Original Research Article

Immune-boosting effect of natural remedies and supplements on progress of, and recovery from COVID-19 infection

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Abstract

Purpose: To investigate the effect of natural remedies and supplements on the progress of and recovery from COVID-19 infection, and the role of safety precautions in controlling the spread of its causative pathogen.

Methods: A questionnaire was designed and electronically distributed among previously infected individuals across countries. The survey included questions about the participants' demographic information, medical history, how they were infected, symptoms they have experienced, where they were isolated, the degree of precautions taken against the virus, and their consumption of natural remedies or supplements before and during the infection period.

Results: The results showed that natural remedies and supplements are widely consumed among COVID-19 patients both before and during infection, either as a single remedy or in combination with other remedies. As the age of the participants increased, the incidence of their hospitalization increased. Significant results were observed when comparing the severity of infection with the number of natural remedies and supplements taken before (P 0.000) and during the infection (P 0.003).

Conclusion: Increasing the intake of natural remedies and/or supplements before and during COVID-19 infection lowers the severity of the infection. Vitamin C, honey, and citrus fruits such as orange and lemon were the major remedies consumed before and during infection. A large number of the participants that experienced severe COVID-19 conditions, did not consume any natural remedies or supplements.

Keywords: Immunity; COVID-19; Natural remedies; Supplements; Risk of hospitalization

INTRODUCTION

Our environment contains a wide range of pathogenic microbes that replicate, spread and threaten normal host functions by a variety of mechanisms, including the production of cytotoxic free radicals, for instance [1]. Our bodies combat these pathogens through the immune

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system, which is comprised of a complex set of organs, cells, chemicals and processes [2,3].

Common factors that significantly challenge immune functions are, nutrition, age, stress, smoking, sleep, autoimmune diseases, immunosuppressive agents, diseases such as diabetes mellitus type 2, etc [4-6].

The Coronavirus disease (COVID-19) first appeared in Wuhan, China in December of 2019 and World Health Organization named the causative virus as SARS-CoV-2. The disease spread rapidly in China causing an epidemic, and this was followed by an international spread. The disease was then announced as a global pandemic in March of 2020 [7].

Coronavirus is an enveloped, non-segmented, positive single-strand RNA virus of the family of Coronaviridae [8]. Human-to-human transmission of SARS-CoV-2 can occur through inhalation of the airborne virus found in respiratory droplets or aerosols, as well as by touching a surface contaminated with the virus, then touching mucosal surfaces of the eyes, nose or mouth. Some of the commonly recognized non-specific symptoms of COVID-19 are fever, dry cough, shortness of breath, fatigue, sore throat, and chest pain [9,10].

In recent times, populations have been using natural remedies for the prevention and treatment of diseases. Studying the roles of these remedies and supplements in altering the immune response is of great importance. Popular examples are honey, ginger and citrus fruits such as orange and lemon. Supplements have also been widely used, and the main ones are vitamin C and vitamin D. Immune-boosting active constituents in these plants possess antioxidants and antimicrobial mechanisms that are capable of combating the harmful effects of pathogenic microbes and the cytotoxic free radicals produced from them [11].

The aim of this study was to investigate the effect of natural remedies on progress of and recovery from COVID-19 infection as well as the contribution of other relevant factors to this.

METHODS

Study design

A survey was designed with the purpose of collecting relevant information that would assist in achieving the purpose of the study. The survey provided questions about the participants' demographic information, including their age, gender, weight, nationality, level of education, occupational status, as well as questions related to their lifestyle asking about their diet, exercise, sleeping habits, smoking habits, and alcohol consumption. Another section included questions about the participants' past medical history, and asked the female participants whether they were pregnancy or breast-feeding during the infection period. Other questions were more directly related to the COVID-19 infection and asked about the suspected reason for infection, symptoms experienced, length of the infection period, isolation area (home, hotel or hospital) and the degree of precautions taken to avoid the infection. The rest of the questions were about the participants' consumption of natural remedies both before and during the infection period as well as the consumption of synthetic drugs during the infection period.

Sample size

The survey was constructed online using Google Forms and was accessed through a link that was randomly distributed among individuals who were previously infected with COVID-19. The survey was designed in three languages; Arabic, English and Persian, and the participants where from a variety of countries and of different nationalities. The survey results were collected over a period of 7 months (September 2020 - March 2021) and there were of 349 participants throughout.

Ethical statement

This study was approved by the Research and Ethical Committee in Dubai Pharmacy College, Dubai, UAE (approval no. REC/UG/2020/03), and followed the International Ethical Guidelines for Health-related Research Involving Humans prepared by the Council for International Organizations of Medical Sciences (CIOMS) [12]. This study did not utilize any National Health Service sites and is entirely observational (non-invasive and non-interactive). The questionnaire did not include personal, recognizable, sensitive and/or confidential data, therefore the study did not require ethical approval. The patients gave full and free consent to participating in the online research and they agreed to the use of the collected data for scientific research and publication purposes.

Data analysis

The results were analyzed using IBM SPSS software v.26.0. One-way ANOVA test was used, $P < 0.05$ was considered as a statistically significant result.

RESULTS

Demographic information

According to Table 1, most participants were female (n=227, 64.5 %) while 35.5 % were male. 57.3 % were between the age of 16 and 30, followed by those aged 31 to 45 (26.07 %). In addition, most of the participants weighed between 60 to 79 Kg (40.97 %) followed by those who weighed 40 to 59 Kg (25.79 %) and 80 to 99 Kg (24.93 %). Most of the participants were of Asian nationalities (71.64 %), and the majority of those were Iranian (31.81%), followed by those of African nationalities (23.21 %) who were mainly from Egypt (19.77 %). The rest of the participants were from European, North American, and South American countries. The participants varied with regards to their educational status. The majority were highly educated; holding a bachelor's degree or a higher certification (79.94 %), followed by those holding a secondary school degree (16.33 %). Only 3.72 % held a degree below secondary school. Moreover, 51.58 % of the participants were employed, 27.51 % were unemployed, and 20.92 % were students. When the participants were asked about their diet, those who consumed plenty of fruits and vegetables, and had low fat, sugar and salt intake were considered to be on a healthy diet, while an unhealthy diet was considered to be high in fats, sugars and salts, and low in fruits and vegetables. As shown in Table 2, 66.76 % of the participants consumed a combination of both diets, 29.49 % consumed a healthy diet, and the rest consumed an unhealthy diet. According to what the participants have stated regarding their exercise habits, most of them (41.55 %) rarely exercised, while 36.96 % exercised quite often, and the rest either exercised always or did not exercise at all. Moreover, 63.04 % of the participants slept between 6 to 9 h a day, while 29.79 % slept between 3 to 6 h a day. Others either slept for less than 3 h or for more than 9 h a day. Furthermore, 80.81 % of the participants were non-smokers, while 19.19 % were smokers, and 93.41 % did not consume alcohol while the rest did. Most of the participants were not suffering from any other health-related problems apart from COVID-19 (81.94 %) while the rest suffered from a variety of health problems including cardiovascular, hematological, digestive, endocrine, renal, respiratory, nervous, skeletal, and immunological disorders. Out of the severe COVID-19 cases, 65.38 % had one or more comorbid conditions.

Table 1: Demographic profile of the participants (N = 349)

Variable	Response	N (total=349)	Frequency
Gender	Male	124	35.53%
	Female	225	64.47%
Age	0-15	11	3.15%
	16-30	200	57.31%
	31-45	91	26.07%
	45+	47	13.47%
Weight range (Kg)	20-39	3	0.86%
	40-59	90	25.79%
	60-79	143	40.97%
	80-99	87	24.93%
	100-119	20	5.73%
	120-139	6	1.72%
Continent of nationality	Asia	250	71.64%
	Africa	81	23.21%
	Europe	11	3.17%
	North America	6	1.72%
	South America	1	0.29%
Continent of residency	Asia	300	85.96%
	Africa	31	8.89%
	Europe	16	4.58%
	North America	2	0.58%
Level of education	Below secondary school	13	3.72%
	Up to secondary school	57	16.33%
	Bachelor's degree	169	48.42%
	Higher than a bachelors	54	15.47%
	Studied a medical filed	56	16.05%
Occupational status	Working	180	51.58%
	Not working	96	27.51%
	I'm a student	73	20.92%

Table 2: Lifestyle and past medical history of the participants (N = 349)

Variable	Response	N (total=349)	Frequency
Diet pattern	Healthy	75	21.49%
	Unhealthy	41	11.75%
	A combination of both	233	66.76%
Exercise pattern	Always	40	11.46%
	Often	129	36.96%
	Rarely	145	41.55%
	Never	35	10.03%
Daily hours of sleep	0 to 3	1	0.29%
	3 to 6	104	29.79%
	6 to 9	220	63.04%
	More than 9	24	6.88%
Smoking habit	Smoking	67	19.19%
	Not smoking	282	80.81%
Alcohol drinking habit	Drinking	23	6.59%
	Not drinking	326	93.41%
Diseases and Health Problem State (Affected body system)	None	286	81.94%
	Cardiovascular system	17	4.87%
	Hematological system	3	0.85%
	Digestive system	10	2.86%
	Endocrine system	34	9.74%
	Renal system	1	0.28%
	Respiratory system	11	3.15%
	Nervous system	2	0.57%
	Skeletal system	3	0.85%
	Immune system	6	1.71%

Approximately half of the participants (50.72 %) were infected due to their direct contact with a suspected COVID-19 case, 41.55 % were unsure of the reason for their infection, while the rest suspected that their infections were because they often went to crowded places, were traveling, or did not follow the COVID-19 precautions properly, as shown in Table 3. Most of the participants (57.02 %) claimed that they "always" followed the COVID-19 safety precautions (i.e., handwashing for at least 20 seconds, wearing a mask, social distancing, etc.), 28.65 % responded with "often", while the rest responded with "sometimes", "rarely" or "never". Most the participants (92.55 %), who also had mild or moderate COVID-19 conditions, were either isolated at home or in a hotel room, while those with a severe condition were hospitalized. It is also shown that only 2.87 % of the female participants were breastfeeding during the infection period, and 1.15 % had transferred the infection to their babies (Table 3). Additionally, according to Table 4, body ache, fatigue, fever, headache, and loss of taste or smelling sensations were each experienced by more than half of the participants (59.89, 59.03, 57.88, 56.73 and 52.44 % respectively). Other commonly experienced symptoms were dry cough (42.98 %), stuffy nose (35.53 %), sore throat (35.24 %) and shortness of breath (30.95 %). The symptoms that were experienced less frequently were sweating, sneezing, diarrhea, nausea, and vomiting. In contrast, 10.03 % of the

participant did not experience any symptoms. Most of the participants were considered to have had a mild to moderate infection, as they were either asymptomatic or had symptoms lasting for 13 days or less, while the rest were considered to have had severe conditions, as they were hospitalized and their symptoms lasted for 14 days or more. Regarding the time taken to obtain a negative COVID-19 PCR test, 32.66 % of the participants were unsure of when their test result appeared negative, 28.08 % obtained the negative result by 7 to 14 days and 17.48 % obtained it by 15 to 21 days from the day of infection. The rest obtained the negative result either after 6 days or less (mild), or after 22 days or more (severe). The main medications taken during the infection period were paracetamol or ibuprofen (53.01 %), and azithromycin (28.08 %). Other medications that were taken were aspirin, hydroxychloroquine, levofloxacin, naproxen, remdesivir, prednisolone, famotidine, and a combination of lopinavir and ritonavir.

Questions related to the use of natural remedies before and during infection

Answers to the questions related to the administration of natural remedies before COVID-19 infection shown in Table 5 indicate that approximately more than 80 % of the participants consumed a combination of supplements and natural remedies simultaneously.

Table 3: Suspected reason for infection with COVID-19, place of isolation, and infection transfer from a breastfeeding mother to her baby (N = 349)

Question	Response	N (total = 349)	Frequency
Suspected reason for infection	Direct contact with a suspected case	177	50.72%
	Travelling	15	4.30%
	Going to crowded places	27	7.74%
	Not followed the COVID-19 precautions properly	14	4.01%
	Unsure	145	41.55%
Degree of following COVID-19 precautions	Always	199	57.02%
	Often	100	28.65%
	Sometimes	41	11.75%
	Rarely	6	1.72%
	Never	3	0.86%
Place of isolation	Home	307	87.97%
	Hospital/clinic	26	7.45%
	Hotel room	16	4.58%
Breastfeeding status	Breastfeeding	10	2.87%
	Not breastfeeding	215	61.60%
	Not applicable	124	35.53%
Transfer of infection to baby	Transferred	4	1.15%
	Not transferred	6	1.72%
	Not applicable (Male/Not breastfeeding)	339	97.13%

Table 4: Symptoms experienced by the participants, synthetic drugs taken during the infection period, and time to obtain negative PCR test result (N=349)

Question	Response	N (total = 349)	Percentage (%)
Symptoms experienced	No symptoms	35	10.03%
	Fever	202	57.88%
	Dry cough	150	42.98%
	Shortness of breath	108	30.95%
	Sneezing	85	24.36%
	Sore throat	123	35.24%
	Stuffy nose	124	35.53%
	Sweating	102	29.23%
	Headache	198	56.73%
	Body ache	209	59.89%
	Fatigue	206	59.03%
	Diarrhea	92	26.36%
	Nausea/vomiting	60	17.19%
	Loss of taste/smelling sensation	183	52.44%
	Other	37	10.60%
Duration of symptoms	No symptoms	35	10.03%
	Less than 7 days	83	23.78%
	7 to 13 days	161	46.13%
	14 to 21 days	45	12.89%
	More than 21 days	25	7.16%
Time taken to get the COVID-19 PCR test negative	Less than 7 days	50	14.33%
	7 to 14 days	98	28.08%
	15 to 21 days	61	17.48%
	More than 21 days	26	7.45%
	Unsure	114	32.66%
Synthetic drugs taken during infection	None	125	35.82%
	Hydroxychloroquine	18	5.16%
	Azithromycin	98	28.08%
	Levofloxacin	9	2.58%
	Remdesivir	7	2.01%
	Lopinavir/Ritonavir (combination)	6	1.72%
	Paracetamol or Ibuprofen	185	53.01%
	Aspirin	24	6.88%
	Naproxen	9	2.58%
	Prednisolone	7	2.01%
	Famotidine	6	1.72%
	Other	52	14.89%

These remedies included vitamin C supplement, (56.16 %), orange or lemon fruits (46.42 %), honey (42.98 %), vitamin D supplement (38.40 %), ginger (29.51 %), zinc supplement (26.65 %), multivitamin supplement (23.78 %), and black seeds (15.76 %). On the other hand, some participants had taken Echinacea, turmeric, garlic, cinnamon, thyme, clove, chamomile, star anise, frankincense, and other remedies. However, 19.20 % of the participants did not consume any natural remedies or supplements before their infection. An increase in the percentage of participants who consumed natural remedies and supplements was observed during infection as shown in Table 5, compared to the percentage of consumption before infection. Examples of the consumed remedies and supplements during infection were vitamin C, honey, orange or lemon fruits, vitamin D supplements, zinc supplements, ginger, multivitamin supplements, black seeds, garlic and turmeric (71.63, 60.17, 58.17, 47.28, 44.13, 42.12, 26.36, 23.78, 18.62 and 15.76 % respectively). Other natural remedies were onion, star anise, costus, frankincense, etc. Only 12.32 % of the participants did not consume any natural remedies or supplements during their infection period.

Mild, moderate and severe cases

To classify the participants according to the severity of their infection, factors like the duration of symptoms, time taken to obtain a negative PCR test result and the place of isolation (home, hotel, or hospital) were considered. About 65.04 % of the participants were classified as mild, 27.51 % as moderate and 7.45 % as severe cases. Correlating the percentage of each class with the intake of natural remedies and/or supplements revealed that a large percentage of the mild cases have consumed vitamin C, citrus fruits, honey, vitamin D, ginger, zinc and black seed (55.07, 48.90, 42.73, 37.00, 32.16, and 26.87 % respectively) before infection. Additionally, 18.94 % consumed multivitamins, garlic, cinnamon, thyme and Echinacea. On the other hand, 18.94 % of the mild cases did not consume any natural remedies or supplements. Furthermore, during the infection period, an increase in the percentage of the mild cases that consumed natural remedies and/or supplements was observed compared to before infection. These natural products included vitamin C, honey, citrus fruits, vitamin D, zinc, ginger, multivitamin supplements, black seed, and garlic (68.72, 55.95, 53.30, 43.61, 40.09, 39.65, 21.59, 21.15 and 20.26 % respectively). Additionally, 15.86 % consumed other remedies such as cinnamon, thyme and chamomile. Only 14.98 % of the mild cases did not consume any natural remedies or supplements during infection (Figure 1).

Looking at the moderate cases shown in Figure 2, it is clear that almost the same remedies were also consumed either individually or in combination. These included vitamin C, honey, orange or lemon, vitamin D, multivitamin supplement, zinc, ginger, and black seeds (59.38, 51.04, 47.92, 45.83, 36.46, 29.17, 28.13, and 16.6 % respectively).

Table 5: Natural remedies and supplements taken by the participants before and during their infection period (N = 349)

Natural remedy	Number of patients that have taken these natural remedies before infection N (total = 349)	Frequency	Number of patients that have taken these natural remedies during infection N (total = 349)	Frequency
None	67	19.20%	43	12.32%
Vitamin C	196	56.16%	250	71.63%
Vitamin D	134	38.40%	165	47.28%
Multivitamin supplements	83	23.78%	92	26.36%
Zinc	93	26.65%	154	44.13%
Ginger	103	29.51%	147	42.12%
Orange or Lemon	162	46.42%	203	58.17%
Honey	150	42.98%	210	60.17%
Blackseed	55	15.76%	83	23.78%
Echinacea	13	3.72%	17	4.87%
Turmeric	43	12.32%	55	15.76%
Garlic	49	14.04%	65	18.62%
Cinnamon	7	2.01%	11	3.15%
Thyme	10	2.87%	19	5.44%
Others	24	6.88%	59	16.91%

Only 15.63 % of the moderate cases did not consume or drink any natural remedies or supplements before infection. Similar to mild cases, the percentage of moderate condition who received natural remedies during the infection increased compared to the percentage before infection. Only 4.17 % of the participants did not take any supplements or remedies before infection. The consumed remedies were vitamin C, orange or lemon, honey, vitamin D, zinc, ginger, multivitamin supplement, black seeds, garlic and turmeric (80.21, 71.88, 59.38, 52.08, 51.04, 40.63, 27.08, 19.79 and 19.79 % respectively). Other 23.93 % of the participants with moderate conditions consumed other remedies such as thyme and cinnamon.

On the other hand, a high percentage of the severe cases (34.62 %) did not consume any natural remedies before infection, while 53.85, 23.08 and 19.23 % of them consumed vitamin C, vitamin D and citrus fruits respectively (Figure 3). Zinc, honey, and black seeds were collectively taken by 15.38 % of the severe cases. Others consumed ginger, turmeric, garlic, thyme, and other natural remedies like marjoram. Conversely, during infection, the severe cases consumed vitamin C supplements, honey, zinc, orange or lemon, vitamin D supplements, black seeds, and ginger (65.48, 53.86, 50.00, 50.00, 34.62, 34.62, and 30.77 % respectively). Nevertheless, 19.23 % of the severe cases did not consume any natural remedies during their infection period.
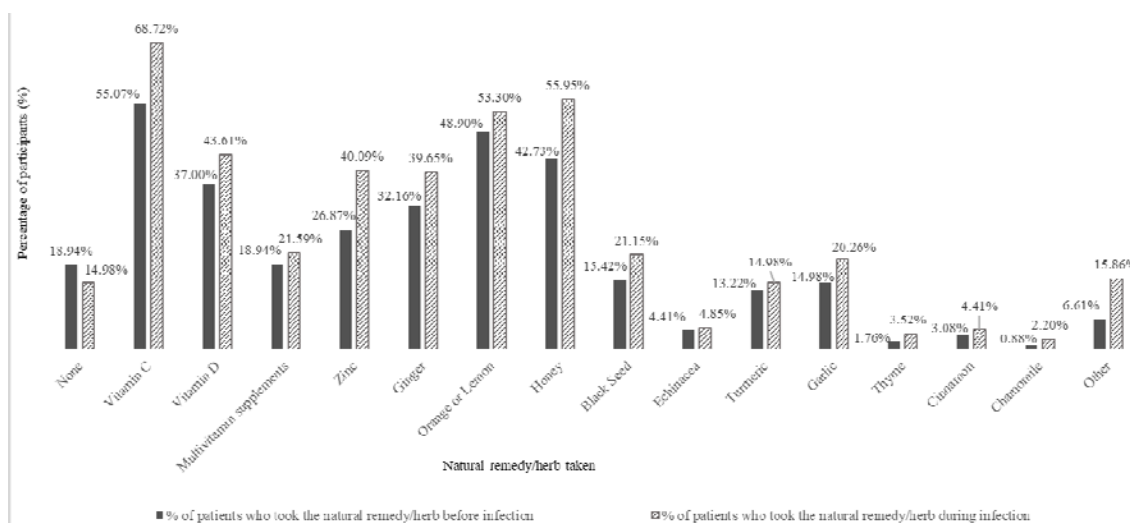

Figure 1: Natural remedies and supplements consumed by the mild cases before and during infection (65.04 % of the participants are considered as mild cases)
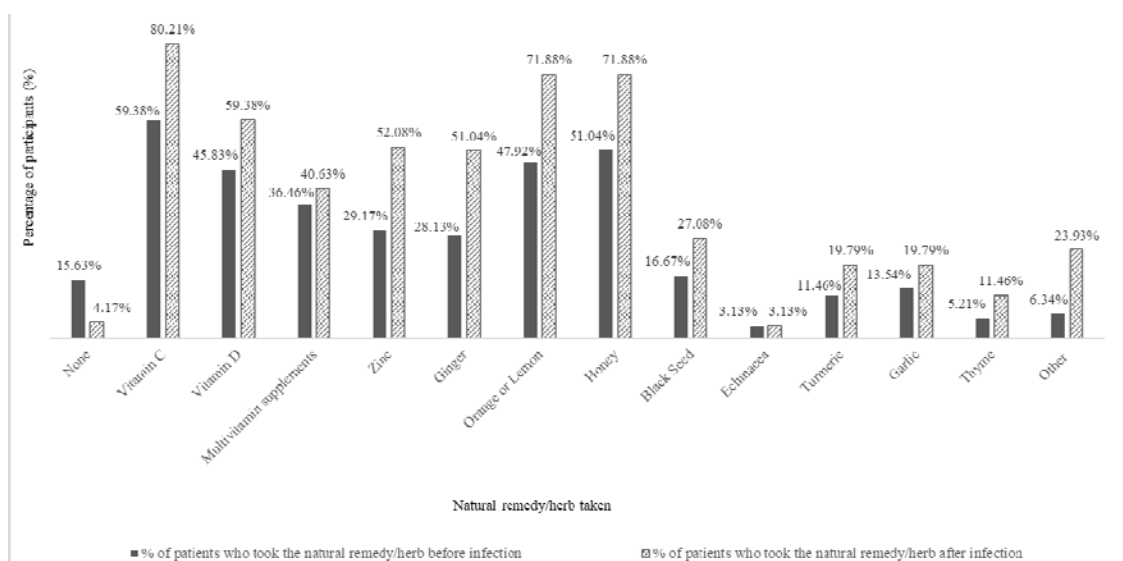

Figure 2: Natural remedies and supplements consumed by the moderate cases before and during infection (27.51 % of the participants are considered as moderate cases)
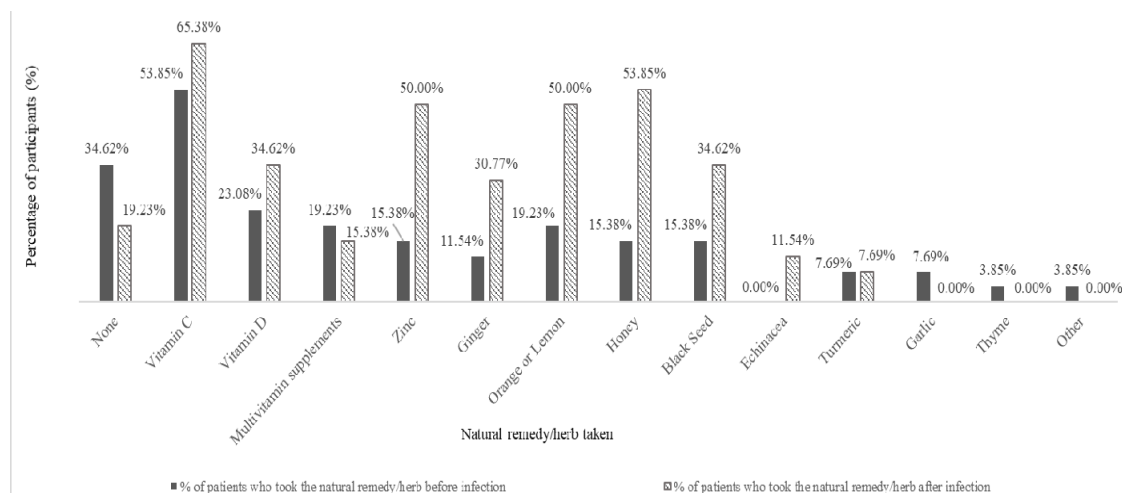
Figure 3: Natural remedies and supplements consumed by the severe cases before and during infection (7.45 % of the participants are considered as severe cases)

Table 6: One-way ANOVA test for analysis of the protective effect of natural remedies/supplements against COVID-19 infection and reducing the severity of the infection

Variable	Sum of Squares	df	Mean square	F	Sig.
Intake of natural remedies before infection (Took natural remedies/ didn't take natural remedies)	0.301	1	0.301	0.762	0.383
Intake of natural remedies during infection (Took natural remedies/ didn't take natural remedies)	0.476	1	0.476	1.207	0.273
Amount/number of natural remedies taken before infection (high/low)	6.803	1	6.803	18.099	0.000*
Amount/number of natural remedies taken during infection (high/low)	3.384	1	3.384	8.772	0.003*

$P < 0.05$ significant

One-way ANOVA test results

The results of the statistical analysis performed using ANOVA test are displayed in Table 6. No significant results were observed when comparing the severity of the COVID-19 infection and the intake of natural remedies or supplements either before (P 0.383) or during (P 0.273) infection. However, a statistically significant difference was observed when comparing the severity of the COVID-19 infection with the intake of natural remedies or supplements before (P 0.000) and during (P 0.003) infection.

DISCUSSION

This study shows that natural remedies and supplements were widely consumed before and during the infection period among COVID-19 patients, either in combination or alone. Moreover, it was shown that the higher the level of education, especially if the participants had studied in a medical field, the higher was the degree of them following the COVID-19 safety precautions and the intake of natural remedies, compared to those with a lower educational status. It was also observed that severe conditions were more likely to occur within higher age groups. Therefore, the incidence of hospitalization due to severe conditions was directly related to the age of the participants in our study. Over half of these severe cases had one or more comorbid conditions.

Approximately half of the participants were infected due to their direct contact with a suspected COVID-19 case, whereas the others were infected because they were often going to crowded places, traveling, or not following the COVID-19 precautions properly. In addition, most of the participants with mild and moderate cases claimed that they always followed the COVID-19 safety precautions (i.e., hand washing for 20 seconds, wearing a mask, keeping a safe distance, etc.), while the rest stated that they sometimes, rarely or never following them.

Overall, this study shows that the increase in the number of natural remedies or supplements taken by the participants before and during a COVID-19 infection decreased the severity of the infection. It is also shown that vitamin C, honey, and citrus fruits were the most consumed remedies by participants having mild or moderate conditions. On the other hand, most of the participants who did not consume any natural remedies or supplements were categorized as severe cases. These natural remedies were shown to be capable of combating the harmful effects of the cytotoxic free radicals produced by common harmful pathogens [11].

Vitamin C and Vitamin D work by supporting various cellular functions of both the innate and adaptive immune systems. They provide potential protection against oxidative stress by supporting epithelial barrier function against pathogens, as well as by promoting the oxidant scavenging activity of the skin. These vitamins accumulate in phagocytic cells (e.g., neutrophils) and enhance chemotaxis, phagocytosis, generation of reactive oxygen species, and ultimately microbial killing [13,14].

Honey is another remedy that is rich in vitamins and minerals. It possesses antioxidant activity owing to its phenolic acid content that scavenges free radicals to prevent them from attacking macromolecules and causing cell damage or homeostatic disruption. Additionally, honey has antimicrobial activity against microorganisms as well as immune-stimulatory effects that trigger the production of immunological mediators, such as tumor necrosis factor α, interleukin-1β, and IL-6 [15]. Another popular plant is ginger, which contains zingiberene in its volatile oil, and also contains terpenes and phenolic compounds. Ginger has powerful antioxidant activity, as well as an antimicrobial activity against bacteria such as salmonella. Ginger extract has also been shown to significantly raise the thymus index, spleen index and phagocytosis rate [16].

Limitations of the study

One of the study limitations is that the participants were limited to those having access to the internet. In addition, a high percentage of the participants were from Middle Eastern countries. Another limitation is that there is possibility of dishonest answers to the questions asked in the survey.

CONCLUSION

The findings of this study show that the intake of natural remedies and supplements decreases the severity of a COVID-19 infection. Therefore, it is recommended that individuals infected with COVID-19, or those who seek protection from the infection, consume a variety of natural remedies and/or supplements before and during the period of infection to minimize the severity of infection, reduce the duration of their symptoms, as well as the risk of hospitalization as a result of the infection. In addition, we advise the individuals to follow the usual COVID 19 safety protocols, including hand washing, mask wearing and keeping a safe physical distance to control the spread of COVID-19.

DECLARATIONS

Conflict of Interest

The authors declare that no conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Dr. Naglaa Gamil Shehab, Prof. in the Clinical Pharmacy and Pharmacotherapeutics Department, Dubai Pharmacy College, Dubai, UAE conceived and designed this study. All authors contributed in data collection, analysis, manuscript writing and proofreading for publication.

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