

Factors Predicting the Outcome of Non invasive Ventilation in Acute Respiratory Failure Secondary to Chronic Obstructive Pulmonary Disease Exacerbation

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ABSTRACT

Introduction: Non invasive Mechanical Ventilation (NIV) is a better alternative for treating respiratory failures of any cause compared to invasive ventilation. Various factors influence the outcomes of patients treated with NIV in acute respiratory failure secondary to Chronic Obstructive Pulmonary Disease (COPD).

Aim: To determine the possible early predictors and associated factors influencing the outcome of NIV in acute respiratory failure due to COPD patients.

Materials and Methods: This was hospital-based observational study undertaken at SRM Medical Hospital and Research Centre in the Respiratory Medicine Department, after obtaining ethical clearance and informed patient consent. All patients with COPD exacerbation were admitted to the respiratory medicine ward. An Arterial Blood Gas (ABG) analysis was carried out, and those patients with type 2 respiratory failure were included in the study. This study included 42 patients with acute respiratory failure secondary to COPD requiring NIV. Data of patient's ABG parameter, heart rate, blood pressure, and respiratory rate baseline values at an interval of one hour, six hours, and

every 24 hours were recorded. The outcome was divided into two categories depending upon whether patients improved or required invasive ventilation. Data were entered in Microsoft Excel datasheet and was analysed using Statistical Package for Social Sciences (SPSS) 22.0 version software.

Results: Of 42 patients, 30 (71.42%) were treated successfully with NIV, while 12 (28.57%) required invasive ventilation and were declared NIV failure (requiring invasive ventilation). Among the patients, it was observed that patients with mean age >60 years, BMI >26.5, baseline pH <7.2, PaCO₂ >78, heart rate >120, respiratory rate >40, co-morbidities and infective exacerbation were requiring invasive ventilation. It was also observed that among the failure category patients treated with conventional Spontaneous and Timed (S/T) mode showed more failure rates than Average Volume Assured Pressure Support (AVAPS) S/T mode.

Conclusion: Patients with acute respiratory failure secondary to COPD responds well to NIV. The baseline pH, PaCO₂, HR and Respiratory Rate (RR) before initiation of NIV predicts outcome. Also, age, BMI, associated comorbidities and mode of NIV predicts the outcome.

Keywords: Arterial blood gas, Average volume assured pressure support, Haemodynamic instability

INTRODUCTION

"Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterised by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormality usually caused by significant exposure to noxious particles or gases and influenced by host factors including abnormal lung development" [1] as per The Global Initiative of Chronic Obstructive Lung Disease (GOLD) 2020. COPD is a progressive, chronic disease, and eventually, many patients develop respiratory failure. Patients with COPD exacerbations are treated with oxygenation, bronchodilators, antibiotics, and corticosteroids. Patients who fail to respond to the traditional treatment are managed with mechanical ventilation which can be invasive or Non invasive [2,3].

NIV is considered superior and safer than invasive ventilation because of its significant advantage in the ventilatory management of acute type 2 respiratory failure secondary to COPD [1]. The NIV use is associated with a significant reduction in the need for endotracheal intubation and its complication. Although the success rate is higher with NIV treatment, failure also has been observed to a small extent [4-6]. Therefore, patients on NIV must be observed closely for signs of treatment failure and should be intubated promptly before a catastrophe occurs. So, identifying the early predictors in managing those patients for a better outcome is mandatory.

The study aimed to determine the possible early predictors and associated factors influencing the outcome of NIV in acute respiratory failure due to COPD.

MATERIALS AND METHODS

This was a hospital-based observational and analytical study that was undertaken in the Respiratory Medicine Department at SRM Medical Hospital and Research Centre, Jaipur, Rajasthan, India. The study duration was one and a half years (February 2019-August 2020) from the date of obtaining ethical clearance (1636A/IEC/2019). A total of 42 patients with respiratory acidosis secondary to COPD (pH <7.35 and PaCO₂ >45 mmHg) attending respiratory medicine Outpatient Department (OPD).

Sample size: Mean PaCO₂ after treatment in two groups was 53.2±9, 45.4±7.9 based on a previous study [7] with 95% confidence and 80% power. The sample size was 42; 21 members in each group.

Inclusion and Exclusion criteria: COPD patients with respiratory acidosis (pH <7.35 mm Hg) and type 2 respiratory failure (PaCO₂ >45 mmHg) were included. Low Glasgow Coma Scale (GCS), Haemodynamic instability, facial deformity, obstruction of the upper airway from recent trauma/surgery, pneumothorax, cardiogenic pulmonary oedema, cardiopulmonary arrest, patients with Arterial Blood Gas (ABG) showing pH <7.10, haemoptysis or haematemesis, other causes of type 2 respiratory failure except for COPD were excluded.

Demographic data, history including co-morbidities, relevant investigations, modes of NIV setting AVAPS or S/T, sputum organism growth and clinical outcomes of all the patients were recorded in a structured pro forma. Data of patient's ABG parameter, heart rate, blood pressure, and respiratory rate baseline values were noted and at an interval of one hour, six hours, and every 24 hours. The baseline parameters between two modes of NIV ventilation (AVAPS and S/T mode) among the NIV failure category were also compared. The duration and severity of COPD illness were not considered. There were two study endpoints:

- **Success [7,8]:** Decrease of at least 20% in respiratory rate compared with spontaneous breathing, refinement in ABGs with pH >7.35, decrease in PaCO₂ of the atleast 15% compared with spontaneous breathing while maintaining Saturation of Peripheral Oxygen (SPO₂) (with or without oxygen) 88-92% or when the subjective criteria showed improvement in the patient dyspnea and a significant decrease in PaCO₂ of >15% (compared with the initial PaCO₂ value under spontaneous breathing) after one hour of therapy and successful clinical and ABG improvement at the time of discharge.
- **Failure [8]:** During NIV if patient develops respiratory arrest, bradycardia (50/minute) with loss of consciousness, hypotension (Systolic BP <70 mmhg), and refractory hypoxemia inability to maintain a SPO₂ more than 90% (despite high Fraction of Inspired Oxygen (FIO₂) more than 60%), increased respiratory rate compared with its initial value at admission (assessed at regular interval) these are the criteria for terminating NIV (NIV failure) and switching to invasive ventilation. If the patient develops these signs/symptoms during NIV, then those patients will be considered as failure as early as within one hour of initiation of NIV.

STATISTICAL ANALYSIS

Parameters were tabulated and analysed by SPSS software version 22.0. The quantitative variables were analysed using Student's t-test and qualitative variables were analysed using the Chi-square test. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Of 42 patients, there were 27 male and 15 female with a mean age of 56.83 years. Among them, 30 (71.42%) patients improved with NIV and 12 (28.58%) patients were considered NIV failure as per the criteria specified in the methodology [Table/Fig-1].

Among 42 patients, the mean age of patients in the success category was 55.13±5.823, while in the failure category, it was 61.08±5.452. It was observed that patients with age >60 years had a poor outcome in NIV management of acute respiratory failure secondary to COPD. On comparing the mean BMI between success (19.62±3.22) and failure category (26.65±5.649), it was noted that patients who were overweight (BMI >25) were predominantly present in failure category than in success category.

In the success category, the mean baseline pH was 7.26±0.034 while in failure category it was 7.2±0.049 which was statistically significant. It is evident that patients who present with initial pH >7.25 have a better outcome without any need for invasive ventilation. Out of 42 patients, 35 patients (83.33%) showed improvement in pH after one hour of initiating NIV treatment. At the same time, 7 (16.66%) had deterioration within one hour itself. Within the 35 patients who showed an initial improvement, five patients had decline in pH when ABG was repeated after six hours interval and clinically these patients deteriorated. So, these patients were also considered failure and were intubated.

Overall, 30 patients had successful outcome with respect to PaCO₂. The mean baseline PaCO₂ in success category was 69.98±7.102 while in failure category it was 78±5.461 [Table/Fig-1]. Out of 42 patients, 34 patients (80.95%) showed improvement in PaCO₂ after one hour of initiating NIV treatment. In contrast, 8 (19.04%)

Parameters	NIV Success (n=30)	NIV Failure (n=12)	p-value	CI 95%
Age	55.13±5.823	61.08±5.452	0.0041	-9.90101 to -1.99899
Sex				
Male	19	8	0.8386	-
Female	11	4		
BMI (kg/m ²)	19.62±3.22	26.65±5.649	0.0001	-9.81645 to -4.24355
pH (Baseline)	7.26±0.034	7.2±0.049	0.0001	0.03328 to 0.08672
PaCO ₂ (Baseline)	69.98±7.102	78±5.461	0.0011	-12.63896 to -3.40104
Heart rate (Baseline) (beats/min)	115.33±5.033	120.92±8.393	0.0111	-9.83070 to -1.34930
Respiratory rate (Baseline) (breath/min)	34.33±3.089	40.33±3.367	0.0001	-8.18688 to -3.81312
Sputum organism growth				
Yes	4	6	0.0117	-
No	26	6		
Co-morbidities				
Yes	9	9	0.0077	-
No	21	3		

[Table/Fig-1]: Comparison of baseline parameters between NIV success and failure category.

*Co-morbidities- diabetes; hypertension; chronic kidney disease and ischemic heart disease

had deterioration within one hour itself. Within the 34 patients who showed an initial improvement, four patients had a decline in PaCO₂ when ABG was repeated after six hours interval. So, these patients were also declared as NIV failure and were intubated. Therefore, a patient who presents with initial PaCO₂ <70 and patients who show improvement within one hour of initiating NIV appears to a good predictor was successful NIV outcome.

At the time of admission, all patients presented with tachycardia and tachypnoea. The mean baseline HR was 116.92 while the RR was 36.04. The success category patients had significantly lesser HR (115.33±5.033) and RR (34.33±3.089) than the failure category (HR=120.92±8.393, RR=40.33±3.367), which was statistically significant with p-value <0.01 [Table/Fig-1]. So patients who present with tachycardia and tachypnoea on the lower limit (HR <120 and RR <35) have a better outcome.

Co-existing co-morbidities and infective exacerbation (in sputum) also play a significant role in predicting the outcome of NIV success. Out of 42 patients, 18 (42.85%) had co-morbidities, among which 9 (21.42%) were in failure category. With respect to sputum examination, 10 patients (23.8%) had growth, among them 6 (14.2%) were in failure category [Table/Fig-1].

Overall, 23 (54.76%) patients received AVAPS-S/T mode, and 19 (45.23%) patients received S/T mode of NIV treatment. Among the failure category with 12 patients, it was observed that only 4 (33.33%) were on AVAPS mode and 8 (66.67%) were in S/T mode [Table/Fig-2].

Also, in failure group it was observed that the mean baseline of pH, PaCO₂, HR and RR was comparable between AVAPS and S/T group. This implies that the AVAPS and S/T group has the same baseline value, but still, the incidence of failure in S/T group was higher.

In this study, 23 patients received AVAPS mode of ventilation in which 4 (9.52%) patients belonged to NIV failure category while remaining 19 patients received S/T mode in which 8 (19.04%) patients were NIV failure [Table/Fig-2]. Although the baseline values in the AVAPS group and S/T group were comparable and statistically insignificant, the incidence of NIV failure was significantly higher in the S/T mode when compared to AVAPS mode. Hence, it can be concluded that the selection of mode ventilation also plays an essential role in the outcome of NIV success rate among COPD patients.

Parameters	AVAPS (n=4)	S/T (n=8)	p-value	CI 95%
Age	60.75±4.113	61.25±6.274	0.8892	-8.29401 to 7.29401
Sex				
Male	3	5	0.665	-
Female	1	3		
BMI (kg/m ²)	26±6.683	26.98±5.535	0.7918	-9.03420 to 7.07420
pH (Baseline)	7.205±0.067	7.19±0.042	0.6401	-0.05433 to 0.08433
PaCO ₂ (Baseline)	76.75±4.992	78.63±5.902	0.5984	-9.58154 to 5.82154
Heart rate (Baseline) (beats/min)	120.25±11.615	121.25±7.246	0.8563	-12.99054 to 10.99054
Respiratory rate (Baseline) (breath/min)	40.25±3.096	40.38±3.701	0.9532	-4.94706 to 4.68706
Sputum organism growth				
Yes	2	4	0.4652	-
No	2	4		
Co-morbidities				
Yes	3	6	1	-
No	1	2		

[Table/Fig-2]: Comparison of baseline parameters between AVAPS and S/T mode among NIV failure category.

*Co-morbidities- diabetes, hypertension, chronic kidney disease and ischemic heart disease

DISCUSSION

In this study, the possible early predictors and associated factors influencing the outcome of NIV in acute respiratory failure due to COPD were assessed. Previous studies have provided some predictors for successful outcome of NIV which includes lower age group, lower APACHE II score, patient-ventilator synchrony, better GCS, hypercarbia ($45 < \text{PaCO}_2 < 92$ mmHg), acidosis ($7.35 < \text{pH} < 7.10$), oxygenation and heart and respiratory rates within the first 1-2 hour after the initiation of NIV [7,8].

From the present study, it can be concluded that patients with age >60 years had a poor outcome in NIV management of acute respiratory failure secondary to COPD. This was similar to a study conducted by Van Gemert A et al., the authors stated that older age and low GCS are an essential factor for conversion of NIV to IMV in AHRF secondary COPD [9,10]. In another study by Kida Y et al., NIV failure rate was higher in elderly patients with acute hypercapnic respiratory failure [11].

In the success category, the mean baseline pH was 7.26 ± 0.034 , so it can be concluded that patients who present with initial pH >7.25 have a better outcome without any need for invasive ventilation. Fewer studies have shown that the improvement in pH within a short period after initiation of NIV predicts the outcome. A study conducted by Claude KH et al., proved that improvement in pH and reduction in PaCO₂ observed within 2 hours of initiation of NIV in COPD patients [12]. Lightowler JV et al., did a similar study showed that patients with baseline pH <7.22 went for NIV failure in COPD patients [13]. Another study was done by Liu J et al., also concluded that severe acidosis is a significant predictor for NIV failure in COPD patients [10]. Cavalleri M et al., in his study, has shown that patients with initial pH <7.23 are more prone to NIV failure [14].

The mean baseline PaCO₂ in success category was 69.98 ± 7.102 while in failure category it was 78 ± 5.461 . Therefore, a patient who presents with initial PaCO₂ <70 appears to a good predictor of successful NIV outcome. Liu J et al., did a similar study showed that patients with baseline PaCO₂ >88 went for NIV failure in COPD patients [10]. Cavalleri M et al., showed that patients with initial PaCO₂ >85 mmHg were liable for NIV failure [14].

The mean baseline HR was 116.92 while the RR was 36.04. The success category patients had significantly lesser HR and RR than the

failure category, which was statistically significant. So, patients who present with tachycardia and tachypnoea (HR <120 and RR <35) have a better outcome. Liu J et al., also showed that patients with initial mean HR >121 and RR >30 have a poor outcome and went for NIV failure [10].

In this study, the percentage of co-morbidities was higher in NIV failure group. Moretti M et al., showed that incidence of comorbidities were more in NIV failure category than in success category [15]. But Talwar D and Dogra V concluded that the incidence of comorbidities was equal both in success and failure group [16]. Also, while weaning the COPD patients from mechanical ventilation both groups had equal outcomes.

It can be concluded that the selection of mode ventilation also plays an important role in the management of COPD patients in terms of reducing the incidence of NIV failure. Similar studies were done by Claudett KH et al., and Shaaban L et al., they concluded that Bilevel Positive Airway Pressure (BiPAP)-AVAPS mode is an effective and safer mode compared to BiPAP-S/T mode in non invasive ventilatory management of acute respiratory failure in COPD patients [12,17].

Limitation(s)

The fact that it was an observational study in which patients were not randomised. A randomised control trial can be conducted in future to assess the other outcomes. Also, in future the technology and modes of ventilation used in NIV may change and these predictors cannot be used to assess the outcome in COPD patients.

CONCLUSION(S)

In this study, it was observed that patients with acute respiratory failure secondary to COPD who were treated with NIV had a better outcome with reduced incidence of NIV failure. Among the failure group, elder age (>60 years), obese patients, severe acidosis (pH <7.2), hypercarbia (PaCO₂ >78), HR >120 /min and RR >35 /min at the time of presentation predicts the NIV failure. And also we observed that NIV failure was higher in patients who received S/T mode than AVAPS-S/T mode of NIV.

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PLAGIARISM CHECKING METHODS: [\(Lain H et al.\)](#)

- Plagiarism X-checker: Nov 26, 2020
- Manual Googling: Mar 17, 2021
- iThenticate Software: Apr 24, 2021 (12%)

ETYMOLOGY: Author Origin**AUTHOR DECLARATION:**

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Nov 23, 2020**Date of Peer Review: **Jan 28, 2021**Date of Acceptance: **Apr 08, 2021**Date of Publishing: **Jun 01, 2021**