

Original Research

Perception and Knowledge of Students of Medical Colleges towards Dietary Supplements Use for Prevention and Treatment of COVID-19

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Received (first version): 14-Apr-2023

Accepted: 13-Jun-2023

Published online: 24-Oct-2023

Abstract

Background: Dietary supplements (DSs) have grown in popularity over the last two decades, particularly during the COVID-19 pandemic. It is critical to educate medical students, the future health care providers, about the appropriate and safe use of DSs. **Objective:** The aim of this study was to assess the knowledge, use, and attitude of undergraduate students at medical colleges at Jouf University towards DSs use for prevention and treatment of COVID-19. **Methods:** The present descriptive cross sectional questionnaire based study involved undergraduate medical students at Jouf University, KSA. After ethical approval, data were collected using an online questionnaire through Google forms during the second term of academic year 2021-2022. The questionnaire was divided into two sections composed of four components including Demographics data, health status, use and attitude, and students' perceptions toward dietary supplements use. Data were analyzed by employing GraphPad Prism[®]9 software. **Findings:** The questionnaires were completed by 574 students, with 256 (44.5.0%) males and 318 (55.4%) females. Participants who never used DSs (25.78%) were excluded from the study. The most commonly used supplement was multivitamins (24.8%), followed by vitamin D (21.1%). 26.29% used DSs based on HCP advice, while 24.41% made their own decision. The majority (65%) believed that DSs could boost their immune systems, while 35% believed that dietary supplements could always lower the risk of infecting with COVID-19. Approximately 43.7% of participants believed that DSs had no side effects. The majority of participants (46%) believed that DSs intake was not required after COVID-19 vaccination, and 56.6% believed that healthy food could be used instead of DSs. 62% of study participants continued to use DSs after being prescribed them. Approximately 67.6% said they would recommend DSs for COVID-19 prophylaxis and 63.4% said they would recommend DSs for treatment. **Conclusion:** The current study's findings highlighted the significant prevalence of DSs consumption among students at medical colleges, at Jouf university, based on HCP advice and self-decision. The study suggests educating undergraduate students on the proper use of DSs for COVID-19 treatment or prophylaxis.

Keywords: COVID-19; dietary supplements; perception; vitamins; minerals; treatment; prophylaxis; medical students

INTRODUCTION

The Food and Drug Administration (FDA) defines a dietary supplement (DS) as "a product intended for ingestion that contains a "dietary ingredient" intended to add additional nutritional value to (supplement) the diet".¹ All vitamins, minerals, amino acids, and even herbs are considered dietary

ingredients and are used to supplement essential nutrients and protect against certain diseases.¹

DS consumption has increased in many countries over the last few decades.¹ The media played a significant role in attracting public attention through advertisements, informative articles, and study reports linking Dietary supplements (DSs) to well-being and health conditions.¹ As natural products, DSs are thought to be safe and free of side effects when used to treat and/or prevent diseases.² Consequently, this has resulted in an increase in their sales.²

During the coronavirus disease 2019 (COVID-19) pandemic in 2020, advertisements claiming DSs are useful in the treatment and prevention of COVID-19 have increased, and hence their consumption¹ specially in the first period and the during the second wave (2). Despite scientific evidence that many DSs have immune-boosting, anti-inflammatory, antioxidant, and antiviral properties, COVID-19 treatment guidelines do not comment on their use (3). The worldwide increase in DSs consumption has highlighted the importance of educating medical staff so that they can properly use it and counsel patients on its use to avoid interactions and harmful effects.¹ Regardless of the uncertainty about possible efficacy against COVID-19, people believed that taking DSs would provide some protection by boosting immunity and reducing disease severity in those infected with COVID-19.⁴ The applied COVID-19 vaccines, either in an

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inactivated DNA or mRNA form as well as protein subunit have demonstrated different levels of effectiveness.⁵ Therefore, continuous optimization of these vaccines is a necessity in order to increase their efficacy. As new variants of viruses continue to emerge, boosting the individuals' immune system may enhance the effectiveness of the vaccines.⁵ Because of the aforementioned factors, serious concerns have been raised about people's perceptions and knowledge of DSs as well as their benefit and safety during COVID-19.⁴ Mukattash *et al.* conducted a multinational Middle Eastern study to determine knowledge and patterns of DS intake as a prophylactic modality during the second wave of the COVID-19 pandemic. According to the study, DS consumption was not guided by institutional recommendations or information.⁴

Adequate knowledge of DSs use for prophylactic against and treatment of COVID-19 among medical students (i.e., future health care providers) could play a significant role in controlling their use and limiting their harmful effects.

To the best of our knowledge, no previous studies have been conducted among students of medical colleges at Jouf University to assess their perception and knowledge of the consumption of DSs and their efficacy for COVID-19 prevention and treatment. This study aims to provide a thorough understanding of medical students' perceptions and knowledge of the use of DSs for COVID-19 treatment and/or prevention. The findings of this study can shed light on those medical students' knowledge gaps about DSs and inform necessary strategies to provide proper future education about DSs for COVID-19. Furthermore, this may help to close the knowledge gap, which in turn influences the attitude and behavior of medical students (future healthcare providers) positively and benefits their patients.

MATERIALS AND METHODS

The purpose of this study was to determine students' perceptions and knowledge of dietary supplement intake as a prophylactic and treatment modality for the COVID-19 pandemic at Jouf University.

The two primary objectives were to:

Determine the perception and knowledge of dietary supplements among Jouf university medical students.

Evaluate the use of DSs among students of the medical colleges at Jouf University and how the pandemic changed the pattern of DSs intake and to compare their use of DSs prior to and following vaccination against COVID-19.

Study design

This study was a cross-sectional study. Sampling was carried out conveniently through an online survey using a Google-Form web survey platform which was sent to all registered students of medical Colleges at Jouf University (Medicine, Pharmacy, Dentistry, and Applied Medical Sciences) in the second semester of academic year 1443 H via e-mail and social media platforms (Twitter, WhatsApp, and Instagram) from

February 2022 to April 2022. Students were also asked to share the questionnaire with one another.

The online sample size software (Raosoft®) (6) was used to calculate the target sample size according to the total number of the registered students in the second semester of academic year 2021-2022 which was estimated as 2780 students. A total of 574 students were included in the study.

Inclusion criteria: Any undergraduate student registered at Jouf University's medical colleges (Medicine, Dentistry, Pharmacy, and Applied Medical College) who was willing to participate and give consent in the study was included.

Exclusion criteria: Students who were not registered in Jouf University's medical colleges, did not use DSs, or did not give consent were excluded from the study.

The targeted sample size ($n = 338$) and calculated with a 5% margin of error, 95% confidence interval, and 50% response distribution.

The questionnaire consists of nineteen close-ended questions with predefined options, divided into two sections preceded by a script. This script containing information about the study nature, purpose, privacy rights, and estimated time to complete the survey before filling the questionnaire.

The questionnaire consisted of two main sections: The first section contained four questions comprehended demographic information which included gender, Student's college, consumption of dietary supplements and if the participant was infected with Corona virus before or not. The second section retrieved the participants' perception and knowledge of DSs and its role in treatment and or prophylaxis against COVID -19, vaccination, smoking, general health status, DSs intake and rate of intake during the pandemic and whether or not they would recommend DSs to a friend DSs or family.

We assessed their knowledge and perceptions of DSs use for COVID-19 prevention and treatment, taking into account that these students see themselves as future medical staff of healthcare workforce and the importance of these students playing a role in the pandemic process.

Students were informed in the invitation about the study's voluntary and anonymity nature and the option to discontinue filling out the questionnaire at any time. All participants were randomly selected and their confidentiality was maintained throughout the study no personal information was reported on the survey form. The google form's cover page included an introductory section outlining the purpose of the study, and completion of the questionnaire was considered as written consent for participation in the study as it was voluntarily.

The questionnaire was created by the study's authors after an extensive literature review, by modifying a previously published and validated questionnaire that had been shown to be a practical and reliable instrument, successfully used for knowledge and attitude assessment towards DSs during COVID-19.^{4,7} To reduce the risk of ambiguity, the questionnaire was pre-checked by two academic members who were



not involved in the survey's creation, and a pilot study was conducted on a group of 13 students (their answers were later not included in the analysis). The questionnaire was approved by the Local Committee of Bioethics and distributed to registered students at Jouf University's medical colleges after all of the corrections listed after the pre-check process. After making all of the corrections listed after the pre-check process, the questionnaire was approved by the Bioethics Committee and distributed to registered students at Jouf University's medical colleges.

The data was then automatically transferred via the link to the designated server, and at the end of the research period, the collected data was transferred to an Excel spreadsheet for analysis.

Statistical analysis

The collected data was analyzed using Descriptive analysis with categorical variables expressed as a percentage value. Analysis and graphics were performed by GraphPad Prism®9 and Microsoft Excel. A paired-sample t-test and the chi-square independence test were used to determine differences between variables and any values of $P < 0.05$ were considered

statistically significant.

The study design and conduction followed the World Medical Association's Declaration of Helsinki. The study proposal (No. 16-10-43) was approved by the Local Committee of Bioethics of Jouf University.

RESULTS

Sociodemographic findings

A total of 574 students responded to the questionnaires, 256 (44.5.0%) male, and 318 (55.4%) females, that registered at Jouf University in one of the medical colleges (Medicine, Pharmacy, Dentistry, and Applies Medical Sciences) at second semester of academic year 2021-2022. The majority were Pharmacy students (53.6%) and the minority were Dentistry students (6.8%). Approximately 37.1% of them reported that they had been infected with COVID-19 (61.9% male and 38.1% female). With regard the usage of DSs, 148 (25.78%) participants never used DSs, therefore, there were excluded from the study and were not allowed to complete the second section of the Questionnaire (Figure 1).

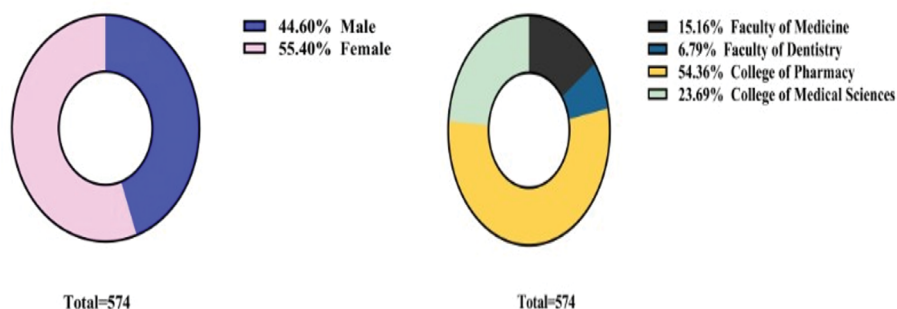


Figure 1. Characteristics of the study participants based on gender and Colleges

Health status of DSs users (n=426)

Only around 12% of participants reported having chronic medical conditions ($n = 51$). Moreover, more than 80% of them stated that their general health was excellent or good and almost similar percentage do not smoke.

As in (Table 1), the results showed that the most common supplements used were multi-vitamins 24.8 ($n=106$) followed by vitamin D 21.1% ($n = 90$). Remarkably, Vit C and Calcium as 5.4% ($n=23$) and 4.9% ($n=21$) respectively. A 36.6% ($n=156$) consumed DSs in an irregular manner.

A comparison of behaviors, type and rate of DSs intake between participants during the pre-pandemic and pandemic periods:

As shown in (Table 1), the intake of DSs during the COVID-19 pandemic period was 38.7 percent higher than before the COVID-19 pandemic period. Multivitamins product was the most commonly used supplement (24.8 percent), followed by vitamin D (21.1 percent), Zinc (10.1%), Omega-3 (8.9%), vitamin B (7%), vitamin A (6.1%), vitamin C (5.4%), and calcium (4.9%). Furthermore, the majority of participants (36.6 percent) admitted using DSs infrequently.

Questionnaire results revealed that 62% of participants continued taking DSs after being vaccinated, while 46% discontinued and believed DSs were unnecessary after receiving COVID-19 vaccination (Figure 2).

When compared to male students, female students used DSs at a significantly higher rate before the COVID-19 pandemic period (Table 2). While there was no significant difference in the rate of use of DSs after COVID-19 vaccination between male and female students. (Table 2).

Perception of participants regarding the use of DSs for treatment and prophylaxis of COVID-19:

The questionnaire included nine questions designed to assess medical students' perceptions and knowledge of using DSs for COVID-19 prophylaxis and/or treatment. While the majority (65%) believed that DSs could boost their immune systems, approximately 12% disagreed and 22.3 percent could not give an affirmative answer. Surprisingly, 35% believed that dietary supplements could always reduce the risk of getting COVID-19 infection, while 36.1 percent disagreed.

Table 1. Participants' attitude towards DSs use (N=426)

Variable	Category	Frequency (N)	Percentage (%)
When did you use the DSs?	Before COVID-19	178	41.8
	During COVID-19	60	14.1
	Before and during COVID-19	83	19.5
	During COVID-19 and discontinued after taking the vaccine	48	11.3
	Before and During COVID-19 and discontinued after taking the vaccine	24	5.6
	During Covid-19 and continued after taking vaccine	33	7.7
Which type of DSs do you use?	Vit A	26	6.1
	Vit B	30	7.0
	Vit C	23	5.4
	Vit D	90	21.1
	Zinc	43	10.1
	Calcium	21	4.9
	Omega-3	38	8.9
	Multi-vitamins	106	24.8
	Multi-vitamins and minerals	49	11.5
How often do you take DSs?	1–2 times /day	126	29.6
	1–3/week	108	25.3
	4–6/week	36	8.5
	Irregularly	156	36.6

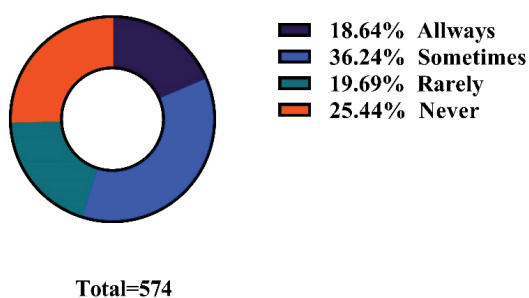


Figure 2. Dietary supplement use among participants

43.7 percent of participants believed DSs were safe, did not cause harm, and had no side effects; interestingly, the same percentage believed DSs could aid in the treatment of COVID-19.

The majority of participants (46%) believed that DSs intake was not required following COVID-19 vaccination, and 56.6%

Table 2. The Impact of Gender on the use of DSs before and after vaccination (N=426)

VARIABLE	CATEGORY	Male students	Female students	P value
Do you use Dietary supplements?	Yes	169 (29.44%)	259 (45.12%)	(0.008)**
	Never	76 (13.24%)	70 (12.2%)	
Did you stop taking DSs after being vaccinated against COVID-19?	Yes	71 (16.6%)	91 (21.3)	(0.61)
	No	110 (25.7)	156 (36.5)	

believed that healthy food is an alternative to DSs.

A sizable proportion of students (67.6 percent and 63.4 percent, respectively) stated that they would recommend DSs for COVID-19 prophylaxis and treatment. Furthermore, 62 percent of study participants continued to take DSs after being immunized against COVID-19 (Figure 3).

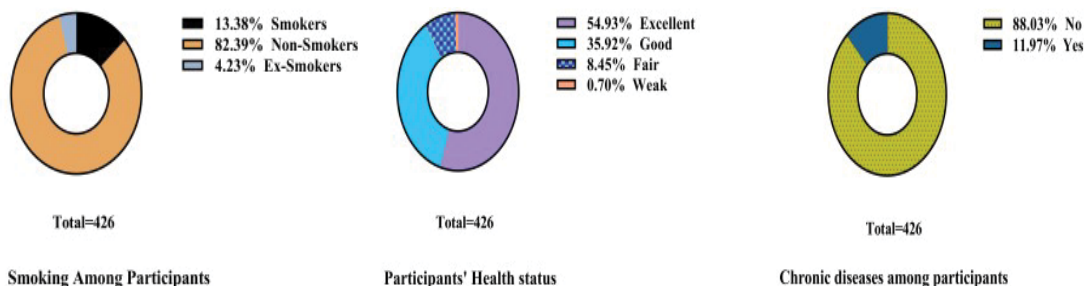


Figure 3. Participants' health status



When asked about the source of information that recommended the use of DSs, it was discovered that the medical practitioner was the most common source of recommendation (26.29%), followed by the participant's own opinion (24.41%) and advice

from friends or relatives (17.84%). Surprisingly, social media, books, and university lessons were the least popular sources of DS recommendations (15.26% and 16.2%, respectively) (Figure 4 and 5).

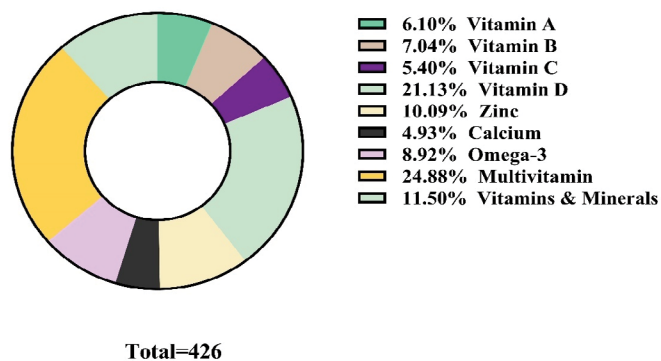


Figure 4. Type of the Dietary supplement used by participants

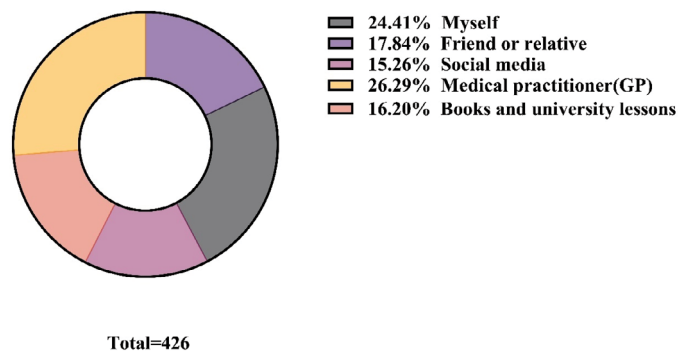


Figure 5. Motivator for Using dietary supplement

DISCUSSION

This cross-sectional study aimed to assess the perception and knowledge of students of medical colleges regarding the consumption of DSs for the prevention and treatment of COVID-19 at Jouf University. The online-survey was conducted between February and April 2022.

The number of students who responded represents nearly a fifth of all registered students at Jouf University's medical colleges in the second term of the academic year 2021-2022. With a participation rate of 53.6%, pharmacy students outnumbered all other medical students. When asked if they had ever been infected with the Corona virus, nearly one-third of those polled said yes. According to the recorded responses, the majority of participants (74.21%) used DSs. Furthermore, DSs intake during the COVID-19 pandemic period was 58.22% higher than before the pandemic. This was consistent with previous studies conducted Saudi Arabia, that found a significant increase in DSs consumption among adult population during the Pandemic time.⁸ DSs are used by many health professionals, including dietitians, physicians, and pharmacists.⁸ and medical students were no exception.

More than 80% of those polled said their overall health was excellent or good, and they did not smoke. Only about 12% of participants (n = 51) reported having chronic medical conditions.

Regarding dietary supplements, the study results revealed 24.8% of the participants used multi-vitamins, and 21.1% used vitamin D. Despite of the limited evidence-based efficiency against COVID-19, these products became popular among people due to the widespread of clinical reports highlighting the role of vitamins in fighting infections including COVID-19.¹⁰ Other studies found that vitamin D consumption increased significantly during the pandemic. Because of its potential link to COVID-19 incidence and importance to overall health.⁸ Participants consumed zinc (10.1%), omega-3 (8.9%), vitamin B (7%), vitamin A (6.1%), vitamin C (5.4%), and calcium (4.9%).

Furthermore, 36.6 percent of participants admitted to using DSs infrequently.

Following vaccination, the DSs intake continued by 62% of participants compared to 46% who stopped using DSs. Comparing male participants to female participants, females used DSs at a significantly higher rate before the COVID-19 pandemic period. These results aligned with a study carried by Merwid-Lad *et al*¹² However, there was No significant influence of gender on the decision to take DSs observed after COVID-19 vaccination between male and female students.

The assessment of medical students' perceptions and knowledge regarding the use of DSs for COVID-19 prophylaxis and/or treatment revealed that the majority (65%) believed that DSs could boost their immune systems, approximately 12% disagreed, and 22.3 percent were unable to provide an affirmative answer. Surprisingly, 35% of respondents believed that dietary supplements could always reduce the risk of infecting with COVID-19, while 36.1 percent disagreed.

A 43.7 percent of participants thought DSs were safe, did not cause harm, and had no side effects; interestingly, the same percentage thought DSs could help with COVID-19 treatment.

The nearly more than half of participants (56.6%) believed that healthy food is an alternative to DSs which was discovered to be an incorrect perception¹¹ but it was corroborated by other study carried among medical students University of Lagos (9). A well-balanced diet supplemented with necessary micronutrients may aid in providing optimal resistance to SARS-CoV-2 and a feasible, safe, and readily available therapeutic option.¹²

A significant proportion of students (67.6 percent and 63.4 percent, respectively) stated that they would recommend DSs for COVID-19 prophylaxis and treatment. Furthermore, 46% of study participants believed that DSs were still necessary after immunization against COVID-19, while 62 percent continued to take DSs.

Vaccination is considered the primary health strategy for



protecting against SARS-CoV-2 infection and has been shown to significantly reduce disease severity and mortality. Having said that, certain populations continue to be at risk for severe disease outcomes, necessitating the use of additional approaches to boost immunity and improve vaccine response, such as insuring adequate DSs status, as reported in numerous observational studies.¹³ The majority of participants (36.6%) used DSs on an irregular basis, while 29.6% used DSs once or twice daily.

Our study Also demonstrated that advice from the medical practitioner (26.29%) and self-knowledge (24.41%) were the main motivators for the participants to use DSs. Surprisingly, social media was the minor cause with only 15.26% These findings are not consistent with a recent cross-sectional study that reported that social media and the Internet were the main sources of suggestions for the participants to take DSs.^{7,11} Furthermore, it suggests a curriculum gap in which there is insufficient material in their standard textbooks to teach them about the role of DSs in both preventive and therapeutic medicine.

Seeking professional advice implies that students have a healthy curiosity and a proactive mindset toward optimal health.¹¹ However, it also implies that the recommendations for using DSs in a well-nourished population are unwise.¹¹

The findings of this study could be beneficial in educating undergraduate medical students and healthcare providers about the use of DSs when personally used or in counseling their patients. For this reason, the following studies were thoroughly evaluated in order to identify physiological mechanisms of selected DSs and their actions in relation to COVID-19 pathogenesis or interventions and outcomes related to the use of DSs in the prevention/treatment of COVID-19:

Vit D

The ability of vitamin D to modulate adaptive and innate immunity, resulting in improved immunological health and antiviral defense, suggested that it could be used to prevent and treat SARS-CoV-2 infections.⁸ Although previous research has found a link between the severity of COVID-19 disease and vitamin D deficiency, and has recommended vitamin D supplementation for COVID-19 patients who are deficient in the vitamin.^{12, 14,15} Having said that, there is no link between vitamin D deficiency and susceptibility to COVID-19 infection. Furthermore, no evidence supports the use of vitamin D for prophylaxis^{14,11}, treatment, or amelioration of disease severity¹¹ Another study suggested that vitamin D may have an additive effect on the antiviral activity of antiviral medications.¹⁶ Through its interaction with its receptor, vitamin D induces intracellular events that regulate many genes, modulating immunity in four ways: improving virus clearance via autophagy;¹⁶ suppressing the inflammatory process and cytokine storm;^{15,17} increasing (Angiotensin converting enzyme) ACE2 concentrations; and also maintaining epithelial layers intact.¹⁸ This suggested that vitamin D had a double-edged effect against COVID-19.^{16,17} The prophylactic and therapeutic potential of vit D against SARS-CoV-2 has emerged from its ability to modulate the adaptive

and innate immunity resulting in improving the immunological health and enhancing the antiviral defense.⁸ There are conflicting claims about the benefits of taking vitamin D before being diagnosed with COVID-19.¹⁸ A meta-analysis study, on the other hand, suggested adding vitamin D to the therapeutic regimen of hospitalized COVID 19 patients as an adjuvant to improve their clinical outcomes. For the treatment of COVID-19-infected patients Serum concentration should be raised above 40–60 ng/mL (100–150 nmol/L).¹⁸ Nonetheless, the optimal dose, duration, and mode of administration of vitamin D supplementation have yet to be determined and require further research.^{17,19}

Vit C

Vitamin C (ascorbic acid) is an antioxidant that functions as a cofactor for many enzyme,^{20,21} including monoxygenase and dioxygenase enzymes,¹⁹ and improves adaptive immunity by supporting numerous intrinsic cellular immune functions.^{20,21} Respiratory infections, such as pneumonia, can be fatal in patients with vitamin C deficiency.²⁰

Tehrani et al.²³ demonstrated that high doses of intravenous vitamin C treatment improved respiratory rate and peripheral oxygen saturation in COVID-19 patients suffering from pneumonia.²⁰ A 2,000 mg daily dose of vit C-complex is effective without causing any side-effect.²⁴ Another study claimed that using vitamin C reduced hospital mortality. More research, particularly randomized clinical trials, is needed to back up these findings.²⁵

Vit A

Retinol, a form of vitamin A, is the precursor to two active metabolites: retinal and retinoic acid. Retinal is required for vision, and retinoic acid acts as an intracellular messenger that regulates gene transcription. The daily recommended dose of vitamin A for adult males is 900 µg and 700 µg for females. Deficiency is common in poor countries, particularly among children and pregnant and lactating women.¹²

To date, no evidence supports the beneficial clinical effects of vitamin A supplementation for the treatment of COVID-19 in adult patients, while in children with severe chronic malnutrition, there are significant effects in preventing lower respiratory tract infections, albeit with limited evidence. Theoretically, it is worth noting that, particularly in the second inflammatory phase of the disease, vitamin A supplementation may be beneficial in COVID-19 treatment.¹² A clinical study, on the other hand, suggested the use of vitamin A supplement to improve some clinical (body ache, weakness, and fever) and paraclinical symptoms such as reduction of White Blood Cells (WBC) and C-reactive protein (CRP) in COVID-19 hospitalized patients.²⁶

Vit E

The lipophilic antioxidant vitamin E is found in cell membranes, lipids, plasma, and red blood cells.²¹ A previous study in elderly male patients with community-acquired pneumonia showed that vitamin E treatment improved their conditions.²¹ It is hypothesized to work by lowering COX and PGE2, modulating



T cell functions, and regulating the cell cycle.²⁷ As a result, it is suggested that supplementing with a nutritional source of Vit E for deficiency treatment in COVID-19 patients may improve the immune response and antioxidant status during the disease.^{21,22}

Vit B

B vitamins are a class of water-soluble vitamins, and each one plays an important role in the treatment of COVID-19. B vitamins are essential for cell functions such as energy metabolism and immunity because they all function as coenzyme.^{28,29} Furthermore, they reduce cytokine levels, maintain endothelial integrity, decrease hypercoagulability, and improve respiratory rate. As a result, hospitalization may be reduced.²⁹

According to the literature, Vit B₁ (Thiamine) plays an important role in immune response and is linked to a lower risk of cardiovascular (CV) disease, type 2 diabetes, and kidney disease, among many others. Thiamine deficiency can lead to abnormal immune responses, CV events, and inflammation.²⁹ Patients infected with SARS-CoV-2 who are deficient in thiamine may develop severe symptoms due to an insufficient antibody response.²⁹ Therefore, adequate thiamine levels may aid in the implementation of appropriate immune responses during SARS-CoV-2 infection.²⁹

Folate or B₉ can be given in 400 g doses to both adult males and females. In addition to its role as a coenzyme in the methylation reaction of nucleic acids, protein synthesis, and ATP synthesis, folate influences NK cell cytotoxicity and cytokine secretion in response to pathogens.¹²

Vit B₁₂ deficiency appears to lower NK cell activity and total lymphocyte count (CD4+ and CD8+ T cells), both of which are associated with COVID 19.^{12,18} Recently, vitamin B₁₂ supplementation in combination with vitamin D and Mg was shown to improve oxygenation rate and reduce the need for intensive care, or both, in elderly COVID-19 patients. These findings necessitate additional research to determine the effect of vitamin B₁₂ on the severity of COVID-19.¹²

Omega-3

Omega-3 (ω 3 or n-3) fatty acids are natural healthy found in abundant in seafood and marine oils fats. They inhibit the formation of proinflammatory/prothrombotic lipid mediators including eicosanoids and docosanoid.³⁰

Many studies considered omega 3 fatty acids to have potential in protecting against infection with or treatment of COVID-19 by reducing duration of symptoms, lowering the risk of developing renal and respiratory failure, and thus decreasing mortality rate.³¹ because they act as substrates for the formation of anti-inflammatory resolvins such as protectins and resolvins.³⁰

Zinc

The importance of Zinc, a naturally occurring trace minerals, emerged from its role in cells growth, development, and proliferation, enzymatic functions, DNA synthesis, and upregulation of translational factors.³² Despite the ubiquity of exact function, Zinc aids in growth and functionality maintenance of immune cells such as neutrophils and NK

cells.^{33,32} Zinc Deficiency severely debilitates the adaptive and the immune system and cause cytokine suppression.³³

Nevertheless, in excess, zinc can weaken of the immune system, therefore, its regulated homeostasis is required for zinc to serve as immunomodulator and anti-inflammatory.³³

Zinc is a common element found in dairy products, red and white meats, beans and nuts.³² However, zinc deficiency is projected to be between 17% to 20% worldwide,³⁴ with over two billion individuals in poor nations are at risk.³² Notably, in high income nations, despite of zinc availability, its deficiency is highly common in vegetarians, the elderly, and patients with chronic disease such as liver cirrhosis and inflammatory bowel disease.³⁴

The antiviral activity of zinc, at dose of 600 mg/day, was reported against many viruses such as Influenza.³⁵ and SARS coronavirus.³² evident by generation of both innate and humoral responses.³⁵ Therefore, a hypothesis was emerged regarding the potential benefit for prophylaxis and treatment of COVID-19.³⁶

Although many mechanisms of action, either direct or indirect, have been proposed to explain antiviral activity.³⁵ the uncertainty about the mechanism of action as an antiviral bursts conflicting claim about its clinical effectiveness for viral infection prevention and/or treatment.³⁵ In the elderly, zinc as a daily supplement at dose of 30 mg/day, is suggested to be adequate for boosting their immune system and decrease their susceptibility to infections such as pneumonia.³⁵ The potential efficacy of zinc as antiviral can be divided into two categories:

As a supplement to boost antiviral activity and systemic immunity in deficient patients.

As a treatment to aid in viral replication suppression and accompanying pathological symptoms.³⁴

Calcium

Calcium inhibits the enzyme dihydroorotate dehydrogenase (DHODH), which is required for pyrimidine biosynthesis in active lymphocytes to meet their pyrimidine requirements. Similarly, viruses use the DHODH of the host cell during replication, implying that it is a promising therapeutic target in the treatment of virus infections such as COVID-19.³⁷ Furthermore, DHODH suppression has innate and adaptive immunomodulatory effects on some antiviral genes. Calcium-containing supplements reduced T cell proliferation and cytokine production in autoimmunity models, implying that the hyperinflammation that frequently accompanies moderate and severe COVID19 hospitalized cases could be reduced by blocking DHODH enzyme.³⁷ Despite the importance of calcium consumption for SARS-CoV-2 cellular invasion, the role of hypocalcemia in COVID-19 infection has yet to be investigated. As a result, likely disease-specific hypocalcemia, which occurs in COVID-19 patients and worsens in severe cases, is associated with a high rate of mortality, prolonged hospitalization, and increased need for ICU. Monitoring calcium serum levels and treating hypocalcemia earlier in COVID-19 patients may help improve prognosis and is also recommended at hospital



discharge.³⁸

In general, respiratory infections are particularly serious in individuals who suffer from malnutrition.³⁰ and COVID-19 is no exception.³⁹ Inevitably, prior to the vaccine and until now, people have used DSs in prophylaxis and curbing COVID-19.¹² As previously stated, numerous studies argued that DSs may have a potential therapeutic effect in COVID-19 patients because they have been shown to be effective as adjuvant therapies in COVID-19 patients.^{12,40} Nonetheless, in terms of safety, these findings should be interpreted with caution due to uncertainty about the overall quality of the included trials. Well-designed RCTs will be required in the future to address in deep their real scientific role.²²

Up to date, there is a lack of adequate scientific evidences to support either their use in the prevention or treatment of COVID-19. However, some of them, such as vitamin D, vitamin C, and zinc, have been widely prescribed by doctors, sometimes in high bolus doses, ignoring potential side effects and interactions.¹² It is important to note that, regardless of how scientifically sound the use of some DSs in COVID-19 therapy might be, the potential beneficial effects should be investigated and evaluated in RCT before administration and the recommended dose should not be exceeded for the general population and age group, with the exception of clinical studies.¹²

More than three years have passed since the announcement of COVID-19 by WHO, however, medical specialists are still searching and learning about the disease. As a result, therapeutic protocols are constantly being updated and improved.¹² However, as new SARS-CoV-2 variants could emerge in the future, people must take precautionary measures and boost their immune systems to protect their lives.¹² A plethora of studies recommended DSs to maintain adequate macromutational status to enhance vaccine immunogenicity and effectiveness.¹³

The most concerning issue right now is post-COVID, for which no therapeutic options have been validated or available.²² In this context, DSs could represent new strategies for developing new therapies to treat post-COVID symptoms and effects.²²

Limitations of the study:

As a cross-sectional study, only a glimpse of participant responses could be provided at the time of the survey, reflecting on the study's causality. Furthermore, because the collected data was self-reported, there is a possibility of under- or over-reporting of information. Furthermore, nearly half of our sample (54.36%) was made up of Pharmacy students, which may have influenced the use of DSs.

Another limitation was the lack of information in medical curricula about viruses like SARS, which impose stigma similar SARS-CoV-19 viruses, prior to the COVID-19 pandemic. Additionally, because this study was conducted among undergraduate students at Jouf University, the findings are limited in their applicability to other medical schools in other parts of the country.

CONCLUSIONS

The current cross-sectional study provided a relatively holistic view of medical students' DSs consumption and perceptions about their role in treating or protecting against COVID-19, and highlighted the role of students' self-acquired knowledge and advice from medical practitioners in DS intake.

The rate of DSs consumption among participants is high, but it is not evidence-based or guided by Ministry of Health recommendations.

There was a lack of evidence-based knowledge about DSs and their efficacy in the treatment and prophylaxis of COVID-19.

The majority of participants (61.3%) consumed DSs before and during the COVID-19 pandemic, believed in its role in boosting immune system as well as treating and protecting against COVID-19, and will recommend DSs to others.

Using self-awareness as a motivator for using DSs was ineffective, leading to certain misconceptions.

The introduction of COVID-19 vaccines has reduced DSs intake, as approximately more than one-third of participants discontinuing DSs following vaccination against COVID-19.

This pioneering effort in the study suggested that more education on DSs is necessary so that future health professionals can provide adequate advice to patients and the community as a whole about appropriate and safe DSs consumption.

Recommendations:

Use of these over-the-counter DSs products either as sole remedies or as prophylactics against COVID-19 must be evidence-based and guided by relevant clinical trials and recommendations of Ministry of health.

Curriculums of medical colleges should be updated regularly regarding DSs and their prophylactic and therapeutic potentials against COVID-19. Until then, extra curriculum activities such as journal clubs and awareness campaigns must be held in the University to improve students' perception and fill the knowledge gaps.

Information about indications, appropriate use, and doses of vitamins and minerals, as per the most recent literature, should be disseminated and taught to all health practitioners and medical students through circulation of online periodical newsletters published by authorized body.

Although these recommendations appear to be simple and insignificant, they pave the way for the safe and effective use of DSs.

ABBREVIATIONS

ACE2	Angiotensin-2 converting enzyme
COVID-19	Coronavirus disease
COX	Cyclooxygenase enzyme
CRP	C-reactive protein



DSs	Dietary Supplements
HCP	Health care provider
HDIVC	High-Dose Intravenous Vitamin C
ICU	Intensive care unit
PEG2	Prostaglandin E2
RCT	Randomized controlled trial
SARS-CoV-2	severe acute respiratory syndrome

FUNDING

No funding received to support the study.

DECLARATIONS

The data collected during the study are available upon request from the corresponding author.

CONFLICTS OF INTEREST

Authors declare no conflicts of interests.

ACKNOWLEDGMENTS

Authors would like to thank all participants students who volunteered their time to make this study possible are greatly appreciated.

This article is original and has not been published elsewhere, nor is it currently being considered for publication by any journal.

AUTHOR CONTRIBUTIONS

E. E. and N. A. conceptualized the study, while all authors contributed to the methodology, data collection, and analysis. E. E. was the primary author, but all authors contributed to the writing, read, and approved the final version of the manuscript.

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