ORIGINAL RESEARCH

Non-invasive ventilation outcome on age and history of past mechanical ventilation

[1]Dr. Ahamed Rafad, [2]Dr. Bency K Thomas, [3]Dr. Mathew Ninan, [4]Dr. P Sukumaran

[1]Senior Resident, Department of Respiratory Medicine, Pushpagiri Institute of Medical Sciences and Research Centre, Thiruvalla, Kerala, India
[2]Assistant Professor, Department of Respiratory Medicine, Pushpagiri Institute of Medical Sciences and Research Centre, Thiruvalla, Kerala, India
[3,4]Professor, Department of Respiratory Medicine, Pushpagiri Institute of Medical Sciences and Research Centre, Thiruvalla, Kerala, India

Corresponding Author
Dr. Ahamed Rafad
Senior Resident, Department of Respiratory Medicine, Pushpagiri Institute of Medical Sciences and Research Centre, Thiruvalla, Kerala, India

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ABSTRACT

Introduction: Non-invasive ventilation (NIV) refers to the provision of ventilator support through the patient's upper airway using a mask or similar device[1]. NIV reduces the need for endotracheal intubation and improves survival. There is no hundred percent success rate with the aid of NIV for managing respiratory failure. There are instances in which management may have to be changed to intubation and invasive mode of mechanical ventilation. Some patients will hold on to NIV for initial period and may ultimately may go for endotracheal intubation. It is important to ascertain the factors associated with NIV failure so that we can identify the high-risk subset of patients who are likely to fail a trial of NIV, to prevent unnecessary mortality.

Objectives

- To determine the association between NIV outcome and age.
- To determine the association between NIV outcome and history of previous mechanical ventilator-management among patients.

Methods

80 adult patients diagnosed with Type 2 respiratory failure were included in this study, on a long observational study basis. Demographic history, physical examination and relevant investigations for type 2 respiratory failure were noted, and NIV-pressure support mode (PSV) were initiated on all patients. Ventilator was equipped with adjustable pressure limits and patients were ventilated as per the predefined inspiratory and expiratory airway pressure settings with each inspiration being triggered by patient's spontaneous breath. The interface used during the study was a well-fitting Oro-nasal mask. Subsequent adjustments were carried out according to the need of the patient and the results of blood gas analysis. All patients were given oxygen and titrated during ventilation to maintain oxygen saturation between 88%-92%. Serial ABG monitoring was done at the end of 1-2-hour, 4-6 hour and any other time if patient's condition required so. Any deterioration of pH (pH<7.25) and increase $PaCO_2$, worsening of mental status (Glasgow coma scale <8), hemodynamic instability, intolerance to NIV, all such patients were proceeded for endotracheal intubation and invasive mechanical ventilation.**Results:** No association was found between age and successful NIV outcome in this study p=0.974 (Chi-square test), whereas it was noted that patients who had a previous history of undergoing mechanical ventilation had poor outcome compared to those who hadn't P=0.002 (Fisher's exact test).**Conclusion:** From the present study it was evident that successful NIV outcome has no association with age of the patient whereas a previous history of mechanical ventilation support has a poor outcome with NIV support.

Key words:ABG-arterial blood gas, BPAP-Bi-level positive airway pressure COPD-chronic obstructive pulmonary disease, pH-potential of hydrogen, NIV-non-invasive ventilation, ETI-endotracheal intubation

INTRODUCTION

Non-invasive ventilation (NIV) is the provision of ventilator support through the patient's upper airway with the help of a mask or similar device[1]. NIV has developed from home ventilation, predominantly for the use of treatment of hypoventilation in patients with neuromuscular disease or sleep apnea. In recent years however its use has expanded to support

patients with type 2 respiratory failure due to Chronic Obstructive Pulmonary Disease (COPD). NIV has effectively been used in high dependency units and even in ward areas. NIV has revolutionized the management of acute respiratory failure, and has been applied in diverse forms of acute respiratory failure. It has been a standard treatment approach to patients with type 2 respiratory failure and is recommended as the initialintervention for most patients with Type 2 respiratory failure unlesscontraindicated.

The frequency of type 2 respiratory failure in patients with acute exacerbation of COPD varies from 16-35% with overall mortality of 35-43%. Ventilatory support through endotracheal intubation (ETI) is the standard mode of therapy, for such patients. However, ETI is associated with several complications like nosocomial pneumonia, injury to upper airways causing ulceration, bleeding and long-term complication like tracheal stenosis. Moreover, patients with COPD are prone to ventilator dependence and may have repeated weaning failures leading to requirement of tracheostomy. It is obvious that avoiding ETI in patients with acute exacerbation of COPD is the key to improving their in-hospital outcomes. To this end, NIV has been claimed to be a safe and effective alternative in patients with acute exacerbation of COPD[2-4].

Particular issues which impact on acute respiratory care and NIV in NMD are:

- Difficulties with cough and ineffective tracheobronchial secretion clearance
- Bulbar weakness-swallowing function may worsen at the time of an acute infection and/or aspiration may be the cause of or have contributed to the current infective episode.
- Upper limb weakness may make it difficult for patients to place and remove interface without assistance or communicate
- Cardiomyopathy complicates a number of neuromuscular diseases including Duchene muscular dystrophy, Emery Dreifuss muscular dystrophy and sarcoglycanopathies; left ventricular function may worsen during a chest infection or conversely an acute decompensation may be caused by the acute cardiogenic pulmonary oedema
- Patients may need high dependency unit care to manage nursing/self-care needs even if there is no acute medical indication for the admission[5].

Obesity hypoventilation syndrome (OHS) is increasingly common, with both increasing obesity and increasing severity of obstructive sleep apnoea. Although the true population prevalence is unknown, it can be demonstrated that significantnumbers of acute medical patients meet the criteria for the diagnosis of OHS, although this often goes unrecognized and untreated, even if it is recognized. Despitethe recognized morbidity and mortality of patients presenting with obesity-related acute decompensated respiratory failure, it remains underrepresented in primary research and guidelines on NIV. Approximately 50% of patients presenting with decompensated OHS will have another contributory acute pathology, such as pneumonia, heart failure, veno-thromboembolism or sepsis. The other half of these patients present with decompensated chronic respiratory failure[5].

Patients presenting with acute decompensated respiratory failure secondary to OHS can be managed successfully with NIV and this should be the preferred mode of ventilator support, with the exception of the most severely unwell or those with the other associated organ dysfunction in whom endotracheal intubation and mechanical ventilation on the ICU is mandated. It is important to acknowledge that the outcome in patients with multi-organ failure complicating decompensated ARF remains poor. Furthermore, the management of obesity-related respiratory failure with oxygen therapy alone, either at high or intermediate concentration is strongly discouraged due to the adverse effect on minute ventilation with subsequent worsening of hypercapnic respiratory failure. The strongest predictor of NIV failure in patients already established on domiciliary therapy for obesity-related respiratory failure is their previous compliance. Indeed, patients with poor adherence to home CPAP or NIV are more likely to fail a trial of acute NIV during a decompensated episode. NIV is also more likely to fail in the super-obese patient with a BMI >60kg/m^2 and in those patients who have a poor initial response to NIV. It is essential that such patients undergo a careful clinical setting which is dependent on the balance between the risk of NIV success or failure[5,6].

The application of NIV in the management of patients with acute respiratory failure is not associated with a 100% success rate. In many patients' application of NIV is clearly insufficient as it does not obtain adequate ventilation and eventually endotracheal intubation and invasive mechanical ventilation is required for the management of respiratory failure. Also, some patients will initially benefit from NIV (for hours to few days) but will then deteriorate and require intubation. The failure rates of NIV can range from 5% to 50 % in different studies depending on the etiology and severity of respiratory failure (Plant et al 2001[7], Nava and Ceriana 2004 [8]; Confalonieri et al 2005 [9]).

Failure to identify the patients who are likely to fail NIV can cause inappropriate delay in intubation; this can lead to clinical deterioration and increased morbidity and mortality. Thus, it becomes important to ascertain the factors associated with NIV failure so that we can identify the high-risk subset of patients who are likely to fail a trial of NIV.

However, there is a paucity of literature from India on NIV despite the fact this modality of treatment can assume significant relevance in resource constrained setting[10].

OBJECTIVES

The two objectives of this study were:

- To determine the association between NIV outcome and age.
- To determine the association between NIV outcome and previous history of mechanical ventilation.

MATERIALS AND METHODS

After getting permission from the Institutional Ethics Committee (No. PIMSRC/E1/388A/43/2019), a longitudinal observational study was conducted on 80 patients diagnosed with Type 2 Respiratory failure admitted to the department of Respiratory Medicine, for a period of 2 years, from November 2019 to October 2021.

All patients above 18 years of age, with diagnosed type 2 respiratory failure (PH<7.35 and $PaCO_2$>45mmHg, PaO_2<60mmHg, SpO_2<92% with 4-6 l/min oxygen by mask), who were conscious and cooperative, and on whom airway was able to be maintained, were included in this study after getting a written informed consent.

Whereas, those who were not conscious nor cooperative, in those whom airway was not able to be maintained and those who suffered from facial injuries, who had hemodynamic instability with life threatening hypoxia were excluded from this study.

NIV (pressure support mode) will be used in all patients. Ventilator is equipped with adjustable pressure limits and patient is ventilated as per the predefined inspiratory and expiratory airway pressure settings with each inspiration being triggered by patient's spontaneous breath. The interface used during the study was a well-fitting Oro-nasal mask. After explaining the details of the process of the NIPPV institution, patient was propped up to 30-degree angle. NIPPV was initiated by the investigators in all the cases. Patient were usually initiated on a pressure support (PS) and end expiratory positive airway pressure (EPAP) of8 cm H_2O and 5 cm H_2O. Subsequent adjustments were carried out according to the need of the patient and the results of blood gas analysis. All patients were given oxygen and titrated during ventilation to maintain oxygen saturation between 88%-92%.

Each patient was encouraged to use the NIV continuously. NIV was discontinued for eating and drinking. After starting treatment each patient was monitored closely. Patient's discomfort and intolerance to mask was looked for. Clinical status such as use of accessory muscles of respiration, increase or decrease of dyspnea, appearance or disappearance of cyanosis, heart rate, respiratory rate, blood pressure was monitored. Level of consciousness were also closely monitored. Continuous arterial oxygen saturation was monitored using pulse oximeter. ABG analysis done at 1–2-hour, 4-6 hour and any other time if patient's condition required so, any deterioration of pH (pH<7.25) and increase PaCO2, worsening of mental status (Glasgow coma scale <8), hemodynamic instability, intolerance to NIV, and such patients shall proceed to invasive ventilation.

All the patients received pharmacological treatment including bronchodilators, steroids, antibiotics, DVT prophylaxis, and nebulization, decided on case-to-case basis and as per the standard guidelines.

Once the patient improved clinically and corroborated by improvements in ABG, weaning was initiated. During the weaning phase, the pressure support was decreased in gradations of 2-3 cm H_2O till the inspiratory positive airway pressure was 8 cm H_2O. The application was switched over to intermittent use. Weaning failure was defined as inability to wean the patient off NIV, due to clinical features such as respiratory distress (tachypnea, tachycardia, and increased work of breathing) or laboratory evidence of worsening or persistent respiratory distress.

Data was entered in Microsoft Excel and analyzed. Categorical data was presented as frequency and percentage and continuous data such as age as descriptive statistics. Association between NIV outcome and demographic and clinical characteristics were done using Chi-square/ Fisher's exact tests. A p -value of <0.05 was considered as statistically significant.

RESULTS

A total of 80 patients who met the inclusion criteria admitted with type 2 respiratory failure during the period of November 2019-October 2021 were included in the study.

DEMOGRAPHIC

- Age of the participants ranged from 25 to 99 with a mean (SD) of 68.95 years. Age distribution is shown in Table: 1 and fig: 1. Majority (70%) were in the age group 61-80.

Table 1: Age wise distribution

Age (Years)	Frequency (*n*)	Percentage (%)
≤40	3	3.75
41-50	3	3.75
51-60	10	12.5
61-70	28	35
71-80	28	35
81-90	6	7.5
>90	2	2.5

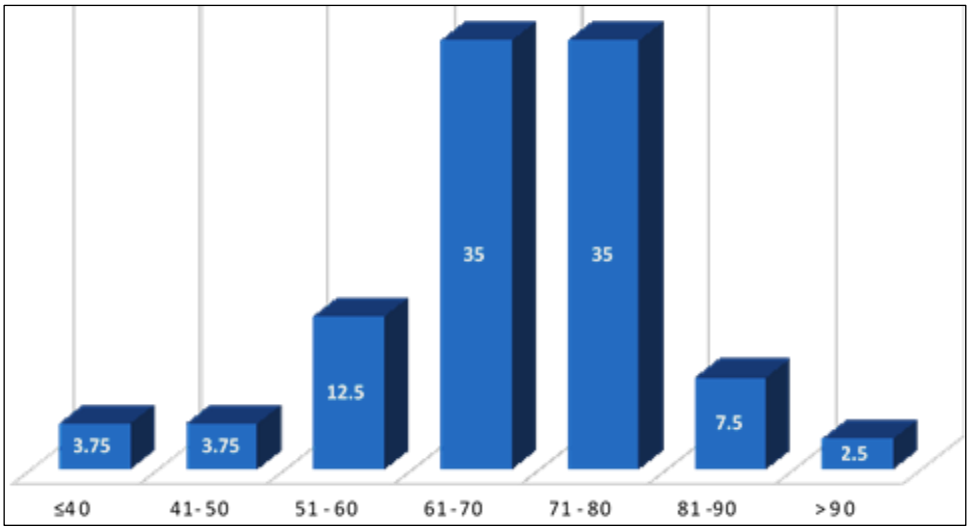

Fig 1: Age class of the study group

- The study group had a male preponderance of 68.75% as given in Table: 2.

Table 2: Gender wise distribution

Gender	Frequency	Percentage (%)
Male	55	68.75
Female	25	31.25

- Prior diagnosis given in Table: 3, fig: 3 and 76.25% had COPD

Table 3: Prior Diagnosis of Acute respiratory failure

Prior Diagnosis	Frequency	Percentage (%)
COPD	61	76.25
Asthma	15	6.25
Chest wall deformities	3	3.75
Neuromuscular abnormalities	1	1.25

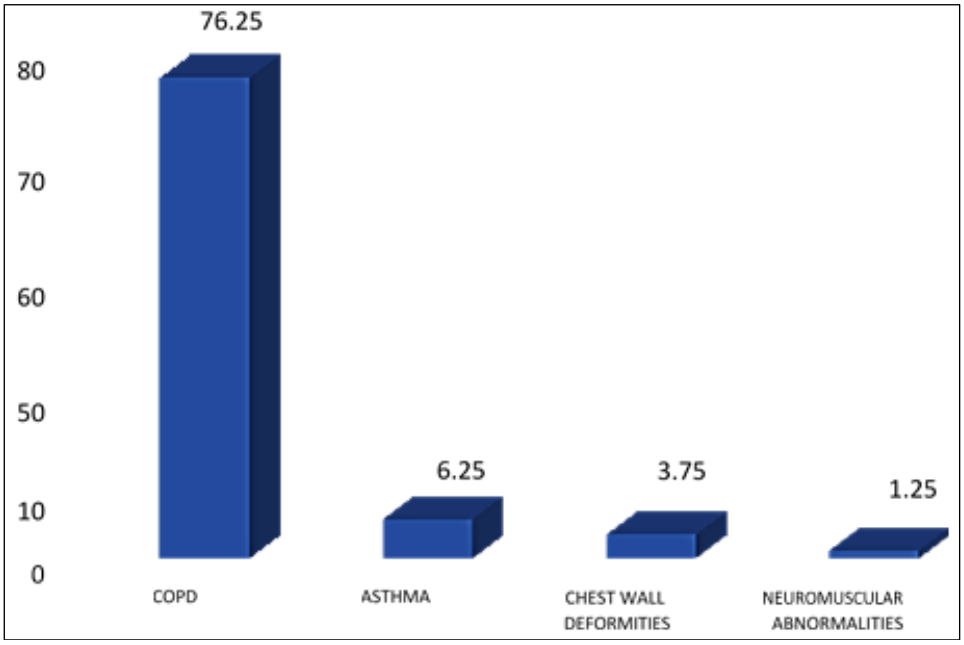

Fig 3: Prior Diagnosis of Acute respiratory failure

HISTORY OF MECHANICAL VENTILATION

Previous history of mechanical ventilation in Fig: 4. 5% of the study population had history of mechanical ventilation in the past.

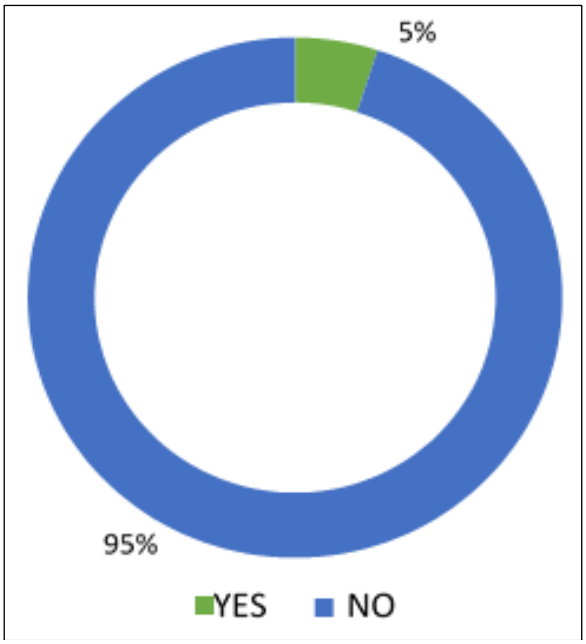

Fig 4: Previous history of mechanical ventilation

ASSOCIATION BETWEEN NIV OUTCOME AND DEMOGRAPHIC DATA

Association between NIV outcome and different age group are depicted intable: 4.

Table 4: Association between NIV outcome and age of the study participants

Age (Years)	Success (%)	Failure (%)	Total
<40	2 (66.7)	1 (33.3)	3
41-50	3 (100)	0	3
51-60	8 (80)	2 (20)	10
61-70	21 (75)	7 (25)	28
71-80	21 (75)	7 (25)	28
81-90	5 (83.3)	1 (16.7)	6
>90	2 (100)	0	2
Total	62	18	80

No association between age and NIV outcome noted in this study group. p=0.974 (Chi-square test).

ASSOCIATION BETWEEN NIV OUTCOME AND PREVIOUS HISTORY OF MECHANICALVENTILATION

Association between NIV outcome and previous history of mechanical ventilation depicted in table: 5.

Table5: NIV outcome in patients with previous history of Mechanical Ventilation

History of Mechanical Ventilation	Outcome Success (%)	Outcome Failure (%)	Total
Yes	0	4 (100)	4
No	62 (81.6)	14 (18.4)	76

As evident above patients with past history of mechanical ventilation had shown poor outcome as compared to another group. The difference was statistically significant, P=0.002 (Fisher's exact test).

DISCUSSION

A study by Singh V K *et al.* [11], A total of 50 patients with type2 respiratory failure put on NIV. The study cohort had a male preponderance (43/50) with a mean age of 62.36 years[12]. The most common symptom on presentation was breathlessness which is seen in all the patients.

In this cohort study, most common clinical diagnosis was COPD exacerbation (95%) with or without

associated co-morbidities. The success rate with NIV was 84% with 42 patients weaned successfully off NIV in this study.[4] Mean age of the patients who failed NIV was significantly higher than those who succeeded. ABG pH value on admission was significantly lower and $PaCO_2$ value at admission was significantly higher in patients who failed NIV.

A study by N Ambrosino *et al.* [13], Aim of the study was to identify simple parameters to predict the success of the NIV use in the treatment of acute respiratory failure in COPD, retrospectively review the data of 47 patients with COPD undergoing fifty nine consecutive episodes of acute respiratory failure. All were chronically hypoxemic and hypercapnic and on long term oxygen therapy. NIV initiated in patients who had undergone acute relapses of their primary disease and developed type 2 respiratory failure.

Non-invasive mechanical ventilation was considered successful when patients reached levels of pH >7.35 during spontaneous breathing without further worsening of neurological signs, and with improvement in tachypnea and in abdominal paradox for at least 48 hours. Failure of non-invasive mechanical ventilation was defined by the need for endotracheal intubation according to the judgement of the physician in charge or death during non-invasive mechanical ventilation.

Comparison of differences of successful versus unsuccessful treatment was performed using a 'Student unpaired t test' with p<0.0.5 being considered significant. Comparison of baseline data with those recorded during non-invasive mechanical ventilation was performed using a 'paired t test', a 'p'value of <0.05 being considered significant. The predictive models were developed using discriminant analysis.

Non-invasive mechanical ventilation was successful in 46 episodes of acute respiratory failure (78%). The overall mortality was 8.5% (four of 47 patients). Three patients died during non-invasive mechanical ventilation, endotracheal intubation not having been offered. In one of them the cause of acute respiratory failure was pneumonia.

The most frequent cause of acute respiratory failure in all patients was an exacerbation of COPD without clinical or radiological signs of pneumonia. Clinical, radiological, and laboratory evidence of pneumonia was found in 38.5% of episodes of acute respiratory failure unsuccessfully treated with non-invasive mechanical ventilation, but only in 8.7% of those successfully treated. Patients in whom non-invasive mechanical ventilation was unsuccessful were significantly underweight in comparison with those in whom non-invasive mechanical ventilation was successful.

Unsuccessful non-invasive mechanical ventilation was associated with reduced body weight expressed both as absolute and as percentage of ideal body weight. The association between malnutrition and COPD has been recognized for many years. Factors related to nutritional status are considered as an independent influence on the course of COPD.

Failure of non-invasive mechanical ventilation was associated also with a worse neurological status and reduced compliance with treatment. The importance of a compromised neurological status is easy to understand in view of the need for cooperation required to perform non-invasive mechanical ventilation.

The results suggest that non-invasive ventilation should be instituted early in every patient before a severe acidosis ensues.

The use of non-invasive ventilation has markedly increased for the past two decades and non-invasive ventilation has now become an integral tool in the management of both acute and chronic respiratory failure in both at home setting and in the critical care unit. Non-invasive ventilation has been used as a replacement for invasive ventilation as its flexibility also allows it to be a valuable complement in patient management. The role of NIV has been studied and was found to be more useful as an effective therapeutic modality along with other standard treatment.

Non-invasive ventilation is a cost effective, readily available technique and can be used readily outside the intensive care settings.The advantages of non-invasive ventilation include patient comfort, preservation of airway defences like cough, ability to speak and eat. The complications of endotracheal intubation such as nosocomial pneumonias, injury to airways, aspiration and post intubation laryngeal stenosis could be avoided.

In our study mean age of the study participants is 68.95 (12.17) years. Most of the people were in the 61-80 years age group accounting for 70%. There is no association between NIV outcome and age of the individuals in the study group.

Table 6: Comparison of age distribution with other authors

Studies	Number	Age (years)
Present study	80	68.95± 12.17
Agarwal *et al.* [10]	63	45.7±16.6
Khilnani GC *et al.* [14]	40	57.25±10.09

In the study conducted by Agarwal *et al.* [10] the mean age of the study participants w a s 45.7±16.6, which was lower when compared to the present study.

In the study conducted by Khilnani GC *et al*. the mean age of the study participants was 55.25±10.09 of which the mean age of the patients who were

randomized to give NIV was 60±11.07 years, which was also comparable to the present study[14].

In a study by Aylin Ozsancak Ugurlu *et al*.,reported that NIV success is similar in different age groups (younger (18-44 y); middle-aged (45-64 y); elderly (65-79 y) and aged (≥ 80 y)[15].

In a study by Alexandru *et al*. older patients required more days ofNIV and a longer length of hospital stay, had a more severe functional impairment and required higher inspiratory pressures but had the same outcome (i.e., NIV failure and in-hospital mortality) as younger patients[16].

This result confirms findings and supports the current recommendation for NIV support regardless of age in type 2 respiratory failure.

In the present study out of 80 people studied, 55 (68.75%) were males and 25 (31.25%) were females, showing a male preponderance.

Table 7: Comparison of sex distribution with other authors

Sex	Present study	Agarwal *et al.* [10]	Khilnani GC *et al.* [14]
Male	55(68.75%)	40 (63.5%)	31(77.5%)
Female	25 (31.25%)	23(36.5%)	9 (22.5%)

This is comparable to the study by Agarwal *et al.* [10] in which 40 (63.5%) were males and 23 (36.5%) were females out of the 63 patients participated.

Khilnani GC *et al.*[14] study also contains 40 patients of which 31 were males (77.5%) and 9 (22.5%) were females, of which 20 were randomized for NIV therapy in which 15 (75%) were males and 5 (25%) were females. The present study was comparable to this study.

This difference in the sex distribution in various studies could be attributed to the outgoing nature (getting exposure to outdoor pollution) and the more prevalence of smoking in males than females in Indian scenario and further care providers do have a gender bias that may affect overall management. Even, the physicians have tendency to classify women as having asthma and men as having COPD despite similar medical histories.

In the present study we found 14 patients having previous history of mechanical ventilation for type 2 respiratory failure, we found a statistically significant poor outcome in patients with previous history of mechanical ventilation.

A study by J.Khatri *et al*., also shows poor NIV outcome (42.86%) in patients with previous history of mechanical ventilation[17].

In our study group, 18 patients eligible for home BPAP and were discharged with home BPAP, Suggesting the use of home BPAP in stable chronic hypercapnic respiratory failure.

In a study by Wang Z *et al*.,Home BPAP was associated with both a statistically and clinically significant reduction in mortality in patients with COPD, fewer hospitalizations, fewer intubations, reduced dyspnea and no change in quality of life. For patients with Thoracic restrictive disease, neuromuscular disease, Obesity hypoventilation and other lung diseases, Home BPAP was also associated with improved exercise tolerance, improved quality of life, reduced dyspnea, improved sleep quality, and shorter length of hospital stay in individual populations[18].

STRENGTHS OF THE STUDY

- The prospective nature of the study.
- The study sample which is relatively large when compared with some of the other Indian studies.
- Since it is a tertiary care Centre study the transition from non-invasive ventilation to invasive mechanical ventilation could be done easily.

LIMITATIONS OF THE STUDY

- The study did not have a control group which had impact on the statistical analysis of group differences.

CONCLUSION

This study which was conducted in a tertiary care hospital, in South Kerala, included 80 patients diagnosed with Type 2 respiratory failure, based on longitudinal observational study pattern. The duration was from November 2019 to October 2021. This study was conducted with an objective to assess Non-invasive ventilatory outcome with age and previous history of mechanical ventilation support. At the end of the study, it was observed that, there was no association between age and NIV outcome noted in the study group; p=0.974 (Chi-square test). Whereas, patients with past history of mechanical ventilation had shown poor outcome as compared to the other group. The difference was statistically significant, P=0.002 (Fisher's exact test).

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