

**“Does early institution of non-invasive ventilation improves outcome in patients of acute exacerbation of copd presenting with hypercapnic respiratory failure”**

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**Abstract**

**Background:** An important well-known event of respiratory failure (RF) is frequently associated with severe exacerbations of chronic obstructive pulmonary disease (COPD). Moreover, the hypercapnia presents during an acute episode of RF, which is found to have higher mortality rate.

**Objectives:** To investigate the role of NIV applied to COPD patients with acute HRF who presents with acute exacerbations and require hospitalization.

**Material and Methods:** This study was a prospective, observational study which was carried out at Apollo Gleneagles Hospital, Kolkata during the period of study was 18 months (from January 2019 to June 2020). A total of 90 patients were recruited in the study. All COPD cases presenting in the Emergency Department during morning shift for arterial blood gases (ABG) data from patient at baseline, i.e., at arrival (0hr) and follow up at the time interval of 2 and 12hrs and patients presenting with Acute Exacerbations of COPD were included in the study.

**Results:** A total of 90 patients were admitted to the emergency department of Apollo Gleneagles hospital due to AECOPD presenting with HRF, was evaluated and treated with NIV for a better outcome concerning ABG parameters. The maximum value (27.80%) was obtained for the age groups of 51-60 years followed by age groups of 61-70 years (21.10%) and a minimum frequency value (3.30%) was observed for the age groups of 91-100 years. The mean  $\pm$  standard deviation of age value was  $66.37 \pm 13.64$  years. The data on the distribution of ICU admission (% frequency), a maximum value showing ICU as NO groups (55.4%), and a minimum value of about (44.6%) of YES groups as ICU admission were obtained among total studied patients. Overall hospital duration revealed that the minimum duration of hospitalization of 1 day and maximum value of 14 days were recorded and the mean  $\pm$  standard deviation of the duration of hospitalization value was  $4.59 \pm 3.31$  days.

**Conclusion:** In the present study, patients present in the age groups of 51-60 years were observed more susceptible and management through NIV was found to be more beneficial. Moreover, the duration of hospital stays, and ICU admission were found to have reduced in number after NIV treatment.

**Keywords:** AECOPD, NIV, ABG, HRF

**Introduction:**

COPD disease develops slowly and found asymptomatic in early phase during which lung functions decreases continuously. The worse condition in relation to ventilation-perfusion mismatch resulted through inflammatory airway, edema, mucous hypersecretion, and bronchoconstriction. An important well-known event of respiratory failure (RF) is frequently associated with severe exacerbations of chronic obstructive pulmonary disease (COPD).<sup>1</sup> Moreover, the hypercapnia presents during an acute episode of RF, which is found to have higher mortality rate. These can occur both earlier and during the successive 12-months of follow-up patients.<sup>2-3</sup> This is specifically in relation with severity of disease, as decided by the requirement for assisted ventilation, since patients who ultimately require ventilation indicated a more adverse 12-month survival, to just about 40% in one arrangement.<sup>1,3</sup> In general, hypercapnia is caused due to the increase in the partial pressure of carbon dioxide (PaCO<sub>2</sub>) >45mm Hg. As per the report in 2000, COPD was the 4th leading cause of mortality in Canada, and was predicted to be the 3rd leading cause by 2020.<sup>4</sup> Multidisciplinary efforts were involved by government sector, public health personals, healthcare service providers to reduce the COPD burden from population which included economic loss and costly health care system. The long-term diagnosis of patients with “acute respiratory failure (ARF)” in COPD specifically worsens when clinical status of the patient spells the need for ventilatory support, irrespective of invasive or non-invasive therapy.<sup>5,6</sup> Notwithstanding these shared characteristics, the presentation of NIV should be granted as one of the significantly advances in respiratory medication along with noteworthy results as far as improved short-and long-term results.<sup>7</sup> In the post 1980s, investigators started using NIV among patients suffered from ARF and they revealed it as an alternative to endotracheal intubation.<sup>44</sup> Some clinicians truly expected that in next twenty years, this procedure would become supportive as a first-line management for some forms of ARF.<sup>9,10</sup> The therapeutic efficacy of NIV for HF treatment is well established and NIV is considered as the standard therapy of AHRF secondary to AECOPD, among patients who had with and without chronic hypercapnia as reported previously.<sup>6,11</sup>

In recent guidelines of NIV, the multidisciplinary committee, comprising of clinicians, professionals and experts in the field, developed recommendations on the basis of “GRADE (Grading, Recommendation, Assessment, Development and Evaluation) methodology” for eleven useful questions recommended within “PICO (population–intervention–comparison–outcome) format”, which has addressed the usage of NIV for various causes of ARF.<sup>12</sup> In recent article by Comellini et al.<sup>13</sup> reported that NIV is useful, focused particularly on patients with acute HRF. In the present prospective and observational study, it has been attempted to determine the therapeutic role and treatment efficacy of early NIV in COPD patients with acute HRF who presented with acute exacerbations and requires hospitalization. This research on effective therapy is lacking in eastern India.

**Aim and Objectives:**

Aim- This study aims to investigate the role of NIV applied to COPD patients with acute HRF who presents with acute exacerbations and require hospitalization.

Objectives- To investigate the role of NIV applied to COPD patients with acute HRF who presents with acute exacerbations and require hospitalization.

**Material and Methods:**

This study was a prospective, observational study which was carried out at Apollo Gleneagles Hospital, Kolkata during the period of study was carried out for 18 months (from January 2019 to June 2020). A total of 90 patients were recruited in the study.

Inclusion criteria-

All COPD cases presenting in the Emergency Department during morning shift for arterial blood gases (ABG) data from patient at baseline, i.e., at arrival (0hr) and follow up at the time interval of 2 and 12hrs. Patients presenting with Acute Exacerbations of COPD.

Exclusion criteria-

1. Patients who presented with hemodynamic instability.
2. Patients who were stupor or drowsy.
3. Patients with other chronic respiratory diseases, e. g. significant fibrothorax, cystic fibrosis, kyphoscoliosis, neuromuscular diseases.
4. Patients with other systemic disease, e. g. Chronic Kidney Disease, Heart Failure.

The study was performed after the approval of the Institutional Ethics Committee (IEC) and Scientific Committee. This study is purely observational and analytical, requiring no patient interview or interventional method. Data was planned and sourced from hospital records and requisition forms anonymously. Risk to the patients in this study was negligible. Therefore, we request for a waiver of consent for this study. Data collection was started after explaining the purpose of the study and obtaining informed consent of the patient or the legal guardian. Baseline information was collected via structured interview using a pre-designed questionnaires. For arterial blood gases (ABG), four important parameters such as pH, partial pressure of arterial oxygen (PaO<sub>2</sub>), partial pressure of arterial carbon dioxide (PaCO<sub>2</sub>) and base excess (BE) were analyzed during admission (baseline), post-2hrs and 12hrs of non-invasive ventilation (NIV). The data was separated for ICU admission and respiratory care unit.

The protocol was followed as per Saure et al.<sup>14</sup> All the patients were sitting upright for at least 15min before the test, samples of 1.5 mL blood was drawn from the radial artery in a self-filling syringe containing 1ml dry heparin for rinsing the syringe. Immediately after sampling, air pockets were expelled. All samples were analyzed within a few minutes of collection in duplicates, on an instrument called as ABG Machine. pH, PaO<sub>2</sub> (mmHg), PaCO<sub>2</sub> (mmHg) and BE (mmol/L) were automatically reported. For statistical analysis, the data was entered into a Microsoft excel spreadsheet and then analyzed by using SPSS (ver. 20). All data has been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. The continuous variables of 2hrs and 12hrs were expressed as a minimum, maximum, mean, median, and standard deviation and compared from baseline using the Wilcoxon Signed Ranks Test. The p-value <0.05 was considered as statistically significant.

**Observation and Results:**

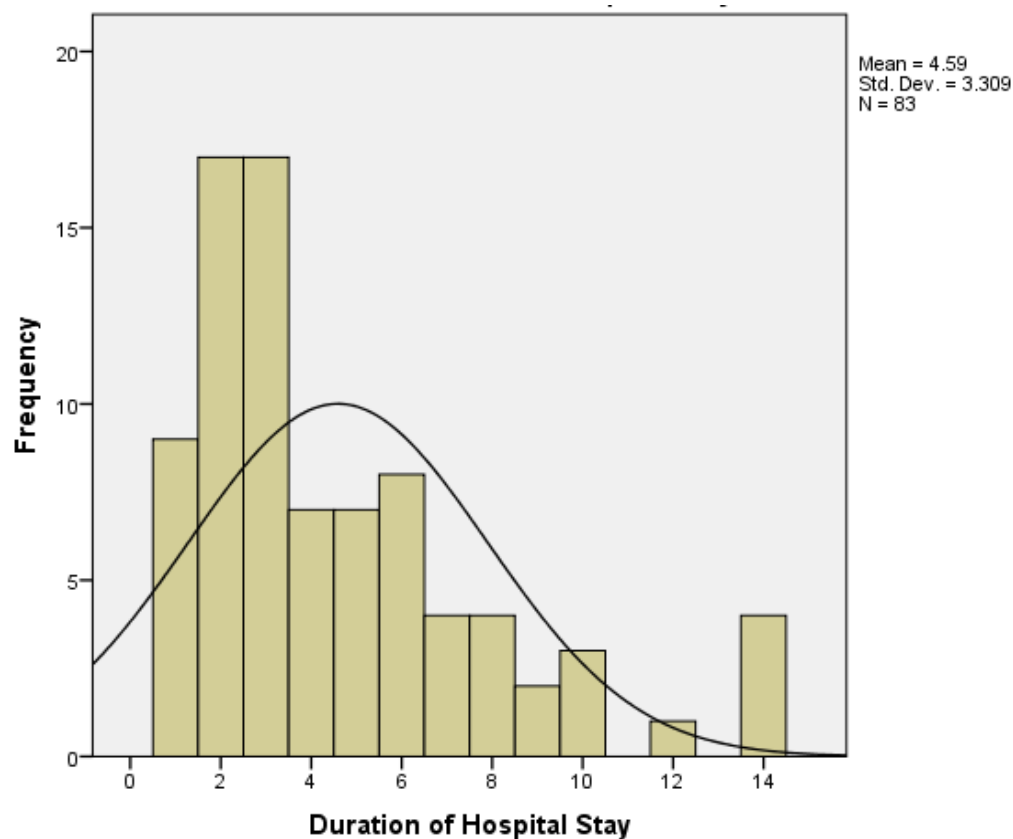
Age groups distribution

Table1: Frequency (%) of age groups among patients

Age (years)	Frequency	Percentage
41-50	13	14.40
51-60	25	27.80
61-70	19	21.10
71-80	17	18.90
81-90	13	14.40
91-100	3	3.30
Total	90	100.0

Above table describes the frequency (%) of age group distribution among the patients. In the age group categorization, the ranges were obtained as 41-50 years, 51-60 years, 61-70 years, 71-80 years, 81-91 years, and 91-100 years, respectively. The higher frequency value (27.80%) was obtained for the age groups of 51-60 years followed by age groups of 61-70 years (21.10%) and a lower frequency value (3.30%) was observed for the age groups of 91-100 years. Among gender distribution showing males (60.0%), and 40.0% of females were obtained among total studied patients.

Fig 1. Histogram for normal distribution of hospitalization among studied patients



In Fig 1, the histogram indicates the duration of hospitalization scores of studied patients. The heights of the bars within a 7-point range. This variable has a mean of 4.59 and a standard deviation of 3.31. These are followed by the shape of the fitted

distribution line found exceeded but nearly normal distribution on the duration of hospitalization parameter.

Table 2: Comparison study of pH between pre (0hr) and post-NIV (2hrs and 12hrs) treatment among patients (n = 90)

pH pre-NIV (0hr)	pH post-NIV (at 2hrs)	pH post-NIV (at 12hrs)
7.26 ± 0.16	7.32 ± 0.11	7.37 ± 0.07
	P<0.001a	P<0.001a
	P<0.001b	

a = Wilcoxon rank comparison between 0hr and 2hrs & 12hrs; b = Wilcoxon rank comparison between 2hrs and 12hrs

In the present study (Table 2), the mean ± standard deviation of pH value for pre or baseline (0hr) data was 7.26 ± 0.16 and post-NIV treatments after 2hrs (7.32 ± 0.11) and 12hrs (7.37 ± 0.07) respectively. A highly significant (P<0.001) increased value of pH was observed in post-NIV treatments (2hrs and 12hrs) when compared to baseline (0hr) in the studied patients. The comparison between 2hrs and 12hrs has also obtained a highly significant difference (P<0.001).

Table 3: Comparison study of PaCO<sub>2</sub> (mmHg) between pre (0hr) and post-NIV (2hrs and 12hrs) treatment among patients (n = 90)

PaCO <sub>2</sub> pre-NIV (0hr)	PaCO <sub>2</sub> post-NIV (at 2hrs)	PaCO <sub>2</sub> post-NIV (at 12hrs)
73.73 ± 16.73	65.37 ± 13.33	59.09 ± 14.63
	P<0.001a	P<0.001a
	P<0.001b	

a = Wilcoxon rank comparison between 0hr and 2hrs & 12hrs; b = Wilcoxon rank comparison between 2hrs and 12hrs

In the present study (Table 3), the mean ± standard deviation of PaCO<sub>2</sub> (mmHg) value for pre or baseline (0hr) data was 73.73 ± 16.73 and post-NIV treatments after 2hrs (65.37 ± 13.33) and 12hrs (59.09 ± 14.63) respectively. A highly significant (P<0.001) increased value of PaCO<sub>2</sub> (mmHg) was observed in post-NIV treatments (2hrs and 12hrs) when compared to baseline (0hr) in the studied patients. The comparison between 2hrs and 12hrs has also obtained a highly significant difference (P<0.001).

Table 4: Comparison study of PaO<sub>2</sub> (mmHg) between pre (0hr) and post-NIV (2hrs and 12hrs) treatment among patients (n = 90)

PaO <sub>2</sub> pre-NIV (0hr)	PaO <sub>2</sub> post-NIV (at 2hrs)	PaO <sub>2</sub> post-NIV (at 12hrs)
65.55 ± 19.87	79.93 ± 26.61	80.84 ± 22.62
	P<0.001a	P<0.001a
	P<0.01b	

a = Wilcoxon rank comparison between 0hr and 2hrs & 12hrs; b = Wilcoxon rank comparison between 2hrs and 12hrs

In the present study (Table 4), the mean ± standard deviation of PaO<sub>2</sub> (mmHg) value for pre or baseline (0hr) data was 65.55 ± 19.87 and post-NIV treatments after 2hrs (79.93 ± 26.61) and 12hrs (80.84 ± 22.62) respectively. A highly significant (P<0.001) increased value of PaO<sub>2</sub> (mmHg) was observed in post-NIV treatments (2hrs and 12hrs) when compared to baseline (0hr) in the studied patients. The comparison between 2hrs and 12hrs is significant (P<0.01).

Table 5: Summary statistics of BE (mmol/L) as ABG parameter for pre and post NIV treatment among patients (n = 90)

Parameter	Minimum	Maximum	Mean	Median	Std. Deviation
BE (at arrival, i.e., baseline or 0hr)	-30.00	24.00	0.47	2.80	8.12
BE post-NIV (at 2hrs)	-16.00	22.40	1.99	2.40	4.74
BE post-NIV (at 12hrs)	-13.00	16.00	1.86	2.10	3.13

The minimum and maximum values for BE (mmol/L) as ABG parameter in case of 0hr or baseline (at arrival) -30.00 and 24.00 while for post-NIV treatment at 2hrs -16.00 and 22.40 and 12hrs -13.00 and 16.00 were observed (Table 5).

Table 6: Comparison study of BE (mmol/L) between pre (0hr) and post-NIV (2hrs and 12hrs) treatment among patients (n = 90)

BE pre-NIV (0hr)	BE post-NIV (at 2hrs)	BE post-NIV (at 12hrs)
0.47 ± 8.12	1.99 ± 4.74	1.86 ± 3.13
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	<b>P&lt;0.001<sup>b</sup></b>	

a = Wilcoxon rank comparison between 0hr and 2hrs & 12hrs; b = Wilcoxon rank comparison between 2hrs and 12hrs

In the present study (Table 6), the mean ± standard deviation of BE (mmol/L) value for pre or baseline (0hr) data was 0.47 ± 8.12 and post-NIV treatments after 2hrs (1.99 ± 4.74) and 12hrs (1.86 ± 3.13) respectively. An increasing trend was observed for BE (mmol/L) value was observed in the post-NIV treatment of 2hrs without significant change, but significant change is found at 12hrs (P<0.01) when compared to baseline (0hr) in the studied patients. The comparison between 2hrs and 12hrs was observed significant change (P<0.001).

### Discussion:

In the present study, it was observed that the age range was 41-100 years. The higher frequency value (27.80%) was observed for the age groups of 51-60 years followed by age groups of 61-70 years (21.10%) and the lower frequency value (3.30%) was observed for the age groups of 91-100 years. The mean ± standard deviation of age value was 66.37 ± 13.64 years among the studied patients. The present observation found a similarity in the recent study by Atiq ul Mannan et al. in Pakistan that average value of age was 61.50 ± 10.77 years and a majority of age groups range between 60 to 80 years,<sup>15</sup> while in an earlier study by Pandey et al. in Nepal, it was observed that 66.5 years was the mean age and ranged between 42-87 years in Nepal. The study also reported that majority of patients were in the age range of 60-80 years of age.<sup>16</sup> In the present study, the findings revealed that the majority of patients were admitted in the RCU (55.4%) as compared to ICU admission (44.6%) due to AECOPD along with HRF. A recent study of Meservey et al. found that 59% of patients were admitted in ICU in the USA due to HRF,<sup>17</sup> and this value is quite high than the present study. In another study by Akyil et al. in Turkey reported that about 27.03% required ICU admission for acute HRF,<sup>18</sup> which is a comparatively lower value than the present study. In the present study, the duration of hospitalization revealed that the minimum of 1 day and a maximum of 14 days were recorded and the mean ± standard deviation of a duration of hospitalization value was 4.59 ± 3.31 days after NIV therapy. Several

researchers have emphasized that during acute HRF in patients, NIV can mitigate complications, which shortens the duration of hospital stay. According to the study by Akyil et al. in Turkey the mean duration of hospital stay especially in the wards, was  $9.2 \pm 5.2$  days,<sup>18</sup> which is a bit higher than the present study. In the present study, arterial blood gases (ABG) tensions were measured through four important parameters viz. pH, the partial pressure of arterial oxygen (PaO<sub>2</sub>), partial pressure of arterial carbon dioxide (PaCO<sub>2</sub>) and base excess (BE). These were analyzed during admission (baseline or 0hr) and post-2hrs and 12hrs of non-invasive ventilation (NIV). Several national and international studies have indicated the changes in ABG parameters after NIV therapy among hospitalized patients of AECOPD and acute HRF.<sup>16,15,19-21,18-23</sup>

In the present study, the mean  $\pm$  standard deviation of pH value for pre or baseline (0hr) data was  $7.26 \pm 0.16$  and post-NIV treatments after 2hrs ( $7.32 \pm 0.11$ ) and 12hrs ( $7.37 \pm 0.07$ ) respectively. A highly significant ( $P < 0.001$ ) improved value of pH was observed in post-NIV treatments (2hrs and 12hrs) when compared to baseline (0hr) in the studied patients. As per published NIV guidelines by the “Indian Society of Critical Care Medicine (ISCM)”, the management of AECOPD and HRF patients, pH should be maintained with a range of 7.25-7.35 for acute or acute-on-chronic respiratory acidosis and patients with AECOPD and acute HRF pH should be 7.35.<sup>21</sup> The present study has observed an elevation of pH after NIV treatment. A similarity has been observed in the earlier international studies and in India in case of a present finding of pH.<sup>15,23,18,24</sup> The present study also observed an increasing trend of PaO<sub>2</sub> (mmHg) after NIV treatment. Some similarities and beneficial impacts were observed related to the earlier studies in national and international contexts for PaO<sub>2</sub>.<sup>23,24</sup> In India, Bhattacharyya and colleagues reported  $56.37 \pm 8.01$ ,  $57.75 \pm 7.78$ , and  $59.1 \pm 7.84$  for 1hr, 4hrs and 24hrs, respectively of post-NIPPV,<sup>23</sup> which is supported with higher efficacy in the present data. The present study is observed a decreasing trend of PaCO<sub>2</sub> after NIV treatment. A similarity on reduction has been observed in the past studies internationally and India with the present finding of PaCO<sub>2</sub>.<sup>15,23,18,24</sup> In Pakistan, Atiq ul Mannan et al. reported the average PaCO<sub>2</sub> value was  $51.32 \pm 6.30$  post-NIV of 12hrs,<sup>15</sup> and in Turkey, Akyil et al. obtained PaCO<sub>2</sub> value of about  $60.0 \pm 12.6$  after 24hrs NIV treatment,<sup>18</sup> while an Indian study by Bhattacharyya et al., it was obtained  $76.3 \pm 13.56$ ,  $71.95 \pm 15.79$ , and  $67.59 \pm 18.84$  for 1hr, 4hrs and 24hrs, respectively of post-NIPPV were obtained.<sup>23</sup> Budweiser et al. reported that BE is a suitable prognostic marker to diagnose chronic HRF and survival rates in COPD and this can help in the intervention like NIPPV.<sup>25</sup> Higgins reported in his article that BE can be a positive or negative value and abnormal BE lead to metabolic acidosis ( $< -3$ ) and alkalosis ( $> +3$ ).<sup>26</sup> According to Morgan, during RF, BE resulted in higher ranges of 19.1-23.5.<sup>27</sup> The data obtained in the present study was within the standard after NIV treatment among studied patients. It is particularly important to note that the therapy by using NIV should be considered carefully in the selection of patients during the hospital stay and it is needed to monitor critically ill patients.<sup>28</sup> Moreover, NIV is used to provide therapy in the acute HRF patients with COPD and the short-term outcome is found to have good results but very less works has been observed about its long-term outcome.<sup>24</sup> Few studies have been reported mortality after hospital discharge.<sup>29,30-31</sup> Additionally, it was reported that long-duration NIV may be used as standard treatment to improve the rate of survival among patients presenting with stable hypercapnic COPD where NIV is focused to largely decrease hypercapnia.<sup>32</sup>

**Conclusion:**

Our study concluded that in the patients of AECOPD presented with acute HRF, the changes in ABG parameters such as pH, PaO<sub>2</sub>, PaCO<sub>2</sub> and BE after NIV treatment of 2hrs and 12hrs were observed in the hospital of eastern India. The respiratory management through NIV indicated significantly higher efficacy after 2hrs and 12hrs treatment among studied patients when compared to baseline data (at arrival or 0hr). In the present study, patients present in the age groups of 51-60 years were observed more susceptible and management through NIV was found to be more beneficial. Moreover, the duration of hospital stays, and ICU admission were found to have reduced in number after NIV treatment. This is a one of its kind prospective and observational study in the hospital of eastern India.

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