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Correlation Of Malnutrition and Disease Development, Prognosis in Old Patients Infected with SARS-CoV-2 From an Observational Study

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ABSTRACT

Background: This research focus on the discussion of malnutrition in elderly COVID-19 patients, primarily including anemia and hypoalbuminemia, and its impact on the severity and prognosis of novel coronavirus pneumonia.

Methods: A retrospective analysis was conducted on clinical data from 163 elderly COVID-19 patients discharged (including deaths) from Shandong Provincial Hospital Affiliated to Shandong First Medical University from December 19, 2022, to February 3, 2023. The patients were divided into four groups based on their hemoglobin levels at admission: normal, mild anemia, moderate anemia, and severe anemia. They were also divided into four groups based on their albumin levels at admission: normal, mild hypoalbuminemia, moderate hypoalbuminemia, and severe hypoalbuminemia. The proportions of severe COVID-19 pneumonia, hospital stay, intubation rate, ICU admission rate, and mortality rate were compared among the groups to determine if there were any statistically significant differences.

Results: Statistical tests were conducted to examine the correlation between anemia and different levels of anemia with the severity of COVID-19. Both of these factors showed no significant correlation ($P>0.05$). A statistical test was also conducted to examine the correlation between anemia and patient outcomes, and it was found that patients with anemia had a positive correlation with the mortality rate ($P<0.05$). However, there was no significant correlation ($P>0.05$) between the severity of anemia and patient outcomes. Statistical tests were performed to examine the correlation between blood levels of albumin and the severity of COVID-19, and a positive correlation was found ($P<0.05$). However, there was no significant correlation ($P>0.05$) between the severity of hypoalbuminemia and the severity of COVID-19. Both the presence of hypoalbuminemia and different levels of albumin were positively correlated with the mortality rate ($P<0.05$).

Conclusion: Patients with anemia have no significant correlation with the severity of COVID-19, but have significant correlation with the mortality rate; while patients with hypoalbuminemia are not only positively correlated with the severity of COVID-19 but also with the mortality rate.

INTRODUCTION

The current trend of population aging in society is becoming increasingly evident. As of the end of 2050, the elderly population aged 65 and above accounted for 16% of the total population in the world, far higher than the 9.3% currently et al. (2021). Elderly individuals often suffer from multiple underlying diseases, which often lead to malnutrition, including anemia and hypoalbuminemia, resulting in a significant decrease in immune function and susceptibility to opportunistic infections Norman et al. (2021). Over the past three years, the COVID-19 pandemic has been raging globally, many elderly people have been infected with the novel coronavirus, leading to severe pneumonia and even death Prendki et al. (2022). Patients over the age of 65 are among the high-risk groups for severe/critical illness Chen. et al. (2021), O'Driscoll et al. (2021).

This study retrospectively analyzed the clinical data of 162 elderly patients with COVID-19 (Coronavirus disease 2019) who had been discharged (including deaths), and explored the correlation between anemia, hypoalbuminemia, and the proportion of severity of COVID-19, hospital stay, tracheal intubation rate, ICU admission rat, and mortality rate. The aim is to provide a method for assessing the severity and prognosis of COVID-19 in elderly patients, assist clinicians in early assessment of the condition and prognosis of COVID-19, provide early intervention and treatment, and reduce

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the risk of further exacerbation and even death.

MATERIALS AND METHODS

General information

The study included a total of 162 discharged (including deceased) COVID-19 patients who were administered and hospitalized at Shandong First Medical University Affiliated Provincial Hospital and met the diagnostic criteria of the trial version 10 of the treatment plan for novel coronavirus infection during the period from January, 2022, to February, 2023. In this study, these old patients (60–96 years of age, average 77.5 ±8, 40 women and 122 men) were sequentially divided four groups based on According to the guideline, Mild: mild symptoms without pneumonia; Moderate:fever or respiratory tract symptoms with pneumonia; Severe: fulfill any of the three criteria: respiratory distress, respiratory rate ≥30 times/min; means oxygen saturation ≤93% in resting state; arterial blood oxygen partial pressure/oxygen concentration ≤300 mmHg (1 mmHg = 0.133 kPa); Critical: fulfill any of the three criteria: respiratory failure and require mechanical ventilation; shock incidence; admission to ICU with other organ failure Shen et al. (2020).

Inclusion and exclusion criteria.

Inclusion criteria: Patients had a history of COVID-19 or were tested positive for SARS-CoV-2 exposure, or who had been in contacted with confirmed COVID-19 patients were included. Patients who meet the diagnostic criteria for mild, moderate, severe and critical cases as outlined in the "Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7) Wei et al. (2020) issued by the National Health Commission of China. Exclusion criteria: Patients with other non-COVID viral infections, a confirmed history of pulmonary tuberculosis, tumors, chronic liver disease, or renal insufficiency. Congenital malformations or developmental disorders, genetic defects, severe malnutrition; Medical diagnosis of coagulation abnormalities (such as coagulation factor deficiency, coagulation disorders, platelet abnormalities) or marked bruising or blood coagulation disorders; A variety of medical, psychosocial, social or other conditions that are contrary to the study protocol or affect the subjects to sign informed consent in the opinion of the researchers. This study has been approved by the Ethics Committee of Shandong University First Hospital, and informed consent has been obtained from all patients.

Groups

According to the levels of hemoglobin, elderly patients were divided into two groups: the normal group with hemoglobin level > 120 g/L, and the anemia group with hemoglobin level ≤12 0g/L. Based on the levels of serum albumin, elderly patients were divided into four groups: Group A, normal albumin group (36-55 g/L); Group B, mild hypoalbuminemia group (30-35 g/L); Group C, moderate hypoalbuminemia group (25-29 g/L); and Group D, severe hypoalbuminemia group (<25 g/L).

Tests

Statistical analysis was conducted to determine the proportion of elderly patients in each group who developed severe/critical COVID-19 after admission, as well as the hospital stay, intubation rate, ICU admission rate, and mortality rate. The levels of hemoglobin were detected by using Blood-Cell-Analyzer (BD company, USA). The levels of albumin and sodium were detected by using biochemical analyzer.

Analysis

The statistical analysis was conducted using SPSS software (SPSS 16.0) and Prism GraphPad Software (GraphPad Prism 8.0). The Cochran-Armitage trend test was used to analyze the correlation between ordered and binary categorical variables. Logistic regression analysis was used to analyze the correlation between binary and ordered variables. spearman correlation analysis was used to analyze the correlation between categorical variables. For continuous data, a normality test was performed, and if the data followed a normal distribution, it was expressed as mean ± standard deviation (x ± s). One-way ANOVA was used for comparing means among the levels of albumin, hemoglobin and sodium groups using Prism. Baseline characteristics of the participants were analyzed using median. Categorical data were expressed as rates, and if the data met the conditions for chi-square test, chi-square test was used; otherwise, Fisher's exact test was used for small sample sizes. Power analysis was used to statement adequate sample size by SPSS. The significance level was set at α=0.05, and a p-value of less than 0.05 was considered statistically significant.

RESULTS

Characters of patients

All detections for the COVID-19 patients were conducted at Shandong First Medical University Affiliated Provincial Hospital, Tengzhou Traditional Chinese Medical Hospital and Tengzhou Central People's Hospital in China. The research protocol was reviewed and approved by Shandong First Medical University Affiliated Provincial Hospital, and Tengzhou Traditional Chinese Medical Hospital and Tengzhou Central People's Hospital. Eligible participants were healthy adults aged 60 years or older. Individuals who had a history of COVID-19 or were tested positive for SARS-CoV-2 exposure, or who had been in contacted with confirmed COVID-19 patients were included. Eligible older participants were required to be generally healthy and 60 to 96 years of age.

General health, assessed during the screening period, was based on clinical laboratory findings, vital signs, physical examination and medical history. The male-to-female ratio was higher in all four groups of enrolled patients, but the difference in gender composition between the groups was not statistically significant (P > 0.05).

Similarly, there was no statistically significant difference in average age (P > 0.05) or disease duration (P > 0.05) among the groups. Power analysis show that sample size in this study can guarantee 90% confidence in obtaining statistical difference (□=0.9, α=0.05, period=12 months). Therefore, the groups are considered comparable (Table 1).

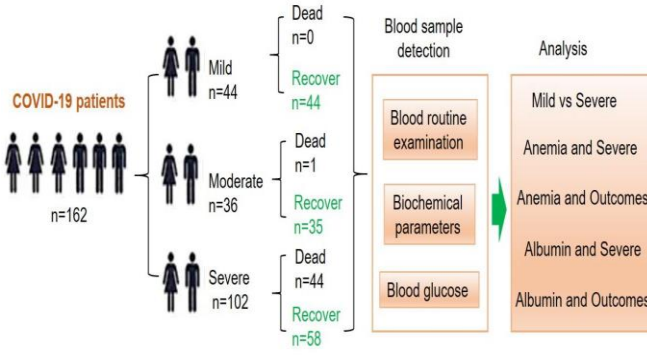
Table 1: Baseline characteristics of the participants classified by gender

Characteristics	(60–70 years)	(71–80 years)	(81–90 years)	(91–100 years)
Age (years)	-	-	-	-
Mean (SD)	67.44(2.08)	75.21(2.56)	84.80(2.45)	92.50(2.25)
Median	68.00	75.00	85.00	91.50
Sex (%)	-	-	-	-
Male	36 (78.26%)	37 (72.55%)	36 (75.00%)	14 (82.36%)
Female	10 (21.74%)	14 (27.45%)	12 (25.00%)	3 (17.64%)
Ethnicity, n （%）				
Han Chinese	46 (100%)	51 (100%)	48 (100%)	17 (100%)
Other	0	0	0	0
High (cm)	-	-	-	-
Mean (SD)	163.31(8.21)	160.63(6.01)	160.31(5.21)	157.24(7.17)
Median	163.15	160.52	160	156.07
Body weight (Kg)	-	-	-	-
Mean (SD)	65.17(11.54)	66.25(11.08)	63.24(5.28)	66.53(8.95)
Median	65.30	68.10	66.00	64.85
BMI (Kg/m2)	-	-	-	-
Mean (SD)	23.23(1.44)	22.25 (3.98)	25.45(3.63)	26.21(1.49)
Median	23.09	21.08	25.43	25.010

Study design and sample collection

In total, 162 blood samples of COVID-19 patients in the Hospital as described in materials and methods were collected (Figure 1). The samples were transported to the laboratory and processed for some analyses. Blood routine examination was conducted by Count Coulter auto-hemocyte analysis instrument. Meanwhile, 44 biochemical parameters were also systematically detected and analyzed in the serum of COVID-19 patients.

Figure 1: Study design and sample collection.



collection and study design from COVID-19 patients. The serum samples of mild patients (n=44), moderate (n=36), and severe patients (n=102) were collected at different time points after diagnosis and before discharge. The blood samples were detected by using blood routine examination, biochemical parameters and blood glucose detection, and these data were compared and correlation was analyzed.

Correlation between anemia and the severity of COVID-19, albumin and the severity of COVID-19

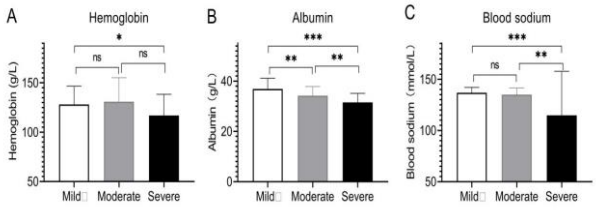
According to the measurement of hemoglobin, patients were divided into two groups: normal control (>120 g/L) and anemice (≤ 120 g/L). A statistical test was conducted to examine the association between anemia status and the severity of COVID-19 using an ordered logistic regression analysis. The p-value obtained was 0.0657, which is greater than 0.05, indicating that there is no significant correlation between the two groups. According to the measurement of hemoglobin, the severity of anemia is divided into three levels: mild group (90-120g/L), moderate (60-90 g/L), and severe (30-60 g/L). A statistical test was conducted to examine the

association between the severity of anemia and the severity of COVID-19 using Fisher's chi-square test. The obtained p-value was 0.217, which is greater than 0.05, indicating that there is no significant correlation between the two. According to the measurement values of albumin, patients with albumin level ≥ 35 g/L are classified as normal, while those with albumin level < 35 g/L are classified as having hypoalbuminemia. A statistical test was conducted to examine the relationship between the presence of hypoalbuminemia and the severity of COVID-19, using ordered logistic regression analysis. The obtained p-value was 1.24e-06 < 0.05, indicating a significant correlation between the two factors. A correlation analysis was also performed, and the Spearman correlation coefficient was found to be 0.3856727, indicating a moderate positive correlation between the presence of hypoalbuminemia and the severity of COVID-19. According to the measurement values of albumin, hypoalbuminemia is classified into three levels: mild, moderate, and severe. mild hypoalbuminemia group (30-35 g/L); moderate hypoalbuminemia group (25-29 g/L); and severe hypoalbuminemia group (<25 g/L). A statistical test was conducted to examine the relationship between the severity of hypoalbuminemia and the severity of COVID-19, using Fisher's chi-square test. The obtained p-value was 0.3382 > 0.05, indicating that there is no significant correlation between the two factors (Table 2, Figure 2A, 2B).

Table 2: Analysis of clinical symptoms and severity of COVID-19/patient outcomes

		Severity of COVID-19		Patient outcomes	
		P-value	**r**	**P-value**	**r**
Anemia	Yes	0.0657	/	0.03204	0.1622748
	Degree	0.217	/	0.5186	/
Hypoproteinemia	Yes	1.24E-06	0.3856727	3.03E-05	0.3035322
	Degree	0.3382	/	0.03032	0.2100583

Figure 2: Comparation of levels of hemoglobin, albumin and sodium in blood.

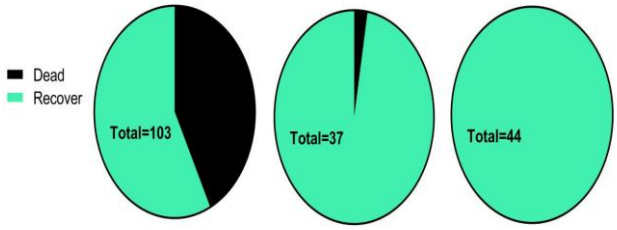


Blood samples were collected in mild, moderate and severe patients separately, and levels of hemoglobin (A), albumin (B) and sodium (C) were detected. ns, no significance, *<0.05, **p<0.01, ***p<0.001.

Correlation between anemia and patient outcomes, albumin and patient outcomes

A statistical test was conducted to examine the correlation between anemia in patients and patient outcomes using the chi-square test. The obtained p-value was 0.03204, which is less than 0.05, indicating a significant correlation between the two factors. Further correlation analysis using Spearman's correlation coefficient revealed a coefficient of 0.1622748, indicating a positive weak correlation. This suggests that there is a positive correlation between patients with anemia and mortality rate. A statistical test was conducted to examine the correlation between the severity of anemia in patients and patient outcomes using the Cochran-Armitage trend test. The obtained p-value was 0.5186, which is greater than 0.05, indicating that there is no significant correlation between the two factors. The statistical test conducted examined the relationship between whether patients had hypoalbuminemia and patient outcomes using the chi-square test. The obtained p-value was 3.028e-05 < 0.05, indicating a significant correlation between the two factors. A correlation analysis was performed, and the Spearman correlation coefficient was 0.3035322, indicating a moderate positive correlation. Patients with hypoalbuminemia were positively correlated with mortality rate. The statistical test conducted examined the relationship between the severity of hypoalbuminemia in patients and patient outcomes using the Cochran-Armitage trend test. The obtained p-value was 0.03032, indicating a significant correlation between the two factors. In the correlation analysis, the Spearman correlation coefficient was 0.2100583, indicating a positive correlation between different degrees of hypoalbuminemia and patient mortality rate (Table 2, Figure 3).

Figure 3: The percent of dead in different groups.



In severe group (A), no patient died, in moderate group

DISCUSSION

Over the past three years, the COVID-19 pandemic has been spread all over the world, many elderly people have died for this. Patients over the age of 65 are among the high-risk groups for SARS-Cov-2 infection Prendki et al. (2022), Chen et al. (2021). Currently, the Omicron variant strain EG.5 may induce the third peak of infection in this winter, which will influence the survival condition of old people especially who have the underlying disease, such as malnutrition Abbasi et al. (2023), Faraone et al. (2023). Our research focused on the study of relations between the malnutrition and severity and outcomes of COVID-19 patients, especially explored the correlation between anemia, hypoalbuminemia, and the proportion of severity of COVID-19 and mortality rate. In this study, it was found that patients with anemia had a positive correlation with the mortality rate. However, there was no significant correlation between the severity of anemia and patient outcomes. Meanwhile, a positive correlation was found between blood levels of albumin and the severity of COVID-19. Both the presence of hypoalbuminemia and different levels of albumin were positively correlated with the mortality rate. The levels of blood sodium also decreased in severe patients which was another indicator for prognostic prediction (Figure 2C). These results showed us the importance of malnutrition during the virus infection in old patients Norman et al. (2021), Prendki et al. (2022), Chen et al. (2021), Tosato et al. (2023), especially the levels of albumin in patient blood. Thus, nutrition parameters test should be carried out when SARS-CoV-2 infected patient is admitted to the hospital. The levels of albumin, hemoglobin and sodium should be paid more attention, and intervened this condition early. Usually, the common treatments against virus, such as taking anti-virus medicine, antiphlogistic medicine, relieve cough and Reduce Phlegm medicine, and hormones are the solutions to improve symptom of COVID-19. Meanwhile, the Chinese herbs did the great job to improve symptom and rehabilitate the patients. In our study, all patients accepted this treatment, and some patients accepted special nutrition treatment based on our observation of these parameters. At last, most of them recovered. Thus, these parameters will become the indicators for clinicians when they are dealing with these patients, to assist clinicians in early assessment of the condition and prognosis of COVID-19, provide early intervention and treatment, and reduce the risk of further exacerbation and even death.

CONCLUSIONS

Before the spread of Omicron variant strain EG.5, the old people who have the anemia and hypoalbuminemia underlying disease should pay more attentions to find useful ways to defense SARS-Cov-2 infection, such as inoculation with effective vaccine about Omicron variant strains.

DECLARATIONS

Ethics approval and consent to participate

All studies were conducted in accordance with Provincial Hospital Affiliated to Shandong First Medical University Committee guidelines (HRE-SLYY-015). This study has been approved by the Ethics Committee of Shandong University First Hospital, and informed consent has been obtained from all patients.

Consent for publication

Submission is approved by all authors.

Availability of data and materials

The datasets generated during the current study are available in contacting with the correspondence author.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

All authors discussed the results and implications of the manuscript. J.Y. and J.F. conceived the study, supervised the project. W.R., G.J., J.M., Z.T., and H.F. performed experiments. G.J. analyzed data and wrote the paper. R.W. and G.J. contributed equally to this work.

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