VOLUME - 11, ISSUE - 04, APRIL - 2022 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

General Medicine

PLASMA ALBUMIN LEVELS AND HOSPITAL MORTALITY IN COVID-19 PATIENTS- A CROSS-SECTIONAL STUDY

Dr. Prasad Ugargol Assistant Professor, Department Of General Medicine, Snmc And Hsk Hospital

Dr. Mallu Surendra Reddy 3rd Year Postgraduate, Department Of General Medicine, Snmc And Hsk Hospital

ABSTRACT

Background: Albumin is a key protein found in the human body that has anti-inflammatory properties. It binds to the reactive oxygen and nitrogen species (ROS and RNS) generated during inflammation, preventing cellular damage. In hospitalized COVID-19 patients, low serum has a direct effect on mortality and severe sequelae, according to a few studies. We conducted this study to find out the prediction of survival in Terminally Ill COVID-19 Patients using Plasma Albumin Levels.

Settings and Design: It is a retrospective study carried out at HSK hospital, Bagalkot, Karnataka. We included 100 patients of RT-PCR positive COVID-19 confirmed cases. All the cases of COVID-19 were reviewed with thorough history, clinical examination, and lab investigations. Severity of COVID-19 was determined using Ct severity index.

Results: Elderly patients and patients with co-morbidities had severe COVID and mortality rate was high among severe cases ($p<0.05$). Total leucocyte count and albumin were significantly altered in moderate and severe cases. Neutrophil-lymphocyte ratio was altered in all COVID-19 cases. Platelet count was significantly decreased in severe cases. The mortality rate in our study was 34%. Majority of the mortality was from aged patients, who were diabetic and had IHD.

Conclusions: Hypoalbuminemia is associated significantly with severity and mortality of COVID-19.

KEYWORDS : COVID-19, Serum Albumin, Hypoalbuminemia.

INTRODUCTION

Coronavirus disease (COVID-19) is an infectious disease caused by the SARS-CoV-2 coronavirus, which has spread fast over the world. The World Health Organization (WHO) has declared COVID-19 as pandemic in March, 2020. The pandemic has wreaked havoc on worldwide health systems, as well as economic and social growth. As of April 7th, 2022, 42,510,428 verified COVID-19 cases and over 5,21,530 deaths had been reported in India.[1]

The majority of persons (80%) have a moderate illness and recover without hospitalization, whereas the other 20% may become more gravely ill. Although the COVID-19 pandemic is still evolving, numerous studies have found a considerable rise in death due to non-COVID-related illnesses since the beginning of the pandemic.[2] These findings underscore the pandemic's far-reaching consequences, which go far beyond the immediate death caused by SARS-CoV-2. According to some recent data, case-fatality rates are decreasing, regardless of confounding factors.[3] These findings back up the notion that better treatment options and a better understanding of prognostic markers can help minimize case fatality. Clear signs that might predict a bad clinical outcome early on and identify people who might be good candidates for existing therapeutic choices are still elusive. The characteristics of patients with severe COVID-19 have been studied in the past.

The presence of high levels of inflammatory markers such as c-reactive protein (CRP), interleukin-6 (IL-6), lactate dehydrogenase (LDH), and ferritin in individuals who have poor outcomes indicates an excessive inflammatory response. At the outset, those patients were elderly and had co-morbidities. Low serum albumin levels have been documented in patients with more serious consequences.[4-7]

Albumin is a key protein found in the human body that has anti-inflammatory properties.[8,9] It binds to the reactive oxygen and nitrogen species (ROS and RNS) generated during inflammation, preventing cellular damage.[10] In hospitalized COVID-19 patients, low serum has a direct effect on mortality and severe sequelae, according to a few studies.[11-13] We conducted this study to find out the prediction of survival in Terminally Ill COVID-19 Patients using Plasma Albumin Levels.

MATERIALS AND METHODS

It is a retrospective study carried out in the department of General Medicine at HSK hospital, Bagalkot, Karnataka after obtaining institutional ethical committee approval. We included 100 patients of RT-PCR positive COVID-19 confirmed cases. Consent was not taken from subjects as it was retrospective study, however required permissions were obtained from hospital authority. We excluded patients with incomplete data.

All the cases of COVID-19 were reviewed with thorough history, clinical examination, and lab investigations. Severity of COVID-19 was determined using CT severity index.

As defined by WHO guidelines, infections were defined as severe in cases of fever or suspected respiratory infection, plus one or more of the following: respiratory rate >30 breaths/min, severe respiratory distress or SpO2 ≤93% on room air.[14] The secondary outcome of the study was the death of the patient within 30 days of the first ED evaluation. Mortality was reconstructed using death charts or by directly contacting the registry office. Critical patients fulfill any of the three criteria: respiratory failure and require mechanical ventilation; shock incidence; admission to ICU with another organ failure. The serum albumin levels <35 g/L was defined as hypoalbuminemia. All laboratory findings were collected from COVID-19 patients at three time points including weeks 1, 2 and 3–4 from onset or the first positive nucleic acid test to blood collection. To ensure the accuracy and completeness of the data, all authors reviewed the extracted data and revised errors immediately by checking the original case data after the errors were found.

Statistical Analysis

Statistical analysis was performed using SPSS 22.0. Continuous variables are assessed as mean ± SD or median [IQR] and analyzed using Student's *t* test and Mann–Whitney *U*-test for normal distributed data or non-normal distributed data, respectively. Categorical variables are presented as frequency and percentages and analyzed using $\chi 2$ test or Fisher's exact test as appropriate. p value of < 0.05 is considered statistically significant.

RESULTS

Demographic characteristics

Among the total 100 cases, 77% were males and 23% were females with a mean age of 52.9± 14.9 years. Patients were grouped as mild, moderate and severe COVID based on CT severity score. A total of 44 patients were identified to be admitted with severe COVID. Table 1 shows the patients' demographic and clinical characteristics in the study and the differences between the three groups based on the severity of COVID.

As expected, older patients and patients with co-morbidities had severe COVID and mortality rate was high among severe cases (p<0.05).

Table 1:Demographic and clinical status of COVID-19 patients

Variables		COVID severity			p-value
		Mild (n=46)	Moderate (n=10)	Severe (n=44)	
Mean Age in years		49.02± 14.5	43.4±16.6	59.05±12.6	**<0.001**
Age	**20-40 years**	16 (34.8%)	5 (50%)	4(9.1%)	**0.007**
	41-60 years	17 (37%)	4 (40%)	20(45.5%)	
	>61 years	13 (28.3%)	1 (10%)	20(45.5%)	
Gender	**Male**	35 (76.1%)	8 (80%)	34 (77.3%)	0.963
	Female	11 (23.9%)	2 (20%)	10 (22.7%)	
Co-morbidities	**Hypertension**	4 (8.7%)	4 (40%)	14 (31.8%)	**0.01**
	Diabetes Mellitus	5 (10.9%)	2 (20%)	19 (43.2%)	**0.002**
	IHD	0	0	5 (5%)	**0.035**
	Asthma	0	0	2 (4.5%)	0.189
Outcome	**Death**	2 (4.3%)	0	32 (72.7%)	**<0.001**
	Discharge	44 (95.7%)	10 (100%)	12 (27.3%)	

Several laboratory tests were done in COVID-19 cases. Total leucocyte count and albumin were significantly altered in moderate and severe cases. Neutrophil-lymphocyte ratio is altered in all COVID-19 cases. Platelet count was significantly decreased in severe cases.

Table 2: Laboratory parameters of COVID-19 patients

Laboratory Parameters	COVID severity			p-value
	Mild (n=46)	Moderate (n=10)	Severe (n=44)	
Hemoglobin (g/dl)	12.3±1.3	12.4±1.3	12.1±1.5	0.84
Total count (per ml)	7858.7± 3071.1	12290± 7749.3	11927.3 ±8053.8	0.005
Neutrophil-lymphocyte ratio	4.23±2.6	4.1±2.2	5.5±2.9	0.073
Platelet count (lac per ml)	2.51±0.99	2.46±1.4	1.85±1.3	0.027
Albumin (g/dl)	4.02±0.13	3.85±0.21	3.21±0.19	<0.001

The mortality rate in our study was 34%. Table 3 shows the distribution of demographic and clinical characteristics among dead and discharged COVID patients. Majority of the mortality was from aged patients, who were diabetic and had IHD. This was statistically significant with p value less than 0.05.

Table 3: Demographic And Clinical Status Of COVID-19 Patients According To Outcome

Variables	Outcome		p-value
	Death (n=34)	Discharge (n=66)	
Mean Age in years	61±11.2	48.7±14.9	<0.001
Age 20-40 years	2 (5.9%)	23 (34.8%)	0.001
41-60 years	14 (41.2%)	27 (40.9%)	
>61 years	18 (52.9%)	16 (24.2%)	
Gender Male	24 (70.6%)	53 (80.3%)	0.274
Female	10 (29.4%)	13 (19.7%)	
Co-morbidities Hypertension	11 (32.4%)	11 (16.7%)	0.073
Diabetes Mellitus	16 (47.1%)	10 (15.2%)	0.001
IHD	4 (11.8%)	1 (1.5%)	0.026
Asthma	0	2 (3%)	0.305

The mortality rate in our study was 34%. Table 3 shows the distribution of demographic and clinical characteristics among dead and discharged COVID patients. Majority of the mortality was from aged patients, who were diabetic and had IHD. This was statistically significant with p value less than 0.05.

Table 4: Laboratory parameters of COVID-19 patients according to outcome

Laboratory Parameters	Outcome		p-value
	Death	Discharge	
Hemoglobin (g/dl)	12±1.5	12±1.3	0.339
Total count (per ml)	13547.1±8541.9	8312.1±4219.4	<0.001
Neutrophil-lymphocyte ratio	6.17±2.8	4.05±2.4	<0.001
Platelet count (lac per ml)	171705.9±138992.8	247348.5± 105367.7	0.003
Albumin (g/dl)	3.08±0.83	3.95±0.71	<0.001

DISCUSSION

The most relevant observation of this retrospective observational study was that in a sample of 100 confirmed COVID-19 patients from our teaching hospital, on admission albumin levels were much lower in severe cases and also was affected mortality.

In our study, factors such as age, presence of co-morbid conditions like diabetes and IHD, increased total count, increased neutrophil-lymphocyte ratio and most importantly hypoalbuminemia were associated with mortality in COVID-19 severe cases. This fact was in the same line of evidence as previously reported findings.[15-19]

The mortality rate (34%) of our study was similar to that by Prof Yu (28.4%), but significantly higher than that from other studies (1.4, 3.2, 11 and 15%).[4,20-21] The present study shows that low serum albumin levels on admission of confirmed COVID-19 infected patients were associated with mortality. Similar to our study, Huang et al., reported hypoalbuminemia in almost 81% of non-survivors of severe COVID-19 patients.[11] Lower albumin and platelet levels were found to be linked to the severity of COVID-19 pneumonia and death.[22]

The causes causing COVID19 hypoalbuminemia have not been adequately investigated or explained. In a prior study[7] and the current investigation, hypoalbuminemia was detected more frequently in severe COVID19 cases compared to mild instances.[23] Albumin is generated in the liver and has a serum half-life of about 21 days. This phenomenon is not explained solely by liver damage as a result of hepatocellular dysfunction.

Study Limitations:

1. This is single center retrospective study.
2. No follow-up was done to assess the long-term effects of hypoalbuminemia.
3. COVID-19 patients with abnormal liver function will have hypoalbuminemia. Unfortunately, our data had no available data on liver function.

CONCLUSION:

The present study has shown a significant association

between serum albumin levels, platelet count and NLR with mortality. Hypoalbuminemia is associated with higher mortality in COVID-19 patients.

REFERENCES:

1. MoHFW | Home [Internet]. Mohfw.gov.in. 2022 [cited 8 April 2022]. Available from: https://www.mohfw.gov.in/
2. Woolf S, Chapman D, Sabo R, Weinberger D, Hill L. Excess Deaths From COVID-19 and Other Causes, March-April 2020. JAMA. 2020;324(5):510.
3. Horwitz L, Jones S, Cerfolio R, Francois F, Greco J, Rudy B et al. Trends in COVID-19 Risk-Adjusted Mortality Rates. Journal of Hospital Medicine. 2020;16(2):90-92.
4. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020 15; 395(10223):497–506.
5. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020 28; 395 (10229):1054–62.
6. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ. 2020 26; 368:m1091
7. Zhang Y, Zheng L, Liu L, Zhao M, Xiao J, Zhao Q. Liver impairment in COVID-19 patients: A retrospective analysis of 115 cases from a single centre in Wuhan city, China. Liver Int. 2020; 40(9):2095–103.
8. Artigas A, Wernerman J, Arroyo V, Vincent J-L, Levy M. Role of albumin in diseases associated with severe systemic inflammation: Pathophysiologic and clinical evidence in sepsis and in decompensated cirrhosis. J Crit Care. 2016; 33:62–70.
9. Rozga J, Piątek T, Małkowski P. Human albumin: old, new, and emerging applications. Ann Transplant. 2013 May 10; 18:205–17.
10. Galley HF. Oxidative stress and mitochondrial dysfunction in sepsis. British Journal of Anaesthesia. 2011 Jul; 107(1):57–64.
11. Huang J, Cheng A, Kumar R, Fang Y, Chen G, Zhu Y et al. Hypoalbuminemia predicts the outcome of COVID-19 independent of age and co-morbidity. Journal of Medical Virology. 2020;92(10):2152-2158.
12. 5. Violi F, Cangemi R, Romiti G, Ceccarelli G, Oliva A, Alessandri F et al. Is Albumin Predictor of Mortality in COVID-19?. Antioxidants & Redox Signaling. 2021;35(2):139-142.
13. Kheir M, Saleem F, Wang C, Mann A, Chua J. Higher albumin levels on admission predict better prognosis in patients with confirmed COVID-19. PLoS One. 2021; 16(3):e0248358
14. Ticinesi A, Lauretani F, Nouvenne A, et al. C-reactive protein (CRP) measurement in geriatric patients hospitalized for acute infection. Eur J Intern Med 2017;37:7–12.
15. Carrasco-Sánchez, F.J.; López-Carmona, M.D.; Martínez-Marcos, F.J.; Pérez-Belmonte, L.M.; Hidalgo-Jiménez, A.; Buonaiuto, V.; Suárez Fernández, C.; Freire, C.S.J.; Luordo, D.; Pesqueira, F.P.M.; et al. Admission hyperglycaemia as a predictor of mortality in patients hospitalized with COVID-19 regardless of diabetes status: Data from the Spanish SEMI-COVID-19 Registry. Ann. Med. 2021, 53, 103–116.
16. Mesas, A.E.; Cavero-Redondo, I.; Álvarez-Bueno, C.; Cabrera, M.A.S.; De Andrade, S.M.; Sequí-Dominguez, I.; Martínez- Vizcaíno, V. Predictors of in-hospital COVID-19 mortality: A comprehensive systematic review and meta-analysis exploring differences by age, sex and health conditions. PLoS ONE 2020, 15, e0241742.
17. Kuderer, N.M.; Choueiri, T.K.; Shah, D.P.; Shyr, Y.; Rubinstein, S.M.; Rivera, D.R.; Shete, S.; Hsu, C.Y.; Desai, A.; de Lima Lopes, G., Jr.; et al. COVID-19 and Cancer Consortium. Clinical impact of COVID-19 on patients with cancer (CCC19): A cohort study. Lancet 2020, 395, 1907–1918.
18. Viana-Llamas, M.C.; Arroyo-Espliguero, R.; Silva-Obregón, J.A.; Uribe-Heredia, G.; Núñez-Gil, I.; García-Magallón, B.; Torán-Martínez, C.G.; Castillo-Sandoval, A.; Díaz-Caraballo, E.; Rodríguez-Guinea, I.; et al. Hypoalbuminemia on admission in COVID-19 infection: An early predictor of mortality and adverse events. A retrospective observational study. Med. Clin. 2021, 156, 428–436.
19. Ceriello, A.; De Nigris, V.; Prattichizzo, F. Why is hyperglycaemia worsening COVID-19 and its prognosis? Diabetes Obes. Metab.2020, 22, 1951–1952.
20. 6. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lancet. 2020;395(10223):507-513.
21. 7. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J et al. Clinical Characteristics of Coronavirus Disease 2019 in China. New England Journal of Medicine. 2020;382(18):1708-1720.
22. Li, J.; Li, M.; Zheng, S.; Li, M.; Zhang, M.; Sun, M.; Li, X.; Deng, A.; Cai, Y.; Zhang, H. Plasma albumin levels predict risk for nonsurvivors in critically ill patients with COVID-19. Biomark. Med. 2020, 14, 827–837.
23. Rothschild MA, Oratz M, Schreiber SSJH. Serum albumin. Hepatology. 1988;8(2):385-401.