ORIGINAL ARTICLE

Impact of PF Ratio and Oxygenation on Non-Invasive Ventilation Failure during Acute Exacerbations of COPD

Syed Ali Abbas[1], Yusra Arshad[2], Kulsum Ghous[3], Nimra Akhtar[4], Ayesha Shahnawaz[5], and Hudaibya Ayub[5]

ABSTRACT

Objective. This research aims to investigate the role of P/F ratio and oxygenation in predicting non-invasive ventilation failure in patients going through acute exacerbation of chronic obstructive pulmonary disease.
Methodology: A Quasi Single Arm Study was carried out in the Medical ICU and medicine ward of a tertiary care hospital, including 170 patients presenting with acute exacerbations of chronic obstructive pulmonary disease. Data were collected using a structured pro forma after obtaining informed consent. The duration of the study was 6 months.
Results: The research involved a total number of 170 individuals who were admitted with acute exacerbation of chronic obstructive pulmonary disease. Among them, 38% experienced non-invasive ventilation (NIV) failure during treatment. The observed rate of mortality in this study was 23.5%. Within the NIV success group, 45% were males and 55% were females. Fraction of inspired oxygen and arterial oxygen saturation differed significantly at admission, 1 hour, 48 hours, and beyond, while Partial pressure of oxygen varied at admission and 1 hour but not after 48 hours. The PF ratio showed significant differences at all time points.
Conclusion: This study examined the outcomes of non-invasive ventilation (NIV) and the mortality rates in patients undergoing acute exacerbation of chronic obstructive pulmonary disease. The analysis of oxygenation metrics revealed significant variations between patients who had NIV failure and those who had not, as well as in relation to mortality. These findings contribute to the understanding of treatment outcomes in acute COPD exacerbation and can help in clinical decision making. More researches can be conducted for further evaluation.

Keywords: Acute exacerbation, acute respiratory failure, chronic obstructive pulmonary disease, mortality, non-invasive ventilation, P/F ratio

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common and extremely fatal illness that occurs globally. It arises from abnormal functioning in the airways and alveolar sacs, leading to an irreversible restriction of airflow. It is predicted that COPD will become one of the primary contributors to global mortality by 2030[1]. Individuals diagnosed with COPD encounter 1 to 4 episodes of acute exacerbation of COPD (AECOPD) annually, which also have a significant financial burden, comprising 50-70% of all costs associated with COPD. Furthermore, these episodes elevate the risk of developing subsequent AECOPDs, hospitalization, and mortality.

The occurrence of AECOPDs is associated with noteworthy breathlessness, which typically persists for a duration of 7 to 10 days. In certain instances, complete recovery may not be achieved for weeks or even months[2]. The mortality rate associated with acute exacerbations of COPD (AECOPD) is considerable. Following hospitalization for an exacerbation, only around half of COPD patients survive beyond a five-year period. The mortality rate within one year after an AECOPD ranges from 12% to 33%, while after two years, it increases to 26% to 40%[3]. Noninvasive ventilation (NIV) refers to a ventilation method that does not require the use of an invasive artificial airway. NIV relieves the workload of respiratory muscles, enhances alveolar ventilation, alleviates dyspnea,

Consultant Physician and Associate Professor, Head of Department of Pulmonology and Critical Care[1] / Registrar[2]/ Registrar, Department of Medicine[3] / Registrar, Community Medicine[4], Dr. Ziauddin Hospital[5], Karachi, Pakistan

Correspondence: Dr. Yusra Arshad, Registrar, Dr. Ziauddin Hospital, Karachi, Pakistan

Email: dryusra76@gmail.com

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reduces respiratory rate, and ultimately enhances arterial oxygenation, hypercapnia, and associated respiratory acidosis[4]. Due to these benefits, the utilization of "noninvasive ventilation (NIV)" for patients experiencing "acute exacerbation" of "chronic obstructive pulmonary disease" (COPD) has witnessed a steady rise in recent times. Furthermore, existing guidelines strongly support the use of NIV for individuals facing acute exacerbation[5].

While noninvasive ventilation (NIV) decreases the necessity for intubation in COPD patients, the mortality rate rises substantially in cases of NIV failure. Furthermore, when patients encounter 'NIV' failure, postponed intubation increases the risk of mortality[6]. The indications for intubation include ongoing respiratory distress characterized by a rate over 35 breaths per minute, persistent respiratory acidosis, and the inability to maintain a PaO2/FiO2 ratio above 100 mmHg, emergence of circumstances requiring intubation for airway safeguarding (such as coma or seizure disorders), management of excessive tracheal secretions, hemodynamic instability unresponsive to fluids and vasoactive medications and instances of respiratory or cardiac arrest.

NIV failure was identified as the necessity for intubation or mortality while undergoing noninvasive ventilation[7]. The success of NIV hinges upon several crucial factors, including meticulous patient selection, timely intervention and the use of a well-fitted interface, motivation and assistance offered to patients along with careful supervision by skilled team of healthcare professionals[8]. The causes of NIV ineffectiveness are frequently associated with the inability to enhance oxygenation levels, failure to alleviate breathlessness, discomfort from the mask, restlessness, anxiety, hemodynamic instability, and worsening of respiration[9]. The use of NIV in circumstances lacking definitive evidence to back its recommendation also increases the likelihood of failure.

Late recognition of patients at risk of NIV failure may experience a delay in starting invasive mechanical ventilation. This delay is significant as it can lead to avoidable complications and fatalities[10]. Impairment in oxygenation, indicated by a decreased ratio of partial pressure of arterial oxygen (PaO2) to fraction of inspired oxygen (FiO2) which is also known as the P/F ratio, is a widely supported risk factor and predictor of NIV failure. Patient outcomes are likely more influenced by the root cause instead of the initial severity of hypoxemia itself. The majority of endotracheal intubation (ETI) cases were attributed to NIV's failure to improve gas exchange (62%).

While the initial arterial blood gas (ABG) values at the start of the study did not demonstrate predictive value, severe hypoxemia (P/F =146) after one hour of NIV treatment was identified as an independent predictor of NIV failure according to the multivariate analysis[11]. The PaO2/FiO2 (P/F) ratio is commonly used to assess the lung's capability to oxygenate the blood in acute respiratory distress syndrome (ARDS)[12]. However, recent research indicates that including positive end-expiratory pressure (PEEP) in the P/F ratio (P/FP ratio) enhances prognostic capability in ARDS[13].

In the context of acute exacerbation of chronic obstructive pulmonary disease (COPD), previous studies have not specifically examined the role of the P/F ratio and oxygenation. Additional research is necessary to assess the significance and usefulness of the P/F ratio and oxygenation in acute exacerbation of COPD[14]. This study was carried out to examine the role of P/F ratio and its inability to improve after NIV and increased requirements of oxygen after NIV application in predicting NIV failure during acute COPD exacerbation.

The purpose of the study is to see the significance of proper maintenance of oxygenation and PF ratio during acute COPD exacerbation, as well as the role of inadequate oxygenation and PF ratio in non-invasive ventilation failure.

METHODOLOGY

IRB/ERC Approval:

A Quasi Single Arm Study was done in three campuses of the Ziauddin Hospital Karachi after taking approval from Ethical Research Committee (4930222YAMED) of Ziauddin University Hospital. Written informed consent was obtained from all the patients.

Patients admitting in Medical ICU and medicine ward with acute COPD exacerbation were part of this research. Inclusion criteria was 1) Age above 40 years, 2) Both genders 3) Known case of COPD, diagnosed by spirometry, 4) Having history of smoking or treated as COPD by attending Physician, 5) Admitting with acute exacerbation. Exclusion criteria was 1) Patients diagnosed with disease other than COPD like pneumonia, heart failure, acute myocardial infarction, pleural effusion, and 2) Patients whose attendants signed "Do not Resuscitate" code.

The calculated sample size was 170 via the WHO calculator, with a 95% confidence interval. The absolute precision required was 0.07. Anticipated population proportion 1 was 0.115 and anticipated population

proportion 2 was 0.119, considering in-hospital mortality rates reported by Correa et al. in 2015 (20.6% for NIV failure and 69.4% for success). Informed consent was taken from patient or family. Data were collected within a duration of six months from Sep 2024- Feb 2025 using a pro forma.

SPSS version 27 was used for data analysis. Shapiro Wilk test checked the normality of continuous variables (like age). Mean and standard deviations were calculated for normally distributed variables (like age in our data), while the median (IQR) was reported for non-normality distributed ones. Mann-Whitney U test compared continuous data. Percentages and frequencies measured qualitative variables like gender, weak cough reflex, non-invasive ventilation failure, and in-hospital mortality.

RESULTS

The research encompassed a sample of 170 individuals who were admitted to both the Medicine ward and medical ICU due to acute respiratory failure. Within the participant pool, there were 80 (47%) males and 90 (53%) females, as shown (Fig. 1) their average age was 66 ± 12 years (ranging from 40 to 80 years). The findings revealed that 66 (38%) of the patients encountered unsuccessful outcomes with non-invasive ventilation (NIV), whereas 104 (61%) achieved favorable results with NIV. Furthermore, a mortality rate of 23.5% was observed among the patients during their hospital stay.

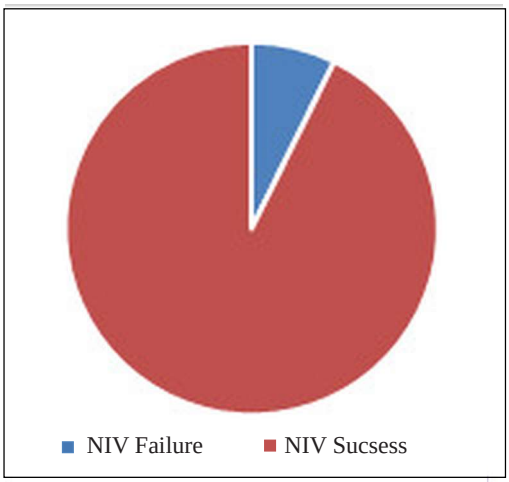

Figure 1: NIV Failure Among Patients

The patients who encountered non-invasive ventilation (NIV) failure, had equal distribution of genders, with 50% males and 50% females. Conversely, within the NIV success group, 45% were males and 55% were females as shown in (Fig. 2). These proportions indicate that there is no statistically significant correlation between gender and outcomes of NIV (p-value=0.636).

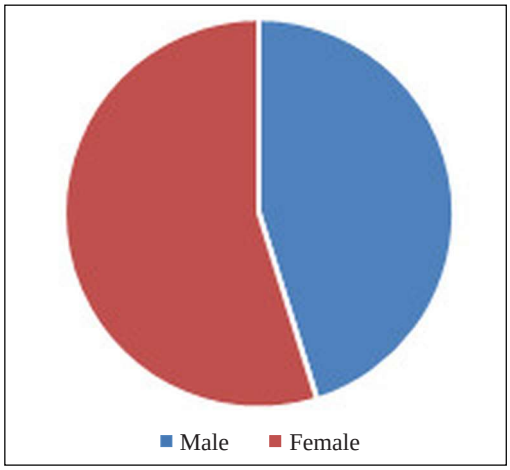

Figure 2: Gender Distribution of NIV Success

Shapiro-Wilk test was used to check the normality of data. The normality test showed that the data was non parametric therefore we used non-parametric statistical test for the analysis of the data.

The comparison of FiO2, SaO2 and PaO2 and PF Ratio among patients with and without non-invasive ventilation failure is presented in Table 1. FiO2 at the time of admission ($p<0.001$), FiO2 at 1 hour ($p<0.001$), FiO2 at 48 hours ($p<0.001$) and FiO2 after 48 hours ($p<0.001$) had highly significant median differences between those patients who developed and those who did not develop non-invasive ventilation failure, respectively. Also, statistically significant median differences in SaO2 at the time of admission ($p<0.001$), SaO2 at 1 hour ($p<0.001$), SaO2 at 48 hours ($p<0.001$) and SaO2 after 48 hours ($p=0.023$) were observed in both groups of patients, respectively. We observed significant difference in the PaO2 at the time of admission ($p<0.001$), PaO2 at 1 hour ($p<0.001$), PaO2 at 48 hours ($p<0.001$) between the patients who developed and those who did not develop non-invasive ventilation failure respectively but we found that PaO2 after 48 hour showed statistically insignificant median difference in patients with and without non-invasive ventilation failure ($p=0.120$). We also observed highly significant difference in the PF ratio at the time of admission ($p<0.001$), PF ratio at 1 hour ($p<0.001$), PF ratio at 48 hours ($p<0.001$) and PF ratio after 48 hours ($p<0.001$) between patients with and without non-invasive ventilation failure respectively.

The comparison of FiO2, SaO2 and PaO2 and PF Ratio among patients with and without mortality is presented in Table 2. We observed significant difference in the FiO2 at the time of admission ($p<0.001$), FiO2 at 1 hour ($p<0.001$), FiO2 at 48 hours ($p<0.001$) and FiO2 after 48 hours ($p<0.001$) between patients with and without mortality respectively. SaO2 at the time of admission ($p=0.007$), SaO2 at 1 hour ($p<0.001$), SaO2 at 48 hours ($p<0.001$) and SaO2 after 48 hours

Table 1: Comparison of Mean Arterial Blood Gas in Patients With and Without NIV Failure

	NIV Failure		P-value
	Yes Median (IQR)	No Median (IQR)	
FiO2 at time of admission	0.53(0.24)	0.41(0.20)	<0.001*
FiO2 at 1 hour	0.81(0.01)	0.61(0.28)	<0.001*
FiO2 at 48 hour	1.00(0.19)	0.49(0.20)	<0.001*
FiO2 after 48 hour	1.00(0.00)	0.33(0.20)	<0.001*
SaO2 at time of admission	72(16)	82(11)	<0.001*
SaO2 at 1 hour	88(10)	93(10)	<0.001*
SaO2 at 48 hour	95(7)	96(3)	<0.001*
SaO2 after 48 hour	97(4)	97(2)	0.023*
PaO2 at time of admission	49(17)	59(18)	<0.001*
PaO2 at 1 hour	75(30)	104(36)	<0.001*
PaO2 at 48 hour	104(44)	124(23)	<0.001*
PaO2 after 48 hour	125(62)	125(32)	0.120
PF Ratio at time of admission	111(79.95)	153(81)	<0.001*
PF Ratio at 1 hour	96(35.50)	186.80(87)	<0.001*
PF Ratio at 48 hour	104(34)	253(136)	<0.001*
PF Ratio after 48 hour	128(63)	346(194)	<0.001*

Mann-Whitney U test is applied
*P=0.05 indicates statistical significance

Table 2: Comparison of Mean Arterial Blood Gas in Patients With and Without Mortality

	NIV Failure		P-value
	Yes Median (IQR)	No Median (IQR)	
FiO2 at time of admission	0.49(0.22)	0.41(0.26)	0.001
FiO2 at 1 hour	0.81(0.01)	0.61(0.24)	<0.001*
FiO2 at 48 hours	1.00(0.19)	0.57(0.40)	<0.001*
FiO2 after 48 hours	1.00(0.0)	0.41(0.40)	<0.001*
SaO2 at time of admission	76(20.50)	81(16)	0.007*
SaO2 at 1 hour	88(9.50)	92(10)	<0.001*
SaO2 at 48 hours	90(15)	96(3)	<0.001*
SaO2 after 48 hours	95(20)	97(3)	<0.001*
PaO2 at time of admission	52(19.40)	57(18)	0.033*
PaO2 at 1 hour	84(36.50)	101(42.50)	<0.001*
PaO2 at 48 hours	87(37.50)	123(24)	<0.001*
PaO2 after 48 hours	78(47.50)	128(32)	<0.001*
PF Ratio at time of admission	123(62.57)	144(99.10)	0.002*
PF Ratio at 1 hour	113.50(47.75)	173(108.90)	<0.001*
PF Ratio at 48 hours	92(28.50)	221(163)	<0.001*
PF Ratio after 48 hours	78(47.50)	312(251.20)	<0.001*

Mann-Whitney U test is applied
*P=0.05 indicates statistical significance.

(p<0.001) had significant median differences between patients with and without mortality, respectively. Statistically significant median differences in PaO2 at the time of admission (p=0.033), PaO2 at 1 hour (p<0.001), PaO2 at 48 hours (p<0.001) and PaO2 after 48 hours (p<0.001) were observed among patients with and without mortality, respectively. We observed significant difference in the FiO2 at the time of admission (p<0.001), FiO2 at 1 hour (p<0.001), FiO2 at 48 hours (p<0.001) and FiO2 after 48 hours (p<0.001) between patients with and without mortality, respectively. We also observed significant difference in the PF ratio at the time of admission (p=0.002), PF ratio at 1 hour (p<0.001), PF ratio at 48 hours (p<0.001) and PF ratio after 48 hours (p<0.001) between patients with and without mortality, respectively.

DISCUSSION

The study analyzed 170 patients presented to the Medicine Ward and ICU with acute respiratory failure caused by COPD exacerbation. The sample included 80 males and 90 females, with an average age of 66 years. The study evaluated NIV outcomes and rates of mortality in patients. The findings showed NIV success in 61% of patients, while 38% had unfavorable outcomes.

The mortality rate during the hospital stay was observed to be 23.5%. The mortality rate due to NIV failure in AECOPD was 11.2% in a previous study[15]. When analyzing the subset of patients with NIV failure, we found an equal distribution of genders. However, within the NIV success group, there were slightly more females than males. The Statistical Analysis found no significant link between gender and NIV outcomes.

The researchers also compared various parameters related to oxygenation, such as FiO2 (fraction of inspired oxygen), SaO2 (arterial oxygen saturation), PaO2 (partial pressure of arterial oxygen), and PF ratio (ratio of arterial oxygen partial pressure to FiO2), between patients who developed NIV failure and those who did not develop NIV failure, as well as among patients who died and those who survived. The results revealed significant median differences in FiO2, SaO2, PaO2, and PF ratios over time between NIV success and failure groups. FiO2 and SaO2 differed significantly at admission, 1 hour, 48 hours, and beyond, while PaO2 varied at admission and 1 hour but not after 48 hours. The PF ratio showed significant differences at all time points. After 1 hour of NIV, patients who did not show improvement in PF ratio were more likely to develop NIV failure.

Similarly, significant median differences in FiO2, SaO2, PaO2, and PF ratio were noted at various time points between patients with and without mortality. FiO2 varied significantly at all points of time, while SaO2 and PaO2 showed significant differences at admission, 1 hour, and 48 hours. Finally, the P/F ratio showed significant differences at all points of time. Specially, failure to show improvement in PF ratio after 1 hour of NIV administration is a useful predictor of in-hospital morality after NIV failure. PF ratio can serve as the optimal parameter for evaluating a patient's oxygenation status. Individuals exhibiting a PF ratio below 150 are at a heightened risk of NIV failure[16].

CONCLUSION

The results indicated that NIV was effective in most of the cases, although a notable number of patients encountered failure with NIV. The analysis of oxygenation parameters showed significant differences between the groups of patients who did and who did not develop NIV failure, as well as between the groups of patients who survived and who died. These findings contribute to our understanding of the factors influencing treatment results in individuals with acute respiratory failure and may have implications for clinical decision-making.

Limitations of Study: This research is conducted in different campuses of same hospital setup. Results can be different if the same research is conducted in multiple hospitals including private and public setups.

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Conflict of interest: Authors declare that there is no conflict of interest.

Authors' Contribution: YA: Developed the concept of this research under the guidance of Dr. Syed Ali Abbas. **YA** and **KG:** searched literature and drafted the manuscript; **AS**, **NA** and **HA:** Contributed in collection and analysis of data

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