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Original Research Article

A correlation of disease severity and outcome with malnutrition status in adults with COVID-19

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ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) pathology increases catabolism and depletes the protein stores, causing malnutrition. However, nutrition assessment in COVID-19 is often overlooked in the current pandemic. The Controlling Nutritional Status (CONUT) score is a validated score to assess nutritional status in hospitalized patients. The objective of the study was to estimate malnutrition among hospitalized adult patients with COVID-19 using the - The Controlling Nutritional Status (CONUT) score and study its effect on the disease severity and outcomes.
Methods: The study was a retrospective study on 146 patients with COVID-19. The history, demographic details were noted and the following parameters were noted at baseline and time of outcome- COVID-19 disease severity, radiological severity, CONUT score, inflammatory markers- serum LDH, CRP, Ferritin, D-Dimer. The outcome parameters- mortality, duration of hospital stay and severity of disease at outcome were measured.
Results: Out of the 146 patients, 84 (57.53%) were male and 62 (42.47%) were female. 97.26% patients had malnutrition at baseline with 42 (28.77%) mild, 70 (47.95%) moderate and 30 (20.55%) severe malnutrition based on CONUT score. The CONUT scores were greater at outcome compared to baseline ($p<0.001$). Higher grades of malnutrition were associated with greater baseline and outcome disease severity ($p<0.001$), radiological severity ($p<0.001$), higher levels of inflammatory markers ($p<0.001$) and a higher mortality ($p<0.001$). However, there was no significant difference in duration of hospital stay ($p=0.67$).
Conclusions: Malnutrition results in worse outcomes and greater mortality in COVID-19. Individual tailored nutritional support in the hospitalized COVID-19 patients, can thus potentially improve outcomes.

Keywords: COVID-19, Malnutrition, Nutrition, CONUT score, Disease severity, Outcome

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an ongoing global pandemic which is caused by the Severe Acute Respiratory Syndrome Corona virus 2 (SARS-CoV-2). The clinical spectrum of this infection ranges from asymptomatic infection to a potentially fatal severe acute respiratory infection.[1] There are multiple factors influencing the susceptibility of an infected individual to develop severe disease.[2] These factors may promote the occurrence of an exaggerated abnormal host immune response called cytokine storm, which results in severe illness.[3]

In hospitalized patients, malnutrition has been found to be an independent risk factor for the development of increased complications and a higher mortality.[4] This is because malnutrition causes hypoproteinemia which affects immune function and tissue healing.[5] Malnutrition in the hospitalized can be due to a decreased intake prior to the illness (seen in elderly and co-morbid) which is worsened by the reduced food intake secondary to the illness and a lack of appropriate nutritional support during hospitalization. In India, malnutrition among hospitalized adults is estimated to be around 31% at the time of hospitalization and is found to increase to around 44% during the course of hospital stay.[6]

The CONUT score is a simple validated screening tool for assessing malnutrition among the hospitalized patients which considers the total lymphocyte count, serum albumin and total cholesterol levels. Here, based on the score, nutritional status can be normal nutrition (0-1), Mild (2-4), Moderate (5-8) or severe (9-12) malnutrition.[7,8]

COVID-19 pathology results in a hyper-catabolic state that depletes the skeletal muscle mass which is an important store of proteins. This causes a reduction in total protein, albumin and pre- albumin, thus affecting immunity and tissue repair. In COVID-19, there are healthcare related and treatment related barriers to adequate nutritional therapy during the hospital stay. Nutrition in COVID-19 hospitalized patients has not received much attention in the current pandemic setting, due to a high patient burden, scarcity of healthcare workers and the risk of potential transmission of the infection to the caregivers.[9] Thus, there is a need to estimate the occurrence of malnutrition among patients hospitalized with COVID-19. In this study, the CONUT score has been used for this purpose.

Thus, the primary objective of the study was to estimate the frequency of malnutrition among hospitalized adult patients with COVID-19 using the CONUT score.

Our secondary objective was to correlate the effect of malnutrition on disease severity and outcomes in hospitalized adult patients with COVID-19.

METHODS

The study was a retrospective study conducted from June 2021 to January 2022 in the hospitals affiliated to Bangalore Medical College and Research Institute. The inclusion criteria for the selection of subjects were patients 18 years of age and above diagnosed to have SARS- CoV-2 infection through a positive Reverse transcription polymerase chain reaction (RTPCR)/ Rapid Antigen test, admitted during the study period to the study hospital. The exclusion criteria (having included) were patients who were discharged against medical advice or transferred to another hospital prior to completion of the full course of hospital stay.

The tool used for screening the nutritional status in the study population was the CONUT score. In this, based on the serum albumin, total lymphocyte count and total cholesterol, the serum albumin score, total lymphocyte count score and total cholesterol score are calculated respectively. These scores are then added to get the CONUT score. A CONUT score of 0-1 indicates normal nutrition, 2-4 is mild malnutrition, 5-8 is moderate malnutrition and 9-12 is severe malnutrition (Table 1).[7]

Among the patients meeting the inclusion criteria, the history and demographic details were noted retrospectively. The baseline vitals – heart rate, blood pressure, oxygen saturation, respiratory rate, temperature, arterial blood gases and oxygen requirement as well as the clinical COVID-19 disease severity and radiological severity were noted. The baseline blood investigations were used to calculate the CONUT score from the serum albumin, total lymphocyte count and total cholesterol. The baseline inflammatory markers of serum C-reactive protein (CRP), D-Dimer, Lactate dehydrogenase (LDH) and ferritin collected. Similarly, the vitals and clinical COVID-19 disease severity, radiological severity, CONUT score and inflammatory markers at the time of outcome also noted. The potential outcomes included discharge from the hospital or death. The duration of hospital stay, COVID-19 disease severity at outcome and the mortality were considered as outcome parameters.

The COVID-19 clinical disease severity was graded into mild, moderate, severe and critical disease as per the World Health Organization (WHO) guidelines.[10]

The data obtained was analyzed.

RESULTS

A total of 146 patients were included in the study out of whom 84 patients (57.53%) were male and 62 patients (42.47%) were female.

Table 1: The COUNT score.

Parameter	Undernutrition degree			
	None	Mild	Moderate	Severe
Serum albumin (g/dl)	≥3.50	3.00-3.49	2.50-2.99	<2.50
Serum albumin score	0	2	4	6
Total lymphocyte count (/mm^3)	≥1600	1200-1599	800-1199	<800
Total lymphocyte count score	0	1	2	3
Total cholesterol (mg/dl)	≥180	140-179	100-139	<100
Total cholesterol score	0	1	2	3
Conut score = serum albumin score + total lymphocyte count score + total cholesterol score				

Table 2: Baseline malnutrition and baseline clinical disease severity.

Malnutrition severity / Baseline disease severity	Normal	Mild malnutrition	Moderate malnutrition	Severe malnutrition	P value
	N (%)	N (%)	N (%)	N (%)	
Mild	2 (50)	15 (36)	2 (3)	1 (3)	<0.001
Moderate	2 (50)	19 (45)	20 (29)	5 (17)	
Severe	0 (0)	7 (17)	44 (63)	20 (67)	
Critical	0 (0)	1 (2)	4 (6)	4 (13)	

Table 3: Baseline malnutrition and disease severity at outcome.

Malnutrition severity / Outcome disease severity	Normal	Mild malnutrition	Moderate malnutrition	Severe malnutrition	P value
	N (%)	N (%)	N (%)	N (%)	
Mild	4 (100)	41 (98)	29 (41)	5 (17)	<0.001
Moderate	0 (0)	1 (2)	6 (9)	1 (3)	
Severe	0 (0)	0 (0)	1 (1)	1 (3)	
Critical	0 (0)	0 (0)	34 (49)	23 (77)	

Table 4: Baseline malnutrition and change in disease severity from baseline to outcome.

Malnutrition severity / Change in severity at outcome	Normal	Mild malnutrition	Moderate malnutrition	Severe malnutrition	P value
	N (%)	N (%)	N (%)	N (%)	
Same	0 (0)	6 (14)	0 (0)	1 (3)	<0.001
Improved	4 (100)	36 (86)	35 (50)	4 (13)	
Worse	0 (0)	0 (0)	35 (50)	25 (83)	

Table 5: Baseline malnutrition and baseline CT severity score.

	Normal	Mild malnutrition	Moderate malnutrition	Severe malnutrition	P value
Baseline median CT severity score (out of 25)	7 (3,12)	8 (4,13)	17.5 (13,21)	18.5 (16,21)	<0.001

Table 6: Baseline malnutrition and baseline serum inflammatory markers.

	Normal	Mild malnutrition	Moderate malnutrition	Severe malnutrition	P value
Baseline LDH median u/l	341.5 (235.5,464)	326 (244,433)	468 (376,626)	580.5 (383,864)	<0.001
Baseline ddimer median (ng/ml)	280.5 (219.5,435.5)	287 (201,342)	560 (359,936)	984 (560,1050)	<0.001
Baseline ferritin median (ng/ml)	455.0 (63.62,932.85)	212.8 (127.4,542.6)	987.4 (469.9,2000)	1729.75 (766,2000)	<0.001
Baseline CRP median (mg/l)	43.47 (4.245,149.32)	16.32 (3.78,45.68)	94.15 (48.5,167.93)	166.44 (79.21,254.2)	<0.001

Table 7: Baseline malnutrition and outcome- discharge and mortality.

Malnutrition severity	Normal	Mild malnutrition	Moderate malnutrition	Severe malnutrition	P value
Outcome	**N (%)**	**N (%)**	**N (%)**	**N (%)**	
Discharged without oxy	4 (100)	40 (95)	26 (37)	4 (13)	<0.001
Discharged with oxy	0 (0)	2 (5)	9 (13)	1 (3)	
Dead	0 (0)	0 (0)	35 (50)	25 (83)	

Table 8: Malnutrition and duration of hospital stay.

	Normal	Mild malnutrition	Moderate malnutrition	Severe malnutrition	P value
Total duration of hospital stay (days)	7.5 (6,9.5)	9 (7,12)	8 (5,12)	4.5 (3,12)	0.67

Table 9: comparison of CONUT score at baseline and outcome.

Time	CONUT score		Mean change (95% CI)	P value[¥]
	Mean	**SD**		
Baseline	5.83	2.63	1.09 (-1.39, -0.79)	<0.001
At outcome	6.93	2.79		

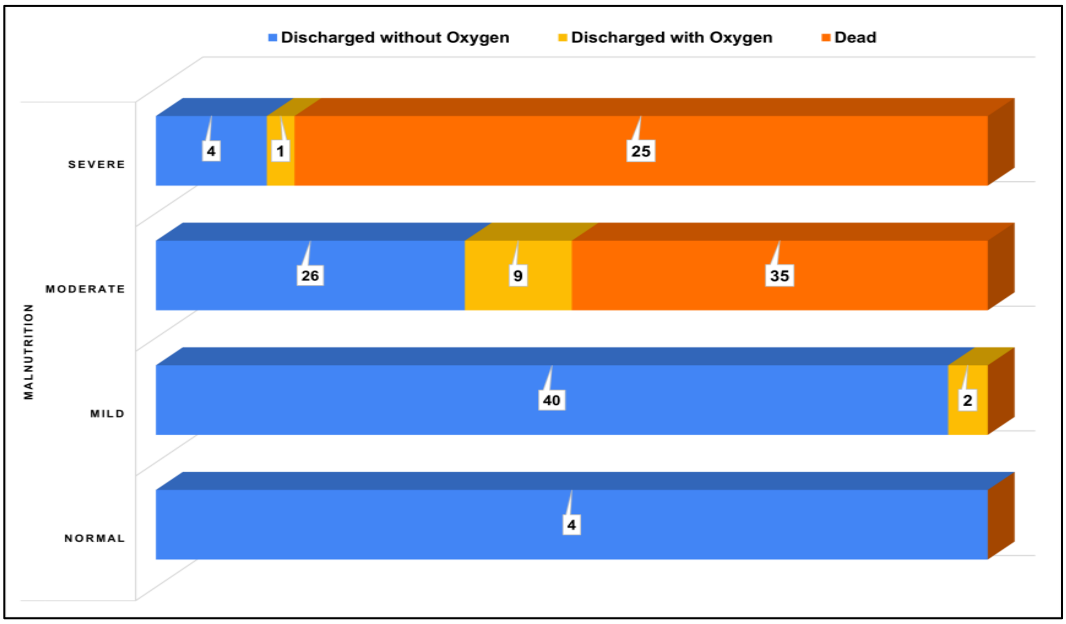

Figure 1: Baseline malnutrition and outcome- discharge and mortality.

In terms of baseline clinical disease severity, 20 patients (13.7%) had mild disease, 46 patients (31.51%) had moderate disease, and 71 patients (48.63%) had severe disease and 9 patients (6.16%) had critical disease. At baseline, it was seen using the CONUT score those 142 patients (97.26%) had some degree of malnutrition. Thus 4 patients (2.74%) had normal nutrition status, 42 (28.77%) had mild malnutrition, 70 (47.95%) had moderate malnutrition and 30 patients (20.55%) had severe malnutrition. In terms of serum inflammatory markers at baseline, the median LDH was 431.5 (331,606) U/L, median D-Dimer was 461 (301,917.5) ng/ml, median CRP was 79.46 (23.4,173) mg/L and median ferritin was 840.1 (227.1,1791.5) ng/ml.

When the outcomes of discharge and deaths were considered, a total of 86 patients were discharged (58.9%) and 60 patients (41.1%) died. Among the discharged patients, 74 patients (84.05%) were discharged without oxygen and 12 patients (13.95%) were discharged with oxygen. The median duration of hospital stay was 7.5 (6, 9.5) days for those with normal nutrition status, 9(7, 12) days for those with mild malnutrition, 8 (5, 12) days for those with moderate malnutrition and 4.5 (3, 12) days for those with severe malnutrition.

The clinical disease severity at outcome was mild disease in 79 (54.11%) patients, moderate disease in 8 (5.48%) patients, severe disease in 2 (1.37%) patients and critical disease in 57 (39.04%) patients. Using the CONUT score calculated at outcome, 0 (0%) patients had normal nutrition, 22 (20.37%) patients had mild malnutrition, and 55 (50.93%) patients had moderate malnutrition and 31 (28.7%) patients had severe malnutrition. At outcome, among the serum inflammatory markers, the median LDH was 378 (294, 576) U/L, median D-Dimer was 413 (292, 867) ng/ml, median CRP was 35.29 (10.86, 130.96) mg/L and median Ferritin was 596.4 (170.2, 1178) ng/ml.

Analysis

The data was analyzed using R software version 4.1.1. R Core Team (2021). The Fischer Exact test was used to assess the association between each of the outcome parameters respectively with the severity of malnutrition. Kruskal Wallis test was used to assess the association between baseline median serum inflammatory markers and the severity of malnutrition. Paired sample T Test was used to compare the mean CONUT scores at baseline and outcome.

Baseline malnutrition and baseline clinical disease severity

A higher severity of baseline malnutrition was significantly associated with a higher grade of baseline clinical disease severity ($p<0.001$) (Table 2).

Baseline malnutrition and outcome clinical disease severity

A higher severity of baseline malnutrition was significantly associated with a higher grade of clinical severity at outcome ($p<0.001$) (Table 3).

Baseline malnutrition and change in disease severity from baseline to outcome

A higher severity of malnutrition at baseline was significantly associated with worsening of the clinical disease severity at outcome compared to baseline ($p<0.001$) (Table 4).

Baseline malnutrition and baseline CT severity score (out of 25)

A higher baseline degree of malnutrition was significantly associated with a higher median CT severity score ($p<0.001$) (Table 5).

Baseline malnutrition and baseline serum inflammatory markers

A higher baseline degree of malnutrition was significantly associated with higher baseline median serum inflammatory markers- LDH, D-Dimer, Ferritin and CRP respectively ($p<0.001$) (Table 6).

Baseline malnutrition and outcome- discharge and mortality

A higher severity of malnutrition at baseline was significantly associated with a higher mortality rate while normal nutrition and milder malnutrition was associated with a significantly higher discharge rate ($p<0.001$) (Table 7) (Figure 1).

Baseline malnutrition and duration of hospital stay

There was no significant association between severity of malnutrition and duration of hospital stay ($p=0.67$) (Table 8).

Comparison of CONUT score at baseline and outcome

The mean CONUT score at outcome was significantly higher (6.93 ± 2.79) in comparison to baseline (5.83 ± 2.63) ($p<0.001$) (Table 9).

DISCUSSION

From the results of our study, it was seen that most of the study population, that is 142 patients (97.26%) had some degree of malnutrition. Further, it was seen that with a greater severity of malnutrition, the baseline COVID-19 disease severity was significantly worse in terms of a worse baseline clinical severity, higher baseline CT-severity score and higher baseline serum inflammatory markers of LDH, D-Dimer, CRP and Ferritin. In addition, a greater severity of malnutrition was also associated with a greater mortality rate and worse clinical disease severity at outcome. Further, there was a significant worsening of the clinical severity at the time of outcome in comparison to the baseline. Thus, malnutrition at the time of admission is associated with adverse outcomes in COVID -19 patients. This is probably due to COVID-19 associated catabolism that depletes the proteins needed for tissue repair and immunity. The catabolism also causes raised blood urea nitrogen, derived from the protein metabolism, which by itself is associated with adverse outcomes and increased mortality in the hospitalized.[9,11] Further, as seen in our study, the serum inflammatory markers were higher in association with the malnutrition severity indicating that malnutrition probably contributes to the abnormal exaggerated immune response called the cytokine storm. This cytokine storm results in extensive vascular inflammation, which can cause disseminated intravascular coagulation, shock, multi-organ failure and death.[3]

Our study also demonstrated that the CONUT scores increased significantly from baseline to the time of outcome, signifying a possible worsening of the nutrition status post admission. This could indicate inadequate nutritional support among the hospitalized COVID-19 patients, who are already in a catabolic state.[2,3] However, in our study, there was no significant association with the severity of malnutrition and the duration of hospital stay. This can be explained by the greater mortality rate among those patients with a greater severity of malnutrition, which could have cut-short the total duration of hospital stay.

A retrospective study by Wei et al on 348 patients with severe COVID-19 showed that the CONUT score was an independent predictor of death in COVID-19 (p=0.009) and was associated with worse cardiac outcomes.[5] Similar associations of the score with mortality were also demonstrated by Wang et al in a retrospective study among 445 COVID-19 patients in Wuhan.[12] Both studies showed a higher CONUT score to be associated with an elevated CRP.[5,12] Also, studies using other tools for nutritional screening instead of or in addition to the CONUT score like those by Allard et al and Song et al have all demonstrated that nutrition risk or baseline nutritional status were significantly associated with COVID-19 disease severity and in-hospital mortality.[13,14] Our results are in concordance with the above mentioned studies. A meta-analysis by Abate et al; estimated the pooled prevalence of malnutrition among hospitalized patients with COVID-19 to be 49.11% with the odds of mortality being ten-times higher in COVID-19 patients with malnutrition.[15]

There are multiple tools available for screening of the nutritional status among hospitalized COVID-19 patients. In comparison to other scales, the CONUT score was seen to have better prognostic potential and was also less expensive and needed less skill to learn. However, there is a lack of uniformity in the cut- offs of the CONUT score to classify the severity of malnutrition.[16] In our study, considering its simplicity, the CONUT score was used. Further, it is less time consuming as it is calculated using lab investigations and does not require elaborate body measurements.

Thus, improving the nutritional status, can potentially improve COVID-19 disease outcomes. Brugliera et al highlight the ways to providing in-hospital nutritional rehabilitation to COVID-19 patients.[17] It involves calculating the protein, energy requirement, adding appropriate levels of carbohydrate and lipids and supplementing the micronutrients and essential and branched chain amino acids. This therapy is individually tailored and enteral nutrition is preferred over parenteral nutrition.[17]

There were a few limitations to the study. One was that we did not consider the effect of pre-existing co-morbidities, gender and age on the nutritional status. Also, the sample size was smaller.

CONCLUSION

Malnutrition increases the mortality and disease severity in hospitalized adult patients with COVID-19. There is a deterioration of the nutritional status during the course of hospitalization indicating inadequate nutritional support. Thus, in- hospital screening of COVID-19 patients for malnutrition and providing them with individually tailored appropriate nutritional support can potentially help reduce the deleterious effects of malnutrition on COVID-19 disease severity and outcomes.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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