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Clinical outcomes in mechanically ventilated patients in pediatric intensive care: A cohort study

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ABSTRACT

Introduction. Mechanical ventilation (MV) is a common intensive care intervention associated with increased resource use and a risk of complications. Therefore, this study aimed to characterize ventilated patients with acute hypoxemic respiratory failure (AHRF) and pediatric acute respiratory distress syndrome (PARDS).

Population and Methods. We conducted a prospective cohort study in the pediatric intensive care unit of a high-complexity hospital between June 2021 and August 2022. The study analyzed the outcomes of patients with MV, the incidence of AHRF and PARDS, and their respective outcomes.

Results. The study recorded 1354 admissions; 273 required mechanical ventilation (306 cycles). 19.4% had AHRF and 6.6% had PARDS. Morbidity upon discharge from the intensive care unit was 18.7%, and mortality was 12.1%. In-hospital mortality was 13.2%; 10.2% required a tracheostomy. In the univariate analysis, PIM-2, failed and unscheduled extubations, tracheostomy, days on mechanical ventilation and length of hospital stay, AHRF, and PARDS were associated with morbidity and mortality. In the multivariate analysis, PIM-2 and tracheostomy remained significant.

Conclusion. One in five patients admitted to the pediatric intensive care unit required mechanical ventilation, and approximately seven out of ten ventilated patients survived without acquired morbidity. AHRF was associated with longer duration of mechanical ventilation and hospital stay, a higher likelihood of tracheostomy, and higher morbidity and mortality. The results for patients with PARDS show a trend toward more days on a ventilator, longer hospital stays, and higher mortality.

Keywords: *mechanical ventilation; respiratory failure; acute respiratory distress syndrome; morbidity; mortality.*

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INTRODUCTION

Pediatric intensive care has improved significantly in recent decades thanks to a better understanding of pathophysiology and advances in monitoring and life-support technologies.[1] In this context, mechanical ventilation (MV) is essential for patients with respiratory failure, for airway protection, or for postoperative support.[2] While invasive mechanical ventilation is a timely intervention, its use requires safe, high-quality care to minimize its risks.[3]

In recent years, there has been a gradual increase in the number of children with complex chronic conditions (CCC), who in some units account for up to 50% of patients.[4] This population has a higher rate of hospitalizations, higher mortality, and greater use of highly complex resources, such as mechanical ventilation.[5] The prevalence of CCC in our setting is unknown.

In this context, it is important to characterize ventilated patients, evaluate their clinical outcomes, and determine the incidence of acute hypoxemic respiratory failure (AHRF) and pediatric acute respiratory distress syndrome (PARDS). This information helps identify at-risk groups and optimize management.[3] However, in our setting, there is currently little data available on this subject.

Therefore, the objectives of this study were to describe the characteristics and outcomes of a cohort of ventilated children, to identify variables associated with morbidity and mortality, and to determine the prevalence and course of AHRF and PARDS in the Pediatric Intensive Care Unit (PICU).

POPULATION AND METHODS

This study was conducted in the PICU of a general university hospital accredited by Joint Commission International since 2015. It has two multidisciplinary units—one with 20 beds and the other with 6—located at different sites, with approximately 1100 admissions per year, about 50% of which are for elective surgeries. The unit provides respiratory and cardiovascular support, renal replacement therapies, and extracorporeal membrane oxygenation (ECMO).

We conducted a prospective cohort study including all patients admitted to MV between June 2021 and August 2022. Follow-up was conducted from admission to the PICU through hospital discharge.

Demographic variables such as age, weight, sex, risk of mortality at admission as measured by the Pediatric Index of Mortality 2 (PIM 2) score, diagnosis at admission, reason for admission to the PICU, complex chronic conditions, comorbidities, postoperative status, elective admission, vasoactive medications, days spent in the PICU and total hospital stay, and functional status upon admission to and discharge from the PICU, as well as upon hospital discharge, measured using the Functional Status Scale (FSS).[6,7]

Acute hypoxemic respiratory failure was defined as PaO_2/ FiO_2(P/F) ≤300, with one or more infiltrates on chest X-ray or CT scan and respiratory support with PEEP (positive end-expiratory pressure) or CPAP ≥5 cm H_2O.[8-11]

For patients without arterial blood gas results, the P/F ratio was replaced with arterial saturation/ FiO_2 (S/F), considering an S/F of 264 to be equivalent to a P/F of 300.

To calculate it, the FiO_2 is reduced until the SaO_2 is ≤97%, and the saturation value is divided by the FiO_2.[12-14] The diagnosis required two measurements consecutive periods separated by at least one hour, with day 1 of AHRF defined as the first day on which the diagnostic criteria were met.[15] In patients with cyanotic heart disease, impaired oxygenation was defined as a decrease of ≥20% in PaO_2 or arterial oxygen saturation from baseline.[16] The causes of AHRF were classified based on chest X-ray findings as pleural effusion, atelectasis, loss of lung volume, or unilateral or bilateral pulmonary parenchymal disease.[11-13]

The diagnostic and severity criteria for PARDS are those defined by the Pediatric Acute Respiratory Distress Syndrome Incidence and Epidemiology (PARDIE) Investigators and the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network.[12,13] Severity was categorized according to the highest OI recorded during hospitalization as mild (OI ≥4 and <8 or OSI ≥5 and <7.5), moderate (OI ≥8 and <16 or OSI ≥7.5 and <12.3), or severe (OI ≥16 or OSI ≥12.3).

In patients diagnosed with AHRF or PARDS, the following were recorded daily for 5 days: P/F ratio; S/F ratio; index of oxygenation (OI = FiO_2 × mean airway pressure × 100) / PaO_2); oxygen saturation index (OSI = FiO_2 × mean airway pressure × 100) / SaO_2); MV parameters; and blood gas analysis.

Failed extubation was also analyzed (reintubation within 48 hours),[17] along with unscheduled extubation, conventional and volumetric capnography, esophageal pressure

monitoring, chest CT scan, prone positioning, recruitment maneuvers, high-frequency oscillatory ventilation (HFOV), extracorporeal membrane oxygenation (ECMO), bronchoalveolar lavage (BAL), use of surfactant, presence of a balloon in the endotracheal tube, nitric oxide (NO), and airway endoscopy.

We recorded whether a tracheostomy was performed during the PICU hospitalization, the number of days until the procedure, and the duration of the tracheostomy until hospital discharge. Morbidity acquired during the PICU hospitalization was defined as an increase of ≥3 points on the FSS scale, or >2 in a single domain, when comparing the FSS score at admission to that at discharge from PICU and hospital discharge.[18]

We also recorded mortality during PICU hospitalization and at hospital discharge.

We constructed the combined morbidity-mortality variable to highlight the clinical significance of adverse outcomes and to more accurately reflect the total burden of disease associated with mechanical ventilation.[18]

Ethical considerations

The Research Ethics Committee of the Italian Hospital approved the study protocol under number 1261. An exemption from the informed consent procedure was requested and granted for the inclusion of data in the registry, as the data were processed anonymously, with the utmost confidentiality, and with access restricted solely to authorized personnel in accordance with current legal regulations: National Law 25326 on the Protection of Personal Data and Law 26529 on Patient Rights, Medical Records, and Informed Consent.

Statistical analysis

We analyzed variable characteristics and distributions and used means and standard deviations, medians and interquartile ranges, or proportions as appropriate.

We performed univariate analyses based on variable distribution. For continuous variables, we used Student's t-test to compare means and the Mann-Whitney test to compare medians. For categorical variables, we used the chi-square test. We set the statistical significance level at p <0.05. To evaluate the association between the independent variables and the morbidity-mortality outcome, we constructed a logistic regression model. We performed a univariate analysis and included variables with p <0.10 and clinical relevance in the multivariate analysis. Before this, we assessed multicollinearity among candidate variables by calculating variance inflation factors (VIFs). We observed no significant multicollinearity (VIF >5 indicates multicollinearity), so we excluded no variables for this reason. We converted categorical variables into dummy variables and dichotomized continuous variables or retained them as continuous. We retained variables with a significant association, clinical relevance, or improved predictive power. We maintained a 1:10 ratio between independent variables and events.

The analysis was performed using Stata 13® (StataCorp, College Station, TX, USA).

RESULTS

During the 14-month study period, 1354 patients were admitted (1035 at the main campus and 319 at the San Justo campus). Of these, 273 (20.1%) required 306 MV cycles (*Figure 1*). The characteristics of the study population are summarized in *Table 1* (see also *Supplementary material 1*).

Of the 273 patients included in the study, 53 (19.4%) experienced one episode of AHRF and 9 (3.3%) experienced two episodes of AHRF. The most common diagnoses associated with AHRF were atelectasis (22.5%), loss of lung volume (19.3%), and pulmonary infection (16.1%).

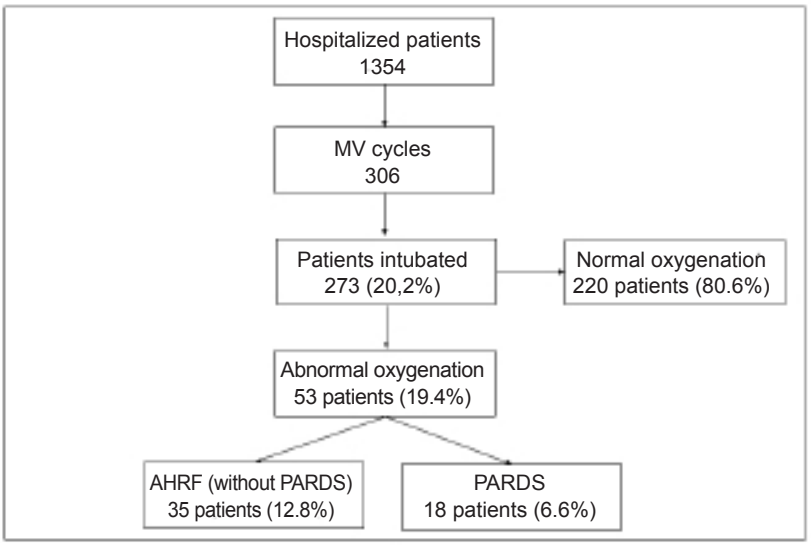
Eighteen patients (6.6%) met the criteria for PARDS; the most common triggers were respiratory infection (38.9%) and bronchoaspiration (22.2%). Regarding PARDS severity, 27.8% were mild, 50% were moderate, and 22.2% were severe.

Of 273 cases, 28 (10.2%) required a tracheostomy; 18.7% (51/273) developed complications during their stay in the PICU; 12.1% of the patients (33/273) died in the ICU, and 3 patients died after discharge from the PICU; thus, the in-hospital mortality rate was 13.2% (36/273). The in-hospital morbidity rate was 11.7% (32/273).

There were 43 (14.1%) failed extubations and 11 (3.6%) unscheduled extubations. After extubation, the high-flow cannula was the most commonly used form of support (32.5% in the first cycle and 29.1% in the second), followed by the low-flow nasal cannula (25.1% and 29.1%).

In the univariate analysis, PIM 2, failed and unscheduled extubations, tracheostomy, days on mechanical ventilation and length of hospital stay, AHRF, and PARDS were associated with

Figure 1. Distribution of patients with acute hypoxemic respiratory failure and pediatric acute respiratory distress syndrome



MV: mechanical ventilation; AHRF: acute hypoxemic respiratory failure; PARDS: pediatric acute respiratory distress syndrome.

morbidity and mortality.

Table 2 summarizes the multivariate analysis. *Table 3* shows differences between patients who did not develop AHRF and those who did. *Table 4* compares patients who developed PARDS with those who had AHRF but did not progress to that syndrome.

DISCUSSION

This study describes a cohort of children requiring acute mechanical ventilation in pediatric intensive care units in our region. One in five patients required at least one cycle of MV (20.2%), similar to Spain (21%)[19] and lower than other series, where it reaches up to 56% of admissions.[20] The incidence of AHRF and PARDS among all admissions was 3.9% and 1.3%, respectively—results comparable to those reported by López-Fernández et al., who, in a cohort of 6545 admissions across 22 units, found that 2.8% had AHRF and 1.4% had PARDS.[19] The frequency of PARDS reported in the PARDIE study is slightly higher: 3.2% of total admissions.[12]

Of the total number of ventilated patients (n = 273), 1 in 5 had AHRF, and 1 in 15 had PARDS. López-Fernández and the PARDIE study report similar results.[12,19] The former reports that, in a population of 1374 ventilated patients, 13.2% had AHRF and 6.6% had PARDS. The latter reports a 6% incidence of PARDS.

Regarding the incidence of PARDS in patients with AHRF, 33.9% (18/53) developed PARDS in our study, while 50.2% (91/181) developed PARDS in the study by López-Fernández.[19]

In our population, 33 patients died and 51 experienced morbidity. Upon reviewing our records and studies previously published by our group,[21,22] we found that none of these events occurred in patients who did not require MV. Thus, morbidity and mortality were 6.2% (84/1354) of total admissions, but 30.7% (84/273) in the ventilated subgroup. This difference prompts reflection on how to measure outcomes. Typically, mortality and morbidity are reported based on total admissions and severity-adjusted models (PIM, PRISM), along with new paradigms that integrate morbidity and mortality and trichotomous models, which also refer to the entire patient population.[23-25] However, since mechanical ventilation is a strong predictor of mortality[26,27] and defines cohorts of high risk,[28,29] we believe that reporting the results for the subgroup of ventilated patients could help identify populations with the greatest potential for improvement. This, in turn, helps reduce the bias associated with low complexity.

Another significant finding was the tracheostomy rate, which was close to 10%. The literature reports rates ranging from 5% to 10%.[30,31]

The frequency observed in our cohort may

Table 1. Characteristics of the population (n = 273)

Variable	Unit	Summary statistics	Value
Age	Months	Median (25-75)	16 (5-74)
Male	n	(%)	157 (57.5)
Weight	Kg	Median (25-75)	9.8 (5.6-19)
Center	n	(%)	
HIBA Central			227 (83.1)
HIBA San Justo			46 (16.9)
Diagnosis upon admission	n	(%)	
Cardiovascular			138 (50.5)
Neurologic			34 (12.4)
Respiratory			32 (11.7)
Hepatologic			20 (7.3)
Oncologic			13 (4.7)
Renal			5 (1.8)
Others			31 (11.3)
PIM2	(%)	Median (25-75)	3.8 (2.1-7.1)
Complex chronic condition	n	(%)	191 (69.9)
Comorbidities	n	(%)	119 (43.5)
Postoperative	n	(%)	163 (59.7)
Elective admission	n	(%)	154 (56.4)
Reason for admission to MV	n		
Postoperative			170 (62.27)
Neurological disease			30 (10.99)
Shock			28 (10.26)
Respiratory disease			24 (8.79)
Airway protection			19 (6.96)
Neuromuscular disease			2 (0.73)
Days in MV	n	Median (25-75)	2 (1-8)
Days in the PICU	n	Median (25-75)	9 (5-17)
Days of hospitalization (total)	n	Median (25-75)	15 (7-38)
Unscheduled extubation	n	(%)	11 (3.6)
Failed extubation	n	(%)	43 (14.1)
Patients with 1 episode of AHRF	n	(%)	53 (19.4)
Patients with 2 episodes of AHRF	n	(%)	9 (3.3)
Duration of the 1° episode of AHRF	Days	Median (25-75)	2 (1–4)
Duration of the 2° episode of AHRF	Days	Median (25-75)	2 (1–4)
Patients with PARDS	n	(%)	18 (6.6)
Duration of PARDS	Days	Median (25-75)	3 (2–7)
FSS upon admission to PICU	Score	Median (25-75)	6 (6–10)
Morbidity upon admission (FSS >6)	n	(%)	122 (44.7)
FSS of patients with morbidity upon admission	Score	Median (25-75)	10 (8–14)
New tracheostomy	n	(%)	28 (10.2)
Days in MV until tracheostomy	n	Median (25-75)	16 (15-22)
Tracheostomy at discharge from PICU	n	(%)	51 (18.7)
Tracheostomy at hospital discharge	n	(%)	47 (17.2)
Acquired morbidity at discharge from PICU	n	(%)	51 (18.7)
Acquired morbidity at hospital discharge	n	(%)	32 (11.7)
In-PICU mortality	n	(%)	33 (12.1)
In-hospital mortality	n	(%)	36 (13.2)

HIBA: Italian Hospital of Buenos Aires; PIM 2: Pediatric Index of Mortality 2; MV: mechanical ventilation; PICU: pediatric intensive care unit; AHRF: acute hypoxemic respiratory failure; PARDS: pediatric acute respiratory distress syndrome; FSS: Functional Status Scale.
Data are expressed as the median and interquartile range (25-75) or as a percentage (%).

Table 2. Multivariate analysis of morbidity and mortality events in pediatric intensive care (n = 84 events)

Variable		OR	95% CI	*p*
PIM2	Continuous	1.05	1.02–1.08	<0.05
Effective admission	Categorical	1.05	0.50–2.23	0.88
Failed extubation	Categorical	1.45	0.65–3.27	0.36
Unscheduled extubation	Categorical	2.09	0.44–9,78	0.34
New tracheostomy	Categorical	10.20	3.08–33.74	<0.05
Days in MV	Continuous	1.00	0.98–1.01	0.34
AHRF	Categorical	2.26	0.87–5.84	0.09
PARDS	Categorical	0.73	0.17–3.02	0.66

OR: odds ratio; 95% CI: 95% confidence interval; PIM 2: Pediatric Index of Mortality 2; MV: mechanical ventilation; ARF: acute hypoxemic respiratory failure; PARDS: pediatric acute respiratory distress syndrome.
A multivariate logistic regression analysis was performed.

Table 3. Differences between patients with acute hypoxemic respiratory failure (n = 530) and those without acute hypoxemic respiratory failure (n = 220)

Variable	Measure	No AHRF	AHRF	*p*
Patients	n	220	53	
Age (months)	Median (25-75)	14.5 (4-70)	51 (9-151)	0.006
Male	%	56.36	62.26	0.26
Complex chronic condition	%	70.45	67.92	0.74
Comorbidities	%	42.73	47.17	0.64
Postoperative	%	64.09	41.51	0.002
Elective admission	%	62.73	30.19	0.001
Days in MV	Median (25-75)	2 (1-5)	11 (3-42)	0.001
Unscheduled extubation	%	3.64	5.66	0.45
Failed extubation	%	8.18	32.08	0.001
New tracheostomy	%	4.09	35.85	0.001
Days in PICU	Median (25-75)	8 (5-14)	22 (11-52)	0.001
Days in hospital	Median (25-75)	12 (6-29)	46 (18-67)	0.001
O_2 upon discharge from PICU	%	14.55	18.87	0.12
O_2 upon hospital discharge	%	6.36	11.32	0.07
MV upon PICU discharge	%	5.45	3.77	0.25
MV upon hospital discharge	%	1.82	3.77	0.07
NIV upon PICU discharge	%	13.64	18.87	0.11
NIV upon hospital discharge	%	12.73	16.98	0.10
Acquired morbidity upon discharge from PICU	%	13.64	39.64	0.001
Acquired morbidity upon discharge from hospital	%	7.73	28.30	0.01
In-PICU mortality	%	10	20.75	0.03
In-hospital mortality	%	10.91	22.64	0.02

ARF: acute hypoxemic respiratory failure; MV: mechanical ventilation; PICU: pediatric intensive care unit; NIV: noninvasive ventilation.
Data are expressed as the median and interquartile range (25-75) or as a percentage (%).
We used the Mann-Whitney test for continuous variables and the chi-square test for categorical variables.

be related to the high prevalence of patients with CCC (of the 28 patients who required a tracheostomy, 21 had CCC) and to the use of tracheostomy to simplify care for critically ill patients.

Univariate analysis identified multiple variables associated with morbidity and mortality. Among these, failed and unscheduled extubations are potentially preventable events.

Failed extubations occurred in 14% of the ventilatory cycles (43/306). Our results are higher than those reported in the literature, which range from 5.5% to 11.5%.[32,33] This could be due, in part, to the high proportion of patients with CHD.

Unplanned extubations occurred in 3.6% of ventilation cycles. These results are similar to

Table 4. Differences between patients with pediatric acute respiratory distress syndrome (n = 18) and those with acute hypoxemic respiratory failure (who did not develop PARDS) (n = 35)

Variable	Measure	AHRF	PARDS	*p*
Patients	n	35	18	
Age (months)	Median (25-75)	17 (6-67)	150.5 (58-173)	0.001
Male	%	65.71	55.56	0.47
Complex chronic condition	%	65.71	72.22	0.63
Comorbidities	%	42.86	55.56	0.38
Postoperative	%	51.43	22.22	0.04
Elective admission	%	37.14	16.67	0.12
Days in MV	Median (25-75)	9 (3–50)	15.5 (6-42)	0.32
Unscheduled extubation	%	8.57	0	0.20
Failed extubation	%	34.29	27.78	0.63
New tracheostomy	%	34.29	38.89	0.74
Days in PICU	Median (25-75)	17 (8–50)	28 (14-57)	0.18
Days in hospital	Median (25-75)	32 (16–64)	52.2 (21-80)	0.37
O_2 upon discharge from PICU	%	17.14	23.53	0.58
O_2 upon hospital discharge	%	11.43	11.76	0.97
MV upon PICU discharge	%	2.86	5.88	0.59
MV upon hospital discharge	%	2.86	5.88	0.59
NIV upon PICU discharge	%	22.86	11.76	0.34
NIV upon hospital discharge	%	20	11.76	0.46
Acquired morbidity upon discharge from PICU	%	56.67	33.33	0.17
Acquired morbidity upon discharge from hospital	%	40	25	0.35
In-PICU mortality	%	14.29	33.33	0.15
In-hospital mortality	%	17.14	33.33	0.30

AHRF: acute hypoxemic respiratory failure; PARDS: pediatric acute respiratory distress syndrome; MV: mechanical ventilation; NIV: noninvasive ventilation; PICU: pediatric intensive care unit.
Data are expressed as the median (25^{th}-75th percentile) or as a percentage. We used the Mann-Whitney test for continuous variables and the chi-square test for categorical variables.

those reported in the literature, ranging from 2.8% to 5.3% of ventilation cycles.[34,35]

In the multivariate analysis, PIM 2 and tracheostomy were independently associated with morbidity and mortality. Variables such as failed extubation, unscheduled extubation, AHRF, and PARDS, although not statistically significant, showed clinically relevant associations with the event (odds ratios with high upper limits of the 95% CI).

On the other hand, patients with AHRF are older and have a higher frequency of unscheduled hospitalizations compared to patients without AHRF. Regarding outcomes, they are more likely to experience failed extubation, spend more time on the MV, have longer stays in both the PICU and the hospital, and are more likely to require tracheostomy and to experience morbidity and mortality during hospitalization.

When we compared patients with AHRF who did not progress to PARDS with patients with PARDS, the latter were older and had a lower frequency of postoperative readmissions. Although not statistically significant, they had more days on a ventilator, longer lengths of stay in the PICU and in the hospital, and twice the mortality rate in the PICU.

This study has limitations. First, the results may have limited external validity because this population has specific characteristics that may differ from those of other units. Second, the study population was small. However, patients from two units were included over 14 months; the frequency of morbidity and mortality events, PARDS, and other independent variables meant the multivariate analysis allowed clinical inference about the significance of certain associations that were not statistically verified.

CONCLUSION

One in five patients admitted to the PICU required mechanical ventilation, and

approximately seven out of ten ventilated patients survived without acquired morbidity. AHRF was a common complication and was associated with longer duration of mechanical ventilation and hospital stay, a higher likelihood of tracheostomy, and higher morbidity and mortality. The results for patients with PARDS show a trend towards more days on a ventilator, longer hospital stays, and higher mortality. ■

The supplementary material provided with this article is presented as submitted by the authors. It is available at: https://www.sap.org.ar/docs/publicaciones/archivosarg/2027/11108_AO_Eulmesekian_Anexo.pdf

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