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Study of Indications, Associated Comorbid Conditions and Outcome of Patients Requiring Bi-level Type of Non-Invasive Positive Pressure Ventilation in a Tertiary Care Hospital

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Abstract

BiLevel non-invasive positive pressure ventilation (BiPAP) is the most utilised supportive treatment in the world of medicine for respiratory failure. COPD is the most common indication for its use. We investigated the indications and effects of comorbidities on BiPAP outcomes because there have been few studies on it. It is a descriptive, observational, cross-sectional study conducted over period of 12 months, wherein 60 patients fulfilling the inclusion criteria for the requirement of BiPAP were included in the study and evaluated. The indications, associated comorbid conditions and the outcomes of NIV therapy were studied. COPD exacerbation with Type II Respiratory failure was the most common indication (71.4%), followed by asthma [near fatal/severe] (21.4%). Success with BiPAP in COPD was 67.6% . In COPD patients with co-morbidities, success came down to 47.4%. Pneumonia, ILD & Cardiogenic Pulmonary Edema (CPE) had success rates of 0%, 16.7% and 66.7% respectively with BiPAP therapy,with higher mortality rates for pneumonia and ILD. Comorbidities were present in 51.7% of patients and Hypertension (35%) and Diabetes Mellitus (21.7%) were the most common. In patients who had co-morbidities, the mean hospital stay was 12 days, which was higher than the mean hospital stay of 9.3 days in patient with no co-morbidities. The presence of co-morbidities was associated with higher failures with BiPAP (51.6%) comapred to ones with no co-morbidities (13.8%) (p value <0.05). Higher respiratory rate (>28/min), lower ABG pO2, pCO2 and bicarbonate levels and higher blood glucose and total leucocyte counts were associated with higher BiPAP failures and mortality. The conclusion was that the most common indication of BiPAP was a COPD exacerbation with type II respiratory failure and presence of comorbidities led to a poorer outcome with prolonged hospital stay. ABG parameters, blood glucose levels and total leucocyte counts has an effect on NIV outcome and mortality.

Keywords: indications, comorbidities and outcomes, bilevel positive airway pressure ventilation

INTRODUCTION

Assisted ventilation is an integral part of critical care which has significantly improved the outcome of patients. It is of two types – Invasive and Non-invasive. Conventional invasive mechanical ventilation is

associated with several complications, a large portion of which are related to endotracheal intubation. Non-invasive ventilation refers to provision of provision of inspiratory pressure support plus positive end expiratory pressure (PEEP) via a nasal or face mask. The use of NIV therapy in selected patients with acute respiratory failure is associated with significantly reduced need for endotracheal intubation and ventilation. A major driving force behind the increasing use of non-invasive ventilation has been the desire to avoid the complications of invasive ventilation. Although invasive mechanical ventilation is highly effective and reliable in supporting alveolar ventilation, endotracheal intubation carries well-known risks of complications. NIV is mostly used for hypercapnic acute respiratory failure but there are evidences that show benefit in hypoxaemic respiratory failure too. However, the evidence of use of NIV remains strongest in patients with hypercapnic respiratory failure due to exacerbation of COPD. The use of NIV in hypoxaemic respiratory failure is however controversial. Two recent meta-analysis of randomized control trials found no robust evidence to support the role of NIV in hypoxaemic respiratory failure and acute lung injury. In a meta-analysis it has been shown that NIV has reduced the mortality in a patient of ARF due to cardiogenic pulmonary oedema.[1]

MATERIALS AND METHODS

This Descriptive, Observational, Cross-sectional study was carried out in the department of Respiratory Medicine, RG Kar Medical College and Hospital Indoor, wherein 60 patients requiring BiLevel type of non-invasive positive pressure ventilation from April 2020 to April 2021 were included in the study.

Inclusion criteria for study*:* In patients with Acute Respiratory Failure (COVID-19 RTPCR- negative) defined by the presence of following criteria: (A+B or A+ C or D)

A) Patients with clinical symptoms and signs of acute respiratory distress such as severe dyspnea, respiratory rate >30 breaths/min, use of accessory muscles of respiration, presence of paradoxical movement of the abdomen, retraction of intercostal spaces.

B) ABG analysis showing pH< 7.35 with PaO2/FiO2 <300 mmHg or PaO2 <60 mmHg while the patient was breathing room air

C) ABG analysis showing respiratory acidosis (arterial pH < 7.35 and/or $PaCO2 \geq 45$mm Hg)

D) Patient received NIV for early weaning after extubation

Exclusion criteria for study Non cooperative/ agitated patient, patient unwilling to give consent, obtunded patient/coma, recent facial/upper airway trauma or burns, facial deformity, poor cough reflex , undrained pneumothorax , upper gastrointestinal breathing, upper airway obstruction

After inclusion into this study, the patients will be evaluated as mentioned below:

A. Detailed history taking and clinical examination

B. Baseline and other investigations as deemed necessary during the study as mentioned below

Baseline- Blood investigations-- Hb%, Total leucocyte count, Differential count, Platelet count, Fasting and post prandial glucose, Random glucose, HBA1C, Urea, Creatinine, Liver function test, electrolytes, arterial blood gas analysis (most crucial parameters)

Radiological investigations -Chest Xray PA view (or lateral view if needed), CECT Thorax (if required), USG Thorax (if required), pulse oximetry, COVID-19 RTPCR report

Descriptive statistics was done by using mean and standard deviation and frequency distribution tables and then inferential statistics was done according to what is needed, using latest version of SPSS software.

RESULTS

A total of 420 admissions took place during the study period in Respiratory Care Unit (RCU) and Indoor ward, and out of them 60 patients required BiLevel type of Non-Invasive Positive Airway Pressure (BiPAP) ventilatory support during admission and during stay in hospital for varied etiologies resulting in acute respiratory failure and were enrolled for the study

Mean Age of the study group was 59.23 yrs (S.D- 13.24 yrs)

- The number of the males in the study were greater and M:F ratio was 1.4:1. Patients with Type II respiratory failure (70%) were greater than with Type I respiratory failure (30%).
- The overall BiPAP success in preventing IMV was 66.7%. The success rate was higher in patients with Type II RF (83.3%) when compared to Type I RF (27.7%). The patient mortality was higher in Type I RF (66.7%) than Type II RF (14.3%). Overall BiPAP failure of the study was 33.3%. Overall mortality in the study was 30%.
- Amongst Type II RF, COPD exacerbation was the most common underlying disease (71.4%), followed by asthma [near fatal/severe] (21.4%).
- Success with BiPAP in COPD was 67.6% and in asthma was 100%. When COPD patients had associated co-morbidities, BiPAP success came down to 47.4%.
- Amongst Type I RF, Pneumonia, Diffuse Parenchymal Lung Disease (DPLD) & Cardiogenic Pulmonary Edema (CPE) had 6 cases each and had success rates of 0%, 16.7% and 66.7% respectively with BiPAP therapy. Pneumonia had no success and CPE had the best success rate.
- Patients who had underlying co-morbidities had higher death rates of 45.2%, when compared to those without co-morbidities- 13.8% (p value < 0.05)
- Mortality rates were higher for patients presenting with Pneumonia (83.3%) and DPLD (83.3%) being treated by BiPAP. COPD (20%) and CPE (33.3%) had relatively lower mortality rates. All 9 patients with Asthma survived and were henceforth discharged (100% survival). 1 such patient of asthma had allergic bronchopulmonary aspergillosis. (ABPA)
- In this study population, out of 60 patients, comorbidities were present in 31 patients (51.7%). Hypertension (HTN) and Diabetes Mellitus (T2DM) were the most common with prevalence of 35% and 21.7% respectively among subjects. Ischaemic heart disease (IHD) and chronic kidney disease (CKD) were present in 8.3% and 5% of patients, respectively. Chronic liver disease (CLD) and hypothyroidism were present in 1 subject each.
- The presence of co-morbidities was associated with higher failures with BiPAP (51.6%) comapred to ones with no co-morbidities (13.8%). Statistical significance was found. (p value <0.05)
- Deaths were seen more in patients with Type I RF (66.7%) when compared to Type II RF (14.3%) (p-value <0.05).
- Average BiPAP duration in patients who had success (66.7% of total) was 6.7 days.
- Higher respiratory rates (RR) >28/min were associated with higher BiPAP failures and patient deaths. (p-value <0.05)
- Lower ABG pO_2 values < 42 mmHg were associated with greater failures with BiPAP and patient mortality (p-value <0.05). Higher pCO_2 values >58mmHg were associated with greater BiPAP success and gradual reduction in those values leading to patient survival (p-value <0.05). ABG HCO_3^- values lower than 27 meq/L was associated with higher failures (p-value <0.05). However, ABG pH values did not have a significant impact on BiPAP and patient outcome.

- Mean CBG of 60 patients at presentation in the study was 151.2 mg/dl. Patients with CBG > 200mg/dl had BiPAP failures rate as high as 76.9%, with maximum failures at CBG >250mg/dl. Patients who had CBG<200 mg/dl had failure rate of only 21.2%, i.e, higher the CBG values, higher are the chances of BiPAP failure. (p value <0.05).
- Mean WBC count (TC) of 60 patients was 15,197/microl. It was seen that in patients with TC >15,000/microl, the chances of BiPAP failure was 56.7% compared to 13.3% in patients with TC <15,000/microl, i.e., higher the TC, higher are the chances of BiPAP failure. (p-value <0.05).
- CBG values (in mg/dl) had a positive correlation (coefficient +0.53) on the duration of hospital stay, i.e., higher is the CBG value, higher is the number of days of hospital stay.
- Total WBC counts per microl (TC) had a positive correlation (+0.53) on the duration of hospital stay, i.e., higher is the TC value, higher is the number of days of hospital stay
- In 42 patients who survived, mean hospital stay was 12.4 days. In patients who had co-morbidities, the mean hospital stay was 12 days, which was higher than the mean hospital stay of 9.3 days in patient with no co-morbidities.

TABLE 1- BASELINE PARAMETERS

PARAMETERS	VALUE
MEAN AGE	59.23 YEARS
GENDER MALE FEMALE	 58.3% (35) 41.7% (25)
RESPIRATORY FAILURE TYPE I TYPE II	 30% (18) 70% (42)
COMORBIDITIES PRESENT ABSENT	 51.7% (31) 48.3% (29)
NIV OUTCOME SUCCESS (PREVENTING IMV) FAILURE	 66.7% (40) 33.3% (20)
RESPIRATORY RATE (per min)	27
TOTAL WBC COUNTS (TC) (per microL)	15,917
CAPILLARY BLOOD GLUCOSE (CBG) (in mg/dl)	151

TABLE 2--DISTRIBUTION OF PATIENTS BASED ON UNDERLYING DISEASE

CO-MORBIDITY	FREQUENCY	PERCENTAGE
HYPERTENSION (HTN)	21	35%
DIABETES MELLITUS (T2DM)	13	21.7%
CHRONIC KIDNEY DISEASE (CKD)	3	5%
ISCHAEMIC HEART DISEASE (IHD)	5	8.3%
CHRONIC LIVER DISEASE	1	1.7%
HYPOTHYROIDISM	1	1.7%

TABLE 3--CO-MORBIDITY DISTRIBUTION

UNDERLYING DISEASE	FREQUENCY	PERCENTAGE
COPD	30	50
ASTHMA	9	15
CARDIOGENIC PULMONARY EDEMA (CPE)	6	10
PNEUMONIA	6	10
DPLD	6	10
CONGENITAL KYPHOSCOLIOSIS	1	1.7
GUILLAIN-BARRE SYNDROME	1	1.7
MYASTHENIA GRAVIS	1	1.7
TOTAL	**60**	**100**

TABLE 4A--NIV OUTCOME ANALYSIS

PARAMETERS	SUCCESS	FAILURE	p-value
Sex Male Female	 74.3% (26) 56% (14)	 25.7% (9) 44% (11)	 0.22
Respiratory Failure Type I Type II	 27.7% (5) 83.3% (35)	 72.3% (13) 16.7% (7)	 0.0003
COPD	67.6% (23)	32.4% (11)	0.049
CARDIOGENIC PULMONARY EDEMA	66.7% (4)	33.3% (2)	0.05
ASTHMA	100% (9)	0	0.05
PNEUMONIA	0	100% (6)	0.001
DPLD	16.7% (1)	83.7% (5)	0.02
COMORBIDITIES PRESENT ABSENT	 48.4% (15) 86.2% (25)	 51.6% (16) 13.8% (4)	 0.036
T2DM PRESENT	 30.8% (4)	 69.2% (9)	 0.016

ABSENT	76.6% (36)	23.4% (11)	
HYPERTENSION			
PRESENT	42.9% (9)	57.1% (12)	0.025
ABSENT	79.5% (31)	20.5% (8)	
IHD			
PRESENT	40% (2)	60% (3)	0.4
ABSENT	69.1% (38)	30.9% (17)	
CKD			
PRESENT	0	100% (3)	0.059
ABSENT	70.2% (40)	29.8% (17)	
CLD			
PRESENT	100% (1)	0	1
ABSENT	66.1% (39)	33.9% (20)	

TABLE 4B--NIV OUTCOME ANALYSIS (contd.)

PARAMETER	p-value	COMMENT
AGE	0.000017	Higher the age(>60yrs), more is the chance of failure with NIV
RESPIRATORY RATE	0.02	Higher the respirate rate, more is the chance of failure with NIV
ABG PARAME-TERS		
pH	0.59	No correlation of pH with NIV outcome
pO2	0.0002	Lower the pO2, more is the chance of failure with NIV
pCO2	0.008	Lower the pCO2, more is the chance of failure with NIV
HCO3-	0.001	Lower the HCO3-, more is the chance of failure with NIV
CAPILLARY BLOOD GLU-COSE	0.00006	Higher the CBG (>200mg/dl), more is the chance of failure with NIV
TLC	0.0001	Higher the TLC (>15000/cmm), more is the chance of failure with NIV

TABLE 5--IMPACT OF CO-MORBIDITIES ON THE BiPAP (NIV) OUTCOME

CO-MORBIDITY	SUCCESS	FAILURE
PRESENT (n=31)	48.4% (15)	51.6% (16)

ABSENT (n=29)	86.2% (25)	13.8% (4)

Test of significance	p-value
Chi-square test	0.036

FIGURE 1 - BARPLOT SHOWING INTERNAL COMPOSITION OF BIPAP OUTCOME

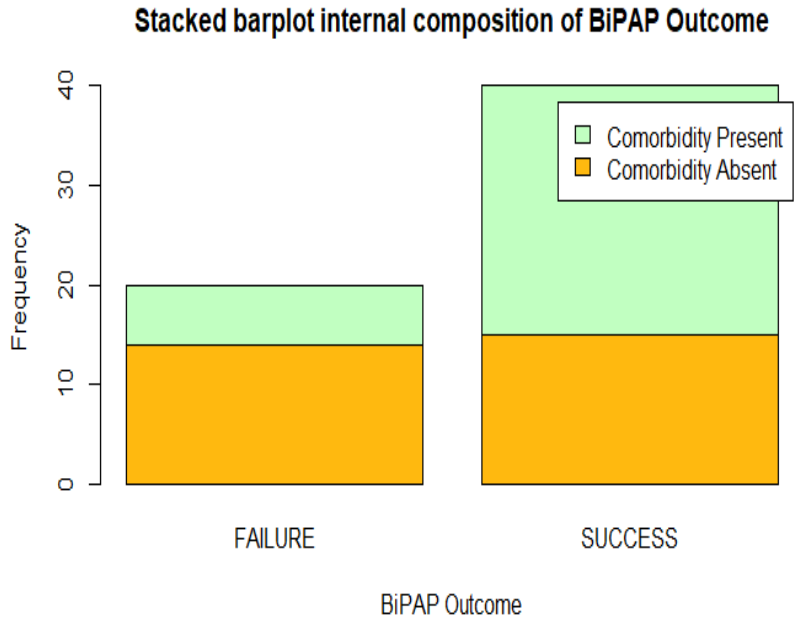
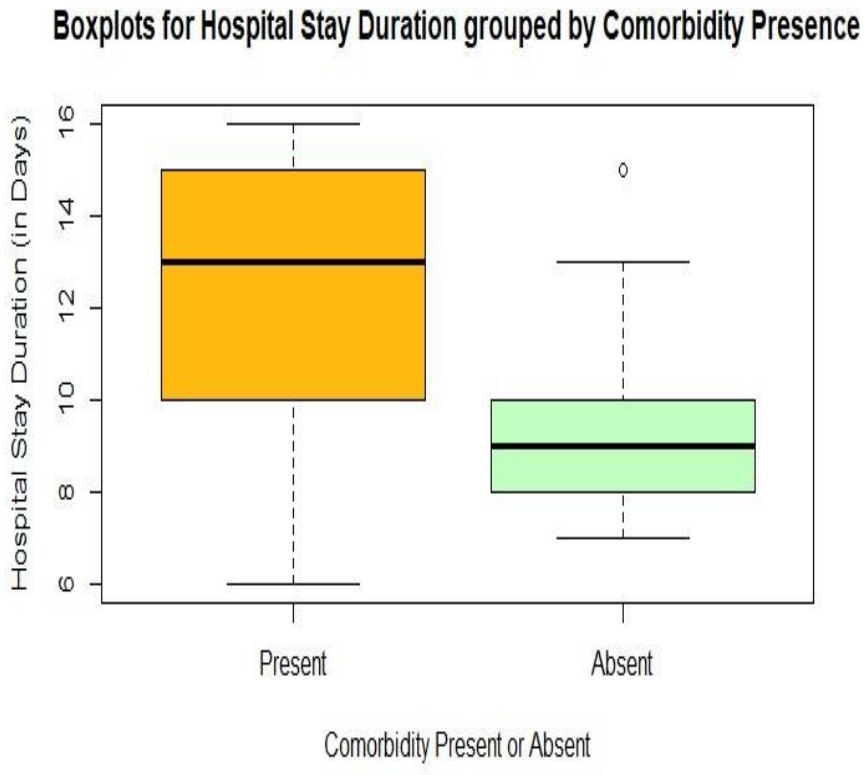


TABLE 6--EFFECT OF CO-MORBIDITIES ON DURATION OF HOSPITAL STAY

CO-MORBIDITY	HOSPITAL STAY (in days)	
	MEAN	MEDIAN
PRESENT (n=17)	12	13
ABSENT (n=25)	9.3	9

Test of significance	p-value
T- test	0.0043

FIGURE 2-BOXPLOT SHOWING HOSPITAL STAY (IN DAYS) GROUPED BY PRESENCE OF COMORBIDITIES



DISCUSSION

Non-invasive ventilation (NIV) has assumed an important role in the management of respiratory failure in acute-care hospitals . It is likely that NIV rests the respiratory muscles and reduces pulmonary micro-atelectasis by the positive pressure it generates. In COPD, NIV likely produces improvement by partly offsetting auto-PEEP and reducing the work of breathing. Although the use of NIV in several forms of acute respiratory failure (ARF) has been validated, the goals of NIV in many of these situations are disparate.

In type I respiratory failure, the aim is to decrease hypoxemia until the process responsible for ARF has resolved.

Keenan SP, Sinuff T, Cook DJ et al[7] showed that patients with acute hypoxemic respiratory failure are less likely to require endotracheal intubation when NPPV is added to standard therapy. However, the effect on mortality is less clear, and the heterogeneity found among studies suggests that effectiveness varies among different populations. As a result, the literature does not support the routine use of NIPPV in all patients with acute hypoxemic respiratory failure. In our study too , the success rate was higher in patients with Type II RF (83.3%) when compared to Type I RF (27.7%). The patient mortality was higher in Type I RF (66.7%) than Type II RF (14.3%)

The beneficial effects of positive pressure have long been known in patients with acute pulmonary edema. It improves compliance and oxygenation by increasing functional residual capacity and opening collapsed air spaces. For patients with pulmonary edema, CPAP should be the noninvasive modality first offered; NIV can be subsequently used if work of breathing remains high or if CO2 retention is

problematic.[14] In our study too CPE had the best success rate amongst patients with Type 1 Respiratory failure.

There are no large prospective studies looking at the impact of NIV on IPF with acute hypoxaemic respiratory failure. A recent retrospective study by Vianello *et al*. showed the overall poor outcome of NIV, with more than 50% needing intubation and all they died in hospital.[17] In our study too the success rate of NIV therapy was low (16.67%).

The evidence is weak for the use of NIV in asthma patients with ARF.

A subsequent randomized pilot study in 33 patients with acute asthma, but not ARF showed improved flow rates and decreased hospitalizations with NIV versus sham NIV.[18] .

However, a Cochrane analysis by Ram *et al*. concluded that large RCTs are needed before recommending NIV use in status asthmaticus.[19] Pallin et al elucidated that NIV can be safely used in acute severe asthma although further work is needed to delineate the precise patient selection process.[30]

Sangeeta Mehta, Nicholas S. Hill1 showed in a study that patients with exacerbations of COPD constitute the largest single diagnostic category among reported recipients of NPPV with success rates in avoiding intubation have ranged from 58 to 93%.[21] In our study, success with BiPAP in in asthma was 100%, however the number of patients were only 9.

Agarwal R, Gupta R, Aggarwal AN et al[11] conducted a study in which during the study period, 248 patients were admitted in the ICU and of these 63 were given NIPPV therapy. The clinical improvement was faster in ARF due to COPD than in ARF due to other causes. The mean hospital stay and mortality were similar in the two groups. In our study amongst Type II RF, COPD exacerbation was the most common underlying disease (71.4%). Success with BiPAP in COPD was 67.6% and when associated with co-morbidities, BiPAP success came down to 47.4%.

B Chakrabarti, RM Angus, S Agarwal et al[24] showed that in acute decompensated ventilatory failure complicating COPD, hyperglycemia upon presentation was associated with a poor outcome. Baseline respiratory rate and hyperglycemia are as good at predicting clinical outcomes as the APACHE II score.

Abigail Bishopp, Nadia Sayeed, Biman Chakraborty et al[25] showed in a study that that the presence and severity of chronic kidney disease has no influence on the duration of NIV required in acute hypercapnic respiratory failure.

Nicholas Lane, Tom Hartley, John Steer et al[26] showed that cardiovascular disease in patients with COPD is prevalent and in patients requiring NIV mortality is higher with increasing comorbidity. In LVSD lack of ACEi/ARB therapy on admission was associated with higher mortality.

Raffaele Scala, Mario Naldi, Sandra Bartolucci et al[27] in a study showed that Chronic and acute co-morbidities are common in COPD patients AHRF needing NIPPV and their presence influences short and longer-term outcome.

A S Sandhya, Brijesh Prajapat, Deepak Talwar[28] showed in a study that NIV was equally successful in COPD with Acute exacerbation with hypercapnic respiratory failure with comorbidities with nearly same outcome

in NIV failure cases. In our study, the presence of co-morbidities was associated with higher failures with BiPAP (51.6%) comapred to ones with no co-morbidities (13.8%). Statistical significance was found. (p value <0.05)

CONCLUSION

In this observational study of patients receiving BiLevel (BiPAP) type of Non-Invasive Ventilation, it was found to be a useful mode of management in type II respiratory failure of various etiologies, COPD being the most common one with high success and mortality prevention. BiPAP was also found to be successful in cases of asthma (near-fatal) with type II respiratory failure after proper patient selection with high success and mortality prevention.

BiPAP can also be used in type I respiratory failure in some selected cases and chances of failure are substantial like as in pneumonia and DPLD but except in cases of cardiogenic pulmonary edema (CPE), where BiPAP proved to be highly successful.

Higher respiratory rates (>28), lower pO2 (<42mmHg), lower pCO2 (<58mm Hg) , lower bicarbonate (<27 meq/l), capillary blood sugar >200mg/dl and total leukocyte count (>15,000/) µL is associated with NIV failure and higher mortality. Higher CBG and total leucocyte counts were also associated with prolonged hospital stay, so these parameters need to kept in mind in patients being treated with BiPAP.

Presence of co-morbidities especially, hypertension and type 2 diabetes mellitus were associated with higher BiPAP failure, increased mortality and prolonged hospital stay.

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