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The Association of Hemoglobin and Body Mass Index and the Outcomes of COVID-19: A Prospective Cohort Study

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ABSTRACT

Background: Previous studies indicated the risk factors for COVID-19. It is known that nutritional status is one of the main causes of immune system failure. This study aims to investigate the association of nutritional status and the outcomes of COVID-19 in participants of Yazd Health Study (YaHS).

Methods: 279 people who had taken a blood test before contracting COVID-19 were included in this study in 2022. Data of PO2 level, rate of hospitalization, "supplementation with oxygen" rate, BUN, and creatinine were extracted. Hemoglobin levels and body mass index (BMI) were also evaluated. The authors applied analysis of variance (ANOVA) and independent sample t-test to show differences between levels of BMI and hemoglobin. All statistical analyses were conducted using IBM SPSS version 22.0 software.

Results: The results showed a significant difference between hemoglobin levels and different BMI levels (P = 0.03). However, there was no significant relationship between different BMI levels and BUN (P = 0.34), creatinine (P = 0.42), BUN/Cr (P = 0.14), PO2 (P = 0.34), supplementation with oxygen (P = 0.26), and hospitalization rates (P = 0.97). The results according to the normal and abnormal hemoglobin levels were not significant.

Conclusion: According to the criteria used in this study to assess nutritional status (BMI and hemoglobin levels), there was no significant relationship between nutritional status (different levels of BMI and hemoglobin) and COVID-19 outcomes, including hospitalization rate, “supplementation with oxygen” rate, and low PO2 levels. Further studies in different countries using other nutritional status assessment tools are needed to confirm these findings.

Keywords: Body mass index, COVID-19, hemoglobin, nutritional status

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Introduction

Considering the spread of COVID-19 from the beginning of its emergence and the resulting critical situation, many studies have been conducted with the aim of identifying risk factors for the severe form of COVID-19 (1). Currently, there is consensus on the main clinical risk factors for COVID-19. These include being 65 years and above, male (2), smoking tobacco (3), having comorbidities such as diabetes, hypertension, coronary heart disease, chronic obstructive pulmonary disease (2, 4), and obesity (5, 6). The effect of obesity on the severity of COVID-19 could be due to different mechanisms:

1) A higher baseline inflammatory state among obese individuals (7), which makes them more prone to generate a "cytokine storm,"
2) Lower respiratory capacity (8), which may increase disease severity,
3) Increased lipid peroxidation (9), and higher levels of angiotensin-converting enzyme 2 (-ACE2, a functional receptor for COVID-19) in adipose tissue (10, 11), which may act as a virus reservoir and activate immunity and strengthen cytokines (12).

On the other hand, malnutrition is considered the most important cause of immune system failure worldwide (13). In fact, at least four out of ten hospitalized patients (including the obese (14)) suffer from some forms of malnutrition (15). The rate of malnutrition increases with age (14) and in the presence of concomitant diseases (16). Malnutrition leads to increased hospital length of stay (LOS) (17, 18), hospital mortality (18, 19), and medical costs (19). However, the number of malnourished patients is often underestimated in hospitals, which has led to underreporting of this disease (20, 21). Studies have shown that extracting clinical data directly from electronic medical records (EMR) is more valuable than hospital data (discharge data) for estimating the prevalence of malnutrition (22). nutritional status of patients can be identified using various tools; more than 20 of these tools have been reported so far (23-25) some cases of which include:

1) Malnutrition Universal Screening Tool (MUST),
2) Short Nutrition Assessment (MNA),
3) Nutritional Risk Screening (NRS)
4) Blood factors such as hemoglobin, albumin, BUN, and creatinine.

Malnutrition is a proven risk factor for severe pneumonia (26). Several studies have shown that pneumonia patients with malnutrition are at higher risk of ICU admission, longer hospital stay, and higher mortality (27). Malnutrition affects several metabolic systems and appears to be a pathogenic factor for COVID-19 (28). Figure 1 summarizes the possible mechanisms by which malnutrition can affect the body response to COVID-19 (28). Based on these elements, expert statements and practical guidelines have been published to help healthcare professionals identify at-risk patients and malnourished people with COVID-19 and guide the nutritional management of this population (29).

These observations suggest that nutritional status may affect the severity and outcomes of COVID-19. Therefore, the present study was conducted with the aim of investigating the association of nutritional status based on BMI and hemoglobin levels and the outcomes of COVID-19 in a large population of Iranian adults.

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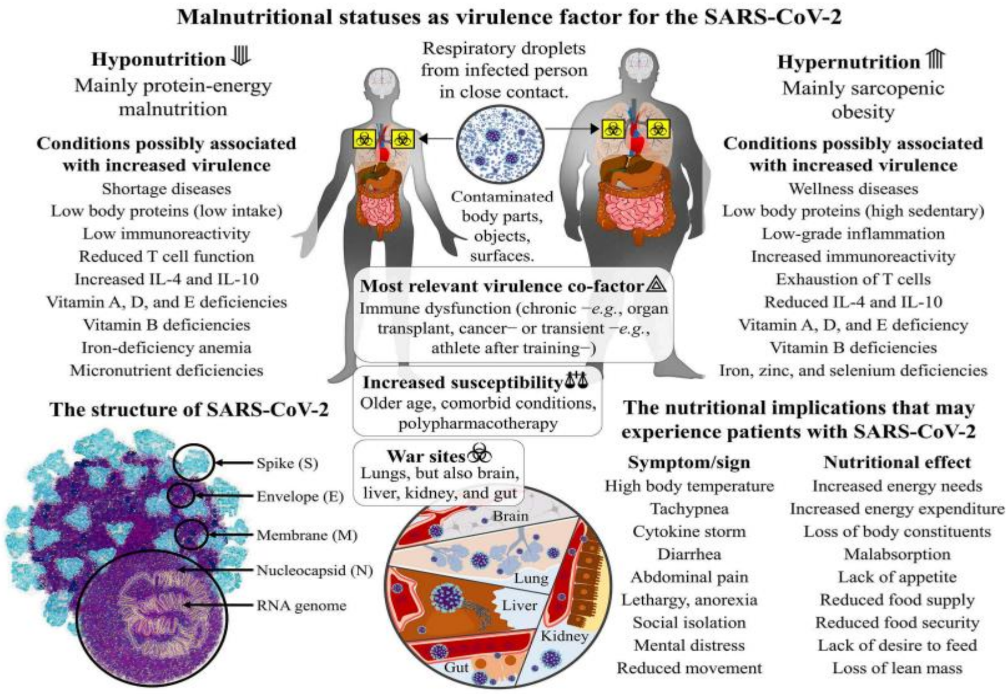

Figure 1. Possible mechanisms of malnutrition as a risk factor for COVID-19

Methods

Study selection

Using data linkage with Yazd Central Lab database, information on blood tests of participants in Yazd Health Study (YaHS) in 2018 and 2019, including hemoglobin and CBC, was collected. The information of people infected with COVID-19 was also collected. About 1,600 adults infected with COVID-19 virus in the age range of 20-70 participating in the enrollment phase of YaHS were also assessed. Finally, all people who had taken a blood test before contracting COVID-19 were included in this study in 2022 (n = 279).

Data extraction

The interviewers (H.V, F.M) made phone interviews with the participants. Information related to CBC, BUN, Cr, BUN/Cr, PO2, supplementation with oxygen, and hospitalization rate were extracted from YaHS database. Furthermore, at the beginning of the study, the authors asked participants to go to the clinic to measure their weight, but the cooperation of participants were low, so they were asked to measure their weight themselves and inform the study team.

Diagnosis of COVID-19

COVID-19 has been diagnosed using real-time polymerase chain reaction tests or CT-Scan positive signs or diagnosis by physicians. In addition, the presence of Immunoglobulin M (IgM) and Immunoglobulin G (IgG) antibodies were evaluated in both symptomatic and asymptomatic patients who recovered from the virus.

Hemoglobin and Body Mass Index assessment

Hemoglobin and BMI of the participants in the study were assessed using data from the first stage of YaHS (BMI < 18.5, and anemia (Hb < 12 gr/dl in women and Hb < 13.5 gr/dl in men)).

Statistical analysis

Statistical analysis was conducted using IBM SPSS version 22.0 software. Descriptive results were expressed as the number of patients (%) for categorical variables and as median (interquartile range) or as mean and standard deviation for continuous variables. This study used Chi-square tests or Fisher's exact test for categorical variables and Student's t-test or Kruskal-Wallis test for continuous variables. In addition, analysis of variance (ANOVA) was applied to show differences between levels of BMI.

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Results

Study population characteristics

A summary of the characteristics of YaHS participants is shown in Table 1. In this study, 52.4% of the participants were female. The mean age of the participants was 49. The BMI mean value of the participants in the study was in the overweight range (27.9). The average levels of Hb, BUN, Cr, and Cr/BUN of the participants were in the normal range. The average percentage of PO_2 of participants was 87.9%, and a small percentage of the participants were intubated (6.4%) or hospitalized (7.1%) (Table 1).

Table 1. Summary of the general characteristics of the participants in the enrollment phase of Yazd Health Study - YaHS (2014-2015) (n = 279)

Variables	Mean±SD or number (percentage)
Sex (female)	140 (52.4%)
Age (year)	49.4 ± 12.9
BMI (kg/m2)	27.9 ± 4.9
PO2	87.9 ± 9.5
Hemoglobin (g/dL)	14.3 ± 1.7
Blood urea nitrogen (mg/dL)	29.1 ± 9.0
Creatinine (mg/dL)	1.1 ± 0.5
Blood urea nitrogen /Creatinine	27 ± 10.3
"Supplementation with oxygen" rate (%)	17 (6.4%)
Hospitalization rate (%)	19 (7.1%)

Data were reported as mean and standard deviation or number (percentage). BMI: Body Mass Index

Comparison of biochemical parameters according to BMI

Table 2 presents the comparison of biochemical parameters based on BMI. The results showed a significant difference in Hb level based on different levels of BMI (P = 0.03). However, there was no significant relationship between different levels of BMI and BUN, Cr, BUN/Cr, PO2, supplementation with oxygen, and hospitalization rate.

Table 2. Comparison of biochemical parameters according to BMI in Yazd Health Study

Variables	BMI < 25 (n = 44)	25 ≤ BMI < 30 (n = 87)	BMI ≥ 30 (n = 48)	P-values[1]
Hemoglobin (g/dL)	14.3 ± 2	14.7 ± 1.6	13.9 ± 2	0.03
Blood urea nitrogen (mg/dL)	27.7 ± 8.2	30.1 ± 9.3	30.1 ± 10.7	0.34
Creatinine (mg/dL)	1.10 ± 0.2	1.1 ± 0.2	1.1 ± 0.3	0.42
BUN/Cr	25.5 ± 7.6	26.9 ± 7.9	29.8 ± 16.2	0.14
PO_2				0.34
< 80%	6 (21.4%)	5 (12.5%)	2 (8%)	
≥ 80%	22 (78.6%)	35 (87.5%)	23 (92%)	
"Supplementation with oxygen" rate (%)				0.26
Yes	2 (4.9%)	6 (7.3%)	6 (14.3%)	
No	39 (95.1%)	76 (92.7)	36 (85.7%)	
Hospitalization rate (%)				0.97
Yes	3 (12.5%)	7 (11.3%)	3 (10.3%)	
No	21 (87.5%)	55 (88.7%)	26 (89.7%)	

BMI: Body Mass Index; BUN, Blood Urea Nitrogen
Data were reported as mean and standard deviation or number (percentage). P-value was calculated based on ANOVA or chi-square.

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Comparison of biochemical and anthropometric parameters based on hemoglobin levels

Table 3 presents the comparison of biochemical and anthropometric parameters based on Hb levels. The results showed that there was no significant difference in BMI, Cr, BUN/Cr, PO2, supplementation with oxygen, and hospitalization rate based on normal and abnormal hemoglobin levels.

Table 3. Comparison of biochemical and anthropometric parameters according to hemoglobin levels in Yazd Health Study

Variables	Abnormal levels of hemoglobin (n = 22)	Normal level of hemoglobin (n = 240)	P-value [1]
BMI (kg/m^2)	27.7 ± 6	27.93 ± 4.8	0.33
Blood urea nitrogen (mg/dL)	25.6 ± 7.1	29.5 ± 9.1	0.66
Creatinine (mg/dL)	1 ± 0.2	1.2 ± 0.6	0.54
BUN/Cr	24.8 ± 5.7	27.4 ± 10.6	0.18
PO_2			0.54
< 80%	1 (10%)	19 (17.4%)	
≥ 80%	9 (90%)	90 (82.6%)	
"Supplementation with oxygen" rate (%)			0.65
Yes	1 (5.9%)	17 (9.1%)	
No	16 (94.1%)	170 (90.9%)	
Hospitalization rate (%)			0.44
Yes	1 (5.3%)	13 (10.9%)	
No	18 (94.7%)	106 (89.1%)	

BMI: Body Mass Index; BUN, Blood Urea Nitrogen
Data were reported as mean and standard deviation or number (percentage). P-value was calculated based on the independent sample t-test or chi-square

Discussion

The results showed that the average hemoglobin level differed between different BMI levels, and the lowest level was in individuals with a BMI above 30 kg/m2. However, no significant difference was observed between the outcomes of COVID-19, such as supplementation with oxygen, low PO2 level, and hospitalization based on different levels of BMI and hemoglobin. It is well known that nutritional assessments play an important role in the health status of patients (30-32). Hence, the European Society for Clinical Nutrition and Metabolism (ESPEN) provides practical guidelines for the nutritional management of individuals infected with SARS-CoV-2. According to ESPEN recommendations, the prevention, diagnosis, and treatment of malnutrition should be considered an integral part of the ongoing care of patients with COVID-19 (33). In addition, a study showed that among the hematological parameters, reduction in Hb is one of the dominant factors in COVID-19 patients (34). The results of a study showed a link between a previous malnutrition diagnosis and severe COVID-19. In this study, the effect of malnutrition on severe COVID-19 was the highest in younger children (less than 5 years) in the pediatric population (35). A study in China showed that one-third (34%) of overweight patients were at risk of malnutrition. In this study, malnutrition was assessed using NRS-2002 score, and the findings indicated that a higher NRS-2002 score was associated with an increased LOS and greater disease severity (36). A study revealed that among hospitalized patients with COVID-19, a higher BMI was associated with a higher risk of severe organ failure or in-hospital death, which dissipates after adjustment for CRP level (37). Another study showed that obese patients were at a higher risk of severe development of SARS-CoV2 infection and associated mortality (38). The observed findings were due to the alteration of the body's immune system due to malnutrition caused by excessive food consumption (obesity). Obesity induces an inflammatory state by altering TCD4 cell response, resulting in increased leptin

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production (39, 40) which is characterized by the reduction of effective and cytotoxic functions. Micronutrient deficiency is another issue in malnourished individuals, since vitamins and micronutrients play an important role in the proper functioning of innate and acquired immune responses (41, 42). Malnutrition combined with micronutrient deficiencies, excessive metabolism, and excessive nitrogen loss, predisposes individuals to infection and increases the associated outcomes (43). However, the results of previous studies were not in the same direction as the present study. One possible cause of the observed conflicting results could be attributed to the criteria used to evaluate the nutritional status in the study. Previous studies have shown the association of nutritional status and COVID-19 using screening and assessment tools of nutritional status CONUT, GNRI, NRS2000, and GLIM. Studies have also shown that biological markers are poor predictors of nutritional status, as they may be affected by critical illness, infection, and liver and kidney disease (44). Therefore, it is necessary to conduct further studies using other nutritional status evaluation criteria.

Strengths and limitation

The present investigation scrutinizes the association between nutritional standing based on hemoglobin and BMI levels and the severity of COVID-19 among adult inhabitants of Yazd Greater Area, Iran, using data from a large-scale prospective study (YaHS) that covered both urban and rural populations. However, this study entailed a certain limitation. The principal limitation of this study pertained to the criteria utilized for evaluating the nutritional status, as the authors were unable to employ NRS, NUTRIC, MUST, MNA, etc. criteria due to insufficient data. Therefore, it is necessary to conduct further studies using other nutritional status assessment criteria. In addition, due to the study design, it was not possible to examine the causal relationship.

Conclusion

There was no significant relationship between nutritional status (different levels of BMI and hemoglobin levels) and COVID-19 outcomes, including hospitalization rate, supplementation with oxygen rate, and low PO2 levels. However, more studies in different countries using other nutritional status assessment criteria should be conducted to confirm these findings.

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Conflict of interest

The authors declared no conflict of interests.

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Ethical considerations

This project was approved by the Medical Ethics Committee of Shahid Sadoughi University of Medical Sciences, Yazd, Iran. Moreover, written informed consent was obtained from all of the participants.

Code of ethics

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Author contributions

Design and conception of the paper were done by, M. M and Sh. H; Data acquisition or analysis/ interpretation was conducted by, H. V, F. M. and Sh. H; Manuscript was drafted by, Sh. H, HV. MM and A. N, were engaged in revision of the manuscript; M. M, supervised the study and was responsible for the integrity and accuracy of all study data. Ultimately, the final version was read and approved by all the authors.

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