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ORIGINAL ARTICLE

Noninvasive Ventilation on Acute Hypoxemic Respiratory Failure: Analysis of Therapeutic Impact in an Observational study

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ABSTRACT

Background. Patients with acute hypoxemic respiratory failure (AHRF) represent a heterogeneous group of conditions, often associated with pneumonia and characterized by varied etiopathogenesis. Pathophysiologically, pulmonary involvement may be alveolar, interstitial, or alveolo-interstitial. Oxygen therapy is the first-line treatment. The lack of clinical improvement with high-concentration oxygen therapy and the absence of immediate intubation criteria suggest the potential benefit of non-invasive ventilation (NIV). **Objective.** The aim of this study was to assess the impact of NIV on intubation and mortality in patients admitted to the ICU for AHRF of various etiologies and to identify predictive factors associated with NIV failure. **Methods**. This is an observational cohort study using data collected prospectively over a one-year period in the medical intensive care unit of Sétif University Hospital. **Results.** Among 35 patients treated with NIV for AHRF, 23 were not intubated. NIV significantly reduced the respiratory rate from 41.85 ± 7.91 cycles/min at admission to 29.06 ± 7.29 cycles/min (p = 0.001), without improving the PaO_2/FiO_2 ratio (p = 0.69). The effectiveness of NIV varied according to the etiology of AHRF and the severity of hypoxemia. Interstitial lung disease was significantly associated with NIV failure (OR: 7.39; 95% CI [1.44–37.9], p = 0.01). A PaO_2/FiO_2 ratio < 150 mmHg was an independent risk factor for failure (OR: 5.2; 95% CI [1.02–27.75], p = 0.04). Patients requiring intubation had a very high ICU mortality rate. **Conclusion.** The impact of NIV on preventing intubation was 65.7% across all cases of AHRF. NIV may serve as first-line ventilatory support when the PaO_2/FiO_2 ratio is > 150 mmHg. Conversely, 75% of patients with a PaO_2/FiO_2 ratio < 150 mmHg required intubation, resulting in increased mortality.

Keywords: Acute hypoxemic respiratory failure, non-invasive ventilation failure, NIV for acute hypoxemic respiratory failure, intubation rate, interstitial lung disease, NIV failure risk factor.

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1. INTRODUCTION

Acute hypoxemic respiratory failure (AHRF) is primarily caused by injuries to the lung parenchyma, mainly affecting previously healthy lung tissue. These injuries lead to hypoxemia (PaO2/FiO2 < 300 mm Hg), clinically manifesting as respiratory distress and SpO2 < 90%. Untreated, AHRF can progress to acute respiratory distress syndrome (ARDS). Hypoxemia results from inadequate gas exchanges due to shunts and/or varying degrees of intrapulmonary diffusion disorders. This condition increases the workload on respiratory muscles leading to hyperventilation with hypocapnia. However, excessive and escalating inspiratory efforts can harm the patient, causing self-inflicted lung injuries (P-SILI) [1].

Mechanical ventilation, particularly invasive ventilation, remains the primary intervention for managing severe AHRF [2]. Nonetheless, the complications associated to intubation must be carefully considered [3]. Non-invasive ventilation (NIV) represents an alternative therapeutic modality, administered via an interface, typically an oronasal mask, which delivers inspiratory pressure support (PS) coupled with positive end-expiratory pressure (PEEP) during the respiratory cycle. NIV effectively reduces polypnea and corrects hypoxemia [4-6]. In clinical practice, NIV is used to avoid intubation. Indeed, it is still frequently used in this indication [7]. Its efficacy in improving gas exchange has been demonstrated [8]. Also, NIV enhances patient comfort and prevents sedation and invasive mechanical ventilation complications [9,10]. However, NIV failure associated with increased mortality risk [11,12].

In the Algerian healthcare context, the widespread adoption of non-invasive ventilation (NIV) was historically constrained by limited interface availability. While increasing equipment accessibility has facilitated preliminary experimental studies [15] and clinical trials, persistent gaps in clinician training and practical expertise continue to impede optimal implementation.

This study aims to (1) assess the impact of NIV on morbidity and mortality outcomes in acute hypoxemic respiratory failure (AHRF) patients and (2) delineate clinically relevant predictive factors associated with therapeutic success or failure.

2. MATERIAL AND METHODS

This cohort study is a prospective, observational investigation involving thirty-five (n:35) consecutive adult patients diagnosed with acute hypoxemic respiratory failure (AHRF). The cohort study it was conducted in the medical intensive care unit of Setif University Hospital (Algeria). Given the observational nature of the study and its intention-to-treat approach, written consent was not sought from either the patient or their family. As such, our study complies with the ethical guidelines outlined in the Declaration of Helsinki, with due regard for the anonymity of individual patient data in any subsequent publication.

Inclusion Criteria

Our study includes adult patients who are admitted to the intensive care unit with an acute respiratory distress attributable to acute hypoxemic pneumonitis. Acute hypoxemic respiratory failure (AHRF) was diagnosed on the basis of a combination of clinical indicators that include a respiratory rate (RR) exceeding 25 cycles per minute, peripheral oxygen saturation (SpO_2) below 90% despite supplemental oxygen, intercostal retraction, and cyanosis. Additionally, AHRF was confirmed by arterial blood gas analysis demonstrating a partial pressure of oxygen (PaO_2) below 60 mm Hg and a corresponding PaO_2/FiO_2 ratio below 300 mm Hg while the patient was receiving oxygen via a reservoir mask. The fraction of inspired oxygen (FiO_2) was calculated using the formula (21% + 3% x flow rate in Liters per minute of oxygen). The etiology of AHRF was ascertained through imaging studies, echocardiography, and biological analyses, including polymerase chain reaction (PCR).

Non-inclusion criteria

Patients with a documented history of chronic respiratory or cardiac failure notably acute cardiogenic pulmonary edema, and those with a history of smoking were not included in the study. Additionally, those in a state of shock, with disturbances in consciousness or psychomotor agitation requiring sedation, and needing urgent intubation were also not included.

Study protocol

On admission, patients were examined and monitored by multiparametric scope. Before initiating non-invasive ventilation (NIV), an initial arterial blood gas analysis was performed. Patients were positioned in a semi-seated orientation, and the procedure was meticulously explained to them. The oronasal mask was gently placed over the patient's face by a nurse without sticking it.

Initial settings for pressure support (PS) and positive end expiratory pressure (PEEP) were configured to 8 and 5 centimeters of water, respectively, accompanied by an initial fraction of inspired oxygen (FiO_2) of 0.6. Subsequently, the oronasal mask was fixed and tightened. Monitoring was stringent during the first two hours, conducted at the bedside without limb restraint.

Ventilation Modality

The integrated NIV mode of the Hamilton G5 ICU ventilator was utilized, featuring a flow generator, a heated humidifier, and a dual-limb circuit with an oronasal mask interface. This mode incorporates a leak compensation algorithm that dynamically adjusts for air leaks, prevents over-tightening of mask straps, and ensures stable ventilation and oxygenation. It provides BiPAP-equivalent functionality, including Inspiratory Pressure Support (IPAP), which has demonstrated benefits in augmenting tidal volume, reducing respiratory muscle workload, and preventing diaphragmatic fatigue, as well as Positive Expiratory Pressure (EPAP/PEEP) to maintain alveolar recruitment and prevent airway collapse.

The inspiratory trigger was fixed at 2 L/min (flow-triggered), with a preset ramp time between 0 and 100 milliseconds, later adjusted based on patient needs or patient-ventilator asynchronies. Cycling (I:E ratio) was initially set at 25%, with standardized settings later personalized according to clinical progression. While monitoring for intolerance, NIV pressure was incrementally increased by 1-2 cm of water, not exceeding a maximum of 16 cm, with the primary goal of reducing respiratory rate. FIO2 and PEEP (capped at 10 cm of water) were adjusted to maintain SpO2 above 92%.

Settings were fine-tuned at two-hour and six-hour intervals, followed by periodic adjustments guided by arterial gasometry results. NIV was maintained overnight if well-tolerated, with periodic hydration breaks, and automatically reactivated if SpO2 dropped below 88%. In cases of mask leakage exceeding 50%, a stepwise algorithm was applied: first, readjusting the oronasal mask through gentle pressing; second, reducing PEEP by 1 cm of water; third, decreasing the NIV level by 2 cm of water; and fourth, considering mask replacement. Any side effects were meticulously identified and addressed.

The weaning process involved gradual reductions in NIV pressure, FiO_2, PEEP, and duration, with discontinuation once the patient stabilized. Intubation was indicated in cases of NIV failure, defined by worsening or persistent polypnea, poorly tolerated respiratory distress (respiratory rate > 35 cycles/min, signs of struggle, SpO2 < 85%), agitation or decreased alertness (Glasgow < 12), the need for noradrenaline, or hypercapnia with PaCO2 > 45 mm Hg. Success criteria included respiratory rate < 25 cycles/min, heart rate < 100 bpm, SpO2 ≥ 92% on 5 L/min oxygen, absence of respiratory distress signs, pH between 7.35 and 7.42, and improvement in the PaO2/FiO2 ratio.

Data collection and analysis

Patient demographic data and NIV parameters—including inspiratory pressure support (IPAP), positive end-expiratory pressure (PEEP), fraction of inspired oxygen (FiO_2), and expired tidal volume (Vte) normalized to predicted body weight—were prospectively collected at predetermined intervals: admission, 2-hour and 6-hour timepoints, and at NIV discontinuation.

Statistical analyses were performed using SPSS Statistics (version 22; IBM Corp.). Continuous variables are reported as mean ± standard deviation, while categorical variables are presented as counts and percentages. Between-group comparisons employed Student's t-test for independent or paired samples as appropriate. Qualitative data underwent comparison utilizing Fisher's exact test or χ^2 tests, whatever the number is.

We first performed univariate analysis to identify potential predictors of NIV outcomes. All variables demonstrating marginal association ($p \leq 0.20$) in univariate analysis were subsequently entered into a multivariable logistic regression model to identify independent predictors of NIV failure. Results are reported as adjusted odds ratios (aOR) with corresponding 95% confidence intervals. Statistical significance was set at p-value ≤ 0.05.

3. RESULTS

Pre-treatment baseline patient characteristics

The description of the population to whom NIV was applied is reported in Table 1.

Initial impact of NIV

Arterial gasometric data were procured from thirty-one patients, constituting 88.6% of the cohort. Table 2 reports the results which are obtained at the second hour of NIV intervention.

A clinically significant reduction in respiratory rate (mean decrease: 12 cycles/min) was achieved in 24 patients (68.6%), demonstrating statistical significance ($p<0.001$). While SaO_2 showed marked improvement, the mean PaO_2/FiO_2 ratio remained stable overall, despite a clinically relevant increase (≥30 mm Hg) observed in 62.8% of cases. Of note, one patient (2.9%) required intubation at this stage secondary to hemodynamic instability.

Final impact of NIV and patients' outcome

Longitudinal analysis (Table 3) demonstrated only marginal, non-significant improvements in both respiratory rate (RR) and PaO_2/FiO_2 ratio between hours 2 and 6 of NIV therapy. The overall NIV failure rate reached 34.3% (12/35 cases), with a median time-to-intubation of 12 hours following NIV initiation. Indications for intubation included: emergency procedures (n=2), refractory hypoxemia (n=7), hemodynamic instability (n=2), and mask intolerance (n=1). The intervention demonstrated a favorable safety profile, with only minor adverse effects observed and no reported cases of barotrauma or facial pressure ulcers. ICU mortality was recorded at 31.4% (11/35 patients).

Table 1. Baseline characteristics of included patients with AHRF before NIV (n=35).

Variable	Number & (%)	Means ± standard deviation
Gender (M/F)	17/18(48.6/51.4)	
Age (years)		51.3±18.77
SAPS II		34.6 ± 12 .07
Vital signs at admission		
Intercostal retractions	35 (100)	
Cyanosis	10 (28.6)	
Respiratory rate (c/min)		41.85 ± 7.91
SPO2 (%)		71.65 ± 14.4
Heart rate (beats/min)		118.91 ± 13.37
Systolic blood pressure (mm Hg)		130.51 ± 23.92
Temperature (°C)		38.34 ± 0.96
chest x-ray		
Unilateral alveolar infiltrate	07 (20)	
Bilateral alveolar infiltrate	17(48.7)	
Interstitial infiltrate	11(31.4)	
Comorbidities		
None	18 (51.4)	
Diabetes	12 (34.3)	
Heart disease	4 (11.4)	
Hematological disease	7 (20)	
Chronic renal failure	3 (8.6)	
HIV infections	2(5.7)	
Long-term corticosteroids	2(5.7)	
Breast neoplasia	1(2.9)	
ABG data at admission		
pH		7.41±0 .11
SaO2 (%)		81.21 ± 10.85
PaCO2 (mm Hg)		31.8 ± 9.77
PaO2 (mm Hg)		51.8 ± 14.03
PaO2/FIO2 (mm Hg)		162.65 ± 56.08
HCO3-(m mol/l)		20.9 ± 4.0
Etiology of AHRF		
bacterial pneumonia	12 (34.3)	
Influenza A pneumonia	9 (25.7)	
Acute interstitial pneumonia	10 (28.6)	
Pneumocystis pneumonia	2 (5.7)	
Miliary tuberculosis	1 (2.9)	
Diffuse alveolar hemorrhage	1 (2.9)	

Data represented as frequency (%) for categorical variables and mean , (SD) and range for continuous variables. SAPS II: Simplified Acute Physiology Score II; SPO_2: pulse oximetry ; HIV: Human Immunodeficiency Virus ; ABG, arterial blood gas ; pH: Potential of Hydrogen; ***SaO_2 (%)****: Arterial Oxygen Saturation ;* ***$PaCO_2$ (mmHg)****: Partial Pressure of Arterial Carbon Dioxide;* ***PaO_2 (mmHg)****: Partial Pressure of Arterial Oxygen;* ***PaO_2/FiO_2 (mmHg)****: Ratio of Arterial Oxygen Partial Pressure to Fraction of Inspired Oxygen;* ***HCO_3^- (mmol/L)****: Bicarbonate Concentration; AHRF: acute hypoxemic respiratory failure.*

Table 2. Comparison of NIV outcomes between admission and 2-hour treatment in patients with AHRF(n:35).

Variable	On admission	At the 2nd hour	*p*
Respiratory rate/min	41.85 ± 7.91	29.06 ± 7.29	0.001
SPO_2 (%)	71 .65 ± 14.4	94.8 ± 3.9	0.001
Heart rate (beats/min)	118.91 ± 13.37	109.68 ± 15.95	0.05
Systolic blood pressure (mmHg)	130.51 ± 23.92	129.15 ± 15.81	1 (NS)
Intercostal indrawing	35 (100)	18 (51.4)	0.05
Cyanosis	10 (28.6)	1 (2.8)	0.01
pH	7.41 ±0.11	7.4 ± 0.1	0.63(NS)
SaO_2 (%)	81.21 ± 10.85	93.59 ± 5.03	0.001
$PaCO_2$ (mm Hg)	31.8 ± 9.77	33.31 ± 6.7	0.08(NS)
PaO_2 (mm Hg)	51.8 ± 14.03	80.53 ± 24.54	0.001
PaO_2/FiO_2 (mm Hg)	162.65 ± 56.08	165 ± 48.92	0.69 (NS)
↑PaO_2/FiO_2 (n %)		22 (62.8%)*	-

Data represented as mean, and (SD); SPO_2 : pulse oximetry, NS: NS non-signifcant diference ($p > 0.05$). pH: *Potential of Hydrogen; SaO_2 (%): Arterial Oxygen Saturation ; $PaCO_2$ (mmHg): Partial Pressure of Arterial Carbon Dioxide; PaO_2 (mmHg): Partial Pressure of Arterial Oxygen; PaO_2/FiO_2 (mmHg): Ratio of Arterial Oxygen Partial Pressure to Fraction of Inspired Oxygen.* Number (%) of patients with improved PaO_2/FiO_2 ratio at 2 hours.*

Table 3. Comparison of non-invasive ventilation outcomes between 6-hour assessment and final discontinuation in patients with AHRF(n=35).

Variable	At the 6th hour	At the end of VNI	*p*
Respiratory rate/min	28.09 ± 9.24	20.29 ± 7.08	<0.001
SPO_2 (%)	94 ± 2.1	96.3 ± 3.2	0.06(NS)
Heart rate (beats/min)	102.8 ± 16.91	89.88 ± 14.72	<0.001
Systolic blood pressure (mmHg)	131.21 ± 13.20	124.23 ± 17.32	0.9 (NS)
Intercostal retractions (n, %)*	15 (45.4)	6 (17.1)	0.04
Cyanosis (n, %)*	1 (2.8)	1 (2.8)	1 (NS)
pH	7.41 ± 0.08	7.4 ± 0.07	0.90(NS)
SaO_2	94.30 ± 4.96	96.58 ± 3.65	0.87(NS)
$PaCO_2$ (mmHg)	33.7 ± 5.7	34.45 ± 3.77	0.69(NS)
PaO_2 (mmHg)	80.64±28.31	83.96±13.18	0.74(NS)
PaO_2/FiO_2 (mm Hg)	189.67±7.34	315.19±120.91	<0.001

Data are presented as mean ± standard deviation; Significance = p < 0,05. P values were calculated by t -test or chi-square as appropriate. SPO_2 : pulse oximetry, NS: NS non-signifcant diference (p > 0.05), pH: *Potential of Hydrogen; SaO_2 (%): Arterial Oxygen Saturation ; $PaCO_2$ (mmHg): Partial Pressure of Arterial Carbon Dioxide; PaO_2 (mmHg): Partial Pressure of Arterial Oxygen; PaO_2/FiO_2 (mmHg): Ratio of Arterial Oxygen Partial Pressure to Fraction of Inspired Oxygen.* Number (%) of patients.*

Table 4. Summary of patient outcomes in intensive care.

Variable	Number & (%)	Means ± standard deviation
NIV failure	12(34.3)	
Length of stay		6.6 ± 3.72 (2 – 30 days)
Mortality after NIV failure	11/12 (91.6)	
Intensive care mortality	11/35 (34.3)	
Mortality by etiology		
bacterial pneumonia	3/12 (25)	
Acute interstitial pneumonitis	7/10 / (70)	
Influenza A pneumonia	1/9 (11.1)	

Data represented as mean, and (SD) and number (%) of patients; NIV: noninvasive- ventilation, ICU: intensive care unit.

Table 5. Univariate analysis of factors predictive of NIV failure in AHRF patients (n=35).

Variable	Success (n: 23)	Failure (n: 12)	*p*
Age (years)	49.38 ± 20.49	52.45 ± 18.07	0,20
Gender (M/F)	9 / 14	8 / 4	0.11
SAPS II	33.13 ± 11.13	37.15 ± 13.59	0.19
Hematological disease	3 (42.8)	4 (57.2)	0.62
bacterial pneumonia	8 (66.7)	4 (33.3)	0.16
Acute interstitial pneumonia	3 (30)	7 (70)	0.05
Influenza A pneumonia	8 (88.9)	1 (11.1)	0.001
Respiratory rate (c/min)	41.9 ± 7.8	41.6 ± 8.3	0.92
Heart rate (beats/min)	117.1 ± 13.4	121.9 ± 13.2	0.31
pH	7.43 ± 0.11	7.38 ± 0.10	0.12
SaO_2 (mm Hg)	82.5 ± 7.9	78.9 ± 14.6	0.55
$PaCO_2$ (mm Hg)	30.4 ± 9.5	34.1 ± 10	0.28
PaO_2 (mm Hg)	52.4 ± 15.5	50.7 ± 11.5	0.74
PaO_2/FiO_2 (mm Hg)	163.3 ± 59.5	161.5 ± 51.9	0.93
PS (cm/ H_2O)	13.3 ±2.1	12.8 ± 4.1	0.87
PEEP (cm/ H_2O)	7.2 ± 2.0	7.5.0 ± 1.8	0.64
Vte (ml)	560 ± 124	645 ± 135.1	0.09
Length of stay in ICU (days)	6.95 ± 3.09	6.0 ± 4.67	0.47

Data are presented as mean ± standard deviation; Significance = p < 0,05; SAPS II: Simplified Acute Physiology Score II ;pH: Potential of Hydrogen; SaO_2 (%): Arterial Oxygen Saturation ; $PaCO_2$ (mmHg): Partial Pressure of Arterial Carbon Dioxide; PaO_2 (mmHg): Partial Pressure of Arterial Oxygen; PaO_2/FiO_2 (mmHg): Ratio of Arterial Oxygen Partial Pressure to Fraction of Inspired Oxygen. PS: pressure support; PEEP: Positive End-Expiratory Pressure; Vte: Expired Tidal Volume.

Predictors of NIV Failure

Univariate analysis (Table 5) revealed no significant differences in initial SAPS II scores between patient groups. However, respiratory rate (RR), positive end-expiratory pressure (PEEP), and expiratory tidal volume (Vte) were significantly elevated in NIV failure cases (645 ± 131.5 vs. 560 ± 134.5 ml, p = 0.09). No between-group differences were observed in duration of hospital stay.

Multivariate analysis (Table 6) identified a PaO_2/FiO_2 ratio <150 mmHg at admission as an independent predictor of NIV failure (adjusted OR 5.2, 95% CI 1.02-27.75; p=0.04). Notably, acute interstitial lung disease emerged as a significant risk factor for intubation, demonstrating a markedly increased likelihood (adjusted OR 7.39, 95% CI 1.44-37.9; p=0.01).

Table 6. Multivariate analysis of predictors of failure NIV in patients with AHRF (n=35).

Variable		NIV failure (n, %)	OR ; IC 95%	P
Gender	M	8 (66.7)	3.93 [0.91 – 17.01]	0.06
	F	4 (33.3)		
Age **(years)**	<65	10 (83.3)	1.25 ; [0.25 - 6.16]	0.78
	≥ 65	2 (16.7)		
SAPS II	<34	3 (25)	0.44 ; [0.105 – 1.88]	0.26
	≥34	9 (75)		
Influenza A pneumonia	**Yes**	1 (8.3)	1.14 ; [0.01 - 1.34]	0.08
	No	11 (91.7)		
Bacterial pneumonia	**Yes**	4 (33.3)	1.34 ; [0.32 – 5.61]	0.68
	No	8 (66.6)		
Acute interstitial pneumonia	**Yes**	7 (58.3)	7.39 ; [1.44 – 37.9]	**0.01**
	No	5 (41.7)		
PaO_2/FiO_2 (mm Hg)	< 150	9 (75)	5.2; [1.02 - 27.75]	**0.04**
	≥ 150	3 (25)		
Vte (ml)	< 8 ml/kg	4(33.3)	2.09 ; [0.98-3.76]	**0.08**
	≥ 8 ml/kg	8(66.6)		

Data represented as mean, and (SD) and number (%). SAPS II: Simplified Acute Physiology Score II PaO_2/FiO_2 (mmHg): Ratio of Arterial Oxygen Partial Pressure to Fraction of Inspired Oxygen; Vte: Expired Tidal Volume.

4. DISCUSSION

Clinical Impact of Hypoxemia and NIV Outcomes: hypoxemia has deleterious effects and is associated with an increased risk of mortality within the first 24 hours of hospitalization [13]. In cases of acute hypoxemic respiratory failure, non-invasive ventilation (NIV) often demonstrates high failure rates and increased mortality [14]. In this study, we enrolled patients requiring respiratory support but not immediate intubation. Initial NIV application led to improved pulse oximetry (SpO_2) and a rapid reduction in respiratory rate and distress signs. However, by the sixth hour (H_6), tachypnea persisted despite notable increases in partial pressure of oxygen (PaO_2) and arterial oxygen saturation (SaO_2). Interestingly, these improvements did not translate into a significant change in the PaO_2/FiO_2 ratio—a finding consistent with prior research [15-17]. This discrepancy may be attributed to the combined effects of high FiO_2 and positive end-expiratory pressure (PEEP), which enhance oxygenation without altering the PaO_2/FiO_2 ratio, as FiO_2 inversely influences this parameter.

NIV Success Rates and Patient Severity: the NIV success rate in our cohort study was 65.7%, lower than in some studies [18-19], likely reflecting the severity of our patients' conditions rather than NIV application technique. Notably, acute interstitial lung disease (ILD) patients had a particularly high intubation rate (70%), with NIV discontinuation leading to rapid desaturation. This subgroup, representing 28.6% of cases, included heterogeneous etiologies such as chemotherapy toxicity and congenital disease complications. Given their immunocompromised status, avoiding intubation was a key advantage. However, abrupt NIV cessation resulted in rapid gas exchange deterioration, with hypoxemia being the primary intubation trigger (58.3%). The impact of NIV on outcomes varied with hypoxemia severity. A PaO_2/FiO_2 ratio >150 mm Hg at admission emerged as a critical threshold for avoiding intubation, irrespective of ARDS presence [15,21]. Additionally, NIV success depended on underlying pathophysiological mechanisms [22].

Influenza A-Related ARDS and NIV Outcomes: our hospital implemented a rapid-response network for severe influenza A (confirmed via PCR), admitting 13 ARDS patients to the ICU. Three required immediate intubations, while NIV was attempted in the remaining ten, achieving a 90% success rate (9/10).

NIV Failure and Mortality Risks: NIV failure correlated with high mortality, particularly in acute acute interstitial lung disease patients, where outcomes remain poor regardless of intubation [23,24]. NIV failure itself is an independent ICU mortality risk factor [22,25]. While delayed intubation (median 12 hours after NIV initiation) did not appear detrimental [15], late ICU admission may have influenced outcomes.

Persistent tachypnea at H_6 suggested ongoing excessive inspiratory effort [26], potentially contributing to self-inflicted lung injury and NIV failure [1,27-30]. Elevated expired tidal volume (Vte) was also associated with NIV failure and mortality in severe hypoxemia [16]. Notably, intubated patients did not exhibit higher severity scores or respiratory rates than others [31].

This prospective study evaluating the efficacy of non-invasive ventilation (NIV) in the management of acute hypoxemic respiratory failure (AHRF) yielded several key findings: *1. Initial efficacy of NIV:* NIV significantly improved oxygenation (SpO_2, PaO_2) and reduced respiratory rate within the first hours of application. However, the lack of improvement in the PaO_2/FiO_2 ratio suggests that the benefits were primarily due to high FiO_2 and PEEP rather than enhanced gas exchange. *2. Failure rates and predictive factors:* the overall NIV failure rate was 34.3%, with high mortality (91.6%) in cases of failure. A baseline PaO_2/FiO_2 ratio < 150 mmHg and acute interstitial lung disease were independent predictors of NIV failure. Patients with AILD had a 7-fold higher risk of intubation, highlighting the severity of this condition. *3. Mortality and etiological specificities:* overall ICU mortality was 31.4%, primarily driven by NIV failure. Influenza A pneumonia had a favorable response to NIV (90% success rate), whereas AILD was associated with significantly higher mortality (70%). *4. Clinical implications and limitations:* NIV may be an effective alternative in patients with a PaO_2/FiO_2 ratio > 150 mmHg, but caution is warranted below this threshold. Close monitoring (particularly of respiratory rate and expired tidal volume) is essential for early detection of NIV failure. Delayed intubation did not appear to increase mortality, though late ICU admission may have influenced outcomes.

Several limitations should be noted in this study. This was a single-center observational study. Although NIV (non-invasive ventilation) was systematically initiated after the failure of standard oxygen therapy, our primary objective was to evaluate its role as an intermediate approach between conventional oxygen therapy and invasive ventilation (IV). Although recruitment was conducted exhaustively, the small sample size (n=35 over one year) results in insufficient statistical power to draw clinically relevant conclusions. This limitation is partly attributable to stringent selection criteria**.**This limitation was particularly evident in the “NIV failure” subgroup, which may affect the reliability of the predictive factors identified by logistic regression analysis. Heterogeneity in treatment decisions: although standardized protocols (including NIV) were available, treatment decisions (transition to IV or treatment adjustments) depended on the attending physicians, introducing uncontrolled heterogeneity, especially during on-call periods. Limitations of statistical analyses,conclusions regarding predictive factors for failure should be interpreted with caution, as the small size of the “failure” group may limit the power of the analyses.

Potential unmeasured biases, several factors could not be assessed, such as: the delay between admission and NIV initiation, the degree of adherence to the NIV protocol, the rigor of follow-up data collection at scheduled time points. However, the use of objective endpoints (intubation rate and mortality) may partially compensate for these biases. These limitations highlight the need for prospective, randomized, and multicenter studies to confirm our observations and clarify the optimal role of NIV in this indication.

5. CONCLUSIONS

First-line NIV remains a valuable tool in the management of acute hypoxemic respiratory failure. However, its success largely depends on the underlying etiology and the severity of hypoxemia, requiring particular caution when the PaO_2/FiO_2 ratio is below 150 mmHg. The impact of NIV on intubation rates is less than 35%. Strict patient selection, based on blood gas parameters and disease-specific risk factors, is crucial to optimize outcomes and avoid the high mortality associated with NIV failure. Further prospective randomized trials are needed to refine NIV application protocols in this setting.

Abbreviations

NIV Non-invasive ventilation
AHRF Acute hypoxemic respiratory failure
ICU intensive care unit
ARDS acute respiratory distress syndrome
ABG Arterial blood gases
FiO_2 Fraction of inspired oxygen
RR Respiratory rate

SpO_2 Oxygen saturation
SAPS II: Simplified Acute Physiology Score II
PaO_2/FiO_2 : Ratio of Arterial Oxygen Partial Pressure to Fraction of Inspired Oxygen
Vte Expired Tidal Volume
pH Potential of Hydrogen
SaO_2 Arterial Oxygen Saturation
$PaCO_2$ Partial Pressure of Arterial Carbon Dioxide
PaO_2 Partial Pressure of Arterial Oxygen
PS: pressure support
PEEP Positive End-Expiratory Pressure

Authors' contributions: First, A.C participated in data collection, interpretation, and manuscript writing. Then H.H contributed to data collection and manuscript revision. A-M.H took part in the study's data collection. M.H participated in data analysis and manuscript revision. M.N was involved in study conception. Finally, all authors contributed to study design, reviewed, and approved the final manuscript before submission.

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