

## Predictors of Noninvasive Ventilation Failure in Intensive Care Unit

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### Abstract:

**Background:** : Non-invasive ventilation (NIV) has emerged as a preferred alternative to invasive mechanical ventilation, offering benefits such as reduced intensive care unit, respiratory center unit stay, lower complication rates, and improved patient outcomes. However, NIV failure remains a critical concern. **Aim of Work:** Identification of the predictors of noninvasive ventilation failure among patients admitted in RCU in Benha University hospital. **Methods:** This prospective observational study was conducted to 100 Patients presented with Acute Renal Failure (ARF) and was admitted to Respiratory Critical Unit (RCU), Chest Department in Benha University Hospitals from June 2022 to June 2023. Patients were divided into two groups: successful NIV (n=63) and failed NIV (n=37). **Results:** Significant predictors of NIV failure included higher heart rate, systolic blood pressure, and respiratory rate, along with lower diastolic blood pressure ( $P < 0.001$ ). Conditions such as chronic obstructive pulmonary disease and pneumonia were more common in the failed NIV group ( $P < 0.001$ ), while pulmonary oedema was more prevalent in the successful NIV group ( $P < 0.05$ ). Cardiac and renal comorbidities were significantly associated with successful NIV. PaCO<sub>2</sub> levels, acute physiology and chronic health evaluation scores were higher in the failed NIV group. Multivariate regression identified weight, body mass index, cardiac and renal comorbidity, acute admissions, APACHE score, and sex,

weight, BMI, cardiac and renal comorbidity, acute admission, types of lung disease, were independent predictors of failed NIV ( $P < 0.05$ ) while sex was not. **Conclusion:** Weight, BMI, cardiac, renal comorbidity, acute admission, APACHE and BiPAP were independent predictors of NIV failure in RCU patients.

**Keywords:** Noninvasive Ventilation Failure, Acute Respiratory Failure, Respiratory Center Unit stay.

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## Introduction

Acute respiratory failure (ARF) has a steady increase in the number of ICU hospitalization at an average annual rate of 11.8% in 2015 to 2021 with a decrease in inpatient mortality in the United States<sup>[1]</sup>.

ARF characterized by the impaired respiratory system to exchange gases and to oxygenate the blood, resulting in hypoxia with or without hypercapnia. Two main mechanisms of ARF include failure in pulmonary ventilation caused by neuromuscular diseases, chest wall deformities, obstructive pulmonary diseases, and failure in gas exchanges caused by adult acute respiratory distress syndrome, acute cardiogenic pulmonary oedema, pneumonia, airspace collapse (atelectasis) and pulmonary embolism<sup>[2]</sup>.

Non-invasive ventilation (NIV) refers to the delivery of mechanical ventilation without using an invasive artificial airway (endotracheal tube or tracheostomy tube) that markedly increases over the past two decades worldwide among patients admitted in RCU<sup>[3]</sup>.

NIV has become an alternative to invasive mechanical ventilation for the management of ARF, since it can decrease the length of stay in the RCU, reduce the number of possible complications, increase the quality of life, reduce risk of infection and improve the chance of survival, compared to conventional invasive ventilation<sup>[4]</sup>.

The effectiveness of NIV varies according to the etiology of respiratory failure NIV for ARF should be performed in a clinical environment with adequate nurse-to-patient ratios and monitoring. The choice of facility level should be selected according to disease severity and the co-existence of other organ failure<sup>[5]</sup>.

NIV failure has been defined as the need for endotracheal intubation (ETI) or death. Its rate greatly varies between 5 and 60%, depending on numerous factors, including the cause of ARF. Unsuccessful NIV was found to be independently associated with

death, especially in patients with de novo ARF<sup>[4]</sup>.

The aim of this work: Identification of the predictors of non-invasive ventilation failure among patients admitted in RCU in Benha University hospital.

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## Patients and Methods:

This prospective observational study was conducted to 100 Patients presented with (ARF) and was admitted to the (RCU), Chest Department in Benha University Hospitals during the period between June 2022 to June 2023 after the approval of the Institutional Ethical Committee with **approval code (Ms 37-10-2022)**.

There are adequate provisions to maintain privacy of participants and confidentiality of the data.

### Inclusion Criteria:

Patients from 20 to 60 years old, with ARF due to difficult etiology resulting from all kinds of diseases such as pneumonia, acute respiratory distress syndrome (ARDS), Chronic obstructive pulmonary disease (COPD), asthma, and cardiogenic pulmonary edema, and Eligible for Non-Invasive ventilation were included in the study

### Exclusion Criteria:

While patients with disturbed conscious level, excessive secretion, vomiting or uncooperative, females who were pregnant or with facial deformity and facial surgery and major causes requiring RCU admission were excluded Eligible for non – invasive ventilation NIV.

### Methods:

All patients were subjected to history taking(Age, sex, Body mass index (BMI), Weight, previous hospital admission, previous Intensive Care Unit admission, previous need of NIV and other comorbidities), complete clinical examination was included (Blood Pressure, Heart rate, Respiratory rate, Temperature, Diastolic blood pressure, Systolic blood pressure, Conscious level by Glasgow Coma Scale), local examination (Clinical Evaluation by The

Sequential Organ Failure Assessment (SOFA)), Routine laboratory investigation (CBC, liver functions test, kidney functions test, random blood sugar, arterial blood gas and serum electrolytes), radiological investigations (Chest X-Ray, CT-Chest, ECHO).

### Statistical analysis

This prospective observational study was conducted on 100 patients presented with ARF and were admitted to ICU Benha University Hospitals and divided into two groups

Statistical analysis was done by SPSS v26 (IBM Inc., ARMONK, IL, USA). Shapiro-Wilks test and histograms were used to evaluate the normality of the distribution of data. Quantitative parametric variables were presented as mean and standard deviation (SD) and compared between the two groups utilizing unpaired Student's t-test. Quantitative non-parametric data were presented as median and interquartile range (IQR) and were analyzed by Mann Whitney-test. Qualitative variables were presented as frequency and percentage (%) and were analyzed utilizing the Chi-square test or Fisher's exact test when appropriate. Univariate regression was used to estimate the relationship between a dependent variable and one independent variable. Multivariate regression was also used to estimate the relationship between a dependent variable and more independent variables. A two tailed P value < 0.05 was considered statistically significant.

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### Results:

Weight and BMI were significantly higher in the Successful NIV group compared to the Failed NIV group (P < 0.001). Heart rate, systolic blood pressure, and

respiratory rate were significantly lower, while diastolic blood pressure was higher in the Successful NIV group (P < 0.001). COPD and pneumonia were less prevalent in the Successful NIV group (P < 0.001), whereas pulmonary oedema and cardiac issues were more common (P < 0.05 and P = 0.004, respectively). Renal issues and acute admissions were also higher in the Successful NIV group (P = 0.009 and <0.001). Leukocytes were significantly lower in the Successful NIV group (P < 0.001), while kidney functions (creatinine and urea) and serum potassium were better in the Successful NIV group (P < 0.001). Other variables, including liver functions and serum Na, Mg, Ca, and haematocrit, showed no significant differences between the groups. **Table 1**

pH and HCO<sub>3</sub> were insignificantly different at admission, 6h, 12h, 24h and 48h between both groups. PaCO<sub>2</sub> was significantly higher at admission, 6h, 12h, 24h and 48h in Failed NIV than Successful NIV (P value<0.001). **Table 2**

APACHE score was significantly lower in successful NIV compared to failed NIV (P<0.001). NIV (BiPAP) was significantly higher in successful NIV group than failed NIV (P<0.001). **Table 3**

In univariate and multivariate regression, sex, weight, BMI, cardiac and renal comorbidity, acute admission, types of lung disease, APACHE and BiPAP, weight, BMI, cardiac and renal comorbidity, recurrent or acute admission, types of lung disease, APACHE and BiPAP were independent predictors of failed NIV (P <0.05) while sex wasn't.

### Table 4

**Table 1:** Demographic data, vital signs, type of lung disease, associated comorbidity and recurrent or acute admission of the studied groups

		Successful NIV(n=63)	Failed NIV (n=37)	P
	Age (years)	42.71±10.51	43.08±10.49	0.866
Sex	Male	28(44.44%)	27(72.97%)	<b>0.006*</b>
	Female	35(55.56%)	10(27.03%)	
	Weight (kg)	80.1±14.08	70.11±10.9	<b>&lt;0.001*</b>
	Height (m)	1.65±0.08	1.66±0.07	0.767
	BMI (kg/m <sup>2</sup> )	30.67±5.43	25.6±4.35	<b>&lt;0.001*</b>
	HR (beats/min)	80.75±10.02	106.27±11.15	<b>&lt;0.001*</b>
	DBP (mmHg)	76.89±8.14	49.62 ± 3.01	<b>&lt;0.001*</b>
	SBP (mmHg)	127.03±12.76	155.14±9.15	<b>&lt;0.001*</b>
	Respiratory rate (breaths/min)	18.92±3.42	41.51±3.36	<b>&lt;0.001*</b>
	COPD	9(14.29%)	31(83.78%)	<b>&lt;0.001*</b>
	Pulmonary edema	42(66.67%)	7(18.92%)	<b>&lt;0.001*</b>
	Pneumonia	21(33.33%)	30(81.08%)	<b>&lt;0.001*</b>
	Obstructive Sleep Apnea	30 (47.6%)	7 (18.92%)	<b>0.005*</b>
	DM	23(36.51%)	10(26.32%)	0.383
	HTN	8(12.7%)	7(18.42%)	0.402
Associated comorbidity	DM and HTN	12(19.05%)	6(16.22%)	0.793
	Hypothyroidism	1(1.59%)	2(5.41%)	0.553
	Cardiac	19(30.16%)	2(5.41%)	<b>0.004*</b>
Recurrent or acute admission	Renal	6(9.52%)	11(29.73%)	<b>0.009*</b>
	RA	48(76.19%)	14(37.84%)	<b>&lt;0.001*</b>
	AA	15(23.81%)	23(62.16%)	
<b>Laboratory Parameters</b>				
CBC	Hematocrit (%)	40.92±9.64	42.11±0.11	0.560
	Leukocytes (x 10 <sup>9</sup> /L)	8.78±2.51	17.55±4.21	<b>&lt;0.001*</b>
Liver function test	AST (U/L)	51.97±17.24	50.68±17.32	0.719
	ALT (U/L)	52.57±24.18	59.86±26.5	0.163
	Albumin (mg/dl)	28.54±7.34	28.59±6.92	0.971
	Bilirubin (mg/dl)	0.33±0.1	0.35±0.1	0.286
Kidney function test	Creatinine (mg/dl)	3.1 ± 0.98	6.06±1.76	<b>&lt;0.001*</b>
	Urea (mg/dl)	149.97±18.16	183.7±19.7	<b>&lt;0.001*</b>
Electrolytes	Serum Na(mEq/L)	136.03±5.85	136.65±5.99	0.615
	Serum K (mEq/L)	4.02±0.48	2.33±0.28	<b>&lt;0.001*</b>
	Serum Mg(mg/dL)	2.23±0.36	2.28±0.41	0.508
	Serum Ca (mg/dL)	8.89 ± 0.9	8.56 ± 0.86	0.079

Data are presented as mean ± SD or frequency (%). \* Significant p value <0.05. NIV: Non-invasive ventilation, BMI: Body mass index, HR: Heart rate, DBP: Diastolic blood pressure, SBP: Systolic blood pressure, COPD: Chronic Obstructive Pulmonary Disease, DM: diabetes mellitus, HTN: hypertension, AA: acute admission, RA: recurrent admission, CBC: complete blood count, AST: Aspartate aminotransferase, ALT: Alanine transaminase.

**Table 2:** ABG of the studied groups.

	Successful NIV (n=63)	Failed NIV (n=37)	P
<b>pH</b>			
<b>At admission</b>	7.2±0.03	7.2±0.03	0.355
<b>6h</b>	7.2±0.04	7.21±0.03	0.312
<b>12h</b>	7.21±0.06	7.21±0.06	0.671
<b>24h</b>	7.22±0.09	7.22±0.09	0.963
<b>48h</b>	7.3±0.15	7.28±0.16	0.612
<b>PaCO<sub>2</sub> (mmHg)</b>			
<b>At admission</b>	56.29±12.77	77.57±8.83	<0.001*
<b>6h</b>	53.35±13.71	75.54±9.77	<0.001*
<b>12h</b>	45.81±13.35	67.57±9.86	<0.001*
<b>24h</b>	43.57±13.31	65.59±9.47	<0.001*
<b>48h</b>	39.14±17.29	59.51±19.84	<0.001*
<b>HCO<sub>3</sub> (mEq/L)</b>			
<b>At admission</b>	19.89±5.82	21.14±6.17	0.569
<b>6h</b>	19.05±3	19.22±3.47	0.798
<b>12h</b>	19.35±3.32	19.22±4.24	0.862
<b>24h</b>	19.46±3.66	19.59±4.52	0.872
<b>48h</b>	18.08±7.86	18.86±7.16	0.619

Data are presented as mean ± SD. \* Significant p value <0.05. NIV: Non-invasive ventilation, HCO<sub>3</sub>: Bicarbonate, PaCO<sub>2</sub>: Partial pressure of carbon dioxide.

**Table 3:** APACHE score, NIV mode of the studied groups

	Successful NIV (n=63)	Failed NIV (n=37)	P
<b>APACHE score</b>	14(12-19.5)	30(28 – 32)	<0.001*
<b>NIV mode</b>			
<b>CPAP</b>	18 (28.57%)	27 (69.23%)	<0.001*
<b>BiPAP</b>	45 (71.43%)	12 (30.77%)	

Data are presented as frequency (%) or median (IQR). \* Significant as P value ≤0.05. APACHE: Acute physiology and chronic health evaluation, NIV: Non-invasive ventilation, CPAP: Continuous positive airway pressure, BiPAP: Bilevel positive airway pressure.

**Table 4:** Univariate and multivariate regression to predict failed NIV

	Odds ratio	Univariate		Odds ratio	Multivariate	
		95% CI	P		95% CI	P
<b>Sex</b>	0.2963	0.1230 to 0.7139	<b>0.006*</b>	0.2396	0.0341 to 1.6846	0.151
<b>Weight(kg)</b>	0.920	0.885-0.957	<0.001*	0.851	0.780-0.928	<0.001*
<b>BMI (kg/m<sup>2</sup>)</b>	0.816	0.739-0.901	<0.001*	0.823	0.744-0.909	<0.001*
<b>Cardiac comorbidity</b>	0.132	0.028-0.607	<b>0.009*</b>	0.09	0.016-0.492	<b>0.005*</b>
<b>Renal comorbidity</b>	4.019	1.341-12.045	<b>0.01*</b>	3.517	1.02-12.125	<b>0.046*</b>
<b>Recurrent or acute admission</b>	4.728	1.913-11.68	<0.001*	0.395	1.504-10.371	<b>0.005*</b>
<b>Types of lung disease</b>						
<b>COPD</b>	31.00	10.079	<0.001*	147.63	19.473-1119.23	<0.001*
<b>Pneumonia</b>	8.571	3.232-22.72	<0.001*	13.99	4.159-47.05	<0.001*
<b>Obstructive Sleep Apnea</b>	0.256	0.098-0.670	<0.001*	1.262	1.156-1.378	<0.001*
<b>APACHE score</b>	1.272	1.166-1.388	<0.001*	1.262	1.156-1.378	<0.001*
<b>BiPAP</b>	0.192	0.079-0.462	<b>0.002*</b>	0.213	0.063-0.720	<b>0.01*</b>

\*Significant as P value≤0.05, CI: Confidence interval. COPD: Chronic obstructive pulmonary disease, SBP” Systolic blood pressure, DBP: Diastolic blood pressure, APACHE: Acute physiology and chronic health evaluation.

## Discussion

Chen et al<sup>[10]</sup> carried out a retrospective clinical study on 46-bed mixed ICU aged more than 18 years, having indications for NIV: ARF resulting from all kinds of diseases such as pneumonia, ARDS, COPD, asthma, and cardiogenic pulmonary oedema. They showed that failed patients were more associated with ideal body weight (IBW) than successful patients. Also, Liu et al<sup>[11]</sup> who conducted a retrospective observational study at 29-bed ICU patients who underwent cardiac surgery and developed ARF after extubation. They demonstrated that BMI was significantly higher in successful NIV group than in failed NIV group and they noted that sex was insignificantly different between both groups. The smaller sample size and older mean age (59.4 years) may explain this difference from our results.

In the current study, heart rate, systolic blood pressure and respiratory rate were significantly lower in successful NIV than in failed NIV. Diastolic blood pressure was significantly higher in successful NIV than in failed NIV, in agreement with our results, Wafy et al<sup>[12]</sup> carried out a prospective observational study on 150 patients who had non-invasive ventilation. They showed that high heart rate at admission was associated with NIV failure.

This came in line with Chen et al<sup>[10]</sup> who noted that NIV failure appeared to have higher heart rate at the first day of ICU admission and had higher heart rate during NIV treatment. Also, Pons-Òdena et al<sup>[13]</sup> carried out a prospective cohort study included all ARF patients that received NIV in a 14-bed Paediatric ICU. They demonstrated that patients with higher heart rates were more prone to non-invasive support failure.

However, Al-Rajhi et al<sup>[14]</sup> performed a retrospective cohort study on 163 consecutive patients with community acquired pneumonia requiring ventilator support. They found that mean arterial pressure was insignificantly different

between successful NIV and failed NIV groups. The different age and sample size may explain this difference from our results.

Our results revealed that chronic obstructive pulmonary disease (COPD) and pneumonia were significantly lower in successful NIV group than in failed NIV group. Pulmonary edema was significantly higher in successful NIV group than in failed NIV group.

our results are supported by Liu et al<sup>[11]</sup> who found that COPD and pneumonia were significantly lower in successful NIV group than in failed NIV group.

In disagreement with our results, Wafy et al<sup>[12]</sup> reported that obstructive lung disease was significantly higher in successful NIV group than in failed NIV group. The different sample size, different age and respiratory failure type may explain this difference from our results, Furthermore, Al-Rajhi et al<sup>[14]</sup> found that COPD was significantly higher in successful NIV group than in failed NIV group.

Regarding the present study, APACHE score was significantly lower in successful NIV compared to failed NIV. This came in line with Wafy et al<sup>[12]</sup> who demonstrated that patients with failed NIV had significantly higher APACHE-II score in comparison to those with successful NIV.

Our results revealed that in univariate and multivariate regression, sex, weight, BMI, cardiac and renal comorbidity, acute admission, types of lung disease, APACHE and BiPAP, weight, BMI, cardiac and renal comorbidity, recurrent or acute admission, types of lung disease, APACHE and BiPAP were independent predictors of failed NIV ( $P < 0.05$ ) while sex wasn't.

## Limitations

- It was a single center study
- Small sample size that may produce insignificant results
- Short follow up.

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## Conclusions:

Physicians must be alert when applying NIV for different types of respiratory failure patients and keep predictors of NIV failure (BMI, cardiac and renal comorbidity, recurrent or acute admission, types of lung disease, APPCHE and mode of NIV ) into consideration for better outcome.

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## List of Abbreviations

NIV	Noninvasive Ventilation
ICU	Intensive Care Unit
RCU	Respiratory Center Unit
ARF	Acute Respiratory Failure
COPD	Chronic Obstructive Pulmonary Disease
ETI	Endotracheal Intubation
BMI	Body Mass Index
SOFA	Sequential Organ Failure Assessment
APACHE	Acute Physiology and Chronic Health Evaluation
BiPAP	Bilevel Positive Airway Pressure
CPAP	Continuous Positive Airway Pressure
AST	Aspartate Aminotransferase,
ALT	Alanine Transaminase
HR	Heart Rate
DBP	Diastolic Blood Pressure
SBP	Systolic Blood Pressure
DM	Diabetes Mellitus
HTN	Hypertension
AA	Acute Admission
RA	Recurrent Admission

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