

# Association of HbA1c with Outcomes in Patients of Acute Exacerbation of COPD in Tertiary Care Hospital

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## Abstract

**Background:** Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is a major cause of morbidity, mortality, and hospitalization worldwide. Hyperglycemia is a common response to acute illness; however, the influence of chronic glycemic status, as reflected by glycated hemoglobin (HbA1c), on clinical outcomes in AECOPD remains uncertain. This study aimed to evaluate the association between HbA1c levels and clinical outcomes in patients admitted with AECOPD. **Material and Methods:** A hospital-based cross-sectional study was conducted in the Department of Respiratory Medicine over 18 months and included 205 patients aged  $\geq 40$  years admitted with AECOPD. HbA1c was measured at admission, and patients were categorized into HbA1c  $\leq 6\%$  and  $>6\%$  groups. Clinical outcomes assessed included duration of hospital stay, mortality, need for non-invasive ventilation (NIV), invasive mechanical ventilation (IMV), and ICU outcomes. Statistical analysis was performed using the independent t-test and Chi-square test, with  $p < 0.05$  considered statistically significant. **Results:** The mean age of the study population was  $63.74 \pm 9.46$  years, and 82.0% of patients were male. Most participants were smokers (85.4%) and from rural areas (65.4%). Patients with HbA1c  $>6\%$  had a significantly longer hospital stay than those with HbA1c  $\leq 6\%$  ( $8.08 \pm 2.20$  vs.  $7.44 \pm 2.19$  days;  $p = 0.042$ ). A significantly higher proportion of patients with HbA1c  $>6\%$  required NIV support (51.1% vs. 38.5%;  $p = 0.036$ ). However, HbA1c showed no significant association with mortality ( $p > 0.05$ ), invasive mechanical ventilation requirement ( $p = 0.50$ ), or ICU outcomes ( $p = 0.55$ ). **Conclusion:** Elevated HbA1c was associated with prolonged hospitalization and an increased requirement for non-invasive ventilation among patients with AECOPD, suggesting that poor long-term glycemic control adversely influences disease severity. However, HbA1c was not associated with mortality, invasive mechanical ventilation, or ICU outcomes. Routine assessment of HbA1c at hospital admission may help identify patients at greater risk of adverse in-hospital outcomes and facilitate appropriate risk stratification and management.

**Keywords:** Acute exacerbation of COPD; HbA1c; Non-invasive ventilation; Mortality; Hospital stay.

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## INTRODUCTION

Chronic respiratory symptoms like dyspnea, coughing, sputum production, &/or exacerbation are the hallmarks of chronic obstructive pulmonary disease (COPD), a diverse lung illness. These symptoms, which cause persistent & frequently worsening airflow obstruction, are caused by abnormalities of the airways (such as bronchitis, bronchiolitis) &/or alveoli (such as emphysema).<sup>[1]</sup> Patients with COPD frequently experience acute exacerbations (AECOPD), which necessitate hospitalization. Compared to patients treated as outpatients, hospitalized patients have greater mortality rates & expenses.<sup>[2]</sup> An exacerbation of chronic obstructive pulmonary disease (ECOPD) is characterized by increased dyspnea, cough, & sputum that worsens in less than 14 days. It may also be accompanied by tachypnea &/or tachycardia, & it is frequently linked to increased systemic & local inflammation brought on by pollution or infection,

etc.<sup>[3]</sup>

Numerous variables, such as elevated cortisol, catecholamines, glucagon, growth hormone, gluconeogenesis, & glycogenolysis, contribute to hyperglycemia linked to critical illness (also known as stress hyperglycemia or stress diabetes).<sup>[4]</sup> Since insulin resistance has been shown in over 80% of critically sick patients, it may possibly be a contributing factor.<sup>[5]</sup> Regardless

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of baseline glucose tolerance, any critically ill patient may have abrupt hyperglycemia if their condition is bad enough. Poor outcomes from a variety of acute diseases, such as myocardial infarction,<sup>[6]</sup> stroke,<sup>[7]</sup> trauma,<sup>[8]</sup> & pneumonia,<sup>[9]</sup> are linked to acute hyperglycemia. Thus, a poor prognosis from a variety of acute disorders is linked to hyperglycemia. However, it is still unclear how blood glucose levels & clinical outcomes in AECOPD are related. Hence the present study was undertaken to determine the relationship HbA1c levels and clinical outcomes in patients of AECOPD.

## MATERIALS AND METHODS

The present cross-sectional study was conducted in the Department of Respiratory Medicine; TMMC & RC after approval from Institute ethics research committee till 18 months.

**Sampling Strategy:** Purposive Sample

**Size Estimation:** 205

$$n = \frac{Z_{\alpha/2}^2 p(\%)q(\%)}{d(\%)^2}$$

where p is the observed prevalence

q = 100- p

d is the margin of error

$Z_{\alpha/2}$  is the ordinate of standard normal distribution at  $\alpha\%$  level of significance

p= 7%

d = 3.5%

= 1.96 at  $\alpha = 5\%$  level of significance

$n = (1.96)^2 * 7 * 93 / (3.5)^2$

= 204.07"

Reference: "Sundeep Salvi, Deesha Ghorpade. What is the true burden of chronic obstructive pulmonary disease in India & what are its implications at a national level? 2021 Indian Chest Society, Lung India 2021;38:503-5".<sup>[10]</sup>

### Equipment Utilized with feasibility:

1. HbA1c estimation was done using HPLC method by Bio-Rad D10.
2. Radiology- Chest Xray- M/s Shimadzu corporation, Model-RADSPEED 80; Equipment Id-g-XR-69248, Made in Japan

### Operational Definitions:

Cases – Patients with age more than 40 Years of age with acute exacerbation of COPD

### Inclusion Criteria

1. Patient attending EOPD/OPD of age  $\geq 40$  years of both sexes.
2. Patient diagnosed with acute exacerbation of COPD.
3. Patient giving informed written consent.

### Exclusion Criteria

1. Patients with any active lesions radiologically (Pneumonia/Pulmonary Tuberculosis/lung Abscess etc.), Bronchial asthma, & Interstitial Lung Disease.
2. Patient of acute exacerbation of COPD with myocardial infarction & or cerebrovascular accident, requiring surgery, reduced ejection fraction, CKD.
3. Patient receiving hyperglycemic agent like corticosteroids.

**Methodology:** The study group consists of COPD patients over 40 who have given their agreement to participate in the trial, were previously diagnosed by history & examination, & were admitted with an acute exacerbation of COPD whose severity was assessed using GOLD criteria. The Rome proposal defined the severity of an exacerbation as mild, moderate, or severe based on the patient's clinical parameters. At the time of admission, a 2 ml peripheral venous blood sample would be obtained for HbA1c determination. A history of risk factors such as diabetes mellitus, smoking, hypertension, dyslipidemia, & any other chronic illness was asked.

Each patient's hospital stay duration (in days) was noted. The date of death was noted if a patient passed away. Until they were released from the hospital or until they passed away, the patients were monitored. When a patient is clinically stable, they are released from the hospital.

**Statistical analysis:** Excel was used to tabulate the data using a statistician. Each group's means & standard deviations were used for statistical analysis. Data for each evaluation point was statistically analyzed using the t & chi square tests. The significance level was set at  $p < 0.05$ .

## RESULTS

The mean age was  $63.74 \pm 9.46$  years, with most patients aged 56–65 years (34.6%). The majority were male (82.0%), from rural areas (65.4%), and smokers (85.4%). Chest tightness was the most common associated symptom (37.1%). Mild and severe COPD were equally prevalent (39.5% each). Most patients were receiving inhaler therapy (97.1%), predominantly LABA + LAMA + ICS (70.7%), while 50.2% were compliant with treatment. Nearly half of the patients had no chronic illness (49.7%), whereas diabetes mellitus was the most common comorbidity (35.6%) as shown in [Table 1].

**Table 1: Baseline demographic and clinical characteristics of the study population (N = 205)**

| Variable       | Category        | n (%) / Mean $\pm$ SD |
|----------------|-----------------|-----------------------|
| Age (years)    | Mean $\pm$ SD   | 63.74 $\pm$ 9.46      |
| Gender         | Male            | 168 (82.0)            |
|                | Female          | 37 (18.0)             |
| Residence      | Rural           | 134 (65.4)            |
|                | Urban           | 71 (34.6)             |
| Smoking status | Smoker          | 175 (85.4)            |
|                | Non-smoker      | 30 (14.6)             |
| Other symptoms | Chest tightness | 76 (37.1)             |
|                | Fever           | 33 (16.1)             |
|                | Fatigue         | 20 (9.8)              |
|                | None            | 76 (37.1)             |

|                                 |                        |            |
|---------------------------------|------------------------|------------|
| Severity of COPD                | Mild                   | 81 (39.5)  |
|                                 | Moderate               | 43 (21.0)  |
|                                 | Severe                 | 81 (39.5)  |
| Use of inhaler                  | Yes                    | 199 (97.1) |
| Type of inhaler*                | LABA + ICS             | 13 (6.3)   |
|                                 | LABA + LAMA            | 45 (22.0)  |
|                                 | LABA + LAMA + ICS      | 145 (70.7) |
| Compliance with inhaler therapy | Yes                    | 103 (50.2) |
| Chronic illness                 | None                   | 102 (49.7) |
|                                 | Diabetes mellitus (DM) | 73 (35.6)  |
|                                 | Hypertension (HTN)     | 17 (8.3)   |
|                                 | DM + HTN               | 13 (6.4)   |

LABA = Long-acting  $\beta$ 2-agonist; LAMA = Long-acting muscarinic antagonist; ICS = Inhaled corticosteroid.

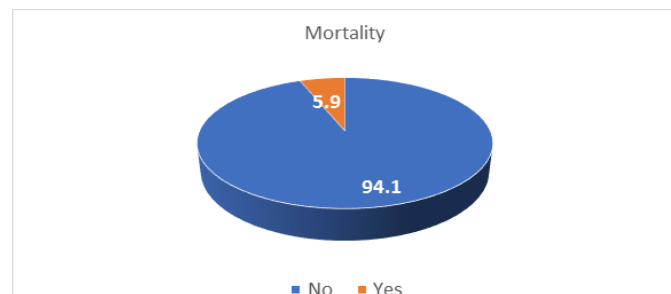


Figure 1: Mortality

Mortality was reported among 5.9% of the subjects [Figure 1].

When we compared overall duration of hospital stay based on HbA1c levels irrespective of admission glucose groups, patients with HbA1c >6 had a longer mean hospital stay (8.08

$\pm$  2.20 days) compared to those with HbA1c  $\leq$ 6 ( $7.44 \pm 2.19$  days). This difference was found to be statistically significant ( $t = 4.19$ ,  $p = 0.042$ ) as shown in [Table 2].

Among patients with HbA1c  $\leq$ 6 ( $n = 117$ ), 86 patients were in Group I & 31 in Group II. Mortality was observed in 5 patients in Group I & 1 patient in Group II. The difference in mortality between these subgroups was not statistically significant ( $p = 0.49$ ). In the HbA1c >6 group ( $n = 88$ ), 32 patients were in Group I & 56 in Group II. Mortality occurred in 2 patients in Group I & 4 patients in Group II. Again, no statistically significant association was found between admission glucose groups & mortality within this HbA1c category ( $p = 0.78$ ). Overall, mortality rates were comparable across both HbA1c categories & admission glucose groups, with no clear trend indicating increased risk with higher HbA1c levels [Table 3].

Table 2: Association of HbA1c & Duration of Hospital Stay in surviving patients. (N=193)

|                                  | HbA1c $\leq$ 6 (n=111)           |                      | HbA1c >6 (n=82)                  |                      |
|----------------------------------|----------------------------------|----------------------|----------------------------------|----------------------|
|                                  | Group I ( $\leq$ 140mg/dl)       | Group II (>140mg/dl) | Group I ( $\leq$ 140mg/dl)       | Group II (>140mg/dl) |
| Number of patients               | 81                               | 30                   | 30                               | 52                   |
| Duration of hospital stay (days) | $7.58 \pm 2.11$                  | $7.91 \pm 2.35$      | $7.41 \pm 2.16$                  | $7.55 \pm 2.32$      |
| t test                           | 1.13                             |                      | 0.094                            |                      |
| p value                          | 0.29                             |                      | 0.76                             |                      |
|                                  | HbA1c $\leq$ 6 (n=111)           |                      | HbA1c >6 (n=82)                  |                      |
|                                  | Duration of hospital stay (days) |                      | Duration of hospital stay (days) |                      |
|                                  | $7.44 \pm 2.19$                  |                      | $8.08 \pm 2.20$                  |                      |
| t test                           | 4.19                             |                      |                                  |                      |
| p value                          | 0.042*                           |                      |                                  |                      |

\*: statistically significant

Table 3: Association of HbA1c & mortality

|                    | HbA1c $\leq$ 6 (n=117)     |                      | HbA1c >6 (n=88)            |                      |
|--------------------|----------------------------|----------------------|----------------------------|----------------------|
|                    | Group I ( $\leq$ 140mg/dl) | Group II (>140mg/dl) | Group I ( $\leq$ 140mg/dl) | Group II (>140mg/dl) |
| Number of patients | 86                         | 31                   | 32                         | 56                   |
| Mortality          | 5 (5.81%)                  | 1 (3.23%)            | 2 (6.25%)                  | 4 (7.14%)            |
| p value            | 0.49                       |                      | 0.78                       |                      |

The proportion of patients requiring invasive mechanical ventilation appears comparable between the two HbA1c categories, with no evident increase in ventilatory requirement in patients with higher HbA1c levels. Statistical

analysis using the Chi-square test revealed no significant association between HbA1c levels & the need for invasive mechanical ventilation ( $\chi^2 = 0.42$ ,  $p = 0.50$ ) as shown in [Table 4].

Table 4: Association of HbA1c & invasive mechanical ventilator

| HbA1c Category | Invasive Mechanical Ventilator |       |     |       | Total |
|----------------|--------------------------------|-------|-----|-------|-------|
|                | No                             |       | Yes |       |       |
|                | N                              | %     | N   | %     |       |
| <6             | 108                            | 92.31 | 9   | 7.69  | 117   |
| >6             | 79                             | 89.77 | 9   | 10.23 | 88    |

|            |      |       |    |      |     |
|------------|------|-------|----|------|-----|
| Total      | 187  | 91.22 | 18 | 8.78 | 205 |
| Chi square | 0.42 |       |    |      |     |
| p value    | 0.50 |       |    |      |     |

The proportion of NIV use is notably higher in patients with HbA1c >6 compared to those with HbA1c <6, suggesting a possible association between poorer long-term glycemic control & increased need for ventilatory support. Statistical

analysis using the Chi-square test demonstrated a significant association between HbA1c levels & NIV use ( $\chi^2 = 4.41$ ,  $p = 0.036$ ) as shown in [Table 5].

**Table 5: Association of HbA1c & NIV use**

| HbA1c Category | NIV USE |       |     |       | Total |
|----------------|---------|-------|-----|-------|-------|
|                | No      |       | Yes |       |       |
|                | N       | %     | N   | %     |       |
| <6             | 72      | 61.54 | 45  | 38.46 | 117   |
| >6             | 43      | 48.86 | 45  | 51.14 | 88    |
| Total          | 115     | 56.09 | 90  | 43.91 | 205   |
| Chi square     | 4.41    |       |     |       |       |
| p value        | 0.036*  |       |     |       |       |

\*: statistically significant

The ICU outcomes were divided into Alpha category (1-3 days of ICU stay), Beta category (4-6 days of ICU stay), Delta category (7-9 days of ICU stay), Gamma category ( $\geq 10$  days of ICU stay) & Mortality as the extreme outcome. The

distribution of ICU stay duration & mortality appears comparable between the two HbA1c groups, with no clear trend indicating prolonged ICU stay or increased mortality with higher HbA1c levels [Table 6].

**Table 6: Association of HbA1c with ICU outcomes**

| HbA1c Category | ICU OUTCOMES     |                |                  |                     |           | Total |
|----------------|------------------|----------------|------------------|---------------------|-----------|-------|
|                | Alpha (1-3 days) | Beta (4-6days) | Delta (7-9 days) | Gamma ( $\geq 10$ ) | Mortality |       |
| <6             | 12               | 17             | 1                | 6                   | 6         | 42    |
| >6             | 10               | 13             | 2                | 5                   | 6         | 36    |
| Total          | 22               | 30             | 3                | 11                  | 12        | 78    |
| Chi square     | 2.89             |                |                  |                     |           |       |
| p value        | 0.55             |                |                  |                     |           |       |

## DISCUSSION

AECOPD is a major cause of chronic morbidity and mortality worldwide and represents a significant public health challenge due to its high prevalence, frequent hospitalizations, and substantial healthcare resource utilization. Hyperglycemia is a well-recognized physiological response to acute illness and commonly occurs during AECOPD. The underlying mechanisms include increased hepatic glucose production and peripheral insulin resistance mediated by elevated levels of glucocorticoids, catecholamines, and pro-inflammatory cytokines. In addition, infections, which are among the most common triggers of AECOPD, can further impair glucose metabolism by promoting hepatic glucose overproduction and peripheral insulin resistance, resulting in stress-induced hyperglycemia.<sup>[11,12]</sup> Despite these established mechanisms, the relationship between HbA1c and clinical outcomes in patients with AECOPD remains inadequately understood.

In the present study, males constituted the majority of patients with AECOPD (82.0%), indicating a marked male predominance. This finding is likely attributable to greater exposure to established risk factors, particularly smoking and occupational hazards, among men. Similar male predominance has been reported by Steriade AT et al,<sup>[13]</sup> Vaudan S et al,<sup>[14]</sup> Sanjay Tandon et al,<sup>[15]</sup> and Kamlesh Kumar Gupta et al.<sup>[16]</sup>

The mean age of the study population was 63.74 $\pm$ 9.46

years, with most patients belonging to the 56–65 and 66–75 year age groups. These findings suggest that AECOPD predominantly affects older adults and are consistent with previous studies by Sanjay Tandon et al,<sup>[15]</sup> Kamlesh Kumar Gupta et al,<sup>[16]</sup> and Pramila Devi R et al,<sup>[17]</sup> which also reported a higher burden of disease among patients in the sixth and seventh decades of life.

A greater proportion of participants were from rural areas (65.4%), possibly reflecting increased exposure to biomass fuel smoke, poor indoor air quality, and limited healthcare access in rural settings. In contrast, Sanjay Tandon et al,<sup>[15]</sup> reported a higher proportion of patients from urban areas.

Smoking was highly prevalent in the present study, with 85.4% of patients being smokers, reaffirming its pivotal role as a major risk factor for COPD and its exacerbations. This observation is in agreement with the findings of Sanjay Tandon et al,<sup>[15]</sup> who reported that 81% of patients were smokers, and Pramila Devi R et al,<sup>[17]</sup> who found that nearly all male patients (97.65%) had a history of smoking.

Patients were further categorized according to random blood glucose levels ( $\leq 140$  mg/dL and  $>140$  mg/dL) to evaluate the association between HbA1c and length of hospital stay among survivors. Within both HbA1c categories ( $\leq 6\%$  and  $>6\%$ ), no significant difference in hospital stay was observed between the two blood glucose groups ( $p>0.05$ ). However, when patients were analyzed according to HbA1c irrespective of admission blood glucose levels, those with HbA1c  $>6\%$  had a significantly

longer hospital stay than those with HbA1c  $\leq 6\%$  ( $8.08 \pm 2.20$  vs.  $7.44 \pm 2.19$  days;  $p=0.042$ ). These findings suggest that chronic glycemic status, rather than admission blood glucose alone, may have a greater influence on hospitalization duration in patients with AECOPD.

These findings are consistent with those of Kamlesh Kumar Gupta et al,<sup>[16]</sup> who also reported a significantly longer hospital stay among patients with HbA1c  $>6\%$  compared with those having HbA1c  $\leq 6\%$  ( $9.78 \pm 1.74$  vs.  $6.77 \pm 2.08$  days). Collectively, these observations indicate that poor long-term glycemic control is associated with prolonged hospitalization in AECOPD, although the impact of acute hyperglycemia varies across studies owing to differences in glucose assessment methods, patient characteristics, and treatment strategies.

**Limitations:** This study's generalizability to other populations is limited because it was conducted in a single hospital within the Western UP area. The confounding effects of corticosteroids are still present even though we were able to standardize the timing of blood glucose measurement (i.e., at the time of admission). This is because we were unable to ascertain whether participants were taking steroids prior to admission, & the severity of the airflow obstruction was not compared due to the absence of recent spirometric reports in a few patients.

## CONCLUSION

Patients with acute exacerbation of COPD and elevated HbA1c ( $>6\%$ ) experienced significantly longer hospital stays and were more likely to require non-invasive ventilation compared with those having HbA1c  $\leq 6\%$ , indicating that poor long-term glycemic control is associated with increased disease severity during hospitalization. However, HbA1c was not significantly associated with mortality, invasive mechanical ventilation, or ICU outcomes. These findings suggest that HbA1c may serve as a useful prognostic marker for predicting hospitalization burden and the need for ventilatory support in patients with AECOPD. Routine HbA1c assessment at admission may aid in early risk stratification and optimization of clinical management. Larger multicenter prospective studies are warranted to further establish the prognostic value of HbA1c and determine its role in improving outcomes in patients with AECOPD.

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## Conflicts of interest

There are no conflicts of interest.

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