



## PH, CRP as Prognostic Indicators for the Success of Treatment with Non-invasive Ventilation in Patients with Chronic Respiratory Failure Type II

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### Authors' contributions

This work was carried out in collaboration among all authors. Author HA designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors MH and MIK managed the analyses of the study. Author AA managed the literature searches. All authors read and approved the final manuscript.

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### ABSTRACT

**Background:** Non-invasive mechanical ventilation (NIMV) provides an alternative option to the initiation of invasive mechanical ventilation in patients with acute respiratory failure, avoiding the associated adverse events.

**Objective:** the present study aimed to assess the outcome of the patients who were initially treated with NIMV and identify the prognostic predictive value of PH and CRP for NIMV failure.

**Materials and methods:** This was observational analytical study conducted in the Department of Pulmonology in Tishreen University Hospital –Lattakia- Syria from January 2019 to January 2020. Adult patients with the diagnosis of acute on chronic respiratory failure type 2 were enrolled in the study.

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**Results:** A total of 67 patients with acute on chronic respiratory failure type 2 were included in the study. The median age was 63 years and 62.7% were male. The patients in the PH group (7.20-7.25) presented higher rates of mortality and admission to intensive care unit (ICU) which represented 25% and 50% respectively. The NIMV failure rate was 22.4%. Frequency of patients with  $\text{PH} \leq 7.31$ ,  $\Delta\text{PH} \leq 0.04$ , or  $\text{CRP} \geq 53.5$  were higher in NIMV failure group; (33.3% vs. 3.8%,  $p: 0.001$ ), (46.7% vs. 23.1% -,  $p: 0.03$ ), and (53.3% vs. 32.7%,  $p: 0.04$ ) respectively. Independent predictors for NIMV failure were:  $\text{PH} \leq 7.31$ (OR 3.3[0.6-7.8],  $p: 0.01$ ) and  $\Delta\text{PH} \leq 0.04$ (OR 2.1[1.1-3.9],  $p: 0.02$ ).

**Conclusion:** NIMV is an effective treatment for hypercapnic respiratory failure. Identification independent predictors for NIMV failure may be useful to avoid the possible complications.

*Keywords: Non-Invasive Mechanical Ventilation (NIMV); respiratory failure; mortality; hypercapnic.*

## 1. INTRODUCTION

Chronic respiratory failure is a long-term long-term condition, usually occurring over a period of months or years [1]. It may be due chronic lung diseases such as COPD, cystic fibrosis or pulmonary fibrosis [2,3]. Neuromuscular disease and chest wall abnormalities may also cause chronic respiratory failure [3]. It may be classified as occurring with hypoxia (Type 1) or hypercapnea (Type 2) [4]. NIMV has emerged as a new and important tool in the treatment of acute respiratory failure (ARF) for all diagnosis including patients with and without chronic obstructive pulmonary disease (COPD) regardless of the supporting evidence for the later [5,6]. It can reduce substantially the need for endotracheal-intubation, incidence of complications associated with mechanical ventilation (MV), stay in the ICU, and mortality [7,8]. Recently, NIMV application outside the ICU has been reported. It can be attractive for many reasons, such as cost-effectiveness and the possibility to treat patients at an early stage [9]. Predictors of failure NIMV are not well described in the literature, could include baseline abnormal blood gas, disease severity, malnutrition and higher baseline CRP and white blood cell count [10]. CRP is a pentameric protein that exists in the plasma. An elevation in CRP plasma levels is usually the result of an inflammatory or infectious process. This protein is of hepatic origin and rises in response to IL-6 secreted from macrophages and T-cells therefore, described as an acute phase protein. The main clinical value of CRP is evaluating both the severity of the disease and the overall response to treatment through monitoring its levels [11]. PH stands for Power of Hydrogen [12]. This power of Hydrogen or PH is mainly a scale used to measure the degree of acidosis or alkalosis in fluids and most importantly the blood. Normal blood PH falls between (7.36-

7.44). Hereby, Acidemia occurs when  $\text{PH} < 7.36$ , whereas Alkalemia occurs when  $\text{PH} > 7.44$  [13].

The aim of the study was to elucidate the prognostic value of PH and CRP for NIMV failure in patients with chronic respiratory failure type 2.

## 2. MATERIALS AND METHODS

### 2.1 Study Design and Data Collection

This study includes all the adult patients who were admitted to the department of Pulmonology in Tishreen University Hospital –Lattakia- Syria from January 2019 to January 2020 with a diagnosis of acute on chronic respiratory failure type 2. The following data were recorded: demographic data (age, sex), laboratory parameters including CRP and arterial blood gas (ABG) analysis on admission and after 2 hours of NIMV. Exclusion criteria were patients with: metabolic acidosis, unconscious patients.

### 2.2 Definitions

**Acute on chronic exacerbation of type 2 respiratory failure:** An acute deterioration in an individual with significant pre-existing hypercapnic respiratory failure. Arterial blood gas (ABG) with:  $\text{PH} < 7.35$ , partial pressure of oxygen concentration ( $\text{FiO}_2$ ) ratio less than 200 (or  $\text{PaO}_2$  less than 60 mmHg)[14].

### 2.3 Statistical Analysis

Statistical analysis was performed by using IBM SPSS version 20. Basic Descriptive statistics included means, standard deviations (SD), Frequency and percentages. Independent t student test was used to compare 2 independent groups, and one way Anova to compare

between the three groups. Differences of distribution examined by using chi-square test or Fisher exact test if it need. Binary logistic regression was performed to identify the risk factors associated with NIMV outcome. Statistical significance was accepted at a p value of <0.05.

### 3. RESULTS

A total of 67 patients with chronic respiratory failure Type 2 were identified. The median age was 63 ( range,20-94 years), and 62.7% were male. As shown below, 62.7% were in PH group ( 7.31-7.36). There were significant differences between three groups regard to PH and  $\Delta$  PH

( $p < 0.05$ ). Rates of mortality and admission to ICU were more frequently in PH group (7.20-7.25) which represented 25%, 50% respectively, whereas survival rates were higher in PH group (7.31-7.36) and (7.26-7.30) which represented 97.6% and 88.2% respectively.

The rate of NIMV failure was 22.4%. As shown below, successful treatment with NIMV was associated with significant improvement in PH value compared to NIMV failure group. Serum CRP levels were higher in the NIMV failure group without significant difference ( 53.5± 47.1 vs. 41.3 ±48.2 , $p < 0.4$ ).

**Table 1. Demographic characteristics of the study population by comparison of the three groups of PH. We can notice that demographics were statistically insignificant .PH(1) and Delta PH showed statistically significant variations regarding outcome**

Variable	PH groups (N%)			p-value
	7.20-7.25	7.26-7.30	7.31-7.36	
	<b>8(11.9%)</b>	<b>17(25.4%)</b>	<b>42(62.7%)</b>	
Age	66[39-88]	62[20-76]	63[37-94]	0.6
Sex				0.9
Male	5(62.5%)	11(64.7%)	26(61.9%)	
Female	3(37.5%)	6(35.3%)	16(38.1%)	
C-reactive protein(CRP) mg/dL	46.1[3.30-147]	46.2[0.40-227]	42.9[3.78-140]	0.9
PH(1)	7.23±0.02	7.27±0.01	7.35±0.05	0.0001
$\Delta$ PH	0.11±0.07	0.06±0.05	0.02±0.06	0.001
<b>Outcome</b>				0.06
Survival	2(25%)	15(88.2%)	41(97.6%)	
Mortality	2(25%)	1(5.9%)	0(0%)	
Admission to ICU	4(50%)	1(5.9%)	1(2.4%)	

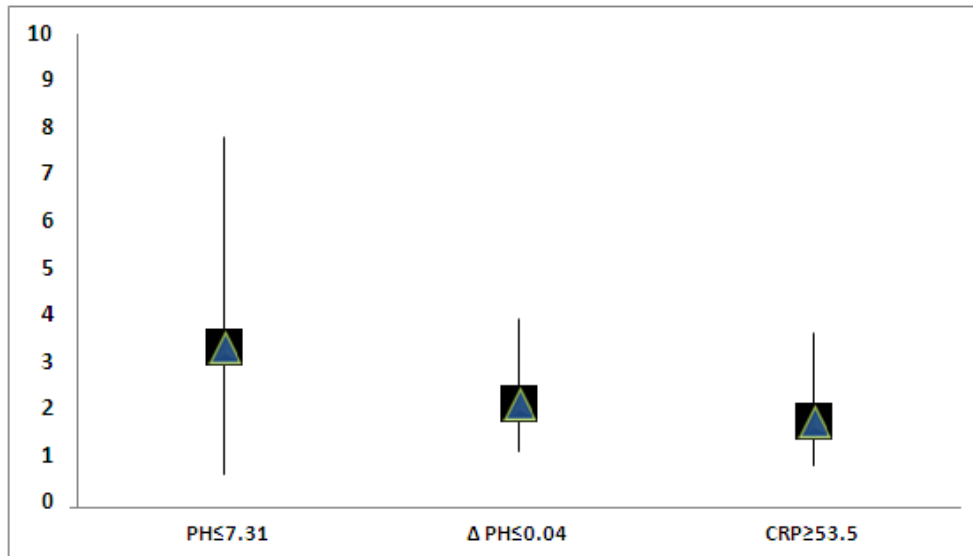
**Table 2. Comparison of demographic characteristics and laboratory findings according to the outcome of patients. failure of treatment with NIMV was associated with PH(2)= 7.39±0.06 and PH≤ 7.3**

Variable	NIMV success (n=52)	NIMV failure (n=15)	p-value
Age	62[20-90]	68[55-94]	0.05
Sex			0.8
Male	33(63.5%)	9(60%)	
Female	19(36.5%)	6(40%)	
<b>Laboratory findings</b>			
CRP	41.3±48.2	53.5±47.1	0.4
PH(1)	7.31±0.06	7.35±0.05	0.07
PH(2)	7.39±0.06	7.31±0.05	0.0001
$\Delta$ PH	0.07±0.04	0.04±0.03	0.02
PH≤ 7.31, n(%)	2(3.8%)	5(33.3%)	0.001
$\Delta$ PH≥0.04 , n(%)	12(23.1%)	7(46.7%)	0.03
CRP ≤53.5, n(%)	17(32.7%)	8(53.3%)	0.04

**Table 3. Risk factors for NIMV failure in the study population by multivariate logistic regression**

Factor	OR(95% CI)	p-value
PH $\geq$ 7.31	3.3[0.6-7.8]	0.01
$\Delta$ PH $\geq$ 0.04	2.1[1.1-3.9]	0.02
CRP $\leq$ 53.5	1.7[0.8-3.6]	0.3

These risk factors are represented in the Fig (1).



**Fig. 1. Risk factors for NIMV failure in the study population. This figure represents the findings demonstrated in Table 3**

To determine the factors associated with NIMV failure, binary logistic regression analysis was carried out, and PH $\leq$  7.31 and  $\Delta$ PH  $\leq$  0.04 were found to be risk factors for NIMV failure, Table (3).

#### 4. DISCUSSION

This analytic study demonstrated characteristics and predictive ability of PH and CRP for NIMV failure in patients with chronic respiratory failure Type 2.

Patients with a PH value < 7.25 had significantly greater rates of mortality and admission to ICU compared to patients with a PH value > 7.25. Successful treatment with NIMV was associated with significant improvement in PH (p:0.0001) after two hours of NIMV, and patients who failed NIMV were more likely to be with PH $\leq$  7.31,  $\Delta$ PH  $\leq$  0.04, and CRP  $\geq$  53.5. There were no significant differences between two

groups (success and failure) in regard to sex and age. The most important risk factors for NIMV failure in the present study were: PH $\leq$  7.31 and  $\Delta$ PH  $\leq$  0.04.

Risk factors and predictors of NIMV failure are numerous. The PH level which is an indicator of the severity of hypercapnia has been reported to be a critical factor in determining the success of NIMV. Although some reports failed to show any relationship between baseline ABGs and success of NIMV [15,16], a large body of evidence clearly indicated that a lower baseline PH is a risk factor for NIMV failure, and PH < 7.25 was associated with NIMV failure [17].

Studies related to the role of CRP levels, which is used as an inflammatory marker, are inconsistent and found to lack sensitivity and specificity to predict NIMV failure [18].

In comparison to other studies, Salturk et al. [19] found that NIMV is effective in respiratory failure,

and  $\text{PH} < 7.31$ ,  $\Delta\text{PH} < 0.30$  between baseline and control, peak CRP, and  $\text{PaO}_2/\text{FiO}_2$  ratio  $< 200$  on baseline were found to be the risk factors for NIMV failure in COPD patients with ARF [19].

Confalonieri et al. [20] pointed out that a  $\text{PH} < 7.25$  after 1 h of NIMV use, was associated with an increased risk of failure. Also, that risk of failure was even greater when  $\text{PH}$  levels were  $< 7.25$  at admission [20].

Wang et al. [21] demonstrated that high serum CRP levels predict NIMV failure for patients with acute exacerbation of COPD ( $39.48 \pm 16.77$  vs  $7.85 \pm 6.23$ ,  $p: 0.001$ ) [21].

## 5. CONCLUSION

This study was able to establish a strong connection between lower  $\text{PH}$  levels and failure in treatment with NIMV. Two cut-off points were determined to predict failure in treatment with NIMV;  $\text{PH} \leq 7.31$ ,  $\Delta\text{PH} \leq 0.04$ .

Also, lower CRP levels were associated with higher rates of successful treatment but those findings were statistically insignificant. Clinicians should be aware of the predicted parameters of NIMV failure because of the strong link between failure and poor outcome.

This study will best serve as a pilot study for future research with larger sample size and more parameters to study

## CONSENT AND ETHICAL APPROVAL

As per international standard or university standard guideline patients consent and ethical approval has been collected and preserved by the authors.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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