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EFFECTIVENESS OF NON-INVASIVE VENTILATION FOR TYPE 2 RESPIRATORY FAILURE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) EXACERBATION

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Abstract

Background: *Acute exacerbations of COPD often result in Type 2 respiratory failure (T2RF), marked by hypercapnia and respiratory acidosis. Non-invasive ventilation (NIV) has emerged as the primary treatment for these kinds of conditions, decreasing the necessity for intubation and enhancing results. Our study findings illustrated the essential importance of NIV in the management of acute hypercapnic respiratory failure during COPD exacerbations within our local community.*

Objectives: *To determine the effectiveness of non-invasive ventilation, for type 2 respiratory failure in chronic obstructive pulmonary disease (COPD) exacerbation in patients presenting to tertiary care hospital.*

Methodology: *This six-month cross-sectional study (September 2024-February 2025) at PIMS, Islamabad assessed the efficacy of NIV in patients with COPD and T2RF. We enrolled 178 adult males and females (ages 18-60) who met GOLD criteria for acute exacerbation (pH 7.25-7.35, $PaCO_2$ 55-75 mmHg). Patients were given standardized non-invasive ventilation with a full-face mask, with an initial inspiratory positive airway pressure of 10 cm H_2O and an expiratory positive airway pressure of 4-5 cm H_2O, titrated to a maximum of 20 cm H_2O. Oxygen saturation levels maintained between SpO_2 88-92%. The primary outcome (treatment efficacy) required three criteria at 48 hours: pH ≥7.35, symptom relief, and a normalized respiratory rate. The data was methodically input and analyzed using SPSS version 25.0. Effect modifiers were addressed via stratification, the chi-square test was employed, and a p-value of ≤0.05 was considered statistically significant.*

Results: *The study included 178 T2RF COPD patients. The average age was 35.39±11.26 years, with 62.9% of persons under 40. The majority of patients (66.3%) were male. 66.9% (n=119) of COPD patients with Type 2 respiratory*

failure responded well to non-invasive ventilation (NIV), while 33.1% (n=59) did not. Infection and NIV non-compliance aggravated 28 (47.5%) and 31 (52.5%) of those who failed to respond. Gender, age, BMI, and PCO_2 levels did not significantly impact outcomes. Long-term COPD (≥5 years) was linked to improved responsiveness, possibly due to disease management techniques.

Conclusion: *The effectiveness of NIV was observed in 66.9% of cases involving COPD exacerbations, with pH normalization and extended disease duration serving as predictors of successful outcomes. The findings provide evidence for the efficacy of NIV as the primary treatment for Type 2 respiratory failure.*

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a widespread disorder that accounts for almost 1 million hospitalizations annually and ranks as the third highest cause of death in the United States. Patients hospitalized due to acute exacerbations of COPD (AE-COPD) display a broad spectrum of disease severity, ranging from short hospitalizations to extended hospital stays and mortality. Approximately 12–18% of patients with acute exacerbations of chronic obstructive pulmonary disease (AE-COPD) necessitate intensive care unit (ICU) admission, with mortality rates nearing 15% within this cohort. In Pakistan, the burden of COPD is substantial, with studies reporting a prevalence of 13.6% in adults over 40 years, attributed to high smoking rates, indoor air pollution from biomass fuels, and poor healthcare access. Acute exacerbations of COPD (AECOPD), characterized by increased dyspnea, cough, and sputum production, may result in acute hypercapnic respiratory failure (AHRF), a critical situation need immediate attention. Pakistan encounters distinct obstacles in COPD management attributable to insufficient pulmonary healthcare infrastructure, protracted diagnostic processes, and poor compliance with long-term treatment regimensA considerable percentage of patients arrive late with severe exacerbations, heightening the risk of Type 2 respiratory failure (T2RF). The Global Burden of Disease (GBD) Study 2019 identified COPD as the third foremost cause of mortality in Pakistan, with elevated death rates predominantly in rural regions attributed to biomass smoke exposure and insufficient spirometry screening.

Non-Invasive Ventilation (NIV) is a crucial intervention for type 2 respiratory failure. NIV has demonstrated efficacy in the management of acute respiratory failure in postoperative patients, pulmonary edema, COPD exacerbations, obstructive sleep apnea, and in aiding the weaning process from mechanical ventilation.[i,ii] NIV is particularly effective for alert, cooperative COPD patients during exacerbations. While numerous studies describe NIV use across conditions, most randomized controlled trials (RCTs) focus on COPD.[iii] Current guidelines strongly recommend NIV over standard care for moderate-to-severe COPD exacerbations, though only two small RCTs directly compare NIV to invasive mechanical ventilation (IMV), showing NIV reduces complications and readmissions without affecting mortality. A survey of 99 AE-COPD patients in French ICUs and a large US administrative study found NIV significantly reduced mortality compared to IMV.[12] Stefan et al. reported an 86.7% NIV success rate for type 2 respiratory failure in COPD exacerbations.[iv] Identifying predictors of NIV success is crucial to optimize patient selection and resource allocation, particularly in resource-limited settings like Pakistan, where ICU beds and ventilators are scarce. While international guidelines strongly recommend NIV for AHRF in COPD, most evidence derives from Western populations, with limited data from our local population, where disease phenotypes and healthcare barriers differ. Understanding the effectiveness of NIV in this context is essential for optimizing treatment strategies and improving patient care. There is limited recent data regarding the NIV treatment modality and its effectiveness in patients with severe AE-COPD. We aimed to evaluate the effectiveness of NIV in patients hospitalized for severe COPD exacerbations, addressing a gap due to limited local studies. Our findings will enhance patient counseling and provide valuable insights for future research in this area.

MATERIAL AND METHODS

To evaluate the efficacy of non-invasive ventilation (NIV) in controlling acute exacerbations of chronic obstructive pulmonary disease (COPD) with Type 2 respiratory failure, this cross-sectional study was conducted at the Department of Pulmonology, Pakistan Institute of Medical Sciences (PIMS), Islamabad over a six-month period from September 2024 to February 2025. The investigation utilized precise operational definitions to guarantee consistent patient evaluation. The diagnosis of COPD was made following the criteria set by the Global Initiative for Chronic Obstructive Lung Disease (GOLD). This involved the presence of documented symptoms such as chronic cough, sputum production, or dyspnea lasting for over three months each year for two consecutive years, alongside confirmation through post-bronchodilator spirometry that indicated a FEV_1/FVC ratio of less than 70%. Acute exacerbations were categorized according to the GOLD severity staging system (1-4), utilizing percentage predicted FEV_1 values. An exacerbation is defined as an acute clinical worsening accompanied by increased disease severity within a one-week period. Type 2 respiratory failure is characterized by arterial blood gas values indicating hypercapnia ($PaCO_2$ ≥45 mmHg) alongside acidosis (pH <7.35) and clinical signs of tachypnea (respiratory rate >22 breaths per minute).

A total of 178 participants were enrolled in the study, with the sample size determined using the WHO sample size calculator, which was based on an expected NIV effectiveness rate of 86.7%, a 5% margin of error, and a 95% confidence level. Consecutive non-probability sampling was utilized to identify suitable adult patients aged 18-60 years who were presenting with AE-COPD and Type 2 respiratory failure (pH 7.25-7.35, $PaCO_2$ 55-75 mmHg). Exclusion criteria were meticulously implemented to eliminate potential confounding variables, thereby excluding patients with significant cardiopulmonary compromise, bronchogenic malignancy, or active pulmonary tuberculosis.

A standardized NIV protocol was established under the guidance of consultant pulmonologists who possess at least five years of post-fellowship experience. The initiation of treatment required the use of a full-face mask for the initial 24 hours, with the possibility of transitioning to a nasal mask afterwards, contingent upon the patient's tolerance. The initial ventilator settings were established at IPAP 10 cm H_2O and EPAP 4-5 cm H_2O. Adjustments were made progressively, increasing by 2-5 cm H_2O every 10 minutes as tolerated, with a goal of reaching a maximum pressure of 20 cm H_2O or until a therapeutic response was observed. Supplemental oxygen was meticulously adjusted to ensure that peripheral oxygen saturation remained within the range of 88-92%. Thorough monitoring encompassed ongoing pulse oximetry, electrocardiographic assessment, and hourly arterial blood gas evaluations, while bronchodilator therapy was provided during NIV-free periods to enhance medication delivery. The main outcome measure of NIV effectiveness was rigorously defined as the attainment of three simultaneous endpoints after 48 hours of treatment: pH normalization (≥7.35), full resolution of presenting symptoms, and return to a normal respiratory rate. The analysis encompassed a range of demographic and clinical parameters as secondary outcomes. The data collection involved thorough baseline characteristics such as age, body mass index, disease duration, and GOLD stage classification. The statistical analysis utilized descriptive statistics, presenting mean±standard deviation for continuous variables and frequencies and percentages for categorical variables, with a specific emphasis on assessing the diagnostic accuracy of pH normalization as the main efficacy endpoint. The data was systematically entered and analyzed utilizing SPSS version 25.0. Effect modifiers were managed through stratification, the chi-square test was utilized, and a p-value of ≤0.05 was deemed statistically significant.

RESULTS

The research encompassed 178 COPD patients exhibiting T2RF. The average age was 35.39±11.26 years, with 62.9% of individuals under 40 years old. The majority of patients were male (66.3%), and the average BMI was 23.89±5.18 kg/m², with 59% classified as normal (≤24.99). At baseline, the mean PCO_2 was 65.25±5.61 mmHg, and the pH was 7.30±0.03, with 53.4% exhibiting mild acidosis (pH 7.25–7.30). Following 24 hours of non-invasive ventilation, PCO_2 improved to 60.46±6.25 mmHg, with 73.6% of patients achieving a pH greater than

7.30. At 48 hours, 85.4% exhibited PCO_2 ≤60 mmHg (mean 52.60±6.11 mmHg), and 57.9% had adjusted pH (>7.35). These results underscore the efficacy of non-invasive ventilation in swiftly rectifying hypercapnia and acidosis during exacerbations of chronic obstructive pulmonary disease. The comprehensive analysis of all examined quantitative and qualitative factors, together with the categorization of diverse clinico-demographic data, is presented in Tables 1 and 2. Non-invasive ventilation (NIV) proved helpful in 66.9% (n=119) of COPD patients experiencing Type 2 respiratory failure, whereas 33.1% (n=59) exhibited inadequate response (figure 1). Among those who did not respond satisfactorily, infection and non-compliance with NIV were contributing factors to aggravation in 28 (47.5%) and 31 (52.5%) of patients, respectively. Gender, age, BMI, and PCO_2 levels did not significantly affect outcomes. The normalization of pH (baseline and post-NIV) emerged as the most significant predictor of NIV performance. A prolonged duration of COPD (≥5 years) was associated with an enhanced response, potentially attributable to established disease management practices. Table 3, Figure 2, and Figure 3 provide a comprehensive stratification analysis.

Table 1: Clinical and demographic details of the quantitative variables of the study subjects (n=178)

Quantitative Variables	Minimum	Maximum	Mean	± SD
Age (Years)	18.00	60.00	35.39	11.26
Weight (kg)	40.00	78.00	57.34	11.27
Height (cm)	140.00	169.00	155.53	8.75
BMI (kg/m^2)	14.20	38.20	23.89	5.18
Duration of Disease (years)	3.00	7.00	4.48	.98
Baseline PCO_2 Value	55.00	75.00	65.25	5.61
Baseline pH Value	7.25	7.35	7.30	0.03
24 Hours of NIV PCO_2 Value	47.00	73.00	60.46	6.25
24 Hours of NIV pH Value	7.28	7.38	7.32	0.02
48 Hours of NIV PCO_2 Value	40.00	67.00	52.60	6.11
48 Hours of NIV pH Value	7.30	7.45	7.36	0.03

Table 2: Distribution of study subjects on the basis of various clinical and demographic qualitative variables as well as in the categorizes of various quantitative variables (n=178)

Variables		Frequency	Percentage (%)
Gender	Male	118	66.3
	Female	60	33.7
Age Groups	<40 Years	112	62.9
	≥40 Years	66	37.1
BMI Groups	≤24.99 Kg/m^2	105	59.0
	25-29 Kg/m^2	44	24.7
	>29 Kg/m^2	29	16.3
Duration of Disease	<5 Years	89	50.0
	≥5 Years	89	50.0
Baseline PCO_2	55-69 mmHg	130	73.0

Variables		Frequency	Percentage (%)
Gender	Male	118	66.3
	Female	60	33.7
Age Groups	<40 Years	112	62.9
	≥40 Years	66	37.1
BMI Groups	≤24.99 Kg/m^2	105	59.0
	25-29 Kg/m^2	44	24.7
	>29 Kg/m^2	29	16.3
	>69 mmHg	48	27.0
Baseline pH Value	7.25-7.30	95	53.4
	>7.30	83	46.6
24 Hours of NIV PCO_2 Value	≤60 mmHg	88	49.4
	>60 mmHg	90	50.6
24 Hours of NIV pH Value	≤7.30	47	26.4
	>7.30	131	73.6
48 Hours of NIV PCO_2 Value	≤60 mmHg	152	85.4
	>60 mmHg	26	14.6
48 Hours of NIV pH Value	≤7.35	75	42.1
	>7.35	103	57.9

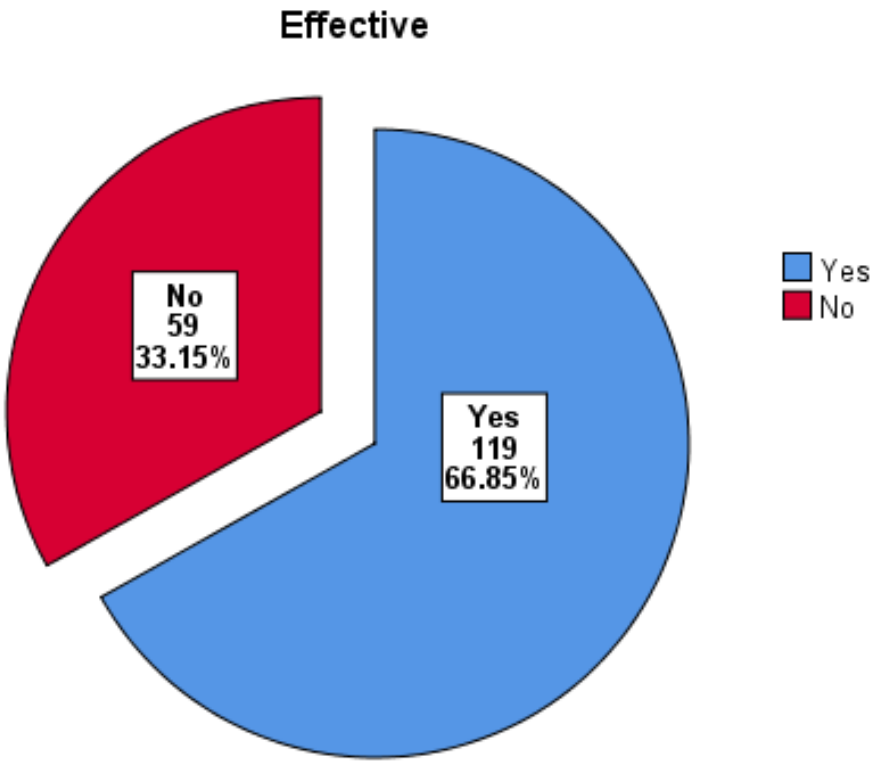

Figure 1: Effectiveness of NIV for T2RF in patients with COPD exacerbation

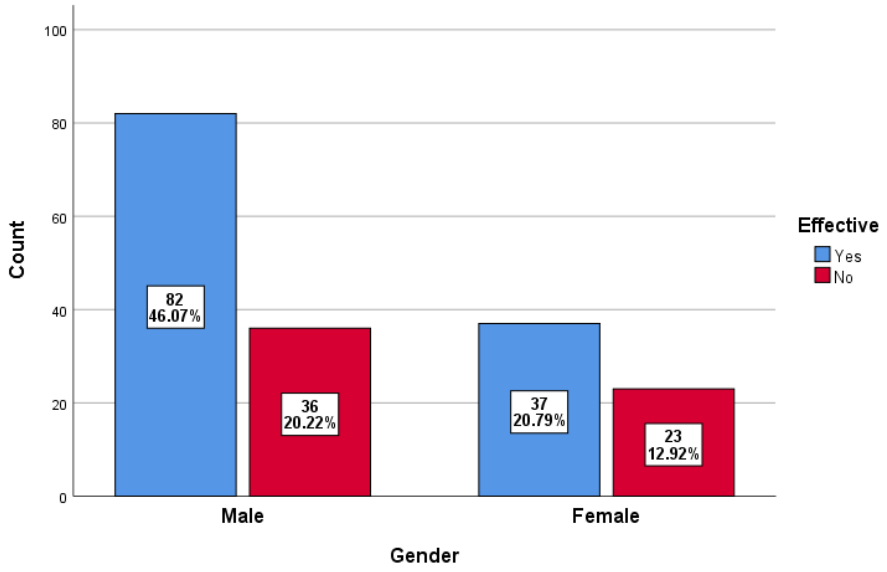

Figure 1: Effectiveness of NIV for T2RF in patients with COPD exacerbation (gender-based stratification) p-value = 0.294

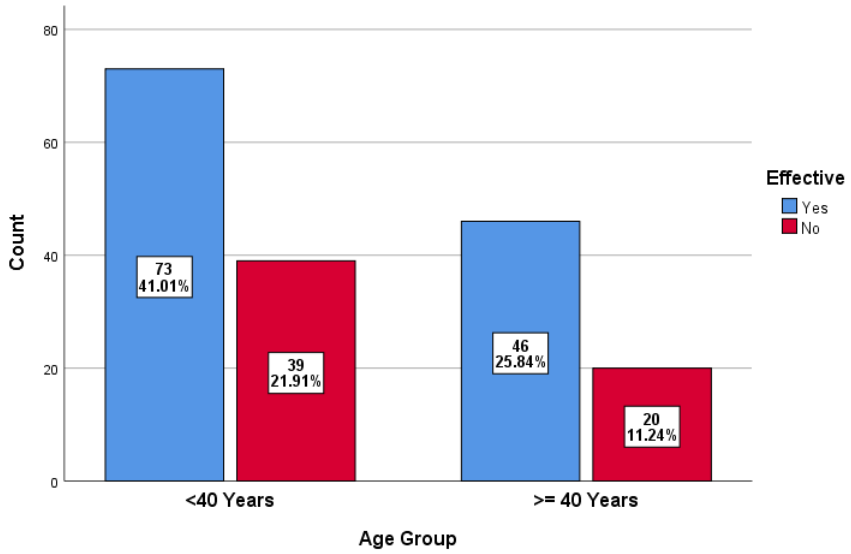

Figure 1: Effectiveness of NIV for T2RF in patients with COPD exacerbation (age-based stratification) p-value = 0.536

Table 3: Stratification of NIV effectiveness for T2RF in patients with COPD exacerbation on the basis of various clinical and demographic variables

Variables		Effective		p-Value (x^2-test)
		Yes	No	
BMI Groups	≤24.99 Kg/m^2 25-29 Kg/m^2 >29 Kg/m^2	73 (61.3%) 26 (21.8%) 20 (16.8%)	32 (54.2%) 18 (30.5%) 9 (15.3%)	0.451
Duration of Disease	<5 Years ≥5 Years	53 (44.5%) 66 (55.5%)	36 (61.0%) 23 (39.0%)	0.038
Baseline PCO_2	55-69 mmHg >69 mmHg	87 (73.1%) 32 (26.9%)	43 (72.9%) 16 (27.1%)	0.974
Baseline pH Value	7.25-7.30 >7.30	36 (30.3%) 83 (69.7%)	59 (100.0%) 0 (0.0%)	0.000
24 Hours of NIV PCO_2 Value	≤60 mmHg >60 mmHg	62 (52.1%) 57 (47.9%)	26 (44.1%) 33 (55.9%)	0.313
24 Hours of NIV pH Value	≤7.30 >7.30	04 (3.4%) 115 (96.6%)	43 (72.9%) 16 (27.1%)	0.000
48 Hours of NIV PCO_2 Value	≤60 mmHg >60 mmHg	101 (84.9%) 18 (15.1%)	51 (86.4%) 8 (13.6%)	0.781
24 Hours of NIV pH Value	≤7.35 >7.35	16 (13.4%) 103 (86.6%)	59 (100.0%) 0 (0.0%)	0.000

DISCUSSION

NIV is a critical method for managing acute hypercapnic respiratory failure in patients with exacerbations of COPD. Focusing on clinical and biochemical indicators of therapy success, this study assessed the effectiveness of non-invasive ventilation in 178 COPD patients with T2RF. Our findings show that NIV was successful in 66.9% of cases, with pH normalization found to be the most important predictor of positive results. On the other hand, demographic factors like age, gender, and body mass index (BMI) had no impact on treatment effectiveness. These results provide latest views on the impact of disease duration and acid-base balance on the efficacy of NIV while matching present studies.

The total success rate of 66.9% seen in our study aligns with prior findings, which have recorded NIV efficacy rates between 60% and 80%. This indicates that NIV continues to be a dependable first-line treatment for acute hypercapnic respiratory failure in individuals with COPD. The 33.1% failure rate underscores the necessity for meticulous patient selection and prompt identification of those who may necessitate escalation to invasive mechanical breathing. In our sample, the equalization of pH was the main predictor of NIV success. While none of the patients with a pH of 7.30 or lower had a good response to NIV, those with a baseline pH over 7.30 had a 69.7% success rate. Early therapy is emphasised by this finding since severe acidosis is linked to impaired respiratory muscle function and reduced ventilator efficacy. Long-term success was significantly predicted by the swift pH change within the first 24 hours of NIV, given that 96.6% of respondents maintained a pH >7.30 at this time. At 48 hours, 86.6% of successful patients attained a pH >7.35, but none in the failure group did. These findings substantiate the notion that pH serves as a more dependable indicator of NIV efficacy than partial pressure of carbon dioxide (PCO_2), which exhibited no significant link with treatment outcomes in our investigation.

Unexpectedly, greater COPD duration was linked to higher NIV success rates. Though many studies show that advanced COPD is linked to negative outcomes because of fixed airway obstruction, our findings suggest that people with chronic disease could respond better to NIV, perhaps because of increased knowledge with COPD management programs or adaptive physiological mechanisms. This finding requires for more investigation, particularly in relation to patient compliance and comorbidities. On the other hand, demographic variables including age, gender, and BMI had no significant impact on NIV outcomes. Although men had a higher response rate, this difference was not statistically relevant. Younger age and obesity also found not associate with reduced effectiveness, hence refuting previous concerns about NIV performance in these groups.

The physiological effects of acidosis on respiratory function provide the mechanistic basis of our results. Severe acidosis reduces diaphragmatic contractility and increases the effort of breathing, hence impairing the effectiveness of non-invasive ventilation in providing enough ventilation. On the other hand, rapid pH correction improves gas exchange and reduces respiratory muscle weariness, hence clarifying why early pH normalization was such a success indicator. Moreover, patients with chronic COPD may develop compensatory metabolic alkalosis, which mitigates acute hypercapnia and improves the efficiency of non-invasive ventilation. These discoveries underscore the necessity of real-time monitoring of acid-base equilibrium to inform therapeutic decision-making.

Despite various advantages, our research has notable limitations. The single-center design could limit the generalizability of our results, and the lack of long-term follow-up data prevents conclusions on post-discharge outcomes including rehospitalization or death. Moreover, we did not collect detailed information on NIV settings—e.g., pressure levels, interface type—which could influence therapy effectiveness. Future studies have to address these shortcomings by include multicenter systems, lengthening follow-up times, and using consistent NIV deployment techniques.

Conclusively, this study verifies that with pH normalisation being the most reliable predictor of efficacy, NIV is an effective treatment for nearly more than half of COPD patients with T2RF. In patients with moderate acidosis, doctors must emphasize the quick start of non-invasive breathing and carefully track pH trends over the first 24 hours of therapy. The lack of relationship between demographic factors and NIV results suggests that age, gender, and BMI should

not prevent a trial of NIV in appropriate people. Future research should focus on maximizing NIV settings, looking at comorbidity impacts, and evaluating long-term findings to improve patient selection and clinical outcomes. Incorporating these results into practice will help clinicians to maximize the use of NIV as a key treatment for COPD flare-ups, hence reducing the need for invasive breathing and improving patient outcomes.

CONCLUSION

The research indicated that NIV was beneficial for more than half of COPD patients with T2RF, with pH normalization recognized as the primary predictor of its efficacy. Patients exhibiting a baseline pH greater than 7.30 and those with a disease duration of five years or longer demonstrated significantly enhanced outcomes. Demographic characteristics, including age, gender, and BMI, did not significantly influence efficacy. However, the robust correlation between early pH enhancement and treatment success underscores its importance as a therapeutic indicator. The data support the use of NIV as a primary approach for managing COPD exacerbations, particularly in resource-limited settings. Future research should examine optimal ventilator settings and comorbidities to enhance the efficacy of non-invasive ventilation across diverse patient populations.

REFERENCES

Roh JA, Kim KI, Jung HJ. The efficacy of manual therapy for chronic obstructive pulmonary disease: A systematic review. PLoS One. 2021;16(5):e025129

Liu X, Du C, Hu F, Zhao Y, Zhou J, Wang Q, et al. Management of acute exacerbation of chronic obstructive pulmonary disease under a tiered medical system in China. Ther Adv Respir Dis. 2022;16:17534666221075499.

Jafar TH, Haaland BA, Rahman A, Razzak JA, Bilger M, Naghavi M, Mokdad AH, Hyder AA. Non-communicable diseases and injuries in Pakistan: strategic priorities. Lancet. 2013;381(9885):2281-90.

Khan MA, Khan MA, Walley JD, Khan N, Imtiaz Sheikh F, Ali S, et al. Feasibility of delivering integrated COPD-asthma care at primary and secondary level public healthcare facilities in Pakistan: a process evaluation. BJGP Open. 2019;3(1):1-5.

Baba M, Khan S, Hasnain F, Sakina R, Talat A, Irfan A. Exploring the Treatment Types and Challenges in Patients with Chronic Obstructive Pulmonary Disease: A Qualitative Study. World Fam Med. 2022;20(1):23-9.

1. Fallahzadeh A, Sharifnejad Tehrani Y, Sheikhy A, Ghamari SH, Mohammadi E, et al. The burden of chronic respiratory disease and attributable risk factors in North Africa and Middle East: findings from global burden of disease study (GBD) 2019. Respir Res. 2022;23(1):268-70.

Zubair T, Abbassi A, Khan OA. Early Detection of Chronic Obstructive Pulmonary Disease in Apparently Healthy Attendants of Tertiary Care Hospital and Assessment of its Severity. J Coll Physicians Surg Pak. 2017;27(5):296-300.

Patel SM, Nair GP, Tuppekar BG, Uppe AG. Effectiveness of non-invasive ventilation in patients with type 2 respiratory failure. Int J Res Med Sci. 2021;9(3):794-7.

Hartley T, Lane ND, Steer J, Elliott MW, Sovani MP, Curtis HJ, et al. The Noninvasive Ventilation Outcomes (NIVO) score: prediction of in-hospital mortality in exacerbations of COPD requiring assisted ventilation. Eur Respir J. 2021;58(2):2004042.

Khilnani GC, Mani RK, Ramakrishnan N, Sidhu US. Guidelines for noninvasive ventilation in acute respiratory failure. Indian J Crit Care Med. 2013;17:42-70.

Hogea SP, Tudorache E, Fildan AP, Fira-Mladinescu O, Marc M, Oancea C. Risk factors of chronic obstructive pulmonary disease exacerbations. Clin Respir J. 2020;14(3):183-97.

Stefan MS, Nathanson BH, Higgins TL, Steingrub JS, Lagu T, Rothberg MB, et al. Comparative Effectiveness of Noninvasive and Invasive Ventilation in Critically Ill Patients With Acute Exacerbation of Chronic Obstructive Pulmonary Disease. Crit Care Med. 2015;43(7):1386-94.

Abraham SV, Azeez AK, Padmanabhan A. NIV failure in respiratory failure: an analysis. Egypt J Bronchol. 2023;17; 1-4.

Bruno CM, Valenti M. Acid-base disorders in patients with chronic obstructive pulmonary disease: a pathophysiological review. J Biomed Biotechnol. 2012;2012:915150.

Osadnik CR, Tee VS, Carson-Chahhoud KV, Picot J, Wedzicha JA, Smith BJ. Non-invasive ventilation for the management of acute hypercapnic respiratory failure due to exacerbation of chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2017;7(7):CD004104.

Mirza S, Clay RD, Koslow MA, Scanlon PD. COPD Guidelines: A Review of the 2018 GOLD Report. Mayo Clin Proc. 2018;93(10):1488-1502.

Forbes R, Duce B, Hukins C, Ellender C. Factors associated with noninvasive ventilation usage in patients with hypoventilation disorders. Sleep Adv. 2024;5(1):1-5.

Yanos J, Wood LD, Davis K, Keamy M 3rd. The effect of respiratory and lactic acidosis on diaphragm function. Am Rev Respir Dis. 1993;147(3):616-9