Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Original article

The importance of nutritional status on clinical outcomes among both ICU and Non-ICU patients with COVID-19

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SUMMARY

Background and aims: The current Covid-19 outbreak becomes a tremendous public health concern worldwide. Since a little information is available on nutritional status and its devastating effects on covid-19 complications in Iran, in the present study, we aimed to evaluate nutritional status of covid-19 population and its related factors.

Methods: We performed this observational study by recruiting 400 hospitalized covid-19 subjects. Thereafter, the needed clinical and para clinical data were collected and their nutritional status was then assessed using NRS-2002.

Results: Approximately 36% of the total sample size and 100% of the ICU- admitted cases were at the severe risk of malnutrition. The patients with NRS$\geq$ 5 were significantly older ($p < 0.0001$). Non-survivals obtained higher scores in terms of both severity of disease (86%) and impaired nutritional status (67%), and this relationship was found to be statistically significant ($p < 0.0001$). In regard to the obtained prognostic inflammatory scores, 86% of the non-survivals obtained significantly highest scores for GPS ($P = 0.015$).

Conclusion: Nutritional status has a considerable effect on clinical outcomes of covid-19 patients, which should be evaluated. Thereafter, rapid subsequent nutritional interventions must be implemented in this regard. As well, special attention must be paid to both elderly population and individuals with underlying diseases.

1. Introduction

Coronaviruses, which belong to the family of enveloped single-stranded RNA viruses, have been firstly identified in 1966. These viruses have four subtypes, including alpha, beta, gamma, and delta. Accordingly, alpha and beta subtypes are most commonly found in mammals. A new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) firstly appeared in Wuhan, China, on December 2019 [1]. Thereafter, different variants of this virus even with more infectivity and virulence, were detected worldwide [2,3]. The Covid-19 pandemic is rapidly spreading worldwide, which has posed some unpredictable challenges and threats to patients and health care systems [4]. Up to now, nearly 174 million cases have been infected, and 3.74 million deaths due to this virus have been reported worldwide, of which 2.97 million infected cases, 2.74 recovered individuals, and more than 81,000 deaths have been registered in Iran. Of note, the latest statistics can be followed from the Johns Hopkins university website [1]. Usually,

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the associated symptoms appear within approximately 5 days, and the estimated time from the onset of symptoms to recovery or death, depends on patients' age, underlying diseases, immune system conditions, body weight, and nutritional status [5], which can last between 6 and 41 days. Usually, Pneumonia is the first symptom, which could lead to the disease's identification. However, recent evidence indicated the occurrence of gastrointestinal symptoms and those symptoms associated with the involvement of other organs and systems, including fever, cough, headache, the increased salivation, the decreased appetite, the decreased taste and smell, nausea, diarrhea, vomiting, fatigue, and sepsis [6,7]. Although most people with this disease show mild symptoms and a subsequent speedy recovery [8], a number of affected individuals experience symptoms of cytokine storm syndrome. Accordingly, it is a known inflammatory syndrome with sudden and fatal hypercytokinemia and multiple organ failure (MOF), which is mostly caused by overactive immune system [9,10].

Supportive therapies are considered as the most common therapeutic approaches for covid-19; however, some appropriate nutritional assessments and subsequent interventions could effectively improve the clinical outcomes in patients and also reduce the length of hospital stay and ICU admission [4,9].

The reduced food intake, inflammation-related catabolism, decreased appetite, diarrhea, and decreased physical activity due to the increased length of hospital stay are among the most important factors, which increase the risk of malnutrition among patients with Covid-19.The food availability may also be impaired during confinement and affect dietary pattern to a great extent. According to the recent guidelines proposed by American society for enteral and parenteral nutrition (ASPEN) and European society for parenteral and enteral nutrition (ESPEN), nutritional interventions should be considered as an integral part of both the management and treatment processes of these patients [11–13].

Malnutrition might lead to the weakened immune system, the development of respiratory failure, and the increased need for ventilator support. Therefore, nutritional disorders should be urgently identified and then managed in these patients [14,15]. The goal of the nutritional screening is predicting the likelihood of better or worse consequences of nutritional factors and indicating whether nutritional strategies are effective [16]. We found no published report on the prevalence of malnutrition among covid-19 Iranian population, but a report from Iranian hospitals in 2018 revealed that approximately 30% of patients are malnourished and at the risk of malnutrition [17]. The present research aimed to evaluate the nutritional status of hospitalized covid-19 patients with different levels of disease's severity, as well as its association with morbidity and mortality using Nutritional Risk Screening tool-2002 (NRS-2002).

2. Patients & methods

This cross-sectional study was performed in a 6-week period from May to July 2021.We recruited 400 confirmed cases of covid-19 recognized by polymerase chain reaction (PCR) and their clinical symptoms who were hospitalized at *Peymaniye hospital* of Jahrom, Iran. This study was approved by the ethic committee of Jahrom University of Medical Sciences (IR.JUMS.REC.1400.020) and conducted in accordance with the Declaration of Helsinki. The patients were not enrolled in the study if they were under 18 years old, pregnant, had a length of intensive care unit (ICU) stay <24 h, and if they did not sign any informed consent form.

Weight and height were measured by a trained nurse at the time of admission. Demographic information, drug history, underlying diseases, initial symptoms, laboratory values, and diagnostic tests were obtained through the patients' medical records. Information on appetite status, weight loss, daily calorie intake (and its comparison with actual calorie requirements), and respiratory and nutritional support methods (Enteral/parenteral) were completed through both interview and observations. Parenteral nutrition (PN) was defined as the use of intravenous infusion (central or peripheral) of at least 2 energy-supplying nutrients, including dextrose, fat emulsions, and amino acids for at least 3 days, in order to provide more than 10 kcal/kg/day energy. As well, enteral nutrition (EN) was considered as the continuous use of commercial formulas in the form of gavage for at least 3 days and energy supply for more than 10 kcal/kg of body weight per day. In addition, the use of nutritional and dietary supplements was recorded.

Nutritional status was evaluated by two well-trained nutritionists using NRS-2002, which was recommended by ESPEN for the assessment of nutritional status of the hospitalized patients [4,18,19]. Accordingly, it is designed based on the two main parts, including nutritional status consisting of weight loss, Body mass index (BMI), and food intake; and disease severity. Each parameter is given a score ranged from 0 to 3, and those patients aged 70 years old or older receive an additional 1 point. According to the severity of Covid-19, the patients admitted to the ICU were given a score of 3 and the patients admitted to other units were given a score of 2. Finally, the patients were categorized as follows: NRS<3: at nutritional risk; NRS 3–4: moderate malnutrition; and NRS$\geq$ 5: severe malnutrition [20].

We also measured Glasgow prognostic score (GPS), which is an inflammation-based score consisting of albumin and CRP [21]. Moreover, it is known as a reliable scoring system in many clinical conditions, including cancer, cardiovascular diseases, and covid-19. More details about GPS can be obtained from Table 3 [22]. The clinical outcome of each participant included in this study (either discharged or died) was recorded until July 1, 2021. Additionally, the length of hospital stay was calculated by deducting the date of discharge or death from the date of admission.

Statistical analysis: Normality of variables was analyzed using shapiro-wilk test. Afterward, normal quantitative variables were presented as Mean ± SD and non-normal ones were reported as median (IQR). The qualitative variables were reported as number (percent). The comparison was performed using Kruskal–Wallis or one-way ANOVA for quantitative and Chi-square test or Fishers exact test for qualitative and categorical variables, respectively. Next, both Univariate and multivariate logistic regression were performed to detect the risk factors of poor nutritional outcomes among the COVID-19 patients. Finally, all the obtained data were analyzed using SPSS-25 and p-value <0.05 was considered as a statistically significant level.

3. Results

3.1. Characteristics of the study population

A total of 400 COVID-19 patients, including 235 (59%) men and 165 (41%) women, with the median age of 55 years old (ranged from 42 to 69 years old), were enrolled in this study. Approximately, 17% of the patients were admitted to ICU. Most common comorbidities were found as follows: Hypertension, diabetes, and cardiovascular diseases (as 33%, 25.5%, and 13.5%, respectively). Furthermore, Fever (92%), impaired appetite (89.5%), cough (82%), and nausea (79.5%) were the most observed initial symptoms among these patients. The median time from hospital admission to transfer to ICU was 1 day (3-0). As well, the overall length of hospital stay was estimated as 19 (24-15) days and the median time for the ICU and non-ICU cases was 26 (30-18) and 18 (23-15), respectively. Accurately, 80% of the ICU-care-admitted patients

received ventilation. The total mortality rate was estimated at about 5%, which was much higher among the critically ill patients (up to 74% compared to 0.9% in the non-ICU participants). More detailed information is shown in Table 1.

3.2. Nutritional risk and outcomes

Using NRS-2002, we categorized the included participants into nutritionally at risk (3.25%), moderate malnutrition (60.5%), and severe malnutrition (36.25%) groups. The comparison of these groups in terms of the clinical characteristics and laboratory indices is demonstrated in Table 2. Nearly 97% of the total study population and 100% of the ICU cases were suffering from malnutrition. Those patients classified in the severe category were significantly older ($p < 0.0001$) and had lower BMI ($p < 0.0001$) compared to others. In addition, hypertension and cardiovascular diseases were found as significantly higher in the cases at moderate and severe nutritional risks ($P = 0.009$ and $P = 0.0$ 16, respectively). The subjects in moderate and severe categories were more likely to suffer from impaired appetite and loss of smell or taste ($p = 0.002$ and $p = 0.014$, respectively). Subjects in the severe nutritional risk group had significantly different levels of both albumin ($p < 0.0001$) and CRP ($p < 0.0001$) compared to the two moderate and at risk groups. Notably, about 43 patients had GPS = 0, 134 subjects had GPS = 1, and 223 individuals had GPS = 2. A significant association was also detected between nutritional risk score and GPS ($p < 0.0001$). Of note, up to 69% of the ICU patients had GPS = 2, which was significantly higher than that of the non-ICU subjects ($p = 0.033$). The mortality rate was significantly higher in the severe category ($p < 0.0001$) and among the ICU care patients ($p < 0.0001$). Subsequently, supportive nutritional therapy was provided for about 80 cases. Rout of nutrition revealed a significant relationship with NRS score ($p < 0.0001$). Thereafter, about 20% of patients received enteral and parenteral nutrition supports and nearly 70% of the patients receiving enteral nutrition had severe malnutrition. The total mortality rate was estimated at about 5%, in which 76% of dead patients exhibited unfavorable nutritional condition.

As shown in Table 3, the non-survivals had higher scores for both factors of severity of disease (86%) and the impaired nutritional status (67%), and this relationship was found to be statistically significant ($p < 0.0001$).

The baseline significant clinical and laboratory variables were included in logistic regression analysis (as shown in Table 4). Multivariate logistic regression analysis revealed that age, poor appetite, Headache, chest pain, and serum level of LDH are significantly associated with higher nutritional risk screening scores.

Table 1
Characteristics of study participants.

Variable		N (%)
Patients		400
Age, median (IQR), years		55 (69–42)
Age Score	<70	305 (76.2)
	≥70	65 (23.8)
Gender	Male	235 (59%)
	Female	165 (41%)
Unit	ICU	70 (17.5)
	Non-ICU	330 (82.5)
Comorbidities	Diabetes	102 (25.5)
	Hypertension	132 (33)
	Cancer	13 (3.25)
	CVD	54 (13.5)
	CKD	12 (3)
	Hyperlipidemia	15 (3.75)
	Hypothyroidism	14 (3.5)
	History of CVA	26 (6.5)
	Asthma	13 (3.25)
	COPD	8 (2)
	Autoimmune disorders	20 (5)
	TB	1 (0.25)
	Parkinson	3 (0.75)
	IBD	3 (0.75)
	Chronic liver failure	4 (1)
	HIV	1 (0.25)
	SCA	1 (0.25)
Signs & Symptoms	Nausea	318 (79.5)
	Vomiting	59 (14.75)
	Diarrhea	62 (15.5)
	Constipation	48 (12)
	Impaired appetite	358 (89.5)
	Loss of Smell or Taste	109 (27.25)
	Dyspnea	309 (77.25)
	Fever	368 (92)
	Cough	328 (82)
	Headache	151 (37.75)
	Chest Pain	210 (52.5)
	Fatigue	300 (75)
Clinical outcome	Discharge	379 (94.8)
	Death	21 (5.2)

4. Discussion

The current covid-19 outbreak with an increasing prevalence become a huge public health concern worldwide [23]. The involvement of various organs and a wide range of complications made the treatment process of this disease more complicated [24], which could result in nutritional and metabolic derangements [14]. Malnutrition, in particular, is a known risk factor for both morbidity and mortality resulted from viral infections and community acquired pneumonia [25]. Some of the Covid-19 effects, including diarrhea, nausea, vomiting, anorexia, dysgeusia, dyspnea, and hyper-metabolism may eventuate in severe weight loss, malnutrition, the prolonged length of hospital stay, and worsen complications [25,26]. Therefore, performing an early nutritional assessment to assure appropriate interventions and avoid adverse outcomes should be considered as an integral part of the covid-19 management [26,27]. In the current study, NRS-2002, which has been proved to have a high sensitivity in identifying unfavorable nutritional outcomes compared to other tools [27,28], was applied as a valid tool for the assessment of the nutritional status as well as screening at risk ICU and non-ICU patients. NRS-2002 consists of the following three domains: defective nutritional status, severity of disease, and age [20].

Our observations are in line with most of recent papers that investigated the nutritional status of covid-19 patients. In our study, out of 400 covid-19 patients with the median age of 55 years old, approximately 76% were under 70 years old and up to 80% of them were admitted to non-ICU units. Our findings suggest that older individuals mostly are at moderate and severe nutritional risks ($p < 0.0001$). Moreover, in line with the results of a similar study [28–31], multivariate regression analysis indicated that older age could significantly predict poor nutritional outcomes. A recent cross-sectional study has evaluated the nutritional statuses of 182 covid-19 individuals, and proved that older patients obviously are at a greater risk of malnutrition [32]. In general, cognitive, emotional, and physical dysfunctions become more prevalent along with people aging [33]. Moreover, dental problems, dysgeusia, and dysphagia prevent older population to maintain healthy dietary habits [34]. As revealed by some other investigators, it can also be concluded that diabetes and hypertension are among the most prominent underlying diseases [8,28,32,35]. In contrast, Maguire et al. displayed that the majority of Covid-19 cases have no underlying diseases [36]. Hypertension and cardiovascular diseases were found to be significantly

Table 2
Comparison of clinical characteristics and initial laboratory indices among patients with high and low nutritional risk.

Variables		NRS-2002 SCORE			P-Value
		At risk n = 13	Moderate n = 242	Severe n = 145	
Age (year)		50 (61–32)	50 (64–40)	68 (77–49)	**<0.0001**[a]
Gender					0.981[b]
Female		5 (3.0)	101 (61.2)	59 (35.8)	
Male		8 (3.4)	141 (60.0)	86 (36.6)	
BMI (Kg/m^2)		23 (24–21)	22 (24–21)	21 (23–19)	**<0.0001**[a]
Smoking history (n (%))		0	11 (61.1)	7 (38.9)	0.866[b]
Comorbidities (n (%))					
Diabetes		3 (2.9)	59 (57.8)	40 (39.2)	0.787[b]
Hypertension		5 (3.8)	66 (50.0)	61 (46.6)	**0.009**[b]
Cancer		0	5 (38.5)	8 (61.5)	0.181[c]
CVD		4	24 (48.0)	26 (52.0)	**0.016**[b]
CKD		0	7 (58.0)	5 (42.0)	0.845[c]
Hyperlipidemia		0	11 (73.0)	4 (27.0)	0.467[b]
Hypothyroidism		0	9 (64.0)	5 (36.0)	1.000[b]
History of CVA		1 (4.0)	10 (38.0)	15 (58.0)	0.075[b]
Asthma		0	7 (54.0)	6 (46.0)	0.719[c]
COPD		0	5 (62.5)	3 (37.5)	1.000[c]
Autoimmune disorders		2 (10.0)	10 (50.0)	8 (40.0)	0.200[b]
TB		0	0	1 (100.0)	0.395[c]
Parkinson		0	1 (33.0)	2 (67.0)	0.601[c]
IBD		0	1 (33.0)	2 (67.0)	0.601[c]
Chronic liver failure		0	1 (25.0)	3 (75.0)	0.256[c]
HIV		0	0	1 (100.0)	0.362[d]
SCA		0	1 (100.0)	0	0.638[d]
Signs & Symptoms (n (%))					
Nausea		10 (3.0)	197 (62.0)	111 (35.0)	0.526[b]
Vomiting		2 (3.4)	32 (54.2)	25 (42.4)	0.538[b]
Diarrhea		1 (1.6)	41 (66.0)	20 (32.4)	0.511[b]
Constipation		1 (2.1)	19 (39.6)	28 (58.3)	**0.005**[b]
Impaired appetite		6 (1.7)	216 (60.3)	136 (38.0)	**0.002**[b]
Loss of Smell or Taste		0	76 (69.7)	33 (30.3)	**0.014**[b]
Dyspnea		10 (3.2)	178 (57.6)	121 (39.2)	0.077[b]
Fever		11 (3.0)	223 (60.6)	134 (36.4)	0.744[b]
Cough		13 (4.0)	204 (62.0)	111 (34.0)	**0.036**[b]
Headache		11 (7.3)	99 (65.6)	41 (27.1)	**<0.0001**[b]
Chest Pain		11 (5.2)	121 (57.6)	78 (37.2)	**0.047**[b]
Fatigue		10 (3.3)	188 (62.7)	102 (34.0)	0.266[b]
SBP (mmHg)		132 (136–114)	125 (137–114)	132 (139–120)	**0.027**[a]
DBP (mmHg)		90 (94–78)	84 (92–79)	92 (99–82)	**<0.0001**[a]
O2 Saturation	≤93%	13 (3.3)	236 (60.0)	145 (36.7)	0.147[c]
	>93%	0	6 (100.0)	0	
Respiratory Rate	≥30 breaths/min	11 (3.0)	228 (60.0)	141 (37.0)	0.084[b]
	<30 breaths/min	2 (10.0)	14 (70.0)	4 (20.0)	
Unit admission					**<0.0001**[b]
ICU		0	14 (20.0)	56 (80.0)	
Non-ICU		13 (4.0)	228 (69.0)	89 (27.0)	
Laboratory Findings					
WBC (10^3/ul)		6 (10–4)	6 (9–4)	8 (12–5)	**0.002**[a]
HCT (%)		39 (44–38)	38 (41–35)	33 (37–30)	**<0.0001**[a]
FBS (mg/dl)		109 (181–89)	120 (200–100)	120 (218–92)	0.421[a]
Albumin (gr/dl)		3.9 (4–3.3)	3.4 (3.8–3)	3 (3.3–2.7)	**<0.0001**[a]
ALT (u/l)		25 (45–15)	27 (45–17.7)	30 (58.5–18.5)	0.216[a]
AST (u/l)		23 (45–16)	25 (37–18)	28 (50–20)	**0.044**[a]
ALP (u/l)		170 (189–107)	169 (230–127)	168 (256–139)	0.298[a]
BUN (mg/dl)		12 (15–10)	15 (20–12)	20 (29–15)	**<0.0001**[a]
Cr (mg/dl)		1 (1.2–0.8)	1.1 (1.3–1)	1.1 (1.5–0.9)	0.568[a]
CRP (mg/l)		30 (34–11)	40 (84–12)	60 (100–25)	**<0.0001**[a]
CPK (u/l)		90 (205–57)	132 (290–70)	166 (424–80)	0.226[a]
LDH (u/l)		535 (907–450)	547 (718.2–427)	650 (970–470)	**0.002**[a]
Fibrinogen (mg/dl)		445 (556–385)	474 (580–373)	492 (652–365)	0.835[a]
GPS					**<0.0001**[b]
CRP≤ 10 mg/l, ALB ≥3.5 g/dl		3 (7.0)	36 (83.7)	4 (9.3)	
CRP≥ 10 mg/l, ALB ≥3.5 g/dl or CRP≤ 10 mg/l, ALB ≤3.5 g/dl		7 (5.2)	93 (69.4)	34 (25.4)	
CRP≥10 mg/l, ALB ≤3.5 g/dl		3 (3.3)	113 (60.5)	107 (36.3)	
Clinical Outcome					**<0.0001**[b]
Death		0	5 (23.8)	16 (76.2)	
Discharge		13 (3.4)	237 (62.5)	129 (34.0)	
Nutrition support					**<0.0001**[b]
Oral		13 (4.1)	217 (68.2)	88 (27.7)	
Enteral		0	22 (31.0)	49 (69.0)	

Table 2 (*continued*)

Variables	NRS-2002 SCORE			P-Value
	At risk n = 13	Moderate n = 242	Severe n = 145	
TPN	0	1 (50.0)	1 (50.0)	
Enteral + Parenteral	0	2 (22.2)	7 (77.8)	

Abbreviations: BMI, Body mass index; CVD, cardiovascular disease; CKD, chronic kidney disease, cardiovascular accident; Chronic obstructive pulmonary disease; TB, Tuberculosis; IBD, Inflammatory bowel disease; HIV, Human immunodeficiency virus; SCA, sickle cell anemia; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, White blood cells; HCT, hematocrit; FBS, Fasting blood sugar; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; BUN, blood urea nitrogen; Cr, creatinine; GPS, Glasgow Prognostic Score; CRP, C-reactive protein; CPK, creatine phosphokinase; LDH, lactate dehydrogenase; ALB, Albumin.
[a] Bonferroni correction on multiple Kruskal–Wallis tests.
[b] Chi-square test.
[c] Fisher's exact test.
[d] Linear-by-Linear Association.

Table 3
Comparison of NRS-2002 & GPS among survivals and non-survivals.

Item	Score	Survivals	Non- Survivals	P-Value
NRS-2002				
Age score (year)				**0.002**
<70	0	295 (96.7)	10 (3.3)	
≥70	1	84 (88.4)	11 (11.6)	
Severity of disease				**<0.0001**[a]
Normal nutritional requirements	0	0	0	
Hip fracture, chronic patients, in particular with acute complications	1	0	0	
Major abdominal surgery, Stroke, Sever pneumonia, Hematological malignancy	2	328 (99.1)	3 (0.9)	
Head injury, Bone marrow transplantation, ICU patients	3	51 (73.9)	18 (26.1)	
Impaired nutritional status				**<0.0001**
Normal	0	22 (100.0)	0	
Wt loss>5% in 3 months or FI <%50-75	1	70 (93.3)	5 (6.7)	
Wt loss>5% in 2 months or BMI 18.5–20.5+ impaired general condition or FI %25-60	2	187 (98.9)	2 (1.1)	
Wt loss>5% in 1 months or BMI<18.5+ impaired general condition or FI %0-25	3	100 (87.7)	14 (12.3)	
GPS				**0.015**
CRP≤ 10 mg/l, ALB ≥3.5 g/dl	0	43 (100.0)	0	
CRP≥ 10 mg/l, ALB ≥3.5 g/dl or CRP≤ 10 mg/l, ALB ≤3.5 g/dl	1	131 (97.8)	3 (2.2)	
CRP≥10 mg/l, ALB ≤3.5 g/dl	2	205 (91.9)	18 (8.1)	

P-Value obtained by chi-square test unless indicated.
Abbreviations: Wt, weight loss; FI, food intake.
[a] Fishers Exact test.

Table 4
Independent prognostic factors using univariate and multivariate logistic regression.

	Univariate				Multivariate			
	Moderate		Severe		Moderate		Severe	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Age	1.02 (0.98–1.06)	0.211	1.07 (1.03–1.11)	<0.0001			1.07 (1.02–1.12)	**0.005**
BMI	0.99 (0.84–1.18)	0.987	0.83 (0.69–0.99)	<0.046			0.94 (0.74–1.24)	0.696
Hypertension	0.60 (0.18–1.90)	0.385	1.16 (0.36–3.72)	0.801				
Constipation	1.02 (0.12–8.29)	0.983	2.87 (0.35–23.01)	0.320				
Impaired appetite	5.19 (1.58–17.05)	0.007	9.44 (2.56–34.83)	0.001	5.74 (1.47–22.33)	0.012	8.43 (1.84–38.63)	**0.006**
Headache	0.12 (0.02–0.58)	0.008	0.07 (0.01–0.33)	0.001	0.19 (0.03–1.02)	0.053	0.12 (0.02–0.74)	**0.016**
Chest pain	0.18 (0.03–0.83)	0.029	0.21 (0.04–0.98)	0.048	0.15 (0.02–0.87)	0.034	0.12 (0.02–0.74)	**0.023**
SBP	0.98 (0.95–1.01)	0.254	0.99 (0.96–1.02)	0.777				
DPB	0.99 (0.94–1.05)	0.836	1.04 (0.98–1.10)	0.129				
WBC	1.03 (0.90–1.17)	0.654	1.07 (0.94–1.22)	0.292				
HCT	0.91 (0.83–1.00)	0.056	0.78 (0.70–0.86)	<0.0001				
FBS	1.00 (0.99–1.00)	0.992	0.99 (0.99–1.00)	0.726				
AST	0.99 (0.99–1.00)	0.118	1.00 (0.99–1.00)	0.839				
BUN	1.07 (0.97–1.18)	0.151	1.10 (1.00–1.22)	0.041			1.04 (0.94–1.15)	0.382
CRP	1.02 (1.00–1.04)	0.031	1.03 (1.01–1.05)	0.005	1.03 (1.00–1.05)	0.024	1.03 (1.00–1.06)	**0.011**
LDH	1.00 (0.99–1.00)	0.643	1.00 (0.99–1.00)	0.498				

associated with the adverse nutritional outcomes. Patients with diabetes are more susceptible to viral infections. Correspondingly, this can be due to the immune–endocrine interaction in which many intracellular pathways are similar in both immune and hormone receptors. More specifically, type-2 diabetic subjects also experience resistance to leptin. Leptin is a key element in promoting proliferation and activating immune cell [37]. Although many contradictions exist regarding both hypertension and immunosuppression, a more potent mechanism could be referred to the sympathetic outflow, which may debilitate the full activation of T-lymphocytes. On the other hand, it was hypothesized that the expression of angiotensin converting enzyme II

(ACE2) is elevated in individuals infected with covid-19 with underlying comorbidities like hypertension. ACE2 promotes the entrance of SARS-COV-2 into cells and also exacerbates the resulted infection [38]. Hypertension is more prevalent among elderly [39] and as already mentioned, older age is known as a potential risk factor for the adverse nutritional outcomes. In the current study, we indicated that patients experiencing more constipation, impaired appetite, and loss of smell or taste, can be categorized as having a moderate to severe nutritional risk. High nutritional derangements were observed to be significantly related to higher levels of WBC, BUN, and CRP as well as a lower level of albumin. These results were also confirmed by other researchers [8,20,28,29,31]. Conversely, *Bedock* et al. reported no significant association between nutritional status neither with any underlying disease nor with their clinical outcomes [25]. In consistent with this finding, the presence of GPS = 2, which is known as an inflammatory prognostic factor, was found as a strong predictor for the detrimental nutritional status, so that 90% of dead subjects had highest GPS scores. In line with these reports, the results of a study performed in turkey also demonstrated that dead patients display a significantly greater CRP level, so GPS = 2 can be considered as a significant prognostic factor for death and transfer to ICU [22]. The reduced albumin and the elevated BUN are the signs indicating that these patients are at a sever nutritional risk [20]. As described earlier, GPS is an inflammatory-based prognostic factor in different situations, including covid-19, in such a manner that GPS = 2 illustrates hypoalbuminemia as well as greater levels of CRP. The interaction between inflammation and the detrimental nutritional outcomes appears similar to a vicious cycle. SARS-COV-2 virus has great potentials in stimulating inflammatory pathways and leakage of pro-inflammatory cytokines, which could consequently increase metabolism, suppress appetite, and reduce food intake [40,41]. On the other hand, poor nutritional status weakens immune system [42], which consequently causes the accumulation of more immune cells in the lung as well as the overproduction of pro-inflammatory mediators [43].

In this study, nearly 20% of the participants received nutritional support; either total EN (18%) or EN in addition to PN (2%). Accordingly, of them, nearly 70% were classified as having the elevated nutritional risk.

NRS score among the non-survivals and patients admitted at ICU was higher than that of the survivals and patients admitted at other units. Accordingly, these findings were highlighted in two recent cross-sectional studies conducted in china and Italy [11,35]. In agreement with these findings, *Zhang* et al. have demonstrated that non-survival covid-19 subjects manifest higher modified-NUTRIC scores [44]. As expected, severity of disease and deleterious nutritional outcomes were observed to be considerably higher among non-survivals. On the contrary, *Bedock* et al. by assessing the nutritional status of 160 covid-19 patients via the Global Leadership Initiative on Malnutrition (GLIM) criteria, have reported no significant relationship among nutritional status, death, and rate of admission to ICU, maybe due to limited sample size and selection bias [25].

It can be stated that our prognostic model, including NRS, CRP, and albumin, could extremely reflect nutritional and inflammatory statuses, so it might be considered as a reliable tool to assess nutritional status and predict possible outcomes among covid-19 patients.

Our research is among the first studies providing data regarding the nutritional status of Iranian patients infected with covid-19. Nevertheless, this study had some limitations like selection bias due to single-center data gathering. Moreover, considering self-report of history of weight loss, this parameter may also be affected by the recall bias. In addition, the cross-sectional design of this study was another limitation.

5. Conclusion

Based on NRS score moderate to severe nutritional risk was observed in 96% of patients. Detrimental nutritional status acts like a vicious cycle and is considerably related to adverse outcome of covid-19. We strongly recommend rapid nutritional screening upon admission time. Our suggested prognostic parameters may assist health care providers for timely diagnosis of at risk patients and implementing appropriate interventions for high risk individuals. Special attention should be paid to older patients and people with underlying disease.

Authors' contributions

Hosseinikia M and Pourmahmoudi A equally contributed to the conception and design of the research; Shabanpur M and Jafarnia Jahromi A contributed to data gathering; Roustaei N contributed to the acquisition and analysis of the data; Roustaei N, Hosseinikia M and Nicolau J contributed to the interpretation of the data; Hosseinikia M, and Veronese N drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

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Declaration of competing interest

None declared.

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