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## Factors leading to poor outcome of noninvasive positive pressure ventilation in acute exacerbation of chronic obstructive pulmonary disease

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### ABSTRACT

**Objective:** To determine frequency of factors leading to poor outcome of non-invasive positive pressure ventilation in acute exacerbation of chronic obstructive pulmonary disease.

**Methods:** This cross sectional study was conducted at our center between May 2012 and November 2012. A total of 195 diagnosed patients of acute exacerbation of chronic obstructive pulmonary disease meeting the inclusion criteria were selected from the ER department. At the time of admission age was inquired BP, respiratory rate and oxygen saturation will be noted and pedal edema was assessed and investigations were sent for pH assessment. Noninvasive positive pressure ventilation (NIPPV) using BiPAP was applied in spontaneous mode by the help of oronasal mask. Presence of respiratory rate (less than 12/min), systolic blood pressure <90 mmHg, GCS <13 and PaO<sub>2</sub> ≤65, pH <7.2 and heart rate >140 bpm was taken as poor outcome.

**Results:** The average age of the cases was 61.9±9.3 years with male to female ratio being 1.5:1. NIPPV was successful in 151 (77.4%) cases and 44 (22.6%) cases were underwent endotracheal intubation. About 38 (44.7%) of patients with oxygen saturation (82%–86%) had poor prognosis. A total of 40 (55.6%) of patients with pH range 7.20–7.26, required endotracheal intubation, 43 (66.2%) with pedal edema underwent endotracheal intubation. While 29 (24.16%) patients of age >60 years needed endotracheal intubation.

**Conclusions:** In this study, NIPPV was successful in 77.4% cases and 22.6% cases were underwent endotracheal intubation. Pedal edema was the most common factor leading to poor outcomes while age >60 years was the least common factor, 66.2% and 24.2% respectively.

## 1. Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality worldwide. It is among top 10 global contributors to the global burden of disease as measured by disability-adjusted life years[1]. The global burden of disease study has projected that COPD, which ranked sixth as the cause of death in 1990, will become the third leading cause of death worldwide by 2020, thus, among

all major chronic diseases, COPD is the only disease that shows rising mortality[2–4].

Acute exacerbation of COPD (AECOPD) is largely responsible for morbidity and mortality associated with the disease[5]. An exacerbation of COPD is an event in the natural course of the disease characterized by a change in the patient's baseline dyspnea, cough and/or sputum beyond day-to-day variability sufficient to warrant a change in management[6]. Noninvasive positive pressure ventilation (NIPPV) is claimed to be safe and effective modality in treating patients with AECOPD[5]. It helps in preventing endotracheal intubation in acute respiratory failure secondary to COPD as compare to other causes[7]. However, NIPPV is not successful in all cases of AECOPD,

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with a failure rate of 66% in an Indian study and 18.18%, 50% and 23% in different western studies[8–11]. One of the retrospective studies done in Aga Khan University hospital showed that coexisting sepsis and hypercapnic acute respiratory failure have high hospital mortality on NIPPV with failure rate of 23.5%[12].

Out of 250 patients enrolled in the study, 29 (24.16%) patients aged 60–75 years had to undergo endotracheal intubation. Patients with oxygen saturation in the range 82%–86% at the time of admission, 75 (50%) of these had poor prognosis. Patients with pH range 7.20–7.26 carry poor prognosis and 100 (66.66%) required endotracheal intubation. Out of 100 patients with pedal edema, 70 (70%) had to undergo endotracheal intubation[8].

The aim of the study is to determine the factors leading to poor outcome in patients with AECOPD who are treated with NIPPV. So that protocol could be developed for such patients and endotracheal intubation could be applied without giving trial of NIPPV, which fasten recovery and decrease the morbidity.

## 2. Materials and methods

### 2.1. Place of study

This cross sectional study was conducted from May 2012 to November 2012 in Department of Chest Medicine in Jinnah Postgraduate Medical Centre. Patients with the diagnosis of AECOPD as defined in the operational definition, meeting the inclusion criteria were selected from the ER department, Jinnah Postgraduate Medical Centre, Karachi. Permission from ethical committee of Jinnah Postgraduate Medical Centre and written consent from the patients was taken. At the time of admission age was inquired BP, respiratory rate and oxygen saturation will be noted and pedal edema was assessed and investigations were sent for pH assessment. NIPPV using BiPAP (vision Respironics INC. USA. BiPAP S/T 30) was applied in spontaneous mode by the help of oronasal mask with head straps to minimize the leak. A single, more than 4 years' experienced operator, was applied BiPAP to control operator bias and researcher himself monitored the response. Calibration of the machine was done to control instrument bias. Therapy was initiated with an inspiratory positive airway pressure (10 cm H<sub>2</sub>O) and expiratory positive airway pressure (5 cm H<sub>2</sub>O) and it was optimized according to patient's comfort and blood pressure.

Patient's response was monitored clinically at 30 min, 1 h and at the end of 2 h. Presence of respiratory rate (less than 12/min), systolic blood pressure < 90 mmHg, GCS < 13 and PaO<sub>2</sub> ≤ 65, pH < 7.2 and heart rate > 140 bpm was taken as poor outcome and the patient was underwent endotracheal intubation. This information along with the demographics was entered into the proforma attached as annexure. Required sample size was 195 patients calculated by using

WHO sample size determination software with 24.16% COPD treated with non-invasive mechanical ventilation patients and 95% confidence interval and 6% level of precision[8]. Sample was collected by non-probability purposive sampling. Age between 40–80 years and duration of COPD more than 6 months were defined as inclusion criteria while cardiac and respiratory arrest, upper gastrointestinal bleed, comatose patients, hypotension even with ionotropes support, arrhythmias, poor gag reflex, hyponatraemia serum sodium < 120 mmol/lit and patients with pneumothorax were excluded from study.

### 2.2. Data analysis procedure

Data was entered and analyzed through SPSS version 15. Continuous variables like age, systolic blood pressure, heart rate, respiratory rate, GCS, pH and SaO<sub>2</sub> were expressed as mean ± SD. Whereas categorical variables like poor outcome, older age group (age more than 60 years), gender, pedal edema and academia were presented in frequencies and percentages. Effect modifiers were controlled through stratification of age and gender to see the effect of these on outcomes by applying *Chi* square test and  $P \leq 0.05$  was taken as significant.

## 3. Results

A total of 195 diagnosed case of AECOPD were included in this study. Out of 195 patients, 116 (59.5%) were male and 79 (40.5%) were female with 1.5:1 male to female ratio.

The average age of the patients was 61.9 ± 9.3 years. Minimum age was 40 years and maximum age was 78 years. Most of the patients had age > 60 years [111 (56.9%)].

After 2 h of NIPPV, mean systolic blood pressure was (121.9 ± 22.5) mmHg and mean respiratory rate was 20.2 ± 4.6, heart rate was 120 ± 15.3, pH was 7.25 ± 0.09, GCS was 10.4 ± 2.2 and mean SaO<sub>2</sub> was 87.5 ± 7.9 (Table 1).

**Table 1**

Characteristics of patients with an AECOPD after 2 h of treatment (n=195).

Parameters	Mean ± SD
SBP	121.9 ± 22.5
Respiratory rate (Breaths/min)	20.2 ± 4.6
GCS	10.4 ± 2.2
pH	7.25 ± 0.09
SaO <sub>2</sub>	87.5 ± 7.9
Heart rate (Beats/min)	120.0 ± 15.3

SBP=Systolic blood pressure; GCS=Glasgow coma scale.

NIPPV was successful in 151 (77.4%) cases and 44 (22.6%) cases were underwent endotracheal intubation (poor outcomes).

Stratification was done with regards to gender and age to see the effect of these on outcomes. Poor outcomes of NIPPV were significantly high in male [33 (28.4%)], and low in female [11 (13.9%)] ( $P=0.028$ ). While 29 (24.16%) patients of age > 60 years had to undergo endotracheal intubation ( $P=0.026$ ).

Patients with oxygen saturation were in the range 82%–86%. About 38 (44.7%) of these had poor prognosis. Patients with pH range 7.20–7.26, 40 (55.6%) of these required endotracheal intubation while 43 (66.2%) with pedal edema had to undergo endotracheal intubation (Table 2).

**Table 2**

Other factors leading to poor outcomes ( $n=195$ ).

Factors	Number of cases	Poor outcomes	Percent
SaO <sub>2</sub> (82%–86%)	85	38	44.7%
Acedemia (pH 7.2 – 7.26)	72	40	55.6%
Pedal edema	65	43	66.2%

#### 4. Discussion

The use of noninvasive ventilation (NIV) in the management of COPD is now supported by a number of randomized controlled trials<sup>[13–17]</sup>. It has been shown to reduce intubation rates, mortality, and length of hospital stay<sup>[13–17]</sup>. It has the advantage that it can be applied intermittently, avoids the need for sedation, and allows the patient to eat, drink, and speak. The incidence of nosocomial pneumonia during NIV is lower than in intubated patients. However, NIV is not successful in all cases of acute on chronic respiratory failures owing to COPD, with reported failure rates of 7%–50%<sup>[16]</sup>. There has also been concern that NIV may delay intubation, leading to a worse outcome<sup>[18,19]</sup>.

In this study, NIPPV was successful in 77.4% cases and 22.6% cases were underwent endotracheal intubation (poor outcomes) which is similar to reintubation rates described elsewhere from India and the European–American countries<sup>[20–23]</sup>. There is little doubt on the efficacy of NIV in AECOPD and cardiogenic pulmonary edema<sup>[8,24]</sup>. A study from India reported the success rate of NIPPV was 87.5% for AECOPD<sup>[7]</sup>. One of the retrospective studies done in Aga Khan University hospital showed that coexisting sepsis and hypercapnic acute respiratory failure had high hospital mortality on NIPPV with failure rate of 23.5%<sup>[12]</sup>. However, NIPPV is not successful in all cases of acute exacerbation of COPD, with a failure rate of 66% in an Indian study and 18.18%, 50% and 23% in different western studies<sup>[8–11]</sup>.

In this study, pedal edema has been shown to predict death or patient requiring endotracheal intubation owing to acute exacerbation of COPD; 66.2% of the cases with pedal edema had to undergo endotracheal intubation. The evidence for the use of NIV remains strongest in patients with hypercapnic acute respiratory failure due to exacerbations of COPD and cardiogenic pulmonary edema<sup>[8,24]</sup>. Shameem *et al.*

*al.* reported that out of 100 patients with pedal edema 70% required endotracheal intubation<sup>[8]</sup>.

Acidosis was also strong indicator of endotracheal intubation owing to acute exacerbation of COPD<sup>[10,14]</sup>. In this study, patients with pH range 7.20–7.26 carry poor prognosis and 55.6% of these required endotracheal intubation. Ambrosino *et al.* found that patients in whom NIV treatment failed were significantly more academic at baseline than those successfully treated<sup>[18]</sup>. Brochard *et al.* found that success was less likely with a lower starting pH<sup>[17]</sup>. Shameem *et al.* also reported the similar results; they reported that patients with pH range 7.20–7.26 carried poor outcome and 66.7% required endotracheal intubation<sup>[8]</sup>.

Oxygen saturation (SaO<sub>2</sub>) at the time of admission can predict outcome of the patient. As in this study, patients oxygen saturation were in the range of 82%–86%; 44.7% of these had poor prognosis. Shameem *et al.* also reported that patients with oxygen saturation were in the range of 82%–86% at the time of admission; 75 (50%) of these had poor prognosis<sup>[8]</sup>.

Stratification was done with regards to gender and age to see the effect of these on outcomes. Poor outcomes of NIPPV were significantly high in male 33 (28.4%) ( $P=0.028$ ). While 29 (24.16%) patients of age > 60 years had to undergo endotracheal intubation ( $P=0.026$ ). These facts are consistent with the observations of other authors<sup>[10,25,26]</sup>. Shameem *et al.* studied 250 patients in the study; 24.16% patients of age 60–75 years had to undergo endotracheal intubation.

The results of this study suggest, management of patients with acute exacerbation of COPD, in addition to medical therapy, should include NIV if they present with moderate respiratory acidosis (pH < 7.35). Patients who fail to respond or have contraindication to NIV should be evaluated for endotracheal intubation and mechanical ventilation. NIV is a welcome advancement in the management of respiratory failure. In selected patients with acute exacerbations of chronic obstructive pulmonary disease, NIV can reduce the need for endotracheal intubation, the length of the hospital stay, and the in-hospital mortality rate.

In this study, NIPPV was successful in 77.4% cases and 22.6% cases were underwent endotracheal intubation (poor outcomes). Pedal edema was the most common factor leading to poor outcomes while age > 60 years was the least common factor, 66.2% and 24.2% respectively. While patients with pH range 7.20–7.26, 55.6% of these required endotracheal intubation. Other factor was oxygen saturation (82%–86%). In conclusion, this study demonstrates that NIPPV is an effective modality in preventing endotracheal intubation due to COPD.

#### Conflict of interest statement

The authors report no conflict of interest.

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