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Non-Invasive Ventilation in Infants Attending a Tertiary Care Center: A Retrospective Review

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ABSTRACT

Bronchiolitis was the most significant worldwide cause of infant hospitalization, presenting with symptoms of cough, wheezes, difficulty in breathing, decreased feeding, and apneas. It is estimated that 1-3% of hospitalized infants will require treatment in an intensive care unit, especially when risk factors are present. This study analyzes the use of Non-invasive ventilation (NIV) in severe bronchiolitis and its role in reducing the rate of ventilator-associated pneumonia (VAP) and the duration of oxygen requirement. Data were collected retrospectively through PHENIX, a hospital electronic system for infants less than one year old. Shortness of breath, cough, apnea, cyanosis, N-CPAP immediate or later after few hours, mechanical ventilation (MV), length of hospital stay, and survival status were the outcome variables. Mann-Whitney U test was performed via SPSS version 25.0. Fifty-five infants with bronchiolitis were admitted with forty-nine episodes receiving NIV or MV. A total of thirty-seven infants were treated with NIV, while 15 infants were treated with MV. Fever was the major indication for initiating NIV among infants, followed by cough, apnea, and shortness of breath. Insignificant evidence was reported between baseline respiratory parameters and infants receiving NIV and MV. In the first four hours, changes in respiratory variables showed a significant increase for infants receiving NIV than those receiving MV. Infants receiving NIV had significantly fewer days in NIV and PICU but insignificant fewer days in the hospital stay. The experience of using NIV in infants admitted for bronchiolitis recommends that NIV might be an adjunct to mechanical ventilation. This strategy was related to a lower rate of pneumonia and a shorter duration of oxygen therapy.

Keywords: Apnea, Infants, Length of Stay, Non-invasive Ventilation, Respiratory Distress

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INTRODUCTION

Acute respiratory failure is accountable for 4.25 million deaths globally from influenza, pneumonia, respiratory syncytial virus and is the predominant cause of mortality in low and middle-income countries [1]. Bronchiolitis elevates the cause of infants' hospitalization across the world, specifically in Europe and North America [2-6]. Approximately 7% of bronchiolitis admissions need intensive care for ventilator support in the United Kingdom [7]. Respiratory failure has been reported in one-third of unplanned infant admissions to pediatric intensive care units (PICUs), majorly because of bronchiolitis. These admissions need a prolonged hospital stay and invasive mechanical ventilation [8]. The need to develop effective and safe alternatives to PICU admission and invasive ventilation is acute in countries with no retrieval infrastructure [9]. On the contrary, none of the interventions is supported by robust evidence of advantage for clinically significant findings commonly used for infants admitted with bronchiolitis, making this a subject of debate for future studies [10]. In particular, intensive respiratory is an intervention with identified complications in infants that occurred through invasive mechanical ventilation. The use of non-invasive ventilation (NIV) in pediatric acute respiratory failure of variable outcomes has been supported in a study [11]. Despite the fact that clinical approval is not universal and published best practice guidelines are not easily accessible, evidence suggests an increased usage of non-invasive ventilation in bronchiolitis [12]. Continuous positive airway pressure (CPAP) has been used differently since the 1970s. While in the year 2000, other non-invasive modalities were also introduced [13].

In this retrospective study, the use of NIV decreased the rate of ventilator-associated pneumonia and reduced the duration of oxygen requirement without prolonging the hospital stay. The objective was to analyze the use of NIV in severe bronchiolitis and its role in decreasing the rate of ventilator-associated pneumonia (VAP) and reducing the duration of oxygen requirement, therefore, shortening the hospital stay. The secondary outcome was to evaluate the final diagnoses, which will be based mostly on lower respiratory tract infections in infants and the mortality rate if the infants survived or died.

During the period of last two years, which was named as the period of NIV, the attending physicians were encouraged to use NIV as the primary ventilation support strategy when the infants required ventilator support, and the aim is to analyze the feasibility and efficacy of this strategy starting from the pediatric emergency department. Moreover, to show more evidence as well as predict process success.

METHODS

A retrospective review was conducted for infants who received NIV and invasive ventilation for bronchiolitis from January 2016 to July 2017. The data was retrieved from the hospital electronic system (PHENIX) after receiving the ethical approval committee to initiate the work. The data were gathered for all infants with one year and less who came to the pediatric emergency department with lower respiratory symptoms. All infants had a daily medical review at least twice a day at handover ward rounds. Patient observations included respiratory rate, oxygen saturation recordings, inspired oxygen concentration, continuous positive airway pressure (CPAP), and hourly heart rate as charted by nursing staff.

This study has also collected data for shortness of breath (SOB), cough, Apnea, cyanosis to the symptoms, cause of ARF, the severity of dyspnea, the BROSJOD score for bronchiolitis, and measurement of ARF before treatment using the Wood-Downes score for asthma. The study has collected data for infants who require N-CPAP immediately or later after few hours. The study has also collected data for infants who required mechanical ventilation (MV) from the start as they were very sick or required MV after failed to improve the N-CPAP. The final outcome was followed from the electronic files of the patients who with the length of hospital stay, survival, or died. Length of hospitalization was reviewed and should be correlated with early initiation of N-CPAP to the infants.

The hospital record of infants was then cross-checked to confirm agreement with the coded diagnosis or where bronchiolitis was not coded. However, none of the observations were missed related to symptoms attributed to bronchiolitis for patients receiving NIV. All infants were included who received NIV and/or invasive ventilation for bronchiolitis. Diagnostic criteria were based on clinical features of auscultation findings of bilateral crackles, a history of cough, and/or wheeze, with supporting chest X-ray findings of hyperinflation. For respiratory viruses, all infants underwent nasopharyngeal aspirate investigation.

The indication of NIV/CPAP was noted when the patient had severe or moderate dyspnea or if apneas were reported. Some particular contraindications were included for avoiding complications throughout transport. NIV or CPAP was excluded too when the stabilization time was anticipated to be greater than the transport duration. NIV failure was explained as

the requirement for removing the NIV initiated by the transport team due to lack of appropriate trigger, the requirement for intubation because of disease progression, and inadequate subject interfaces.

Two different ventilators were provided for non-invasive support: the Crossvent 2 (Bio-Med Devices, Guilford, Connecticut) or the Oxylog 3000 (Dra¨ger Medical, Lu¨- beck, Germany). CPAP values varied between 5 and 10 cm H2O pressure; NIV included maximum expiratory positive airway pressure of 5-8 cm H2O with inspiratory positive airway pressure of 18 cm H2O.

Criteria for severity for additional respiratory support include exhaustion secondary to increased work of breathing, apnea or irregular respiratory effort, and refractory hypoxia [14]. In addition, hypercarbia with acidosis defined as pH <7.25 and PCO2 ≥ 84 mm Hg were included for bronchiolitis. CPAP was included in NIV modes via a nasal mask or nasal prongs, either variable or pre-set for accomplishing levels between 4-6 cms H2O. Extra-thoracic negative pressure ventilation was also included through biphasic cuirass ventilation [15].

Inspired helium-oxygen mixture (Heliox, BOC, Guilford, UK) was provided in combination with biphasic cuirass ventilation or CPAP as rescue therapy. CPAP via a nasal mask or nasal prongs either pre-set for achieving levels between 4-6 cms H2O were included in NIV modes (Infant Flow1 System, Viasys Healthcare Inc, CA) or variable level (Infant Flow1 Advance System, Viasys; and AutosetTM, Resmed, Sydney, Australia); and extra-thoracic negative pressure ventilation via biphasic cuirass ventilation (RTXTM, Medivent, London, UK). A respiratory backup rate was provided by variable level CPAP and biphasic cuirass ventilation.

Gender, age, and weight at admission, chronic lung disease, immune deficiency or congenital cardiac disease, clinical presentation, status on initiation of ventilation, recorded methylxanthine use, nasopharyngeal aspirate results and history of prematurity were included as information from patient case notes via a standardized data collection instrument. Evidence of bacterial co-infection was noted, which includes radiological signs, clinical signs, white blood cell count > 20 X 109/L, C-reactive protein > 50 mg/L, and positive bacterial cultures. Outcome data had a non-invasive start in ER immediately. Invasive started 1-4 hours, invasive started after >24 hours, duration of invasive in days, MV after CPAP, PICU stay, and total hospital stay (HS) in days.

Details of complications included: increased oral or nasopharyngeal secretions, pneumothorax, interface issues such as nasal cannulae or tube, leak or skin complications, mask intolerance, aspiration of gastric contents, gastric distension, elevated inflammation markers, and new growth in sputum with chest X-ray modifications, and any issues leading to sedation if administered.

Using SPSS 25 (Chicago, IL), was conducted Statistical data. Differences between the three groups (responders, non-responders, and mechanical ventilation from the start) were examined using the Kruskal-Wallis test. Differences between the two groups (Survived and died) were investigated using the Mann-Whitney U test. Fisher's exact test was used for comparisons between two groups for data with contingency tables, indicating expected cell counts of <5. Two-tailed tests were used throughout with P-values of 0.05.

RESULTS

Fifty-five infants with bronchiolitis were admitted to the hospital over the period of 18 months. Forty-nine episodes were identified in 55 patients who received either NIV or mechanical ventilation. All episodes for severity and respiratory support have fulfilled formal criteria. In total, 55 patients were treated with NIV, out of which 37 infants required non-invasive ventilation in ER and 15 infants required mechanical ventilation.

Figure 1 shows diagnosis status and reported bronchiolitis among majority of the infants (n = 14), followed by pneumonia (n = 7), sepsis (n = 7), pneumonia and other respiratory disorders (n = 5), and bronchopneumonia (n = 4).

Table 1 summarizes and admission characteristics. The female to male ratio was 1.04:1, which shows that female infants were majorly admitted to the hospital. The mean age at the time of admission was 4.378 ± 3.1796 months. The majority of the infants were classified as full-term (92.7%), while only four infants were classified as preterm (7.3%). Indications for initiating NIV were fever (n = 37, 67.3%), cough (n = 37, 67.3%), apnea (n = 39, 70.9%), and shortness of breath (n = 41, 74.5%). Mechanical ventilation was provided to 8 infants (14.5%) after CPAP; whereas, non-invasive ventilation was majorly provided to infants in ER (67.3%).

Table 2 summarizes the data for baseline respiratory parameters for responders, non-responders, and mechanically ventilated from the initial presentation. Responders and non-

responders had the highest rates of PH but did not reach any significance. Similarly, responders and those mechanically ventilated had the highest rates of PCO3 but did not reach any significance. Responders and mechanically ventilated cases had the highest rates in HCO3 and base excess but did not reach any significance, respectively.

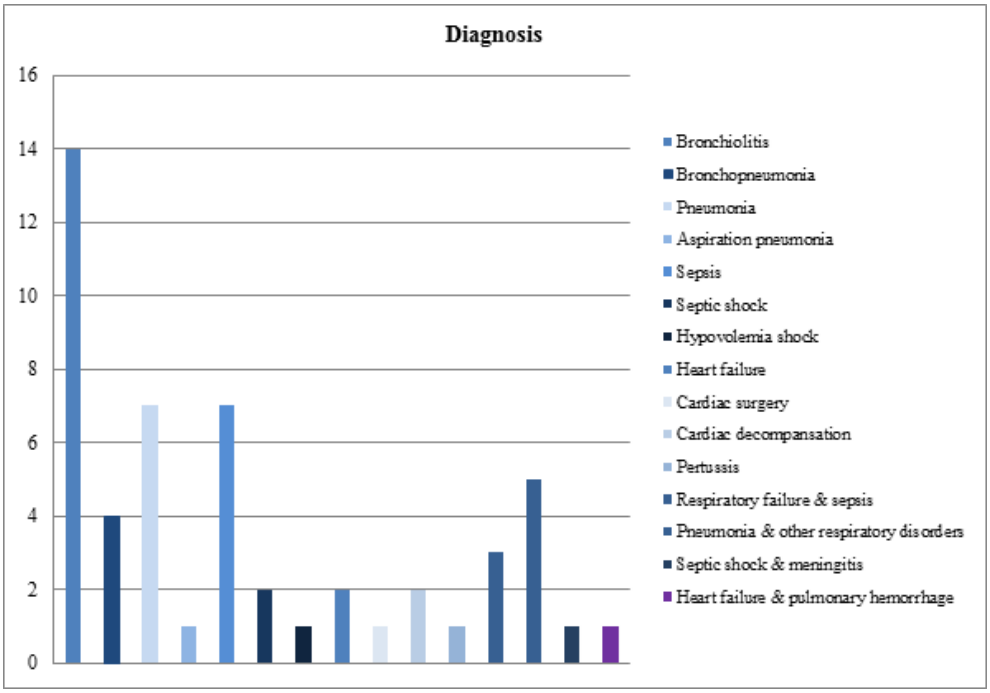

Figure 1: Diagnosis Status.

Table 3 shows changes in respiratory variables in the first four hours from pre-ventilation to 1 and 4 hrs after initiation of ventilation. The non-responders showed significant increase in PH, PCO3, and HCO3 as compared to responders and mechanically ventilated, but did not reach to any significance.

Table 4 shows short-term outcomes and compared them with the survival status. It was observed that those patients who managed on NIV had significantly more days in non-invasive than patients who died (P = 0.039). Patients who survived with NIV had significantly fewer days in PICU than patients who died in PICU stay (p = 0.022). However, patients who survived with NIV showed fewer days in hospital stay but did not reach any significance.

The severity of dyspnea was classified as severe in 22 subjects (40%). Moderate respiratory failure was reported in 27 subjects (49%), while only six issues had a mild respiratory failure (Table 5).

This study explains that infants with respiratory issues due to severe bronchiolitis can be effectively and safely stimulated by NIV regardless of long-term sequela, preventing complications related to exposure to high concentrations of oxygen, mechanical ventilation, and lengthy hospital stays [16-20].

Findings encouraging the use of NIV in bronchiolitis are amassing, but evidence of large prospective randomized trials is interesting, as shown by their scarcity in the literature [21-26]. Few attempts have explored the outcomes of responders and non-responders, and this study has presented short-term results of a cohort of infants with severe bronchiolitis treated with NIV [27]. The advantages are enormous regarding resource utilization, which is an important parameter globally since over 75% are treated without invasive ventilation. For infants, the PICU stay and hospital stay were longer for patients with severe bronchiolitis [28, 29].

CPAP is assumed to enhance oxygenation and gas exchange in bronchiolitis by reducing breathing and recruiting at electric lungs, but its contribution to apnea treatment is not well-established [30,31]. The extent of infants reacted to CPAP for apnea, but the inclusion of methyl-xanthines in some episodes makes it complicated to be treated. None of the patients responded to CPAP who received methyl-xanthines. It might be because of the fact that initial application of a modality might be more effective with a backup rate for such infants in NIV is to be used.

A decrease in oxygen requirement was associated with a ventilation strategy based on NIV as the primary ventilation support and therefore tends to reduce the length of stay, as shown

in the previous study [32]. This difference can be explained by the use of sedative drugs in intubated infants. On the contrary, this was not related to a substantial decrease in ventilation duration. The paucity of a standardized weaning protocol can demonstrate the lack of reduction in ventilation duration with NIV for infants treated by NIV [33]. The mean hospital length of stay was higher (6 days for the NIV group) as compared to those reported in previous studies [34, 35]. Due to different reasons, the hospital stay of infants with severe bronchiolitis can be prolonged, which includes differences in the discharged policy, social problems, and feeding troubles. The findings do not deem to be demonstrated by a lower severity in infants throughout the NIV period. The comorbidities of severe pneumonia infection are majorly associated with pre-existing factors.

Table 1: Admission characteristics

	Frequency	Percent	
Sex*	Female	25	45.5
	Male	24	43.6
	Total	49	89.1
Age at the time of admission (months)			4.378 ± 3.1796
Oxygen requirement on admission*			3.128 ± 2.6971
Delivery	Term	51	92.7
	Preterm	4	7.3
	Total	55	100.0
Fever*	No	4	7.3
	Yes	37	67.3
	Total	41	74.5
Cough*	No	4	7.3
	Yes	37	67.3
	Total	41	74.5
Apnea*	No	2	3.6
	Yes	39	70.9
	Total	41	74.5
Shortness of Breath*	Yes	41	74.5
	No	3	5.5
Non-invasive ventilation in ER	Yes	37	67.3
	MV	15	27.3
	Total	55	100.0
Non-invasive ventilation in 1-4 hr	No	40	72.7
	Yes	1	1.8
	MV	14	25.5
	Total	55	100.0
Non-invasive ventilation after >24 hr	No	39	70.9
	Yes	2	3.6
	MV	14	25.5
	Total	55	100.0
MV after CPAP	No	32	58.2
	Yes	8	14.5
	MV	15	27.3
	Total	55	100.0
Survival	Yes	48	87.3
	No	7	12.7
	Total	55	100.0
PICU Stay (days)			6.37 ± 5.490
Total HS (days)			16.60 ± 12.150

* Variables showed missing observations

Table 2: Respiratory parameters for responders, non-responders, and mechanically ventilated from outset*

		Responders (N = 3)	Non-responders NIV (N = 37)	Mechanical ventilation (N = 1)	P (test)
Ph	Median	7.28	7.27	7.21	0.526
	Range	7.28-7.36	7.12-7.41	0-7.21	
PCO2	Median	54	47	49	0.678
	Range	46-56	31-68	0-49	
HCO3	Median	23	19.2	19.2	0.386
	Range	18.3-28.5	13-29.4	0-19.2	
Base excess	Median	5.3	4.3	5.6	0.778
	Range	1.2-6.3	2.1-8.3	0-5.6	

* Variables showed missing observations

Table 3: Changes in respiratory variables in the first 4 hours (1-4) in infants*

		Responders (N = 3)	Non-responders NIV (N = 37)	Mechanical ventilation (N = 1)	P (test)
Ph	Median	7.27	7.36	7.21	0.356
	Range	7.12-7.41	0-7.36	0-7.21	
PCO2	Median	47	54	49	0.777
	Range	31-68	0-54	0-49	
HCO3	Median	19.2	28.5	19.2	0.097
	Range	13-29.4	0-28.5	0-19.2	
Base excess	Median	4.3	5.3	5.6	0.852
	Range	2.1-8.3	0-5.3	0-5.6	

* Variables showed missing observations

Table 4: Comparison between short-term outcomes and survival group

	Survived (N = 36)	Died (N = 4)	P (test)
Total days in non-invasive	3.11 ± 2.18	2.75 ± 3.5	0.039
PICU Stay (days)	5.72 ± 3.82	12.25 ± 13.02	0.022
Total HS (days)	16.33 ± 12.1	19 ± 13.61	0.683

Table 5: Severity of respiratory failure

	Responders	Non-responders	Mechanical Ventilation	Total
Mild ARF, n (%)	0 (0)	5 (83.3)	1 (16.7)	6 (11)
Moderate ARF, n (%)	2 (7.40)	24 (88.9)	1 (3.70)	27 (49)
Severe ARF, n (%)	1 (4.55)	20 (90.90)	1 (4.55)	22 (40)

A threshold for intubation has been recommended in guidelines for NIV use in the adult population, such as complications or deterioration of therapy. However, similar procedures were absent for infant bronchiolitis. A trial of NIV is suggested as non-responders had similar findings to those mechanically ventilated from the initial admission in most cases. It is assumed that guideline construction should consider hypercarbia degree at presentation, where pre-set CPAP might be less influential as a sole modality. That reaction should guide the requirement for elevation or adjustment of therapy, even as early as throughout the first 4 hr. This approach equals treatment strategy with invasive ventilation, where adjustment and troubleshooting are needed if the preferred response is not produced but has not previously been detected with respect to NIV for bronchiolitis.

Infants successfully managed with NIV were likely less effective than those who were mechanically ventilated and might have controlled regardless of respiratory support. It was unlikely that an unrepresentative group was examined because a total of 55 patients were admitted to the hospital with bronchiolitis over the 18-months study period. On the contrary, almost all of the patients had achieved the objective criteria for respiratory support.

CONCLUSION

NIV was effectively and safely used over 18 months for supporting infants with pneumonia due to bronchiolitis with a low requirement to elevate to invasive ventilation. Evidence on presentation and clinical course assist in developing guidelines for the use of NIV in bronchiolitis for infants. The retrospective nature of the data and the small sample sizes were the limitations of this study. Some biological data were lacking, such as blood gas analysis. No written standardized protocols were used for setting and weaning for the NIV group over the study period. On the contrary, the study was conducted in the same PICU over 18-months with the same physicians to postulate that habits did not change over the study. The prospective controlled trial will be necessary for confirming the efficiency of NIV compared with intubation for evaluating possible advantages in the length of hospital stay and PICU.

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Authors' contributions

The participation of each author corresponds to the criteria of authorship and contributorship emphasized in the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals of the International Committee of Medical Journal Editors. Indeed, all the authors have actively participated in the redaction, the revision of the manuscript, and provided approval for this final revised version.

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Conflict of interest

The author declares no competing interest.

Data Availability

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Supplementary Materials

None

Ethical approval

Although this is not a direct human study, no patient identifying data were used in the present study, but still, the authors declare that all the ethical principles were obeyed while designing and conducting the present study. In the time this study was designed and conducted, our institution did not have any research or ethics committee, but the protocol for the present study was officially approved by the institutional academic council (Reference no: 181-3/9/2016).

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