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Measurement and Prognostic Value of Serum Albumin among Hospitalized Sudanese Patients with COVID-19

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Abstract

Background: Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), roles of serum albumin level in prediction of clinical outcome and severity in COVID-19 patients.

Aim: This study focuses on measurement of serum albumin level in Sudanese patients with COVID-19 and determining the severity and outcome of those patients.

Methods and Material: Data was collected during the period from January 2021to March 2021 using the laboratory database of Jabra Hospital- COVID19 isolation center, Khartoum, Sudan. All patients were tested positive for COVID-19. The data included age, gender, wards, length of hospitalization and serum albumin level, Information regarding patient outcomes was also analyzed.

Result: The study comprises of 140 patients, 80 (57%) of the patients were male and 60 (43%) were female, 128 patients (91.40%) had hypoalbuminemia (serum albumin <3.5g/dL) and 12 patients (8.60%) had normal serum albumin level. High mortality rate among patients with hypoalbuminemia, regarding the outcome of those patients 100 (71%) died, while 40 (28.6%) recovered. There was insignificant difference in the serum albumin level between the age groups (P value of 0.659). However, there was significant difference in the serum albumin level between patients in different wards (P. value of 0.016). The serum albumin level was significantly low in patients in ICU 79 (95.2%) had hypoalbuminemia. The mean of albumin for the COVID-19 died group 2.8 ± 46 was significantly lower than COVID-19 recovered group 3 ± 40 with (P. value 0.04). There was a significant different in the outcome between patients in different wards, ICU patients had high mortality than other wards and that occur within short hospitalization period.

Conclusion: These findings highlight the prognostic value of albumin on admission, hypoalbuminemia is strongly associated with severity and poor prognosis in Sudanese patients with COVID-19.

Keywords: *COVID-19; SARS-CoV-2 age; Albumin; Hypoalbuminemia; Prognosis; Severity; Sudanese*

Introduction

COVID- 19

Coronaviruses are enveloped, positive single-stranded large RNA viruses that infect humans and animals. There are four main subgroups of coronaviruses, known as alpha, beta, gamma and delta. SARS-CoV-2 belongs to beta subgroup of coronavirus family, along with SARS-CoV, which caused worldwide epidemic in 2003 [1,2]. Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a novel viral disease first discovered in December 2019 in Wuhan, China. Within 1 month, it was confirmed in 19 countries [3]. The disease caused by SARS-CoV-2 is now officially called COVID-19 according to WHO. Like SARS-CoV, SARS-CoV-2 mainly attacks respiratory system. In symptomatic patients, the clinical manifestations of the disease usually present as fever, cough, fatigue and other signs of respiratory tract infections [4,5]. In severe cases, individuals elicit symptoms of pneumonia with abnormal chest CT, associated with complications of severe acute respiratory distress syndrome, acute cardiac injury, kidney failure and eventually death. Liver impairment has been reported as a common clinical manifestation in patients with SARS-CoV

infection [6,7]. The symptoms of COVID-19 infection appear after an incubation period of approximately 5.2 days [8]. The period from the onset of COVID-19 symptoms to death ranged from 6 to 41 days with a median of 14 days. This period is dependent on the age of the patient and status of the patient's immune system. It was shorter among patients >70 years old compared with those under the age of 70 [9]. Children mainly acquire SARS-CoV-2 infection from their family members but seem to experience less severe COVID-19 than adults [10]. According to scientific reviews smokers are more likely to require intensive care or die compared to non-smokers [11,12].

All patients with COVID-19-infected pneumonia received antibacterial agents, 90% received antiviral therapy, and 45% received methylprednisolone [13]. Recent pathogenic coronaviruses, i.e., SARS-COV and Middle East Respiratory Syndrome Coronavirus (MERS-COV). These two viruses had striking genetic similarity (especially SARS-COV) with the novel coronavirus, i.e., SARS-CoV-2 and, therefore, hepatic involvement in this is not entirely unexpected [14]. Albumin in adult humans is the most abundant plasma protein with a concentration ranging from 3.5 to 5.5 g/dL. Albumin represents 50% of the total protein content of plasma, with globulins making up most of the rest. It is a single peptide chain of 585 amino acids in a globular structure. Albumin is exclusively synthesized by the liver, initially a pre-proalbumin and then proalbumin, which in the Golgi apparatus is converted to albumin, which is the final form secreted by the hepatocyte. Factors that stimulate albumin synthesis include the action of hormones such as insulin and growth hormone. Albumin production may be inhibited by pro-inflammatory mediators such as interleukin-6 (IL-6), interleukin-1 (IL-1) and tumor necrosis factor [15]. Typically, hypoalbuminemia is ascribed to diminished synthesis (eg, malnutrition, malabsorption, or hepatic dysfunction) or increased losses (eg, urinary losses with nephropathy or protein-losing enteropathy). Diversion of synthetic capacity to other proteins (acute-phase reactants) is another cause of hypoalbuminemia. Inflammatory disorders can accelerate the catabolism of albumin while simultaneously decreasing its manufacture. During critical illness, capillary permeability increases dramatically and alters albumin exchange between intravascular and extravascular compartments [16,17].

Relation between serum albumin and COVID 19

Based on recent studies, in a comprehensive systematic review and meta-analysis study of Coronavirus disease (COVID-19) and the liver, this study Concluded that the most frequent abnormality in liver functions was hypoalbuminemia followed by derangements in gamma-glutamyl transferase and aminotransferases, and these abnormalities were more frequent in severe COVID-19 disease, however, limited by heterogeneity in definitions of severity and liver function derangements [18]. In a retrospective cohort study conducted in adult patients with COVID-19 disease hospitalized in the Third People's Hospital of Yichang, this study included adult patients with confirmed COVID-19. The relationship between hypoalbuminemia and death was studied using binary logistic analysis. A total of 299 adult patients were included, 160 (53.5%) were males and the average age was 53.4 ± 16.7 years. Hypoalbuminemia (<35 g/L) was found in 106 (35.5%) patients. The difference in albumin was considerable between survivors and non-survivors (37.6 ± 6.2 vs 30.5 ± 4.0, $P < .001$). This study concluded that hypoalbuminemia is independent predictive factors for mortality and associated with the outcome of COVID-19 [19]. Another retrospective, single-center study was conducted on 115 confirmed cases of COVID-19 in Zhongnan hospital of Wuhan University, ALT and AST slightly increased in COVID-19 patients, they were not of predictive value for the outcome. However, hypoalbuminemia was seen predominantly in severe COVID-19 cases compared with mild cases in a previous study [20]. The roles of hypoproteinemia in the clinical outcome and liver dysfunction of COVID-19 patients. In a retrospective study, extracted data from 2,623 clinically confirmed adult COVID-19 patients at Tongji Hospital, Wuhan, China. The patients were divided into three groups—non-critically ill, critically ill, and death groups, during hospitalization this study suggests that COVID-19-induced cytokine storm causes hepatotoxicity and subsequently critical hypoalbuminemia, which are associated with exacerbation of disease-associated inflammatory responses and progression of the disease and ultimately leads to death for some critically ill patients [21]. My study to explore this relationship further with the hypothesis that low serum albumin at presentation can predict serious outcomes among Sudanese patients with COVID-19 infection.

Method

Study population and data collection

This is a retrospective study includes 140 hospitalized COVID-19 patients in Jabra Hospital- COVID19 isolation center, Khartoum, Sudan. Data was collected during the period from January to March 2021 using the laboratory database of Jabra COVID-19 Isolation Center Khartoum, The Republic of Sudan. Patients included in this study were diagnosed with COVID-19 according to the Clinical Guidance for COVID- 19 and Diagnosis published by WHO.

- All patients have typical medical history and imaging characteristics of COVID-19.
- Positive real-time polymerase chain reaction (RT-PCR) assay from naso-pharyngeal swab specimens.
- Complete clinical data.

- Patients younger than 18 years old, had acute hepatitis within one month, and with history of liver or renal dysfunction were excluded from this study.

All the protocol has approved and carried out according to ethical guidelines of the declaration of Helsinki for human research. Jabra Hospital provided the authorization. The data included age, gender, serum albumin level and length of hospitalization. Information regarding patient outcomes was also analyzed.

Statistical analysis

Continuous variables were expressed as means ± SD. Categorical variables were expressed as percentages. The t test (for variables normally distributed) and Mann-Whitney U test (for variables non-normally distributed). The difference between categorical variables was examined with the chi-squared ($\chi 2$) test. A comparison of serum albumin level in each group (dead group, recovered group) was carried out using chi-squared test all statistical analyses were performed using the SPSS 26.0 (SPSS Inc) software package. A P value <.05 was considered statistically significant.

Result

The study comprises of 140 patients, n= 80 (57%) of the patients were male and 60 (43%) were female. According to patients ages were categorized into three groups, patients aged below 40 years old, aged from 40-60 years old and above 60 years old, mean age of the participants was 66.41 ± 11.85 years old with a minimum of 24 years old and maximum of 90 years old.

Table 1: *Relationship between gender and serum albumin level.*

	<3.5	3.5-5.5	P value
Male	75(93.8%)	5 (6.3%)	0.257
Female	53 (88.3%)	7 (11.7%)	

Those patients were admitted into three wards according to their disease severity n=83 (59.3%) in ICU, n=23 (16.4%) in HDU and n= 34 (24.3%) in Covid-19 Ward were presented in severe cases, moderate cases and mild cases respectively. Regarding hospitalization duration was classified into three periods, patients hospitalized less than 10 days, from 10-20 days and more than 20 days. Normal serum albumin level ranges from 3.5-5.5 g/dL and below 3.5 indicates hypoalbuminemia based on clinical guidelines. Result showed high proportion of patients count for 128 patients (91.40%) had hypoalbuminemia and while only 12 patients (8.60%) had normal serum albumin. Regarding the outcome of those patients n=100 (71%) patients died, while 40 (28.6%) patients recovered. Results showed insignificant difference in the serum albumin level between male and female (P. value of 0.257), 75(93.8%) of male patients had hypoalbuminemia and 5(6.3%) male patients had normal serum albumin level, 53(88.3%) female patients had hypoalbuminemia and 7(11.7%) female patients had normal serum albumin level (Table 1). There was insignificant difference in the serum albumin level between the age groups (P value of 0.659), 4(100%) patients aged below 40 years old had hypoalbuminemia. Patients aged from 40-60 years old 35(87.5%) had hypoalbuminemia and only 5 (12.5%) patients of this age group had normal serum albumin level, 85(92.4%) patients aged above 60 years old had hypoalbuminemia and only 7(7.6%) of this age group had normal serum albumin level (Table 2).

Table 2: *Relationship between patients in different age groups and serum albumin level.*

	<3.5	3.5-5.5	P value
<40 years old	4(100%)	0(0%)	0.649
40-60 years old	35(87.5%)	5(12.5%)	
>60 years old	85(92.4%)	7(7.6%)	

However, there was significant difference in the serum albumin level between patients in the three wards (P. value of 0.016). Hypoalbuminemia was dominantly in patients admitted to ICU n=79 (95.2%) and only 4(4.8%) patients in this ward had normal serum albumin level. Among patients in HDU n=22(95.7%) had hypoalbuminemia and 1 (4.3%) patient in this ward had normal serum albumin level. While in the COVID19 ward 27(79.4%) patients had hypoalbuminemia and 7(20.6%) had normal serum albumin level (Table 3).

Table 3: *Relationship between patients in different wards and serum albumin level.*

	<3.5	3.5-5.5	P value
ICU	79(95.2%)	4(4.8%)	0.016
HDU	22(95.7%)	1(4.3%)	
Covid-19 Ward	27(79.4%)	7(20.6%)	

The mean of serum albumin for the COVID-19 died group 2.8 ± 46 was significantly lower than COVID-19 recovered group 3 ± 40 with (P. value 0.04) (Table 4).There was 93(93%) patients died with hypoalbuminemia while only 7(7%) patients died had normal serum albumin level, regarding recovered group 35(87.5%) patients had hypoalbuminemia and 5(12%) patients recovered had normal serum albumin level (Table 5).

Table 4: *Mean of albumin level in died and recovered group.*

Outcome	Albumin mean ± SD	P value
Died	2.8±46	0.04
Recovered	3±40	0.04

Table 5: *Relationship between died and recovered group and serum albumin level.*

	<3.5	3.5-5.5	P value
Died	93(93%)	7(7%)	0.294
Recovered	35(87.5%)	5(12.5%)	

Table 6: *Relationship between gender and outcome.*

	Died	Recovered	P value
Male	54(67.5%)	26 (32.5%)	0.235
Female	46(76.7%)	14 (23.3%)	

Table 7: *Relationship between patients in different age groups and outcome.*

	Died	Recovered	P value
<40 years old	4 (100%)	0 (0%)	0.587
40-60 years old	27(67.5%)	13(32.5%)	
>60 years old	66 (71.7%)	26(28.3%)	

Table 8: *Relationship between patients in different wards and outcome.*

	Died	Recovered	P value
ICU	77(92.8%)	6(7.2%)	0.000
HDU	17 (73.9%)	6(26.1%)	
COVID-19 ward	6(17.6%)	28(82.4%)	

When comparing the outcome result between the various variables, there was insignificant difference between male and female in the COVID-19 infection outcome (death/recovery) since (P. value 0.235) (Table 6). Also, there was an insignificant difference between the age groups in the disease outcome (P. value 0.587) (Table 7). Although There was a significant different in outcome between patients in different wards high mortality rate was among patients in ICU compared to patients in other wards. Mortality rates demonstrate 77 (92.8%) patients died in ICU, 17 (73.9 %) patients died in HDU, on the other hand only 6(17.6 %) patients died in COVID-19 ward (P value of 0.000.) (Table 8).

Table 9: *Relationship between length of hospitalization and outcome.*

	Died	Recovered	P value
<10 days	63(76.8%)	19(23.2%)	0.114
10-20 days	36(66%)	18(34%)	
>20 days	2(40%)	3(60%)	

Patients who hospitalized less than 10 days 63(76.8%) of them died, 19(23.2%) of them recovered, patients who hospitalized from 10-20 days 17(73.9%) of them died, 6 (26.1%) of them recovered and patients who hospitalized more than 20 days 2(40%) of them died, 3(60%) of them recovered (P value of 0.114) (Table 9).

Discussion

Since the pandemic started much research have been conducted of which some are focused on the clinical remarks while others described the laboratory finding characteristics of patients. Hypoalbuminemia in severe COVID-19 has been repeatedly addressed in the literature to predict the severity of COVID-19 as mentioned above in the literature review. This study supports that low serum albumin level on admission can predict the outcome of COVID-19. My study focusses on serum of albumin measurement in COVID-19 patients. I discovered that a substantial number of COVID-19 patients exhibited significant reductions in the serum levels of albumin, this study found that the proportion of hypoalbuminemia (<3.5 g /dL) accounted for 91.40 % of all the 140 patients on admission, hypoalbuminemia has a strong association with high mortality rate among COVID-19 patients and result mortality within short period of hospitalization. Hypoalbuminemia was seen predominantly in severe COVID-19 cases in ICU compared to moderate and mild cases in other wards and this finding agrees with findings in previous published research. In addition, I found that gender have no significant effect on serum albumin level and the outcome among Sudanese patients. This study included only 140 cases because serum albumin test is not a routinely investigation for patients during admission, therefore this created a limitation in the number of cases, and this may affect the result of demographic character analysis. So, this point needs more analysis in the future studies with inclusion of large-scale population, a prospective study should be conducted along with measurement of serum albumin multiple times during hospitalization to monitor the progression of serum albumin this can give a better understanding of COVID-19 influence on the liver. Elderly patients have a great chance to develop severe type of infection and mortality, compare to patients of younger age, 66 patients aged over 60 years died compared to only 4 patients of

those under 40 years died due to COVID-19 infection. Additionally, the highest proportion of patients with hypoalbuminemia were over 60 years died due to the COVID-19 infection. This is documented in many studies that have proved advanced age is a characteristic features of immune response dysfunction affecting albumin level. The identification of relatively low serum albumin concentrations in hospitalized COVID-19 patients might assist with appropriate risk stratification and selection of suitable care pathways, even taking into consideration that age can be an important confounding factor. This research has its limitations. This research studied a single-center experience; however, the baseline factors are consistent with the presently available literature and the single-center experience may not be a limitation. I only showed the value of baseline albumin level for outcome of Sudanese COVID-19 patients, yet the changes in serum albumin levels during the developments of COVID-19 disease in human body were not reflected because as I mentioned earlier it was not ordered routinely. Also, at this COVID-19 isolation center albumin therapy for the management of COVID-19 has not been used, prospective trials/studies with albumin treatment may answer the question in whether albumin infusion treatment could improve the prognosis. In this study I analyzed the death and recovery frequency between different hospitalization periods I found that high proportion of patients died within less than 10 days, However, in this study I compared a COVID-19 died group with a recovered group of patients to determine the effect of the albumin in the COVID-19 outcome, These findings highlight the prognostic value of albumin at time of admission, which can be helpful in tailoring a prompt response for early interventions in Covid-19 disease patients. Claiming that albumin is a marker of severity and poor outcome in Covid-19 patients.

Conclusion

Hypoalbuminemia defined as a serum albumin level of less than 3.5 g/dL, is associated with the severity and outcome of Sudanese patients with COVID-19. My study demonstrates that albumin is a specific prognostic marker of COVID-19 infection outcome particularly albumin among COVID-19 patients particularly elderly patients and could help physician to predict patients with poor prognosis earlier and hypoalbuminemia is strongly associated with the severity of COVID-19. Based on the results of our study, I therefore propose that urgent albumin transfusion treatment should be taken into consideration when treating patient with COVID-19 infection. Further studies with larger cohort are required to better understand the value of albumin count in diagnosis and treatment of the COVID-19 infection.

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