SMJ- Sohag Medical Journal, Vol. 28 No(3) 2024

Print ISSN1687-8353 Online ISSN2682-4159

Original Article

Non-Invasive Ventilation in Patients with Acute Hypoxemic Respiratory Failure

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Abstract

Background: NIV has long been effective in the treatment of acute hypercapnic respiratory failure secondary to cardiogenic pulmonary edema and COPD while its use in the management of *de novo* acute hypoxemic respiratory failure (AHRF) has been met with mixed results associated with higher risks of intubation (failure of therapy) and higher risks of mortality.

Objectives: This study was designed to determine efficiency of non-invasive ventilation (NIV) in treating individuals with *de novo* acute hypoxemic respiratory failure.

Patients and Methods: The present work involved individuals with *de novo* acute type I RF hospitalized to Respiratory Intensive Care Unit (RICU), Department of Chest Diseases, Sohag University Hospitals during the period from November 2020 to May 2023.

Results: 126 patients (50.79% males) were included with a mean age of 57.76 years, all participants were diagnosed with ARDS due to pneumonia (61.11% viral and 38.89% bacterial) with 39.60% had mild, 45.24% moderate and 15.08% severe ARDS. NIV success rate was 62.7%. Severe ARDS was correlated with increased risk of NIV failure (84.21%). Refractory hypoxemia was the main cause of NIV failure (48.94% of NIV failure group). NIV failure group had longer duration of mechanical ventilation and longer ICU length of stay.

Conclusion: This study confirmed that NIV had an impact in managing of acute hypoxemic respiratory failure and ARDS due to pneumonia especially in early cases with mild to moderate ARDS.

KeyWords: NIV, ARDS, AHRF.

Abbreviations:NIV: Non-Invasive ventilation, AHRF: Acute hypoxemic respiratory failure, PEEP: Positive end expiratory pressure, DM: Diabetes mellitus, HTN: Hypertension, RICU: Respiratory intensive care unit, CXR: Chest X-ray, BMI: Body mass index, APACHE: Acute physiology and chronic health evaluation, ARDS: Acute respiratory distress syndrome.

DOI: **10.21608/SMJ.2024.298264.1478** **Received:** June 20, 2024 **Accepted:** June 26, 2024

Published: September 01, 2024

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Citation: : Hesham G. A. Ismail et al., Non-Invasive Ventilation in Patients with Acute Hypoxemic Respiratory Failure SMJ,2024 Vol. 28 No(3) 2024: 25- 41.

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Introduction

Non-invasive ventilation (NIV) is the delivery of respiratory assistance without the use of intrusive methods such as a tracheostomy tube or endotracheal tube. NIV has shown a significant rise in usage over the last twenty years. It has become an essential method for treating both chronic and acute respiratory failure, both at home and in critical care units. [12] The NIV therapy has established a reputation for effectively managing acute hypercapnic respiratory failure that arises as a result of COPD. NIV has been the primary therapy of choice for over 40 years in the treatment of acute-on-chronic diseases, including COPD and cardiogenic pulmonary edema.[22] Nevertheless, the utilization of NIV as a broad strategy for treating respiratory failure without hypercapnia has had inconsistent outcomes, especially in those with hypoxemic RF. Various causes have been examined, including acute cardiogenic pulmonary edema, immunosuppression, community-acquired pneumonia (CAP), postoperative care, post-extubation care, and ARDS. The findings have been inconclusive, with a combination of positive and negative outcomes.[15,20] NIV has shown mixed outcomes when treating de novo acute hypoxemic respiratory failure (AHRF), which refers to acute RF among individuals without hypercapnia, cardiac issues, or underlying chronic pulmonary disease. This procedure has been associated with increased risks of intubation (therapy failure) and increased mortality rates.[22,27]Notwithstanding these issues, studies indicate that NIV is being utilized more often among individuals with AHRF and is being started as the primary method of ventilatory support in 20% to 30% of these patients.[9,24] NIV has been utilized as the primary method of ventilatory support in patients meeting clinical criteria for acute respiratory distress syndrome (ARDS)[4,1,] with rates of success above 50%, particularly among individuals who have rapid improvement in oxygenation. Several studies have provided evidence for the growing popularity of NIV among individuals with AHRF. These studies have shown that NIV significantly decreases the need for intubation and reduces death rates in immunosuppressed patients and certain surgical patients with AHRF.[6,27]

Patients and methods

Prospective observational non-randomized clinical trial conducted at the Respiratory Intensive Care Unit (RICU), Department of Chest Diseases, Sohag University Hospitals from November 2020 to May 2023. Acceptance of Ethical Committee was gotten. This study was conducted on 126 patients (62 females and 64 males) with acute type I RF as characterized by the sudden appearance of clinical indications, such as rapid breathing and increased effort to breathe, within a period of less than 7 days. It is also identified by radiologic indicators, which may include opacities shown on a chest X-ray that might be present on one or both sides of the chest, absence of any chronic chest or cardiac problems, post-operative, post-cardiac arrest, post trauma or post extubation respiratory failure and hypoxemia described as a condition when the PaO_2 remains consistently below 60 mmHg for a duration of 6 to 8 hours, or when the SpO_2 is consistently below 90% while inhaling conventional oxygen at a maximum concentration of 60% and low or normal $PaCO_2$.

Ethical consideration

Written consent was taken from each patient or the first of kin of each patient to participate in the study and the study was approved by the Ethical Committee of Medical Research of Faculty of Medicine, Sohag University.

Criteria for inclusion

Participants hospitalized at the respiratory ICU with *de novo* AHRF requiring ventilatory support due to:

1. Tachypnea with respiratory rate >30 breath/min.
2. Other signs of respiratory distress as usage of accessory muscles of respiration and/or paradoxical breathing with thoraco-abdominal asynchrony.
3. PaO_2/FiO_2 ratio <300.

Patients Exclusion criteria

1. Age less than 18 years old.
2. individuals with hypercapnic respiratory failure ($PaCO_2$ more than 50 mmHg) on admission.
3. individuals with underlying chronic pulmonary disorders (e.g., COPD, bronchial asthma, ILD).
4. requirement for emergency invasive mechanical ventilation and endotracheal intubation.

5. individuals who admitted to RICU after cardiopulmonary arrest outside RICU.
6. Contraindications to the utilization of NIV as:

a) Recent injuries or surgical procedures involve-ng the esophagus, face, or skull.
b) Tracheotomy or other conditions affecting the upper airway.
c) Current occurrence of bleeding in the upper gastrointestinal tract.
d) Vomiting.
e) Inability to clear respiratory secretions.
f) Hemoptysis.
g) Persistent hemodynamic instability with SBP below 90 mmHg or mean MAP below 65 mmHg after giving a bolus of crystalloid fluid (30 ml/kg) and use of vasoactive agents or life-threatening arrhythmias.

7. Patients with chronic cardiac, hepatic or renal diseases.
8. individuals already diagnosed lung cancer.
9. individuals under chemotherapy due to extra-pulmonary malignancies.
10. Patients with post-operative, post-extubation or post trauma respiratory failure.

Methods

Each participant had been exposed to:

1 .comprehensive taking of history.

2 .comprehensive clinical assessment: General examination, cardiac, abdominal and local chest examination.

Utilization of accessory respiratory muscles by **Patrick scale.** [(22)]:

The following scale was used:

0. There is no observable utilisation of neck muscles, either in a phasic or tonic manner.
1. The neck muscles are tense, yet there is no variation in respiration (i.e., tonic activity).
2. Modest respiratory adjustment with contraction of the neck muscles.
3. There is a moderate level of phasic activity, with no signs of intercostal or supraclavicular indrawing.
4. Intense phasic contractions with indrawing.
5. Intense phasic contractions with paradoxical movement of the abdomen.

3 .Chest imaging:

- Chest X-Rays P.A. & Lateral views.
- Chest C.T. scan.
- CT pulmonary angiography if required.
- Chest ultrasound.

4 .Echocardiography or ECG if required.

5. Laboratory tests:

- Full blood picture that includes differential count.
- Full metabolic profile (serum creatinine, serum urea, liver enzymes, serum total proteins, serum albumin, serum bilirubin, serum glucose, serum alkaline phosphatase, serum electrolytes (NA^+, K^+, Ca^{++}) and coagulation profile (PT, PC, INR and aPTT).
- Arterial blood gases using ABL800 FLEX Blood Gas Analyzer (Denmark), we recorded the following variables: pH, $PaCO_2$, PaO_2, SaO_2, HCO_3^- and PaO_2/FiO_2 ratio.

6. Sputum sample for bacterial culture and sensitivity was taken.
7. Nasopharyngeal swab for serological detection of Influenza A, H1N1 and H5N1 virus in suspected cases.
8. Nasopharyngeal swab for PCR testing for SARS-CoV-2 in suspected cases.
9. Evaluation of severity of disease:

a) **Acute Physiology and Chronic Health Evaluation II (APACHE II)** scoring was adopted as a severity scoring on admission .[(18)]
b) **Sequential Organ Failure Assessment (SOFA)** was used for assessment of Severity of organ failure at baseline and daily to assess for the appearance of septic shock and sepsis.[(29)]
c) **The ratio of partial pressure of arterial oxygen (PaO_2)** to the fraction of the inspired oxygen (FiO_2) [PaO_2/FiO_2] ratio for assessment of severity of hypoxemia and ARDS based on the Berlin Definition of ARDS, 2016.

ARDS category according to the Berlin definition

PaO_2/FiO_2 ratio (mmHg)	ARDS category
>300	None
>200 and ≤300	Mild
>100 and ≤200	Moderate
≤100	Severe

10. Criteria for detection of septic shock and sepsis were endorsed based on **The Third International Consensus Definitions for Sepsis and Septic Shock.** [26]:

a) Sepsis is characterized as a potentially fatal condition when the body's reaction to infection becomes disordered, leading to failure in vital organs.
b) Organ dysfunction may be defined as a sudden increase in the overall SOFA score by 2 or more points due to the infection.
c) In individuals without documented previous organ failure, the baseline SOFA score is believed to be zero.
d) Septic shock is a kind of sepsis characterized by severe hemodynamic and cellular/metabolic abnormalities that significantly raise the risk of death.
e) Patients who have septic shock may be recognized by a clinical definition of sepsis, where they have low blood pressure that requires vasopressors to keep their MAP at or above 65 mmHg. Additionally, they have a serum lactate level greater than 2 mmol/L (18 mg/dL) even after receiving enough fluids to restore their volume.

10 **Initiation of NIV*:***

a) After fulfillment of inclusion criteria, the studied patients were connected to Carescape R860 ventilator (GE, USA), via double limb circuit with the interface of a clear non-vented oronasal face mask with a soft cushion seal. The mask was secured with head straps avoiding a tight fit.
b) The ventilator is switched to NIV mode with the following initial settings:

i) PEEP 10 cmH_2O and increased in 2 cmH_2O increments every 1 hour if needed to maintain SpO_2 above 92% provided that PaO_2 not exceeding 110 mmHg.
ii) Pressure Support at 6 cmH_2O and increased in 2 cmH_2O increments to maintain expiratory tidal volume between 4 and 6 ml/kg, a RR of fewer than 30 breaths/minute.
iii) FiO_2 60% and adjusted by 5% every 2 hours to keep PaO_2 of more than 65 mmHg or PaO_2/FiO_2 ratio of more than 120.
iv) Expiratory Trigger 25%.
v) Inspiratory Trigger 5 L/min.
vi) NIV was interrupted only during meals and was replaced by high flow nasal cannula (HFNC) when available.

c) In the event of leaks, an algorithm had been implemented. This algorithm consisted of four steps: first, adjusting the location of the mask; second, decreasing the PEEP level by 2 cmH2O; third, gradually lowering the pressure-support level by 2 cmH2O increments until the minimum expiratory tidal volume was achieved; and fourth, replacing the mask interface.
d) The head of the bed was raised to a 30-degree angle in each participant. The ventilator settings were modified based on continuous oximetry and sequential ABG readings. The patients were not sedated.

11 **Monitoring during NIV**:

a. Continuous monitoring was conducted for HR, MAP, RR, and oxygen saturation SpO_2.
b. Follow up of **clinical data** including utilization of accessory respiratory muscles by Patrick scale every 6 hours.
c. **ABGs** at baseline before application of NIV and after 1 h, 6 h to assure **initial stability** and after 24 h to assure **sustained stability** and every 6 hours thereafter, before weaning and if needed in case of deterioration.

- **The improvement of gas exchange** has been characterized as the capacity **to raise the PaO_2/FiO_2 ratio over 200 or to boost this ratio by over 100 from the initial value.** The evaluation of gas exchange improvements was conducted within one hour of the commencement of NIV to assess the **initial improvement.** Additionally, the assessment was also done throughout time to determine the **sustained improvement. Sustained improvement** in gas exchange refers to the capacity to sustain an established increase in the ratio of PaO2/FiO2 until NIV is stopped, as demonstrated by repeated measurements of ABG.

d. **Ventilator parameters**:

i. **Minute Ventilation $\dot{V}_E$.**
ii. **Tidal Volume V_T.**
iii. **Peak Inspiratory Pressure PIP.**
iv. **Inspiratory Time to Total Cycle Time ratio (Inspiratory Duty Time) T_i/T_{tot}.**
v. **Leak L/min.**

12 **Weaning from NIV** was achieved on a gradual concept:

i. Decrease FiO_2 to 40%, then
ii. Decrease pressure support every 2 hours by 2 cmH_2O down to 8 cmH_2O, then
iii. Decrease PEEP by 2 cmH_2O every 2 hours down to 5 cmH_2O.

13 **Outcome measures**:

- **The primary outcome** of the research was to determine the occurrence of endotracheal intubation and invasive mechanical ventilation throughout the trial, as well as identify the variables that increase the risk of NIV being unsuccessful.

1-Successful outcome is defined as discontinuation of NIV for 72 hours after weaning to conventional oxygen therapy with:

a. RR <24 BPM.
b. HR <110 BPM.
c. SpO_2 >90% on FiO_2 <35%.

If the patient has difficulty breathing or a decrease in oxygen levels after being removed from NIV, they are returned to NIV.

2-Failure of non-invasive ventilation is defined by criteria that necessitate **endotracheal intubation** using cuffed endotracheal tubes (internal diameters 7.5-8.5 mm) and shifting the patient to invasive mechanical ventilation.

The research participants were promptly intubated without any hesitancy in order to prevent the negative consequences of delayed intubation.

Intubation

was conducted for those receiving NIV if any of the following conditions were met;

1-Disturbed level of conscious in the form of agitation hindering nursing care and requiring sedation or GCS < 8 or seizures disorders.

2-Severe hemodynamic instability defined as **persistent hypotension is characterized by a SBP < 90 mmHg or a MAP < 65 mmHg,** even after fluid resuscitation**. It may also refer to the necessity for over 300 ng/kg/min of norepinephrine** support in order to preserve a SBP above 90 mmHg or electrocardiographic instability with **life threatening arrhythmias**.

3-Severe respiratory distress with **RR > 40 breaths/min**.

4-Severe hypoxemia with **PaO_2 /FiO_2 < 100** or **SpO_2 remaining below 90%** despite **FiO_2 100%**.

- **The secondary outcomes** included:

a. Length of time on mechanical ventilation.
b. The duration of time a patient spends in the ICU,

Statistical methods used for data analysis

STATA version 17.0 (Stata Statistical Software: Release 17.0 College Station, TX: StataCorp LP.) was used to analyze the data. The Shapiro-Wilk normality test was implemented to ascertain the distribution of various variables. The quantitative data was expressed using statistical measures such as the mean, standard deviation, median, and range. The data was subjected to analysis utilizing a student t-test in order to contrast the means of two groups. The Mann-Whitney test was implemented when the data did not follow a normal distribution. The qualitative data was given in numerical form as both absolute numbers and percentages, and was contrasted utilizing either the Chi-square test or the Fisher exact test. Roc curve analysis has been employed to identify the optimal threshold for many indicators that might indicate the failure of NIV. Additionally, sensitivity, specificity, positive predicted value, and negative predictive value were computed. Logistic regression analysis yielded odds ratios. The graphs were generated employing the Excel, STATA, or Medcalc for Windows (version 11.0) software programs. A P value was deemed significant if it was below 0.05 and very significant if it was below 0.001.

Results

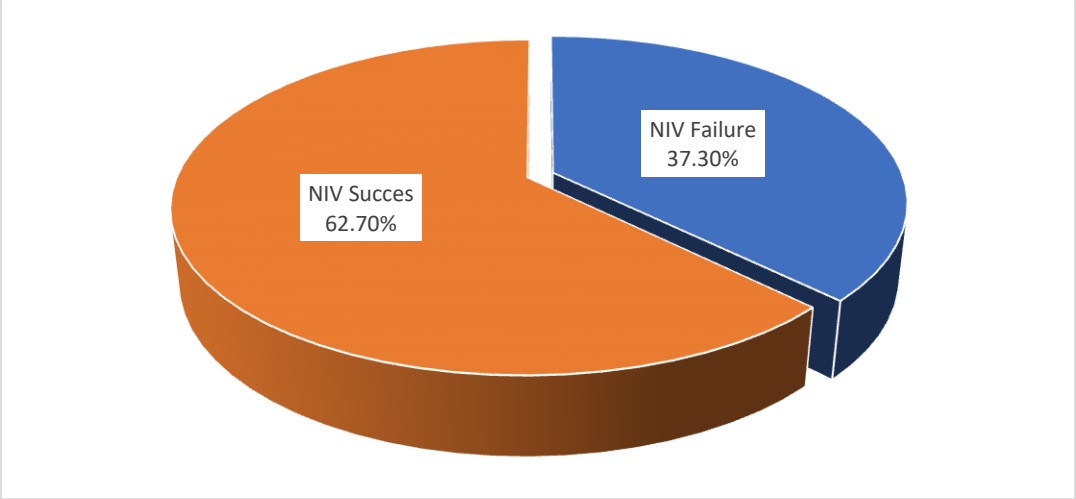

Figure 1: Outcome of NIV in studied patients

Our study was conducted on 126 patients selected after application of exclusion and inclusion criteria. The outcome of NIV showed 79 participants (62.7%) had successful NIV while 47 patients failed the NIV trial (37.3%).

Table 1: Comparison between NIV success and failure groups regarding demographic data

Variable	Total N=126	NIV Success group N=79	NIV Failure group N=47	P value
Age/year				
Mean ± SD	57.76±13.37	49.38±8.91	71.85±5.27	**<0.0001**
(range)	(29-82)	(29-62)	(64-82)	
Gender				
Female	62 (49.21%)	38 (48.10%)	24 (51.06%)	0.75
Male	64 (50.79%)	41 (51.90%)	23 (48.94%)	
Pregnancy				
No	58 (93.54%)	34 (89.47%)	24 (100%)	0.29
Yes	4 (6.45%)	4 (10.50%)	0	
BMI				
Mean ± SD	24.33±1.38	24.27±1.32	24.43±1.50	0.55
(range)	(20.91-27.21)	(20.91-27.21)	(20.91-27.21)	

NIV: Non-invasive ventilation ***BMI: Body mass index***

NIV success group had significantly younger **age** in comparison to NIV failure group (mean 49.38 years versus 71.85 years respectively, P value <0.0001). No statistically significant variations were existed among other demographic parameters and NIV outcome.

Table 2: Comparison between NIV success and failure groups regarding the clinical criteria

Variable No (%)	Total No (126)	NIV Success No (79)	NIV Failure No (47)	P value
Pneumonia				
Bacterial	49 (38.89%)	29 (36.71%)	20 (42.55%)	**0.01**
Viral	77 (61.11%)	50 (63.29%)	27 (57.45%)	
Causative organism				
K. Pneumoniae	12 (9.52%)	5 (6.33%)	7 (14.89%)	
MRSA	9 (7.14%)	3 (3.80%)	6 (12.77%)	
MSSA	10 (7.94%)	7 (8.86%)	3 (6.38%)	**0.03**
Pneumococci	18 (14.29%)	14 (17.72%)	4 (8.51%)	
Influenza virus	7 (5.56%)	2 (2.53%)	5 (10.64%)	
SARS-COV-2	70 (55.56%)	48 (60.76%)	22 (46.81%)	
ARDS severity				
Mild	50 (39.60%)	38 (48.10%)	12 (25.53%)	
Moderate	57 (45.24%)	38 (48.10%)	19 (40.43%)	**<0.0001**
Severe	19 (15.08%)	3 (3.80%)	16 (34.04%)	
Septic shock				
No	109 (86.51%)	72 (91.14%)	37 (78.72%)	**0.04**
Yes	17 (13.49%)	7 (8.86%)	10 (21.28%)	
DM				
No	104 (82.54%)	68 (86.08%)	36 (76.60%)	0.18
Yes	22 (17.46%)	11 (13.92%)	11 (23.40%)	
Hypertension				
No	114 (90.48%)	74 (93.67%)	40 (85.11%)	0.13
Yes	12 (9.52%)	5 (6.33%)	7 (14.89%)	

ARDS: Acute respiratory distress syndrome **DM:** Diabetes mellitus
MRSA: methicillin resistant staphylococcus aureus **MSSA:** methicillin sensitive staphylococcus aureus
SARS-COV-2: severe acute respiratory syndrome coronavirus 2

A statistically significant relation was existed among the **type of pneumonia** (bacterial or viral) and the **causative organism** and NV outcome (**P value 0.01 and 0.03 respectively**). A very significant statistical relation between the **degree of ARDS** and NIV outcome with NIV failure group had more severe ARDS (**P value <0.0001**). NIV failure group had more patients with **septic shock on admission** than NIV success group and that was statistically significant (21.28% of patients in NIV failure groups versus 8.86% in NIV success group, **P value 0.04**). No statistically significant relations were existed among presence of systemic hypertension nor diabetes mellitus and NIV outcome.

Table 3: Baseline clinical parameters of studied patients in relation to NIV outcome

Variable	Total N=126	NIV Success N=79	NIV Failure N=47	P value
GCS				
Mean ± SD	14.21±0.91	14.61±0.63	13.55±0.93	**<0.0001**
(range)	(12-15)	(13-15)	(12-15)	
Heart rate (bpm)				
Mean ± SD	114.39±11.67	107.33±8.59	126.26±11.67	**<0.0001**
(range)	(110-154)	(89-125)	(110-154)	
SBP (mmHg)				
Mean ± SD	106.07±21.82	113.86±17.63	92.98±22.08	**<0.0001**
(range)	(40-150)	(60-150)	(40-120)	
DBP (mmHg)				
Mean ± SD	66.23±16.18	70.57±14.46	58.94±16.45	**0.0001**
(range)	(20-80)	(20-95)	(20-80)	
Respiratory rate (cpm)				
Mean ± SD	34.50±6.41	30.68±3.10	40.94±5.28	**<0.0001**
(range)	(23-60)	(23-38)	(34-60)	
Temperature (˚C)				
Mean ± SD	37.46±2.90	37.71±0.78	37.68±0.81	0.81
(range)	(36.4-39)	(36-39)	(36.5-39)	
Patrick scale				
Mean ± SD	1.51±1.29	0.67±0.55	2.91±0.90	**<0.0001**
(range)	(0-4)	(0-2)	(1-4)	

GCS: Glasgow Coma Scale **SBP:** Systolic blood pressure **DBP:** Diastolic blood pressure
bpm: beat per minute **cpm:** cycle per minute ˚ **C:** degree Celsius

Patients with higher NIV success rate had significantly higher **GCS**, higher **SBP** and **DBP** levels in comparison to patients with NIV failure (mean 14.61, 113.68 mmHg and 70.57 mmHg versus 13.55, 92.98 mmHg and 58.94 mmHg respectively, **P values <0.0001**). Patients with higher NIV success rate had significantly lower **heart rate**, lower **respiratory rate** and lower **Patrick scale** in comparison to patients with NIV failure (mean 107.33 bpm, 30.68 cpm and 0.67 versus 126.26 bpm, 40.49 cpm and 2.91 respectively, **P value <0.0001**). no statistically significant relationship was existed among body temperature and NIV outcome.

Table 4: Baseline ABG parameters in relation to NIV outcome

Variable	Total N=126	NIV Success N=79	NIV Failure N=47	P value
pH Mean ± SD (range)	7.45±0.05 (7.35-7.59)	7.45±0.05 (7.35-7.59)	7.44±0.05 (7.36-7.5)	0.30
SaO_2 (%) Mean ± SD Median (range)	80.47±4.19 (68-86)	81.47±3.40 (71-86)	78.79±4.86 (68-86)	**0.004**
PaO_2 (mmHg) Mean ± SD (range)	47.53±3.78 (38-53)	48.42±3.20 (40-53)	46.04±4.21 (38-53)	**0.005**
$PaCO_2$ (mmHg) Mean ± SD (range)	32.02±4.52 (24-40)	31.96±4.57 (24-40)	32.11±4.47 (25-40)	0.86
P/F ratio Mean ± SD (range)	94.75±7.38 (76-107)	96.44±6.43 (80-107)	91.89±8.04 (76-107)	**0.0007**
HCO_3^- (mEq/L) Mean ± SD (range)	23.37±2.37 (20-27)	23.27±2.39 (20-27)	23.55±2.37 (20-27)	0.51

ABG: Arterial blood gas **pH:** Power of Hydrogen ion **SaO_2:** Oxygen saturation of arterial blood **HCO_3^-**: Bicarbonate ions **PaO_2:** Partial pressure of oxygen O_2 in arterial blood **$PaCO_2$:** Partial pressure of carbon dioxide CO_2 in arterial blood **P/F ratio:** Ratio of pressure of O2 in arterial blood PaO_2 to fraction of inspiratory oxygen concentration FiO_2

There was a significant statistical relation between **SaO_2, PaO_2 and P/F ratio** and NIV outcome as NIV success group had significantly higher baseline **SaO_2, PaO_2 and P/F ratio** in comparison to NIV failure group (mean 81.47%, 48.42 mmHg and 96.44 versus 78.79%, 46.04 mmHg and 91.89, **P values 0.004, 0.005 and 0.0007 correspondingly**). There was no statistically significant difference between **pH**, **$PaCO_2$** and **HCO_3^-** in NIV success and failure groups (mean 7.45, 48.42 mmHg and 23.27 mEq/L versus 7.44, 32.11 mmHg and 23.55 mEq/L, **P values 0.30, 0.86 and 0.51 correspondingly**). there were no statistically significant relationships among other baseline gasometric parameters (pH, $PaCO_2$ and HCO_3^-) and NIV outcome.

Table 5: APACHE II score, 1st, 2nd and 3rd day SOFA score in relation to NIV outcome

Variable	Total N=126	NIV Success N=79	NIV Failure N=47	P value
APACHE II score Mean ± SD (range)	23.33±4.77 (17-33)	20.30±2.53 (17-26)	28.43±2.96 (23-33)	**<0.0001**
SOFA score on 1st day Mean ± SD (range)	2.52±1.54 (2-8)	1.66±0.77 (1-4)	3.96±1.44 (2-8)	**<0.0001**
SOFA score on 2nd day Mean ± SD (range)	0.93±1.36 (0-5)	0.52±0.60 (0-2)	4.56±0.53 (4-5)	**<0.0001**
SOFA score on 3rd day Mean ± SD (range)	0.38±0.90 (0-5)	0.23±0.45 (0-2)	4.33±0.58 (4-5)	**0.0001**
SOFA score before weaning Mean ± SD (range)		0.20±0.40 (0-1)		

APACHE II: Acute physiology and chronic health evaluation **SOFA:** Sequential organ failure assessment **P value <0.05:** significant **P value ≥0.05:** non-significant

NIV success group had significantly lower **APACHE II score** in comparison to NIV failure group (mean 20.30 versus 28.43 respectively, **P value <0.0001**). NIV success group had significantly lower **SOFA score on 1st, 2nd and 3rd days** in comparison to NIV failure group (mean 1.66, 0.52 and 0.23 versus 3.96, 4.56 and 4.33, **P value <0.0001, <0.0001 and 0.0001 correspondingly**).

Table 6: Baseline laboratory investigations in relation to NIV outcome:

Variable	Total N=126	NIV success N=79	NIV Failure N=47	P value
WBCs (thousand/cc)				
Mean ± SD	14.46±10.43	12.85±9.27	17.16.5±11.74	0.06
(range)	(3.5-40)	(3.5-36)	(3.8-40)	
HGB (gm/dl)				
Mean ± SD	12.53±1.77	12.39±1.92	12.76±1.47	0.26
(range)	(3.5-16)	(3.5-15)	(9.8-16)	
PLTs (thousand/cc)				
Mean ± SD	375.12±122.75	358.0±116.84	403.9±128.2	0.09
(range)	(152-678)	(158-625)	(152-678)	
Creatinine (mg/dl)				
Mean ± SD	1.19±0.76	1.01±0.50	1.49±1.0	**0.002**
(range)	(0.4-4)	(0.4-2.8)	(0.4-4)	
Na^+ (mEq/L)				
Mean ± SD	134.88±7.00	135.2±6.72	134.34±7.49	0.51
(range)	(120-147)	(120-147)	(120-147)	
K^+ (mEq/L)				
Mean ± SD	3.67±0.84	3.64±0.84	3.72±0.85	0.60
(range)	(1.9-5.1)	(1.9-5.1)	(2.4-5.1)	
Ca^{2+} (mmol/L)				
Mean ± SD	1.0±0.11	1.00±0.11	0.995±0.11	0.75
(range)	(0.8-1.2)	(0.8-1.2)	(0.8-1.2)	
AST (IU/L)				
Mean ± SD	31.70±10.47	33.47±10.57	28.74±9.72	0.05
(range)	(15-52)	(15-52)	(15-51)	
ALT (IU/L)				
Mean ± SD	34.52±11.72	34.00±11.00	35.40±10.28	0.48
(range)	(15-52)	(20-52)	(15-52)	
Total bilirubin (mg/dl)				
Mean ± SD	1.25±0.42	1.21±0.38	1.31±0.47	0.28
(range)	(0.5-2.5)	(0.6-2.5)	(0.5-2.5)	
Albumin (g/dl)				
Mean ± SD	3.73±0.57	3.86±0.56	3.52±0.53	**0.001**
(range)	(2.5-5)	(2.7-5)	(2.5-4.3)	
Total protein (g/dl)				
Mean ± SD	6.21±0.45	6.22±0.47	6.18±0.43	0.61
(range)	(5.5-7)	(5.5-7)	(5.5-6.8)	
CRP (mg/dl)				
Mean ± SD	70.96±37.01	58.46±30.69	91.98±37.48	**<0.0001**
(range)	(18-154)	(20-140)	(18-154)	

WBCs: White blood cells. **HGB:** Hemoglobin. **PLTs:** Platelets.
Na: serum sodium ions. **K:** serum potassium ions. **Ca:** serum calcium ions.
AST: Aspartate transaminase. **ALT:** Alanine transaminase **CRP:** C ***reactive protein.***

NIV success group had a significantly higher level of serum **albumin** (mean 3.86 g/dl) than NIV failure group (mean 3.52 gm/dl, **P value 0.001)**. NIV success group had a significantly lower level of serum **creatinine** (mean 1.01 mg/dl) and lower level of serum **CRP** (mean 58.64 mg/dl) than NIV failure group (mean 1.49 mg/dl and 91.98 mg/dl respectively, **P value 0.002 and <0.0001 correspondingly**). there were no statistically significant relationships between other baseline laboratory tests and NIV outcome.

Table 7: Time of NIV failure

Time of NIV failure (hour)	Number (%)
2	20 (42.55%)
6	6 (12.77%)
12	13 (27.66%)
24	4 (8.51%)
48	3 (6.38%)
72	1 (2.13%)

Regarding **the time of NIV failure**, 20 patients (42.55%) failed the NIV after 2 hours of NIV, 6 patients (12.77%) failed the NIV 6 hours following NIV initiation, 13 patients (27.66%) failed NIV 12 hours after NIV initiation, 4 participants (8.51%) after 24 hours, 3 participants (6.38%) after 48 hours and 3 participants (6.38%) following 72 hours.

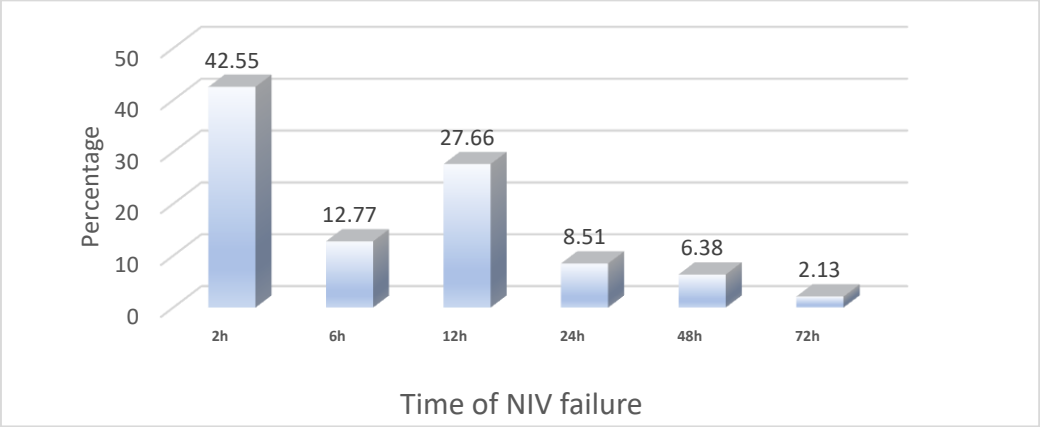

Figure 2: Time of NIV failure

Table 8: Causes of NIV failure

Causes of NIV failure	Number (%)
Refractory hypoxemia	23 (48.94%)
Excessive work of breathing	12 (25.53%)
Hemodynamic instability	9 (19.15%)
DCL (GCS<12)	3 (6.38%)

DCL: Disturbed conscious level
GCS: Glasgow coma scale

Regarding the cause of NIV failure, 23 patients (48.94%) failed NIV because of the inability to correct the **refractory hypoxemia** using NIV, 12 patients (25.53%) due to **excessive work of breathing** not relieved by NIV, **hemodynamic instability** and **DCL (GCS<12)** (9 and 3 patients accounting for 19.15% and 6.38% of the failure group respectively).

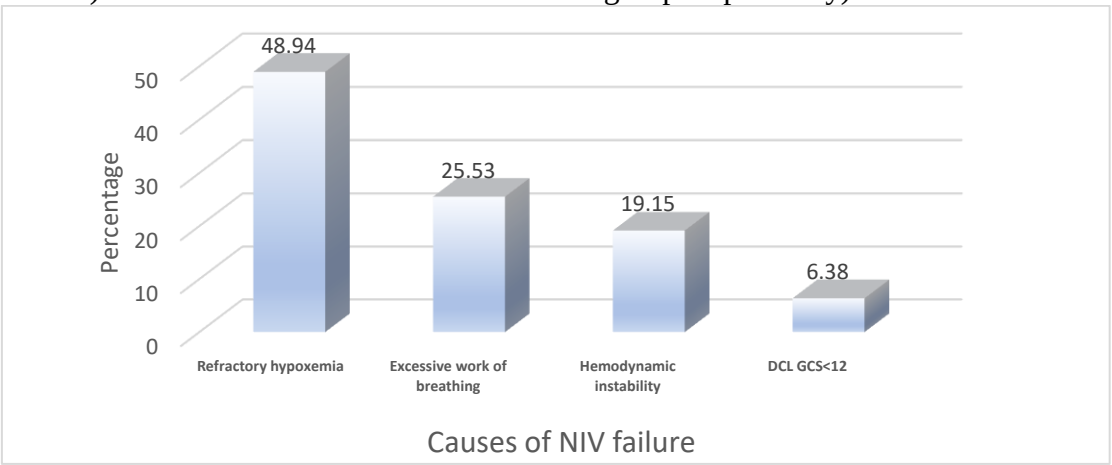

Figure 3: Causes of NIV failure

Table 9: Relation between time of NIV failure and cause of failure

Causes of NIV failure	Number	Time of NIV failure	
		Time/hour	Number (%)
Refractory hypoxemia	23	2 6 12	19 (82.61%) 3 (13.04%) 1 (4.35%)
Excessive work of breathing	12	6 12	3 (25.00%) 9 (75.00%)
Hemodynamic instability	9	2 12 24 48	1 (11.11%) 3 (33.33%) 3 (33.33%) 2 (22.22%)
DCL (GCS<12)	3	24 48 72	1 (33.33%) 1 (33.33%) 1 (33.33%)

DCL: Disturbed conscious level
GCS: Glasgow coma scale

Of the 23 patients who failed NIV due to inability to correct **refractory hypoxemia** using NIV, 19 patients did so after 2 hours of NIV initiation (82.61%), 3 patients after 6 hours (13.04%) and 1 after 12 hours (4.35%). Regarding the 12 patients who failed NIV due to persistence of **excessive work of breathing**, 3 patients failed NIV after 6 hours (25%) and 9 after 12 hours (75%). Meanwhile, of the 9 participants who failed NIV due to **hemodynamic instability**, 1 patient failed NIV after 1 hour (11.11%), 3 patients after 12 hours (33.33%), another 3 after 24 hours (33.33%) and 2 patients after 48 hours from NIV initiation (22.22%). 3 patients failed NIV due to **depressed consciousness** (GCS <12), 1 after 24 hours, another one after 48 hours and the last one after 72 hours (33.33% each).

Table 10: MV duration and ICU length of stay in relation to NIV outcome

Variable	Total N=126	NIV Success N=79	NIV Failure N=47	P value
Duration of mechanical ventilation in days Mean ± SD (range)	5.96±3.28 (2-14)	3.81±1.37 (2-7)	9.60±2.15 (6-14)	**<0.0001**
ICU Length of stay Mean ± SD (range)	7.62±3.06 (4-16)	5.73±1.32 (4-9)	10.78±2.47 (6-16)	**<0.0001**

P value <0.05: significant
P value ≥0.05: non-significant

NIV success group had significantly shorter **duration of being mechanically ventilated** and shorter **ICU length of stay** than NIV failure group (mean 3.81 days and 5.73 days, versus 9.6 days and 10.78 days and respectively, **P value <0.0001 each**).

Discussion

Our study was conducted on 126 patients (64 males and 62 females). The **outcome** of NIV showed 79 patients (62.7%) had successful NIV while 47 patients failed the NIV trial (37.3%), agreeing with the results by **Watson et al., 2023** .[30] with 59% NIV success rate among individuals with AHRF owing to community acquired pneumonia, **Ferrer et al., 2003** .[12] with 75% NIV success rate among individuals with severe hypoxemic RF, **Antonelli et al.,** .[5] with NIV success in 70% of patients, **Salwa et al., 2019** .[24] who found 68.33% NIV success rate among individuals with acute RF, **Bellani et al., 2017** .[7] who found 62.5% success rate of NIV in ARDS patients, **Dargent et al.,** .[9] with 58% NIV success in COVID-19 patients, **Duan et al.,** .[11] with 56% NIV success among individuals with de novo AHRF and **Buell et al., 2023** .[8] who

reported 30-50% failure rate among individuals with de novo AHRF, and contrasting to the findings by **Thille et al.,** [28] with 46% NIV success rate in AHRF, **Jayasimhan et al., .(** [17] whose study revealed that the NIV success rate was 35.8% and **Yaroshetskiy et al.,** [31] with NIV success 28.7% among individuals with COVID-19 mild to moderate ARDS.

In present work, we revealed a highly significant statistical correlation among older **age** and NIV failure (mean age 49.38 years Vs 71.85 years in NIV success and failure groups respectively, P value <0.0001) as older age is usually correlated with elevated disease severity and complications agreeing with the results by **Duan et al.,** [11] (mean age 57 years Vs 60 years in success and failure groups respectively, P value <0.01), **Habtamu et al.,** [14] who found that COVID 19 patients with AHRF older than 60 years are more liable to NIV failure, **Yaroshetskiy et al., .(** [31] (mean 62 years Vs 73 years in successful and failure groups respectively, P value 0.005), **Salwa et al.,** [24] (mean age 56.24 years Vs 62.52 years in successful and failure groups respectively, P value 0.039), **Ibrahim et al.,** [15] (mean age 56 years Vs 70 years in success and failure groups respectively, P value 0.036), **Dargent et al.,**[9] (mean age 58 years Vs 66 years in success and failure groups , P value 0.042) and disagreeing with the findings by **Jayasimhan et al., 2022**[17] who found no significant correlation among patients' age and NIV outcome (P value 0.809), **Bellani et al.,** [7] (P value 0.081), **Antonelli et al.,** [5] (P value 0.05), **Thille et al.,** [28] (P value 0.142), **Ferrer et al.,** [12] (P value 0.774).

Our study revealed no significant relationship between patient **gender** and NIV outcome (P value 0.75) agreeing with the results by **Jayasimhan et al.,** [17] (P value 0.646), **Bellani et al., .**[7] (P value 0.727), **Yaroshetskiy et al.,** [31] (P value 0.412), **Salwa et al., 2019 .**[24] (P value 0.705), **Thille et al.,** [28] (P value 0.551), **Ferrer et al.,** [12] (P value 0.602), **Antonelli et al., 2001** .[5] (P value 0.09) and contrasting to findings by **Duan et al.,** .[11] who found that male gender was associated with NIV success (P value <0.01) and **Dargent et al.,** [9] who found that female gender was associated with NIV success (P value 0.001).

All the studied population were diagnosed with pneumonia on admission to the respiratory ICU and according to the Berlin definition of ARDS, all were diagnosed as having ARDS. We found a highly significant statistical relationship between **ARDS severity** and NIV outcome with increased ARDS severity associated with NIV failure (P value <0.0001) in line with the findings by **Bellani et al.,** [7] who reported that presence of ARDS on admission was correlated with elevated risk of NIV failure (P value 0.009) and that mild and moderate ARDS were associated with NIV success while severe ARDS was correlated with elevated risk of NIV failure (P value 0.001), **Thille et al.,** [28] who found that moderate and severe ARDS were correlated with NIV failure (P value <0.0001), and **Duan et al.,** [11] who reported that existence of ARDS was correlated with NIV failure (P value <0.01).

Our study revealed that the presence of **septic shock on admission** to the respiratory ICU was correlated with elevated risk of NIV failure (P value 0.049) as shown in the results by **Duan et al.,** [11] who reported increased incidence of NIV failure an patients with septic shock and on vasopressor therapy (P value <0.01), **Antonelli et al.,** [5] who reported that presence of sepsis on admission was correlated with increased incidence of NIV failure and endotracheal intubation (P value <0.001) and in contrast to the work by **Bellani et al.,** [7] who found no difference in NIV outcome in patients requiring vasopressor agents for management of septic shock and those who didn`t. Also, **Thille al.,** [28] who found no difference in NIV outcome among individuals with and without septic shock and sepsis (P value 0.913), **Ferrer et al.,** [12] who revealed no variation in NIV outcomes among individuals with and without shock on admission (P value 0.519) as they included in their study patients with mild septic shock that was corrected rapidly with IV fluids and minimal vasopressor drugs.

In line with our findings, **Yaroshetskiy et al.,** [31] revealed no significant relation between existence of **DM** or **HTN** and NIV outcome (P value 0.751 each), also **Duan et al.,** [11] (P value 0.26 and 0.18 for DM and HTN respectively), **Ferrer et al.,** [12] (P value 0.685 for DM) and **Antonelli et al., .**[5] (P value 0.05 and 0.50 for DM and HTN respectively), while **Bellani et al.,** [7] found that diabetic patients are at increased risk of NIV failure (P value 0.035) disagreeing with our results as DM was associated with more severe disease.

Regarding **baseline vital signs**, our study revelaed that NIV successful group had significantly elevated **GCS** (mean 14.61 in success Vs 13.55 in

failure groups, P value <0.0001) agreeing with the results by **Salwa et al.,** [24] (mean 13.7 and 11.4 in success and failure groups respectively, P value <0.001), **Duan et al.,** [11] (mean 14.7 Vs 14.4 in success and failure groups respectively, P value <0.01) and ***González et al.,*** [19] (mean 13.8 Vs 14.3 in success and failure groups respectively, P value 0.007) and disagreeing with the results by **Jayasimhan et al.,** [17] (mean 15 in each group, P value 0.407), **Thille et al., .(** [28] (mean 14.9 and 14.6 in successful and failure groups respectively, P value 0.098).

Also, in our study NIV success group had significantly higher baseline **SBP and DBP** (mean 113.68 mmHg and 70.57 mmHg Vs 92.98 mmHg and 58.94 mmHg in success and failure groups respectively, P value <0.0001) agreeing with the results by **Duan et al.,** [11] (mean systolic blood pressure 133 mmHg Vs 129 mmHg in success and failure groups respectively, P value <0.01 while mean diastolic blood pressure 77 mmHg Vs 76 mmHg in success and failure group, P value 0.19) and **González et al., .(** [19] (mean SBP 138 mmHg Vs 129 mmHg in success and failure groups respectively, P value 0.002) and contrasting to the findings by **Thille et al.,** [28] (mean systolic blood pressure 134 mmHg and 124 mmHg in successful and failure groups respectively, P value 0.055) as they excluded shocked patients from their study.

We found that patients with higher NIV success rate had significantly lower **heart rate**, lower **respiratory rate** in comparison to patients with NIV failure (mean 107.33 bpm and 30.68 cpm versus 126.26 bpm and 40.49 cpm respectively, P value <0.0001 both) agreeing with **Duan et al.,** [11])(mean heart rate 114 bpm vs 117 bpm, mean respiratory rate 30 cpm Vs 33 cpm in success and failure groups respectively, P value 0.02 and <0.01 respectively), **Antonelli et al.,** [5] (mean respiratory rate 35 cpm Vs 38 cpm in success and failure groups respectively, P value 0.02) and contrasting to the findings by **Thille et al.,** [28] (mean heart rate 114 bpm vs 110 bpm, mean respiratory rate 32.7 cpm Vs 33.3 cpm in success and failure groups respectively, P value 0.467 and 0.517 respectively), **Ferrer et al.,** [12] (mean heart rate 116 bpm vs 115 bpm in success and failure groups, mean respiratory rate 37 cpm in each group, P value 0.892 and 0.764 respectively), **González et al.,** [19] (mean HR 104.5 bpm Vs 106.5 bpm, mean RR 28.2 cpm Vs 31.4 cpm in success and failure groups respectively, P value 0.39 and 0.001 respectively) and **Dargent et al.,** [9] (mean respiratory rate 26 cpm Vs 25 cpm in success and failure groups respectively, P value 0.798).

Also, in our study lower baseline **Patrick scale of accessory respiratory muscle use** was significantly associated with NIV success (mean 0.67 Vs 2.91 in success and failure groups respectively, P value <0.0001) agreeing with the results by **Yaroshetskiy *et al.,*** [31] (mean 1 versus 2 in success and failure groups respectively, P value <0.001) and **Dargent et al.,** [9] who found that the Respiratory comfort scale score was significantly higher in NIV success group (P value 0.004).

Regarding the **baseline gasometric parameters**, our study revealed that NIV success group had significantly higher baseline **SaO_2**, **PaO_2** and **P/F ratio** in comparison to NIV failure group (mean 81.47%, 48.42 mmHg and 96.44 versus 78.79%, 46.04 mmHg and 91.89, P values 0.004, 0.005 and 0.0007 respectively) agreeing with the results by **Bellani et al.,** [7] (mean P/F ratio 171 Vs 165 in success and failure groups respectively, P value <0.001) while no significant difference in PaO_2 (mean 88.6 mmHg Vs 83.1 mmHg in success and failure group respectively, P value 0.097), **Thille et al.,** [28] (mean P/F ratio 211 Vs 163 in success and failure groups respectively, P value 0.003) while no significant difference in PaO_2 (mean 78.7 mmHg Vs 84.1 mmHg in success and failure group respectively, P value 0.517), **Agarwal et al.,** [2] (mean P/F ratio 144.2 Vs 103.8 in success and failure group respectively, P value 0.01), **González et al.,** [19] (mean P/F ratio 148.6 Vs 118.5 in success and failure groups respectively, P value <0.001) and **Duan et al., .(** [11] (mean P/F ratio 167 Vs 145 in success and failure groups respectively, P value <0.01, mean SaO_2 90% Vs 87% in success and failure groups respectively, P value <0.01) and in contrasting to the findings by **Jayasimhan et al., 2022** [17] (mean P/F ratio 105 and 109.5 in success and failure groups respectively, P value 0.945), **Dargent et al.,** [9] (mean P/F ratio 109 and 79 in success and failure groups respectively, P value 0.05), **Ferrer et al.,** [12] (mean P/F ratio 102 Vs 103 in success and failure groups respectively, P value 0.735, mean PaO_2 58 mmHg Vs 56 mmHg in success and failure groups respectively, P value 0.682) and **Antonelli et al.,** [5] mean P/F ratio 119 and 120 in success and failure groups respectively, P value 0.8).

We revealed no statistically significant difference among **pH**, **$PaCO_2$** and **HCO_3^-** in NIV success and failure groups (mean 7.45, 48.42 mmHg and 23.27 mEq/L versus 7.44, 32.11 mmHg and 23.55 mEq/L, P values 0.30, 0.86 and 0.51 respectively) agreeing with the results by **Thille et al., 2013** [28] (mean 7.44, 34.8 mmHg and 24.4 mEq/L versus 7.44, 35.3 mmHg and 25.5 mEq/L, P values 0.685, 0.669 and 0.547 respectively), **Ferrer et al.,** [12] (mean pH was 7.42 Vs 7.41, mean $PaCO_2$ was 37 mmHg Vs 36 mmHg in success and failure groups respectively, P values 0.392 and 0.178 respectively), **Antonelli et al.,** [5] (mean pH was 7.4, mean $PaCO_2$ was 41 mmHg in both success and failure groups respectively, P values 0.7 and 0.6 respectively), **Bellani et al.,** [7] (mean pH was 7.38 in both success and failure groups, P value 0.967) while in their study lower $PaCO_2$ was correlated with elevated incidence of NIV failure (mean $PaCO_2$ was 44 mmHg Vs 34 mmHg in success and failure groups, P value 0.009), **Duan et al.,** [11] (mean $PaCO_2$ was 33 mmHg in both success and failure groups, P value 0.18) while higher pH was associated with NIV success (mean pH was 7.43 Vs 7.42 in both success and failure groups respectively, P value 0.02) and **Dargent et al.,** [9] (mean $PaCO_2$ was 31 mmHg Vs 35 mmHg in success and failure groups respectively, P value 0.231).

Regarding the **baseline laboratory investigations**, we found that NIV success group had a significantly higher level of serum **albumin** (mean 3.86 g/dl) than NIV failure group (mean 3.52 gm/dl, P value 0.001), NIV success group had a significantly lower level of serum **creatinine** (mean 1.01 mg/dl) and lower level of serum **CRP** (mean 58.64 mg/dl) than NIV failure group (mean 1.49 mg/dl and 91.98 mg/dl respectively, P value 0.002 and <0.0001 respectively) in line with the findings by **Jayasimhan et al.,** [17] (mean serum creatinine was 0.76 mg/dl Vs 1.11 mg/dl in success and failure groups respectively, P value 0.018), **Yaroshetskiy et al., .(** [31] (mean serum creatinine was 0.75 mg/dl Vs 0.92 mg/dl in success and failure groups respectively, P value 0.002) while they found that serum CRP had no variation among NIV success and failure groups (mean was 32 mg/dl Vs 42 mg/dl, P value 0.807), **González et al.,** [19] (mean serum creatinine 1.5 mg/dl in both groups, P value 0.88, mean serum albumin 3.1 gm/dl Vs 2.5 gm/dl in success and failure groups respectively, P value <0.001) and **Salwa et al., .** [24] (mean serum creatinine was 1.25 mg/dl Vs 2.01 mg/dl in success and failure groups respectively, P value <0.001) while serum albumin had no role in predicting NIV failure in their study (mean was 3.38 g/dl Vs 3.33 g/dl in success and failure groups respectively, P value 0.702).

Disagreeing with our results, **Salwa et al., .(** [24] found that baseline **WBCs** count was lower in NIV success than in failure group (mean WBCs count was 11.25 thousand/cc Vs 15.38 thousand/cc in success and failure groups respectively, P value 0.004) and **González et al.,** [19] who revealed that serum **hematocrit** level was significantly decreased in failure contrasted to in the success group (mean 32.1% Vs 36% in failure and success groups correspondingly, P value <0.001) while serum **bilirubin** was significantly lower in the success group (mean 0.7 mg/dl Vs 1.5 mg/dl respectively, P value <0.001).

In our study we adopted the **APACHE II score** and **SOFA score** as **severity scores**.

Our study revealed that NIV success group had significantly lower **APACHE II score** than NIV failure group (mean was 20.30 Vs 28.43 respectively, P value <0.0001) in line with the findings by **Jayasimhan et al., .(** [17] (mean was 16 Vs 20.5 in success and failure groups, P value 0.002) and **Salwa et al.,** [24] (mean was 19.39 Vs 26.90 in success and failure groups, P value <0.001) and contrasting to the findings by **Agarwal et al.,** [2] who found no relation between APACHE II score and the outcome of NIV in AHRF patients (P value 0.85).

In our study, NIV success group had significantly lower **SOFA score** on 1st, 2nd and 3rd days in comparison to NIV failure group (mean 1.66, 0.52 and 0.23 versus 3.96, 4.56 and 4.33, P value <0.0001, <0.0001 and 0.0001 respectively), which agrees with the results by **Watson et al.,** [30] who reported that the SOFA score was higher in patients with NIV failure at both ICU admission (7 vs. 4, P value < 0.001) and after 24 h (8 vs. 3, P value < 0.001)**, Bellani et al., .(** [7] (mean 1st day SOFA was 2 versus 3 in success and failure groups respectively, P value 0.019), **Yaroshetskiy et al.,** [31] (mean 1st day SOFA was 3 versus 4 in success and failure groups respectively, P value 0.001), **Duan et al., .(** [11] (mean 1st day SOFA was 4.8 Vs 6.1 in success and failure groups respectively, P value <0.01) and contrasting to the

findings by **Dargent et al.,** [9] (mean 1st day SOFA was 2 Vs 3 in success and failure groups respectively, P value <0.097).

Regarding the **time of NIV failure**, our study showed that 42.55% of the failure group failed the NIV after 2 hours of NIV, 12.77% after 6 hours, 27.66% after 12 hours, 8.51% after 24 hours, 6.38% after 48 hours and 2.13% after 72 hours as shown in the findings by **Salwa et al.,** [24] who found that of the AHRF patients who failed the NIV trial, 41.67% failed NIV trial after 2 hours, 8.33% after 4 hours, 8.33% after 6 hours, 25% after 12 hours, 8.33% after 48 hours and 8.33% after 72 hours, **Antonelli et al., .(** [5] who found that 68% of patients were intubated within 48 hours from NIV initiation and **Ozyilmaz et al.,** [20] who found that 68% of the failure group had early NIV failure (within 48 hours of initiation of NIV) and 17% of the NIV failure group had late NIV failure (beyond 48 hours on NIV initiation).

Regarding the **cause of NIV failure**, our study showed that 48.49% of patients failed NIV because of the inability to correct the refractory hypoxemia using NIV, 25.53% due to excessive work of breathing not relieved by NIV, 19.15% due to hemodynamic instability and 6.38% due to DCL (GCS<12), while **Salwa et al., .(** [24] found that 58.33% of the AHRF patients who failed the NIV trial failed due to inability to correct dyspnea and ABG values, 25% due to excessive secretions and 16.67% due to hemodynamic instability, while **Ferrer et al.,** [12] reported that the cause of NIV failure was the excessive work of breathing with signs of exhaustion in 84.62% of the NIV failure group and 15.38% failed due to refractory hypoxemia and **Antonelli et al., .(** [5] who found that 62% of the NIV failure was due to inability to correct hypoxemia, 13% due to inability to manage secretions, 11% due to hemodynamic instability, 9% due to mask intolerance and 5% due to inability to correct dyspnea.

Our study showed that NIV success group had significantly shorter **duration of mechanical ventilation** than NIV failure group (mean 3.81 days Vs 9.6 days, P value <0.0001), agreeing with the findings by **Jayasimhan et al., 2022** [17] (mean 5 days Vs 11 days in success and failure groups respectively, P value 0.013) and disagreeing with the findings by **Yaroshetskiy et al., .(** [31] who found no significant variation in duration of mechanical ventilation between NIV success and failure groups (mean 4 days Vs 6 days respectively, P value 0.103), the results by **Bellani et al., .(** [7] (9 days Vs 8 days in success and failure groups respectively, P value 0.293) and **Antonelli et al., .(** [5] (mean 2 days Vs 1 day in success and failure groups respectively, P value 0.06).

Also, our study showed that NIV success group had significantly decreased **ICU length of stay** contrasted to NIV failure group (mean 5.73 days, versus 10.78 days respectively, P value <0.0001) in line with the findings by **Habtamu et al.,** [14] (mean 4 days versus 8 days respectively, P value 0.02), **Dargent et al.,** [9] (mean 5 days Vs 25 days in success and failure groups respectively, P value <0.001), **Watson et al., .(** [30] (mean 4 days versus 8 days respectively, P value < 0.001), **Bellani et al.,** [7] (mean 7 days Vs 10 days in success and failure groups respectively, P value <0.001), **Ibrahim et al., .(** [15] who found that NIV failure group had significantly longer ICU stay (P value <0.001) and **Antonelli et al.,** [5] (mean 5 days Vs 9 days in success and failure groups respectively, P value <0.001) and contrasting to the findings by **Jayasimhan et al.,** [17] who found no difference in ICU length of stay (mean 4.69 days Vs 4.90 days in success and failure groups respectively, P value 1.0), ***Ferrer et al., .(*** [12] (mean 8.0 days Vs 10.1 days in success and failure groups respectively, P value 0.339) and **Duan et al.,** [11] (mean 7 days Vs 8 days in success and failure groups respectively, P value 0.92).

Conclusion

NIV has a role in managing of *de novo* AHRF and ARDS. The rate of NIV success in patients with *de novo* AHRF and ARDS is 62.70%. NIV is effective in managing of patients with mild to moderate ARDS but not in severe ARDS. Patients with more severe disease at presentation as revealed by the significantly more severe ARDS degree, the presence of septic shock on admission, higher APACHE II and higher SOFA score on the 1st day and on subsequent days are more liable to fail NIV. Refractory hypoxemia and the excessive work of breathing are the main causes of NIV failure.

Recommendation:

NIV should be an integral part in managing of individuals with de novo AHRF and ARDS in the absence of immediate indications for endotracheal intubation and/or any contraindication for NIV, particularly in mild to moderate ARDS and less severe disease at presentation. Close monitoring

of AHRF and ARDS patients put on NIV for the detection of any sign of deterioration and/or complication which necessitate invasive mechanical ventilation and endotracheal intubation. A low threshold for invasive mechanical ventilation and endotracheal intubation should be adopted upon any sign of deterioration and/or complication or failure to achieve improvements in gas exchange and/or improvement in signs of respiratory distress.

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