



Serum Albumin And C - Reactive Protein/ Albumin Ratio On Admission As Prognostic Predictors In Sars-Cov-2 Infection: A Retrospective Study

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Abstract

The salient objective of this research was to assess the serum albumin levels and C - reactive protein /albumin ratio in the admitted cases of SARS-CoV-2 in a tertiary care hospital, we tried to predict the severity of the disease like increased oxygen requirement during the hospital stay and on discharge, intensive care unit (ICU) requirement, longer hospital stay and secondary infections during the hospital stay by assessing by the C - reactive protein /albumin ratio biomarker. The study was conducted as a retrospective observational one, a total of 200 SARS-CoV-2 infected subjects were considered for the study, and each subject was carefully examined and data collected. Based on the objective of interest we correlated Serum Albumin levels and C - reactive protein /Albumin Ratio at the time of admission and subsequent clinical course of patient was noted. As per the findings, the mean CRP was 2.68 g/L in mild cases; moderate was 6.38 g/L, and severe was 7.44 g/L. The higher CRP is significantly associated with a tendency for respiratory distress, increased requirement of high flow oxygen treatment and patients requiring mechanical ventilation. CRP/Alb ratio on the mean differences was 0.386, the serum albumin level significantly differed at 1% level. In conclusion, CRP/alb ratio is a valid Biomarker for treating SARS-CoV-2 patients and provides substantial information to the clinicians for making a valid decision at the right time.

Keywords: SARS-CoV-2, CRP, albumin ratio, Covid induced mortality, Survivor

1093

DOI Number: 10.48047/NQ.2022.20.17.NQ880141

Neuroquantology 2022; 20(17):1093-1099

INTRODUCTION

Ever since the pandemic began, SARS-CoV-2 has taken the world by a storm. The infection may be asymptomatic, mild, and often progressing to severe form leading to death. Colossal research is underway pertaining to the disease detection, prevention, varied clinical manifestations, treatment, and complications. It has become cardinal to find biomarkers that can help predict clinical worsening, requirement of longer stay in the hospital, complications post recovery and finally mortality. In a study by Das et al it was found that, several biomarkers that include IL-6, NT Pro BNP, hs Troponin I, PCT, CRP, Ferritin, LDH, Creatinine, BUN, AST, ALT, tend

to increase in SARS-CoV-2 patients. Markers like PO₂, SO₂, Total protein, Albumin, tend to decrease in such patients. ⁽¹⁾ Albumin is a protein synthesized in the liver and its main role is to maintain oncotic pressure, provide nourishment to tissues, binding and transporting substances, and maintaining acidbase equilibrium. During critical illness, inflammatory mediators decrease albumin synthesis in order to prioritize synthesis of other acute phase reactants. Aziz et al. performed a meta-analysis of four studies that found an increased risk for severe SARS-CoV-2 (defined as respiratory distress, ICU admission, and/or death) with hypoalbuminemia. ⁽²⁾ In a retrospective cohort study of 299 patients,



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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest

Huang et al. showed that hypoalbuminemia was an independent predictor for mortality in COVID-19 patients. ⁽³⁾Moreover, low serum albumin concentrations in critical illness have been associated with poor outcomes.⁽⁴⁾ In a study by Kheir M et al, A total of 109 patients (60.2%) had hypoalbuminemia (albumin level <3.3 g/dL). Patients with higher albumin levels on admission had a 72% decreased risk of developing venous thromboembolism, were associated with a lower risk of developing ARDS, admission to the ICU and were less likely to be readmitted within 90 days. Furthermore, higher albumin levels were associated with fewer total adverse events (p<0.001) ⁽⁵⁾Hypoalbuminemia was an early predictor of in-hospital mortality in SARS-CoV-2, regardless of age, comorbidity and inflammatory markers as seen in a study done by María C. Viana-Llamaset al where 609 patients were studied⁽⁶⁾ CRP is an acute phase protein released from hepatocytes after stimulation by various cytokines in response to infection, ischemia, trauma, and other inflammatory conditions. High CRP levels have been found in critically ill patients in relation to prognosis and mortality. The CRP/Albumin ratio, which is the result of the ratio of these two parameters to each other, has just been started to be used. The CRP/Albumin ratio was first reported to identify patients with serious illness in an acute medical ward. ⁽⁷⁾ The CRP/Albumin ratio is believed to be a more reliable predictor of inflammatory status than CRP or albumin alone. ⁽⁸⁾CRP/albumin ratio was an independent risk factor for 30-day mortality rate in patients with SARS-CoV-2as seen in the study by Mohamed El-Shabrawy et al, where 116 patients were studied, and it showed lower survival in patients with elevated CRP/Albumin ratio (log rank test p<0.0001) ⁽⁹⁾ Being vigilant about these affordable yet critical markers in SARS-CoV-2 patients may lead to early identification of

patients at risk for developing in-hospital complications, close monitoring, and follow-up for complications during hospital stay. The field of SARS-CoV-2 research is rapidly growing;a few studies have examined whether serum albumin levels and CRP/albumin ratio in SARS-CoV-2 infection can be used as a factor to predict severity and outcome in the global and the Indian scenario. Hence the idea of this study was born. The salient objective of the present research to assess the Serum Albumin levels and C - reactive protein /Albumin Ratio on admission in patients admitted with COVID19 infection can predict severity of disease (like increased oxygen requirement during hospital stay and on discharge, Intensive care unit ICU requirement, longer hospital stay and secondary infections during hospital stay) and also correlated the Serum Albumin levels and C-Reactive Protein /Albumin Ratio on admission in patients admitted with SARS-CoV-2 infection can predict adverse events (like venous thromboembolism, acute respiratory distress syndrome(ARDS), cerebrovascular accidents, acute coronary syndrome and acute kidney injury).

1094

Methodology

The study was conducted at Department of General Medicine in a tertiary care hospital. The recruitment procedure was done after the patient's satisfied the inclusion criteria. Retrospective case records design was adopted for conducting the research. We reviewed the admission files of patients, collected demographic profile of the cases, the duration of hospital stay, institutional permission was obtained for reviewing the patients with Standard protocol of SARS-CoV-2. All laboratory parameters were taken into consideration from our hospital's central laboratory. Patients diagnosed with chronic liver disease, chronic kidney disease and congestive cardiac failure (with or without treatment) have been excluded as hypoalbuminemia is known to be associated in these conditions and can lead to false results.



Inclusion Criteria

- a) Males and females ≥ 18 years presenting with Covid 19 symptoms (e.g., fever, chills, cough, dyspnoea, gastrointestinal disturbances, loss of smell, loss of taste, etc)
- b) COVID 19 positive by RT PCR only.

Exclusion Criteria

- a)Pregnancy
- b)Diagnosed cases of chronic liver disease, chronic kidney disease and congestive cardiac failure.

Study design: Observational cross-sectional study was conducted .
 Sample size :200 admitted in thehospital wards during the study period.

Outcomes of the research

Severity of COVID 19 diseaseand Adverse events were noted- (like venous thromboembolism, acute respiratory distress syndrome(ARDS), cerebrovascular accidents , acute coronary syndrome and acute kidney injury) .

Statistical analysis

Descriptive statistical measures like percentages mean and standard deviation will be applied. Inferential statistical measures like Chi-square test will be applied to find out the relationship between predictors and covid-19 infection prognosis. Data will be represented in tables and graphs as relevant. Difference will be interpreted as statistically significant if P value is less than 0.05.

Results

Table 1: Descriptive statistics of SARS-CoV-2 infected cases (study subjects)

Variable	Category	n	%
Age (Years)	≤ 20 yrs.	3	1.5%
	21-40 yrs.	63	31.5%
	41-60 yrs.	92	46.0%
	61-80 yrs.	42	21.0%
	Mean Age (Years)	47.84±14.21	
Sex	Males	102	51.0%
	Females	98	49.0%

A total of 200 SARS-CoV-2 infected patients were recruited for the study of which males comprised 102 (51.0%) and females were 98(49.0%) . Age-wise incidence was observed, the highest prevalence was seen in 41-60years (46.0%) followed by 21-40 years 31.50%; 61-80 years 21.0% and least prevalence was seen in ≤ 20 yrs (1.50%). The mean age of the infected patients was 47.84 with 14.21 SD years and an IQR of 19- 67 years. Logistic regression was employed to test the age-specific incidence of SARS-CoV-2, the older age was found to be highly correlated and prone to infection in the early incubation period odds of 3.68 hazard rate was 6.14 times higher risk for transmitting the infection.

Table 2 Distribution of Chief Complaints among study patients

Complaints	n	%
Fever	146	73.0%
Cough	142	71.0%
Breathlessness	63	31.5%
Head Ache	24	12.0%
Myalgia	21	10.5%
Tiredness	15	7.5%
Anosmia	14	7.0%
Sore Throat/ Throat pain	10	5.0%
Ageusia	10	5.0%
Loose Stools	7	3.5%
Running Nose / Cold	7	3.5%
Chest Pain	3	1.5%
Giddiness	3	1.5%
Abdominal Pain	3	1.5%
None	3	1.5%
Distribution of co morbidity among study patients		
Diabetes Mellitus	55	27.5%
Hypertension	29	14.5%
Hypothyroidism	10	5.0%
IHD	8	4.0%
Bronchial Asthma	7	3.5%
Neurological Disorder	3	1.5%
Carcinoma	2	1.0%
CKD	1	0.5%
TB	1	0.5%
Anaemia	1	0.5%
None	119	59.5%

The sign and symptoms was correlated by using unpaired t-test , as per the findings fever (73.0%) p<0.001 Cough (71.0%) p<0.001 ;Breathlessness (31.50%) p<0.001 ; Head Ache (12.0%) p<0.001 ; Myalgia (10.50%) p<0.001 ; Tiredness (7.50%) p<0.001 ;Anosmia (10.50%) p<0.001 ; Sore Throat/ Throat pain (5.0%) p<0.001 ; Ageusia (7.0%) p<0.001 ; Loose Stools (3.50%) p<0.001 ; Running Nose / Cold



(3.50%) $p < 0.001$ and Chest Pain (1.50%) $p < 0.001$ were found to be significantly correlated with severity of disease and hospitalization of the patients, 40.50% of the cases had one or more co-morbidity, the diabetes mellitus (27.50%); hypertension (14.50%); Hypothyroidism (5.0%); IHD 4.0%; Bronchial Asthma 3.50% and other co-morbidity was (4.0%). The comorbidity and sign both are found to be statistically significant with the survival of the patient AUC was 0.855, $p < 0.001$ Table 2. Duration of hospital stay was tested by chi-square test, the mean hospital stay was 5.39 with SD 2.80 days IQR (2.15 days). 78.50% cases were shown worsening of clinical status and need for Oxygen and NIV requirement was (65.50%) and 5.50% respectively and it was found to be statistically significant $p < 0.001$ odds 3.87 CI 95% 56-78%. Ventilator (2.00%) and ICU (5.50%) requirement significantly correlated with mean hospital stay was < 5 days (3.0%) $p < 0.001$ hazard risk was 10.85 times more chance need oxygen requirement within 5 days after infection. Severity was correlated by ANOVA, the moderate severity was reported (58.0%), mild (28.50%), and severe (13.50%) Fisher F value was significantly correlated with severity and outcome, majority of the cases (97.50%) survived, the fraction of numerator CFR was $< 5.0\%$ (actual CFR was 2.5%) of SARS-CoV2 (F=4.55, $P < 0.001$). Based on the occurrence and adverse effects of the drug tested by paired t-test, the results found that 14.0% had ARDS followed by AKI (3.0%) $P < 0.01$. The hematological perimeters were estimated and it was tested by suitable statistical tools, the percent prevalence of a higher rate of Eosinopenia 43.0%, NLR was 45.50% AUC was 0.81

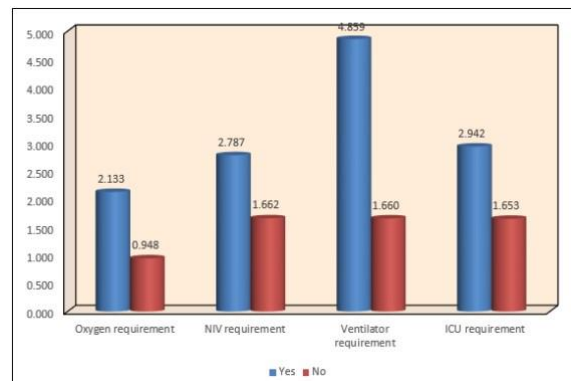


Figure 1: Distribution of cases for the SARS-CoV-2 supportive treatment

Table 3 Comparison of mean Serum Albumin levels & CRP / Albumin ratio based on the survival status of patients using Mann Whitney Test

Parameters	Outcome	N	Mean	SD	Mean Diff	p-value
Serum albumin (g/dl)	Non-Survivor	5	3.100	0.301	-0.393	0.06
	Survivor	195	3.493	0.519		
CRP/Alb ratio	Non-Survivor	5	1.347	1.015	-0.386	0.58
	Survivor	195	1.734	2.460		

The severity of SARS-CoV-2 in admission cases was graded as mild, moderate, and severe based on the SOP of the World health organization. Comorbidity was assessed during the study period and was summarized using the Charlson comorbidity index. All laboratory investigations were done. Table 4 The CRP (normal range < 5 g/L) and albumin (normal range 40-48 g/L) concentrations were determined in addition to other hematological and clinical parameters. the CAR was calculated as CRP (mg/l) to albumin (g/l). The mean CRP was 2.68 g/L in mild cases; moderate was 6.38 g/L and severe was 7.44 g/L. The higher CRP and CAR were highly associated with a tendency for respiratory distress, increased requirement of high flow O₂ treatment and patients needing mechanical ventilation, higher occurrence of deep venous thrombosis and lower incidence of myocardial infarction. By using the Kruskal Walis test we tested many associated vital parameters with life support treatment of SARS-CoV-2. Each variable was assessed carefully during the study intervention. The results are presented in Table 3, it shows that, 64.86% of average Neutrophils (%) were seen in mild, 70.54% in moderate, and severe was 84.79%. Lymphocytes (%), the mean was 25.18 in mild; moderate 20.60 and severe was 13.54; Eosinophils (%) 0.87 in mild; moderate was 0.39 and severe was 0.17; Monocytes (%) average 8.46 in mild, 3.59 is moderate and 6.12 in severe cases. Basophils (%) 0.36 in mild;



moderate 0.35 and severe was 0.19 % respectively .All parameters were found to be statistically significant at a 1% level of significance. Table 3 depicted that, the Comparison of mean Serum Albumin levels & CRP / Albumin ratio based on the survival status of patients using Mann Whitney Test, the result shows that the mean difference between survivors and nonsurvivors on the serum albumin level was 0.301 (g/dl) and CRP/Alb ratio on the mean differences was 0.386 serum albumin was significantly differed at 1% level and CRP /Alb ratio was significantly differed(p<0.05) .

with a higher procalcitonin, higher white blood counts or cells, lower absolute lymphocyte counts, higher platelets, higher Ferritin (mean 330.85 ng/ml), higher D – dimers (mean 442.59 ng/ml), Table 4 higher serum albumin 3.1 g/L, higher SGOT, and SGPT will increase the mortality of the SARS-CoV-2 and takes more time to discharge from the hospital, an average duration of hospital stay for nonsurvivors significantly more as compared with survivors, all vital parameters will fall on the marginal reference range.

Discussion

The present study discusses salient features and

Table 4:
Significance of different haematological and laboratory parameters of SARS-CoV-2

Parameters	Mild		Moderate		Severe		p-value	Mann Whitney Post hoc Test		
	Mean	SD	Mean	SD	Mean	SD		Mi vs Mo	Mi vs Se	Mo vs Se
Neutrophils (%)	64.86	14.01	70.54	16.33	384.79	1577.71	<0.001*	0.006*	<0.001*	<0.001*
Lymphocytes (%)	25.18	11.07	20.60	12.57	13.54	8.65	<0.001*	0.009*	<0.001*	0.009*
Eosinophils (%)	0.87	1.34	0.39	0.76	0.17	0.48	<0.001*	0.003*	<0.001*	0.06
Monocytes (%)	8.46	3.95	7.39	3.59	6.12	2.71	0.03*	0.09	0.008*	0.11
Basophils (%)	0.36	0.52	0.35	0.69	0.19	0.14	0.04*	0.404	0.02*	0.03*
Platelet count (10 ³ µL)	224.98	80.69	227.05	79.08	247.00	107.59	0.79
ANC(10 ³ µL)	4.07	2.11	5.40	3.21	6.84	3.74	0.002*	0.02*	0.001*	0.04*
ALC(10 ³ µL)	1.43	0.68	1.23	0.74	0.95	0.79	<0.001*	0.02*	<0.001*	0.009*
NLR	3.694	3.037	6.445	5.975	10.07	8.513	<0.001*	0.002*	<0.001*	0.007*
Ferritin (ng/ml)	144.85	170.74	351.87	375.52	386.16	330.85	<0.001*	<0.001*	<0.001*	0.38
CRP (mg/dl)	2.68	3.85	6.38	8.13	7.44	5.29	<0.001*	<0.001*	<0.001*	0.04*
D-DIMER (ng/ml)	270.05	77.58	418.58	350.50	442.59	290.74	<0.001*	<0.001*	0.001*	0.51
LDH (U/L)	196.02	53.84	286.81	159.55	348.89	109.82	<0.001*	<0.001*	<0.001*	0.001*
Creatinine (mg/dl)	0.82	0.58	0.90	0.47	0.86	0.32	0.01*	0.004*	0.04*	0.63
Urea (mg/dl)	27.28	16.71	31.47	25.98	38.89	27.46	0.005*	0.04*	0.004*	0.03*
Na (mEq/L)	136.78	3.33	135.90	3.29	134.90	4.72	0.14
K (mEq/L)	4.09	0.48	4.09	0.49	4.16	0.62	0.81
SGOT (U/L)	30.67	15.06	44.98	43.81	52.26	45.09	<0.001*	0.001*	0.001*	0.26
SGPT (U/L)	31.98	21.73	50.76	72.21	48.07	27.99	0.001*	0.001*	0.004*	0.31
Serum albumin (g/dl)	3.727	0.473	3.452	0.468	3.1	0.561	<0.001*	<0.001*	<0.001*	0.003
CRP/Alb ratio	0.795	1.242	1.987	2.812	2.554	2.037	<0.001*	<0.001*	<0.001*	0.023

These findings resemble those observed in the context of SARS-CoV-2-associated chronic inflammatory diseases. Nevertheless, clinical and laboratory investigations strongly correlated respiratory distress (ARDS) and increased Case fatality rate and its prognostic significance in the relationship of life supportive treatment, only ten cases Covid 19 induced mortality were seen in those who are suffering from one or more underlying comorbidities like hypertension, diabetes, CVD and AKI. Higher CAR was also associated

research findings on the SARS-CoV-2 infected subjects, with support of previously published research articles, certain features and characteristics of the parameters are discussed briefly ⁸. Yi Li et al., 2021¹⁵ studied the early prediction of disease progression in patients with COVID19 using the C reactive and albumin ratio, the results show that CRP/Alb ratio had the strongest positive correlation with the sequential organ failure assessment score and length of hospital stay in the survivor group, the results also revealed that the oxygen saturation Spo2, D- dimer level and CRP/Alb ratio were key and risk factors for the



geometric progression of the disease ^{6,7}. In the present study, Spo2, D dimer, and CRP/alb values were found to be higher and significantly correlated with covid19-induced mortality and increased morbidity > 95% . The majority of the cases died of multiple organ failure and were statistically significant with CFR P<0.001. Higher the ratio and it closely approximated ICU admission, invasive mechanical ventilation and longer duration of hospital stay ^{4,5}. The CRP /Alb ratio can predict the risk of progression of the disease and the critical stage of admitted cases of covid19. The clinical course, the morbidity and mortality of SARS-CoV-2 shows significant differences worldwide. In the present study, the mortality was 5% which was lower than that of the above study. The CRP/Alb ratio seems to forecast various path physiological processes and different aspects of inflammation. In contrast to CRP where elevation reflects the severity of acute inflammatory response, a decrease in albumin can reflect different processes including inflammation in internal organs, nephritic range proteinuria, damaged liver function, and worse nutritional status. As we noticed during the study period CRP /Alb ratio expressed in higher values, too many underlying adverse outcomes functionally correlated to morbidity and mortality AUC was 0.86 ^{1,2,3}. The Ratio is associated with a number of unfavourable features in admitted cases of SARS-CoV-2. We notice worse clinical course including more rapid respiratory deterioration and a higher need for an intensive level of care as well as higher mortality have been reported ¹⁶. Among the inflammatory markers, CRP, Serum Ferritin, and LDH were significantly associated with mortality, it has been suggested as an early marker to predict in-hospital mortality. Some of the cases showed an increase in Ferritin levels during their hospital stay, especially in non-survivors, higher reference range was recorded and it was found to be statistically significant p<0.001 ^{9,10,11}. The mean D dimer of all cases at admission was above the normal limits as compared with survivors and nonsurvivors, an elevated d dimer increasing

the severity and geometric progression of the diseases.

Limitation of The study

The present study was conducted at the sample level during the second wave of the pandemic, a few drawbacks were found in the study because the disease has now exponentially distributed, and it is difficult to document and correlate the biochemical parameters with a varied set of population. Further study at the population level is necessary to describe the various diagnostic biomarkers to assess the mortality of SARS-CoV-2 accurately . Another limitation was that the present study was conducted in a hospital setup and it was not correlated for the comparison with a varied infected populations in different variants of concern .

Conclusion

Summing of the results concludes that our study identified different clinical and laboratory tests for assessing and early screening prediction SARS-CoV-2 infected population mortality . Many of these are simple and inexpensive tests in low-resource settings that can help in the rational use of scarce resources and help us to early identification of cases for the inception of suitable therapy. CRP/alb ratio is a valid Biomarker for treating SARS-CoV-2 patients and provides substantial information to the clinicians for taking a valid decision at the right time.

Acknowledgement

All doctors and patients who worked tirelessly for the pandemic.

Consent and others

Waiver of the consent was taken due to retrospective nature of the study.

Safety information

It is Not applicable , because it is a observational retrospective design .

Conflict of interest

There is no conflict of interest between Institution and funding agency



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