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Tailoring nutrition therapy amid the COVID-19 pandemic: Does it work?

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SUMMARY

Background: The COVID-19 pandemic has been a challenge for nutrition monitoring and delivery. This study evaluates clinical and nutritional characteristics of patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and investigates the relationship between nutrition delivery and clinical outcomes.
Methods: Prospective observational study of adults admitted for >24 hrs to a tertiary-care hospital during a period of 2months. Data was collected on disease severity, energy, protein delivery and adequacy, use of mechanical ventilation (MV), hospital length of stay (LOS). Multivariate logistic regression models were used to determine the associations with mortality as the primary outcome.
Results: 1083 patients: 69% male (n = 747), 31% females (n = 336), mean age 58.2 ± 12.8 with 26.6 ± 4.32 BMI were analysed. 1021 patients survived and 62 deaths occurred, with 183 and 900 patients in the ICU and ward, respectively. Inadequate calorie and protein delivery had significantly higher mortality than those with adequate provision ($p < 0.001$) among the ICU patients. In bivariate logistic regression analysis, inadequacy of energy and protein, disease severity, comorbidities ≥3, NRS score ≥3 and prone ventilation correlates with mortality ($p < 0.001$). In multivariate logistic regression analysis of the ICU patients, energy inadequacy (OR:3.6, 95%CI:1.25–10.2) and prone ventilation (OR:11.0, 95%CI:3.8–31.9) were significantly ($p < 0.05$) associated with mortality after adjusting for disease severity, comorbidities and MV days.
Conclusion: Most patients infected with SARS-CoV-2 are at nutrition risk that can impact outcome. Our data suggest that addressing nutritional adequacy can be one of the measures to reduce hospital LOS, and mortality among nutritionally risk patients.

1. Introduction

The COVID-19 pandemic has brought about a rapid change in healthcare practices, with a focused demand for nutrition support to prevent and treat marked nutritional consequences during COVID-19 infection.

The novel SARS CoV-2 virus infection, in its severe form, clinically resembles acute respiratory distress syndrome (ARDS), pneumonia, and septic shock requiring mechanical ventilation [1]. It is also characterized by a pro-inflammatory response to infection and hyper-catabolism, with increased energy expenditure linked to mechanical ventilation, all of which significantly raise calorie, protein and other nutrient demands [2,3]. Several earlier studies have shown that patients with severe pneumonia are at risk for protein energy malnutrition (PEM) and clinical cachexia that severely impair respiratory muscle function, affecting long term lung efficiency [4,5] and making PEM an independent mortality risk

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predictor [6,7]. Malnutrition further impacts other physiological processes, including hematopoiesis and the immune response, compromising the body's response to infection. The worsening of malnutrition should therefore be tackled by an appropriate nutritional strategy, including adequate protein-energy delivery and stimulation of physical activity.

Other factors like anorexia secondary to infection, dyspnea, dysosmia, dysgeusia, stress, need to quarantine, etc. impact nutrient intake adequacy. In a study conducted by Lechien et al., in 12 European hospitals, 85.6% of patients with documented COVID-19 reported olfactory dysfunction, while 88% reported gustatory changes, with females being more affected than males [8]. Some patients experience diarrhoea, nausea, vomiting, stomach pain, and in some instances, gastrointestinal bleeding before developing respiratory symptoms. Such symptoms will make it difficult to initiate timely nutrition therapy or attain nutrient adequacy. Evidence also suggests that the severity of GI symptoms reflects the severity of the disease [9] in addition to contributing to poor appetite and decreased food intake.

Severe SARS-CoV-2 infection was most frequently seen in the elderly in the ICU [10]. Analyses by the Italian national Health Institute (ISS) and other published studies from China on mortality from SARS-CoV-2 showed that older age, with an average of 78 years, and the presence of 3 or more comorbidities, including chronic non-communicable diseases (NCDs) such as ischemic heart disease, hypertension, diabetes, chronic obstructive pulmonary disease (COPD) and malignancies, are at highest risk [11–17].

Nutritional status is the most easily identifiable, distinct, and modifiable risk factor [18,19] that affects clinical outcomes, given the prevalence of malnutrition in SARS-CoV-2 positive patients on admission according to the NUTRICOV study [20], and with 42% in ward and 66% in ICU in other studies [21]. The NRS score can be used both in wards and ICUs to identify at-risk patients [22] who will benefit from aggressive NT [19,23].

According to global recommendations, early initiation of nutrition therapy, in conjunction with pharmacological therapies, will prevent and help resolve the infectious process with greater ease, minimize hospital length of stay (LOS) [24] and reduce complications, that will also apply for COVID-19 patients too. The rapid emergence of scientific data on COVID-19 has prompted the impetus towards research.

Simultaneously, guidance and recommendations were released by The European Society for Clinical Nutrition and Metabolism (ESPEN) [25] and the American Society for Parenteral and Enteral Nutrition (ASPEN), specific to nutrition support therapy of COVID-19 patients admitted in critical care units [26]. Although there is evidence to indicate malnutrition among COVID patients at admission, there is paucity of data on adequacy of nutrition provision and its link to outcomes of mortality and length of hospital stay (LOS).

Our study aims: 1) to evaluate clinical and nutrition characteristics of SARS Cov-2 patients admitted in ward and in the ICU 2) to investigate the relationship between nutrition delivery and adequacy and clinical outcomes in terms of length of hospital stay (LOS) mortality and other health-related outcomes in SARS Cov-2.

2. Methods

All hospitalized patients with a laboratory-confirmed diagnosis of COVID-19 by Reverse Transcription Polymerase Chain Reaction (RT-PCR), between 05 June 2020 and 15 August 2020, were included in the study. Institutional Ethical Committee approval was obtained for the study (SIEC/2020/411). Retrospective data of the patients was reviewed prior to the finalization of this study protocol.

All adult in-patients >18yrs of age with >24 h stay in the hospital ward or ICU were included. Data was collected at admission on age, gender, and body mass index (BMI). Nutrition information regarding oral nutrition, use and type of enteral or parenteral nutrition were collected. Daily nutrition monitoring data was collected for 14 days. The retrospective data of previously admitted patients in this hospital showed that the average LOS in the hospital ranged from 5 to 12 days. Therefore, 14 days was considered to monitor food or feed provision to the patients admitted during the hospital stay.

Length of hospital stay, whether in the ward or ICU, was collected. Hospital discharge data with patient outcomes like hospital mortality, and transfer to home, were also recorded.

Patients were grouped into mild (predominantly upper respiratory disease), moderate (pneumonia without hypoxia) and severe disease (pneumonia with hypoxia) categories according to the National Clinical Management Protocol as advised by the Ministry of Health [27].

Baseline nutritional screening by NRS-2002 was performed. SOFA and APACHE II scores for the ICU patients were calculated on the day of admission. Patients were classified as having a high NRS-2002 score (≥3) and low (<3) risk of malnutrition.

Patient information regarding disease severity, number of days of mechanical ventilation (MV), number of hours prone ventilation in the ICU was collected. Number of comorbidities, use of dialysis, vasopressors and propofol were logged during the data collection period. The primary clinical outcome of interest-mortality and its association with nutrition adequacy, were analyzed separately for ward and ICU patients. Furthermore, hospital LOS were analyzed and compared.

Caloric requirements were calculated as 25 kcal/kg/day and protein 1.2–1.5 gms/kg/day, as referred to in the guidelines [28]. The ideal body weight was used to determine energy requirements for up to the first 5 days of admission in this study. After the acute phase of the illness was over and the tolerance to feeding had been established over 5 days, the nutritional needs were then calculated and implemented using the actual body weight. The retrospective data of the previously admitted COVID-19 patients in this hospital showed that the average BMI was 26–28 kg/m^2. Ideal body weight instead of actual body weight was taken initially after admission as per the guidelines [29], and to avoid overfeeding over the first 5–7 days of acute illness. This was also an attempt to achieve at most 70% energy requirements of actual body weight calculations.

Daily nutrition data, which included the initial feeding strategy, type and amount of nutrition received, was collected from admission until 14 days, hospital discharge, or death. Daily total calorie and protein prescribed and delivered were captured for every patient for 14 days. Cumulative energy and protein prescribed and delivered were recorded accordingly. Inadequate calorie and protein delivery were defined as calorie or protein adequacy <80%.

Training was provided to the nurses in Covid-19 units, outlining the goals of nutrition provision to COVID patients and the feeding methodology. Dietitians, in close contact with nurses, kept track of nutritional data and monitored the patients.

Oral diet, or enteral nutrition (EN), was started as per the hospital feeding protocol.

The patients on oral diet were assessed for plate wastage during hospital stay. Plate wastage refers to the volume or percentage of the served food that is discarded [30]. At the end of the meal, the amount of food consumed is visually evaluated and the proportion of food on the plate consumed by each subject estimated on a Comstock 6-point scale (all, ¾, ½, ¼, <¼, and none) [31] and recorded. The energy and protein content of each meal served to the patients was calculated. Patients on both normal and therapeutic diets were considered. Enteral feeding with scientific formulas was started as per hospital protocol and monitored for feed delivery, and interruptions were recorded.

2.1. Statistical analysis

SPSS Windows version 24.0 was used for statistical analysis. Data was presented as either mean ± standard deviation (SD), median; inter quartile range (IQR), or proportions and compared using t-test, Chi-square test, logistic regression, and log rank tests, respectively. Normality was checked using mean, median, mode.

For the analysis, all statistical tests were evaluated with a 2-tailed p-value, and p-values less than 0.05, a 95% confidence interval (CI) were deemed significant. All potential risk factors were compared between survivors and non-survivors by univariate analysis using Chi-square/Fisher's exact tests, and Student's t test/Mann Whitney U tests for continuous variables. Univariate and multivariate logistic regression analysis was performed with mortality outcome for all the patients. In the second part of the analysis, 14-day energy and protein adequacy were categorized as ≥80% and <80%, and their association with the mortality outcome for ward and ICU patients separately was determined. We also investigated nutrition delivery in a subclass of patients who received MV ≥ 24 h and during prone ventilation.

3. Results

1083 patients out of 1134 were eligible for the study analysis. 51 patients were excluded because of incomplete data, including patients who Left Against Medical Advice (Figure 1).

3.1. General characteristics of patients

Of the 1083 patients, 69% were male (n = 747) and 31% were females (n = 336) with a mean age of 58.2 ± 12.8 years and BMI of 26.6 ± 4.32 kg/m^2. The subjects admitted in ward 83% (n = 900) and ICU 17% (n = 183) were considered individually for analysis as shown in Figure 1, with prevalent comorbidities 61% (n = 656) and those with no comorbidities 39% (n = 427) as in Table 1. Of the 656 patients with comorbidities at admission, 70% (n = 456) being type 2 diabetic, 19% (n = 126) hypertensive, and 11% (n = 74) with other underlying diseases (Figure 1). The nutritional screening was done using NRS 2002 tool to identify patients at risk for malnutrition. According to the NRS-2002, 714 and 369 patients (66% and 34%) were categorised respectively at low and high risk of malnutrition in our study. The mean ± SD of NRS 2002 score was 2.21 ± 0.41 and 3.2 ± 0.35 for ward and ICU patients, respectively. Patients were admitted with symptoms like loss of taste 8% (n = 87), diarrhoea 6% (n = 66), nausea 3% (n = 28), and loss of appetite 22% (n = 242) (Table 1).

There were 83% (n = 900), 7% (n = 75), 10% (n = 108), patients who were categorized with mild, moderate, and severe disease, respectively, on admission. The mean serum albumin levels (gm/dl) at admission were 3.63 ± 0.497, 3.53 ± 0.467, and 3.02 ± 0.545 for patients with mild, moderate and severe disease respectively. At the end of the follow-up period of each patient, there were 1021 (94%) patients who survived and 62 (6%) dead (Table 1).

98% of the patients (n = 1066) were initiated with nutrition support (oral, or/and EN), within 24–48 h as per the hospital feeding protocol. Overall, there were 10% (n = 112) patients who received EN in the ICU and 90% (n = 971) patients on oral diet both in ICU and ward. Of the 183 ICU patients, 61% (n = 112) were on EN and 39% (n = 71) on oral diet (Tables 1 and 2). Among the patients on oral diet, 65% of 971 patients (n = 636) were advised oral nutrition supplements (ONS) along with the oral diet to meet the nutritional requirements, and 35% (n = 335) patients sustained their nutrition needs only on oral diet without ONS (Table 1). None of the patients received parenteral nutrition.

Patients receiving medical therapy like renal replacement therapy (RRT), vasopressors, propofol, cytoSorb therapy, motility agents and insulin are indicated in Table 1. Additionally, in the ICU, there were 32 patients who were on prone ventilation which is used as a rescue therapy for patients with ARDS. 14% (n = 155) patients received > 24 h of mechanical ventilation. The mean ± SD of the APACHE score for the patients admitted in ICU was 16.58 ± 5.18 (Tables 1 and 2).

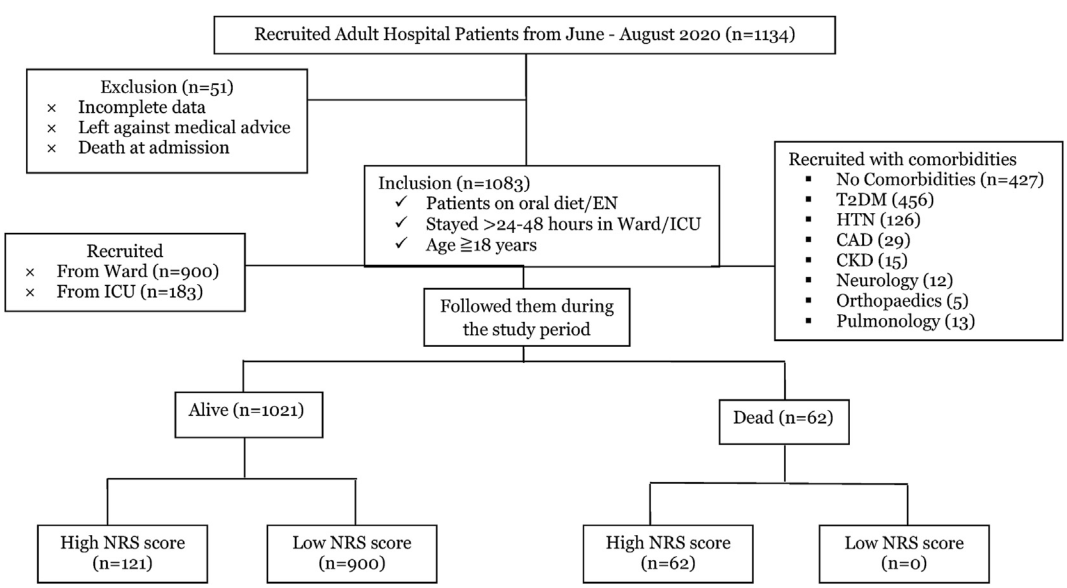

Fig. 1. Flow diagram of patients selected for analysis.

Table 1
Patient Characteristics categorised by mortality outcome.

Total Number (%)		Total patients (n = 1083)		
		Survivors 1021 (94)	Non-survivors 62 (6)	P-value
Number of patients in ICU (%) (n = 183)		121 (66)	62 (34)	<0.001
Number of patients in Ward (%) (n = 900)		900 (100)	–	
BMI, kg/m^2, mean (SD)		27 ± 4.26	26.2 ± 4.38	0.878
Age, years, mean (SD)		51.5 ± 14.37	64.9 ± 11.3	<0.001
Male number n = 747 (69%) (%)		696 (93)	51 (7)	0.02
Female number n = 336 (31) (%)		325 (97)	11 (3)	
NRS score, mean (SD)		2.32 ± 0.51	3.31 ± 0.46	<0.001
Low (<3) (n = 900) (%)		900 (100)	–	<0.001
High (≥3) (n = 183) (%)		121 (66)	62 (34)	
Baseline APACHE II, mean (SD)		14.43 ± 4.69	20.89 ± 2.98	<0.001
SOFA score, mean (SD)		4.93 ± 1.41	7.16 ± 1.85	<0.001
R Rate mean (SD)		22.3 ± 5.46	42.53 ± 3.59	<0.001
SPO_2 mean (SD)		94.6 ± 6.33	72.4 ± 7.08	<0.001
LOS, IP days, mean (SD)		17.98 ± 10.71	8.53 ± 3.13	<0.081
Median (IQR) LOS		6 (5–9)	9 (6–11)	
Number of co-morbidities	NIL (n = 427)	420 (98)	7 (2)	<0.001
(n = 537)	1-2 comorbidities	501 (93)	36 (7)	
(n = 119)	≥3 comorbidities	100 (84)	19 (16)	
MV days mean (SD) (n = 155)		6.39 ± 2.89	6.69 ± 2.42	
MV days: Number (%)	1–5days	47 (66)	24 (33)	0.068
	≥6days	46 (55)	38(45)	
Disease Severity: Number (%)	Mild	900 (100)	–	<0.001
	Moderate	75 (100)	–	
	Severe	46 (43)	62 (57)	
Loss of Taste (n = 87)	Yes Number (%)	68 (6)	19 (2)	
(n = 996)	No Number (%)	953 (88)	43 (4)	
Diarrhoea at Admission	Yes Number (%)	57 (5)	9 (1)	
	No	964 (89)	53 (5)	
Presence of Nausea	Yes Number (%)	22 (2)	6 (1)	
	No	999 (92)	56 (5)	
Loss of appetite	Yes Number (%)	195 (18)	48 (4)	
	No	826 (76)	14 (2)	
Patients on enteral feeding Number (%) (n = 112)		50 (45)	62 (55)	
Patients on Oral diet Number (%)		971 (90)	–	
Patients on ONS Number (%)	Yes	636 (65)	–	
	No	335 (35)	–	
Prone ventilation (n = 32)	Yes	25 (81)	7 (19)	0.067
(n = 151)	No	96 (64)	55 (36)	
Feed interruptions during prone ventilation	Yes	16 (50)	2 (6)	
Number (%)	No	9 (28)	5 (16)	
Cumulative Total energy prescribed		12,785 ± 5756	14,366 ± 5528	<0.032
Cumulative Total energy delivered (% delivered)		14,012 ± 6599 (110)	11,941 ± 5733 (83)	
Energy Adequacy median (IQR)		107 (98–118)	85 (64–94)	
Cumulative Total protein prescribed		646 ± 542	700 ± 279	0.655
Cumulative Total protein delivered (% delivered)		684 ± 324 (106)	574 ± 270 (81)	
Protein Adequacy median (IQR)		106 (95–117)	83 (62–96)	
Adequacy of Energy	≥80% Number (%)	967 (89)	35 (3)	<0.001
	<80% Number (%)	54 (5)	27 (3)	
Adequacy of Protein	≥80% Number (%)	956 (88)	39 (4)	<0.001
	<80% Number (%)	65 (6)	23 (2)	

BMI Body mass index; APACHE Acute Physiology and Chronic Health Evaluation; SOFA Sequential Organ Failure Assessment; LOS Length of stay; IP Inpatient; MV Mechanical ventilation; RRT Renal replacement therapy; NRS Nutritional risk screening; ONS Oral Nutrition Supplement.

3.2. Predictors and outcomes

The measured variables in our study are NRS score, mechanical ventilation days, presence of comorbidities, disease severity, prone ventilation and adequacy of energy and protein. The main study outcome is mortality. Length of hospital stay (LOS) was also monitored and compared. Results of the univariate analysis of NRS score, MV, disease severity, and inadequacy of energy and protein revealed an associated with mortality and the hospital LOS (Table 1).

In bivariate logistic regression analysis, energy inadequacy <80% (Odds ratio, OR 13.8, 95% Confidence Interval, CI 7.79–24.48, $p < 0.001$), protein inadequacy <80% (Odds ratio, OR 8.67, 95% Confidence Interval, CI 4.89–15.39, $p < 0.001$), presence of comorbidities ≥3 (Odds ratio, OR 11.4, 95% Confidence Interval, CI 4.67–27.86, $p < 0.001$), and NRS score ≥3 (Odds ratio, OR 1.84, 95% Confidence Interval, CI 0.89–3.77, $p = 0.095$), were significantly associated with mortality.

In-depth analysis of only ICU patients was conducted and compared (because none of the ward patients suffered the main outcome of mortality) so as to draw valid correlations between the variables and the outcome. For the analysis of results, the patients categorized according to disease severity were considered (Table 2). Of the total number of patients, 7 and 12% males (n = 54 and 89) and 6% each among females (n = 21 and 19) were admitted in the ICU with moderate and severe disease respectively as depicted in table (2). It is noted that the percentage of patients with severe disease increased as the number of comorbidities increased. There were 3% with no comorbidities and 20% with ≥3 comorbidities ($p < 0.001$) (Table 2) who was with severe disease in the ICU. Similarly, the number of MV days increased as the disease severity increased ($p < 0.001$) among the ICU patients. The mean (SD) MV

Table 2
Patient Characteristics categorised according to disease severity.

Total Number (%)		Total patients (n = 1083)			
		Mild Disease 900 (83)	Moderate Disease 75 (7)	Severe Disease 108 (10)	P-value
Number of patients in ICU (%)		–	75 (100)	108 (100)	
Number of patients in Ward (%)		900 (100)	–	–	
BMI, kg/m^2, mean (SD)		27 ± 4.29	27.24 ± 3.58	26.3 ± 4.45	0.247
Age, years, mean (SD)		51.2 ± 14.43	50.7 ± 13.66	61.1 ± 13.14	<0.001
Male number n = 747 (%)		604 (81)	54 (7)	89 (12)	0.004
Female number n = 336 (%)		296 (88)	21 (6)	19 (6)	
NRS score, mean (SD)		2.21 ± 0.41	3.05 ± 0.22	3.34 ± 0.47	
Low (<3) (n = 900) (%)		900 (100)	–	–	<0.001
High (≥3) (n = 183) (%)		–	75 (41)	108 (59)	
Baseline APACHE II, mean (SD)		–	13.04 ± 3.95	19.05 ± 4.47	<0.001
SOFA score, mean (SD)		–	4.61 ± 1.25	6.42 ± 1.9	< 0.001
R Rate mean (SD)		20.64 ± 1.53	27.9 ± 1.49	43.4 ± 3.88	<0.001
SPO_2 mean (SD)		96.3 ± 1.47	90.8 ± 3.58	70.4 ± 6.52	<0.001
LOS, IP days, mean (SD)		7.38 ± 3.76	8.21 ± 4.18	13.16 ± 8.24	< 0.001
Median (IQR)		6 (5–9)	7 (5–10)	11 (8–17)	
Number of co-morbidities	NIL (n = 427)	383 (90)	29 (7)	15 (3)	<0.001
(n = 537)	1-2 comorbidities	431 (80)	37 (7)	69 (13)	
(n = 119)	≥ 3 comorbidities	86 (72)	9 (8)	24 (20)	
MV days mean (SD)		–	3.31 ± 3.12	7.05 ± 0.77	<0.001
MV days: Number (%)	1–5days	–	31 (44)	40 (56)	<0.001
(n = 155)	≥ 6days	–	16 (19)	68 (81)	
RRT	Yes (n = 13) %	–	1 (–)	12 (1)	
	No RRT (n = 1070) %	900 (83)	74 (7)	96 (9)	
Vasopressors	Yes (n = 144) %	–	41 (4)	103 (9)	
	No Vasopressors (n = 939) %	900 (83)	34 (3)	5 (1)	
Patients on enteral feeding (n = 112)		–	4 (4)	108 (96)	
Prone Ventilation (n = 32)	Yes	–	–	32 (17)	
(n = 151)	No	–	75 (41)	76 (42)	
Feed interruptions during prone ventilation	Yes	–	–	18 (56)	
	No	–	–	14 (44)	
Motility agents used (n = 103)	Yes	–	47 (4)	56 (5)	
(n = 980)	No	900 (83)	28 (3)	52 (5)	
Propofol used (n = 109)	Yes	–	47 (4)	62 (6)	
(n = 974)	No	900 (83)	28 (3)	46 (4)	
Cumulative Total energy prescribed		12,260 ± 5397	13,254 ± 5444	17,828 ± 6404	< 0.001
Cumulative Total energy delivered (% delivered)		13,505 ± 6674 (112)	13,034 ± 6493 (98)	15,333 ± 6961 (86)	
Energy Adequacy median (IQR)		108 (100–118)	100 (94–103)	88 (73–95)	
Cumulative Total protein prescribed		623 ± 416	661 ± 285	860 ± 314	< 0.001
Cumulative Total protein delivered (% delivered)		656 ± 320 (107)	699 ± 338 (106)	739 ± 318 (86)	
Protein Adequacy median (IQR)		107 (97–118)	105 (99–112)	88 (76–97)	
Adequacy of Energy	≥80% No. (%)	859 (86)	70 (7)	73 (7)	<0.001
	<80% No. (%)	41 (51)	5 (6)	35 (43)	
Adequacy of Protein	≥80% No. (%)	849 (85)	69 (7)	77 (8)	<0.001
	<80% No. (%)	51 (58)	6 (7)	31 (35)	

days increased from 3.31 ± 3.12 days among the patients with moderate disease to 7.05 ± 0.77 days for the severe disease (Table 2). The mean ± SD of the hospital LOS for the patients admitted significantly increased with the severity of disease from 7.38 ± 3.76 days among patients with mild disease, to 8.21 ± 4.18 days in moderate disease and to 13.16 ± 8.24 days with severe disease (Table 2). In multivariate logistic regression analysis of the ICU patients, energy inadequacy <80% (OR: 3.7, 95% CI 1.53–9.17) and protein inadequacy <80% (OR: 2.86, 95% CI: 1.16–7.05), were significantly ($p < 0.05$) associated with mortality after adjusting for the effect of disease severity. The median (IQR) nutritional adequacy for energy reduced with disease severity from 108 (100-118), 100 (94-103) to 88 (73-95) respectively for the patients with mild, moderate, and severe disease (Table 2) ($p < 0.001$).

Among the 183 patients who were admitted in the ICU, 66% (n = 121) patients survived and 34% (n = 62) expired. Of these, 85% (n = 155) were on mechanical ventilation, and 58% (n = 107) suffered from severe disease. Inadequacy of energy and protein <80% significantly increased from 5% (n = 41), and 6% (n = 51) among the ward population to 22% (n = 40), and 20% (n = 37) respectively among the ICU patients (Table 2). There were 18% (n = 32) of the ICU patients on prone ventilation where significant differences in mortality were noted, with 81% (n = 25) survivors and 19% (n = 7) non-survivors. The median (IQR) hospital LOS for survivors on MV in the ICU was 12 (8-18) days, ($p < 0.001$), and the median (IQR) duration of MV was 5 (4-8) days. Similarly, the median (IQR) hospital LOS for dead patients on MV in the ICU was 9 (6-11) days, ($p < 0.001$), and the median (IQR) duration of MV among the dead patients was 7 (5-9) days. The median (IQR) nutritional adequacy for energy and protein for ICU patients was 94(84-100) and 95(81-104) respectively. Considerable inverse association was observed between energy and protein delivered and length of hospital stay among the survivors in the ICU ($p < 0.001$). The multivariate logistic regression analysis of the ICU patients revealed that, prone ventilation (OR: 11.0, 95% CI: 3.8–31.9), and energy inadequacy <80% (OR: 3.6, 95% CI: 1.25–10.2) were significantly ($p < 0.05$) associated with mortality after adjusting the effect of disease severity, presence of comorbidities and MV days.

Significant correlation was also observed between mortality and calorie and protein adequacy among the patients in the ICU. 76% (n = 108) were alive when the calorie adequacy was ≥80% as compared to 33% (n = 13) when calorie adequacy was <80%. Similar significant trend was observed with protein adequacy ($p < 0.001$). Our results suggest an association between nutritional adequacy and mortality. In general, nutritional inadequacy of protein and energy correlated with higher mortality, among the total study population (Figure 2).

4. Discussion

COVID-19 has become a pandemic affecting millions of patients across the globe and posing a challenge to the healthcare system. In our study, 900 (83%) and 183 (17%) patients, were admitted and treated in the ward and ICU, respectively during the study period. Although, all the patients admitted in the hospital were included in the study for evaluation with the study objectives, the results of the ICU patients correlated better with the study objectives than the ward patients.

Of the 183 patients, in the ICU, 85% (n = 155) were on mechanical ventilation. The number of patients on MV was high because the ICU admission policy in the hospital was changed to accommodate the very sick cases, and not all tertiary hospitals in the city are equipped for Covid.

There were 900 patients admitted in the ward and categorised as having mild disease. The adequacy of ≥80% energy and protein were met for 85% of the patients in the ward with the average LOS of 7.38 ± 3.76 and no deaths.

Our study demonstrates that all the 183 patients admitted in the ICU were at risk for malnutrition with a mean NRS score of 3.2 ± 0.35. In our study, a detailed nutritional assessment was not done in order to limit the exposure of the dietitian to Covid in line with our hospital personnel policy. Although there is limited data on nutritional status of COVID patients, studies conducted by Li et al., and Bedock et al. [21,32] have shown that there is high prevalence of malnutrition among this population.

A total of 98% of the patients (n = 1066) were initiated with nutrition support (oral, or/and EN), within 24–48 h as per the hospital feeding protocol. The advantages of early feeding (within 36 h of admission) over delayed feeding on morbidity and mortality have been shown in many meta-analyses and RCTs, and these findings are the foundation of the recommendations by the European Society for Clinical Nutrition and Metabolism (ESPEN) and the American Society for Parenteral and Enteral Nutrition (ASPEN) [29,33].

Our paper is formulated from the nutrition delivery point of view and focussed on the outcomes categorised by energy and protein adequacy especially among patients in the ICU. In this study, significant differences were observed between ICU patients categorised according to disease severity in terms of mortality, wherein 57% among the severe group did not survive, with no deaths in the moderate group ($p < 0.001$).

Nutritional adequacy of energy and protein has a profound impact on the patients' outcome in terms of morbidity and mortality, which has been proven from many studies. It is indicated that COVID-19 has an impact on the nutritional status before admission [34] and inadequacy of nutrition provision during the hospital stay, especially among the ICU patients would worsen the outcomes.

A study [35] conducted in 2017 among regular ICU patients, showed an inverse association between only energy intake with hospital LOS. Notably, cumulative nutritional inadequacy correlated with higher mortality. In our study of the COVID patients, 76% of the ICU patients (n = 108) were alive when the calorie adequacy was ≥80% as compared to 33% (n = 13) when calorie adequacy was <80% ($p < 0.001$). Similar significant trend was observed with protein adequacy ($p < 0.001$). These results indicate that the daily energy and protein deficit is significantly corelated with mortality, and it is probable that daily optimisation of nutritional delivery would result in greater reduction of LOS also. Additionally, the nutritional adequacy may also benefit other clinical outcomes other than LOS and mortality.

A multicentric observational study on 2772 mechanically ventilated patients showed that improvement of 1000 kcal per day was associated with reduced mortality [odds ratio for 60-day mortality 0.76; 95% confidence intervals (CI) 0.61–0.95, p = 0.014] and an increased number of ventilated-free days (VFDs) (3.5 VFD, 95% CI 1.2–5.9, p = 0.003) [36]. An international survey suggested that many centres were able to meet the nutritional adequacy goal of only 62% [37]. In our study overall cumulative nutritional adequacy of 78% was achieved for ICU patients. Thus, nutritional therapy together with pharmacological therapy may undoubtedly help the COVID patient to overcome the acute phase of the disease first and to shorten recovery times.

The strength of our study is that the nutritional delivery along with the calorie and protein deficit associated with interruptions was traced among the COVID patients despite the restrictions preventing some dietitians from entering Covid units. This helped to improve the adequacy by taking necessary steps to reduce the duration and number of feed interruptions. To provide optimal

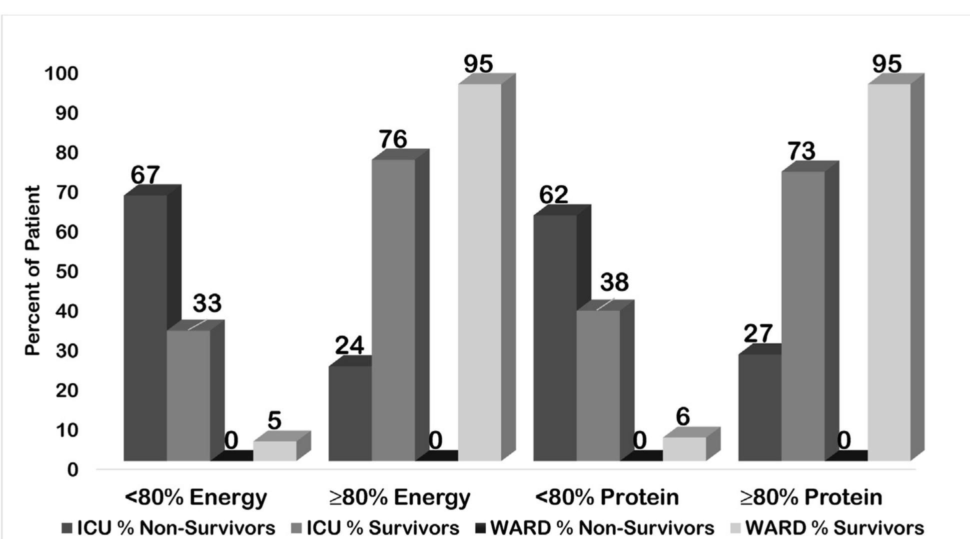

Fig. 2. Graph showing the relation of mortality and nutritional adequacy in ward and ICU.

dietetic care for the patients, the best practice method of having one dietitian for every 30 patients and connecting with each of the treating nurses to have daily updates of the patient intake or feed provision with interruptions was particularly useful.

A few drawbacks of the study must be recognized. Although we have proved that monitoring of nutrition intervention of the COVID patients can be done with good daily coordination with the nurse, it is susceptible to gaps in nutrition care. Our study is a single-centred observational study, where the results of this small sample size may not extrapolate to the larger population. Therefore, larger multi-centric randomised controlled studies are needed to demonstrate the association of adequacy of nutritional delivery with hospital LOS and mortality. The study correlated the outcomes with the adequacy energy and protein, but the amount and impact of micronutrients was not established. It is also to be noted that, in this present population, the standards of medical nutrition therapy have not been protocolised due to limited scientific data that links nutrition adequacy to patient outcome and the impact of other treatments was not considered.

5. Conclusion

This study was taken up to test whether adequacy of nutrition can be achieved in COVID patients given the situation of isolation, and risk of exposure of healthcare staff. In our study, the results of the ICU patient data correlated better with the study objectives than the ward patients. In conclusion, 76% of the ICU patients were alive when the calorie adequacy was $\geq$80% as compared to 33% when calorie adequacy was <80%. With our study, it is proved that daily optimisation of nutrient delivery, surpassing interruptions can improve patient outcomes in COVID-19, and it can be considered as a desired standard of care. Although this study proved the link between adequacy of nutrition and patient outcome, impact of other treatments in conjunction with nutrition therapy should be studied with different disease severity.

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Authors of manuscript

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Statement of authorship

Radha R Chada contributed to the conception and design of the study. Radha R Chada, Sachin Chidrawar, Ayesha Siddiqua, Syeda Amena Omer, Rajiv Medanki, and Balakrishna Nagalla contributed to the acquisition, analysis, and interpretation of data. Radha R Chada, Syeda Amena Omer and Rajiv Medanki drafted the manuscript. Radha R Chada, Sachin Chidrawar, Rajiv Medanki, Ayesha Siddiqua, Syeda Amena Omer, and Balakrishna Nagalla critically revised the manuscript. All the authors gave final approval.

All authors revised the manuscript and agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

Declaration of competing interest

None declared. No author in this study has any conflicts of interest to declare.

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