

RESEARCH ARTICLE

REVISED Practice and knowledge of dietary supplement consumption among Indonesian adults post-delta wave of the COVID-19 pandemic [version 2; peer review: 3 approved]

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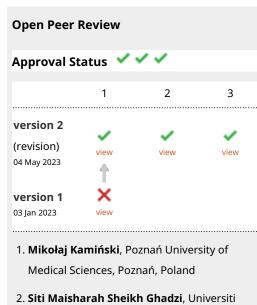
Abstract

Background: Increasing dietary supplement (DS) consumption was observed during the COVID-19 pandemic, including during the post-Delta wave period. This study aimed to measure the practice of DS consumption and respondents' knowledge of DS.

Methods: An internet-based survey was distributed from October-December 2021 and obtained 541 valid and completed responses. Descriptive analysis was performed to present the practice of DS consumption, including frequency, duration, aim, preferable dosage form etc. Level of knowledge on DS principles, side effects and regulation were also measured. Inferential analyses were conducted to determine the predictors of the respondents' DS practice and level of knowledge.

Results: Data from 541 valid responses showed that 77.63% of respondents consumed DS in the last 3 months, with only 59.52% reporting also consuming DS before the COVID-19 pandemic. One half of the respondents had good knowledge about DS; however, some knowledge regarding side effects and possible drug-supplement interaction needed improvement. Their DS consumption practice was affected by their economic status and history of contracting COVID-19. Nevertheless, the level of knowledge was not affected by the sociodemographic factors and DS supplement experience.

Conclusions: Taken together, the practice of self-consumption of DS in Indonesia is increasing; hence, knowledge of DS is necessary to avoid detrimental effects that might occur in the future. Increasing



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access to information on better labelling and educating consumers about DS are important actions to consider.

Keywords

awareness, COVID-19, diet, healthy lifestyle, herbal, mineral, vitamin, sociodemographic



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We did shorten some sentences to increase the clarity and readability of the manuscript.

Any further responses from the reviewers can be found at the end of the article

Introduction

United States Food and Drugs Administration (USFDA) defined dietary supplements (DS) as substances containing vitamins, minerals, amino acids or enzymes, or herb/botanical products that complete the diet's nutritional value. However, DS is not intended for treating, curing, preventing, or diagnosing diseases (FDA, 2022). Despite that definition by the USFDA, much evidence-based research, from fundamental animal studies to randomized clinical trials has shown the effectiveness of DS consumption in preventing disease, improving health, and reducing disease symptoms (Kaviani et al., 2020; Shinto et al., 2014; Sim et al., 2022). Moreover, the global consumption of DS has been steadily increasing for the last decade (Kantor et al., 2016; Kelly et al., 2005). Since 2020, the public's interest in DS use has increased in the wake of COVID-19 worldwide (d'Arqom et al., 2021; Hamulka et al., 2021; Lordan, 2021; Speakman et al., 2021). At the beginning of the pandemic, some DS recorded higher demand and consumption rates due to the perception that DS ingredients might boost immune function and reduce inflammation to help prevent COVID-19 (d'Arqom et al., 2021; Hamulka et al., 2021; Mohsen et al., 2021).

The COVID-19 outbreak has claimed a total of 6,540,487 lives as of October 2022 (WHO, 2022). More than 90% of COVID-19 deaths involved a pre-existing medical condition, of which 66% of the patients had metabolic syndrome, a pathologic condition due to obesity, insulin resistance, hypertension and hyperlipidemia (Li *et al.*, 2021). Patients who present with one or two comorbidities are at a higher risk of low survival following COVID-19 transmission. This is due to impaired function resulting from the secondary effects of HDL cholesterol, as observed by Kitchens *et al.* (2003). Moreover, the decline in respiratory functions is likely caused by prolonged systemic inflammation, as indicated by high c-reactive protein levels (Chen *et al.*, 2014; Kim *et al.*, 2017). Additionally, the high risk of cardiac arrest is attributed to the underlying comorbidities of metabolic syndrome, as highlighted by Hess *et al.* (2017).

All the mentioned medical complications could be prevented by early detection, being active, and meeting the physiological demands of essential vitamins and minerals. It has been established that vitamin C, B6, D, and E deficiency were associated with an increased risk of metabolic syndrome (Beveridge et al., 2015; Godala et al., 2017; Kodentsova et al., 2019). In light of the pandemic, there has been a significant shift in the way healthcare providers and the general public perceive dietary supplements. For example, there has been an increased recognition of their potential to mitigate the severity of COVID-19 infections. Notably, countries such as Indonesia have been increasingly providing essential dietary supplements to high-risk populations to reduce the risk of hospitalization and adverse post-complications of COVID-19 transmission (Kemenkes, 2022; Weir et al., 2020). A study conducted in the UK on 445,850 participants showed a significant association between the use of multivitamins, omega-3 fatty acids and vitamin D₃ supplements with a lower risk for SARS-CoV-2 (Louca et al., 2021). However, uncontrolled and overconsumption of DS might lead to unwanted effects, such as kidney problems, cancer and drug-herbs interactions (Agbabiaka et al., 2018; Asher et al., 2017; d'Argom et al., 2020; Peng et al., 2004).

In Indonesia, although the use of DS is high, little published data is available regarding public practice and knowledge towards DS and their safety. As such, more research on public awareness of DS is essential to gain a better understanding of people's beliefs and expectations regarding DS. Therefore, this study aimed to investigate the practice and knowledge of the general public in Indonesia regarding DS during the post-Delta wave of the COVID-19 pandemic. In addition, the predictive factors of DS consumption and level of knowledge were further analyzed.

Methods

Study design

This research employed a cross-sectional design. The primary data were collected using an internet-based questionnaire (www.surveyplanet.com). The questionnaire was distributed to the adult population in Indonesia through email and social media using convenience sampling methods from October to December 2021, and multiple responds from single device were prevented based on respondents' IP address. This study followed the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) and The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (Eysenbach, 2004; Vandenbroucke *et al.*, 2007). The ethics clearance was issued by the Faculty of Medicine, Universitas Airlangga No. 244/EC/KEPK/FKUA/2021.

Participants

The inclusion criteria were Indonesian adults older than 18 years old and residing in Indonesia during the post-Delta wave of the COVID-19 pandemic. Sample size was calculated using sample size calculator (www.raosoft.com) with 5% margin of error, 95% confidence level, and population number filled with 100,000, resulting in 383 minimum respondents. Respondents were recruited through announcements distributed in social media and email using non-probability sampling.

Data collection

Respondents independently filled in the online questionnaire using their own device, and the estimated survey length was 12 minutes. To measure respondents' practice and awareness on DS, a set of questionnaires containing three sections was distributed online. The sections comprised basic demographic information, supplement consumption practice, and DS knowledge. The first section consisted of basic demographic factors such as age, sex, domicile, education, occupation, field of study/work, COVID-19 infection status, comorbidity, marital status, and self-claimed economic status. The second section consisted of 17 questions regarding their supplement consumption practice, which included respondents' consumption of DS, duration, frequency, numbers, place to buy, aims, benefit, and source of information. And the last section comprised 16 questions to measure DS knowledge, including their knowledge on the regulation, side effects, and benefit. The questionnaire was modified from the Prevalence and Awareness Concerning Dietary Supplement Use among Saudi Adolescents (Alfawaz et al., 2020) and Knowledge about dietary supplements and trust in advertising them: Development and validation of the questionnaires and preliminary results of the association between the constructs (Karbownik et al., 2019). The questionnaire was combined and validated by two pharmacologists, a pharmacist, and a psychologist, and was further tested on 20 respondents to ensure that the content and terms used in the questionnaire were relevant and understandable. The reliability measurement on the survey data showed a Cronbach alpha coefficient of 0.750 for DS knowledge. As the reliability value for the preliminary pilot testing is at an acceptable level, the real data collection for this study was proceed. A copy of the survey instrument can be found under Extended data (d'Arqom, 2022).

Ethical considerations

This study followed the Helsinki declaration and approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Airlangga (No. 86/EC/KEPK/FKUA/2021). The aims of the study, the consent, and the permit to publish their responses anonymously were provided in the landing page, prior completing the questionnaire. The respondents provided their consent by clicking the YES button before starting the questionnaire.

Analytical procedures

Only the complete responses were processed and analysed. Respondents were grouped based on their sociodemographic factors. Supplement practice and awareness were measured using nominal or ordinal scales. Data were processed and analyzed using Microsoft Excel and SPSS 24.0 (IBM, Chicago, IL, USA). Graphs were visualized using GraphPad Prism 5.0. Descriptive statistical analyses were performed, including the frequency for each categorical variable. The answers to the knowledge survey were measured using correct/wrong/does not know options measured as 1/0/0. The total score was the summation of the 16 question scores and was grouped in four categories based on the total score of each respondent: poor (0-4), moderate (5-8), good (9-12) and excellent (13-16). The Chi-square test and Fisher's Exact test were performed to measure the difference between DS consumption and knowledge on each group. To investigate the predictors of DS consumption, binary logistic regression with 95% confidence intervals (95% CIs) was calculated. Moreover, to investigate the predictors of DS knowledge, ordinal logistic regression with 95% CI was performed. Prior to multivariate regression, univariate regression was performed to determine each sociodemographic factor that might affect DS consumption or level knowledge. Sociodemographic factors with p<0.25 were included to further multivariate regression using the backward elimination method (Bursac *et al.*, 2008). Variables with p<0.05 from the multivariate regression analysis were considered significant predictive factors.

Results

Characteristics of respondents

Five hundred forty-eight respondents visited the informed consent page, and 541 completed and valid questionnaires used in the final analysis (completion rate was 98.72%). Around two thirds of respondents comprised young adults, females and unmarried individuals. The majority came from the main island, which is the most developed region in Indonesia (82.26%), with self-reported economic status, were average economic status (73.54%) and never had a COVID-19 positive status (78.19%). Table 1 summarizes the respondents' sociodemographic characteristics. Hundreds (18.48%) were reported to have comorbidities such as obesity (35.65%), hypertension (22.61%), respiratory diseases (21.74%) and others (diabetes mellitus, autoimmune diseases, genetic diseases and cancer) (Figure 1A). The full dataset can be found under *Underlying data* (d'Arqom, 2022).

Table 1. Sociodemographic characteristic of respondents.

Sociodemographic factors	Total respondents (N=541)	Supplement consumer	Non-supplement consumer	X ²	p
Age				14.686	0.005
18-25	338 (62.48%)	245 (72.49%)	93 (27.51%)		
26-35	77 (14.23%)	65 (84.42%)	12 (15.58%)		
36-45	61 (11.28%)	54 (88.52%)	7 (11.48%)		
46-55	51 (9.43%)	45 (88.24%)	6 (11.76%)		
>55%	14 (2.59%)	11 (78.57%)	3 (21.43%)		
Sex				0.006	1
Male	213 (39.37%)	165 (77.46%)	48 (22.54%)		
Female	328 (60.63%)	255 (77.74%)	73 (22.26%)		
Location				0.466	0.501
Main Island	445 (82.26%)	348 (78.20%)	97 (21.80%)		
Outside Main Island	96 (17.74%)	72 (75%)	24 (25%)		
Education				11.203	0.004
High School graduate	240 (44.36%)	171 (71.25%)	69 (28.75%)		
Diploma or Undergraduate	217 (40.11%)	176 (81.11%)	41 (18.89%)		
Post graduate	84 (15.53%)	73 (86.90%)	11 (13.10%)		
Work				12.712	0
Employed	190 (35.12%)	164 (86.32%)	26 (13.68%)		
Unemployed	351 (64.88%)	256 (72.93%)	95 (27.07%)		
Field of work/study				2.783	0.110
Health-related	339 (62.66%)	271 (79.94%)	68 (20.06%)		
Non-health-related	202 (37.34%)	149 (73.76%)	53 (26.24%)		
Confirmed COVID-19				6.741	0.009
Never	423 (78.19%)	318 (75.18%)	105 (24.82%)		
Ever	118 (21.81%)	102 (86.44%)	16 (13.56%)		
Marital status				12.703	0.000
Married	165 (30.11%)	144 (87.27%)	21 (12.73%)		
Unmarried	376 (68.61%)	276 (73.40%)	100 (26.60%)		
Economy status				8.971	0.011
Below Average	29 (5.29%)	16 (55.17%)	13 (44.83%)		
Average	403 (73.54%)	314 (77.92%)	89 (22.08%)		
Upper Average	109 (19.89%)	90 (82.57%)	19 (17.43%)		

Notes: Boldface p-values indicate significant differences between groups using Chi-square or Fisher-Exact test.

Practice of dietary supplement consumption

Our study found that 420 (77.63%) respondents consumed DS during the post-Delta wave of the COVID-19 pandemic. Forty percent reported they had never consumed DS before the pandemic. Several sociodemographic factors were associated with DS consumption, for example, middle-aged adults were more likely to consume DS compared with elderly and young adults (p=0.005). Higher education, higher self-reported economic status, married status, those diagnosed with COVID-19 and working respondents were also more likely to consume DS (p=0.004, 0.011, 0.000, 0.009, 0.000, respectively). No statistically significant differences were found in DS consumption among sex, domicile and field of work/study. The frequency of supplement consumption based on their sociodemographic factors is summarized in Table 1.

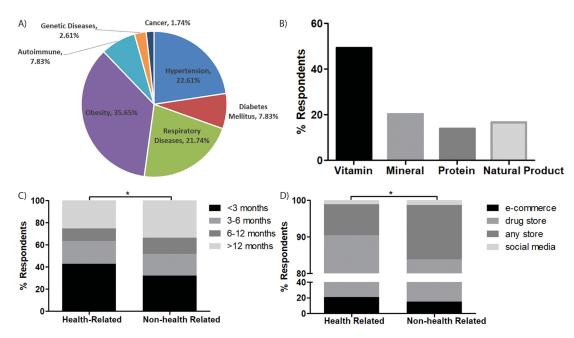


Figure 1. Comorbidity and DS consumption practice. (A) types of comorbidities of the respondents, (B) types of DS consumed by the respondents, (C) duration of DS consumption (D) Source of DS, *p-value<0.05.

Almost one half of respondents consumed vitamins (49.28%), minerals (20.19%), natural products (16.71%) and protein or amino acids (13.82%) (Figure 1B). Their aims of DS consumption were mostly for increasing immunity (81.19%), preventing disease (10.71%), and improving physical appearance (8.10%). Almost 40% of the respondents had consumed DS for less than 3 months, while more than one quarter (28.33%) had consumed DS for more than one year. A different pattern of DS consumption emerged between respondents with health-related backgrounds and non-health-related backgrounds, as most of the last group took DS with longer duration than the first group (p=0.017, Figure 1C).

The most preferred dosage form was capsule (49.76%), tablet (38.57%), liquid (7.62%) and powder (4.05%). Two thirds of the respondents consumed a single type of DS at one time, two types of DS (23.10%) and only 7.62% consumed three or more types of DS simultaneously. More than 40% of respondents consumed 2 to 5 times/weekly (43.10%), less than twice/weekly (33.33%), and 23.57% consumed it more than 5 times/weekly. Two thirds bought DS from drugs stores (69.29%), e-commerce (18.81%) and any store that sold DS (10.71%), while only 1.19% bought DS from social media. Even though the majority of respondents in both groups were more likely to buy DS from drug stores, the health-related groups were more likely to choose e-commerce as the second option, while the second option for non-health-related respondents was any store that sold DS and e-commerce platforms (p=0.025, Figure 1D).

The primary sources of information were family members or friends (49.29%), and health professionals (32.86%), and the rest received information from academic journals, websites and TV/magazine advertisements. Surprisingly, 48.57% consumed DS for more than 3 months without healthcare consultation. Moreover, one half of respondents did not have an exact schedule for consuming DS, while only 30.71% consumed them on a scheduled basis. As expected, more than three quarters of respondents had missed consuming DS (82.62%). Almost three quarters (73.57%) felt the benefit of consuming DS. However, only one third would continue to consume DS if they faced financial difficulty (34.29%). More than one half of respondents consuming DS knew about their side effects and they consumed and endeavored to find information regarding suitable DS (67.38%). Differences in DS consumption between the two groups are summarized in S2 Table. A supplementary material can be found under Extended data (d'Arqom, 2022).

Knowledge on dietary supplements

In a set of questionnaires containing 16 items (S1 Table), respondents' knowledge on DS was measured. The results showed that 7.21% of respondents had excellent knowledge, 59.52% had good knowledge, 31.24% had fair knowledge and 2.03% had poor knowledge on DS. As expected, based on their field of study or work, the level of knowledge was higher in health-related fields compared with non-health-related fields (p=0.000, Figure 2A). The majority of respondents of both groups knew DS function was not to replace food but to increase nutritional value of their diet and improve health conditions (Q4, Q5 and Q8). Unfortunately, almost two thirds remained unaware that DS were still

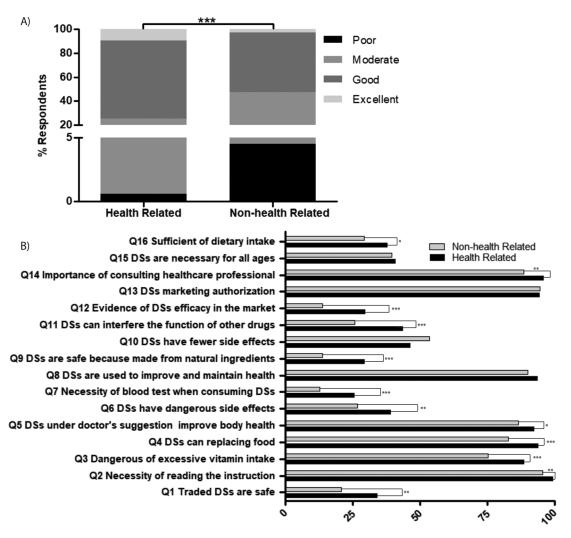


Figure 2. Respondent's knowledge on DS. (A) comparison of respondents' level of knowledge based on their background work/study field, (B) comparison of correct answers based on their background work/study field, *** p-value<0.000

needed even though they already consumed a healthy diet (Q16), so DS were necessary for all ages (Q15). Moreover, almost all respondents understood that prior to consuming DS, they needed to consult a doctor or pharmacist and read the instructions or the label (Q2 and Q14). The respondents were also aware that before releasing to the market, DS needed a permit from an authorized organization in Indonesia (Q13). However, they were still unaware that not all traded DS were safe to consume (Q1), because some were illegally traded and not all provided evidence to support their beneficial claims (Q12). Regarding side effects, most respondents understood that consuming too many vitamins was harmful (Q3), but they still had a mindset that natural products were safe to consume because they come from nature (Q9). However, their awareness about DS side effects (Q6, Q10) and possible DS-drug interaction (Q11) needed improvement. The Kruskal-Wallis test showed significant differences in the answers between the two groups (Figure 2B), except for DS function (Q8), side effect DS side effects (Q10), authorization before releasing to the market (Q13) and the necessity of DS for all ages (Q15).

Determinants of DS consumption practice

To measure predictors of DS consumption of this study, binary logistic regression was performed. For supplement consumption, the univariate analysis of binary logistic regression showed respondents with higher education, working, having confirmed COVID-19 status, married status and have higher self-reported economy status were more likely to consume DS. Using those variables, multivariate analysis of a binary logistic regression model showed significant positive predictors for consuming DS were the health-related field of work or study (AOR: 1.733, 95% CI 1.109-2.709). However, respondents reporting no confirmed COVID-19 status were less likely to consume DS (AOR 0.524,

95% CI 0.291-0.944), and as expected, respondents with a lower self-reported economic status were less likely to consume DS post-Delta wave COVID-19 pandemic (AOR 0.309, 95% CI 0.124-0.769) proving the lack of accessibility due to financial constraints. The model estimated the overall accuracy of 77.8% and explained 9.9% of the variation in supplement consumption for preventing COVID-19 (Omnibus tests of model coefficients chi-square: 36.330, p=0.000). Table 2 showed the predictor factors of DS consumption practice.

Table 2. Predictor factors of DS consumption using binary logistic regression.

	Univariate			Multivariate			
Predictor factors	p-value	COR	95% CI	p-value	AOR	95% CI	
Age							
18-25	0.618	0.718	0.196-2.633				
26-35	0.589	1.477	0.358-6.096				
36-45	0.331	2.104	0.470-9.428				
46-55	0.361	2.045	0.441-9.491				
>55		1					
Sex							
Male	0.939	0.984	0.651-1.488				
Female		1					
Location							
Main Island	0.495	1.196	0.715-1.999				
Outside Main Island		1					
Education							
High School graduate	0.005	0.373	0.187-0.747				
Diploma or Undergraduate	0.235	0.647	0.315-1.328				
Post graduate		1					
Work							
Employed	0.000	2.341	1.454-3.768				
Unemployed		1					
Field							
Health-related	0.096	1.418	0.940-2.138	0.016	1.733	1.109-2.709	
Non-health-related		1					
Confirmed COVID-19							
Never	0.011	0.475	0.268-0.841	0.031	0.524	0.291-0.944	
Ever		1					
Marital status							
Married	0.000	2.484	1.489-4.145				
Unmarried		1					
Economy status							
Below average	0.003	0.260	0.107-0.629	0.012	0.309	0.124-0.769	
Average	0.292	0.745	0.431-1.288				
Upper average		1					

Notes: Chi-square for multivariate analysis 1.505, p=0.982, Variables with p-value<0.25 in univariate analysis were subjected to multivariate analysis. Variables with p-value<0.05 in multivariate analysis were subjected as significant predictive factors. AOR: adjusted odds ratio; COR: crude odds ratio; 95% CI: 95% confidence interval

Predictive factors of DS knowledge

Ordinal logistic regression was performed to investigate the respondents' knowledge of DS. The results of both univariate and multivariate analyses were consistent in showing that sociodemographic factors such as age, sex, domicile, education, work status, COVID-19 experience, marital status, economic status, and work/study background were not significant predictors of respondents' knowledge regarding DS consumption (Table 3). Additionally, DS consumption itself was not found to be a significant factor affecting knowledge.

Table 3. Predictor factors of DS knowledge using ordinal regression.

	Univariate			Multivariate			
Predictor Factors	p-value	COR	95% CI	p-value	AOR	95% CI	
Age							
18-25	0.075	0.361	0.117-1.110	0.171	0.441	0.137-1.421	
26-35	0.347	0.564	0.171-1.858	0.392	0.592	0.178-1.967	
36-45	0.058	0.310	0.092-1.039	0.061	0.312	0.092-1.056	
46-55	0.119	0.376	0.110-1.287	0.123	0.376	0.108-1.303	
>55		1			1		
Sex							
Male	0.134	1.303	0.922-1.840	0.240	1.242	0.865-1.782	
Female		1			1		
Location							
Main Island	0.437	1.189	0.769-1.838				
Outside Main Island		1					
Education							
High School graduate	0.348	0.788	0.480-1.296				
Diploma or Undergraduate	0.900	0.968	0.584-1.604				
Post graduate		1					
Work							
Employed	0.223	1.246	0.875-1.774	0.392	1.261	0.741-2.145	
Unemployed		1			1		
Field							
Health-related	0.275	0.824	0.581-1.167				
Non-health-related		1					
Confirmed COVID-19							
Never	0.445	0.853	0.567-1.284				
Ever		1					
Marital status							
Married	0.428	1.160	0.804-1.672				
Unmarried		1					
Economy status							
Below Average	0.676	1.189	0.527-2.682				
Average	0.324	1.234	0.812-1.874				
Upper Average		1					
Supplement consumption							
No	0.237	1.278	0.851-1.921	0.222	1.294	0.856-1.959	
Yes		1			1		

Notes: Chi-square for multivariate analysis 66.101, p=0.967, Variables with p-value<0.25 in univariate analysis were subjected to multivariate analysis. Variables with p-value<0.05 in multivariate analysis were subjected as significant predictive factors. AOR: adjusted odds ratio; COR: crude odds ratio; 95% CI: 95% confidence interval.

Discussion

The COVID-19 pandemic has changed most aspects of human lifestyle including the economy, transportation and of course, the medical field. It has been three years since WHO announced the pandemic, and despite declining cases, the status has not been revoked. Even now, researchers are still actively seeking and revealing new knowledge on COVID-19, including finding preventive measures and definitive drugs for post-COVID complications and long term COVID symptoms. DS as a preventive measure was highly investigated to avoid advanced stages of COVID-19. Several research studies also explored the possibility of DS to reverse the pathophysiology of COVID-19 (Caballero-García et al., 2021), as well as a complementary therapy for patients with COVID-19 and preventive therapy against lung diseases (Zhang & Liu, 2020). Several studies including clinical trials, endeavored to prove that DS effectively reduced disease severity, shortened the length of stay and prevented infection by boosting the immune system (Pinnawala et al., 2021). Unfortunately, those clinical trials failed to prove DS ability to do so (Amin & Drenos, 2021; Brunvoll et al., 2022; Murai et al., 2021; Thomas et al., 2021). However, increasing DS consumption and sales have been reported worldwide including in the US, Europe and Asia (d'Argom et al., 2021; Hamulka et al., 2021; Karlsson et al., 2021; Khabour & Hassanein, 2021; Lordan, 2021) with self-consumption practice, without consultation with healthcare professionals, and still observed in Asia, Africa and America (d'Arqom et al., 2021, (Quispe-Cañari et al., 2021; Sadio et al., 2021; Wegbom et al., 2021; Yasmin et al., 2022). Even though the self-consumption of DS is considered safe, their side effects in high-risk populations, especially individuals with several genetic backgrounds, comorbidities and patients on prescribed medication, could be unpleasant. They might experience unwanted effects due to drug and disease interaction (Agbabiaka et al., 2018; Asher et al., 2017; Ekor, 2014; Peng et al., 2004).

Practice of dietary supplement consumption and its predictive factors

Our study found increasing DS consumption, as more than three quarters of respondents consumed DS during the Delta wave of the COVID-19 pandemic, with only 59.52% consuming DS before the outbreak. Forty percent of the respondents did not consult with healthcare professionals before consuming DS for more than 3 months. This practice was also found before and during the pandemic, in parallel with other similar studies, such as in 1579 US citizens (Blendon *et al.*, 2013), 105 athletes in Saudi Arabia (Aljaloud & Ibrahim, 2013), 651 students in Saudi Arabia (Almegewly *et al.*, 2022) and 48,925 Japanese adults (Chiba & Tanemura, 2022). This consumption was significantly associated with middle age, higher education, higher economic status, marital status, receiving a diagnosis of COVID-19 and employment status. However, our regression model showed that only health-related field of work or study was a positive predictive factor, while never confirmed COVID-19 status and lower self-reported economic status were negative predictors.

Younger respondents might feel healthier and at lower risk of obtaining severe stage of COVID-19 (Libertini *et al.*, 2019; Perrotta *et al.*, 2020), while older respondents might be unaware of the risk and the disease, despite being more prone to transmission (Wolf *et al.*, 2020). Another possible reason was they might be unaware of the risk of interaction between DS and their diseases or drugs consumed (Agbabiaka *et al.*, 2018; Alkhalidi *et al.*, 2019). However, a high possibility existed that respondents having received a diagnosis of COVID-19 would like to prevent re-infection by consuming DS (Ali, 2020; Shahbaz *et al.*, 2022). Married and working respondents might consume DS due to their responsibilities to avoid infection and need to fulfil their duties to their family members. This finding was similar to the study in Indonesia during the first year of the pandemic (d'Arqom *et al.*, 2021), Saudi Arabia (Radwan *et al.*, 2022) and Lebanon (Mohsen *et al.*, 2021). Higher economic status respondents were able to buy the DS and might have a higher responsibility in their workplace; thus, they had consumed DS. Similar phenomena were also reported in Indonesia and Saudi Arabia (d'Arqom *et al.*, 2021; Radwan *et al.*, 2022). A study on 11,240 US adults from 2011 to 2014 also reported similar finding, as consumption of DS was higher among those earning higher incomes (Cowan *et al.*, 2018).

Among the two groups, respondents with non-health-related background were more likely to consume DS for more than three months compared with respondents with health-related backgrounds. Despite of not being in the medical and healthcare career line, non-health background respondents' have better long-term compliance. According to Biesalski and team, long term compliance in DS such as multivitamin and mineral supplement brings benefit to general health from developing lifestyle disease and was also documented safe in over 10 years of consumption in the clinical trial (Biesalski & Tinz, 2017). However, this miraculous finding does not apply to all DSs. Stranges *et al.* (2007) found that prolonged use of selenium, an ingredient commonly found in mainstream ingestible beauty supplements, can lead to an increased risk of developing type 2 diabetes later in life. Therefore, there are potential detrimental effects of long-term compliance with such supplements (Stranges *et al.*, 2007).

DS consumption practice was also associated with the method in acquiring DS. Drug stores were the primary vendor to purchase DS, followed by e-commerce platform and any store selling DS. This finding supported the significant presence of online shopping, due to its convenience and ease during the COVID-19 pandemic (Eger et al., 2021; Gu et al., 2021). Moreover, respondents with health-related background were more likely to buy using e-commerce platforms than the

non-health-related respondents. A study involving 34,488 Italians did not investigate the work/study background of the respondents as one of the predictive factors for online shopping; however, they found that younger age, higher education, female, good economic status and extended working hours comprised positive predictors for online shopping (Dominici et al., 2021). This might be one of the reasons, because healthcare professionals and medical students have long working hours (Dyrbye et al., 2017; Shreffler et al., 2020), including during the COVID-19 pandemic (Razu et al., 2021). However, this finding raises concerns about the regulatory control of e-commerce platforms and physical stores selling dietary supplements. Unlike drug stores, where pharmacists are available to offer advice and address concerns about supplements and their potential side effects, e-commerce platforms and other stores selling DS may not provide access to experts.

Knowledge on dietary supplements and its predictive factors

Moreover, our study found that one half of respondents possessed good knowledge levels about DS, with only 2% having poor knowledge. However, our findings might be biased because almost two thirds of our respondents had health-related work/study backgrounds. However, the comparison of DS knowledge in both groups showed respondents with non-health-related backgrounds possessed less knowledge about DS, supporting our above-mentioned concern on the purchasing habits out of drug store. This finding differed from that of 351 students in Saudi Arabia, reporting no difference between the knowledge level of health science students with those of non-health science students (Alowais & Selim, 2019). Unfortunately, most were still partially unaware of the safety and side effects of DS on the market and the necessity of DS consumption. This hurdle was also found among 537 US healthcare professionals (Kemper *et al.*, 2003) and 179 US students pharmacist (Axon *et al.*, 2017). Our study found that their level of knowledge was not determined by sociodemographic factors and DS consumption in the post-delta wave of the COVID-19 pandemic, as no significant predictor factors were found in univariate and multivariate analysis.

Even though sociodemographic factors did not affect the respondents' knowledge of DS, we need to be aware about health inequality that has been highlighted during the COVID-19 pandemic and has been discussed extensively (McGrail et al., 2022; Mishra et al., 2021). In Indonesia itself, in 2017, the WHO and Ministry of Health Republic of Indonesia reported an existing gap on health status in Indonesia related to economic status, education level, occupation, employment status, age, sex, place of residence and subnational region. These disparities include low consumption of fruits and vegetables, known as the main source of vitamins and minerals from food (WHO & Kemenkes, 2017). Several other studies also reported these health disparities (Haemmerli et al., 2021; Mulyanto et al., 2019). Reportedly, the implementation of national coverage insurance has resulted in a decrease in health disparities attributed to differences in economic status (Warsito & Adisasmito, 2020). Regrettably, the COVID-19 pandemic has led to an increase in socioeconomic disparity in urban areas, while rural areas with the highest COVID-19 cases have experienced a decrease, yet the impact of this trend on health inequalities remains unreported (Brata et al., 2021).

Limitation and recommendation

Even though the internet-based survey was conducted conveniently and efficiently, the questionnaire might not have reached the respondents in remote areas of Indonesia due to limited internet access. Moreover, limited interaction with the respondents might have created a biased responses to the questionnaire. Furthermore, the sampling methods did not represent the distribution of Indonesian adults. Thus, more respondents and better questionnaire outreach are needed to draw a complete picture of the practices and knowledge level of DS consumption post-delta wave of the COVID-19 pandemic. Despite the limitations, this study brings an important understanding on the practice and knowledge of DSs consumption in Indonesia, which have reconfigured our food and dietary psychology and habits due to the COVID-19 pandemic.

This study showed the practices and knowledge level of DS consumption in Indonesia post-delta wave of the COVID-19 pandemic. Even though the self-consumption of DS is considered safe, its side effects in high-risk populations, namely individuals with several comorbidities and patients on prescribed medication, might experience unwanted effects due to drug and disease interaction. Therefore, collaborative efforts from a multitude of organisations including medical doctors, pharmacists and governmental bodies to uphold their responsibilities to educate and provide essential and easily understandable information available to the general public. Based on this current study, the practice of self-consumption of DS in Indonesia is increasing, and this pattern is expected to increase further in the coming years. Hence, knowledge of DS is necessary to avoid detrimental effects that might occur in the future. This could be done by increasing accessibility of information with better labelling and educating youth, the future consumers to empower users to make wise choices on DS.

Data availability

Underlying data

Mendeley Data: Practice and Knowledge DS Indonesian Adult. doi: 10.17632/n2fdtbwrxb.2 (d'Arqom, 2022)

This project contains the following underlying data:

- Data 514 analysis.xlsx
- Erratum Data 514 analysis.xlsx (correction of coding variables, all started from 0)

Extended data

This project contains the following extended data:

 Supplementary file.docx (contains the survey instrument and differences between DS consumption practice of respondents with health-related background and non-health-related background)

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

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Brief summary:

The reviewed paper, titled "Practice and knowledge of dietary supplement (DS) consumption among Indonesian adults post-delta wave of the COVID-19 pandemic" was an internet-based survey which focused primarily on how dietary supplements was consumed by a statistically determined group of people in Indonesia, during the COVID-19 pandemic, as well as during the post-Delta wave period. The authors utilized descriptive method of analysis to illustrate the consumption pattern (frequency, duration, aim, preferrable dosage form), familiarity with and side-consequences of DS among the respondents.

This is a well written paper which throws more light on the consumption of DS not only in Indonesia but throughout the world. Other reviewers have commented extensively on the statistical analysis and inferences in this paper. Authors should go over the syntaxes and tenses as I have suggested in the review paper which I am submitting with comments and highlighted sentences or words, LINK.

General Comments:

Introduction:

- The subject matter of this manuscript, consumption of DH, is of global concern and the period of study was a time of worldwide pandemic. Currents of vital information on these two issues are vital to the scientific world. The introduction segment of the paper, consisting of four paragraphs, is well written but few sentences therein require correction of typographical errors and tenses.
- Furthermore, the authors should probably have presented DS consumption from a wider area of the world so that readers could have a better idea of the depth of the health problems that the study was trying to unravel.

Method:

- This segment of the manuscript was divided into five segments Study design, Participants, Data collection, Ethical consideration, and Analytical procedures. Here, the authors should probably have given a brief description of the study site, including the population of Indonesia and some geographical information, if the sample size was adequate for statistical inference, though this really depends on the response rate as this was an on-line study.
- One of the minor drawbacks of this section is the syntax of the last sentence in the data collection section which has been referred to and corrected in the review.

Result:

- The Result segment of the reviewed paper contains most of the sentences or words that need correction. First, there is no need to express percentages beyond one decimal place.
 In fact, figures are best expressed as whole numbers. This has been reflected in the reviewed paper.
- Secondly, some of the sentences in this segment of the paper need to be rephrased to make sense to the readers. One minor observation was that the first column in Table 1 may be re-arranged, putting Marital status and Economic status after Sex followed by Education, Work, Field of work/study and lastly Confirmed COVID-19.
- Further, Figure 1 is too compact and should probably be spread out and given a relatively clearer explanation, especially Figures 1 C and D. Figure 1 A refers to co-morbidities of the respondents, but this should be explained further. Is it that these disease entities occur together in the same patient (co-morbidity) or they exist differently, in different prevalence, among the study participants? This should be made clear to readers. The following questions in the questionnaire needs further clarification Q6: DSs have dangerous side effects and Q10: DS have fewer side effects. The reason is that Q6 does not preclude Q10. DSs fewer but dangerous side effects and fewer or more DSs can have dangerous side effects.

Discussion:

- It would be good to include references from different regions of the world, including Africa, which was also ravaged by the COVID-19 pandemic and where DSs are also consumed in large quantities before, during and after the pandemic.
- The authors quoted Biesalski & Tinz, 2017 as having a "miraculous" finding but this word miraculous should be deleted from this manuscript because it is subjective, and others may not find it miraculous. Some statements in this segment of the manuscript are incomplete and authors have been advised to complete them in the reviewed paper.

Limitation and recommendations:

 A statement in the second paragraph in this segment, also highlighted in yellow as others that need correction, has been reconstructed. The authors should take a look at it and possibly effect the recommended changes.

Overall, this is a well-written paper with good ideology. I would like to congratulate the authors for their efforts in producing a splendid work. The authors may wish to go over the reviewed paper and make possible changes to the areas that need correction.

Congratulations again.

Is the work clearly and accurately presented and does it cite the current literature? Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others? Yes

If applicable, is the statistical analysis and its interpretation appropriate?

I cannot comment. A qualified statistician is required.

Are all the source data underlying the results available to ensure full reproducibility? Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Tropical Diseases, Women's Health, Adolescent Nutrition.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 17 July 2023

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Siti Maisharah Sheikh Ghadzi

School of Pharmaceutical Sciences, Universiti Sains Malaysia, Minden Heights, Pulau Pinang, Malaysia

Brief summary

This manuscript was designed with the aim to investigate the practice and knowledge of the general public in Indonesia regarding DS during the post-Delta wave of the COVID-19 pandemic. In addition, the predictive factors of DS consumption and level of knowledge were further analyzed.

General comments

Method

- Questionnaire: more information is needed, especially on the validity tests. What type of validity test was conducted?
- How do the authors determine the eligibility of the pharmacologist, pharmacist and psychologist to validate the questionnaire? Are 4 reviewers sufficient? Please explain with references.
- How do the authors determine whether the number of subjects for the pilot study is sufficient? Please add the reference as well.
- How did the authors determine the level of knowledge based on the score? Were any standard classifications used, (example: Bloom's cut off point)? Please add the explanation and reference.

Results

- Figure 2b describes the results from Kruskal Wallis. But the information on the use of Kruskal Wallis is not described in the method section. Were the data not normally distributed? Please revise accordingly.
- Table 2 and Table 3. It is not clear on why the demographic data was not included in the logistic regression analysis. Please describe the reason, and revise if needed. Perhaps because it was not significant in the univariate analysis? If yes, then my suggestion is to describe in the statistical analysis, in which to add that the significance variables in the univariate analysis is further investigated using univariate and multivariable logistic regression. Please revise accordingly.
- Table 2: why are Education, Work and Marital statuses not included into the multivariable analysis even though it is significant in the univariate regression? Why is Field included in the multivariable logistic regression even though it is not significant in the univariate regression?

Discussion

- Paragraph 1: It would be good to include the examples of side effects in high risk population, and unwanted effects dur to drug and disease interaction.
- Paragraph 2: any potential reason for the results of regression model? It would be good to add the explanation on the potential reason.

Is the work clearly and accurately presented and does it cite the current literature?

Is the study design appropriate and is the work technically sound? Partly

Are sufficient details of methods and analysis provided to allow replication by others? Yes

If applicable, is the statistical analysis and its interpretation appropriate? Partly

Are all the source data underlying the results available to ensure full reproducibility? Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Clinical pharmacy, endocrine, pharmacokinetic/pharmacodynamic modelling, pharmacotherapy

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 19 May 2023

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Mikołaj Kamiński

Department of Treatment of Obesity, Metabolic Disorders and Clinical Dietetics, Poznań University of Medical Sciences, Poznań, Poland

Thank you for the responses. All my comments were responded.

Is the work clearly and accurately presented and does it cite the current literature? Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others? $\mbox{\em Yes}$

If applicable, is the statistical analysis and its interpretation appropriate? Yes

Are all the source data underlying the results available to ensure full reproducibility? Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Public Health

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 30 March 2023

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Mikołaj Kamiński

Department of Treatment of Obesity, Metabolic Disorders and Clinical Dietetics, Poznań University of Medical Sciences, Poznań, Poland

The manuscript presents a study focusing on the practices and knowledge level of dietary supplement (DS) consumption in Indonesia, particularly after the COVID-19 pandemic. The authors have provided a comprehensive background on the topic and presented their findings based on a well-structured questionnaire. However, there are certain aspects that need to be addressed to improve the manuscript's overall quality and clarity.

Major Comments:

- 1. The authors mention that the study was conducted after the COVID-19 pandemic. However, considering that the pandemic is still ongoing and that the WHO has not revoked the pandemic status, it would be better to rephrase the context of the study as "during the COVID-19 pandemic" or "in the post-delta wave of the COVID-19 pandemic" instead of "after the COVID-19 pandemic."
- The manuscript would benefit from a clear description of the study design, including the sampling method, sample size, and the study period. It is essential to provide these details to assess the study's robustness and reliability.
- 3. The authors should consider providing a demographic breakdown of the respondents, including age, gender, geographic distribution, and other relevant characteristics. This information is crucial to understand the generalizability of the study findings.
- 4. The authors should provide more details about the questionnaire, including how it was developed, its validation process, and how the knowledge levels of respondents were assessed.

- 5. The authors have highlighted several limitations of the study, such as the sampling method, questionnaire outreach, and potential bias in the responses. They should consider discussing potential strategies to address these limitations in future studies to provide a more comprehensive understanding of DS consumption practices and knowledge levels in Indonesia.
- 6. The discussion section could be better organized by separating the key findings and relating them to the existing literature. It is essential to highlight the novel aspects of the study and the implications of the findings for policy and practice.
- 7. Given the study's focus on practices and knowledge levels, it would be helpful to include recommendations for public health interventions to promote safe and informed DS consumption, such as educational campaigns or regulatory measures.

Minor Comments:

- 1. In several instances throughout the manuscript, the authors use the term "DS" without defining it first. It would be helpful to define the term "dietary supplements" before using the abbreviation "DS" to improve readability.
- 2. Some sentences are lengthy and could be broken down into shorter, more concise statements for better readability.
- 3. The manuscript would benefit from a thorough proofreading to correct grammatical errors, inconsistencies in citations, and formatting issues.

In conclusion, the manuscript presents an interesting study examining the practices and knowledge level of dietary supplement consumption in Indonesia during the COVID-19 pandemic. However, several aspects need to be addressed to improve the manuscript's quality and clarity. By addressing these concerns, the authors can present a more robust and reliable study that contributes to the understanding of dietary supplement consumption in the context of the ongoing pandemic.

Is the work clearly and accurately presented and does it cite the current literature?

Is the study design appropriate and is the work technically sound?

Are sufficient details of methods and analysis provided to allow replication by others? Partly

If applicable, is the statistical analysis and its interpretation appropriate? Partly

Are all the source data underlying the results available to ensure full reproducibility? Partly

Are the conclusions drawn adequately supported by the results? Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Public Health

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response 28 Apr 2023

Annette d'Argom

Response to Review and Editor Comments

(Manuscript Number: ID 129045)

We are very much thankful to the reviewers for their deep review. I have revised the manuscript in the light of their useful suggestions and comments. We hope the revision improves the paper to a level of their satisfaction. Number wise answers to the specific suggestions/comments are as follows:

Response to Reviewer: 1

Comments to the Author

The manuscript presents a study focusing on the practices and knowledge level of dietary supplement (DS) consumption in Indonesia, particularly after the COVID-19 pandemic. The authors have provided a comprehensive background on the topic and presented their findings based on a well-structured questionnaire. However, there are certain aspects that need to be addressed to improve the manuscript's overall quality and clarity.

Major Comments:

1. The authors mention that the study was conducted after the COVID-19 pandemic. However, considering that the pandemic is still ongoing and that the WHO has not revoked the pandemic status, it would be better to rephrase the context of the study as "during the COVID-19 pandemic" or "in the post-delta wave of the COVID-19 pandemic" instead of "after the COVID-19 pandemic."

Response: Thank you very much for bringing up this matter. We change the sentences into post-delta wave of the COVID-19 pandemic as in the line 350 and 354.

2. The manuscript would benefit from a clear description of the study design, including the sampling method, sample size, and the study period. It is essential to provide these details to assess the study's robustness and reliability.

Response: Thank you very much for pointing out this issue. We did mention the sampling methods and the study period in the line 52-55 ("The questionnaire was distributed to the adult population in Indonesia through email and social media using convenience sampling methods from October to December 2021, and multiple responds from single device were prevented based on respondents' IP address."); and the sample size in the line 62-65 ("Sample size was calculated using sample size calculator (www.raosoft.com) with 5% margin of error, 95% confidence level, and population number filled with 100,000, resulting in 383 minimum respondents.").

- 3. The authors should consider providing a demographic breakdown of the respondents, including age, gender, geographic distribution, and other relevant characteristics. This information is crucial to understand the generalizability of the study findings. Response: Thank you very much for your suggestion. The sociodemographic characteristic of the respondents was provided in table 1.
- 4. The authors should provide more details about the questionnaire, including how it was developed, its validation process, and how the knowledge levels of respondents were assessed.

Response: Thank you very much for bringing up this matter. We did mention about the development of the questionnaire and the validation process as in the line 78-88 ("The questionnaire was modified from the Prevalence and Awareness Concerning Dietary Supplement Use among Saudi Adolescents (Alfawaz et al., 2020) and Knowledge about dietary supplements and trust in advertising them: Development and validation of the questionnaires and preliminary results of the association between the constructs (Karbownik et al., 2019). The questionnaire was combined and validated by two pharmacologists, a pharmacist, and a psychologist, and was further tested on 20 respondents to ensure that the content and terms used in the questionnaire were relevant and understandable. The reliability measurement on the survey data showed a Cronbach alpha coefficient of 0.750 for DS knowledge. As the reliability value for the preliminary pilot testing is at an acceptable level, the real data collection for this study was proceed."). Moreover, the assesment the knowledge level of the respondents was mention in the line 102-105 ("The answers to the knowledge survey were measured using correct/wrong/does not know options measured as 1/0/0. The total score was the summation of the 16 question scores and was grouped in four categories based on the total score of each respondent: poor (0-4), moderate (5-8), good (9-12) and excellent (13-16).")

5. The authors have highlighted several limitations of the study, such as the sampling method, questionnaire outreach, and potential bias in the responses. They should consider discussing potential strategies to address these limitations in future studies to provide a more comprehensive understanding of DS consumption practices and knowledge levels in Indonesia.

Response: Thank you very much for pointing out this matter. We did provide the strategies to address this limitation for better future studies as in the line 348-350 ("Thus, more respondents and better questionnaire outreach are needed to draw a complete picture of the practices and knowledge level of DS consumption post-delta wave.")

- 6. The discussion section could be better organized by separating the key findings and relating them to the existing literature. It is essential to highlight the novel aspects of the study and the implications of the findings for policy and practice.

 Response: Thank you very much for your suggestion. We divide the discussion part into three sections: (1) practice of dietary supplement consumption and its predictive factors, (2) knowledge on dietary supplements and its predictive factors, and (3) limitation and recommendation.
- 7. Given the study's focus on practices and knowledge levels, it would be helpful to include recommendations for public health interventions to promote safe and informed DS consumption, such as educational campaigns or regulatory measures.

Response: Thank you very much for bringing up this matter. We did include the recommendation for promoting the safe and informed DS consumption as in the line 358-361 ("Therefore, collaborative efforts from a multitude of organisations including medical doctors, pharmacists and governmental bodies to uphold their responsibilities to educate and provide essential and easily understandable information available to the general public.") and 364-365 ("This could be done by increasing accessibility of information with better labelling and educating youth, the future consumers to empower users to make wise choices on DS.")

Minor Comments:

8. In several instances throughout the manuscript, the authors use the term "DS" without defining it first. It would be helpful to define the term "dietary supplements" before using the abbreviation "DS" to improve readability.

Response: Thank you very much for pointing out this issue. We did define dietary supplements as DS in the first sentence of the abstract.

9. Some sentences are lengthy and could be broken down into shorter, more concise statements for better readability.

Responses: Thank you very much for the suggestion. We re-write some sentences to increase the readability, for example in the line 19-26, 31-36, 222-226, 290-293, 307-311, and 336-342.

10. The manuscript would benefit from thorough proofreading to correct grammatical errors, inconsistencies in citations, and formatting issues.

Responses: Thank you very much for the suggestion. Our manuscript has been reviewed by a English native speaker. We do hope it meets your expectation.

11. In conclusion, the manuscript presents an interesting study examining the practices and knowledge level of dietary supplement consumption in Indonesia during the COVID-19 pandemic. However, several aspects need to be addressed to improve the manuscript's quality and clarity. By addressing these concerns, the authors can present a more robust and reliable study that contributes to the understanding of dietary supplement consumption in the context of the ongoing pandemic.

Responses: Thank you very much for your review. We do hope that our revision does improve the quality and clarity of the manuscript.

Competing Interests: The authors declare that they have no conflict of interest.

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