Microbial Pathogenesis xxx (xxxx) 105792

Contents lists available at ScienceDirect

Microbial Pathogenesis

journal homepage: www.elsevier.com/locate/micpath

The effect of Nutrition Bio-shield superfood (NBS) on disease severity and laboratory biomarkers in patients with COVID-19: A randomized clinical trial

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ARTICLE INFO

Keywords:
COVID-19
Nutrition bio-shield superfood
Laboratory biomarkers
Clinical trial study
Iran

ABSTRACT

Background: Nutrition Bio-shield Superfood (NBS) is an organic and viable herbal supplement that could improve the function of the immune system. The present study aims to determine the effect of NBS on disease severity and laboratory biomarkers in patients with COVID-19.

Methods: This current study was a randomized, comparative, parallel two-arm and single-blind clinical trial study performed in Tehran, Iran. In total, 70 patients with COVID-19 were included in the present study and assigned to two groups including 1) intervention group (n = 35) and 2) control group (n = 35). All patients included in the intervention group received 4.5 gr daily rate of NBS superfood, three times the daily rate of 1.5 gr for 14 days. In contrast, patients included in the control group received a placebo three times a day for 14 days. The measurement of laboratory parameters including CRP, ESR, D-Dimer, LDH, CPK, SGOT, SGPT, ALP, FBG, WBC count, PLT, and lymphocyte count was performed using standard kits and methods. Moreover, all serum samples were tested to determine the levels of IL-6 and TNF-α using specific commercially available ELISA kits according to the instructions of the manufacturer.

Results: A significant decrease in the mean serum level of several variables including CRP ($p < 0.001$), ESR ($p < 0.001$), D- Dimer ($p = 0.001$), LDH ($p < 0.001$), SGOT ($p = 0.002$), SGPT ($p = 0.019$), ALP ($p < 0.001$), WBC count ($p < 0.001$), body temperature ($p = 0.013$), IL-6 ($p < 0.001$), and TNF-α ($p < 0.001$) was seen 14 days after intervention from baseline in the intervention group than control group. In contrast, in the intervention group, the significant increase from baseline of lymphocyte percentage ($p < 0.001$) and oxygen saturation ($p < 0.001$) was seen 14 days after receiving NBS superfood than the control group.

Conclusion: Results showed that the use of NBS superfood had various beneficial effects on COVID-19 disease severity. These results suggest that NBS superfood can be used as an effective natural supplement in the treatment process of COVID-19 disease.

1. Introduction

Coronavirus disease (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and was declared a pandemic by World Health Organization (WHO) on March 11, 2020 [1,2]. Up to July 20, 2022, around 569, 964, 042 cases of COVID-19 and 6,392,275 deaths have been reported worldwide (https://www.worldometers.info/coronavirus/). To date, there are >7,296,635 confirmed cases in Iran with over >141,564 deaths (https://www.worldometers.info/coronavirus/country/iran/).

Based on the disease state, patients with COVID-19 infection usually exhibit two types of clinical symptoms. Patients with mild to moderate disease (approximately 75–80%) may show several clinical manifestations such as sore throat, cough, and headaches and in most cases, recover after several days. In contrast, severe forms of COVID-19 infection (approximately 10–15%) are related to multi-organ failure, lung infiltrates, and falling oxygen saturation and require care at tertiary hospitals [3–5].

The laboratory findings have revealed that damage to immune effector cells and exacerbation of pro-inflammatory cytokines to COVID-19

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https://doi.org/10.1016/j.micpath.2022.105792
Received 25 February 2022; Received in revised form 20 July 2022; Accepted 14 September 2022
0882-4010/

infection may lead to lung damage, thus contributing to the growing death rate [1,6]. Moreover, it has become clear that the lymphocyte and platelet counts in COVID-19 patients hospitalized in Intensive Care Units (ICU) decrease severely, while the neutrophil count in their blood increases [7].

Moreover, increases in the levels of several factors such as interleukin-1 receptor antagonist (IL-1Ra), IL-1B, IL-2, IL-6, IL-7, IL-8 (cytokine storm), IL-10, Granulocyte-Colony Stimulating Factor (GSCF), interferon γ-induced protein (CXCL10), Monocyte Chemoattractant Protein-1 (MCP-1), Macrophage Inflammatory Protein-1α (MIP1α), serum C-Reactive Protein (CRP), and TNF-α are associated with the severe form of COVID-19 infections [8,9]. Despite the existence of several types of vaccines, treatment of severe forms of COVID-19 infection is the main challenge to physicians, worldwide. Therefore, it is important to find new therapeutic targets to reduce the mortality rates among COVID-19 patients admitted in ICUs.

Vitamins and their supplements have a positive impact on normal functioning of the immune system subjected to infection. Studies have demonstrated that several classes of vitamins and supplements such as vitamin A and D supplementation and high doses of selenium raise the humoral immunity of pediatric patients after influenza vaccination [10]. Moreover, in patients with torque teno virus infection, the use of dietary supplementation with high levels of zinc had a positive effect on the functioning of the immune system [11]. In general, micronutrients, herbals, and natural compounds have antioxidant and anti-inflammatory effects and play a significant role in medicine and pharmaceutical sciences [12].

Nutrition Bio-shield Superfood (NBS) is an organic, healthy and viable herbal supplement that was prepared from wheat. This viable herbal supplement contains macro and micro molecules, different vitamins, and various components including A, B1–B3, B5, B6, B9, C, D, K, magnesium, potassium, phosphorus, sulfur, manganese, calcium, iron, boron, copper, zinc, omega-3, omega-6, omega-9, and other ingredients [13]. NBS has various health benefits and may be used as a good therapeutic target in patients with COVID-19. Administration of this viable herbal supplement could improve the functioning of the immune system [13]. Therefore, the present study aimed to determine the effect of NBS on disease severity and laboratory biomarkers in patients with COVID-19.

2. Materials and methods

2.1. Study design and participants

This present study was a randomized, comparative, parallel two-arm and single-blind clinical trial performed in Aban and Kashani hospitals in Tehran, Iran with the objective of evaluating whether NBS can improve the disease severity and clinical outcomes of patients with COVID-19 infection. All study protocols and procedures were approved by the Ethics Committee of Hamadan University of Medical Sciences (protocol number IR. UMSHA.REC.1399.046; approval date: 2020-05-19) and conducted according to the Helsinki Declaration. The protocol was registered in the Iranian registry of clinical trials at www.irct.ir (IRCT registration number: IRCT20200426047206N1; Registration date: 2020-04-28). In total, 70 patients were included in the present study. The goals of the research were explained to all patients, and written informed consent was signed by all patients.

2.2. Inclusion criteria

Patients are included in the present study only if they meet all of the following criteria: 1) patients with a definitive diagnosis of COVID-19 infection, 2) those with severe clinical manifestations of COVID-19, 3) patients who signed written informed consent, 4) hospitalized patients aged between 25 and 85 years, and 5) male and female patients. Definitive diagnosis of COVID-19 infection was determined through 1) positive Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) assay (Retrieve RT-PCR Ct values) and 2) "50-point or higher severity score" CT scan data from the patients' medical records.

2.3. Exclusion criteria

Patients meeting any of the following criteria are excluded from the study: 1) patients who had been previously included in any other clinical trial study; 2) non-hospitalized patients with COVID-19; 3) patients with other viral infections including human immunodeficiency virus, hepatitis C virus, or hepatitis B virus; 4) those with solid organ transplantation; 5) subjects with an immunosuppressive disease or a history of chronic disease; 6) pregnant patients; 7) patients who received any supplements such as vitamin D, C, A for three months before the start of the research.

2.4. Interventions and randomization

In total, 70 patients were included in the present study and the included patients were assigned based on the randomization method to two groups: 1) intervention group (n = 35) and 2) control group (n = 35). All patients included in the intervention group received daily 4.5 gr NBS superfood, that is, 1.5 gr three times daily for 14 days. In contrast, patients included in the control group received a placebo three times a day for 14 days. All patients included in the intervention and control groups were unaware of the intervention allocation to groups. However, ICU specialists were aware. Patients were enrolled and assigned to intervention by Aref Khalkhali and Manije Nezamdoost. Mortality rate, hospital stay longer than 7 days, and inflammatory markers that were assessed at baseline and the end of patient's hospitalization were the main outcomes of the present study.

2.5. Clinical and laboratory measurements

To measure laboratory parameters namely CRP, Erythrocyte Sedimentation Rate (ESR), D-Dimer (a fibrin degradation product), lactate dehydrogenase (LDH), creatine phosphokinase (CPK), aspartate transaminase (SGOT), alanine transaminase (SGPT), alkaline phosphatase (ALP), Fasting Blood Glucose (FBG), WBC count, platelets (PLT), and Lymphocyte count, blood samples were taken from all the patients using a standard coagulation tube. Serum samples were isolated from all blood samples using a centrifuge at 10,000 rpm for 10 min. All samples were aliquoted and stored at −20 °C before further analysis. All serum samples were tested to determine the levels of IL6 and TNF-α using specific commercially available Enzyme-Linked Immune-Sorbent Assay (ELISA) kits**.** The process of ELISA assay was performed in line with the instructions of the manufacturer.

2.6. Statistical analysis

All demographical data as well as clinical and laboratory findings were included in SPSS v.23.0 (SPSS Inc., Chicago, IL, USA). To compare the mean of variables at baseline and endline (after 14 days), the normal distribution of data was checked by the Kolmogorov–Smirnov test. Data with and without a normal distribution were compared using the Paired *t*-test and Wilcoxon test, respectively. On the other hand, to compare the mean of variables among intervention and control groups, the normal distribution of data was checked by Kolmogorov–Smirnov test. Data with and without a normal distribution were compared using the Unpaired *t*-test and Mann-Whitney *U* test, respectively. Finally, the Chi-Square test was used to the comparison of the mortality rate among patients included in the intervention and control groups. A *P*-value of <0.05 was set as significant.

3. Results

3.1. Comparison of the variables between the intervention and control groups at baseline and that after 14 days

In the case of the intervention and control groups, median age was 48.69 ± 13.00 (29–77) years and 54.54 ± 13.92 (29–81) years, respectively. Of the patients included in intervention and control groups, 54.3% (n = 19/35) and 51.4% (n = 18/35) were male, respectively.

The clinical characteristics of the patients in the intervention and control groups at baseline and those after 14 days of hospitalization are shown in Table 1.

Results illustrated that there was no significant difference between the intervention group 14 days after receiving NBS superfood and that at baseline in the change in several variables such as SGOT ($p = 0.898$), SGPT ($p = 0.561$), FBG ($p = 0.190$), and CT scan score ($p = 1$). We found significant differences and variations in D-Dimer ($p = 0.020$), ALP ($p = 0.031$), WBC count ($p < 0.001$), PLT ($p = 0.006$), lymphocyte percentage ($p < 0.001$), lymphocyte count ($p < 0.001$), and oxygen saturation ($p < 0.001$) 14 days after receiving NBS superfood compared to those at baseline. In contrast, a significant reduction in the mean of serum levels of several variables including CRP ($p < 0.001$), ESR ($p < 0.001$), LDH ($p = 0.003$), CPK ($p < 0.001$), IL-6 ($p < 0.001$), and TNF-α ($p < 0.001$) at baseline was seen 14 days after receiving NBS superfood. The body temperature was significantly lower in the intervention group 14 days after receiving NBS superfood than that at baseline ($p < 0.001$).

The comparison of the variables revealed that there was no significant difference in CRP, ESR, PLT, lymphocyte count, temperature, oxygen saturation, and CT-scan results for the control group at baseline and those after 14 days. Percentage of lymphocytes was significantly lower in the control group at baseline than that 14 days after hospitalization ($p < 0.001$). In contrast, our analyses revealed that there were significant differences in changes in D-Dimer, ($p < 0.001$), LDH ($p = 0.008$), CPK ($p > 0.001$), SGOT ($p = 0.002$), SGPT ($p = 0.001$), ALP ($p < 0.001$), FBG ($p = 0.007$), and WBC count ($p < 0.001$) after 14 days from baseline in the control group. The evaluation of inflammatory markers, including IL-6 and TNF-a, demonstrated that the levels of these markers in the control group were significantly lower after 14 days of hospitalization from baseline ($p < 0.001$).

3.2. Comparison of the variables for both control and intervention groups after the intervention

The clinical characteristics of the patients in the control and intervention groups 14 days after intervention are shown in Table 2. A significant decrease in the mean of serum levels of several variables including CRP ($p < 0.001$), ESR ($p < 0.001$), D- Dimer ($p = 0.001$), LDH ($p < 0.001$), SGOT ($p = 0.002$), SGPT ($p = 0.019$), ALP ($p < 0.001$), WBC count ($p < 0.001$), body temperature ($p = 0.013$), IL-6 ($p < 0.001$), and TNF-α ($p < 0.001$) was observed 14 days after intervention at baseline in intervention group, compared to the control group. We did not find significant differences in CPK ($p = 0.930$), FBG ($p = 0.137$), PLT ($p = 0.222$), and CT scan score ($p = 0.576$) for the groups. In contrast, in the intervention group, the significant increases in the baseline lymphocyte percentage ($p < 0.001$), lymphocyte count ($p < 0.001$), and oxygen saturation ($p < 0.001$) were seen 14 days after receiving NBS superfood, compared to the control group.

4. Discussion

In recent years, the use of natural and plant-derived compounds is increasing all over the world, especially in developed countries. Plant compounds have several properties such as antimicrobial effects and are used frequently in medical and pharmaceutical sciences [13,14].

The NBS superfood is an organic, healthy and viable herbal supplement and has various health benefits and can improve the functioning of the immune system [13]. This study assessed the effects of NBS superfood on disease severity, laboratory biomarkers, and inflammatory cytokines in patients with COVID-19.

Table 1
Compare the variables between intervention and control groups at baseline and after 14 days.

Variables (Units)	Control group N = 35		P-value	Intervention group N = 35		P-value
	(Baseline) Mean ± SD	(After 14 days) Mean ± SD		(Baseline) Mean ± SD	(After 14 days) Mean ± SD	
CRP (mg/L)	52.97 ± 29.596	49.69 ± 30.676	0.629[a]	61.77 ± 41.839	16.20 ± 13.689	**<0.001**[a]
ESR (mm/h)	48.57 ± 17.973	44.86 ± 21.112	0.047[a]	43.69 ± 18.643	19.77 ± 16.582	**<0.001**[a]
D-Dimer (ng/ml)	1134.69 ± 621.467	2512.77 ± 2205.964	**<0.001**[a]	1194.94 ± 1866.862	1614.57 ± 2240.996	**0.020**[a]
LDH (U/L)	996.29 ± 381.722	1599.71 ± 1361.304	**0.008**[a]	993.29 ± 335.253	846.09 ± 859.374	**0.003**[a]
CPK (U/L)	139.23 ± 118.310	222.77 ± 166.473	**<0.001**[a]	291.51 ± 149.917	200.40 ± 135.388	**<0.001**[a]
SGOT (IU/L)	55.29 ± 22.527	70.31 ± 26.079	**0.002**[a]	51.57 ± 18.789	52.26 ± 27.175	0.898[a]
SGPT (IU.L)	52.69 ± 25.608	67.63 ± 27.805	**0.001**[a]	54.20 ± 34.940	55.06 ± 29.077	0.561[a]
ALP (U/L)	123.74 ± 35.873	173.03 ± 55.947	**<0.001**[a]	122.60 ± 37.720	132.46 ± 32.706	**0.031**[a]
FBG (mg/dl)	125.06 ± 38.331	133.77 ± 26.078	**0.007**[a]	131.17 ± 56.979	132.29 ± 42.167	0.190[a]
WBC (Microliter)	10.7220 ± 3.42735	14.5971 ± 3.83256	**<0.001**[b]	10.1571 ± 2.62357	11.4086 ± 2.68486	**<0.001**[a]
PLT (× 10^3/μl)	202.23 ± 45.885	217.09 ± 72.044	0.197[b]	214.80 ± 58.967	236.80 ± 61.498	**0.006**[b]
Lymphocyte (%)	8.7229 ± 3.78100	6.6543 ± 3.28440	**<0.001**[a]	9.9971 ± 5.17974	14.6886 ± 5.27088	**<0.001**[b]
Lymphocyte count	853.23 ± 300.142	905.09 ± 373.622	0.407[b]	1073.51 ± 965.053	1583.29 ± 401.043	**<0.001**[a]
Temperature	37.1171 ± 0.380	37.1286 ± 0.32771	0.837[a]	37.3571 ± 0.52820	36.9371 ± 0.34135	**<0.001**[a]
Oxygen saturation	83.80 ± 4.708	84.42 ± 5.054	1[a]	85.40 ± 5.616	94.85 ± 1.736	**<0.001**[a]
CT-scan	66.00 ± 10.627	66.00 ± 10.627	1[a]	67.71 ± 11.903	67.71 ± 11.903	1[a]
IL-6	89.1600 ± 29.32172	57.4400 ± 32.16835	**<0.001**[b]	76.1829 ± 58.37699	27.5829 ± 19.27868	**<0.001**[a]
TNF-α	6.6096 ± 1.27040	3.4100 ± 2.04239	**<0.001**[a]	6.1548 ± 1.38650	1.3140 ± 1.22726	**<0.001**[a]

Abbreviations: C-Reactive Protein (CRP), Erythrocyte Sedimentation Rate (ESR), D-Dimer (a fibrin degradation product), Lactate Dehydrogenase (LDH), Creatine Phosphokinase (CPK), Aspartate Transaminase (SGOT), Alanine Transaminase (SGPT), Alkaline Phosphatase (ALP), Fasting Blood Glucose (FBG), White Blood Cell (WBC), Platelets (PLT), Interleukin-6 (IL-6), Tumor Necrosis Factor alpha (TNF-α), Computed tomography scan (CT-scan).

[a] Wilcoxon test.

[b] Paired *t*-test.

Table 2
Compare the variables between control and intervention groups after the intervention.

Variables (Unit)	Study groups		P-value
	Control group N = 35	Intervention group N = 35	
CRP (mg/L)	49.69 ± 30.676	16.20 ± 13.689	**<0.001**[a]
ESR (mm/h)	44.86 ± 21.112	19.77 ± 16.582	**<0.001**[a]
D-Dimer (ng/ml)	2512.77 ± 2205.964	1614.57 ± 2240.996	**0.001**[a]
LDH (U/L)	1599.71 ± 1361.304	846.09 ± 859.374	**<0.001**[a]
CPK (U/L)	222.77 ± 166.473	200.40 ± 135.388	0.930[a]
SGOT (IU/L)	70.31 ± 26.079	52.26 ± 27.175	**0.002**[a]
SGPT (IU.L)	67.63 ± 27.805	55.06 ± 29.077	**0.019**[a]
ALP (U/L)	173.03 ± 55.947	132.46 ± 32.706	**<0.001**[a]
FBG (mg/dl)	133.77 ± 26.078	132.29 ± 42.167	0.137[a]
WBC (Microliter)	14.5971 ± 3.83256	11.4086 ± 2.68486	**<0.001**[b]
PLT (× 10^3/μl)	217.09 ± 72.044	236.80 ± 61.498	0.222[b]
Lymphocyte (%)	6.6543 ± 3.28440	14.6886 ± 5.27088	**<0.001**[a]
Lymphocyte count	905.09 ± 373.622	1583.29 ± 401.043	**<0.001**[a]
Temperature	37.1286 ± 0.32771	36.9371 ± 0.34135	**0.013**[a]
Oxygen saturation	84.42 ± 5.054	94.85 ± 1.736	**<0.001**[a]
CT-scan	66.00 ± 10.627	67.71 ± 11.903	0.576[a]
IL-6	57.4400 ± 32.16835	27.5829 ± 19.27868	**<0.001**[a]
TNF-α	3.4100 ± 2.04239	1.3140 ± 1.22726	**<0.001**[a]
Number of deaths	23	9	**0.002**[c]
Length of hospitalization (Day)	12.37 ± 5.191	8.8857 ± 2.836	**0.001**[b]

Abbreviations: C-Reactive Protein (CRP), Erythrocyte Sedimentation Rate (ESR), D-Dimer (a fibrin degradation product), Lactate Dehydrogenase (LDH), Creatine Phosphokinase (CPK), Aspartate Transaminase (SGOT), Alanine Transaminase (SGPT), Alkaline Phosphatase (ALP), Fasting Blood Glucose (FBG), White Blood Cell (WBC), Platelets (PLT), Interleukin-6 (IL-6), Tumor Necrosis Factor alpha (TNF-α), Computed Tomography scan (CT-scan), N: number of samples.

[a] Mann Whitney *U* test.
[b] Unpaired *t*-test.
[c] Chi-Square.

In general, although a few studies have surveyed the effects of nutrition and different vitamin supplements on diseases severity and clinical biomarkers of COVID-19 infection, to our knowledge, this is the first clinical trial study to survey the effects of NBS superfood on COVID-19 infection. In the present study, our analyses revealed that in the intervention group, the serum levels of CRP and ESR had a significant decrease after 14 days of receiving NBS superfood, compared to the control group. CRP is a liver protein that is produced and released into the blood in inflammation conditions. Similar to CRP, ESR is associated with inflammation in the blood. CRP and ESR are produced following chronic disease or autoimmune disorders and are related to pain, swelling, and redness in injured tissues [15,16]. Results of a study performed by Beigmohammadi et al. revealed that significant differences in serum levels of ESR, CRP, IL6, and TNF-α were detected after the intervention compared with the control group. They illustrated that vitamins had a positive role in enhancing the inflammatory response in ICU-admitted patients with COVID-19 [10]. Gönen et al. demonstrated that upon altering serum Cathelicidin-LL37, IL1B, INOS1, IFNg, and ICAM1, vitamin D supplementation shortened the duration of hospitalization and decreased the mortality rate of COVID-19 patients [2].

In the control group, the serum level of LDH experienced a significant increase after 14 days. In contrast, results showed that NBS superfood led to a significant decrease in LDH level in the intervention group after 14 days. This difference between the two groups was significant. LDH was found in different body tissues and plays a significant role in converting sugar into energy. After tissue damaging by diseases such as COVID-19, LDH is released into the body fluids [17]. Previously published studies revealed that an increase in the serum levels of LDH was related to Acute Respiratory Distress Syndrome (ARDS) in 40% of COVID-19 patients [18,19].

The serum level of CPK experienced a significant increase in the control group after 14 days. However, results revealed that the use of NBS superfood for 14 days could reduce the CPK level in COVID-19 patients. In various conditions including muscle inflammation, strenuous exercise, and damaged heart tissue, CPK is released into body fluids such as blood. It was revealed that COVID-19 could damage the heart and led to the release of CPK into the blood [20]. Results of our study revealed that the NBS superfood decreased the serum level of CPK in blood. Therefore, it can be concluded that NBS superfood may prevent heart damage or alleviate heart inflammation.

Based on the results, the serum levels of SGOT and SGPT had a significant increase in the control group after 14 days. In contrast, in the intervention group, the serum level of these two liver enzymes did not have a significant difference at baseline and after 14 days of receiving NBS superfood. In general, similar to the above-mentioned serum markers, SGOT and SGPT are two sensitive liver markers that are released into the blood in tissue damage conditions [21]. These results revealed that NBS can inhibit the secretion of SGOT and SGPT enzymes in COVID 19 patients. Therefore, it can be concluded that use of NBS superfood may prevent liver damage. After 14 days of intervention, WBC count experiences a significant increase in both control and intervention groups compared to the baseline. However, the results obtained from statistical analyses revealed that this increase was greater in the control group. It is observed that the use of NBS superfood for 14 days can balance the WBC count in COVID 19 patients. The lymphocyte percentage had a significant decrease in the control group after 14 days, while results showed that the use of NBS superfood for 14 days increased the lymphocyte percentage in COVID-19 patients. The blood oxygen level exhibited a significant increase after 14 days of consuming NBS superfood. However, the use of NBS superfood did not have a significant impact on lung involvement in COVID-19 patients. Leulseged et al. evaluated the laboratory biomarkers of COVID-19 disease severity. They found that neutrophil-to-Lymphocyte ratio, SGOT, sodium, and potassium were related to COVID-19 disease severity [22]. Results of a study performed by Yamamoto et al. revealed that the serum levels of several markers such as CRP, procalcitonin, ferritin, albumin, LDH and hemoglobin (Hb) A1c were useful tools in differential detection of the severe stage of COVID-19 disease [1]. The results of a study performed by Khan et al. from Pakistan revealed that the serum levels of CRP, SGOT and SGPT enzymes, troponin-I, serum creatinine, and ferritin significantly increased in COVID-19 patients [4]. By and large, the impairment of immune response and a cytokine storm with an overexuberant inflammatory response could affect the severity of COVID-19 infection. In the present study, the serum levels of IL-6 and TNF-α had a significant decrease after 14 days of intervention in both the control and intervention groups. However, our findings revealed that the decrease in serum levels of IL-6 and TNF-α was quite significant after 14 days of receiving the NBS superfood. Mortaz et al. revealed that serum levels of TNF-α were higher in COVID-19 patients than those in healthy subjects. Moreover, the results of their study pointed out that the serum level of soluble TNF-receptor 1 was significantly higher in ICU patients with severe COVID-19 infection [23]. Farid et al. investigated the use of inflammatory biomarkers in diagnosis of the severity of COVID-19 disease and found that an increase in several biomarkers such as D-dimer, serum ferritin, and CRP was related to severe forms of COVID-19 infection. Moreover, Farid et al. revealed that the serum level of IL-6 in patients who suffered from a severe form of COVID-19 disease was very high [7].

IL-6 prevents the production of albumin in hepatocytes and has a pleiotropic activity in the body. IL-6 as a soluble mediator plays several important roles in the body including stimulation of antibody production and stimulation of synthesis of several acute-phase proteins such as

hepcidin, fibrinogen, serum amyloid A, and CRP. However, in response to various infections and tissue damage, dysregulated continual secretion of IL-6 has a pathological effect on immune response, chronic inflammation, and hematopoiesis. In total, the control of IL-6 synthesis and secretion is important after viral infection [24,25]. Our findings illustrated that NBS might have an anti-inflammatory impact on the immune system and can balance the secretion of inflammatory cytokines such as IL-6 in COVID-19 infection.

5. Conclusions

This study assessed the effect of NBS superfood on disease severity and laboratory biomarkers in patients with COVID-19. Based on our findings, the use of NBS superfood has various beneficial effects on COVID-19 disease severity. Decrease in CRP, ESR, D- Dimer, LDH, SGOT, SGPT, body temperature, IL6, and TNF-α and increase in lymphocyte percentage and blood oxygen level were found to be the significant effects of NBS. Moreover, our results showed that the use of NBS superfood reduced the mortality rate and significantly decreased the duration of hospitalization in COVID-19 patients. This result suggests that NBS superfood can be used as an effective natural supplement in the treatment process of COVID-19 disease and may improve and moderate the severity of disease in COVID-19 patients. However, more comparative studies are required to be done to understand the exact and definitive effects of NBS superfood against COVID-19 infection.

CRediT authorship contribution statement

Mehrdad Mosadegh : Writing – review & editing, Writing – original draft, Software, Data curation, Conceptualization. **Aref Khalkhali :** Writing – original draft, Project administration, Methodology, Data curation. **Yousef Erfani :** Writing – review & editing, Writing – original draft, Software. **Manije Nezamdoost :** Writing – original draft, Formal analysis, Data curation.

Conflict of interest

All of the authors declare that there are no commercial, personal, political, and any other potential conflicting interests related to the submitted manuscript.

Acknowledgment

We would like to thank “School of Public Health, Tehran University of Medical Sciences, Tehran, Iran” for their kind cooperation. The authors received no specific funding for this work.

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