

# Serum Albumin Level as a Prognostic Marker for Covid-19 Positive Patients in Western Uttar Pradesh - A Cross Sectional Study

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## ABSTRACT

### BACKGROUND

WHO has declared Coronavirus disease 2019 (Covid-19) as a pandemic. Covid-19 leads to sickness and death. Human serum albumin (HSA) is the most common circulating protein in the body having oncotic as well as non-oncotic properties. The role of albumin in death among Covid-19 subjects, especially in this part of the country has not been frequently reported. The aim of the study was to analyse the role of serum albumin level as prognostic marker for Covid-19 positive patients.

### METHODS

The present study was conducted in the department of Medicine at Chhatrapati Shivaji Subharti Hospital, Subharti Medical College, Meerut, UP. The study comprised of 100 subjects who were Covid positive from May 2020 to July 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 guidelines. 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 expired or survived. Patients' diagnosis was identified along with the comorbidity (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. Collected data was analysed using Statistical Package for the Social Sciences (SPSS) software version 24 and the tests used were t test and Fisher's exact test and the level of significance was set at  $p < 0.05$ .

### RESULTS

The study comprised of 100 subjects, out of which 45 were males and 55 were females. The overall mean age of the study subjects was 37.52 years. In our study, mortality was 35.29 %, 9.33 % and 85.7 % of the subjects having Covid-19+ type 2 diabetes (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.

### CONCLUSIONS

Covid-19 patients had low serum albumin levels and that might play a role in the survival of patient.

### KEYWORDS

Covid-19, Mortality, Albumin

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*DOI: 10.18410/jebmh/2021/39*

*How to Cite This Article:*

*Talera S, Singhal S, Wadhera N, et al.  
Serum albumin level as a prognostic  
marker for Covid-19 positive patients in  
western Uttar Pradesh - a cross sectional  
study. J Evid Based Med Healthc  
2021;8(04):204-207. DOI:  
10.18410/jebmh/2021/39*

*Submission 27-09-2020,  
Peer Review 02-10-2020,  
Acceptance 05-12-2020,  
Published 25-01-2021.*

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**BACKGROUND**

WHO has declared Covid-19 as a pandemic. Coronaviruses (CoV) belongs to family of viruses that lead to threatening disease like middle east respiratory syndrome (MERS-CoV) and severe acute respiratory syndrome (SARS-CoV). Covid-19 is a new strain that became notified in 2019 and has not been previously identified in people. Coronaviruses are zoonotic in nature.<sup>1</sup>

Coronavirus 2019 (Covid-19) leads to sickness and death. Covid-19 affected patients have problems such as respiratory infection with a mortality of 1.4 – 4 %.<sup>2,3</sup> In certain cases of serious or critical disease, with a higher mortality rate (38 - 60 percent), death can be due to massive alveolar injury and irreversible respiratory failure.<sup>4,5</sup> However, little is understood about the clinical risk markers for non survivors in Covid-19 patients. D-dimer and troponin are correlated with low survival among subjects suffering from Covid-19.

There are many antioxidants in extracellular fluids including albumin, which is known as one of the most potent antioxidants.<sup>6</sup> 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 reduces intensely early in the course of illness and often does not surge till the recovery phase started<sup>7</sup> Human serum albumin (HSA) is the most abundant circulating protein in the body having oncotic as well as non-oncotic properties.<sup>8,9</sup>

In this respect, it is interesting that albumin oxidation induces neutrophil extracellular traps by the aggregation of reactive oxidant species (ROS) within neutrophils, which ultimately accumulate in the lungs.<sup>10</sup> There is a growing body of evidence to indicate that ROS is involved in platelet and coagulation activation, so it is possible that both co-oxidation are involved in albumin degradation / oxidation. In fact, the influence of hypoalbuminemia on oxidative stress / inflammation is associated with a trend towards thrombosis and poor survival.<sup>11</sup>

The impact of serum albumin on mortality in Covid-19 patients has been rarely reported so far, especially 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.

**METHODS**

The present cross-sectional study was conducted in the Department of Medicine at Chhatrapati Shivaji Subharti Hospital, Subharti Medical College, Meerut, UP. The study comprised of 100 subjects diagnosed with Covid positive during the May to July 2020. During the study period, total 147 patients were recruited, but 43 failed to provide the informed consent while 4 patients did not satisfy the inclusion criteria. 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 had not given written informed consent.

The study was initiated after obtaining the approval from institutional ethics committee. They were recruited only after written informed consent was obtained from all potential participants. 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 guidelines. Confirmed diagnosis of Covid-19 was done by using real-time reverse transcription-polymerase chain reaction (RT-PCR). 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 expired or survived. Patients' diagnosis was identified along with the comorbidity (if present). Laboratory investigations comprised of complete blood count (CBC), blood sugar, d-dimer, C reactive protein and serum albumin detection.

**Statistical Analysis**

Data so collected was tabulated in an excel sheet, under the guidance of statistician. Collected data was analyzed using SPSS software version 24 and the test used were t test and Fisher's exact 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 and maximum age of 4 months and 78 years respectively (Table 1).

In our study, 75 % of the Covid patients were not having comorbidity, while diabetes mellitus, multiple organ dysfunction syndrome (MODS), hypertension with pneumonia and MODS was reported among 17 %, 7 % and 1 % of the subjects respectively. Mortality was reported 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).

In our study, we found that albumin level was weakly negative correlated with d-dimer ( $r = -0.29$ ,  $p = 0.041$ ) while it was highly significant negatively correlated with C reactive protein ( $r = -0.68$ ,  $p < 0.001$ ) as shown in table 4.

Gender	N	Age (in Years)		
		Mean	SD	Maximum
Female	45	38.2	16.22	72
Male	55	37.52	18.34	78
<b>Total</b>	<b>100</b>	<b>37.82</b>	<b>17.33</b>	<b>78</b>

**Table 1. Gender Distribution According to Mean Age**

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 %
Fisher's exact test		1.3		
P Value		< 0.001*		

**Table 2. Outcome According to Diagnosis**

\* statistically significant

Prognosis		Albumin Levels		Duration of Stay
		Mean	SD	
Death	Mean	2.99		15.79
	SD	.47		6.44
Survivor	Mean	3.85		10.22
	SD	.71		4.26
t test		25.14		5.79
P Value		< 0.001*		0.03*

**Table 3. Outcome According to Albumin Level and Duration of Hospital Stay**

\* statistically significant

Parameter		Value
D-Dimer	r value	- 0.29
	p value	0.041*
C reactive protein	r value	- 0.68
	p value	<.001*

**Table 4. Correlation of Albumin Level with D-Dimer and C Reactive Protein (CRP), mg / L**

\* statistically significant

## DISCUSSION

In this study, variations in clinical symptoms, laboratory testing, severity of therapeutic procedures and risk of death were reported in patients with confirmed Covid-19. Albumin has been established as an independent indicator (cut-off point: 3.5 g / l) of non-survival risk in critically ill patients with reported Covid-19. Our results illustrate the therapeutic importance of concentrating on albumin levels in chronically ill patients with Covid-19 as an indicator of a high likelihood of non-survivors. The state of hypoalbuminemia has been correlated across various therapeutic settings with chronically ill patients and mortality.<sup>12</sup> The pathophysiology underlying disease-state hypoalbuminemia (such as pancreatitis, inflammation, trauma, burning and organ dysfunction) is considered to be secondary to increased capillary permeability, decreased protein synthesis, decreased serum albumin half-life, decreased total serum albumin mass, increased delivery rate and increased vascular endothelial growth factor expression. A cytokine storm and an interplay of any of the above pathways are the hallmark of extreme Covid-19.<sup>13</sup> Therefore, due to reduced albumin levels (less than 35.1 g / l) in chronically ill patients,

we consider using medications such as human albumin (which raises albumin levels) to minimise the risk of death, which can also allow doctors to recognise patients at an early stage with a high risk of non-survivors. Low albumin levels therefore mean that the nutritional health of the patient is poor and the body's immunity is diminished. However, owing to dietary deficiency, which may be ignored during clinical diagnosis and treatment, the host's immune response against RNA viral infection is frequently impaired. Therefore, prior to general therapy, we suggest checking the nutritional status of patients with Covid-19. Related findings were also disclosed by Muhammad Aziz et al.<sup>14</sup> in their meta-analysis.

Li et al.<sup>15</sup> in their study revealed that an increase in the severity of Covid-19 pneumonia was positively associated with lower values of albumin (all  $p < 0.05$ ). In the critical group, the plasma levels of albumin continued to have a significant association for the risk of death ( $p < 0.05$ ), even after adjusting for confounding factors. These results were similar to our study. In their analysis, however, Francesco Violi et al.<sup>16</sup> indicated that decreased albumin levels must be considered as an epiphenomenon in spite of a bad prognosis factor. However, it should be noted that, even after multivariable modification like high sensitivity C-reactive protein (hs-CRP), the correlation they observed between decreased albumin level and mortality was robust. Different reasons could be given for lower serum albumin levels in the overall cohort and, more specifically, among patients who died. Since hypoalbuminemia is a characteristic of acute and chronic inflammation, which is also supported by an inverse association between hs-CRP and albumin levels in their research, their finding could indicate the existence of an over activated inflammatory status underlying it.

## CONCLUSIONS

Based on the findings, it can be inferred that Covid-19 patients have decreased serum albumin levels that could predispose to poor survival. While further research is needed to support such interaction, the measurement of serum albumin levels can be an additional method for early detection of patients who are at a higher risk of mortality.

## Limitations

Limitation of the present study is its cross-sectional design and small sample size.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

Financial or other competing interests: None.

Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

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