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Research Article

High Flow Nasal Cannula Therapy in Infant Bronchiolitis: A Developing Perspective, and A Long-Term Assessment of the Effects on Length of Hospital Stay

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Abstract

Objective: This study investigates the influence of High Flow Nasal Cannula (HFNC) therapy on respiratory effort within the first six hours of treatment and assesses its potential impact on reducing hospital or Pediatric Intensive Care Unit (PICU) length of stay (LOS) for patients diagnosed with bronchiolitis. **Methods:** Using an interrupted time series design, ARIMA models were employed to analyze rates of invasive and non-invasive mechanical ventilation (MV/NIV), as well as PICU and hospital LOS. The effects on respiratory effort were estimated using the Hedges g test. **Results:** Data from 626 bronchiolitis patients (2015-2019) revealed no significant impact on MV/NIV rates post-HFNC introduction. In 2019, a 28% reduction in PICU admissions was estimated. HFNC correlated with reduced hospital LOS, estimated at 1.4 days (2017), 1.8 days (2018), and 2.6 days (2019). Notably, post-HFNC respiratory rates showed improvement (47.3 ± 12 to 37.8 ± 10.3, $p < 0.0001$, Hedges' g -0.83), as did heart rates (145 ± 20 to 138 ± 20, $p = 0.004$, $g = -0.34$) and Wood-Downes-Ferres scores (pre: 5.3 ± 1.24, post: 4.3 ± 1.32, $p < 0.0001$, $g = -0.79$). **Conclusions:** HFNC therapy for bronchiolitis correlated with reduced hospital LOS and PICU admissions over the study period. The observed improvement in respiratory effort suggests a potential contributing factor to these positive outcomes, emphasizing implications for clinical management.

Introduction

Bremains a pivotal concern in pediatric healthcare, affecting children below the age of two [1]. Bronchiolitis stands as the leading cause of hospitalization among infants younger than one year old, constituting approximately 100,000 hospitalizations annually in the United States. The economic impact of this burden is substantial, with estimated costs totaling $734 million. This statistic underscores the significant strain bronchiolitis places on pediatric healthcare resources and highlights the urgent need for effective interventions to alleviate its impact [2].Despite evolving guidelines advocating streamlined care and resource optimization, the burden persists, with approximately 1-3% of cases necessitating hospital admission [3]. Efforts to curtail unnecessary healthcare services, such as chest radiography, have demonstrated limited success [4]. Furthermore, the escalating trends in intensive care unit (ICU) utilization and associated costs underscore the pressing need for novel interventions [5].

The emergence of High-Flow Nasal Cannula (HFNC) as a respiratory support modality injected renewed hope into the landscape of bronchiolitis management [6-8]. Initial expectations centered around reduced pediatric ICU (PICU) admission rates and improved cost-effectiveness [6]. However, pivotal randomized trials, including studies by Kepreotes et al., Franklin et al., and Durand et al., yielded inconclusive evidence regarding HFNC's superiority over standard oxygen therapy [9-11]. Despite the lack of clear-cut superiority, HFNC gained popularity in pediatrics due to its ease of use and excellent tolerability by children, contrasting with other non-invasive ventilation methods such as Continuous Positive Airway Pressure (CPAP) [11].

In the study conducted by Granda et al., which evaluated nine clinical scales, including three newly introduced ones, to predict relevant outcomes in pediatric bronchiolitis patients in an emergency department setting, it is relevant to highlight that no significant differences in performance were identified among the scales. The results indicated an overall uniformity in the ability to predict relevant outcomes, with no single scale statistically outperforming the others. These innovative findings provide important insights for clinical practice, suggesting that, in the context of bronchiolitis, various scales, including the Wood Downes Ferres score, demonstrate comparable performance in predicting relevant clinical outcomes [12].

In light of this context, our study posits a compelling hypothesis: given time for learning and adaptation, HFNC could unveil previously unrealized benefits, particularly in terms of reducing hospital or PICU length of stay. Additionally, we delve into the immediate effects of HFNC on respiratory work within the initial six hours of therapy. Our investigation scrutinizes pre and post-HFNC heart and respiratory rates, as well as the impact on the Wood-Downes-Ferres score, aiming to uncover nuanced insights into the broader implications of HFNC in pediatric bronchiolitis care.

Methods

We conducted an analysis of data from patients needing to be hospitalized in Santa Catarina Hospital, a prominent private tertiary general hospital located in the heart of São Paulo, Brazil. Santa Catarina Hospital boasts a total of 352 hospital beds, including 58 pediatric ward beds and 26 Pediatric Intensive Care Unit (PICU) beds, making it a vital healthcare institution in the region during the seasonal period. The study included information on children aged 24 months or less diagnosed with bronchiolitis according to the criteria of the American Academy of Pediatrics [1,13]. Exclusion criteria comprised congenital heart disease, initial diagnosis of bacterial pneumonia, or incomplete data in medical records. The study received ethics approval (National Research Ethics Commission certificate number 41744620.5.0000.0068), and a waiver of the consent form was granted due to the retrospective nature of the study.

Data were retrospectively collected by reviewing the MV software (an electronic health medical record system) and the admission books of both the PICU and pediatric ward. In the primary data analysis, interrupted time series were constructed for key outcomes, including the rate of patients needing to be hospitalized in the ward or PICU, ventilation time, PICU, and hospital stays.

"Exposure" was defined as the commencement of High Flow Nasal Cannula (HFNC) use. Prior to exposure, protocol training for the initiation and weaning of HFNC with the healthcare team was conducted in the beginning of 2017 (the first three months of the year, before exposure to HFNC), including the use of the Wood-Downes-Ferres score for objective stratification of disease severity before using HFNC. The pre-exposure period encompassed the years 2015 and 2016, preceding the implementation of HFNC. March 2017 marked the initiation of exposure. The analysis extended until the end of the seasonality of each year from 2017 to 2019. Time series were constructed considering the months of seasonality as time points (from the beginning of March to the end of August). We did not study the years 2020 to 2022 due to the coronavirus pandemic. Autoregressive Integrated Moving Average (ARIMA) models were built, taking into account trends and autocorrelations, to estimate the effect of the intervention [14].

In the other arm of the study, we analyzed measurements of respiratory and heart rates, as well as Wood-Downes-Ferres scores, for patients who received HFNC immediately before and 6 hours after the start of therapy. The Wood- Downes-Ferres score categorizes bronchiolitis severity as mild (1–3 points), moderate (4–7 points), or severe (8–14 points) [15]. To describe the standardized mean differences of the effects, we used the Hedges' g test, where "g" between 0.2 and 0.5 indicates a small effect, values between 0.5 and 0.8 denote a moderate effect, and values above 0.8 suggest a large effect. These values are negative when the direction of the effect is a reduction. To compare measurements before and after HFNC, we utilized the paired T-test. Statistical analyses were performed using SPSS software (IBM Corp., Armonk, NY), and R (R Foundation for Statistical Computing, Vienna, Austria)

Results

Patient Demographics

A retrospective analysis encompassing 626 hospitalized bronchiolitis patients from 2015 to 2019 reveals distinctive patient profiles, with annual case distributions as follows: 106 (2015), 76 (2016), 157 (2017), 144 (2018), and 143 (2019). Notable characteristics include a 9.4% prevalence of prematurity history, 1.5% Broncho dysplasia incidence, and 13.8% recurrent wheezing. Respiratory syncytial virus (RSV) predominated, with consistently high positive test rates (Table 1).

	2015	2016	2017	2018	2019
N	106	76	157	144	143
AGE (median, IIQ)- months	6 (2,2-11)	6 (3-11,2)	7 (2-14)	6 (2-11)	7 (3-10)
AGRESPVIR	104(98%)	67 (88%)	151 (96%)	118 (81,2%)	61 (42%)
VSRAG	8 (7,5%)	2 (2,6%)	6 (3,8%)	23 (15,9%)	66 (46,1%)
Steroids	50 (46%)	39 (51%)	83 (52,8%)	65 (45,1)	65 (45,4%)
Nebulization	96 (90%)	71 (93%)	152 (96%)	105 (73%)	116 (81%)
Antibiotics	50 (46%)	32 (42%)	89 (56,6%)	69 (47%)	42 (29,3%)
HFNC	-	-	28 (17,8%)	39 (27%)	33 (23%)
NIV	0	1 (1,3%)	3 (1,9%)	7 (4,8%)	4 (2,8%)
MV	3 (2,8%)	7 (9,2%)	12 (7,6%)	14 (9,7%)	4 (2,8)
HFNC Evolution for/ MV	-	-	9/28 (32%)	6/39 (15,3%)	4/33 (12,1%)
HFNC after extubation	-	-	8/12 (66,6%)	7/14 (50%)	3/4 (75%)
RCP (Mean, DP)	1,23 (1,7)	1,53 (2,8)	1,9 (4,3)	2 (3,7)	1,57 (2,8)
Average length of stay (days, median, IIQ)	5 (3-6,1)	6 (4-6,5)	6 (5-8)	5 (4-7)	5 (4-7)
Admitted in ICU	28 (26,4%)	25 (32,8%)	84 (53,5%)	78 (54,1%)	59 (41,2%)
length of stay in ICU (days, median, IIQ)	4 (3-5,7)	4 (2-4,6)	6 (5-7,1)	5,5 (4-8,2)	5 (4-6,1)

Table 1: Demographic data and other patient characteristics IQR– interquartile range 27-75. Data are in numbers/percentages, except where indicated.

ARIMA Models and HFNC Impact

Utilizing ARIMA models, no discernible effect was noted on the rates of non- invasive and invasive mechanical ventilation post the introduction of high-flow nasal cannula (HFNC). An initial increment in ICU length of stay in 2017 by 2.18 days subsided in subsequent years. Conversely, a reduction in hospital median stay emerged, estimated at 1.4 days (2017), 1.8 days (2018), and 2.6 days (2019). The introduction of HFNC correlated with an initial 13.3% increase in PICU admissions in 2017, followed by a notable 28% reduction in 2019 (Table 2A, 2B) (Figure 1 and 2).

	Effect estimation (coefficient)	Standard error	t	Sig.
Tempo	0,007	,005	1,283	,256
Interact	-0,008	,007	-1,040	0,346
Phase 2017	0,002	,025	0,097	0,926
phase 2018	-0,005	,028	-0,181	0,864
phase 2019	-0,020	,037	-0,547	0,608

Table 2A: ARIMA model for NIV Phase percentages: level effect.

	Effect estimation (coefficient)	Standard error	t	Sig.
Tempo	0,015	0,011	1,376	,227
Interact	-0,045	0,014	-3,320	0,021
Phase 2017	-0,061	0,059	-1,026	0,352
phase 2018	-0,106	0,068	-1,554	0,181
phase 2019	-0,151	0,079	-1,926	0,112

Table 2B: ARIMA model for MV phase percentages.

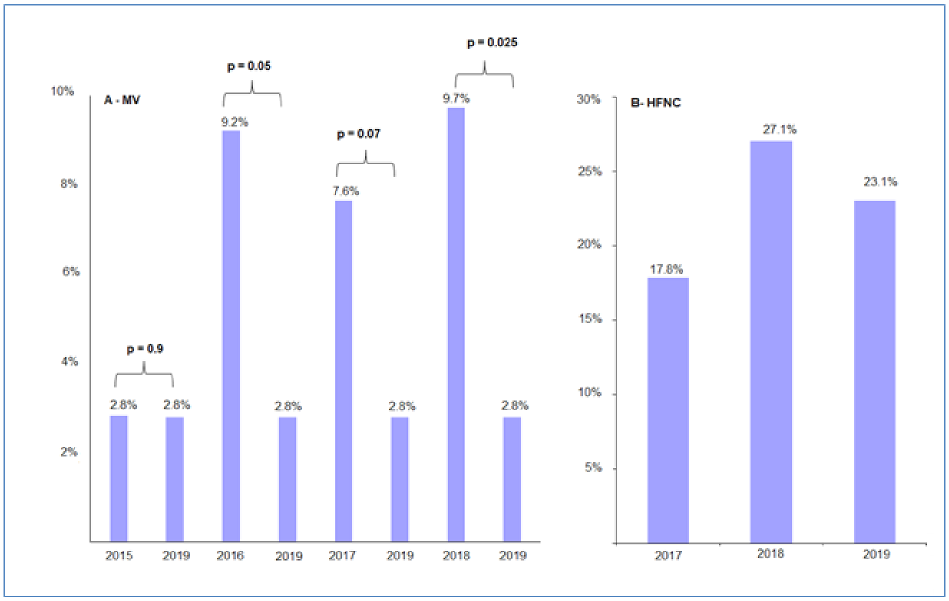


Figure 1: percentage of patients undergoing mechanical ventilation and HFNC in the years. Panel A shows comparisons between the frequencies of the years in relation to the year 2019, the last year of the series, using the chi-square test.

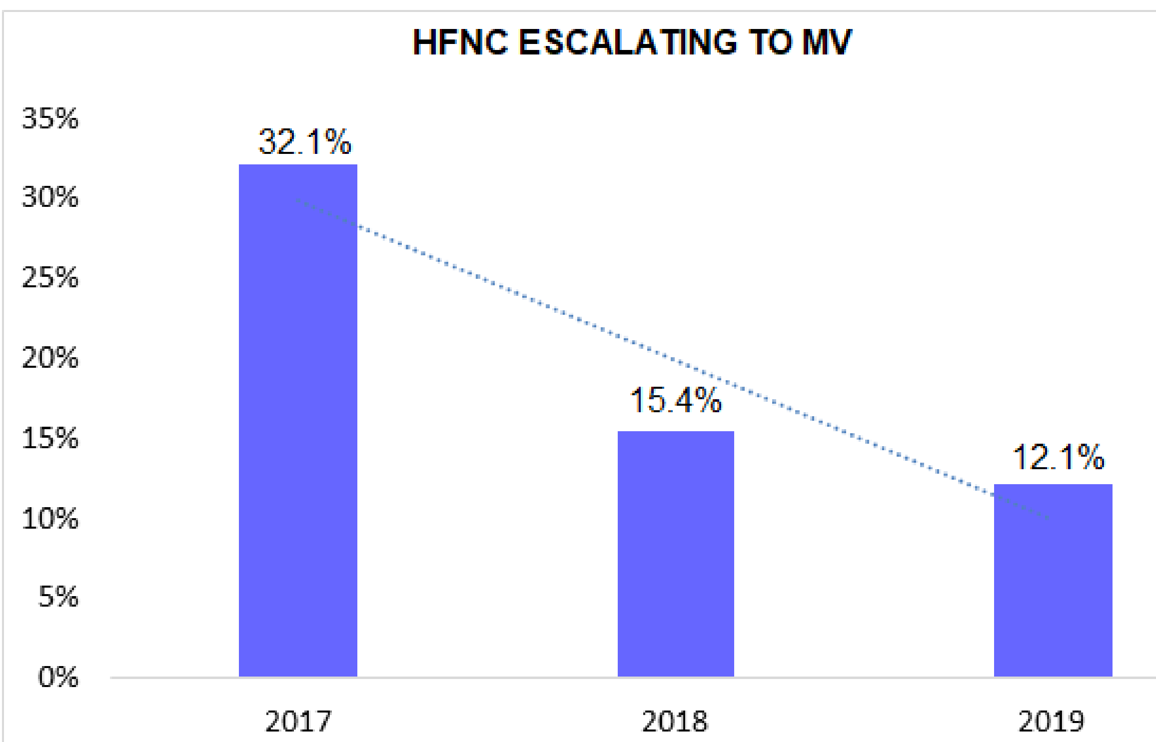


Figure 2: percentage of cases that required HFNC and progressed to mechanical ventilation inthe years 2017 to 2019, with a trend line showing a reduction in the percentage (p = 0.03 by chi-square, comparing the frequencies of 2019 and 2017)

Respiratory and Heart Rate Changes with HFNC

Analysis of respiratory and heart rates, pre and post 6 hours of HFNC initiation in 98 patients (2017-2019), yielded significant findings. Pre-HFNC mean respiratory rates of 47.3 (±12) decreased significantly to 37.8 (±10.3) post- HFNC ($p < 0.0001$, paired T-test), exhibiting a substantial effect size (Hedges' g = -0.83). Similarly, pre-HFNC mean heart rates of 145 (±20) decreased to 138 (±20) post-HFNC ($p = 0.004$, paired T-test) with a smaller effect size (Hedges' g = -0.34) (Figures 3,4,), (Tables 3, 4).

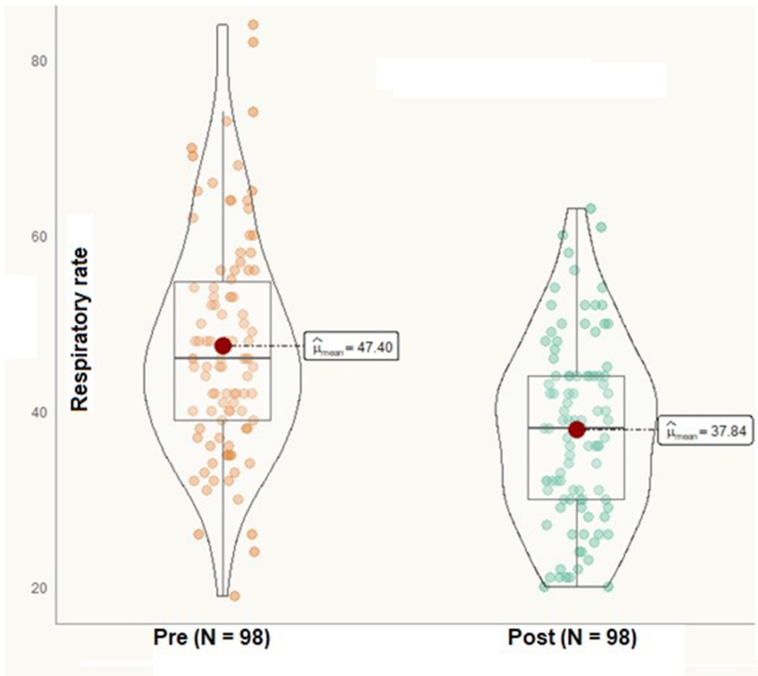


Figure 3: Violin graph highlighting the averages (red dots) of respiratory frequencies of 98 patients, before and after 6 hours of HFNC, with a significant reduction (p <0.0001 by paired T test).

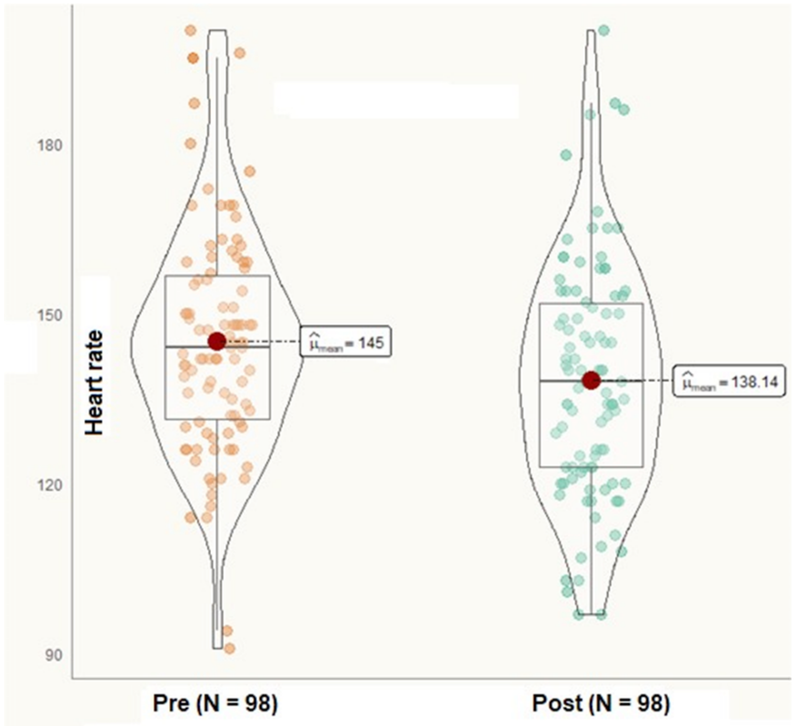
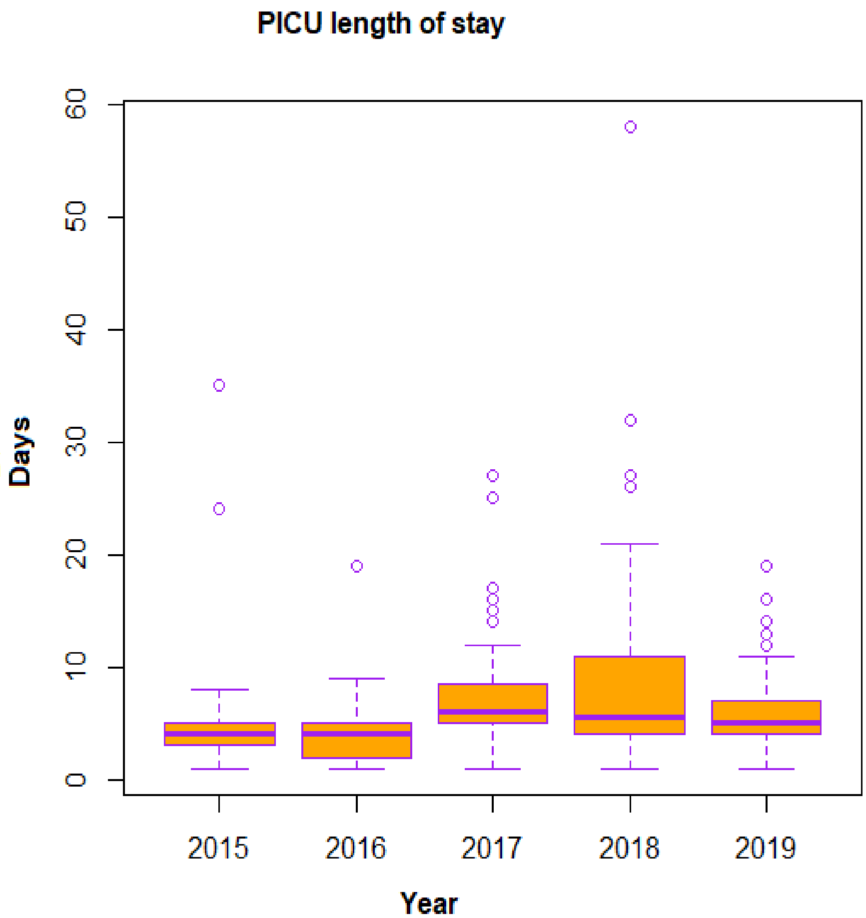


Figure 4: Violin graph highlighting the averages (red dots) of the heart rates of 98 patients, before and after 6 hours of HFNC, with a significant reduction (p = 0.004 by paired T test).

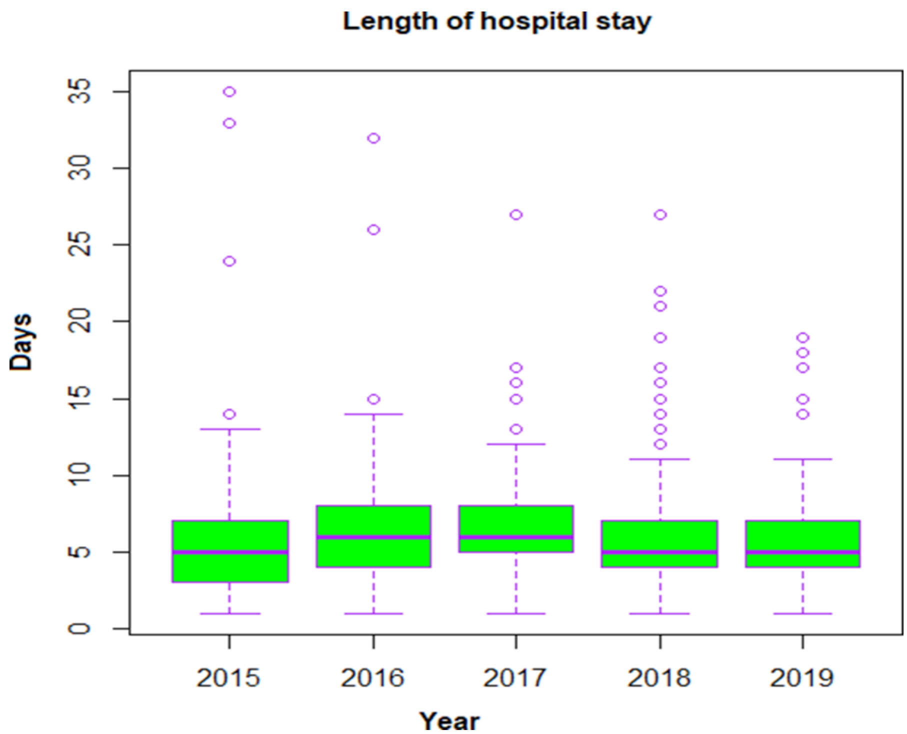
	Effect estimation (coefficient)	**Standard error**	**t**	**Sig.**
Time	0,034	0,148	,231	0,827
Interact	-0,428	0,186	-2,303	0,069
Phase 2017	2,180	0,677	3,222	0,023
phase 2018	0,896	0,917	0,977	0,374
phase 2019	0,467	1,052	0,444	0,675

Table 3: ARIMA model for median ICU length of stay. Phase: level effect.



	Effect estimation (coefficient)	Standard error	t	Sig
Time	0,362	0,119	3,029	0,029
Interact	-0,388	0,159	-2,441	0,059
Phase 2017	-1,438	0,558	-2,579	0,049
phase 2018	-1,826	0,642	-2,844	0,036
phase 2019	-2,602	0,875	-2,973	0,031

Table 4: ARIMA model for median hospital stay times.



Wood-Downes-Ferres Score

Pre-HFNC scores (Mean: 5.3, SD: 1.24) significantly differed from post-HFNC scores (Mean: 4.3, SD: 1.32) ($p < 0.0001$, T-test). The effect size, as determined by Hedges' g, was substantial at -0.79, signifying a moderate to large effect. (Figure 5)

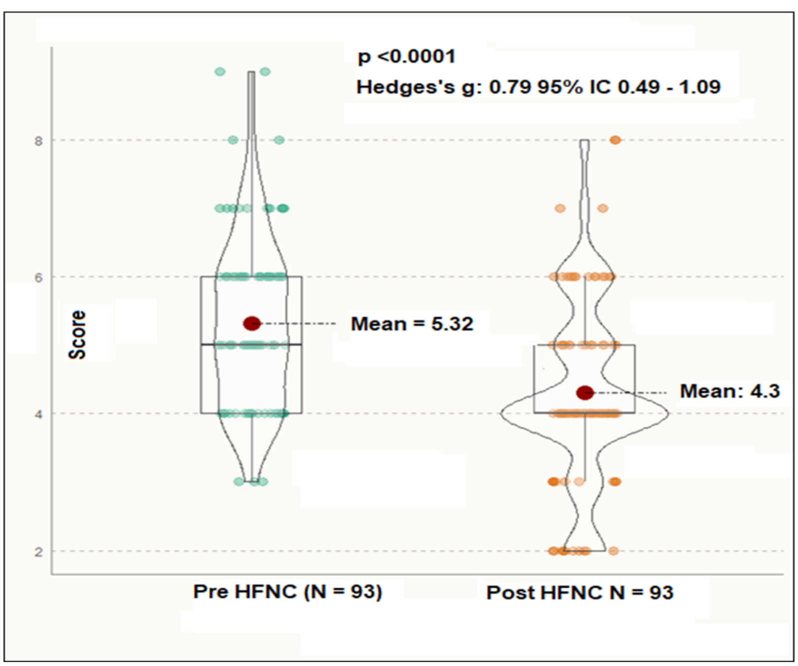


Figure 5: Score Wood-Downes- Ferris.

In summary, the integration of HFNC exhibited nuanced impacts on clinical metrics, suggesting potential benefits in the management of bronchiolitis among hospitalized patients.

Discussion

One of the most intriguing findings in this study is the substantial estimated reduction in the median hospital length of stay. The question surrounding the impact of High-Flow Nasal Cannula (HFNC) on hospital stay yields varied results across different studies. For instance, Franklin et al., in a large randomized study in Australia and New Zealand, comparing HFNC to standard oxygen therapy in children with acute hypoxemic respiratory failure (not exclusively due to bronchiolitis), discovered that the length of hospital stay was longer in the HFNC group, with a median of 1.77 days compared to 1.50 days in the standard oxygen therapy group [10]. Conversely, Murphy et al.'s small study in South Africa found no difference in the length of hospital stay between HFNC and conventional oxygen therapy [16]. In the study by Ergul et al. from Turkey, comparing HFNC with facemask oxygen therapy, patients in the HFNC group exhibited a more rapid recovery, shorter times to weaning off oxygen, and quicker hospital discharge [17]. Huang et al. observed a significant reduction in the median hospital length of stay following the introduction of their protocol- driven approach to HFNC therapy for bronchiolitis patients. This finding is particularly intriguing as it contrasts with some previous studies examining the impact of HFNC on hospital stay [8]. The unique design of our study allows us to observe a progressive reduction in hospitalization time over the years following the introduction of HFNC.

Interrupted time series studies aim to examine whether patterns observed after an intervention differ from those observed pre-intervention, representing one of the most robust quasi-experimental designs [18]. The reported level effects indicate the change defined as the difference between the observed level at the first intervention time point and that predicted by the pre-intervention time trend. This analysis can ascertain whether the intervention had a significantly greater effect than any underlying secular trend [19]. An interesting consideration when utilizing this approach to analyze the effects of incorporating a new technology is the inclusion of the learning curve's impact in the estimate of the effect. In other words, it can analyze the improvement due to learning and increased proficiency over time. In the year of HFNC introduction in the Pediatric Intensive Care Unit (PICU) and emergency department, there was an increase in the length of stay in the PICU, but this effect was not observed in subsequent years. There was also an increase in the percentage of ICU admissions, which changed the following year, followed by a reduction effect. These initial increases can be attributed to the adaptation and recognition of the technology by health professionals, with the benefits of the method becoming clearer over time (Table 5A).

	Effect estimation (coefficient)	Standard error	t	Sig.
Time	0,049	0,009	5,800	0,002
Interact	-0,104	0,011	-9,409	0,000
Phase 2017	0,133	0,037	3,596	0,016
phase 2018	0,029	0,040	,734	0,496
phase 2019	-0,281	0,062	-4,567	0,006

Table 5A: ARIMA model for the percentage of cases admitted to the ICU.

In another arm of the study, we analyzed the effects of HFNC on the physiological parameters of heart rate and respiratory rate. We observed a significant reduction in respiratory rate and a smaller but still significant effect on heart rate. The warm, humidified air in HFNC can improve pulmonary compliance, albeit providing only a small positive end-expiratory pressure [20]. HFNC can also facilitate a washout of the nasopharyngeal dead space, enhancing the clearance of carbon dioxide and promoting more efficient ventilation, thereby reducing the work of breathing [21]. Warming the air to core temperature and humidifying up to 100% can optimize mucociliary clearance, particularly advantageous in hyper secretory states such as bronchiolitis [22]. The observed reduction in heart and respiratory rates leads to a decrease in the Wood-Downes-Ferres score, although it's important to note that this score also incorporates other measures of respiratory effort. These effects on respiratory effort could explain the observed reduction in PICU admissions in the third year of HFNC use.

It is essential to note that this is a monocentric study, and caution should be exercised when generalizing the results. Other critical limitations include the retrospective design and the short time series, interrupted by the coronavirus pandemic, which significantly impacted Brazilian PICUs, resulting in reduced admissions, length of stay, and changes in the epidemiological profile [23]. Another potential critique is the lack of stratification of populations based on the severity of bronchiolitis, which could compromise the comparison of groups from one year to another. Additionally, the low use of Non-Invasive Ventilation (NIV) even before the introduction of HFNC is a characteristic of the unit. While it is a single-center study, the general characteristics of the groups from each year suggest they are very similar and comparable.

Conclusion

Following a period of acclimatization to the technology, the utilization of HFNC demonstrated a correlation with a reduction in both the duration of hospital stays and the incidence of patient admissions to the PICU. The observed impact on heart and respiratory rates, potentially contributing to a perception of clinical amelioration, likely played a pivotal role in influencing the medical team's decision to curtail admissions to the PICU. These findings suggest that the incorporation of HFNC into patient care protocols holds promise for optimizing outcomes, manifesting as abbreviated hospital stays, diminished PICU admission rates, and favorable physiological responses. These implications underscore the potential significance of HFNC in informing and shaping future medical practices and respiratory care interventions.

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Author's contribution

1 Conceptualization

2- Data analysis

3- Data collection

4- Writing – Original Draft Preparation

5- Writing – Review and Editing

6- Supervision

Declaration of Conflicts

None to Declare

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