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Serum albumin level as prognostic marker for Covid-19 positive patients

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Abstract
Background: The aim of the study was to analyse the role of serum albumin level as prognostic marker for Covid-19 positive patients.
Material and Method: The present study was conducted in the CMCH, Ludhiana. The study comprised of 100 subjects reported Covid positive during the June to September 2020. A detailed explanation was given to all the participating respondents regarding the study and their contribution to it. COVID-19 was diagnosed on the basis of the WHO interim guidance. A questionnaire was prepared to collect the Patients demographic profile. Patients date of admission and discharge was recorded along with the outcome i.e. whether patient was expired or survived. Patients diagnosis was identified along with the co-morbidity (if present). Laboratory investigations comprised of CBC and serum albumin detection. Data so collected was tabulated in an excel sheet, under the guidance of statistician. The means and standard deviations of the measurements per group were used for statistical analysis (SPSS 22.00 for windows; SPSS inc, Chicago, USA). Difference between two groups was determined using student t-test as well as chi square test and the level of significance was set at $p < 0.05$.
Results: The study comprised of 100 subjects, out of which 45 and 55 were males and females respectively. The overall mean age of the study subjects were 37.52 years. Death was revealed among 35.29%, 9.33% and 85.7% of the subjects having COVID-19 + T2DM, only COVID-19 and COVID-19 + hypertension respectively with statistically significant difference as $p<0.05$. Albumin level was significantly lower in expired patients (2.99) as compared to survivors (3.85) as $p<0.05$. Hospital stay was also higher in expired patients.
Conclusion: It can be concluded from the results that COVID-19 patients have reduced serum albumin levels, which may predispose to poor survival.

Keywords: covid-19, mortality, albumin

Introduction

WHO have declared COVID-19 as a pandemic. Coronaviruses (CoV) belongs to family of viruses that lead to infection varies from from the cold to threatening disease like Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV). Coronavirus disease (COVID-19) is a new strain that became discovered in 2019 and has not been previously identified in people. Coronaviruses are zoonotic in nature [1]. Coronavirus 2019 (COVID-19) is a pandemic associated with a high risk of morbidity and mortality. Generally, the majority of COVID-19-positive patients are present with general symptoms of respiratory infection with a case fatality rate of 1.4–4% [2, 3]. In some cases that develop severe or critical illness, death may be due to massive alveolar damage and progressive respiratory failure, with a higher mortality rate (38–60%) [4, 5]. However, little is known regarding the clinical markers for the risk of nonsurvivors in patients with COVID-19. Among laboratory variables, D-dimer and troponins are associated with poor survival.

There are many antioxidants in extracellular fluids including albumin, which is known as one of the most potent antioxidants [6]. Serum Albumin appears to be one such prognostic indicator. Its utility as a prognostic indicator has been studied in various contexts including critically ill patients. Albumin being a negative acute phase reactant, its concentration decreases often dramatically early in the course of illness and often does not increase till the recovery phase starts [7]. Human serum albumin (HSA) is the most abundant circulating protein in the body provided of both oncotic and non-oncotic properties [8, 9].

It is interesting, at this regard, that albumin oxidation triggers neutrophil extracellular traps through reactive oxidant species (ROS) accumulation within neutrophils, which eventually accumulate within lungs [10]. There is a growing body of evidence to suggest that ROS are implicated in platelet and clotting activation, thereby it is plausible that in case of albumin degradation/oxidation, both compartments are overactivated. In fact, hypoalbuminemia consequence to oxidative stress/inflammation is associated with thrombosis tendency and poor survival [11]. The impact of serum albumin on mortality in COVID-19 patients has been rarely reported so far, specially in this part of the country. Hence the present study was conducted to analyse the role of serum albumin level as prognostic marker for Covid-19 positive patients.

Material and Method

The present study was conducted in the CMCH, Ludhiana among 100 subjects reported Covid positive during the study period.

The subjects were included and excluded according to the following mentioned criteria:

Inclusion criteria
All Covid 19 positive patients.

Exclusion criteria
Subjects having following characteristics were excluded from the study:
1. Chronic liver disease
2. Nephrotic syndrome
3. Patients who have not given written informed consent

The study was initiated after obtaining the approval from institutional ethics committee of the institution. Only after written informed consent was obtained from all potential participants then they were recruited. A detailed explanation was given to all the participating respondents regarding the study and their contribution to it.
Covid-19 was diagnosed on the basis of the WHO interim guidance. A questionnaire was prepared to collect the Patients demographic profile. Patients date of admission and discharge was recorded along with the outcome i.e. whether patient was expired or survived. Patients diagnosis was identified along with the co-morbidity (if present). Laboratory investigations comprised of CBC and serum albumin detection.

Statistical analysis
Data so collected was tabulated in an excel sheet, under the guidance of statistician. The means and standard deviations of the measurements per group were used for statistical analysis (SPSS 22.00 for windows; SPSS inc, Chicago, USA). Difference between two groups was determined using student t-test as well as chi square test and the level of significance was set at $p < 0.05$.

Results
The study comprised of 100 subjects, out of which 45 and 55 were males and females respectively. The overall mean age of the study subjects were 37.52 years with minimum ans maximum age of 4 months and 78 years respectively (table 1).
In our study, 75% of the Covid patients were not having co-morbidity, while diabetes mellitus, MODS, hypertension with pneumonia and MODS was reported among 17%, 7% and 1% of the subjects respectively. Death was revealed among 35.29%, 9.33% and 85.7% of the subjects having COVID-19 + T2DM, only COVID-19 and COVID-19 + hypertension respectively with statistically significant difference as $p<0.05$ (Table 2).
It can be well appreciated from table 3 that albumin level was significantly lower in expired patients (2.99) as compared to survivors (3.85) as $p<0.05$. Hospital stay was also higher in expired patients (table 3).

Table 1: Gender distribution according to mean age

Gender	N	Age (in years)			
		Mean	SD	Minimum	Maximum
Female	45	38.2	16.22	7	72
Male	55	37.52	18.34	0.33	78
Total	100	37.82	17.33	0.33	78

Table 2: Outcome according to diagnosis

Diagnosis		Outcome		Total
		Death	Survivor	
Covid-19 + with t2dm	N	6	11	17
	%	35.29%	64.71%	100.0%
Covid-19 positive	N	7	68	75
	%	9.33%	90.67%	100.0%
Covid+ with mods	N	0	1	1
	%	0.0%	100.0%	100.0%
Htn with covid pneumonia	N	6	1	7
	%	85.7%	14.3%	100.0%
Total	N	19	81	100
	%	19.0%	81.0%	100.0%
Chi Square		35.59		
p value		<0.01*		

*: statistically significant

Table 3: Outcome according to albumin level and duration of hospital stay

Prognosis		Albumin Levels	Duration Of Stay
Death	Mean	2.99	15.79
	SD	.47	6.44
Survivor	Mean	3.85	10.22
	SD	.71	4.26
Total	Mean	3.68	10.52
	SD	.75	4.75
t test		25.14	5.79
p value		<0.01*	0.03*

*: statistically significant

Discussion
In this study, we identified differences in clinical manifestations, laboratory tests, therapeutic interventions with severity and the risk of nonsurvivors in patients with confirmed COVID-19. We found that albumin may be an independent predictive marker (cut-off point: 3.5 g/l) for the risk of nonsurvivors in critically ill patients with confirmed COVID-19. Our findings highlight the clinical significance of focusing on the levels of albumin as a predictor of a high risk of nonsurvivors in critically ill patients with COVID-19. Hypoalbuminemia status has been associated with critically ill patients and mortality across numerous clinical settings [12]. The pathophysiology behind hypoalbuminemia in disease state (such as pancreatitis, infection, trauma, burn, and organ dysfunction) is thought to be secondary to increased capillary permeability, decreased protein synthesis, decreased half-life of serum albumin, decreased serum albumin total mass, increased volume of distribution, and increase expression of vascular endothelial growth factor. The hallmark of severe COVID-19 includes the cytokine storm and an interplay of some of the aforementioned mechanisms [13]. Therefore, we recommend using drugs such as human albumin (that raise levels of albumin) to reduce risk of nonsurvivors, due to decreased levels of albumin (less than 35.1 g/l) in critically ill patients. This may also help clinicians identify patients with high risk of nonsurvivors at an early stage. Low levels of albumin also indicate that the patient's nutritional status is poor and the body's immunity is reduced. However, the host's immune response against RNA viral infection is often

weakened due to nutritional deficiencies, which may be overlooked during clinical diagnosis and treatment. Therefore, we recommend verifying the nutritional status of patients with COVID-19 before giving general treatments. Muhammad Aziz *et al* [14] in their meta-analysis revealed similar results too.

Juyi Li *et al* [15] in their study revealed that an increase in the severity of COVID-19 pneumonia was positively associated with lower levels albumin (all $p < 0.05$). In the critical group, the plasma levels of albumin continued to have a significant association for the risk of nonsurvivors ($p < 0.05$), even after adjusting for confounding factors. These results were similar to our study.

However Francesco Violi *et al* [16] in their study reported that reduced albumin levels should be considered as an epiphenomenon instead of a determinant of poor prognosis. However, it must be highlighted that the association they have found between reduced albumin level and mortality was robust even after multivariable adjustment including hs-CRP. Reduced serum albumin levels in the overall cohort and more importantly among patients who died, may have different explanations. As hypoalbuminemia is a feature of acute and chronic inflammation, which is also confirmed in their study by an inverse relationship between hs-CRP and albumin levels, their finding might reflect the presence of an underlying overactivated inflammatory status.

Our study demonstrate the association of hypoalbuminemia and COVID-19. A low albumin level can potentially lead to early recognition of severe disease and assist clinicians in making informed decision for their patients.

Conclusion

It can be concluded from the results that COVID-19 patients have reduced serum albumin levels, which may predispose to poor survival. Although the reason for such interplay requires further investigation, the assessment of serum albumin levels may represent an additional tool for early identification of patients at higher mortality risk.

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