, while previous respiratory illness was recorded for 12.0% and 16.0%. Baseline RDAI scores and oxygen saturation did not differ significantly between groups at the prespecified level, and the displayed baseline p-values were all greater than 0.05. The similarity of the recorded characteristics provides context for the subsequent group comparisons, although unmeasured differences cannot be excluded from the available summary results.

Table 1. *Baseline Demographic and Clinical Characteristics of Children With Bronchiolitis (n = 100)*

Variable	3% Hypertonic Saline (n=50)	Ipratropium bromide (n=50)	p-Value
Age (months)	8.7 ± 4.8	9.1 ± 5.1	0.688
Weight (kg)	7.4 ± 1.8	7.6 ± 1.9	0.596
Male Sex, n (%)	29 (58.0)	27 (54.0)	0.689
Female Sex, n (%)	21 (42.0)	23 (46.0)	
History of prematurity, n (%)	8 (16.0)	7 (14.0)	0.775
Previous respiratory illness, n (%)	6 (12.0)	8 (16.0)	0.564
Baseline RDAI Score	8.6 ± 1.8	8.5 ± 1.9	0.788
Baseline SpO_2 (%)	91.4 ± 2.5	91.2 ± 2.4	0.684

Changes in Respiratory Distress and Oxygen Saturation. The time-dependent respiratory observations are summarized in Table 2. Mean RDAI scores declined in both groups, with lower scores observed in the hypertonic saline group at each follow-up assessment. At 30 minutes, the mean RDAI score was 6.3 ± 1.7 after hypertonic saline and 7.2 ± 1.8 after ipratropium bromide (p=0.012). At 60 minutes, the corresponding scores were 5.2 ± 1.6 and 6.4 ± 1.7 ($p < 0.001$). At 24 hours, mean scores were 3.7 ± 1.5 and 5.0 ± 1.6, respectively, and at 48 hours they were 2.6 ± 1.3 and 3.8 ± 1.4; the reported p-values at both time points were below 0.001. The observed RDAI trends across the full assessment period are illustrated in Figure 1.

Oxygen saturation increased from baseline in both study groups, with higher mean follow-up values following hypertonic saline. At 30 minutes, mean SpO_2 was 94.2 ± 2.0% versus 93.3 ± 2.1% (p=0.031). At 60 minutes, the recorded values were 95.3 ± 1.7% versus 94.2 ± 1.9% (p=0.003). The 24-hour values were 96.0 ± 1.4% and 94.9 ± 1.7%, while the 48-hour values were 96.3 ± 1.2% and 95.2 ± 1.5% (both $p < 0.001$). Figure 2 displays the comparative oxygen-saturation trajectory following nebulization. The difference in oxygenation should be interpreted as a measured group outcome rather than evidence that one intervention is routinely indicated in all infants with bronchiolitis.

Table 2. *Changes in RDAI Score and Oxygen Saturation Following Nebulized Treatment (n = 100)*

Assessment Time	3% Hypertonic Saline	Ipratropium bromide	p-Value
RDAI at baseline	8.6 ± 1.8	8.5 ± 1.9	0.788
RDAI at 30 minutes	6.3 ± 1.7	7.2 ± 1.8	0.012
RDAI at 60 minutes	5.2 ± 1.6	6.4 ± 1.7	<0.001
RDAI at 24 hours	3.7 ± 1.5	5.0 ± 1.6	<0.001
RDAI at 48 hours	2.6 ± 1.3	3.8 ± 1.4	<0.001
SpO_2 at baseline (%)	91.4 ± 2.5	91.2 ± 2.4	0.684
SpO_2 at 30 minutes (%)	94.2 ± 2.0	93.3 ± 2.1	0.031
SpO_2 at 60 minutes (%)	95.3 ± 1.7	94.2 ± 1.9	0.003
SpO_2 at 24 hours (%)	96.0 ± 1.4	94.9 ± 1.7	<0.001
SpO_2 at 48 hours (%)	96.3 ± 1.2	95.2 ± 1.5	<0.001

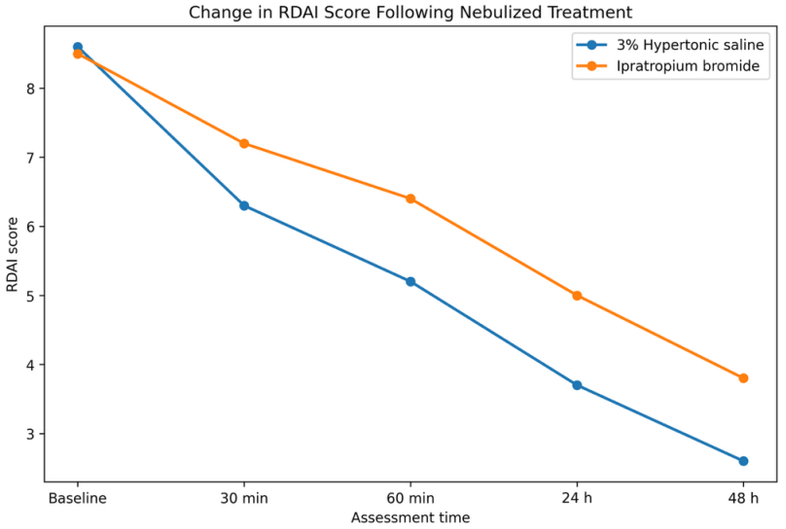


Figure 1. *Changes in Respiratory Distress Assessment Instrument (RDAI) Scores Following Nebulized Treatment*

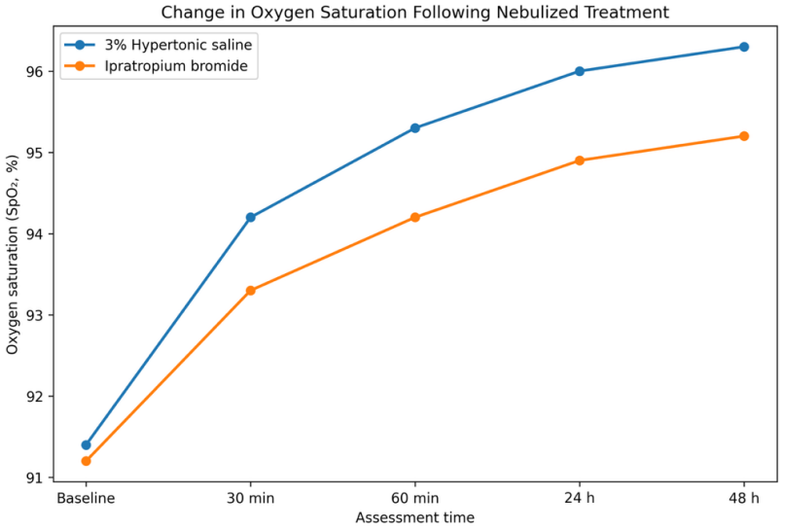


Figure 2. *Changes in Oxygen Saturation Following Nebulized Treatment*

Magnitude of Change From Baseline. Table 3 shows the reported change in RDAI scores and SpO_2 from the baseline assessment. RDAI changes in the hypertonic saline and ipratropium groups were -2.3 ± 1.4 versus -1.3 ± 1.3 points at 30 minutes, -3.4 ± 1.5 versus -2.1 ± 1.4 points at 60 minutes, -4.9 ± 1.6 versus -3.5 ± 1.5 points at 24 hours, and -6.0 ± 1.7 versus -4.7 ± 1.6 points at 48 hours. The reported between-group p-values were below 0.001 at each of these time points. The negative direction of the RDAI change signifies an improvement in clinically observed respiratory distress.

Corresponding increases in oxygen saturation were 2.8 ± 1.7 versus 2.1 ± 1.6 percentage points at 30 minutes (p=0.037); 3.9 ± 1.7 versus 3.0 ± 1.7 points at 60 minutes (p=0.009); 4.6 ± 1.7 versus 3.7 ± 1.6 points at 24 hours (p=0.008); and 4.9 ± 1.6 versus 4.0 ± 1.5 points at 48 hours (p=0.005). Taken together, the observed changes suggest a larger short-term improvement among children assigned to hypertonic saline. However, the clinical implications of the numerical differences must be considered in relation to the whole clinical presentation, the indication for supportive treatment, and subsequent hospital outcomes.

Hospital Outcomes and Adjusted Analysis. The hospital outcomes for both groups are presented in Table 4. Supplemental oxygen was required in 18 children (36.0%) assigned to hypertonic saline compared with 27 (54.0%) assigned to ipratropium bromide (p=0.070). Intravenous fluids were required in 10 (20.0%) and 16 (32.0%) children, respectively (p=0.180). Although both outcomes occurred less frequently in the hypertonic saline group, the reported comparisons did not reach the prespecified level of statistical significance. The mean hospital stay was shorter after hypertonic saline treatment (2.63 ± 1.12 days) than after ipratropium bromide (3.82 ± 1.06 days; $p < 0.001$). Discharge within 72 hours was

reported for 45 of 50 children (90.0%) receiving hypertonic saline and 37 of 50 children (74.0%) receiving ipratropium bromide (reported p=0.044). Correspondingly, hospital stays longer than three days occurred in 10.0% versus 26.0% of children. The comparison of hospital outcomes is depicted in Figure 3.

Table 3. *Change in RDAI Score and SpO_2 From Baseline Following Treatment (n = 100)*

Outcome	3% Hypertonic Saline (n=50)	Ipratropium bromide (n=50)	p-Value
Change in RDAI at 30 minutes	-2.3 ± 1.4	-1.3 ± 1.3	<0.001
Change in RDAI at 60 minutes	-3.4 ± 1.5	-2.1 ± 1.4	<0.001
Change in RDAI at 24 hours	-4.9 ± 1.6	-3.5 ± 1.5	<0.001
Change in RDAI at 48 hours	-6.0 ± 1.7	-4.7 ± 1.6	<0.001
Change in SpO_2 at 30 minutes (%)	2.8 ± 1.7	2.1 ± 1.6	0.037
Change in SpO_2 at 60 minutes (%)	3.9 ± 1.7	3.0 ± 1.7	0.009
Change in SpO_2 at 24 hours (%)	4.6 ± 1.7	3.7 ± 1.6	0.008
Change in SpO_2 at 48 hours (%)	4.9 ± 1.6	4.0 ± 1.5	0.005

Table 5 presents the multivariable analysis of factors associated with discharge within 72 hours. After adjustment for age, weight, baseline RDAI score, sex, and history of prematurity, treatment with hypertonic saline was associated with higher adjusted odds of discharge within 72 hours (aOR 3.08; 95% CI, 1.05–9.06; p=0.040). No individual association for age, weight, baseline RDAI score, male sex, or history of prematurity was statistically significant on the basis of the reported results (all $p > 0.05$). The adjusted estimate was consistent in direction with the observed discharge proportions; nevertheless, interpretation remains dependent on the adequacy of the model and the accuracy of the reported underlying observations. These analyses describe treatment-associated outcomes in the enrolled population and do not establish that the recorded effects will be reproduced in substantially different clinical settings.

Table 4. *Hospital Outcomes Following Nebulized Treatment (n = 100)*

Outcome	3% Hypertonic Saline (n=50)	Ipratropium bromide (n=50)	p-Value
Supplemental oxygen required, n (%)	18 (36.0)	27 (54.0)	0.070
IV fluids required, n (%)	10 (20.0)	16 (32.0)	0.180
Discharge within 72 hours, n (%)	45 (90.0)	37 (74.0)	0.044
Hospital Stay (Days)	2.63 ± 1.12	3.82 ± 1.06	<0.001
Hospital stay > 3 days, n (%)	5 (10.0)	13 (26.0)	0.044
Mean RDAI reduction at 24 hours	4.9 ± 1.6	3.5 ± 1.5	<0.001

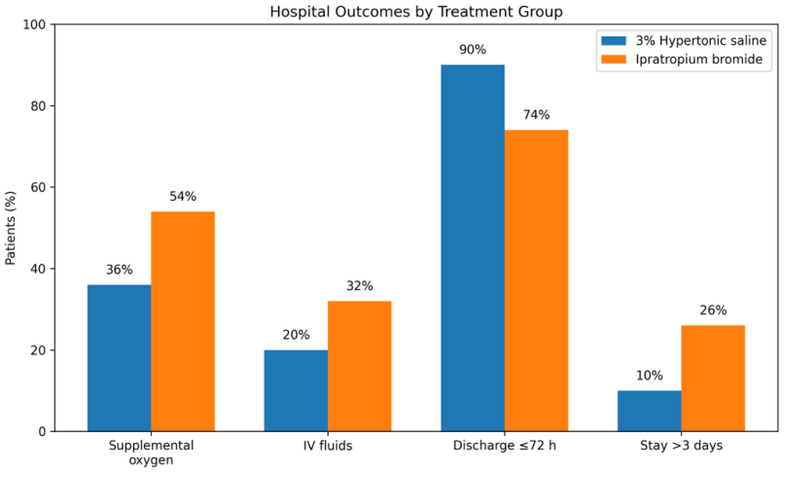


Figure 3. *Comparison of Hospital Outcomes Between Treatment Groups*

Table 5. *Multivariable Analysis of Factors Associated With Discharge Within 72 Hours (n = 100)*

Predictor	Adjusted OR	95% CI	p-Value
3% Hypertonic Saline treatment	3.08	1.05–9.06	0.040
Age (per month increase)	1.02	0.96–1.08	0.524
Weight (per kg increase)	1.08	0.82–1.42	0.583
Baseline RDAI Score	0.82	0.65–1.04	0.098
Male Sex, n (%)	1.14	0.47–2.78	0.774
History of prematurity, n (%)	0.71	0.20–2.49	0.594

4. DISCUSSION

This randomized controlled trial compared nebulized 3% hypertonic saline with ipratropium bromide among 100 children with acute bronchiolitis at a tertiary pediatric service in Rawalpindi, Pakistan. The two groups were similar with respect to the demographic and clinical characteristics recorded at baseline. Children assigned to hypertonic saline subsequently had lower RDAI scores, greater increases in oxygen saturation, and a shorter reported duration of hospital stay than those assigned to ipratropium bromide. The association with earlier discharge persisted in the multivariable model after adjustment for five recorded clinical and demographic variables. These observations describe treatment outcomes in the recruited population; they should not be interpreted as evidence that nebulized therapy is necessarily preferable to established supportive care for every child presenting with bronchiolitis.

The reductions in RDAI scores were apparent from the first post-treatment measurement and continued across the 48-hour assessment period. Mean RDAI decreased from 8.6 $\pm$ 1.8 to 6.3 $\pm$ 1.7 at 30 minutes, 5.2 $\pm$ 1.6 at 60 minutes, 3.7 $\pm$ 1.5 at 24 hours, and 2.6 $\pm$ 1.3 at 48 hours in the hypertonic saline group. Over the same intervals, scores declined from 8.5 $\pm$ 1.9 at baseline to 7.2 $\pm$ 1.8, 6.4 $\pm$ 1.7, 5.0 $\pm$ 1.6, and 3.8 $\pm$ 1.4 in the ipratropium group. Differences in the observed values were reported as statistically significant at all follow-up assessments. The larger decline with hypertonic saline is compatible with improved clearance of airway secretions and less clinically apparent obstruction, although the present clinical observations do not directly establish a biological mechanism. Such scores are useful for describing changes in respiratory signs, but severity assessments are not interchangeable across measurement tools or patient populations. The comparison of bronchiolitis scoring systems published by Rajvanshi et al. underlines the importance of selecting and interpreting standardized measures carefully [12].

Oxygen saturation followed a generally similar pattern. The reported group means rose from 91.4 $\pm$ 2.5% to 94.2 $\pm$ 2.0% at 30 minutes and 96.0 $\pm$ 1.4% at 24 hours in the hypertonic saline group. In the ipratropium group, mean SpO_2 increased from 91.2 $\pm$ 2.4% to 93.3 $\pm$ 2.1% and 94.9 $\pm$ 1.7% at the corresponding intervals. Mean changes from baseline were greater in the hypertonic saline group, including improvements of 4.6 $\pm$ 1.7 and 3.7 $\pm$ 1.6 percentage points at 24 hours. These values support the reported between-group differences in short-term oxygenation. Nevertheless, interpretation of oxygen saturation should also account for the presence or absence of supplemental oxygen, fluctuations in measurement conditions, and whether a difference is accompanied by an important change in clinical status. The clinical significance of pulse-oximetry readings therefore cannot be inferred solely from an isolated statistical comparison.

A previous randomized trial in Pakistan specifically compared nebulized hypertonic saline and ipratropium bromide in 100 children with acute bronchiolitis [9]. That investigation reported improvement in selected respiratory measures and a shorter duration of hospitalization in the hypertonic saline group. Its clinical question and treatment comparison are closely related to those of the present study, and direct acknowledgment of that prior evidence is necessary when considering the results. However, similarities in the direction of an observed effect do not eliminate the need for independent verification of patient-level observations, the treatment protocol, and the statistical analyses. Differences in recruitment dates, participants, treatment schedules, and clinical settings must also be considered before treating the findings as independent confirmation.

The duration of hospitalization showed a considerable difference between the reported groups. Children receiving 3% hypertonic saline had a mean hospital stay of 2.63 $\pm$ 1.12 days, compared with 3.82 $\pm$ 1.06 days in the ipratropium group. The proportion discharged within 72 hours was also higher in the hypertonic saline group, with 45 of 50 children discharged compared with 37 of 50 children in the ipratropium group. By contrast, the observed differences in supplemental oxygen requirements (36.0% versus 54.0%; reported p=0.070) and intravenous fluid requirements (20.0% versus 32.0%; reported p=0.180) were not statistically significant. Consequently, the results do not justify a claim that these latter outcomes were conclusively reduced by hypertonic saline, even though their numerical distributions favored that intervention. Shorter length of stay can be valuable to patients and hospitals, but its interpretation also depends on discharge policies, clinical thresholds, and other factors not completely captured by the summary tables.

Published findings on hypertonic saline have not been consistent across trials. The 2023 Cochrane review found possible modest improvements in symptoms and hospital stay but characterized the certainty of the overall evidence as

low to very low [3]. A randomized trial comparing different durations of hypertonic saline administration evaluated whether a shorter course could yield acceptable clinical outcomes, illustrating the relevance of treatment intensity and timing when interpreting results [5]. In contrast, a Swiss multicenter randomized trial comparing hypertonic saline with standard supportive care found no significant reduction in length of hospitalization in moderate-to-severe bronchiolitis [6]. Likewise, comparisons with normal saline in clinical trials conducted in South Asia have yielded varying estimates of symptom improvement and hospitalization [10, 11]. The interventions used as comparators are especially important: a trial comparing hypertonic saline with an anticholinergic bronchodilator does not directly estimate the benefit of hypertonic saline relative to supportive care alone.

The role of ipratropium bromide also requires contextualization. Earlier randomized evidence showed no clear clinical advantage with nebulized ipratropium in bronchiolitis [7, 8]. These findings are consistent with the limited mechanistic rationale for using an anticholinergic bronchodilator to treat a condition in which viral inflammation, edema, and mucus plugging play prominent roles. Thus, better outcomes with hypertonic saline than with ipratropium should not be interpreted as evidence that either treatment should automatically be given to all eligible children. Current NICE guidance advises against both interventions for routine bronchiolitis management, while the earlier American Academy of Pediatrics guideline offered a more limited and conditional inpatient role for hypertonic saline [1, 2]. The results of the present study should be weighed against those recommendations, the overall quality of the evidence, and the established importance of oxygen, hydration, and respiratory monitoring as required.

The multivariable model reported an adjusted odds ratio of 3.08 for discharge within 72 hours after accounting for age, weight, baseline respiratory distress, sex, and prematurity. Although the reported 95% confidence interval of 1.05–9.06 excludes unity, its width demonstrates considerable imprecision. In addition, only 18 participants were recorded as remaining in hospital beyond 72 hours across the two groups, placing practical limits on how much information the multivariable model can provide. The reported absence of independent associations for the other covariates does not establish that these characteristics are clinically unimportant; such analyses are sensitive to sample size, event frequency, and the accuracy of model specification. The adjusted estimate is therefore best interpreted as a supplementary analysis rather than a definitive explanation of the observed difference in length of hospitalization.

The study has several limitations. It was conducted at one hospital over a relatively short recruitment period, and only 100 children were enrolled. Consecutive recruitment at a single center may limit how well the sample reflects all infants and young children with bronchiolitis. Children with progressive respiratory distress requiring mechanical ventilation, chronic pulmonary or cardiac disease, recurrent respiratory symptoms, or certain recent treatments were excluded. Accordingly, the findings apply primarily to children meeting the study's eligibility criteria and should not be generalized uncritically to those with more complex illness. Follow-up centered on assessments within 48 hours and on in-hospital outcomes, so subsequent illness course, readmissions, and longer-term respiratory outcomes were not evaluated. The available methods also do not report the complete nebulized drug doses, masking procedures, or allocation concealment; these omissions should be resolved against the study protocol where possible. Finally, the observed associations do not replace independent review of the primary trial records, analysis outputs, and individual participant data before firm conclusions are drawn.

Despite these constraints, the comparison addresses an important clinical question in a setting where resource availability and local practice can influence treatment decisions. The results suggest that nebulized 3% hypertonic saline may produce greater improvement in measured short-term respiratory distress and oxygenation than nebulized ipratropium bromide in children similar to those enrolled. Establishing the clinical relevance of these findings requires replication with clearly specified administration schedules, standardized supportive care, adequate allocation concealment, consistent outcome measurement, and transparent reporting of adverse events. Future work should also evaluate meaningful patient outcomes, including safe discharge, symptom progression, and clinically necessary respiratory support, rather than treating a single composite response as conclusive evidence of benefit.

5. CONCLUSION

Among 100 children aged 2–24 months with acute bronchiolitis, nebulized 3% hypertonic saline was associated with a greater decline in RDAI scores and a larger improvement in measured oxygen saturation than nebulized ipratropium bromide over the reported 48-hour follow-up. The hypertonic saline group also had a shorter mean hospital stay, and a higher proportion of children were reported as discharged within 72 hours. The adjusted analysis similarly identified an association between hypertonic saline treatment and earlier discharge. These results are limited by the single-center design, modest sample size, incomplete treatment-protocol details, and the need to verify the reported numerical analyses. They should not be taken as a recommendation for routine hypertonic saline use in bronchiolitis, because major clinical guidelines differ in their interpretation of the evidence and standard supportive management remains essential. Larger, appropriately registered multicenter trials with clearly documented nebulization regimens, standardized assessments, and independent confirmation of the results are needed to establish the clinical value and generalizability of this treatment

comparison.

Author Contributions

All authors contributed to the conception and design of the study and participated in drafting or critically revising the manuscript for important intellectual content. All authors reviewed and approved the final manuscript and agreed to be accountable for their respective contributions.

Ethics Approval and Consent to Participate

Institutional ethical approval was obtained before the recruitment of participants. Written informed consent was obtained from the parent or legal guardian of each enrolled child.

Conflicts of Interest

The authors declare that they have no financial or nonfinancial conflicts of interest relevant to the research described in this manuscript.

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Data Availability

Information concerning access to the underlying study data is subject to confirmation by the corresponding author and the applicable institutional and ethical requirements.

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