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A study on Serum albumin as an indicator for respiratory failure in COPD patients experiencing acute exacerbations, both with and without cor pulmonale in a tertiary care hospital

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ABSTRACT:

Background: COPD is a prevalent disease that can be prevented and treated, marked by ongoing respiratory symptoms and restricted airflow, primarily due to issues in the airways or alveoli, often resulting from significant exposure to harmful particles or gases

OBJECTIVES:

1. To analyze the role of serum albumin in COPD patients with acute exacerbation.
2. To determine whether serum albumin can predict respiratory failure in COPD patients.

MATERIAL & METHODS: Study Design: Prospective hospital-based observational study. **Study area:** The study was conducted in the Department of Pulmonary Medicine**. Study Period:** 1 year. **Study population:** Only males with a smoking history and previously diagnosed COPD patients based on spirometry were included in the study. **Sample size:** The study consisted of 103 subjects. **Sampling method:** Simple random Sampling Technique.

Results: Among the study group, 56 patients (54.4%) have serum albumin <3.8 and 47 patients (45.6%) have serum albumin in the range of 3.8-5.1. respiratory failure is more common among patients with low serum albumin (74.6%) than in patients with a normal serum albumin range (25.4%).

CONCLUSION: The current research indicates that low albumin levels (hypoalbuminemia) are a significant predictor of respiratory failure in patients with acute exacerbations of chronic obstructive pulmonary disease (AECOPD). It also predicts the necessity for non-invasive ventilation (NIV) or invasive mechanical ventilation (IMV) in these patients.

Keywords: COPD, cor pulmonale, non-invasive ventilation, acute exacerbations

INTRODUCTION:

COPD is a prevalent disease that can be prevented and treated, marked by ongoing respiratory symptoms and restricted airflow, primarily due to issues in the airways or alveoli, often resulting from significant exposure to harmful particles

or gases. The chronic airflow limitation seen in COPD arises from a combination of small airway disease (such as obstructive bronchiolitis) and damage to the lung tissue (emphysema), with the specific contributions differing among individuals.[1]

COPD is currently the world's fourth greatest cause of death[2], but it is expected to become the third main cause by 2020. In 2012, more than 3 million people died from COPD, accounting for 6% of total fatalities worldwide[3]. Tobacco use is the leading risk factor for COPD worldwide. Non-smokers can also acquire COPD. COPD is caused by a complex interplay of long-term cumulative exposure to toxic gases and particles, as well as several host factors such as genetics, airway hypersensitivity, and inadequate lung expansion during childhood.[4-6]

COPD is a leading source of morbidity and mortality, affecting roughly 10% of patients. Exacerbation occurs when a person's breathing gets worse than normal, which can result in life-threatening problems depending on the reason and severity, and is a significant event for COPD management due to its negative impact on disease progression, health status, and quality of life. [7,9,10] About 10% of all hospitalizations are directly or indirectly due to COPD, putting a considerable strain on the healthcare system. [11]

Acute exacerbation is strongly associated with higher emergency department visits, respiratory failure, hospitalizations, and fatalities in COPD patients.

Long-term mortality among in-hospital COPD patients treated for AECOPD is high, with a survival rate comparable to lung cancer. [12,13] According to the Intensive Care National Audit and Research Center (ICNARC) case-mix program database, 23.1% of patients die in the ICU and 38.8% during hospitalization [14]. The ICU therapy of these high-risk patients comprises ventilator support (NIV or IMV), inhaled bronchodilators, systemic corticosteroids, and antibiotics, although the evidence for these strategies is essentially nonexistent [15].

Corpulmonale is a right ventricular enlargement caused by structural or functional abnormalities in the respiratory system. The expansion could indicate hypertrophy, dilatation, or both. It occurs from an increase in afterload caused by pulmonary hypertension. The frequency of cor pulmonale is associated with pulmonary hypertension-causing illnesses. Cor pulmonale is responsible for up to 20% of hospital admissions for heart failure and a considerable fraction of all cardiac diseases.[16]

Serum albumin has long been regarded as a biomarker for accurate risk prediction in various clinical scenarios. Low SA levels are linked to an increased risk of all-cause and cardiovascular mortality[17]; dietary status and systemic inflammation influence serum albumin synthesis[18]. Thus, it is important to understand the predictive value of serum albumin in COPD. Proper interpretation of serum albumin, in addition to recognized risk indicators, may give superior risk discrimination and thus present an opportunity to change therapy regimens accordingly.

Corpulmonale in AECOPD causes increased morbidity and death and imposes a significant economic cost. Predicting the role of albumin as a marker of corpulmonale in AECOPD aids in reducing early morbidity and planning future therapies.[19] Because of the foregoing, we conducted a study titled "Comparative analysis of serum albumin as a predicting factor for respiratory failure in COPD patients with acute exacerbation with and without corpulmonale."

OBJECTIVES:

1. To analyze the role of serum albumin in COPD patients with acute exacerbation.
2. To determine whether serum albumin can predict respiratory failure in COPD patients.
3. To determine the association between serum albumin and corpulmonale.
4. To analyze whether a proper interpretation of SA in addition to established risk factors potentially provides better risk discrimination.

MATERIAL & METHODS:

Study Design: Prospective hospital-based observational study.

Study area: The study was conducted in the Department of Pulmonary Medicine**.**

Study Period: 1 year.

Study population: Only males with a smoking history and previously diagnosed COPD patients based on spirometry were included in the study.
Sample size: The study consisted of 103 subjects.
Sampling method: Simple random Sampling Technique.
Inclusion criteria:
1. Age >35 years
2. History of smoking present
3. Known cases of COPD with Cor Pulmonale
4. Known cases of COPD without Cor Pulmonale
5. Room air SpO2<90% in COPD patients
6. Other criteria include positive findings of COPD on clinical examination.
7. Positive radiological, pathological, and other supportive laboratory findings

Exclusion criteria:
1. Community-acquired Pneumonia cases
2. Hospital-acquired pneumonia cases
3. Human Immunodeficiency Virus
4. Malignancy
5. Active tuberculosis
6. COPD patients with room air SpO2>95%
7. Morbidly Obese patients
8. Severe Cardiac Disease
9. Unwilling Patients
10. Recent History of Head Trauma
11. Diagnosed Psychiatrically ill patients
12. Recent History of Drug Abuse
13. Admitted with acute coronary event
14. Bronchiectasis
15. Fibrosis
16.PTB cases

Statistical analysis:
For statistical calculations, data is spread in an Excel sheet descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at a 5% level of significance. The Chi-square/Fisher Exact test has been used to find the significance of study parameters on a categorical scale between two or more groups. A p-value < 0.05 was considered statistically significant. The Statistical software namely SPSS 21.0 was used for the analysis of the data.

OBSERVATIONS & RESULTS:

Table 01. Distribution of study participants based on age(n=103)

group (in years)	**Frequency**	**Per cent**
35- 40	5	4.9

41-50	14	13.6
51-60	30	29.1
>60	54	52.4
Total	103	100.0

The majority of the study participants are in the age group of more than 60 years (52.4%). The mean age of the study participants was observed to be 61.49 ± 11.01 years.

Table No 2-Distribution of study group based on literature

Respiratory Failure					**Total**
Present				**Absent**	
Literature	No	Count	42	20	62
		% within Respiratory Failure	66.7%	50.0%	60.2%
	Yes	Count	21	20	41
		% within Respiratory Failure	33.3%	50.0%	39.8%
Total		Count	63	40	103
		% within Respiratory Failure	100.0%	100.0%	100.0%

Chi-square value = 2.836, P-value = 0.092 (Not Sig)

Out of 103 study participants, 62 patients (60.2%) are illiterates, and 41 patients are literate. Respiratory failure is more common among illiterates 42(66.7%) than among literates with respiratory failure whose number is 21(33.3%).

The majority of study participants are farmers 61 patients (59.2%), followed by Cooli 24 patients (23.3%), followed by teachers i.e 7 patients (6.8%), followed by drivers accounting for 4 patients (3.9%). Respiratory failure is predominant among farmers (55.6%), followed by cool (28.6%) followed by teachers (4.8%).

Table 3-Distribution of study group based on cough and its association with respiratory failure

Respiratory Failure					
Present				Absent	Total
Cough	No	Count	31	30	61
		% within Respiratory Failure	49.2%	75.0%	59.2%
	Yes	Count	32	10	42
		% within Respiratory Failure	50.8%	25.0%	40.8%
Total		Count	63	40	103
		% within Respiratory Failure	100.0%	100.0%	100.0%

Chi-square value = 6.740, P-value = 0.009 (Sig.)

Among the study population, 61 patients (59.2%) did not have a cough and, 42 patients (40.8%) had a cough. Respiratory

failure is more common among patients presenting with a cough (50.8%) than patients presenting without a cough (49.2%).

Among the study group, 65 patients (63.1%) presented without productive cough, and 38 patients (36.9%) presented with productive cough. Respiratory failure is more common among patients presenting without a productive cough (55.6%) than with a productive cough that is (44.4%).

Among the study group, 32 patients (31.1%) presented without dyspnoea, and 71 patients (68.9%) presented with dyspnoea. Respiratory failure is more common among patients presented with dyspnoea (98.4%) than without dyspnoea (1.6%).

Among study participants, 29 patients (28.2%) did not have wheeze, and 74 patients presented with wheeze (71. 8%).respiratory failure is more among patients presented with wheeze (79.4%) than patients without wheeze (20.6%).

Table – 4:-Distribution of study group based on Weight Loss and its association with respiratory failure

Respiratory Failure					Total
Present				Absent	
Weight Loss	No	Count	29	36	65
		% within Respiratory Failure	46.0%	90.0%	63.1%
	Yes	Count	34	4	38
		% within Respiratory Failure	54.0%	10.0%	36.9%
Total		Count	63	40	103
		% within Respiratory Failure	100.0%	100.0%	100.0%

Chi-square value = 20.315, P-value = 0.0001 (Very High Sig.)

Among the study group, 65 patients (63.1%) did not have weight loss, whereas 38 patients (36.9%) had weight loss. Respiratory failure is more common among patients presenting with weight loss (54%) than in patients presenting without weight loss (46%).

Table 5: - Distribution of study group based on serum albumin levels and its association with respiratory failure

Respiratory Failure					
Present				Absent	Total
Albumin_GRP	< 3.8	Count	47	9	56
		% within Respiratory Failure	74.6%	22.5%	54.4%
	3.8 - 5.1	Count	16	31	47
		% within Respiratory Failure	25.4%	77.5%	45.6%
Total		Count	63	40	103
		% within Respiratory Failure	100.0%	100.0%	100.0%

Chi-square value = 26.772, P value < 0.0001 (Very High Sig.)

Among the study group, 56 patients (54.4%) have serum albumin <3.8 and 47 patients (45.6%) have serum albumin in the range of 3.8-5.1. respiratory failure is more common among patients with low serum albumin (74.6%) than in patients with a normal serum albumin range (25.4%).

Among the study group, 8 patients (7.8%) have sodium of <130, 15 patients (14.6%) have serum sodium of >143, and 80 patients have serum sodium in the range of 130-143. respiratory failure is seen among patients with normal serum levels of sodium (71.4%), followed by patients with higher serum sodium levels (19%).

Among the study group, 53 patients (51.5%) have hb<13%, 45 patients (43.7%) have hb between 13 -15 %, and 5 patients (4.9%) have hb of >15%. Respiratory failure is more common among patients with hb<13%(58.7%) followed by (36.5%) in patients with 13- 15%.

Table 6. Association between Cor pulmonale and Respiratory Failure (n= 103)

Cor pulmonale	**Respiratory failure**		Total n (%)	p-value*
	Present n (%)	Absent n (%)		
Present	45 (75)	15 (25)	60 (100)	0.001
Absent	18 (41.9)	25 (58.1)	43 (100)	
Total	63 (61.2)	40 (38.8)	103 (100)	

The chi-square test was applied to test the statistical difference in proportions.

In the study group, corpulmonale is present in 60 patients and absent in 43 patients. Respiratory failure is more common among COPD patients with corpulmonale that is [75%] than in patients without corpulmonale [41.9%]. A higher proportion of patients with respiratory failure are associated with corpulmonale, which is statistically significant with a p-value of 0.001.

Among the 103 study population, 43 patients do not have corpulmonale, and among them, 21 patients have albumin of <3.8g/dl. Of 21 patients, 16 patients presented with respiratory failure.

Of 43 patients, 22 patients have serum albumin in the range of 3.8-5.1g/dl, out of which only two patients had respiratory failure, and 20 patients did not have respiratory failure.

The proportion of patients with hypoalbuminemia, and without cor-pulmonale and presented with respiratory failure is [76.19%].

Table; -7-Sensitivity, specificity, PPV, NPV, of albumin in patients with RF and without

corpulmonale

The specificity and sensitivity of albumin <3.8 g/dL are 80 % and 88.8%, respectively, among patients without Cor pulmonale. The positive and negative predictive values are 76.19 % and 90.9 %, respectively.

Statistic	Formula	Value	95% CI
Sensitivity	$\frac{a}{a+b}$	88.89%	65.29% to 98.62%
Specificity	$\frac{d}{c+d}$	80.00 %	59.30% to 93.17%
Positive Likelihood Ratio	$\frac{Sensitivity}{1-Specificity}$	4.44	2.00 to 9.90
Negative Likelihood Ratio	$\frac{1-Sensitivity}{Specificity}$	0.14	0.04 to 0.52
Disease prevalence	$\frac{a+b}{a+b+c+d}$	41.86% (*)	27.01% to 57.87%
Positive Predictive Value	$\frac{a}{a+c}$	76.19% (*)	58.96% to 87.70%
Negative Predictive Value	$\frac{d}{b+d}$	90.91 % (*)	72.74% to 97.40%
Accuracy	$\frac{a+d}{a+b+c+d}$	83.72% (*)	69.30% to 93.19%

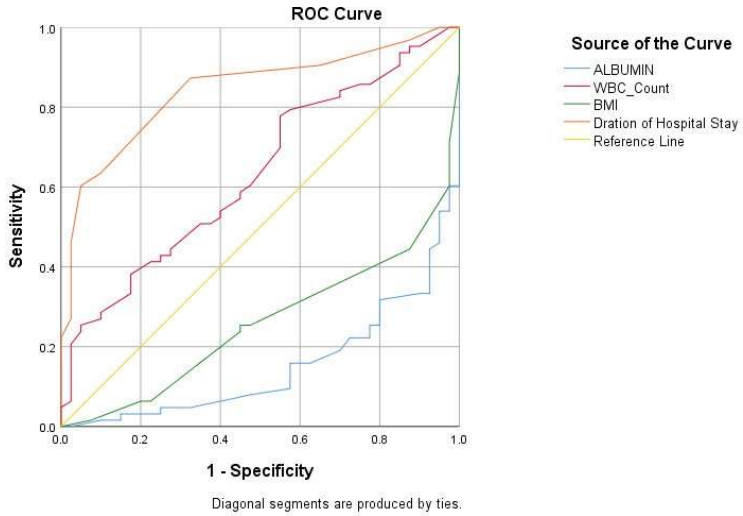
Table: -8-Distribution of study group based on the use of NIV or IMV and its association with RF

Respiratory Failure					
Present				Absent	Total
TYPE_VENT	NIL	Count	2	39	41
		% within Respiratory Failure	3.2%	97.5%	39.8%
	NIV	Count	44	0	44
		% within Respiratory Failure	70.8%	0.0%	42.7%
	Ventilator	Count	18	0	18
		% within Respiratory Failure	28.6%	0.0%	17.5%
Total		Count	63	40	103
		% within Respiratory Failure	100.0%	100.0%	100.0%

Chi-square value = 90.877, P value < 0.0001 (Very High Sig.)

Among the study group, 41 patients (39.8%) were not on any ventilator or NIV support, 44 patients (42.7%) were on NIV support, and 18 patients (17.5%) were on ventilators. A significant proportion of patients presenting with respiratory failure are on NIV, which is [70.8%]. And 28.6% of patients with respiratory failure were connected to the ventilator.

Fig-1:-ROC Curve (Resp_Failure = Present)



Case Processing Summary

Respiratory Failure	Valid N (listwise)
Positive	63
Negative	40

Larger values of the test result variable(s) indicate stronger evidence for an actual positive state.

a. The test result variable(s): BMI has at least one tie between the positive real state group and the negative actual state group.

b. b. The actual positive state is Present.

Table: -9-Area Under the Curve

Test Result Variable(s)	Area	Std. Error	P-Value	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
ALBUMIN	.151	.037	<0.0001 VHS	.078	.223
WBC_Count	.633	.055	.023 SIG	.525	.741
BMI	.260	.048	<0.0001 VHS	.166	.353

Duration of Hospital Stay	.843	.039	<0.0001 VHS	.767	.920

The ROC curve is the receiver operating characteristic curve. Based on AUC, variables that have a value of >0.8 are identified as useful diagnostic variables. That is, these variables have a more exceptional ability to diagnose or predict respiratory failure; they are albumin, WBC count, BMI, and duration of hospital stay. Among this duration of hospital stay, followed by WBC count, followed by BMI, and albumin in descending order have a greater predicting ability of respiratory failure. Duration of hospital stay, BMI, and albumin has a p-value of <0.0001, which is very highly significant, whereas the p-value of WBC count is <0.023, which is statistically significant, but it has a more exceptional ability to predict respiratory failure as per ROC curve.

DISCUSSION:

In the present study, out of 103 patients, 63 patients had respiratory failure, and their mean age was 61.24+/-11.678, and 40 patients did not have respiratory failure but presented with acute exacerbation of COPD, and their mean age was 61.88+/-10.008. There is not much difference in the age group in both the respiratory failure group and the no respiratory failure group. So based on the above results, we conclude that the majority of patients presenting with AECOPD are elderly. In a study conducted by ARAN SINGANAYAGAM ET AL[20] on predictors of mortality in hospitalized adults with acute exacerbation of COPD, twelve prognostic factors were considered, of which nine prognostic factors are associated with long-term mortality. They are age, low BMI, cardiac failure, diabetes mellitus, IHD, malignancy, FEV1, long-term oxygen therapy, and pa02 on admission.

In a study by Seneffe, et al[21] variables associated with hospital mortality were age, weight, dysfunction of respiratory and other organs, and length of hospital stay before ICU admission. In our study, no patients died of respiratory failure due to COPD, though it included elderly patients due to the availability of excellent ICU facilities and ICU care. However, the majority of elderly patients presented with respiratory failure.

In a study conducted by Mark D Eisner et al[22,] lower educational attainment and household income were consistently related to higher disease severity, more reduced lung function, and more significant physical functional limitations in the cross-sectional analysis. Our study also proved the same. In a study conducted by Michal Szczyrek et al.[23] on chronic obstructive pulmonary disease in farmers and agricultural workers, livestock farmers have an increased risk of chronic bronchitis, COPD, and reduced FEV1. Our study also shows that the majority of patients attending hospitals with AECOPD are farmers and have an increased risk of respiratory failure.

DOHERTY et al.[24] investigated the cough reflex sensitivity to capsaicin in COPD and asthma compared with healthy volunteers. In this group of COPD hospital outpatients, with a mean FEV1 of 42% predicted, 81% of patients complained of cough on most of the days. In our study, the number of patients presenting with cough as a symptom is less than 40.8 %, when compared to patients without cough (59.2%)this may be due to the small sample size., but the risk of respiratory failure in patients presenting with a cough is more (50.8%).

According to (Rennard et al.[25]), sputum production, cough, and breathlessness are the major symptoms of which patients complain, although the relative importance depends on the stage of the disease. According to (Von Hertzen et al.[26]), patients with mild to moderate airflow obstruction report cough and sputum production more frequently than those with severe disease. Among the study group, 32 patients (31.1%) presented without dyspnoea, and 71 patients (68.9%) presented with dyspnoea. Respiratory failure is more common among patients presenting with dyspnoea (98.4%) than those without dyspnoea (1.6%). With a very high significant P-value that is <0.0001, and a chi-square test value = 65.835. Holleman andsimel[27] in a prospective study reported that the number of years the patient had smoked cigarettes, the number of years the patient reported wheezing and auscultated wheezing were independent predictors of airflow obstruction, which is a sign of acute exacerbation. Our study also proved that respiratory failure is more common among patients presenting with wheeze than without wheeze with a statistically significant p-value of <0.033.

Among the study group, 56 patients (54.4%) have serum albumin <3.8, and 47 patients (45.6%) have serum albumin in the range of 3.8-5.1. Respiratory failure is more common among patients with low serum albumin (74.6%) than in patients with a normal serum albumin range (25.4%). In a study conducted by char-wenChen et al[28] hypoalbuminemia is a substantial independent risk for respiratory failure in COPD patients with a p-value of <0.001.

Our study also proved that COPD patients having low serum albumin are at increased risk of having respiratory failure. With a p-value of <0.0001, which has very high significance, and the chi-square test value is = 26.772, it shows that albumin and respiratory failure have a strong association. In a study conducted by Nuraimeearsae et al[29], the only factor associated with respiratory failure was low serum albumin levels on the first day of admission with a p-value of 0.003. The study also proved the same. In a study conducted by Gordanapavlisa, et al[30], Hypoalbuminemia is one of the risk factors for respiratory failure in patients with severe exacerbations of COPD requiring invasive mechanical ventilation, with a p-value of 0.010. Our study also proved that low serum albumin is a predicting factor for respiratory failure in AECOPD patients.

Cor pulmonale is defined as an alteration in the structure and function of the right ventricle caused by a primary disorder of the respiratory system. Pulmonary hypertension [PH] is the common link between lung dysfunction and the heart in cor- pulmonale. Cor pulmonale can develop due to various cardiopulmonary diseases. Cor-pulmonale usually has a slow and chronic progression, but acute onset and life-threatening complications can occur. In the study group, corpulmonale is present in 60 patients and absent in 43 patients. respiratory failure is more common among COPD patients with corpulmonale that is [75%], than in patients without corpulmonale [41.9%] higher proportion of patients with respiratory failure are associated with corpulmonale with a chi-square test = 11.581and p-value of = 0.001 which is statistically significant.

In the present study, we have categorized 103 patients into three groups based on the history of exacerbations per year. They are 0-1 exacerbation/year, 2-3 exacerbation/year, and >3 exacerbation/year. Thirty-eight patients have 0-1 exacerbation per year; among them, 23 patients [60.5%] presented with respiratory failure, and 15 patients [39.5%] did not have respiratory failure. Forty-five patients have 2-3 exacerbations per year, of which 26 patients [57.8%] have respiratory failure, and 19 patients [42.2%] do not have respiratory failure. Among the study group, 20 patients are having >3 exacerbations history per year. Out of these 14 patients [70%] have respiratory failure, and three patients [30%] do not have respiratory failure. Based on the above study results, there was no significant association noted between the number of exacerbation episodes and respiratory failure among the study population with a p-value of 0.644 [not significant].

In a study conducted by Yunus Cloak et al[31] on whether the prognosis of COPD depends on the severity of exacerbation, which is a population-based analysis, they found that individuals with COPD and h/o exacerbation carried the poorest prognosis compared to those without exacerbation or h/o medically treated exacerbation, suggesting the difference in risk profile.

CONCLUSION:

The current research indicates that low albumin levels (hypoalbuminemia) are a significant predictor of respiratory failure in patients with acute exacerbations of chronic obstructive pulmonary disease (AECOPD). It also predicts the necessity for non-invasive ventilation (NIV) or invasive mechanical ventilation (IMV) in these patients. In light of the results from this study, we recommend that COPD patients undergo routine nutritional evaluations and consultations once they receive their diagnosis. However, additional prospective research may be necessary to establish whether albumin supplementation or nutritional support can lower the risk of acute respiratory failure (ARF) in COPD patients. According to our findings, serum albumin serves as a crucial indicator of corpulmonale in individuals with AECOPD. Our study further demonstrates that the length of hospital stay is significantly longer for patients experiencing respiratory failure compared to those who do not. Therefore, it holds prognostic importance in assessing recovery duration.

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