

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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Contents lists available at ScienceDirect

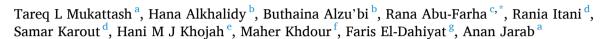
European Journal of Integrative Medicine

journal homepage: www.sciencedirect.com/journal/european-journal-of-integrative-medicine



Research paper

Dietary supplements intake during the second wave of COVID-19 pandemic: A multinational Middle Eastern study



- a Department of Clinical Pharmacy, Faculty of Pharmacy, Jordan University of Science and Technology, P. O. Box 3030, Irbid, Jordan
- b Department of Nutrition and Food Technology, Faculty of Agriculture, Jordan University of Science and Technology, P. O. Box 3030, Irbid, Jordan
- Clinical Pharmacy and Therapeutics Department, Faculty of Pharmacy, Applied Science Private University, Amman, Jordan
- d Pharmacy Practice Department, Faculty of Pharmacy, Beirut Arab University, P.O. Box 11-5020, Riad El Solh, 1107 2809, Beirut, Lebanon
- e Department of Clinical and Hospital Pharmacy, College of Pharmacy, Taibah University, P.O. Box: 30051, 41477, Madinah, Kingdom of Saudi Arabia
- ^f Faculty of Pharmacy, Al-Quds University, Jerusalem, Palestine
- g Clinical Pharmacy Program, College of Pharmacy, Al-Ain University, P. O. Box 64141, Al Ain, United Arab Emirates

ARTICLE INFO

Keywords: COVID-19 Dietary supplements Vitamins Prophylaxis Middle East

ABSTRACT

Introduction: Despite the controversy about the benefits of dietary supplements in treating or preventing COVID-19, their use has increased worldwide even with the introduction of relevant vaccines. Thus, this study aimed to investigate the perception of the Middle Eastern Arab public of dietary supplements as prophylactic or therapeutic agents against COVID-19, and their consumption during the second wave of the COVID-19 pandemic. Methods: A validated, pilot tested online survey was distributed through social networking platforms in Lebanon, the Kingdom of Saudi Arabia, Palestine, Jordan, and the United Arab Emirates. Responses underwent various statistical analyses.

Results: A total of 2,100 responses were included. Around 44% of participants reported changes in their dietary behavior during COVID-19, and 70% believed that healthy habits may prevent the infection. Moreover, 21% believed that dietary supplements surely protect against COVID-19 and 45% thought they aid in treating it. Users of supplements during the second wave of the pandemic counted for 47%, who declared they were influenced by the media, healthcare providers, or close contacts. Most used supplements included Vitamins C and D and zinc. Only 34% of participants read supplement leaflets. The use of supplements was significantly correlated with being female and exercising, as revealed by the odds ratio and logistic regression analysis.

Conclusions: In line with other areas of the world, the use of dietary supplements in the Middle East against COVID-19 is not evidence-based. Competent health authorities should play their role in spreading sound awareness among the public regarding this issue.

1. Introduction

With the increased demand for novel therapies against the rapidly transmissible SARS-CoV-2, several treatment options have been investigated and tried out of desperation. Healthcare communities, scientists, and pharmaceutical and nutri-pharmaceutical companies are struggling to discover novel therapeutic strategies to vanquish COVID-19 [1]. Some of these treatment modalities have shown initial promise with a positive impact while others have led to negative consequences on disease severity and mortality [2,3]. Moreover, worldwide societies have adopted non-pharmacological preventative strategies, such as social distancing, public hygiene and wearing face masks as the most appropriate current measures to protect themselves and reduce community transmission of COVID-19 [4-7].

At the same time, due to the unknown and uncertainty of possible efficacy against COVID-19, individuals have sought additional protective measures through the intake of dietary supplementation and nutraceuticals. It was hoped that these supplements might provide some protection from SARS-CoV-2 infection by boosting the immunity, and may also help reduce disease severity for those who contract COVID-19

E-mail addresses: tlmukattash@just.edu.jo (T.L. Mukattash), haalkhalidy@just.edu.jo (H. Alkhalidy), r abufarha@asu.edu.jo (R. Abu-Farha), r.itani@bau.edu.lb (R. Itani), s.karout@bau.edu.lb (S. Karout), hkhojah@taibahu.edu.sa (H.M.J. Khojah), faris.dahiyat@aau.ac.ae (F. El-Dahiyat), asjarab@just.edu.jo (A. Jarab).

https://doi.org/10.1016/j.eujim.2022.102102

Received 29 October 2021; Received in revised form 24 December 2021; Accepted 9 January 2022 Available online 12 January 2022 1876-3820/© 2022 Elsevier GmbH. All rights reserved.





^{*} Corresponding author.

[8–10]. Despite the fact that different COVID-19 vaccines have been developed and received by more than 31% of the world population, and that many pharmacologic treatments are becoming available, the demand for dietary supplements during the COVID-19 outbreak is drastically increasing [11–13].

Significant concerns were raised about consumer perceptions of nutraceuticals in the time of COVID-19 and their actual clinical benefit and safety [8]. In China, USA, Canada, and France, it was found that customers were significantly interested in nutraceuticals and that their sales has largely increased [10,14–17]. Another American survey has shown that 84% of individuals were confident about the quality and safety of dietary supplements [18]. However, while there is a lack of evidence about the efficacy and safety of many of these ingredients in COVID-19 patients, evidence suggests that the nutritional status of the patient is strongly correlated with COVID-19 severity and mortality [8, 12,19].

Recent studies have found that the administration of high doses of the vitamins C, D, and E, in addition to omega-3 fatty acids and zinc may potentially have a clinical benefit for hospitalized patients. Due to their immunomodulatory and antioxidant effects, these supplements may reduce the viral load, the disease severity, and hence the hospital stay [8,9,17,20–22]. Moreover, the lack of these nutritional substances is associated with higher susceptibility to infections and dysfunction of the immune system [20,23]. However, there are no explicit randomized controlled trials on the role of vitamin supplementation in the context of COVID-19 infection, neither in the prevention nor in the treatment, and their safety profile is questionable. Studies were mainly based on the physiology and pharmacology of vitamin supplementation, and their roles on clinical studies on infections [24–26]. Therefore, clinical trials are needed to confirm the role these dietary supplements may have for COVID-19 treatment.

It is worth noticing that the law does not defend and protect the consumer rights adequately, as nutraceutical companies do not need to get Food and Drug Administration (FDA) approval for registration. Hence responsibilities are ascribed to manufacturing companies to seek approval from the Academy of Sciences to ensure quality, efficacy and safety of these product before manufacturing and selling them [27–29].

To the best of our knowledge, there have been no multinational comprehensive studies conducted in the Middle Eastern countries to assess the prevalence, sources of knowledge, and factors and beliefs related to the consumption of dietary supplements and their efficacy and safety in the era of COVID-19. Investigating these issues would be of extreme importance due to the absence of general agreement and the limited evidence-based research on the use of dietary supplements for this infection. Therefore, this study aimed to identify the perceptions and patterns of intake of dietary supplements as a prophylactic modality during the second wave of COVID-19 pandemic across several Middle East countries.

2. Methods

2.1. Study design

A cross-sectional web-based survey was conducted during the second wave of the COVID-19 pandemic between January 10, 2021, and March 31, 2021. A link to the Google Form questionnaire was distributed through various social networking platforms, targeting adults (age > 18 years) residing in five Middle Eastern Arabic-speaking countries—Jordan, Lebanon, Palestine, Kingdom of Saudi Arabia (KSA), and United Arab Emirates (UAE). Participants' recruitment was conducted using a non-probability snowball sampling technique, where participants were encouraged to share the link with their acquaintances. The questionnaire was self-administered and presented in two languages, English and Arabic, according to participants' preferences.

2.2. Questionnaire development and structure

The questionnaire was designed after a thorough review of relevant studies [13,30–33]. In addition, three experts in public health, pharmacy practice, and clinical nutrition research, other than the research team, reviewed the questionnaire for face and content validity. They assessed the questionnaire items' relevance, specificity, and comprehensiveness. Afterwards, the questionnaire was translated to colloquial Arabic (the participants' native language) by one author, and back-translated by another author, for validation.

The questionnaire consisted of 31 close-ended questions with predefined options, divided into five sections preceded by an introduction. The introduction outlined the study nature, purpose, anonymity, and estimated time for completion followed by an informed consent statement. The first section was dedicated to retrieve participants' sociodemographic data. The second section recorded the participants' general health status. The third section assessed the participants' lifestyle changes and health-related behaviors during the pandemic. The fourth section was concerned with the participants' perception of dietary supplements' efficacy and safety in preventing COVID-19. Finally, the fifth section investigated the pattern of use of dietary supplements during the second wave of the COVID-19 pandemic to prevent contracting the infection.

2.3. The pilot test

A pilot test was performed among 40 volunteers from the general population in Lebanon, KSA, and Jordan (25 completed the English version, and the other 15 completed the Arabic version) to verify its comprehension and cultural acceptability. The participants were requested to evaluate the questionnaire structure, clarity, and length, and to give their overall impression. Then some questions were remodeled based on their feedback. One week later, the questionnaire was retested on the same participants to ensure its reliability and reproducibility. The data obtained from the pilot test were not included in the final data analysis.

2.4. Statistical analysis

The 22nd version of the statistical package for the social science (SPSS®) was used for data analysis. The median \pm interquartile range (IQR) and frequency (or percentages) were used for continuous and categorical variables, respectively. Univariate and multivariate logistic regression were used to screen for predictors of taking dietary supplements. Variables that were found to be significant on a single predictor level (P < 0.25), using univariate logistic regression analysis, were entered into multiple logistic regression analyses. Variables were selected after checking their independence, where Pearson's correlation coefficient (r) of less than 0.9 indicated the absence of multicollinearity between the independent variables in regression analysis. In the multiple logistic regression analysis, variables that were independently associated with taking dietary supplements were identified. Statistical significance was considered at $P \le 0.05$.

2.5. Ethical considerations

The study design and conduction followed the World Medical Association's Declaration of Helsinki guidance [34]. In addition, the study protocol was approved by the Institutional Review Board of King Abdullah University Hospital, University of Science & Technology, Jordan (Reference No. 20210474). Participation in the study was voluntary, and the purpose of the study was explained before accessing the questionnaire. Electronic informed consent of the participants was obtained, and participants had the right to defer from submitting their responses at any time. The anonymity of respondents was preserved.

3. Results

3.1. Demographic characteristics of the study sample

A total of 2100 completed forms from the five selected countries were included. Participants had a median age of 26.0 years (IQR = 19.0) with 71.8% of them (n=1509) having higher education degrees. Around 59% of the participants were females (n=1,245), and almost half of them were married (n=950,45.2%). Finally, around one-quarter of the participants (n=593,28.2%) held a medical-related degree. More details about participants' demographic characteristics are presented in Table 1.

3.2. Medical history of the study sample

Table 2 summarizes the participants' health information. Only 17.0% of the recruited participants (n=357) reported being previously infected with COVID-19, and around 14% of them reported having chronic medical conditions (n=302). The most common reported chronic diseases were hypertension ($n=131,\ 43.4\%$), followed by diabetes mellitus ($n=95,\ 31.5\%$) and bronchial asthma ($n=43,\ 14.2\%$). Moreover, nearly two-thirds of the participants stated that their general health was excellent or very good.

3.3. Health-related behavior and perception of dietary supplements during COVID-19 outbreak

The participants were asked about their dietary behavior during the COVID-19 outbreak (Table 3). Of these, 43.8% (n=920) revealed that their dietary behavior was changed for the better. Interestingly, only 21.3% (n=447) believed that dietary supplements could always reduce the chance of getting COVID-19 infection. In addition, 45.4% of the participants (n=953) thought that dietary supplements could help in treating a person infected with COVID-19.

It was found that 46.6% of the participants (n = 978) reported using dietary supplements for the prevention of COVID-19. When asked about the source of recommendation of the dietary supplements, 37.5% of

Table 1. Demographic characteristics of the study participants (n = 2100).

Variable	n (%)
Age (years)	26.0 ± 19.0^{a}
Sex	855 (40.7)
Male	1245 (59.3)
Female	
Country of residence	568 (27.0)
Jordan	532 (25.3)
Lebanon	348 (16.6)
Kingdom of Saudi Arabia	165 (7.9)
Palestine	487 (32.2)
United Arab Emirates	
Marital status	950 (45.2)
Married	1150 (54.7)
Unmarried ^b	
Educational level	385 (18.3)
School-level or below	208 (9.9)
Diploma	1153 (54.9)
Bachelor	354 (16.9)
Masters/PhD	
Employment	
Student	835 (39.8)
Unemployed	309 (14.7)
Employed	849 (40.4)
Retired	107 (5.1)
Holding a medical-related degree	
No	1507 (71.8)
Yes	593 (28.2)

^a Median \pm inter-quartile range.

Table 2. Medical characteristics of the study participants (n = 2100).

Variable	n (%)
Exercising status	856 (40.8)
Do not exercise	522 (24.9)
Once a week	446 (21.2)
2–3 times a week	163 (7.8)
4–6 times a week	113 (5.4)
Daily	
Previous infection with COVID-19	1743 (83.0)
No	357 (17.0)
Yes	
General health status	495 (23.6)
Excellent	950 (45.2)
Very good	531 (25.3)
Good	97 (4.6)
Fair	27 (1.3)
Weak	
Chronic diseases	1798 (85.6)
No	302 (14.4)
Yes	
Smoking status	1555 (74.0)
Non-smoker	434 (20.7)
Smoker	111 (5.3)
Ex-smoker	

Table 3. Health-related behavior and perception of dietary supplements during COVID-19 outbreak (n = 2100).

Question	n (%)
Have your dietary habit changed since the beginning of the	920 (43.8)
COVID-19?	552 (26.3)
Yes, it changed for the better	396 (18.9)
Yes, it changed for the worse	232 (11.0)
No	
I cannot specify	
Do you think that you need to improve your immunity by	428 (20.0)
changing some unhealthy dietary habits?	1470
No	(70.0)
Yes	202 (9.6)
I do not know	
Do you think that following healthy habits may reduce your	406 (19.3)
chance of getting COVID-19?	1463
No	(69.7)
Yes	231 (11.0)
I do not know	
Do you think that you need to improve your immunity by taking	440 (21.0)
dietary supplements (such as vitamins, minerals, herbs, and	1500
other natural products)?	(71.4)
No	160 (7.6)
Yes	
I do not know	
Do you think that taking dietary supplements may reduce your	423 (20.1)
chance of getting COVID-19?	447 (21.3)
No	320 (15.2)
Yes, always	910 (43.3)
Yes, in case of vitamin deficiency	
I do not know	
Do you think that dietary supplements substitute healthy eating in	1222
enhancing immunity against COVID-19?	(85.2)
No	396 (18.9)
Yes	482 (23.0)
I do not know	
Do you think that dietary supplements are safe and cause no side	866 (41.2)
effects?	609 (29.0)
No	625 (29.8)
Yes	
I do not know	
Do you think that taking dietary supplements helps in treating a	440 (20.9)
person infected with COVID-19?	953 (45.4)
No	707 (33.7)
Yes	
I do not know	

^b Includes single, divorced, and widowed.

these users (n=368) reported following the media such as television and social media platforms, 34.6% (n=338) reported consulting healthcare providers including pharmacists, dieticians, and physicians, and 27.9% (n=272) reported following the advice of relatives or friends. It was found the most common supplements used were vitamin C (n=762, 77.8%), vitamin D (n=545, 55.7%), and zinc (n=420, 42.9%) (Fig. 1). These users were also asked if they read the leaflet attached with the dietary supplements, where 34.0% of them (n=333) reported reading it while the remaining 66.0% (n=645) replied in the negative. Reasons behind reading the leaflet were; to know side effects (n=253, 76.1%), to know benefits (n=234, 70.3%), and to know the proper dose (n=213, 63.9%).

Reasons for not taking dietary supplements are presented in Fig. 2. Not having vitamin deficiency was the most common reported reason for not taking them (n=335, 29.9%) followed by inability to adhere to them (n=263, 23.4%) and the high cost of the supplements (n=259, 23.1%).

3.4. Predictors of taking dietary supplements among the study participants

Logistic regression analysis of factors associated with taking dietary supplements among the study participants (Table 4) revealed that females and those who perform routine exercise showed a significantly higher intake of dietary supplements during the COVID-19 pandemic comparing to others ($P \leq 0.05$). In addition, participants from Lebanon, KSA, and the UAE showed a significantly lower intake of dietary supplements compared to the Jordanians.

4. Discussion

The dearth of effective medications to treat COVID-19 has shifted the public's attention to dietary supplements to augment their immunity and prevent contracting the infection [10,13,35]. These products are exempted from prescreening or any examination to investigate their quality, safety, and efficacy before being released to the public [29,36]. Moreover, marketing and advertising dietary supplements are permitted in several countries, thus exposing consumers' health to falsified hyperbolic health claims, lacking rigorous evidence to support their efficacy [28,37]. The US Food and Drug Administration (FDA) and the Federal Trade Commission (FTC) have issued warnings to several companies selling products that deceive consumers and claim to prevent or

treat COVID-19 [38].

This first multinational study that investigated Middle Eastern Arab public's perception and use of dietary supplements during the COVID-19 pandemic has revealed that the Arab population perceive dietary supplements as immune-boosting agents (71.4%). In addition, they believe these supplements are effective in treating COVID-19 patients (45.4%), and that they are safe with no side effects (29%). Moreover, 21.3% of the participants believed that dietary supplements are essential in preventing COVID-19, while only 15.2% of them recognized dietary supplements to be useful only in cases of deficiencies.

The literature has consistently revealed a common substantial misconception that natural health products and dietary supplements are of good quality, posing no health risk, and generally being safer than prescription medications [39,40]. A recent study has investigated the beliefs about the use of herbal remedies and/or dietary supplements as a protective measure. That study revealed that more than one-third of the participants (34.4%) believe that certain products, such as garlic and Vitamin C, enhance the immunity and reduce the chance of contracting COVID-19 [41]. Noteworthy, the potential prophylactic and therapeutic efficacy of various dietary supplements in mitigating the COVID-19 pandemic has not been established yet [15].

In a large cohort study conducted in the UK, the consumption of omega-3 fatty acids, probiotics, multivitamins, or vitamin D supplements were associated with a lower risk of being infected by COVID-19 virus, while no association was found between the risk of infection and vitamin C, zinc, or garlic supplements intake [31]. In addition, vitamin D and B supplementations were thought to be associated with a decreased risk of mortality among severely infected COVID-19 patients [42]. However, although there is strong scientific evidence supporting the correlation between the mortality rate and severity of COVID-19 infection and blood levels of Vitamin D, still there is an open debate on the causal relationship [43].

A case-control study in Saudi Arabia showed that COVID-19 patients had lower serum levels of vitamin D compared to controls, and severe vitamin D deficiency was a predictor for COVID-19 mortality [44]. Furthermore, it was suggested that zinc supplementation might be beneficial in the prevention and treatment of COVID-19 in patients having cardiovascular diseases, particularly for patients using medications that may increase the risk of being infected by COVID-19 [45]. Various other studies have found that doses higher than the recommended daily dose of Vitamin C, E and zinc may be effective in

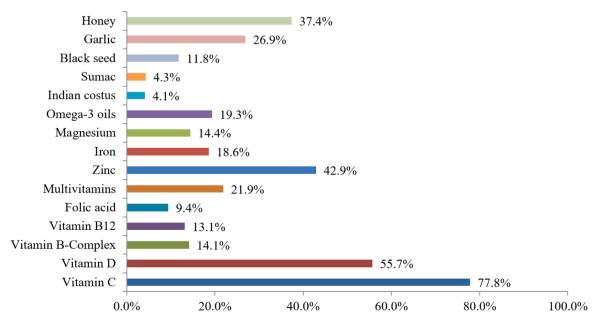


Fig. 1. Most common dietary supplements used to prevent COVID-19 by the study participants. n = 978 out of 2100 (46.6%).

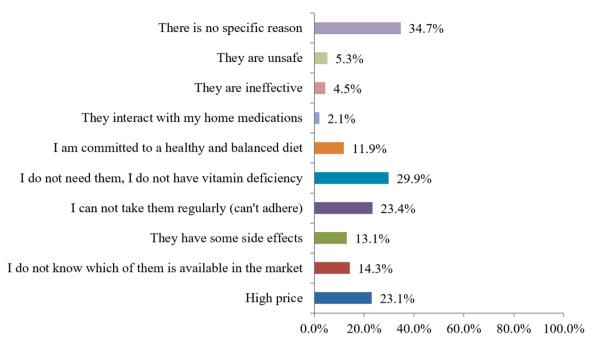


Fig. 2. Reasons for not taking dietary supplements during the COVID-19 pandemic as perceived by the study participants. n = 1122 out of 2100 (53.4%).

Table 4. Assessment of factors affecting participants' behavior of taking dietary supplements during COVID-19 pandemic (n = 2100).

Parameter	Taking dietary suppleme Using simple logistic regression		Using n	ents [0: no, 1: yes] Using multiple logistic regression	
	OR	P	OR	P	
Sex	Reference	<	1.561	<	
Male	1.541	0.001^{a}		0.001^{b}	
Female					
Country of residence	Reference				
Jordan	0.511	<	0.635	0.002^{b}	
Lebanon	0.540	0.001^{a}	0.612	0.001^{b}	
Kingdom of Saudi Arabia	0.855	<	0.801	0.247	
Palestine	0.534	0.001^{a}	0.639	0.001^{b}	
United Arab Emirates		0.376			
		<			
		0.001^{a}			
Marital status	Reference	0.001^{a}	0.834	0.146	
Married	0.736				
Unmarried					
Educational level	Reference	0.003^{a}	1.151	0.203	
Diploma or below	1.332				
Bachelor/postgraduate					
Holding a medical-related degree	Reference	0.001^{a}	1.227	0.060	
No	1.376				
Yes					
Smoking status	Reference	0.675	-	-	
Non-smoker/Ex-smoker	1.046				
Current smoker					
Exercising status	Reference	0.080^{a}	1.384	0.001^{b}	
Do not exercise	1.169				
Exercising					
Do you suffer from any chronic	Reference	0.742	-	-	
disease?	0.960				
No					
Yes					

OR, odds ratio.

decreasing viral load and hospital stay due to COVID-19 [46,47].

Hamulka et al. conducted a Google Trend analysis and crosssectional studies that revealed an increased worldwide interest and consumption of immune-related supplements during the pandemic, in particular vitamin C, vitamin D, zinc, omega-3, garlic, and ginger [13]. These supplements have attracted the public's attention in the desire to boost their immunity and mitigate the COVID-19 pandemic. Nonetheless, despite theoretical support for their immunomodulatory effect, evidence supporting their efficacy in treating or preventing COVID-19 is still controversial, based on retrospective observational studies, and dietary supplements are currently under investigation by several registered randomized controlled trials [15,48-53]. The skepticism surrounding the use of dietary supplements and the lack of profound evidence did not refrain the public from seeking these products [13]. Remarkably, almost half of the current study's participants (46.6%) reported receiving dietary supplements to prevent contracting COVID-19, where the Jordanians were the most common consumers. This finding is supported by a previous study that revealed a high intake of dietary products and herbal remedies among the Jordanians (80%) [54]. The justification for this high intake could be due to the affordability, availability, and acceptability of dietary supplements in the Jordanian culture, which made users more confident with adopting these products for both therapeutic and prophylactic purposes.

Vitamin C (77.8%), vitamin D (55.7%), and zinc (42.9%) were the most used supplements among the Arab populations of this study. Likewise, 37.7% of the Chinese residents were found to consume various dietary supplements, commonly vitamin C and probiotics, to cope with the COVID-19 pandemic16]]. This high intake of dietary supplements is accounted for by the wide-spread of preliminary information through media supporting the use of dietary supplements in enhancing immunity and combating the COVID-19 pandemic, the ready availability of various products in the market for consumers without the need for prescriptions, and the common misconception about the safety of the dietary supplements [55]. On the other hand, the consumption of nutritional supplements may also be influenced by the practices of healthcare providers who use and recommend them. For example, in Turkey, 94.5% of the dietitians preferred the use of dietary supplements (with many of them being encouraged by doctors), 46.1% used medicinal herbs, and 34.9% used functional foods during the pandemic to avoid COVID-19 infection [56].

Worth mentioning is that dietary supplements' adverse effects are not systematically reported and monitored [55]. In fact, high doses of vitamins and minerals can induce toxicity and potentially interact with

^a Eligible for entry into multiple logistic regression.

^b Significant at $P \leq 0.05$.

concurrent medications, leading to sub- or supra-therapeutic effects [57]. For example, a recent study suggested the use of iron chelators or the decreased intake of iron as therapeutic targets in COVID-19 patients due to the negative correlation between COVID-19 severity and the serum levels of iron [58].

The public response once again seems to be highly influenced by lay information sources for adopting dietary supplements, where more than one third (37.5%) of our participants stated receiving dietary supplements based on the recommendations promoted on social platforms. Similarly, Alyami et al. reported that 39.4% of the dietary supplement users in KSA relied on social media or websites [41]. Therefore, the presence of contradicting messages and misleading information mandates raising the public awareness about the evidence-based information provided by healthcare providers [59–61]. In addition, stringent regulations and auditing must be applied to warrant the quality and safety of different dietary health products.

Noteworthy, the theoretical benefit of vitamins in COVID-19, found in systematic reviews and meta-analyses, may not always be extrapolatable to clinical benefit. This could be explained by the fact that a deficiency of a certain vitamin may not necessarily indicate a disease process, rather it might be an outcome. In addition, the administration of vitamins after diagnosis of SARS-CoV-2 infection may not be as effective as a physiological replenished state before the diagnosis [62,63].

Certainly, further clinical studies, particularly randomized control trials, are needed to conclusively determine the prophylactic and therapeutic potentials of different dietary supplements against COVID-19. Until then, the most appreciated, effective preventive measures against SARS-CoV-2 infection include social distancing, wearing face masks, hygiene practices, and receiving the COVID-19 vaccines [64].

5. Limitations

Although this was probably the first larger-scale multinational study that revealed the perceptions and intake of dietary supplements among the Middle Eastern Arabs during the COVID-19 pandemic, some limitations must be pointed out. First, we have recruited our participants using a non-probability snowball sampling technique via social platforms. This had resulted in obtaining skewed sample of participants and introduced selection bias that may limit the generalizability of results to the general Middle Eastern population. Second, we did not investigate the incidence and frequency of intake of dietary supplements before the pandemic. This limitation constrained us from identifying if the intake of dietary supplements has increased during the pandemic, and also stopped us from exploring the associations between the occurrence of COVID-19 and the intake of the dietary supplements. However, this observational study was intended to shed light on the Arabs' perception and intake of supplements during the pandemic, and not to investigate the efficacy of those supplements in reducing the risk of contracting the disease.

6. Conclusions

The high rate of consumption of dietary supplements in the Middle Eastern Arab countries, as in the whole world during the COVID-19 pandemic, is not evidence-based or guided by institutional health recommendations. The advertising content of dietary supplements must be monitored by the competent authorities in the Arab countries, and these authorities should clarify the scientific facts about their uses. Finally, the use of these over-the-counter products either as sole remedies or as prophylactics against COVID-19 must also be guided by relevant clinical trials.

Author contributions

Tareq L Mukattash Conceptualization, Data curation, Methodology, Project administration, Validation, Visualization, Writing – original

draft. Hana Alkhalidy Conceptualization, Methodology, Validation, Visualization, Writing – original draft. Buthaina Alzu'bi Data curation, Methodology, Validation, Visualization, Writing – original draft. Rana Abu-Farha Conceptualization, Data curation, Formal analysis, Validation, Visualization, Writing – original draft. Rania Itani Conceptualization, Methodology, Data curation, Validation, Visualization, Writing – original draft. Samar Karout Data curation, Validation, Visualization, Writing – original draft. Hani M J Khojah Conceptualization, Data curation, Validation, Visualization, Writing – review & editing, Maher Khdour Data curation, Validation, Visualization, Writing – review & editing. Faris El-Dahiyat Data curation, Validation, Visualization, Writing – review & editing. Anan Jarab Data curation, Validation, Visualization, Writing – review & editing. Validation, Visualization, Validation, Visualization, Writing – review & editing.

Financial support

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

The authors would like to thank Pharmacist Rayan El-Hage for her conribution in the data collection.

Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

References

- Y. Heled, A.S. Rutschman, L. Vertinsky, The problem with relying on profit-driven models to produce pandemic drugs, J. Law Biosci. 7 (2020) lsaa060, https://doi. org/10.1093/jlb/lsaa060.
- [2] C.A. Omolo, N. Soni, V.O. Fasiku, I. Mackraj, T. Govender, Update on therapeutic approaches and emerging therapies for SARS-CoV-2 virus, Eur. J. Pharmacol. 883 (2020), 173348, https://doi.org/10.1016/j.ejphar.2020.173348.
- [3] Y. Song, M. Zhang, L. Yin, K. Wang, Y. Zhou, M. Zhou, Y. Lu, COVID-19 treatment: close to a cure? A rapid review of pharmacotherapies for the novel coronavirus (SARS-CoV-2), Int. J. Antimicrob. Agents. 56 (2020), 106080, https://doi.org/ 10.1016/j.ijantimicag.2020.106080.
- [4] V.C.-C. Cheng, S.-.C. Wong, V.W.-M. Chuang, S.Y.-C. So, J.H.-K. Chen, S. Sridhar, K. K.-W. To, J.F.-W. Chan, I.F.-N. Hung, P.-.L. Ho, K.-Y. Yuen, The role of community-wide wearing of face mask for control of coronavirus disease 2019 (COVID-19) epidemic due to SARS-CoV-2, J. Infect. 81 (2020) 107–114, https://doi.org/10.1016/j.iinf.2020.04.024.
- [5] R. Itani, S. Karout, H.M.J. Khojah, F. Jaffal, F. Abbas, R. Awad, L. Karout, R. Abu-Farha, M.B. Kassab, T.L. Mukattash, Community pharmacists' preparedness and responses to COVID-19 pandemic: a multinational study, Int. J. Clin. Pract. 75 (2021) e14421, https://doi.org/10.1111/ijcp.14421.
- [6] D.K. Chu, E.A. Akl, S. Duda, K. Solo, S. Yaacoub, H.J. Schünemann, Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis, Lancet (London, England) 395 (2020) 1973–1987, https://doi.org/10.1016/S0140-6736(20)31142-9.
- [7] H.M.J. Khojah, R. Itani, T.L. Mukattash, S. Karout, F. Jaffal, R. Abu-Farha, Exposure of community pharmacists to COVID-19: a multinational cross-sectional study. J. Taibah Univ. Med. Sci. 16 (2021) 920–928.
- [8] R. Lordan, H.M. Rando, C.S. Greene, Dietary supplements and nutraceuticals under investigation for COVID-19 prevention and treatment, MSystems 6 (2021), https:// doi.org/10.1128/mSystems.00122-21. In press.
- [9] F. Infusino, M. Marazzato, M. Mancone, F. Fedele, C.M. Mastroianni, P. Severino, G. Ceccarelli, L. Santinelli, E. Cavarretta, A.G.M. Marullo, F. Miraldi, R. Carnevale, C. Nocella, G. Biondi-Zoccai, C. Pagnini, S. Schiavon, F. Pugliese, G. Frati, G. D'Ettorre, Diet supplementation, probiotics, and nutraceuticals in SARS-CoV-2 infection: a scoping review, Nutrients 12 (2020) 1718, https://doi.org/10.3390/nu12061718.

- [10] K.K. Adams, W.L. Baker, D.M. Sobieraj, Myth busters: dietary supplements and COVID-19, Ann. Pharmacother 54 (2020) 820–826, https://doi.org/10.1177/ 1060028020928052
- [11] Bloomberg, More Than 4.78 Billion Shots Given: covid-19 Vaccine Tracker, (2021). https://www.bloomberg.com/graphics/covid-vaccine-tracker-global-distribution/ (accessed August 18, 2021).
- [12] J.M. Sanders, M.L. Monogue, T.Z. Jodlowski, J.B. Cutrell, Pharmacologic treatments for Coronavirus Disease 2019 (COVID-19): a review, JAMA 323 (2020) 1824–1836, https://doi.org/10.1001/jama.2020.6019.
- [13] J. Hamulka, M. Jeruszka-Bielak, M. Górnicka, M.E. Drywień, M.A. Zielinska-Pukos, Dietary supplements during COVID-19 outbreak. results of Google trends analysis supported by PLifeCOVID-19 online studies, Nutrients 13 (2020) 1–17, https://doi. org/10.3390/nu13010054.
- [14] J. Grebow, Dietary supplement sales skyrocket during coronavirus pandemic, Nutr. Outlook. (2020). https://www.nutritionaloutlook.com/view/dietary-supplement-sales-skyrocket-during-coronavirus-pandemic (accessed April 24, 2021).
- [15] National Institute of Health, Supplements | COVID-19 Treatment Guidelines, (2021). https://www.covid19treatmentguidelines.nih.gov/supplements/ (accessed April 25, 2021).
- [16] A. Zhao, Z. Li, Y. Ke, S. Huo, Y. Ma, Y. Zhang, J. Zhang, Z. Ren, Dietary diversity among Chinese residents during the COVID-19 outbreak and its associated factors, Nutrients 12 (2020) 1699, https://doi.org/10.3390/nu12061699.
- [17] S. Savant, S. Srinivasan, A.K. Kruthiventi, Potential nutraceuticals for COVID-19, Nutr. Diet. Suppl. 13 (2021) 25–51, https://doi.org/10.2147/nds.s294231.
- [18] J. Grebow, Americans confident in dietary supplement effectiveness and quality in 2020, including during COVID-19 pandemic, CRN surveys show, Nutr. Outlook. (2020). https://www.nutritionaloutlook.com/view/americans-confident-in-dieta ry-supplement-effectiveness-and-quality-in-2020-including-during-covid-19pandemic-crn-surveys-show (accessed April 25, 2021).
- [19] M. Alagawany, Y.A. Attia, M.R. Farag, S.S. Elnesr, S.A. Nagadi, M.E. Shafi, A. F. Khafaga, H. Ohran, A.A. Alaqil, M.E. Abd El-Hack, The strategy of boosting the immune system under the COVID-19 pandemic, Front. Vet. Sci. 7 (2021), 570748.
- [20] P. Kumar, M. Kumar, O. Bedi, M. Gupta, S. Kumar, G. Jaiswal, V. Rahi, N.G. Yedke, A. Bijalwan, S. Sharma, S. Jamwal, Role of vitamins and minerals as immunity boosters in COVID-19, Inflammopharmacology 29 (2021) 1001–1016, https://doi. org/10.1007/s10787-021-00826-7.
- [21] H. Shakoor, J. Feehan, A.S. Al Dhaheri, H.I. Ali, C. Platat, L.C. Ismail, V. Apostolopoulos, L. Stojanovska, Immune-boosting role of vitamins D, C, E, zinc, selenium and omega-3 fatty acids: could they help against COVID-19? Maturitas 143 (2021) 1–9, https://doi.org/10.1016/j.maturitas.2020.08.003.
- [22] J.J. Name, A.C.R. Souza, A.R. Vasconcelos, P.S. Prado, C.P.M. Pereira, Vitamin D Zinc, C. Vitamin, Perspectives for COVID-19 with a focus on physical tissue barrier integrity, Front. Nutr. 7 (2020), 606398, https://doi.org/10.3389/fnut/2020/606398
- [23] S. Maggini, A. Pierre, P.C. Calder, Immune function and micronutrient requirements change over the life course, Nutrients 10 (2018) 1531, https://doi. org/10.3390/nu10101531.
- [24] P.C. Calder, Nutrition, immunity and COVID-19, BMJ Nutr. Prev. Heal. 3 (2020) 74–92. https://doi.org/10.1136/hminph-2020-000085
- 74–92, https://doi.org/10.1136/bmjnph-2020-000085.
 [25] H. Hemilä, E. Chalker, Vitamin C can shorten the length of stay in the ICU: a meta-analysis, Nutrients 11 (2019) 708, https://doi.org/10.3390/nu11040708.
- [26] T.H. Jovic, S.R. Ali, N. Ibrahim, Z.M. Jessop, S.P. Tarassoli, T.D. Dobbs, P. Holford, C.A. Thornton, I.S. Whitaker, Could Vitamins help in the fight against COVID-19? Nutrients 12 (2020) 2550, https://doi.org/10.3390/nu12092550.
- [27] U.S. Food & Drug Administration, Dietary Supplements, (2020). https://www.fda.gov/food/dietary-supplements (accessed April 24, 2021).
- [28] R.L. Bailey, Current regulatory guidelines and resources to support research of dietary supplements in the United States, Crit. Rev. Food Sci. Nutr. 60 (2020) 298–309, https://doi.org/10.1080/10408398.2018.1524364.
- [29] J.T. Dwyer, P.M. Coates, M.J. Smith, Dietary supplements: regulatory challenges and research resources, Nutrients 10 (2018) 41, https://doi.org/10.3390/ nu10010041.
- [30] H.A. Alfawaz, N. Khan, G.A. Aljumah, S.D. Hussain, N.M. Al-Daghri, Dietary intake and supplement use among Saudi residents during COVID-19 lockdown, Int. J. Environ. Res. Public Health. 18 (2021) 1–13, https://doi.org/10.3390/ ijerph18126435
- [31] P. Louca, B. Murray, K. Klaser, M.S. Graham, M. Mazidi, E.R. Leeming, E. Thompson, R. Bowyer, D.A. Drew, L.H. Nguyen, J. Merino, M. Gomez, O. Mompeo, R. Costeira, C.H. Sudre, R. Gibson, C.J. Steves, J. Wolf, P.W. Franks, S. Ourselin, A.T. Chan, S.E. Berry, A.M. Valdes, P.C. Calder, T.D. Spector, C. Menni, Modest effects of dietary supplements during the COVID-19 pandemic: insights from 445 850 users of the COVID-19 Symptom Study app, BMJ Nutr. Prev. Heal. 4 (2021) 149–157, https://doi.org/10.1136/bmjnph-2021-000250.
- [32] A. Alqrache, M. Mostafa, O. Ghabrah, Z. Ghabrah, N. Kamal, T. Ghabrah, H. Atta, Knowledge and patterns of dietary supplement use among students attending King Abdulaziz University in Saudi Arabia: a cross-sectional study, Inquiry 58 (2021), 469580211020882, https://doi.org/10.1177/00469580211020882.
- [33] A.A. Alotiby, L.N. Al-Harbi, Prevalence of using herbs and natural products as a protective measure during the COVID-19 pandemic among the Saudi population: an online cross-sectional survey, Saudi Pharm. J. 29 (2021) 410–417, https://doi. org/10.1016/j.jsps.2021.04.001.
- [34] World Medical Association, Declaration of Helsinki, ethical principles for scientific requirements and research protocols, JAMA 310 (2013) 2191–2194, https://doi. org/10.1001/jama.2013.281053.
- [35] P. Vijayvargiya, Z.E. Garrigos, N.E. Castillo Almeida, P.R. Gurram, R.W. Stevens, R. R. Razonable, Treatment considerations for COVID-19: a critical review of the

- evidence (or lack thereof), Mayo Clin. Proc. 95 (2020) 1454–1466, https://doi.org/10.1016/j.mayocp.2020.04.027.
- [36] R.S. Pawar, E. Grundel, Overview of regulation of dietary supplements in the USA and issues of adulteration with phenethylamines (PEAs), Drug Test. Anal. 9 (2017) 500–517, https://doi.org/10.1002/dta.1980.
- [37] Z. Shi, A. Yan, Dietary supplements: are current policies adequate for promoting health? Nutrients 12 (2020) 1-4, https://doi.org/10.3390/nu12113449.
- [38] U.S. Food and Drug Adminisration, Coronavirus update: FDA and FTC Warn Seven Companies selling fraudulent products that claim to treat or prevent COVID-19, (2020). https://www.fda.gov/news-events/press-announcements/coronavirus-upd ate-fda-and-ftc-warn-seven-companies-selling-fraudulent-products-claim-treat-or (accessed April 25, 2021).
- [39] A.R. Barry, Patients' perceptions and use of natural health products, Can. Pharm. J. 151 (2018) 254–262, https://doi.org/10.1177/1715163518779409.
- [40] G. El Khoury, W. Ramadan, N. Zeeni, Herbal products and dietary supplements: a cross-sectional survey of use, attitudes, and knowledge among the Lebanese population, J. Commun. Health. 41 (2016) 566–573, https://doi.org/10.1007/ s10900.015.0131-0
- [41] H.S. Alyami, M.A.A. Orabi, F.M. Aldhabbah, H.N. Alturki, W.I. Aburas, A. I. Alfayez, A.S. Alharbi, R.A. Almasuood, N.A. Alsuhaibani, Knowledge about COVID-19 and beliefs about and use of herbal products during the COVID-19 pandemic: a cross-sectional study in Saudi Arabia, Saudi Pharm. J. 28 (2020) 1326–1332, https://doi.org/10.1016/j.jsps.2020.08.023.
- [42] S. Lehrer, P.H. Rheinstein, Common drugs, vitamins, nutritional supplements and COVID-19 mortality, Int. J. Funct. Nutr. 2 (2021) 4, https://doi.org/10.3892/ iifn 2021 14
- [43] L. Borsche, B. Glauner, J. von Mendel, COVID-19 mortality risk correlates inversely with Vitamin D3 status, and a mortality rate close to zero could theoretically be achieved at 50 ng/mL 25(OH)D3: results of a systematic review and meta-analysis, Nutrients 13 (2021) 3596, https://doi.org/10.3390/nu13103596.
- [44] A.M. Alguwaines, S. Sabico, R. Hasanato, M.E. Al-Sofiani, M. Megdad, S.S. Albader, M.H. Alsari, A. Alelayan, E.Y. Alyusuf, S.H. Alzahrani, N.M. Al-Daghri, A. A. Jammah, Severe Vitamin D deficiency is not related to SARS-CoV-2 infection but may increase mortality risk in hospitalized adults: a retrospective case-control study in an Arab Gulf country, Aging Clin. Exp. Res. 33 (2021) 1415–1422, https://doi.org/10.1007/s40520-021-01831-0.
- [45] M.M. Karim, S. Sultana, R. Sultana, M.T. Rahman, Possible benefits of zinc supplement in CVD and COVID-19 comorbidity, J. Infect. Public Health. 14 (2021) 1686–1692, https://doi.org/10.1016/j.jiph.2021.09.022.
- [46] A.F. Gombart, A. Pierre, S. Maggini, A review of micronutrients and the immune system-working in harmony to reduce the risk of infection, Nutrients 12 (2020) 236, https://doi.org/10.3390/nu12010236.
- [47] K. Amrein, C. Schnedl, A. Holl, R. Riedl, K.B. Christopher, C. Pachler, T. Urbanic Purkart, A. Waltensdorfer, A. Münch, H. Warnkross, T. Stojakovic, E. Bisping, W. Toller, K.-H. Smolle, A. Berghold, T.R. Pieber, H. Dobnig, Effect of high-dose vitamin D3 on hospital length of stay in critically ill patients with vitamin D deficiency: the VITdAL-ICU randomized clinical trial, JAMA 312 (2014) 1520–1530. https://doi.org/10.1001/jama.2014.13204.
- [48] A. Bassatne, M. Basbous, M. Chakhtoura, O. El Zein, M. Rahme, G.E.-H. Fuleihan, The link between COVID-19 and VItamin D (VIVID): a systematic review and metaanalysis, Metabolism 119 (2021), 154753, https://doi.org/10.1016/j. metabol.2021.154753.
- [49] R. Wang, V. DeGruttola, Q. Lei, K.H. Mayer, S. Redline, A. Hazra, S. Mora, W. C. Willett, D. Ganmaa, J.E. Manson, The vitamin D for COVID-19 (VIVID) trial: a pragmatic cluster-randomized design, Contemp Clin Trials 100 (2021), 106176, https://doi.org/10.1016/j.cct.2020.106176.
- [50] I.H. Murai, A.L. Fernandes, L.P. Sales, A.J. Pinto, K.F. Goessler, C.S.C. Duran, C.B. R. Silva, A.S. Franco, M.B. MacEdo, H.H.H. Dalmolin, J. Baggio, G.G.M. Balbi, B. Z. Reis, L. Antonangelo, V.F. Caparbo, B. Gualano, R.M.R. Pereira, Effect of a single high dose of Vitamin D3 on hospital length of stay in patients with moderate to severe COVID-19: a randomized clinical trial, JAMA 325 (2021) 1053–1060, https://doi.org/10.1001/jama.2020.26848.
- [51] F. Hadizadeh, Supplementation with Vitamin D in the COVID-19 pandemic? Nutr. Rev. 79 (2021) 200–208, https://doi.org/10.1093/nutrit/nuaa081.
- [52] D.A. Jolliffe, L. Greenberg, R.L. Hooper, C.J. Griffiths, C.A. Camargo Jr, C. P. Kerley, M.E. Jensen, D. Mauger, I. Stelmach, M. Urashima, A.R. Martineau, Vitamin D supplementation to prevent asthma exacerbations: a systematic review and meta-analysis of individual participant data, Lancet. Respir. Med. 5 (2017) 881–890.
- [53] C. de Faria Coelho-Ravagnani, F.C. Corgosinho, F.L.F.Z. Sanches, C.M.M. Prado, A. Laviano, J.F. Mota, Dietary recommendations during the COVID-19 pandemic, Nutr. Rev. 79 (2021) 382–393, https://doi.org/10.1093/nutrit/nuaa067.
- [54] F. El-Dahiyat, M. Rashrash, S. Abuhamdah, R. Abu Farha, Z.-U.-D. Babar, Herbal medicines: a cross-sectional study to evaluate the prevalence and predictors of use among Jordanian adults, J. Pharm. Policy Pract. 13 (2020) 2, https://doi.org/ 10.1186/s40545-019-0200-3.
- [55] R.R. Starr, Too little, too late: ineffective regulation of dietary supplements in the United States, Am. J. Public Health. 105 (2015) 478–485, https://doi.org/ 10.2105/AJPH.2014.302348.
- [56] H. Kamarli Altun, M.S. Karacil Ermumcu, N. Seremet Kurklu, Evaluation of dietary supplement, functional food and herbal medicine use by dietitians during the COVID-19 pandemic, Public Health Nutr 24 (2021) 861–869, https://doi.org/ 10.1017/S1368980020005297.
- [57] H. Hamishehkar, F. Ranjdoost, P. Asgharian, A. Mahmoodpoor, S. Sanaie, Vitamins, are they safe? Adv. Pharm. Bull. 6 (2016) 467–477, https://doi.org/ 10.15171/apb.2016.061.

- [58] A. Bastin, H. Shiri, S. Zanganeh, S. Fooladi, M.A. Momeni Moghaddam, M. Mehrabani, M.H. Nematollahi, Iron chelator or iron supplement consumption in COVID-19? The role of iron with severity infection, Biol. Trace Elem. Res. (2021) 1–11, https://doi.org/10.1007/s12011-021-03048-8.
- [59] T.L. Mukattash, A.S. Jarab, W. Al-Qerem, R.K. Abu Farha, R. Itani, S. Karout, I. L. Mukattash, I. Basheti, COVID-19 patients' views and experiences of pharmaceutical care services in Lebanon, Int. J. Pharm. Pract. XX (2021) 1–4.
- [60] R. Itani, H.M.J. Khojah, F. Jaffal, D. Rahme, L. Karout, S. Karout, Provision of pharmaceutical care to suspected high-risk COVID-19 patients through telehealth: a nationwide simulated patient study, BMC Health Serv. Res. 21 (2021) 997, https://doi.org/10.1186/s12913-021-07014-x.
- [61] T.L. Mukattash, A.S. Jarab, W. Al-Qerem, R.K. Abu Farha, R. Itani, S. Karout, I. L. Mukattash, I. Basheti, Providing pharmaceutical care during the COVID-19

- pandemic: attitudes and experiences of home-treated patients in Jordan, J. Pharm. Heal. Serv. Res. 12 (2021) 321–324, https://doi.org/10.1093/jphsr/rmab010.
- [62] D. Rawat, A. Roy, S. Maitra, V. Shankar, P. Khanna, D.K. Baidya, Vitamin D supplementation and COVID-19 treatment: a systematic review and meta-analysis, Diabetes Metab. Syndr. 15 (2021), 102189, https://doi.org/10.1016/j.dsx.2021.102189.
- [63] D. Rawat, A. Roy, S. Maitra, A. Gulati, P. Khanna, D.K. Baidya, Vitamin C and COVID-19 treatment: a systematic review and meta-analysis of randomized controlled trials, Diabetes Metab. Syndr. 15 (2021), 102324, https://doi.org/ 10.1016/j.dsx.2021.102324.
- [64] R. Abu-Farha, T. Mukattash, R. Itani, S. Karout, H.M.J. Khojah, A. Al-Mahmood, K. Alzoubi, Willingness of Middle Eastern public to receive COVID-19 vaccines, Saudi Pharm. J. 29 (2021) 734–739, https://doi.org/10.1016/j.jsps.2021.05.005.