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To Study The Impact Of Anaemia On Survival In Chronic Obstructive Pulmonary Disease With Acute Exacerbations

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ABSTRACT

Background and Aim: The global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease (COPD) defines COPD as a common preventable and treatable disease. Exacerbations and co morbidities contribute to the overall severity in individual patients. Anaemia of chronic disease is relatively common and an important factor in the natural history of COPD. So this study aimed to found out the impact of Anaemia on survival in COPD exacerbations.

Methods: 100 patients of COPD admitted in ICU of Department of Medicine, Mahatma Gandhi Hospital, Jaipur with exacerbation, were included according to inclusion and exclusion criteria.

Results: Out of 100 patients 83 patients needed NIV. Out of these patients 34 patients had NIV failure, 49 patients had successful NIV while 17 patients needed IMV. Mean Haemoglobin and hematocrit for NIV failure patients (11.39 ± 1.69gm/dl, 38.47 ± 3.23%) was significantly lower in comparison to NIV successful patients (13.40 ± 1.34gm/dl, 45.74 ± 3.97%). Duration of hospital stay in anaemic patients (21.91±8.92 days) was significantly higher than the non anaemic patients (18.26±8.09 days). Mean Haemoglobin and hematocrit for non survivors (11.59±1.59 gm/dl, 38.40±3.22%) was significantly lower than survivors (12.79±1.73 gm/dl, 44.20 ± 4.57%).

Conclusion: Anaemia increases the risk of hospital death in severe COPD exacerbations and it also increases requirement of mechanical ventilatory support.

Keywords: Chronic obstructive pulmonary disease, Noninvasive ventilation, Invasive mechanical ventilation, Hemoglobin, Hematocrit

INTRODUCTION:

Chronic obstructive pulmonary disease (COPD) is a name coined for the diseases that were previously known as chronic bronchitis and emphysema [1]. COPD the fourth leading cause of death worldwide represents an important public health challenge that is both preventable and treatable.

In recent years, Anaemia is seen as common co morbidity in COPD patients and associated with reduced functional capacity, impaired quality of life, greater likelihood of hospitalization, and early mortality [2].Any decrease in hemoglobin levels results in a corresponding reduction in the oxygen carrying capacity of the blood. Impairment of this mechanism exerts a negative impact on clinical status [3]. The prevalence of Anaemia in patients with COPD varies from 7.5% to 33% [4].

The systemic inflammation that is now recognized as a feature of COPD makes it a possible cause of Anaemia. If present in COPD, Anaemia could worsen dyspnea and limit exercise tolerance [5]. So, the purpose of our study was to identify whether presence of Anaemia on admission is a risk factor for hospital mortality in COPD exacerbations. We also aim that whether Anaemia effect the outcome of COPD in acute exacerbations in critical care.

METHODS:

100 patients admitted in ICU with COPD exacerbation in the Department of Medicine, Mahatma Gandhi Medical Colege, Jaipur were included according to inclusion and exclusion criteria. Aim of this study was to found out the presence of Anaemia on admission is a risk factor for hospital mortality in COPD exacerbations.

A Hospital based observational study was planned including COPD exacerbations patients who developed acute respiratory failure. Patients with COPD diagnosed according to GOLD criteria were included. Anaemia is defined as Haemoglobin levels <12 gm/dl for females patients and <13 gm/dl for male patients according to the World Health Organisation (WHO). Patients with suspected alternative cause for respiratory failure such as pulmonary embolism, acute respiratory distress syndrome, presence of active bleeding **,** recent operation or transfusion history, presence of a disease associated with bone marrow suppression , renal failure with glomerular filteration rate <30ml/min/1.73m2, malignancy, haematologic disorders and patients who do not give consent for study were excluded.

RESULTS:

Table 1: Distribution of patients on the basis of ventilatory support

Ventilatory support	No. of cases (n)
IMV	17
NIV successful	49

NIV failure	34
Total	100

Out of 100 patients 83 patients were on NIV. Out of these patients NIV failure observed in 34 patients, 49 patients had successful NIV while 17 patients needed IMV. Out of 100 patients 53 were anaemic while 47 were non anaemic.

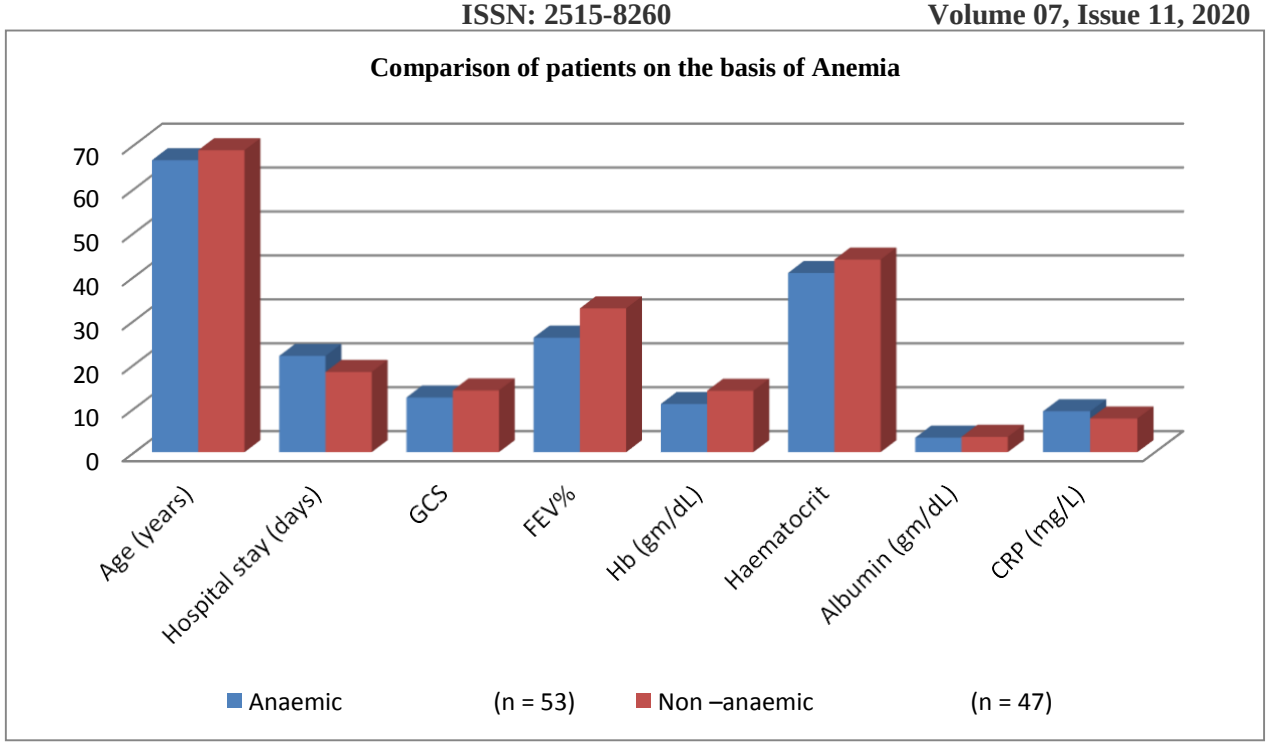
Table 2: Comparison in patients grouped on the basis of NIV outcome

General/ Clinical feature	NIV successful (n = 49)	NIV failure (n = 34)	P-value
Age (years)	66.27 ± 4.53	68.81 ± 6.81	0.044
Hospital stay	13.00 ± 3.97	28.76 ± 5.73	<0.001
GCS	**15.00**	**10.29 + 3.02**	**<0.001**
FEV%	**30.74 + 6.63**	**28.11 + 7.35**	**0.093**
Hb (gm/dl)	**13.40 + 1.34**	**11.39 + 1.69**	**<0.001**
Haematocrit	**45.74 + 3.97**	**38.47 + 3.23**	**<0.001**
Albumin (gm/dl)	**3.54 + 0.31**	**3.23 + 0.33**	**0.000**
CRP (mg/l)	**6.85 + 3.11**	**10.58 + 2.58**	**0.000**

Mean hospital stay for NIV successful patients was 13.00 ± 3.97 days and for NIV failure patients 28.76 ± 5.73 days. This difference was statistically significant (p <0.001). Mean GCS for NIV successful patients was 15.0 and for NIV failure patients 10.29 ± 3.02. This difference was statistically significant (p <0.001). Mean Haemoglobin for NIV successful patients and NIV failure patients was 13.40 ± 1.34gm/dl , 11.39 ± 1.69gm/dl and Haematocrit was 45.74 ± 3.97% , 38.47 ± 3.23% respectively. This difference was statistically significant (p <0.001).

Table 3: Comparison of patients on the basis of Anaemia

General/ Clinical feature	Anaemic (n = 53)	Non-anaemic (n = 47)	P-value
Age (years)	66.47± 4.65	68.74± 4.33	0.420
Hospital stay (days)	21.91±8.92	18.26±8.09	0.035
GCS	12.45 ± 3.24	14.05±2.12	0.005
FEV%	26.06±6.19	32.74±6.22	<0.001
Hb (gm/dl)	10.97±1.04	13.97±0.79	0.000
Haematocrit	40.80±4.51	43.84±5.03	0.002
Albumin (gm/dl)	3.30±0.33	3.49±0.37	0.008
CRP (mg/l)	9.30±3.45	7.66±3.39	0.019



Graph 1: Comparison of patients on the basis of Anaemia

Duration of hospital stay in anaemic and non anaemic patients was 21.91±8.92 days and 18.26±8.09 days respectively. This difference was statistically significant ($p<0.05$). GCS in anaemic and non anaemic patients were 12.45 ± 3.24 and 14.05±2.12 respectively. This difference was statistically significant ($p<0.05$). Mean Hb in anaemic and non anaemic patients were 10.97±1.04 gm/dl, 13.97±0.79 gm/dl

respectively and hematocrit was 40.80±4.51%, 43.84±5.03% respectively. This difference was statistically significant (p<0.001).

Table 4: Distribution of patients on the basis of mortality

General/ Clinical feature	Survivors (n = 66)	Non -survivors (n = 34)	P-value
Age (years)	66.76 ± 4.62	67.85 ± 4.19	0.252
Hospital stay (days)	15.05±5.07	30.18±4.50	<0.001
GCS	14.26±2.08	11.16±3.12	<0.001
Hb (gm/dl)	12.79±1.73	11.59±1.59	<0.001
Hematocrit	44.20 ± 4.57	38.40±3.22	<0.001
Albumin (gm/dl)	3.43± 0.37	3.31±0.34	0.118
CRP (mg/l)	7.38±3.33	10.76±2.68	<0.001

Mean hospital stay in survivors and non survivors were 15.05±5.07 and 30.18±4.50 days respectively. This difference was statistically significant (p<0.001). Mean GCS in survivors and non survivors were 14.26±2.08 and 11.16±3.12 respectively. This difference was statistically significant (p<0.001). Mean Hb in survivors and non survivors was 12.79±1.73 gm/dl, 11.59±1.59 gm/dl respectively and hematocrit was
44.20 ± 4.57%, 38.40±3.22 % respectively. This difference was statistically significant (p<0.001).

DISCUSSION:

COPD is a major cause of health burden throughout the world. COPD often coexists with other co morbidities such as cardiovascular diseases, osteoporosis, skeletal muscle dysfunction, depression, and Anaemia [6]. The mechanism of development of Anaemia and the impact of Anaemia on the prognosis of COPD remain poorly understood. Hence, this study was performed to search acute COPD exacerbation linked with Anaemia and to evaluate the role of Anaemia on the prognosis of COPD.

In this study 83 patients were on non invasive ventilation (NIV) and 17 patients needed invasive mechanical ventilation. Out of 83 patients of NIV 34 patients were not able to maintain saturation on NIV and shifted to IMV. It means 34 patients had NIV failure and only 49 patients had successful NIV. Out of 100 patients 53 were anemic while 47 were non anemic.

In this study mean Hemoglobin for NIV successful patients and NIV failure patients was 13.40 $\pm$ 1.34gm/dl , 11.39 $\pm$ 1.69gm/dl and Hematocrit 45.74 $\pm$ 3.97% , 38.47 $\pm$ 3.23% respectively. This difference was statistically significant ($p < 0.001$). It shows lower hemoglobin and hematocrit levels in NIV failure patients. Our results were in agreement with study done by Begum Ergan et al in 2016 as they observed NIV failure was more in the anemic patients when compared to non anemic group (49% vs 22.6%, respectively; P=0.001) [7]. Another study conducted by Haja Mydin et al in 2013 looked for prognostic factors in hypercapnic respiratory failure and showed that Anaemia was related to increased risk of NIV failure [8]. Possible mechanism for that there is a relationship between muscle oxygenation and peak oxygen consumption which varies extensively in COPD and oxygen consumption is highly influenced by blood oxygenation and oxygen utilization level [9]. Anemic COPD patients also exhibit decreased diffusing capacity of oxygen corrected for hemoglobin. All these changes in transportation of oxygen lead to decrease in aerobic capacity and consequently skeletal muscle dysfunction in severe COPD during exercise. We can expect these changes to be more with patients with low hemoglobin levels, especially during episodes of exacerbations because of increased oxygen demand due to increased work of breathing and impaired cardiopulmonary interactions.

In this study total 83 patients were on NIV. Out of these patients 40 patients had Anaemia and while remaining 43 patients were non-anemic. Out of these, 32.6% patients of Anaemia had successful NIV in comparison 67.4% of non-anemic patients and 70.6% patients of Anaemia had NIV failure while only 29.4% patients who had no Anaemia. It shows anemic patients had significant NIV failure rate in comparison to non anemic patients.

When we compared GCS in anemic and non-anemic patients it was significantly low in anemic patients in comparison to non anemic patients and albumin levels was significantly lower while CRP levels were significantly higher in anemic patients in comparison to non anemic patients. Nutritional factor like a lower serum albumin level was independently associated with the serum hemoglobin level in COPD, suggesting malnutrition is linked with Anaemia in COPD. Previous studies also reported that Anaemia mainly develops due to chronic inflammation in COPD because the low-grade systemic inflammation is associated with an increased risk of major co-morbidities in COPD, irrespective of smoking. However, multiple factors have been suggested to cause Anaemia in COPD in addition to systemic inflammation these are: an increasing age, malnutrition and the use of certain medicines such as theophylline and angiotensin converting enzyme inhibitor.

In our study 24.5 % patients of Anaemia needed IMV in comparison to 8.5% of non- anemic patients while 75.5% patients of Anaemia needed NIV in comparison to 91.5% non-anemic patients. This difference was statistically significant ($p < 0.05$). 40% patients of Anaemia sustained successfully on NIV while remaining 60% patients had NIV failure and 76.7% non-anemic patients maintained on NIV and only 23.3% had NIV failure. It shows significantly higher NIV failure rate in anemic patients in comparison to non anemic patients.

In this study 34 patients died while 66 patients survived. Mean hospital stay in non survivors was significantly higher in comparison to survivors; mean GCS was significantly lower in patients who didn't survived. Mean albumin was lower in non survivors in comparison to survivors while high level of CRP as an inflammatory marker in non survivors. This difference was statistically significant ($p<0.001$)

In this study we found lower hemoglobin and lower hematocrit level in non survivors. This difference was statistically significant ($p<0.001$). It shows Anaemia

was a risk factor for mortality. Study done by Anne Pernille et al in 2016 demonstrates that low concentrations of hemoglobin are associated with increasing mortality after discharge in patients admitted for acute exacerbation of COPD [10]. Previous studies with various cohorts reported that Anaemia is associated with a reduced survival in COPD. Anaemia has been shown to be associated with increased mortality in COPD related acute respiratory failure. All these data suggested that, besides being an important predictor of long term survival, Anaemia should also be considered as a risk factor for short term mortality in severe COPD exacerbations.

The mechanisms of the development of Anaemia in COPD are complex but disease severity seems to be one of the most important factors. Anaemia was proposed as a marker for end stage COPD. COPD is a disease of systemic inflammation in which many cytokines including IL-1, IL-6 and TNF-alpha, play important role. These cytokines are also having role in inhibition of erythropoiesis at different steps of the erythropoietic pathway. Markoulaki et al showed that a severe exacerbation itself caused transient changes in hemoglobin levels with a median decrease of 1.3 gm/Dl [11]. They found a negative correlation between hemoglobin and erythropoietin (EPO) levels which depicts increased EPO resistance during exacerbations. It is well known that erythropoietin resistance is directly correlated with the levels of inflammatory cytokines and therefore the level of systemic inflammation. Repeated exacerbations could cause further inhibition of erythropoiesis and due to this significant decrease in hemoglobin levels can occur in severe COPD. Thus, Anaemia could be accepted as a surrogate of severe systemic inflammation and might be helpful in identifying sicker patients. Additionally, alteration in iron metabolism is another important mechanism responsible for the development of Anaemia of chronic disease. Recently, it was suggested that specific attention should be paid to iron deficiency even in the absence of Anaemia, and iron supplementation may be helpful in anemic COPD patients.

CONCLUSION:

We can conclude from this study that Anaemia is related with increased mortality in acute COPD exacerbations and it is also associated with NIV failure. Further more studies are needed to understand the physiological consequences of Anaemia in COPD exacerbations and its impact on clinical outcomes.

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