Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/8ct1as40

EFFICACY OF 3% HYPERTONIC SALINE NEBULIZATION IN CHILDREN HOSPITALIZED WITH BRONCHIOLITIS

Dr. Samiah Mazhar[1], Dr. Muhammad Faisal Shafiq[2], Dr. Iqra Amjad[3], Dr. Areej Fatima Khan[4], Dr. Syeda Ayesha Mazhar[5], Dr. Muhammad Ali Khan[6]

[1]MBBS, PGR Paediatrics CMH Multan, dr.samiahmazhar@gmail.com
[2]MBBS, FCPS (Pediatric medicine), FCPS (Neonatal Medicine), Assistant Professor & HOD Pediatric Department, CMH Multan, mfaisalshafiq@gmail.com
[3]MBBS, PGR Paediatrics CMH Multan, iqraamjad67@yahoo.com
[4]MBBS, Women Medical Officer Primary and Secondary Healthcare department , areejfatimakhan@gmail.com
[5]MPhil. Pharmaceutics Student at School of Health Sciences and Social work, Griffith University, Australia, syedaayesha.mazhar@griffithuni.edu.au
[6]MBBS, Medical Officer, THQ Hospital Noorpur Thal, Alipitafi007@gmail.com

***Corresponding Author:** Dr. Samiah Mazhar,
*Email:- dr.samiahmazhar@gmail.com

ABSTRACT

Background: Acute bronchiolitis is a prevalent respiratory condition in newborns and young children, often requiring hospitalization.

Objective: The objective of this study is to evaluate the efficacy of nebulization with 3% hypertonic saline in children who are hospitalized with bronchiolitis.

Study Design: Randomized Control Trial (RCT)

Study Setting: This study was conducted at the Department of Pediatrics CMH, Multan From November 2023 to February 2024.

Methodology: Within the Combined Military Hospital in Multan, the department of pediatrics was the location where this study was carried out. A total of 124 individuals diagnosed with acute bronchiolitis were split into two groups for the purpose of this study: The nebulized hypertonic saline was administered to Group A, while the nebulized normal saline was administered to Group B instead. Clinical severity scores (CSS) were assessed at baseline, 12, 24, 48, and 72 hours. Recovery times and length of hospital stay were recorded. The data that was gathered was analyzed using IBM SPSS, specifically version 27.0.

Results: The mean age of patients in Group A was 7.0 months, with a standard deviation of 4.61 months, while in Group B it was 5.97 ± 4.29 months. At the start of the study, Group A had an average oxygen saturation of 92.5±1.25% and Group B had an average of 92.2±0.91% (p=0.075). Group A had a mean oxygen saturation that was 98.3±0.60% higher by discharge than Group B, which was 97.6±0.91% (p<0.001). The mean CSS for the Group A was documented at 7. 9 ± 0. Group A had a mean CSS of 68 at the beginning of the study while that of Group B was 8. 2 ± 0. 68 (p=0. 017). At 12 hours, again there was an overall improvement in CSS and the mean CSS of Group A stood at 6. 9 ± 0. The mean composite satisfaction score of Group A was 65 while that of Group B was mean CSS of 7. 5 ± 0. 62 (p<0. 001). Finally, by 24 hours, Group A had a mean CSS of 4; Therefore, the results indicate that weitinger and colleagues were right to predict that using

preoperative antibiotics for SP will decrease the incidence of SSI. 2 ± 0. 68, compared to 5. 4 ± 0. A total of twenty five percent in the Group B scored 64 percent and above (n = 64, that is p < 0. 001). On the average at 48 hours, the CSS for the Group A was 2. 6 ± 0. 59 which is relatively less compared to total number of respondents belongs to the group B which os only 3. 9 ± 0. 66 (p<0. 001). Within 72 hours, the Group A subjects had a mean CSS of 1. 5 ± 0. A confirmity test for equality of variances leaving to F (2,53) = 2. 7 ± 0. 65 (p<0. 001). The overall use of oxygen therapy showed significantly an increase in Group B (23. 3±2. 37 hours) as compared to Group A (16. 2±2. 47 hours); p<0. 001.

Conclusion: Thus, nebulized hypertonic saline holds the advantage of significantly more favorable such clinical severity, length of hospital stay, and recovery in acute bronchiolitis. These results suggest that hypertonic saline should be used as a better treatment choice of this illness.

Keywords: Bronchiolitis, Clinical Severity Score (CSS), Hypertonic Saline, Hospital Stay, Nebulization, Normal Saline

INTRODUCTION

Bronchiolitis is a common respiratory infection that is common in young children particularly those aged less than two years. Bronchiolitis is a clinical situation characterized by inflammation of the bronchioles; the inflammation is mostly due to viruses, especially RSV.[1,2] The disease is characterized by coughing, wheezing, shortness of breath and the condition could cause serious morbidity in young children, with many required to be hospitalized.[3] Globally, 150 million children under 5 years of age get bronchiolitis every year; and among those, 2-3% are severe enough to require hospitalization. Bronchiolitis affects roughly 100 000 pediatric hospitalizations in the United States per year, and the number of hospitalisation is increasing; the disease is the primary cause of infancy hospitalization, while it costs more than $1 billion per year in healthcare expenses.[4]

Bronchiolitis is mainly due to viral infections, particularly RSV for which it is one of the most common causes. Other viral agents associated with the disease include human metapneumovirus, parainfluenza and rhinovirus among others. The following are considered to predispose someone to bronchiolitis: premature birth, exposure to cigarette smoke, living in crowded places and having chronic lung or heart illness.[5] In bronchiolitis, the disease occurs when the epithelial cells of the bronchioles get infected that resulted to inflammation, oedema, and thickened mucus. This leads to the blockade of airways and since bronchioles in infants are smaller this condition is worsened. Since the airways are blocked, the baby has problems with breathing, he/she chokes with wheezing, cough, and retractions. Bronchiolitis requires that the child's inflammation and mucus be addressed in an attempt to provide symptomatic relief and improve on the child's oxygenation.[6,7]

Some of the diagnostic functions help in supporting bronchiolitis include monitoring of the oxygen saturation and chest X-rays in which hyperinflation and atelectasis may be identifiable. Bronchiolitis does not require any specific therapy; however, supportive care is appropriate, for example, the provision of fluids, clearing of secretions, mainly by means of suctioning of the upper airways and closely monitoring for the development of acute respiratory failure in which mechanical ventilation will be needed only occasionally.[8] Oxygen is administered only when the oxygen saturation is below 90 % on a regular basis. Nebulization is an effective mean of treatment to get rid of the symptoms like wheezing, shortness of breath, and edema of the airways. These persistent nebulization therapy managements include normal saline, bronchodilators, epinephrine, anticholinesterase, and corticosteroids; each with different results and prognosis for the entitled patient.[9] The 3% hypertonic saline nebulization is effective as it has high osmotic pressure and has an ability to draw fluid out of the structures that are oedematous and to also thin mucus lining the airways. It acts by inhalation and has its effect within a few minutes after it has been administered. It is mostly recommended to promote mucociliary clearance thus improving respiratory function and covering the symptoms of bronchiolitis.[10]

This research looks at the effectiveness of 3% hypertonic saline nebulization in the treatment of the common respiratory illness – bronchiolitis in a country that is in dire need of efficient and effective

care to cater for a high disease burden. Therefore, it is appreciable that a locally generated data on the efficacy of this therapy is envisaged to enhance the existing treatment modalities and results in relation to health systems in Pakistan. Some gaps in the current research are the absence of clinical trials/ treatment evaluations from particular regions, hence, regional bronchiolitis management doubts. The findings of this research would be beneficial in providing fresh as good as potentially valuable information that might help to elaborate the guidelines for treating bronchiolitis in the adjusted Pakistani environment.

METHODS

This Randomized Control Trial (RCT) was conducted at Department of Paediatrics at CMH Multan, the research project was carried out from November 2023 to February 2024. Prior to enrolment, informed consent was obtained from the parents or guardians of each and every participant. The WHO tool was used to find a sample size of 124 children, with 62 children in each group (www.openepi.com), with a power of 90% and a margin of error of 5%. The hypertonic group had a 3% longer hospital stay than the normal saline group (74.7±27.2 hours compared to 58.1±22.0 hours) in children admitted with bronchi.[17]

Infants and children under the age of 12 months who were diagnosed with AB and had symptoms within the past 5 days were included in the study. The clinical severity was evaluated utilizing the Wang Score, and only children with a score of 6 or above were included.[11] Children were excluded from the study if they had chronic respiratory conditions such as asthma or cystic fibrosis, congenital heart disease, or other significant congenital anomalies. Those with severe underlying medical conditions, including immunodeficiency or neuromuscular disorders, were also excluded. Additionally, children who had received nebulization treatment within 24 hours prior to admission, had any contraindications to nebulization therapy. The youngsters were randomly divided into two groups using a randomized lottery method. Nebulization with 3% hypertonic saline was given to Group A (n=62), while nebulization with 0.9% normal saline was given to Group B (n=62). Both groups were given nebulization.

CSS was the key assessment of the impact of the intervention, which was assessed at baseline and at 12, 24, 48, and 72 hours following the start of the treatment. The CSS was used to evaluate the overall clinical improvement and severity of symptoms. Additional outcome measures included oxygen saturation levels and the duration of oxygen therapy. Oxygen saturation was measured at admission and discharge using pulse oximetry. The duration of oxygen therapy was recorded as the total number of hours each patient required supplemental oxygen during their hospital stay. Patients were monitored closely throughout their hospital stay. In our study, each child received nebulization every 4 hours throughout the treatment. We conducted vigilant monitoring of patients by calculating their clinical severity score on a daily basis in order to evaluate their development and determine their outcomes. Discharge was granted when the clinical severity score reached 4 or lower.

The data that was gathered was analyzed using IBM SPSS, specifically version 27.0. There is a comparison made using the Chi square test, and it is common practice to report categorical variables using the statistics of frequency and percentage. Mean and SD are used to compare continuous variables using Mann-Whitney U test. The assessment of normality was conducted using measures of kurtosis, skewness, Shapiro-Wilk's test, and Q-Q plots. The results were graphically represented whenever possible to facilitate interpretation. The statistical significance of the results was determined by a p-value that was less than 0.05, together with a confidence range of 95%, with a significance threshold of 5% set.

Result

This study comprised a total of 124 patients, with an even allocation of participation between two groups. Group A (n=62) was administered nebulization treatment using 3% hypertonic saline, whereas Group B (n=62) got treatment with 0.9% normal saline. Table 1 provides a summary of the age and gender distribution of the participants involved in the study. Group A comprised of 21 females, accounting for 33.9% of the group, and 41 males, making up 66.1% of the group. Group B

had 28 females, constituting 45.2% of the group, and 34 males, making up 54.8% of the group. The average age of patients in Group A was 7.0 ± 4.61 months, compared to 5.97 ± 4.29 months in Group B.

Table 1: Age and gender distribution of study participants.

	Group A (n=62)		**Group B (n=62)**	
	n	**%**	**n**	**%**
Gender				
Female	21	33.9%	28	45.2%
Male	41	66.1%	34	54.8%
Age groups (months)				
Less than 6	32	51.6%	39	62.9%
6-12	20	32.3%	15	24.2%
More than 12	10	16.1%	8	12.9%
Age (months), mean ± SD	7.0 ± 4.61		5.97 ± 4.29	

The clinical presentation of patients on admission is shown in Table 2. On admission, both Groups had 100% prevalence of runny nose, cough, breathing difficulty (Group B: 98.4%), chest indrawing, and rhonchi. The prevalence of fever was higher in Group A (64.5%) compared to Group B (51.6%). Over 87.1% of people in Group A wheezed, and over 93.5% of people in Group B did too. Group A had tachypnea in 80.6% of instances, whereas Group B displayed tachypnea in 88.7% of instances. 74.2% of people in Group A and 82.3% of people in Group B had tachycardia. Group B exhibited higher incidence of nasal flaring (24.2%) compared to Group A (16.1%).

Table 2: Clinical presentation of patients on admission.

	Group A		**Group B**	
	n	**%**	**n**	**%**
Runny nose	62	100.0%	62	100.0%
Cough	62	100.0%	62	100.0%
Breathing Difficulty	62	100.0%	61	98.4%
Fever	40	64.5%	32	51.6%
Wheeze	54	87.1%	58	93.5%
Ronchi	60	96.8%	62	100.0%
Chest Indrawing	62	100.0%	62	100.0%
Tachypnea	50	80.6%	55	88.7%
Tachycardia	46	74.2%	51	82.3%
Nasal Flaring	10	16.1%	15	24.2%

At the start of the study, Group A had an average oxygen saturation of 92.5 ± 1.25% and Group B had an average of 92.2 ± 0.91% (p=0.075). Table 3 demonstrated that upon discharge, Group A exhibited a significantly higher average oxygen saturation level (98.3 ± 0.60%) in comparison to Group B (97.6 ± 0.91%) (p<0.001), as in Figure 1.

Table 3: Comparison of oxygen saturation between two groups.

Oxygen saturation (%)	**Group A**	**Group B**	**p value***
	Mean ± SD	**Mean ± SD**	
At admission	92.5 ± 1.25	92.2 ± 0.91	0.075
At discharge	98.3 ± 0.60	97.6 ± 0.91	< 0.001

* Mann-Whitney U test.

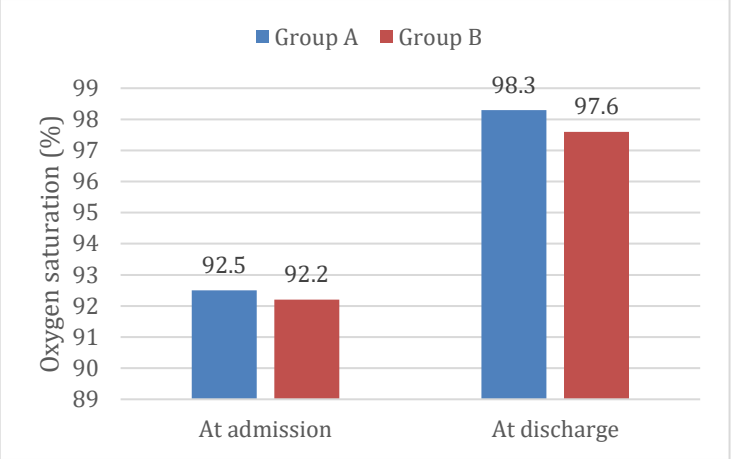

Figure 1: Oxygen Saturation (%) in both groups.

As shown in Table 4, At baseline, the mean CSS was 7.9 ± 0.68 in Group A and 8.2 ± 0.68 in Group B (p=0.017). At 12 hours, Group A's mean CSS decreased to 6.9 ± 0.65, while Group B's mean CSS was 7.5 ± 0.62 (p<0.001). By 24 hours, Group A's mean CSS further reduced to 4.2 ± 0.68, compared to 5.4 ± 0.64 in Group B (p<0.001). After 48 hours, the average CSS for Group A was 2.6 ± 0.59, which was substantially lower than Group B's average of 3.9 ± 0.66 (p<0.001). By 72 hours, Group A's mean CSS was 1.5 ± 0.53, while Group B's mean CSS was 2.7 ± 0.65 (p<0.001). This indicates that Group A experienced a more significant reduction in clinical severity over time compared to Group B.

Table 4: Comparison of mean clinical severity score (CSS) at different time periods of both groups.

Clinical severity score	**Group A**	**Group B**	**p value***
	Mean ± SD	**Mean ± SD**	
Baseline	7.9 ± 0.68	8.2 ± 0.68	0.017
At 12 hours	6.9 ± 0.65	7.5 ± 0.62	< 0.001
At 24 hours	4.2 ± 0.68	5.4 ± 0.64	< 0.001
At 48 hours	2.6 ± 0.59	3.9 ± 0.66	< 0.001
At 72 hours	1.5 ± 0.53	2.7 ± 0.65	< 0.001

* Mann-Whitney U test.

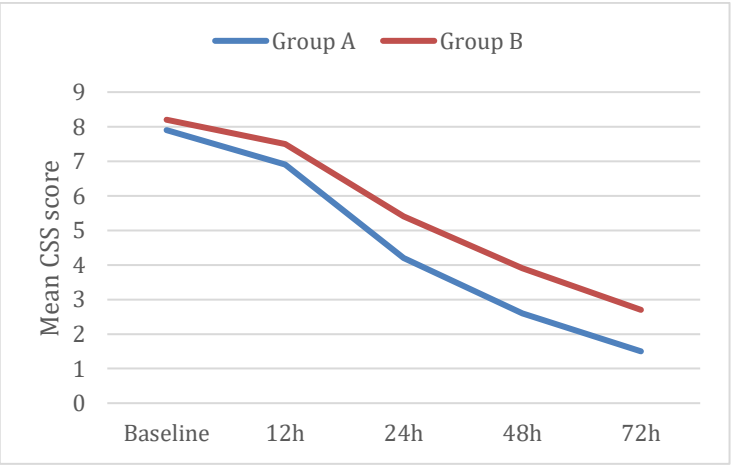

Figure 2: Mean clinical severity score at different times in both groups.

Table 5 indicated that the average duration of oxygen therapy was substantially lower in Group A (16.2 ± 2.47 hours) compared to Group B (23.3 ± 2.37 hours) (p<0.001), as in Figure 3.

Table 5: Evaluation of duration of oxygen therapy between two groups.

	Group A	**Group B**	**p value***
	Mean ± SD	**Mean ± SD**	
Duration of Oxygen Therapy (hours)	16.2 ± 2.47	23.3 ± 2.37	< 0.001

* Mann-Whitney U test.

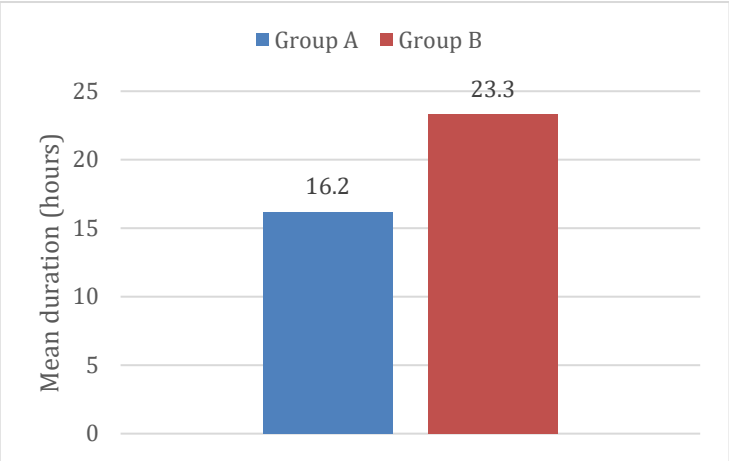

Figure 3: Duration of oxygen therapy in both groups.

Table 6 demonstrates a significant difference in the recovery rate between the two groups. In Group A, 57 patients (91.9%) experienced rapid recovery (≤ 72 hours) compared to 29 patients (46.8%) in Group B (p<0.001). In contrast, five patients (8.1%) in Group A and 33 patients (53.2%) in Group B experienced a prolonged recovery period (> 72 hours).

Table 6: Comparison of recovery between two groups.

Recovery	**Group A**		**Group B**		**p value***
	n	**%**	**n**	**%**	
Rapid (≤ 72 hours)	57	91.9%	29	46.8%	< 0.001
Gradual (> 72 hours)	5	8.1%	33	53.2%	

* Chi square test.

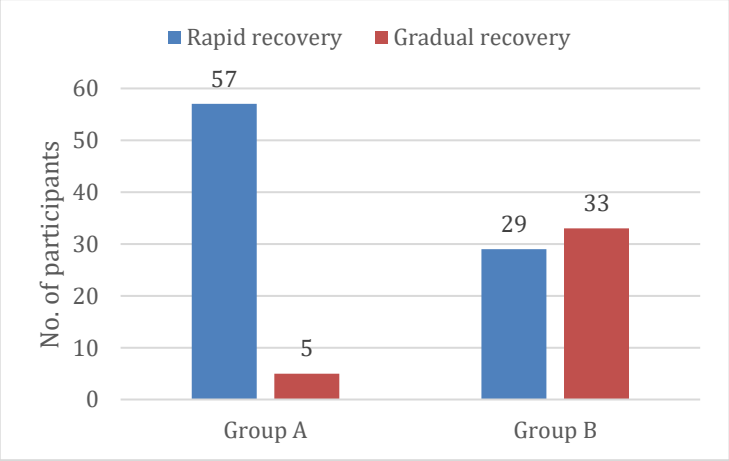

Figure 4: Comparison of recovery in both groups.

Table 7 indicated that Group A had a considerably shorter hospital stay duration (58.2 ± 7.32 hours) compared to Group B (72.7 ± 12.86 hours) (p<0.001), as in Figure 5.

Table 7: Comparison of length of hospital stays between two groups.

	Group A	**Group B**	**p value***
	Mean ± SD	**Mean ± SD**	
Length of Hospital Stay (hours)	58.2 ± 7.32	72.7 ± 12.86	< 0.001

* Mann-Whitney U test.

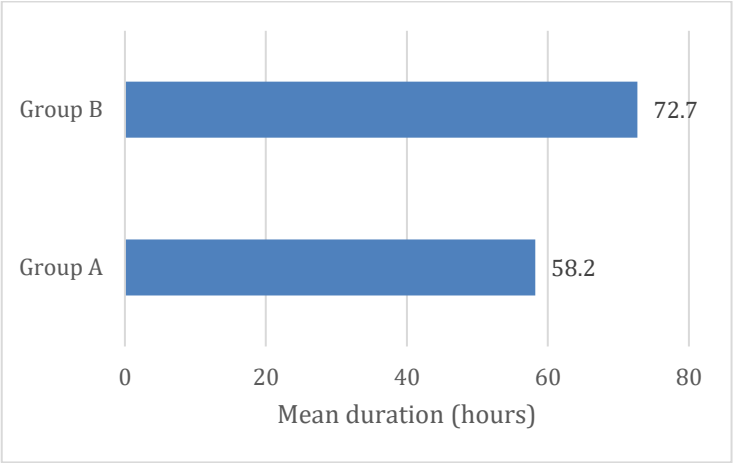

Figure 5: Length of Hospital Stay in both groups.

DISCUSSION

Bronchiolitis is a highly contagious respiratory disease affecting infants, typically caused by viruses such as Respiratory Syncytial Virus (RSV). Despite various treatment approaches including bronchodilators, corticosteroids, and antiviral medications, there remains a lack of consensus on the most effective standardized treatment regimen, leading to ongoing research and clinical trials to identify optimal therapeutic strategies.[12]

Our study observed that Group A had a higher proportion of males (66.1%) compared to Group B (54.8%), consistent with Salman MK et al., who also noted a male predominance in infants with bronchiolitis. Furthermore, the mean age in both groups aligns with their findings, where a significant percentage of infants in both the HS (78.9%) and NS (71.1%) groups were under 6 months. Concerning the gender distribution, the research also found out that there were relatively higher numbers of males among the two groups, with fifty four percent. 8% of the subjects in Group B and 66. 1% in Group A The demographic data of our study also revealed that there were more male infants more than females with bronchiolitis in the study This is in agreement with study conducted by Ralston et al (2014) who also noted we had more males in our cohort of infants with Bronchiolitis. Recently, the authors of the study reported systematically about the average age of 3% hypertonic saline (HS) group were 6 years. 03 ± 3. 71 years, and in the salbutamol group was 5 years. 48 ± 3. 35 years.[15]

This study also demonstrated a 100% prevalence of runny cough, nose, chest indrawing, rhonchi, breathing difficulty and these observations tally with the findings of Eleshet et al (2021) and Islam et al (2018) respectively in regard to symptoms existence. Wheezing was observed among the Group A 87% of the children. In 1% of the cases, while group B had wheezing in 93. Antonio expected poor health and vomiting in 98 % of the cases but recorded it in only 1% of the cases, while Group B had vomiting in 93.From the above tables, we can conclude that the findings of Antonio are quite paradoxical. 5 percent similar to Islam et al study, 93. 33% in group-I, and 95. 55% in group-II, whereas Eleshet et al 88. 8% in group-I and 93. 3% in group-II with the same group division. The rates of incidence of fever were higher in Group A (64. 5%) than those of

Group B (51. 6 %) than the incidence rate reported in the studies by Eleshet et al. (26. 66% in Group-I, 24. 4% in Group-II) and Islam et al. (28. 88% in Group-I 26. 66% in Group-II). The Tic was 80 for tachypnea of the Group A. 6% while the respondents in Group B 88. 7%. Likewise, they are given the rates of tachycardia in Group A which is 74. 2% while from Group B they were 82. 3%. In line with the present study on Nasal flaring, few studies have been performed by Eleshet et al. and Islam et al The frequency distribution of Nasal flaring was higher in our study Group B and 24. 2% more than Group A 16. 1% as compare to Eleshet et al 15. 6% in Group-I and 20% in Group-II and Islam et al 6 These results infer increased fever and nasal flaring prevalence in our study, other symptoms have been discussed in other studies and requires more investigation for these differences.[16,17]

Our study observed that at admission, the mean oxygen saturation was similar between the 3% hypertonic saline nebulization group (92.5 ± 1.25%) and the normal saline group (92.2 ± 0.91%, p=0.075). However, by discharge, the 3% hypertonic saline nebulization group had a significantly higher mean oxygen saturation (98.3 ± 0.60%) compared to the normal saline group (97.6 ± 0.91%, p<0.001). These findings contrast with Islam et al.'s study, which reported a significantly shorter mean duration of oxygen therapy in the hypertonic saline group (15.0 ± 6.0 hours) compared to the normal saline group (26.4 ± 5.4 hours, p=0.02).[17] In a similar study, Eleshet et al. found that the hypertonic saline group needed oxygen supplementation 17.7% of the time, compared to 33.3% in the normal saline group (p=0.14).[16]

In our study, At baseline, Group A's mean CSS was slightly lower than Group B's (7.9 vs. 8.2, p=0.017). Over time, the improvement in CSS was more pronounced in Group A: at 12 hours (6.9 vs. 7.5, p<0.001), 24 hours (4.2 vs. 5.4, p<0.001), 48 hours (2.6 vs. 3.9, p<0.001), and 72 hours (1.5 vs. 2.7, p<0.001), indicating a more rapid and substantial reduction in clinical severity. The results are consistent with the findings of Hossain et al. (2022), who observed that hypertonic saline was superior to normal saline and salbutamol in mitigating the severity of acute bronchiolitis. Their study also highlighted the superiority of hypertonic saline in improving clinical outcomes, which supports our observation of better CSS reduction in Group A.[18]

The results of our study indicate that the duration of hospitalization was considerably shorter in Group A (58.2 ± 7.32 hours) compared to Group B (72.7 ± 12.86 hours) (p<0.001). Literally, Nizam et al. (2024) reported the similar result that the patients receiving hypertonic saline had a mean of 3. 18±1. 11 days of hospital stay as compare to the control group patients those had 4. 44± 1. 08 days hospital stay of total duration (p<0. 001). Moreover, Gupta et al carried a study which showed that the mean length of stay for the hypertonic saline group was 3. 4 ± 1. seven days on the other hand Salbutamol group had a longer mean stay of four days. 9 ± 1. 4 days (p=0. 001). 15,19 Zhang et al. used meta-analysis of four randomized controlled trials that showed that nebulized 3% hypertonic saline in the dosage of 2 ml in one trial and 4 ml in the three others shortened the length of hospital stay and led to quicker improvements in clinical severity of the disease in infants with acute bronchiolitis. In a clinical study by Saleem et al, 2020 the duration of hospital stay of children who underwent nebulization with hypertonic saline was 36.However, it is important to note that this difference did not reach statistical significance. Conversely, our research discovered a noteworthy decrease in the duration of hospitalization for individuals who were administered hypertonic saline.[21]

The constraints of our investigation encompass the comparatively limited sample size and the absence of blinding, which could potentially generate partiality in patient evaluation and treatment results. Moreover, the investigation was carried out in a specific facility, therefore restricting the applicability of the findings to other contexts.

CONCLUSION

In conclusion, nebulized hypertonic saline demonstrates a significant advantage over normal saline in reducing clinical severity, shortening hospital stays, and improving recovery times in acute bronchiolitis. These data provide evidence that hypertonic saline is a superior therapy choice for controlling this illness.

REFERENCES

1. Linssen RS, Teirlinck AC, van Boven M, Biarent D, Stona L, Amigoni A, Comoretto RI, Leteurtre S, Bruandet A, Bentsen GK, Drage IM. Increasing burden of viral bronchiolitis in the pediatric intensive care unit; an observational study. Journal of critical care. 2022 Apr 1;68:165-8.
2. Ghazaly MM, Abu Faddan NH, Raafat DM, Mohammed NA, Nadel S. Acute viral bronchiolitis as a cause of pediatric acute respiratory distress syndrome. European Journal of Pediatrics. 2021 Apr;180:1229-34.
3. Bottau P, Liotti L, Laderchi E, Palpacelli A, Calamelli E, Colombo C, Serra L, Cazzato S. Something is changing in viral infant bronchiolitis approach. Frontiers in Pediatrics. 2022 Apr 14;10:865977.
4. Kawilarang M, Santoso TA, Dharmansyah RP, Angela A, Ferdiaananda MR. Nebulization Therapy in Pediatric Patients with Bronchiolitis: A Literature Review. Jurnal Keperawatan. 2024;16(2):821-40.
5. Mammas IN, Drysdale SB, Rath B, Theodoridou M, Papaioannou G, Papatheodoropoulou A, Koutsounaki E, Koutsaftiki C, Kozanidou E, Achtsidis V, Korovessi P. Update on current views and advances on RSV infection. International Journal of Molecular Medicine. 2020 Aug 1;46(2):509-20.
6. Sebina I, Phipps S. The contribution of neutrophils to the pathogenesis of RSV bronchiolitis. Viruses. 2020 Jul 27;12(8):808.
7. Douros K, Everard ML. Time to say goodbye to bronchiolitis, viral wheeze, reactive airways disease, wheeze bronchitis and all that. Frontiers in pediatrics. 2020 May 5;8:218.
8. Nazif JM, Taragin BH, Azzarone G, Rinke ML, Liewehr S, Choi J, Esteban-Cruciani N. Clinical factors associated with chest imaging findings in hospitalized infants with bronchiolitis. Clinical Pediatrics. 2017 Oct;56(11):1054-9.
9. Katiyar SK, Gaur SN, Solanki RN, Sarangdhar N, Suri JC, Kumar R, Khilnani GC, Chaudhary D, Singla R, Koul PA, Mahashur AA. Indian Guidelines on nebulization therapy. indian journal of tuberculosis. 2022 Jan 1;69:S1-91.
10. Goralski JL, Wu D, Thelin WR, Boucher RC, Button B. The in vitro effect of nebulised hypertonic saline on human bronchial epithelium. European Respiratory Journal. 2018 May 1;51(5).
11. Wang EE, Milner R, Allen U, Maj H. Bronchodilators for treatment of mild bronchiolitis: A factorial randomised trial. Arch Dis Child. 1992; 67:289–93
12. Toivonen L, Karppinen S, Schuez-Havupalo L, Teros-Jaakkola T, Mertsola J, Waris M, Peltola V. Respiratory syncytial virus infections in children 0–24 months of age in the community. Journal of Infection. 2020 Jan 1;80(1):69-75.
13. Salman MK, Ahmed J, Khan M, et al. Comparison of hypertonic saline and normal saline nebulization in treating infants with acute viral bronchiolitis. Pak J Med Sci. 2022;38(5):1174-78.
14. Ralston SL, Lieberthal AS, Meissner HC, et al. Clinical practice guideline: The diagnosis, management, and prevention of bronchiolitis. Pediatrics. 2014;134(5)
15. Gupta HV, Gupta VV, Kaur G. Effectiveness of 3% hyper- tonic saline nebulization in acute bronchiolitis among Indian children: A quasi-experimental study. Perspect Clin Res 2016;7(2): 88-93
16. Elesh H, El-khaleegy H. Efficacy of Nebulized Hypertonic Saline 3% in comparison to Nebulized Normal Saline 0.9% in Children with Acute Bronchiolitis. International Journal of Medical Arts. 2021 Jul 1;3(3):1584-8.
17. Islam KT, Mollah AH, Matin AB, Begum MA. Comparative efficacy of nebulized 3% hypertonic saline versus 0.9% Normal saline in children with acute bronchiolitis. Bangladesh J Child Health. 2018 Dec 17;42(3):130-7.
18. Hossain RM, Shams S, Kader MA, Pervez M, Bhuiyan MF, Hasan MM, Mollah MA. Efficacy of nebulized hypertonic saline versus normal saline and salbutamol in treating acute

bronchiolitis in a tertiary hospital: a randomized control trial. Int J Contemp Pediatr. 2022 Jun;9:523-8.
19. Nizam R, Khalid A, Shafique M, Imtiaz M, Masood S, Masood MK. Comparison of Mean Hospital Stay after Nebulization with 3% Hypertonic Saline vs Salbutamol in Treatment of Bronchiolitis. National Journal of Health Sciences. 2024 Jun 28;9(2):110-4.
20. Zhang L, Mendoza-Sassi RA, Wainwright C, Klassen TP. Nebulized hypertonic saline solution for acute bronchiolitis in infants. Cochrane Database of Systematic Reviews 2018; 4: CD006458
21. Saleem M, Saleem M, Khurshid A. Hypertonic saline versus normal saline nebulization in hospitalized children with acute bronchiolitis. Professional Med J 2020; 27(12):2734-2738.