IAR Journal of Medicine and Surgery Research
https://doi.org/10.70818/iarjmsr.2025.v06i01.0154
Vol. 6, No. 1, 2025

ISSN (Print): 2709-1899
ISSN (Online): 2709-1902

ARTICLE

# Prediction of Non-Invasive Ventilation Failure in Critically Ill COVID -19 Patients

Shahadat Hossain Polash[1], Mohammad Ashrafuzzaman[1a]*, Rocky Das Gupta[2], Nafiza Afroz[3], Shahadat Hossain[4], Manas Kanti Mazumder[5], Farhana Tasnim[6]

[1] Junior consultant (ICU & Critical Care), Dhaka Medical College Hospital, Dhaka, Bangladesh
[1a] Assistant Professor, Department of Anesthesia, Analgesia & Intensive Care Medicine, BSMMU, Dhaka, Bangladesh
[2] Medical Officer, Chattogram Chest Disease Clinic, Attachment: 250 bedded General Hospital, Chattogram
[3] Assistant Surgeon (CCM), National Institute of Burn and Plastic Surgery
[4] Assistant Register (Critical care medicine), Faridpur medical College Hospital
[5] Assistant Professor, Intensive Care Unit division, BSMMU
[6] MD Resident (Phase A), Pathology Department, BIRDEM. Dhaka

## ABSTRACT

**Background:** Non-invasive ventilation (NIV) is recognized as a practical and effective method for assisting selected patients with respiratory issues. The HACOR scoring system evaluates heart rate, acidosis, consciousness, oxygenation, and respiratory rate and has proven to be predictive of NIV failure in critically ill patients like COVID-19 patients. **Aim:** To determine the predictability of HACOR score to identify NIV failure early in patients with respiratory failure linked to COVID-19. **Methods:** This cross-sectional study was carried out at the ICU of Bangabandhu Sheikh Mujib Medical University (BSMMU) and Dhaka Medical College Hospital over a one-year period. It involved 40 patients who were administered NIV via a conventional ventilator in spontaneous mode and selected based on specific inclusion and exclusion criteria. Informed written consent was obtained from each patient's guardians. Upon admission to the ICU, the HACOR score of each patient was measured after one hour of NIV treatment, assessing factors such as heart rate, pH levels for acidosis, and oxygenation through the PaO2/FiO2 ratio, along with respiratory rate. Analysis was performed with both manual methods and software SPSS version 24. **Results:** NIV failure occurred in 33 (82.5%) patients with only 7 (17.5%) achieving successful NIV. Older patients experienced NIV failure significantly higher compared to those with successful outcomes (average ages 61.79±17.28 vs. 47.57±11.92 years, p=0.045), and male patients were predominant (66.66%). The predominating comorbidities were diabetes mellitus (57.5%). The HACOR scores were significantly higher in patients who failed NIV compared to those who succeeded (8.18±2.18 vs. 4.71±1.5, p=0.002). Receiver operating characteristic (ROC) curve analysis established a HACOR score cutoff value of 5 after one hour of NIV treatment for predicting NIV failure in the study population, demonstrating a sensitivity of 93.9% and a specificity of 57.1% (AUC: 0.905). **Conclusion:** Despite the study's limited sample size, findings suggest that the HACOR score may serve as an early indicator of NIV failure in critically ill patients with COVID-19-related respiratory failure. Future research on a larger scale is anticipated to validate and expand upon these important insights.

**Keywords:** HACOR score, NIV, COVID-19

| **Submitted:** 12.10.2024 | **Accepted:** 22.12.2024 | **Published:** 02.01.2025

***Corresponding Author**
Dr. Mohammad Ashrafuzzaman, Assistant Professor, Department of Anesthesia, Analgesia & Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, Email: sojibofmmc@bsmmu.edu.bd

**How to Cite the Article**
Shahadat Hossain Polash, Mohammad Ashrafuzzaman*, Rocky Das Gupta, Nafiza Afroz, Shahadat Hossain, Manas Kanti Mazumder, Farhana Tasnim: Prediction of Non-Invasive Ventilation Failure in Critically Ill COVID -19 Patients. *IAR J Med Surg Res.* 20245;6(1): 1-8.

# INTRODUCTION

Hypoxemic acute respiratory failure often necessitates ICU admission for respiratory support linked with critical issue [1]. Non-invasive ventilation (NIV) is a commonly used intervention in COVID-19 related Acute Hypoxaemic Respiratory Failure (AHRF) [2]. It reduces breathing effort, improves arterial oxygen levels and alveolar ventilation. It can be provided with a face mask, nasal mask, nasal pillows, helmet, or hood [3]. The case fatality rate in the ICU for patients with respiratory failure related to COVID-19 requiring invasive mechanical ventilation was 50% [4]. The "HACOR" scoring system helps predict the failure of non-invasive ventilation (NIV) and has scores that range from 0 to 25 [2]. A score of 5 points or higher indicates an 81.8% chance of NIV failure within the first hour. For patients with scores above 5, early intubation within 12 hours leads to a lower hospital death rate (66% compared to 79%) than intubation done later [2]. This scoring system also effectively measures the risk of in-hospital death for patients with severe respiratory failure [3]. Another study showed that using HACOR at the one-hour mark can help predict NIV failure in patients with pneumonia and acute respiratory distress syndrome (ARDS) [5].

In Bangladesh, most of the patients with COVID-19 associated respiratory failure needs respiratory support. NIV usage has been dramatically increased because of the complications developed from endotracheal intubation and mechanical ventilation. In non-covid respiratory failure, HACOR score can predict NIV failure successfully. But it has not been explored in COVID-19 patients yet. It is crucial to identify patients who cannot benefit from NIV as early as possible, so that they can be timely intubated and ventilated with MV [2, 6-7]. Prediction of NIV failure is very important because of the strong link between failure and poor outcomes. When NIV does not achieve a clear improvement in the respiratory condition, the patient must be rapidly considered for endotracheal intubation [8,9]. Early prediction of NIV failure in COVID-19 patients using the HACOR scoring system can enhance patient outcomes. Timely identification of at-risk patients allows for quicker intubation decisions, potentially reducing ICU mortality and length of stay. In Bangladesh, where ICU resources are scarce, early detection of NIV failure is vital for optimizing resource use and costs. This study evaluates the effectiveness of the HACOR score at one hour in predicting NIV failure in patients with COVID-19 respiratory failure.

# MATERIALS AND METHODS

This cross-sectional study was conveyed in Intensive Care Unit (ICU) of Department of Anesthesia, Analgesia & Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical university (BSMMU), Dhaka and Department of Anesthesia, Pain, Palliative and Intensive Care Medicine, Dhaka Medical college Hospital (DMCH), Dhaka from September 2020 to August 2021. By convenient sampling 40 diagnosed patients of COVID-19 associated respiratory failure age more than 18 years undergoing NIV through conventional ventilator in spontaneous mode based on clinician's decision were included in this study. Patients with indication of immediate invasive mechanical ventilation, any formal contraindication to noninvasive respiratory support, post-extubation use of NIV, NIV intolerance and patient's with 'Do Not Resuscitate' orders were excluded. Data was collected by face-to-face interview with a pre-tested semi structured questionnaire and Case Record Form (CRF).

Socio-demographic information including age, sex & estimated body weight, detailed history regarding clinical manifestations and co- morbidities were recorded for each patient in separate questionnaire. Blood pressure, heart rate, respiratory rate, consciousness level (GCS), Arterial blood gas, $PaO_2/FiO_2$, reason for NIV, starting date and duration were recorded bedside in a Case Record Form (CRF). For oxygenation and acidosis, arterial blood was collected by investigator himself or technician maintaining standard protocol and was analyzed in the one stop laboratory service of ICU of BSMMU & DMCH. NIV was applied through face mask by conventional mechanical ventilator (Newport 360 & Puritan Bennett 840) in spontaneous mode. All patients receiving NIV were assessed at one hour for variables of HACOR score. The patients who were successfully weaned from NIV and those patients who failed NIV as ceiling test or progresses to mechanical ventilation were

recorded. Then HACOR score at one hour of both groups was compared.

***HACOR score:***

The HACOR score helps predict early failure of non-invasive ventilation (NIV) in patients with severe breathing problems. It includes six factors: heart rate, blood acidity (pH level), consciousness (using the Glasgow coma scale), oxygen levels (PaO2/FiO2), and breathing rate. The score is accurate, with a cutoff value of 5; scores above 5 show a higher risk of NIV failure and greater chances of dying in the hospital. Checking the score repeatedly within the first 24 hours can give valuable insights, especially if high scores continue to appear [2,5].

**Statistical Analysis**

After gathering and checking the data for errors, they were edited, categorized, and coded by using SPSS version 24. For categorical variables, results were presented as frequencies and percentages, while numerical variables were summarized using means and standard deviations. Chi-square test for categorical relationships and a T-test for non-categorical comparisons were done. Pearson's correlation analysis was performed to assess the relationship between HACOR scores and ICU stay lengths. Finally, NIV failure predictive ability was evaluated by using the area under the receiver operating characteristic curve, considering a p-value of 0.05 or lower as statistically significant.

**Ethical Implication**

The patients and the key relatives were clearly informed about the scope and limitation of the study. It was explained to the patients and their next to keen that there would be no physical or social risk for the participants and at any point of the study if they wish, they can withdraw themselves from the study at any moment. Proper safety measures were taken in every step of the study. Confidentiality was maintained both verbally and documentary by using separate locker and computer password. Informed written consent of the patient was taken. No incentive was given to the participants for participation to the study. Written permission has also been taken from concerned department where study was undertaken. Ethical clearance was obtained by the Institutional Review Board (IRB) of BSMMU to undertake the current study. Memo-BSMMU/2021/1859, Dated-06/03/2021.

## RESULTS

The main aim of the study was to assess and evaluate HACOR score in early prediction of NIV failure in patients with COVID-19 associated respiratory failure.

**Table 1: Comparison of demographic profiles with NIV outcome (n=40)**

| **Attributes** | **NIV success** n (%) **7 (17.5%)** | **NIV failure** n (%) **33 (82.5%)** | **Significance** |
|---|---|---|---|
| Age (Years) mean±SD | 47.57±11.92 | 61.79±17.28 | 0.045[a] |
| Estimated Body Weight (Kg) mean±SD | 63.86±6.89 | 72.33±8.54 | 0.018[a] |
| Gender n (%) | | | |
| Male | 1 (14.3) | 22 (66.66) | 0.011[b] |
| Female | 6 (85.7) | 11 (33.33) | |
| Comorbidities (Multiple responses) n (%) | | | |
| None | 1(14.2) | 8 (24.2) | |
| Diabetes Mellitus | 4 (57.1) | 19 (57.6) | |
| Hypertension | 3 (42.9) | 16 (48.5) | |
| IHD | 1(14.2) | 6 (18.2) | |

[a]Pearson's chi-square test and [b]independent sample T-test were performed to test the level of significance. P<0.05 was considered as statistically significant

Table 1 stated that NIV was failed in majority 82.5% patients (n=33), while only 17.5% patients (n=7) had experienced successful NIV diagnosed by physicians. mean age and gender was statistically associated with NIV outcome (p<0.05). Diabetes mellitus was the most common co-morbidity found in 57.1% (n=4) in NIV success patients and 57.6% (n=19) in NIV failure patients.

**Table 2: Comparison of mean mode of NIV settings and HACOR (heart rate, acidosis, consciousness, oxygenation, respiratory rate) score between patients by NIV outcome (n=40)**

| Variables | NIV success (n=7) | NIV failure (n=33) | Significance |
|---|---|---|---|
| **Mode** | | | |
| PS (cm of $H_2O$) | 16.86±3.62 | 18.7±2.67 | 0.128 |
| PEEP (cm of $H_2O$) | 9.14±1.07 | 9.58±0.83 | 0.240 |
| $FiO_2$ | 0.87±0.17 | 0.98±0.06 | 0.006 |
| Trig/Sens (cm of $H_2O$) | -2.29±0.49 | -1.94±0.56 | 0.351 |
| **HACOR variables** | | | |
| Heart Rate (per minute) | 88.00±9.66 | 102.3±17.24 | 0.041 |
| pH | 7.49±0.05 | 7.36±0.28 | 0.532 |
| GCS | 15.00±0.00 | 14.24±0.90 | 0.034 |
| PaO2/FiO2 | 123.57±44.1 | 90.24±28.95 | 0.016 |
| Respiratory rate /minute | 27.14±6.99 | 33.64±5.01 | 0.006 |
| Total HACOR score | 4.71±1.5 | 8.18±2.18 | 0.002 |

Independent sample T-test were performed to test the level of significance.P<0.05 was considered as statistically significant

Table 2 described that NIV failure patients had significantly higher HACOR score compared to NIV success patients (8.18±2.18 vs 4.71±1.5, p<0.01). Besides, heart rate, respiratory rate GCS and PaO2/FiO2 were also significantly higher among NIV failure patients compared to NIV success (p<0.05). Mode of NIV settings like PS, PEEP and Trig/Sens were not statistically associated with NIV outcome between patients with NIV failure or success. However, NIV success patients received significantly less $FiO_2$ than NIV failure group (p<0.01).

**Table 3: Prediction of NIV failure according to NIV outcome by using HACOR score (n=40)**

| HACOR score | NIV outcome | | Total |
|---|---|---|---|
| | NIV failure | NIV success | |
| **>5** | 30<br>True Positive (TP) | 3<br>False Positive (FP) | 33<br>TP+FP |
| **≤5** | 2<br>False negative (FN) | 5<br>True Negative (TN) | 7<br>FN+TN |
| | 32<br>TP+FN | 8<br>FP+TN | 40 |

Table 3 showed 30 patients had high HACOR score (>5) (True positive) and 2 patients had HACOR score (≤5) (False negative) among total of 32 patients who had diagnosed as NIV failure by physicians. Among total 8 patients who were diagnosed as NIV success byphysicians, 5 patients had HACOR score ≤5 (True negative) and 3 patients had HACOR score >5 (False positive).

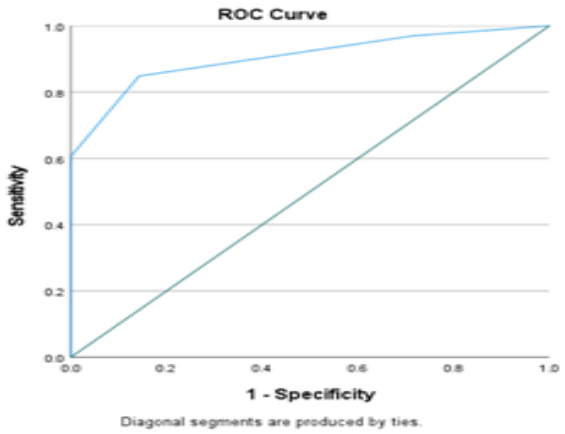


**Figure 1: Receiver operator curve showing performance of HACOR score in predicting NIV failure (n=40)**

| Attribute | AUC | Cut-Off value | Sensitivity | Specificity |
|---|---|---|---|---|
| HACOR score | 0.905 | 5.0 | 93.9% | 57.1% |

Figure 1 shows that receiver operator curve analysis found a cut-off value of 5.0 HACOR score (after 1 hour of NIV) in the prediction of NIV failure among study patients. (Sensitivity: 93.9%, specificity: 57.1%, AUC: 0.905).

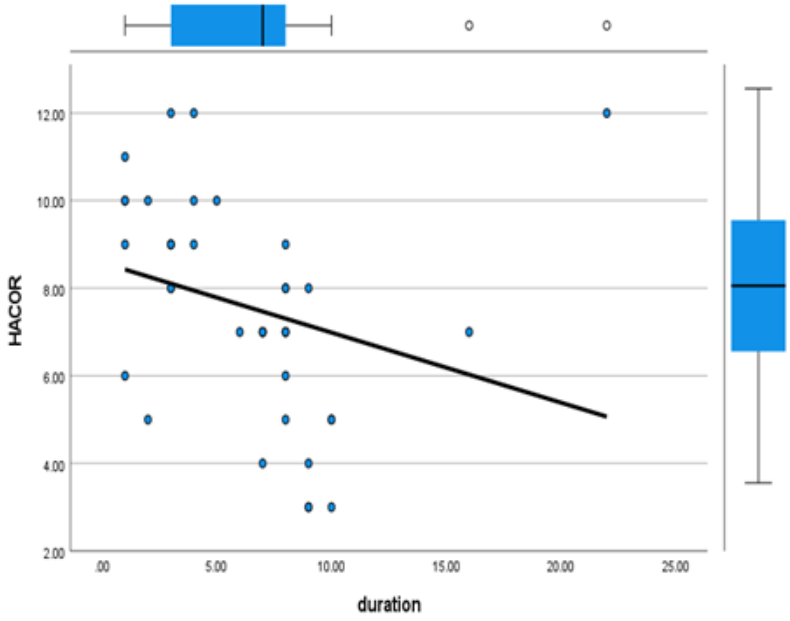


**Figure 2: states that pearson correlation model showed, HACOR score after 1-hour NIV had weak negative correlation with length of ICU stay (r = -0.275). But that was not statistically significant**

## DISCUSSION

Delayed intubation after non-invasive ventilation (NIV) failure significantly increases mortality. Therefore, it's necessary to determine the timing for transitioning to invasive ventilation. The HACOR score—a bedside tool assessing Heart rate, Acidosis, Consciousness, Oxygenation, and Respiratory rate—helps predict NIV failure in non-COVID cases. This study includes 40 newly admitted COVID-19 patients with

respiratory failure undergoing NIV. In this study, only 7 patients (17.5%) had experienced successful NIV. In line with this study findings, previous studies also observed that NIV treatment in COVID-19 critically ill patients has a high failure rate [10,11]. Earlier research on NIV use in acute respiratory failure from viral pandemics revealed dissimilar results, with failure rates ranging from 10% to 70% for influenza, H1N1, and SARS, and up to 92.4% for MERS [12,13]. This high failure rate of NIV in COVID-19 associated respiratory failure can be explained by its complex pathophysiology compared to other diseases causing respiratory failure. In COVID-19, damage to the lungs is induced by direct viral cytopathic effect and by the indirect effects of the cytokine storm [1].

Multiple mechanism including pulmonary embolism, secondary bacterial infection, low compliance of lung causing barotrauma during NIV, all could play a role in NIV failure. Although studies showed high failure rate of NIV, if intubation and MV appear as an inappropriate choice, NIV could still play a vital role. It can recruit collapsed alveoli, increase vital capacity, thus cure a small but not negligible proportion of patients and deliver palliative care to dying subjects with COVID-19-related respiratory failure [10] . In present study, NIV failure patients had significantly higher HACOR score compared to NIV success patients (8.18±2.18 vs 4.71±1.5, p=0.002) after one hour of NIV. Earlier research reported that patients who successfully used non-invasive ventilation (NIV) had a lower HACOR score [2,3,5]. Carrillo et al. (2020) had also confirmed the accuracy of the HACOR score, particularly in pneumonia and ARDS [5]. Similarly, Duan et al. (2017) observed that patients with NIV failure had higher HACOR scores at initiation and after 1, 12, 24, and 48 h of NIV than those with successful NIV [2]. In present study, among the components of HACOR score, heart rate, respiratory rate, GCS and PO2/FiO2 were significantly higher in NIV failure patients. Similarly, in an observational study, Guia et al. (2021) observed that PaO2/FiO2 level at 1 h after starting NIV might be a key determinant [1]. In contrast to present study, Duan et al. (2017) found all components significantly higher in NIV failure group [2]. This can be explained by higher number of patients and the serial measurement of HACOR score in regular interval done in that study. So, in centers with higher resources and logistic supports, HACOR scoring can be done in regular interval to get better predictability.

In present study, receiver operator curve (ROC) analysis found a cut-off value of 5 HACOR score (after 1 hour of NIV) in the prediction of NIV failure among study patients (sensitivity: 93.9%, specificity: 57.1%, AUC: 0.905). In contrast with this finding, Duan et al. (2017) found HACOR score 5 points as the cutoff value with the sensitivity and specificity 72.6 and 90.2%, respectively (AUC=0.88) [2]. This can be explained by the types and number of patients included in the study. Duan et al. (2017) conducted that study in patients with acute hypoxaemic respiratory failure from different diseases like bacterial pneumonia, COPD, pulmonary infarct, pulmonary oedema, ARDS [2]. In contrast, this study was conducted on patients with COVID-19 associated respiratory failure, disease process and prognosis of which is complex unlike other diseases causing respiratory failure, explaining different findings in ROC curve analysis. In current study, NIV failure patients were significantly older than NIV success (61.79±17.28 vs 47.57±11.92 years, p=0.045) with male predominance (66.66%). Comparable to the current study findings, several authors also observed that older aged patients were more prone to NIV failure [1,10]. However, some authors did not found no such association of age with NIV outcome [14,11]. Decreased immunity, thus increased severity of COVID-19 and increases susceptibility of coinfections in older age group can explain the findings in present study.

Distribution of co-morbidities was statistically similar between NIV success vs failure (as p value >0.05). Similarly, another study found no significant association of NIV outcome with comorbidities like diabetes mellitus, hypertension, renal and heart diseases [10]. Small sample size may be the key factor for nonsignificant result in both studies as comorbidities is thought to be associated with worse outcome. There were a number of limitations of the study which includes NIV settings optimization. Moreover, it did not evaluate drug effect among study subject that might affect outcome.

## CONCLUSION

This study observed that HACOR score with a cut off value of 5.0 can predict early NIV failure in critically ill, COVID-19 associated respiratory failure. Hence, HACOR score can be used to predict NIV failure, as it is a simple, bed-side method, easy to implement and that could add valuable information, in lack of a validated tool. However, further study with larger sample size is recommended, which could give us more information about effectiveness of HACOR score in predicting NIV outcome, thus helping the clinicians to manage critically ill COVID-19 associated respiratory failure patients in a

better way. Further larger randomized clinical trial is recommended.

**Declarations**

**Ethics approval and consent to participate**

Before data collection, both verbal and written informed consent was taken from patient's guardian.

**Consent for publication**

All authors have approved this manuscript for publication.

**Availability of data and materials**

The datasets supporting the conclusions of this article are included within the article generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

**Competing interests**

The authors declare that they have no competing interests.

**Funding**

This research received no funding from BSMMU for conduction.

**Authors' contributions**

SHP, MA, RDG participated in the design of the study, data interpretation and drafted the manuscript. NA, SH, MKM, FT contributed to the data design, data interpretation, data analysis and the critical review of the manuscript.

**Acknowledgements**

This researcher acknowledged for the support of the authority and respondents.

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