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Original Research Paper

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TO STUDY PARAMETERS CO-RELATING OUTCOME OF NON-INVASIVE VENTILATION IN ACUTE RESPIRATORY FAILURE

Sanchit Mohan*	MD, DNB, EDARM Pulmonary Medicine,Assistant Professor, Grant Government Medical College, Mumbai. *Corresponding Author
Vishwanath Pujari	MD, DNB Pulmonary Medicine, Associate professor, Grant Government Medical College, Mumbai.
Priti Meshram	MD, DNB Pulmonary Medicine, Head of the Department, Grant Government Medical College, Mumbai.

ABSTRACT **Background:** Respiratory failure is a condition in which the respiratory system fails in one or both of its gas-exchanging functions- oxygenation of pulmonary arterial blood and carbon dioxide elimination from mixed venous blood. NIV is used as a replacement for invasive ventilation in a few conditions, and its flexibility also allows it to be a valuable component in patient management. Its use in acute respiratory failure is well accepted and widespread. **AIM:** This study was conducted to study various parameters such as baseline PCO2 levels, pH, PO2 levels, Heart rate, respiratory rate, and their correlation with the outcome of Non-invasive Ventilation. **Methods:** This is a prospective observational study conducted on 100 patients admitted with either Type-I or Type -II respiratory failure. Results: Respiratory rate <30, Heart rate <130, PCO2 45-70 are associated with good outcomes of Non-invasive ventilation. Type of respiratory failure, sputum aerobic culture are not predictors of NIV outcomes. **Conclusion:** NIV in acute respiratory failure, irrespective of the type of respiratory failure helps in improving gas exchange, reduces intubation and length of hospital stay hence, its use as the first modality of treatment in patients without overt contraindications is recommended. Overall, NIV is safe and effective in patients with acute respiratory failure as there are no major complications associated with its use.

KEYWORDS : Respiratory failure; ABG correlation; Clinical correlation

INTRODUCTION:

Respiratory failure is a condition in which the respiratory system fails in one or both of its gas-exchanging functions- oxygenation of pulmonary arterial blood and carbon-dioxide elimination from mixed venous blood.

The normal partial pressure reference values are: oxygen > 80 mmHg, and carbon-dioxide < 45 mmHg.

The definition of respiratory failure is PO2 < 7kPa (55mmHg). Respiratory failure occurs when gas exchange at the lungs is sufficiently impaired to cause:

- Type I - low oxygen (with normal or low carbon-dioxide)
- Type II - low oxygen, with high carbon-dioxide i.e., PCO_2 > 45mmHg

It may be acute or chronic. Acute respiratory failure is characterized by life-threatening deranged arterial blood gases and acid–base status. Chronic respiratory failure is more indolent and may be clinically inapparent.[1]

Noninvasive ventilation (NIV) refers to the administration of ventilatory support without using any invasive artificial airway (endotracheal tube/tracheostomy tube). Its use in acute respiratory failure is widespread. The role of noninvasive ventilation in chronic respiratory failure is not clear and remains undefined. Guidelines suggest more favorable outcomes when used in patients with chronic obstructive pulmonary disease (COPD) and cardiogenic pulmonary oedema,[2] The use of NIV using nasal masks at night is a widely accepted standard method for patients with chronic hypercapnic respiratory failure caused by chest wall deformity, neuromuscular disease, or impaired central respiratory drive.[3,4]

The advantages of Non-invasive ventilation over endotracheal intubation are obvious. Speech, airway defense mechanisms and swallowing functions remain intact. Limitations are- lack of direct access to airway for removal of secretions, need for patient cooperation, facial trauma and discomfort related to the mask and the potential for abrupt respiratory deterioration if patient breathing is not synchronous with the ventilator or the mask becomes dislodged.[5] With NIPPV, the need for intubation was reported to decline and also the respiratory rate and gas exchange showed rapid improvements.[5] In many studies, NIPPV was associated with a reduced need for invasive mechanical ventilation, decreased mortality and shorter length of hospital stay.[6,7]

METHODS:

This is prospective observational study conducted on 100 cases admitted under Department of Pulmonary Medicine of a tertiary care of hospital.

Inclusion Criteria: -

All cases within age group of 18-70 years presenting with acute respiratory failure with an underlying respiratory disorder.

Exclusion Criteria: -

Any contraindication for NIV[8] i.e.,
A) Patient's inability to protect airway.
B) Systolic blood pressure < 90 mmHg or use of vasopressors.
C) Electrocardiogram instability with evidence of ischemia or ventricular arrhythmias;
D) Agitation, lack of cooperation, facial trauma, burns, or facial surgery.

The demographic characteristics, detailed history including the relevant past and personal history was noted. All the relevant investigations including ABG were noted. All cases received optimum medical management for the underlying disease. Initial NIV settings were noted for every patient and the subsequent changes in the settings with reference to the clinical and/or ABG parameters were noted. The final outcomes like discontinuation of NIV either with improvement or failure requiring invasive ventilation was noted along with the duration of the NIV.

Success of NIV- Improvement in ABG or when NIV was no more needed[9]

Failure of NIV- general condition deteriorated even after NIV

on appropriate medical support[10] or if patient was shifted to invasive ventilator[11,12]

The data was analyzed using SSPS 2016 software.

Machine used for NON-INVASIVE VENTILATION- Stellar 150 (RESMED)

All cases were administered NIV support system, using full face mask or nasal mask. The initial settings (in spontaneous timed mode) were 10 cmH2O of IPAP and 5 cmH2O of EPAP. Both the parameters were titrated as per patient's comfort. Both IPAP as well as EPAP were changed as per clinical status and ABG parameters. FiO2 requirement was assessed by ABG analysis. NIV was applied in propped-up position by face mask.[12] Pressures, both IPAP and EPAP were gradually increased by 2 - 5 cmH2O every 10-15 minutes as per requirement to maintain Spo2 >94%. Cases were assessed every 15 min for initial 2 hours for pulse rate, respiratory rate, GCS, blood pressure, level of co-operation, mental status, oxygen saturation, signs of air leakage around the mask. Appropriate medical management was also given. ABG values were obtained prior to and after 1 hour of NIV, on stabilization and prior to declaring outcome; ABG was also done whenever required to assess the adequacy of ventilation. Initially NIV was given continuously for 24 hours and then depending on response, duration was adjusted. Once patient was weaned off from NIV, daily clinical assessment, ABG were done. Outcome of NIV usage was measured in terms of number of cases treated successfully by NIV and those who deteriorated. Outcome for existing pulmonary disease was corelated with type-I or type-II respiratory failure.

OBSERVATION AND RESULTS

47 cases had type I respiratory failure, while 53 had type II. 49 cases had co-morbidities like DM, hypertension and IHD. 22 cases had history of pulmonary tuberculosis whereas 78 denied the same.

Gradual decrease in mean respiratory rate was seen for both types of respiratory failure. Mean respiratory rate at the time of admission was 32.21 (Type-I) and 32.11 (Type-II), which reduced to 28.81 (type I) and 28.43 (type II) after 1st hour of NIV application and to 22.01 (type I) and 20.83 (type II) before declaring outcome.

Table 1 Correlation Of Outcome With Type Of Respiratory Failure:

	Type-I		Type-II	
	No. of cases (N)	N %	No. of cases (N)	N %
Improved	36	76.6%	48	90.6%
Failure	11	23.4%	5	9.4%
Total	47	100.0%	53	100.0%

Table 2 PCO2 levels in Type II failure with Time:

	PCO2			
	<45mmhg		> 45mmhg	
	No. of cases (N)	N %	No. of cases (N)	N %
0th	0	0.0%	53	100.0%
1 Hour	2	3.8%	51	96.2%
Prior to declaring outcome	38	71.7%	15	28.3%

p-value-0.0005 indicates significance of change in response over the time from 0th till prior to declaring outcome.

Table 3 Correlation Of Heart Rate And Respiratory Rate With Outcome:

	Improvement		Failure		Total	
Heart rate	No. of cases (N)	N %	No. of cases (N)	N %	No. of cases (N)	N %
<130/min	26	96.3%	1	3.7%	27	100.0%
≥130/min	58	79.5%	15	20.5%	73	100.0%
Respiratory rate						
<30/min	32	94.1%	2	5.9%	34	100.0%
≥30/min	52	78.8%	14	21.2%	66	100.0%

p-value for correlation of heart rate with outcome was 0.041(i.e., <0.05), indicating significance of association between HR at 0th hour and Outcome, i.e., cases with Heart Rate of 130 and less have better outcome as compared to cases with baseline heart rate of more than 130.

p-value for correlation of respiratory rate with outcome was 0.048(i.e., <0.05), indicating that cases with Respiratory Rate of less than 30 have better outcome as compared to cases with baseline respiratory rate of 30 and more.

Table 4 Correlation Of ABG Parameters With Outcome:

		Improved		Intubated		Total		p-value
		No. (N)	N %	No (N)	N %	No. (N)	N %	
pH (type I RF)	< 7.25	1	50.0 %	1	50.0 %	2	100.0 %	0.512 i.e., statistically insignificant
	7.25 to 7.35	13	72.2 %	5	27.8 %	18	100.0 %	
	> 7.35	22	81.5 %	5	18.5 %	27	100.0 %	
pH (type II RF)	< 7.25	13	92.9 %	1	7.1 %	14	100.0 %	0.828 i.e., statistically insignificant
	7.25 to 7.35	33	89.2 %	4	10.8 %	37	100.0 %	
	> 7.35	2	100.0 %	0	0.0 %	2	100.0 %	
pCO2 (type II RF)	46 to 70mmhg	34	100.0 %	0	0.0 %	34	100.0 %	.002 i.e., statistically significant
	> 70mmhg	14	73.7 %	5	26.3 %	19	100.0 %	
pO2 (type I RF)	≤55 mmhg	27	75.0 %	9	25.0 %	36	100.0 %	0.640 i.e., statistically insignificant
	>55 mmhg	9	81.8 %	2	18.2 %	11	100.0 %	
pO2 levels (type II RF)	≤55 mmhg	18	90.0 %	2	10.0 %	20	100.0 %	0.913 i.e., statistically insignificant
	>55 mmhg	30	90.9 %	3	9.1 %	33	100.0 %	

Table 4 shows there was no significant association between pH and Outcome in both types of respiratory failure i.e., irrespective of pH outcomes are favorable. There was significant association between PCO2 at 0 and Outcome in Type-II i.e., if initial PCO2 levels are less than 70mmhg, cases are more likely to improve with NIV. However, there was no significance of association between PO2 and Outcome i.e., irrespective of degree of hypoxemia NIV can be applied and its outcome is favorable.

Total 34 cases underwent change in NIV settings, p- 0.013 indicates significance of association between changing NIV settings and outcome.

Table 5 ABG Parameters And Change In NIV Settings:

	Change in NIV Settings			
	Yes		No	
	Mean	Standard Deviation	Mean	Standard Deviation
PCO2_0 hr	61.40	25.62	39.87	19.23
PCO2_1 hr	57.15	21.33	39.62	13.78
PO2_0 hr	53.55	7.33	52.74	9.05
PO2_1 hr	62.72	11.80	64.91	8.36
pH_0 hr	7.32	.11	7.40	.08
pH_1 hr	7.35	.10	7.40	.06

25 cases had difficulty in weaning from NIV i.e., the duration of NIV was more than 3 days with no significant improvement on ABG. They were put on respiratory stimulants. 16 out of these 25 cases improved with additional intervention, however 9 did not.

Out of 47 cases in whom NIV settings were changed, 32 (68.1%) improved, while 15 (31.9%) failed to show any improvement. Among cases who improved, the mean duration of NIV requirement was 2.79 days, while the mean duration of hospital stay was 10.42 days.

Out of 100 cases, 65 showed positive sputum culture. Common organisms isolated were Acinetobacter baumanni and Klebsiella Pneumonia. From those 65 cases, 54 showed improvement on NIV, while 11 deteriorated. P-value was 0.731, indicating no significant association between outcome and positivity of sputum gram culture.

DISCUSSION

This study was conducted in the Pulmonary Medicine ward of a Tertiary Health Care Institute to study the predictors of NIV and factors influencing different outcomes of NIV in cases presenting with acute respiratory failure.

100 consecutive cases with acute respiratory failure were enrolled in our study with almost equal distribution of cases with Type-I (47) and Type-II (53) respiratory failure (Table-1). Cases with different diagnoses were COPD (54), ILD (18), Bronchiectasis (11), Pneumonia (12), Kyphoscoliosis (2), Pulmonary Thromboembolism (2), Pulmonary Tuberculosis (1).

In our study, we found that presence of comorbidities and number of comorbidities did not have any co-relation with outcomes of cases. Similarly, in a study by **Pacilli et al** number of comorbidities was higher in NIV failure group as compared to those cases who succeeded, but the predictive value of the Charlson index was very weak in the failure group and was not accounted. Also, about 20% of the whole group of their cases had complicated or noncomplicated diabetes, but this was not a determinant of success or failure.[13] **Seneff et al** showed that the presence of comorbidity in cases with hypercapnic respiratory failure might be associated with worse prognosis.[14] **Moretti et al** 24 cases who required intubation had significant higher rate of other co-morbidity (58.3% vs 19.7%, $P < 0.05$) at the time of admission.[15]

Respiratory rate reduced significantly from baseline after application of NIV. In a study conducted by **Brochard L. et al**, they reported that respiratory rate was decreased with non-invasive ventilation in cases of acute exacerbations of chronic obstructive pulmonary disease at the end of 1 hour and 3 hours as compared with baseline. [16] This finding is similar to our current study. Similarly, **Agarwal R. et al** concluded that respiratory rate and heart rate were decreased with NIV at the end of 1 and 4 hours when compared with baseline in cases of Acute hypoxemic respiratory failure.[13]

We categorized cases in two groups based on their baseline heart rate (Table-3) and found that if the baseline heart rate was 130 or less, there were more chances that the patient would improve after NIV application. We could not find studies defining cut-off heart rate for improvement/failure of NIV application, however in a study by **Bhattacharyya D et al** failure group had significantly higher HR and RR at the time of enrollment.[17]

We found in our study that if the baseline respiratory rate was less than 30 (Table-3), there are more chances that the patient would improve after NIV application. In the studies conducted by **Phua J et al** and **Aso h et al** it was found that baseline RR of 30 to 34/min and More than 35 per min respectively was a negative predictor for NIV outcome.[18-19] **Jagan Prashanth E. et al** conducted a study wherein they found that there was significant reduction of heart rate and respiratory rate both in the first hour and fourth hour values. They also found that baseline heart rate and respiratory rate were not predictors of failure of NIV by multivariate logistic regression.[20]

Significant improvement was observed in pH for both types of respiratory failure (Table-4). Significant improvement was also observed in PCO2 levels in Type-II respiratory failure after application of NIV (Table-2). These findings are in accordance with study by **Ventrella F. et al** in which improvement in pH was statistically significant at the end of 2 hours and 24 hours as compared with baseline in cases of hypercapnic respiratory failure.[21] Study by **Mclaughlin K. et al** reported that ABG parameters: PH and PCO2 were improved at the end of 1 and 4 hours as compared with baseline in cases of hypercapnic respiratory failure.[22]

In a current study, of 100 cases, 84 improved after applying NIV, however 16 cases were intubated and shifted on mechanical ventilation. **George I. et al** stated that, success rate with NIPPV was 85% in cases of acute respiratory failure admitted to intensive care unit.[6] Study by **Ventrella F. et al** showed NIV was successful in 81% of cases of hypercapnic respiratory failure.[21]

We found that NIV successfully improved gas exchange and V/Q mismatch in both Type-I (76.6%) and Type-II (90.6%), however there was no significant association between type of respiratory failure and outcome. Thus, NIV was effective irrespective of type of respiratory failure. **George I. et al** showed overall success rate of 85% in their cases of acute respiratory failure with NIPPV which is comparable to the current study.[6] Whereas **Kramer N. et al** reported that 69% cases of acute respiratory failure improved with NIPPV.[5] In a study by **Ventrella F. et al** NIV was successful in 81% of cases of hypercapnic respiratory failure.[21]

The baseline pH level is an indicator of hypercapnia and is a critical factor in determining the successful outcome of NIV. Recent trials by **Frutos-Vivar F et al, Rao BK et al, Ferguson ND et al** have shown that a low baseline pH is an important predictor of NIPPV failure.[23-25] In our study we saw that there is no significant relationship between the baseline pH and outcome of the patient (Table-4), suggesting that cases with low pH without other obvious contraindication for NIV, can be treated with NIV as an initial management with successful outcome and it also suggests efficacy of NIV in resource limited set-up. However, in study conducted by **Jagan Prashanth E. et al** lower baseline pH is a significant predictor of NIPPV failure.[20] As per **Bhattacharyya D et al**[26] Baseline pH is found to be able to predict success or failure of NIPPV (mean pH of 7.28 in success group vs 7.22 in failure group) with a sensitivity of 97% and specificity of 71%.9 However, **Poponick et al** found no relationship between baseline ABG parameters and the likelihood of success of NIPPV but the lack of change in blood gases after one hour trial was found to be the predictor for the need for Mechanical Ventilaltion.[27]

As per the multicenter study report published by **Antonelli et al**, baseline arterial blood gas values have no predictive value in determining the outcome of NIPPV,[28] however in our study we observed that baseline PCO2 is a predictor of outcome of NIV in Type II respiratory failure (Table-4), but there was no significant association between baseline PO2 and outcome. In a study by **Jagan Prashanth E. et al**, baseline PO2 and PCO2 values did not predict the failure of NIV.[20]

NIV was initiated with basic settings of 12 cm of H2O:6 cm of H2O (IPAP: EPAP) however settings were changed if there was no improvement in ABG after 1 hour and/or no clinical improvement. Criteria to change settings were PCO2/PO2/pH of 1st hour. Mean values of PCO2 was 61.40 mm of Hg, PO2 was 53 mm of Hg and pH was 7.32 at which settings were changed (Table-5). There was a significant association between change in NIV settings and successful outcome. **Bhattacharyya D et al** showed in their study that with change in NIV settings and with change of interface wherever indicated the overall success rate of NIPPV can be improved.[26] There were 25 cases who required additional intervention, out of which 64% improved and were discharged whereas 36% failed even after adding respiratory stimulants, likely due to disease severity. There are studies on isolated use of respiratory stimulants where NIV couldn't be given or was denied or not tolerated by the patient. However, we could not find studies showing use of respiratory stimulant to improve outcome of NIV.

LIMITATIONS

We had a sample size of 100. We recommend similar study to be conducted with larger sample size and different age groups including pediatric cases which may also help in deriving clinical predictor scores for NIV outcome.

CONCLUSION

Patients with baseline respiratory rate < 30 and heart rate of 130 and less are associated with better outcome. Patients in Type II Respiratory Failure with PCO2 levels between 46-70 have a better prognosis and successful NIV outcome. Type of respiratory failure, sputum aerobic culture are not predictors of NIV outcomes. Usual co-morbidities associated with respiratory failure are Diabetes Mellitus, hypertension, ischemic heart disease and the presence of co-morbidity is not the predictors of NIV outcome. Overall success rate of NIV is 84%. Optimum medical management of the underlying disease condition along with NIV as a supportive measure can decrease intubation rates, mortality, reduces length of hospital stay and morbidity.

NIV in acute respiratory failure, irrespective of type of respiratory failure helps in improving gas exchange, reduces intubation and length of hospital stay hence, its use as a first modality of treatment in cases without overt contraindications is recommended.

Conflicts of Interest: None

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