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Vitamins Sales Before and During the COVID-19 Pandemic at Network Online Pharmacies in Indonesia

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Abstract
The use of vitamins and micronutrients as an immunity enhancer during the COVID-19 pandemic is needed. The use of vitamins and micronutrients as immunity boosters during the COVID-19 pandemic is very much needed. The description of vitamin needs can be predicted from vitamin sales carried out by network online pharmacies in Indonesia. Vitamins C and E are antioxidants that indirectly have a role as an antiviral. Vitamin D can increase immunity, so its availability is important during the COVID-19 pandemic. This study compares vitamin sales before and during the COVID-19 pandemic at online pharmacies in Indonesia as a description of vitamin use in the community, and their availability by the pharmaceutical industry so that the government can take policies to accelerate this period. The study began by taking master data of all vitamin sales from January 2019 to December 2020 at one of the online pharmacies in Indonesia. Data on all sales each year were grouped based on vitamin content, namely single vitamins, containing two vitamins, and multivitamins (more than two vitamins) and then compared them. Data analysis used the independent t-test, and if the data was not normal and homogeneous, it was processed using the Mann-Whitney test by SPSS version 26 software. The results showed that there was a significant difference between sales of vitamin C ($p<0.05$), vitamin E ($p<0.01$), a combination of vitamins B and C ($p<0.05$), vitamins B and E ($p<0.05$), and multivitamins ($p<0.001$) in online pharmacy networks in Indonesia before and during the COVID-19 pandemic. Interestingly, sales of vitamin D did not increase significantly during the COVID-19 pandemic due to limited supplies from pharmaceutical companies even though vitamin D is very important for increasing immunity, thus giving rise to the policy of the Indonesian Ministry of Health to utilize sunlight as the main source of vitamin D.

Keywords: Vitamin, COVID-19, Networking Online Pharmacy, Sun Rays, Immunity.

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1. INTRODUCTION

World Health Organization (WHO) is working with the Indonesian government to monitor the situation and prevent the spread of Covid-19 in Indonesia (World Health Organization, 2022). To bring the pandemic to the end and increase immunity, every country implemented vaccination programs even use traditional medicine combine with "western medicine" (Murdiana et al., 2022). Consumption of micronutrients, i.e., proven vitamins and minerals, increases immunity; thus, it can oppose infection (Philipp et al., 2021). Vitamin sales before and during the pandemic illustrate the consumption of vitamins that increase immunity against COVID-19, but there are exceptions based on Indonesia's geographical location as an equatorial zone rich in sunlight. Acute respiratory distress syndrome (ARDS) causes the most morbidity of COVID-19, which is the result of oxidative stress caused by the formation of cytokines and free radicals. Vitamin C and other antioxidants are recommended for ARDS (Al-Obaidi et al., 2021). Numerous functions of vitamin C include the indirect antiviral effect as immunomodulatory, antiinflammatory effect (Abobaker et al., 2020) and has previously been used to treat septic shock and severe sepsis (Hiedra et al., 2020; Earar et al., 2020; Michele et al., 2020; Darbar, Saha, & Agarwal, 2021). A randomized clinical trial study on COVID-19 survivors aged 20-60 years old in Rome, Italy, found that giving L-arginine plus vitamin C increased patients' ability during COVID-19 (Tosato et al., 2022). Research conducted using the Google Trends website provided by Google stated that Vitamins D and C were the most frequently searched vitamin types in Turkey and worldwide during the COVID-19 pandemic (Cimke & Gurkam, 2020).

Vitamin D also reduces the risk of infection by inducting cathelicidins and defensins thus it decreases the level of virus replication and reduces the concentration of cytokine proinflammatory which causes inflammation as well as increases anti-inflammatory cytokine (Grant et al., 2020). The control of the renin-angiotensin system (RAS), cellular innate and adaptive immunity, and physical barriers are three potential mechanisms by which vitamin D may reduce infection and mortality in Covid-19 (Annweiler et al., 2020). Calcitriol is in the form of active vitamin D, which is metabolically active and influences *hosts'* immunity (Juzeniene et al., 2010). Patients with vitamin D hypovitaminosis are at risk of getting maintenance intensively in the hospital and have a risk of death tall (Carpagnano et al., 2021). Vitamin D deficiency (<20 µg/ml) and insufficiency (<30 µg/ml) of serum 25 hydroxycholecalciferol increase the risk of acute respiratory tract infections. Vitamin D supplementation reduced the relative risk of acute respiratory tract infection by about 8% with the strongest effects in patients receiving daily or weekly boluses (Philipp et al., 2021). Therapy priority for vitamin D in oral form. Vitamin D has a margin of safety-wide and small reporting side effects (Bradley et al., 2020). A study in Jordan using the online Immune Status Questionnaire found that less than 50% did not receive vitamin D supplements in Pandemic COVID-19 (Nawaiseh et al., 2023), supported by research in Japan, productive women stated that during the pandemic they did not get enough vitamin D supplements and sunlight (Tsugawa et al., 2022). Research in Poland describes a decrease in vitamin D levels in pediatrics during the pandemic compared to before (Rustecka et al., 2021) and adult in Korean to prolong healing (Kwon & Kang, 2022).

Vitamin E is already proven as an antioxidant. The supplementation of vitamin E probably decreases the production of pro-inflammatory cytokines (Michele et al., 2020), and indirect by affecting inflammatory mediators generated from other immune cells (Lewis et al., 2019). Supplementation of vitamin E can improve the function of the immune system and reduce the risk of infection. Modulation of immune function by vitamin E has clinical relevance as it affects host susceptibility to infectious diseases such as respiratory infections (Lewis et al., 2019). Vitamin E deficiency affects both humoral and cell-mediated immune processes because it is particularly abundant in the membrane of immune cells (Pae & Wu, 2017).

Vitamin A increasing the response of immunity against respiratory pathogens. Current vitamin A deficiency infection will increase morbidity and mortality risk from pulmonary tract infection. The severe morbidity and mortality from infectious diseases may be decreased by taking vitamin A supplements (Michele et al., 2020). Lack of Vitamin A may hinder the lung's capability to repair damaged epithelial surfaces, which could result in long-lasting scarring, lung fibrosis, and diminished pulmonary function (Stephensen & Lietz, 2021). Enrichment of immunoreaction, suppression of inflammatory response, and biological processes involving reactive oxygen species are some of the ways that Vitamin A attacks SARS-CoV-2 (Li et al., 2020).

Several studies on mice and humans have demonstrated that vitamins B6 and B12 are crucial increase immune response. Their deficiencies have been linked to decreased B lymphocyte production due to their slowed proliferation. Rats with vitamin B6 deficiency have decreased thymus activity, while older individuals with this deficiency have altered T helper cell activities and IL-2 production (Michele et al., 2020).

Soft tissue is guarded against calcification by the matrix gla protein (MGP), a vitamin K-dependent protein. As an autologous defense mechanism to prevent irreversible injury, MGP synthesis is increased. MGP requires vitamin K-dependent activation for functionality, which may deplete vitamin K stores and induce a deficiency in patients with SARS-CoV-2 infection (Visser et al., 2022). Several vitamins are recommended to increase immunity, specifically during the COVID-19 pandemic. Therefore, this study compares the use of vitamins sold by online pharmacy networks in Indonesia before and during the COVID-19 pandemic, which illustrates the need for vitamins by the community and the policy solutions of the Indonesian government if these important vitamins are not available.

2. RESEARCH METHOD

This research uses study survey analytics with a cross-sectional design. The research data were taken from the master data (big data) from one of the largest online pharmacy networks in Indonesia. The sample of this study was all sales populations of vitamins, single, double and multivitamins, that occurred in January 2019 (2019 was the period before the pandemic) to December 2020 (2020 was when the pandemic occurred).

Data collection was carried out in January 2021 after all data was collected. Sales data in 2019 and 2020 from all vitamin brands were grouped based on the vitamin content, namely single vitamins (A, B, C, D, E, K), preparations containing 2 vitamins (A + D, B + C, B + E, C + E, C + D) and multivitamins (more than 3 vitamins). Data analysis was carried out by calculating the number of vitamin sales that occurred before and during the pandemic, the percentage increase in sales for each brand vitamins and than add them, mean ± SD and the significance of the increase in sales.

The analysis of the significance of the number of sales was carried out using the independent t-test if the data was more than two types. Meanwhile, if the paired t-test does not meet the requirements of normality and homogeneity, the Mann-Whitney test is carried out. The analysis was carried out using SPSS 26 software.

3. RESULTS AND DISCUSSION

During the COVID-19 pandemic, there are increasing needs and requests from the public for multivitamins as a prevention effort toward transmission of COVID-19 (Food and Drug Supervisory Agency - Republic of Indonesia, 2023). Many vitamin brands are sold in one online pharmacy in Indonesia. Multivitamins are the most common vitamin combinations. They are reliable supplements that can increase body health. The development of multivitamins to ensure continuous health in an easier way is challenging to fulfill the public's need for health (Shreenidhi & Arivarasu, 2020).

Table 1. The Percentage of sales improvement before the pandemic and during the COVID-19 pandemic.

Types of vitamins	**Types of brands that are sold on the market (n)**	**Sales Amount 2019**	**Sales Amount 2020**	**Percentage Enhancement Sales (%)**
Vitamin A	1	56	64	14,29
Vitamin B	69	4473	13297	197,27
Vitamin C	33	3785	10336	173.08
Vitamin D	24	1427	2456	72,11
Vitamin E	19	399	2188	448,37
Vitamin K	1	280	931	232.5
Vitamins A and D	6	45	140	211,11
Vitamins B and C	31	1306	17355	1228,87*
Vitamins B and E	10	412	983	138.59
Vitamins C and E	3	235	568	141.7
Vitamins C and D	8	203	1147	465.02
Multivitamins	119	3187	16322	412,14

Table 1 shows that all sales of vitamins increased, but most were combinations of vitamins B and C; this is in line with research in Turkey and around the world that interest in vitamins has increased since the start of the COVID-19 pandemic (Cimke & Gurkam, 2020). Deficiency in B vitamins, especially thiamine (B1), can significantly impair cell function, and the body's immune system is needed to eliminate the SARS-CoV-2 virus, as well as cause inflammation so that it causes more severe symptoms (Shakoor et al., 2021). Riboflavin (B2) and UV light are effective against the MERS-CoV virus, which means they can also help fight SARS-CoV-2. Niacin (B3) reduces neutrophil infiltration and exhibits anti-inflammatory effects in patients with ventilator-associated lung injury. Pantothenic acid (B5) has the function of increasing wound healing and reducing inflammation. Pyridoxal 5′-phosphate (PLP) is the active form of pyridoxine, which functions to reduce the symptoms of COVID-19 by regulating the immune response, reducing pro-inflammatory cytokines, maintaining endothelial integrity, and preventing hypercoagulability. Folic acid (B9) is important for DNA and protein synthesis and in adaptive immune responses. Cobalamin (B12) acts as a modulator of the gut microbiota and decreased levels of B12 increase methylmalonic acid and homocysteine, resulting in increased inflammation, reactive oxygen species, and oxidative stress. SARS-CoV-2 can interfere with the metabolism of vitamin B12 (23), so vitamin B12, especially mecobalamin, functions as a damper for the symptoms of COVID-19 (dos Santos, 2020).

Vitamin C (ascorbic acid) is a water-soluble micronutrient that has high antioxidants in enhancing the immune system, supporting the epithelial barrier against the entry of pathogens and the cellular function of the innate and adaptive immune system (João et al., 2020). Vitamin C supplementation increases the oxygenation index in patients infected with COVID-19 (Shakoor et al., 2021). The antiviral effect of vitamin C plays a role in the production of antiviral cytokines (IFN α/β) or even binding to viruses (Bae & Kim, 2020).

Additionally, vitamin C may even directly impact viruses by binding to them and potentially inhibiting their replication. Vitamin C is known for its antioxidant properties, which help protect cells from oxidative stress and inflammation. It also plays a crucial role in supporting the immune system, enhancing the function of both innate and adaptive immune responses. Vitamin C promotes the production of antiviral cytokines, such as interferon-alpha/beta, essential for combating viral infections. Additionally, vitamin C has been shown to have direct antiviral activity, as it can bind to viruses and inhibit their replication (Bae & Kim, 2020).

The multivitamin in this study is a dosage form consisting of 3 or more vitamins. The number of multivitamin trademarks in Indonesia is the highest. The surge in sales of vitamins is primarily observed in the case of vitamin E, as well as combinations of vitamins C and D. This trend can be attributed to the Indonesian population's adherence to the information provided by the Indonesian Ministry of Health regarding the specific benefits of these vitamins in preventing the harshness of SARS-CoV-2. By following the recommendations outlined by the Ministry of Health, individuals seek out these particular vitamins to enhance their immune system and reduce their susceptibility to the virus.

Vitamin E sales showed a high percentage increase of 448.37%, the 3rd highest after the combination of vitamins B and C and the combination of vitamin C and D. Vitamin E is one of the most potent immune-modulating substances available. Vitamin E supplementation improves innate and adaptive immunological responses, increases leukocyte phagocytic capacity, and decreases bactericidal activity (Lewis et al., 2019). Not all vitamins have experienced a significant increase in sales.

Table 2. The sales analysis of significance increases before and during the pandemic.

Types of vitamins	Mean ± SD (Before Pandemic)	Mean±SD (During Pandemic)	p-value	Method Testing
Vitamin A			-	-
Vitamin B	64.82 ± 143.29	192.71 ± 312.27	0.778	Mann Whitney
Vitamin C	114.70 ± 262.09	313.21 ± 519.5	0.033*	Mann Whitney
Vitamin D	59.46 ± 132.04	102.33 ± 215.32	0.247	Mann Whitney
Vitamin E	21.0 ± 23.24	115.16 ± 116.27	0.001**	Independent T-Test
Vitamin K			-	-
Vitamins A and D	7.5 ± 10.37	23.33 ± 25.42	0.211	Independent T-Test
Vitamin B and C	42.13 ± 66.2	559.84±1205.35	0.011*	Mann Whitney
Vitamin B and E	41.2 ± 36.61	98.3 ± 82.80	0.047*	Independent T-Test
Vitamin C and E	78.33 ± 58.31	189.33 ± 134.70	0.628	Mann Whitney
Vitamin C and D	25.37 ± 24.76	143.38 ±198.68	0.085	Independent T-Test
Multivitamins	26.78 ± 43.56	137.16 ± 315.71	0.000***	Mann Whitney

Description: *Significance of increase in vitamin sales before compared to during the pandemic *p<0.05; **p<0.01; ***p<0.001*

Table 2 shows that several vitamins have experienced a significant increase in sales. Vitamin A and single vitamin K only have 1 type of brand circulating in the market; thus, they cannot be compared in significance between before and during the COVID-19 pandemic, and even though there are many types of vitamin B, the increase in sales before and during the Covid19 pandemic did not differ significantly for single vitamin B, but for vitamin B combinations with vitamin C and vitamin E there is a significant difference because the neurotropic B vitamins thiamine (B1), pyridoxine (B6), and cobalamin (B12) have been known as nerve vitamins that maintain nerve survival in different ways. The vitamin B complex continuously protects nerves from damaging environmental influences. Vitamin B1 acts as a nerve antioxidant and facilitates the use of carbohydrates for energy production, vitamin B6 balances nerve metabolism, and vitamin B12 maintains the myelin sheath and remyelination of nerve cells. Vitamins B1, B6, and B12 pave the way for the following essential regeneration by supporting the development of new cell structures (Baltrusch, 2021). Vitamins B1, B6, and B12 function in the peripheral and central nervous systems, including energetic cellular, antioxidant, neuroprotective, and neurotransmitter effects (Calderón-Ospina & Nava-Mesa, 2020).

There is no significant difference in vitamin D sales, either alone or in combination with vitamin A or vitamin C, even though the benefits of vitamin D in preventing COVID-19

are enormous. A high prevalence of hypovitaminosis D was found in COVID-19 patients with acute respiratory failure who were treated in the RICU. Vitamin D deficiency is a marker of poor prognosis in COVID-19 patients and has a high risk of death (Carpagnano et al., 2021). Research confirms race and ethnicity as predictors of severe COVID-19 as well as clinical risk factors for hospitalization and severe COVID-19 that were previously unidentified, namely vitamin D deficiency, hypercholesterolemia, osteoarthritis, and anemia (Mendy et al., 2020). Vitamin D, especially cholecalciferol (Vitamin D3) is an adjuvant in Covid-19 therapy because it has an antiviral effect (Philipp et al., 2021; Ling et al., 2020). A deficiency of vitamin D metabolites identified by low levels of 25(OH)D has an impact on the immune system and on the development of COVID-19 infection by the CoV-2 SAR virus, which results in high hospitalization of COVID-19 patients (Merzon et al., 2020). High-dose calcifediol or 25-hydroxyvitamin D, the primary metabolite of the vitamin D endocrine system, significantly reduces the need for ICU care in hospitalized COVID-19 patients (Entrenas Castillo et al., 2020). Low levels of vitamins C and D in critically ill COVID patients in the ICU are a risk factor for death (Arvinte et al., 2020). The combination of vitamins C and D has also been shown to reduce mild to moderate viral infections in COVID-19 (Hiedra et al., 2020).

The non-significance of sales of vitamin D alone or in combination with onter vitamin in online pharmacy networks in Indonesia is probably due to a shortage of supplies, even though education on the importance of vitamin D in preventing the severity of COVID-19 has been socialized by the Indonesian government. It is also possible because of the Indonesian government's appeal that vitamin D can be obtained from food and sunlight. Vitamin D is cutaneously produced after exposure to UVB rays; its synthesis is influenced by latitude, season, use of sunscreen, skin pigmentation, skin type, age, the actual duration of sun exposure, and the amount of skin exposure (Werneke et al., 2021). At higher latitudes, there is more UVB radiation, with wavelengths between 290 and 315 nm (Werneke et al., 2021). Geographical coordinates determine the intensity of radiation and the length of sunlight received by an area (Arsyad et al., 2021). Indonesia has abundant sunshine every year, with an average radiation intensity of around 4.8 kWh/m a day and an average radiation duration of 12 hours/day (Octavianti et al., 2018). Sunlight contributes to the healing of various health conditions, including respiratory diseases such as influenza, SARS, and COVID-19 (Geier et al., 2018; Tosepu et al., 2020). This study provides an illustration of the overall need for vitamins in Indonesia, because of mobility restrictions during the pandemic, online sales are very representative of the data, although in the outermost areas of Indonesia there may not be online pharmacies available. Recommendations for further research are to look for factors other than vitamins as immune enhancers.

4. CONCLUSION

There was a significant difference in sales of vitamin C, vitamin E, a combination of vitamins B and C, vitamins B and E, and multivitamins in the network of online pharmacies in Indonesia before and during the COVID-19 pandemic. Sales of Vitamin D did not increase significantly due to limited supply, which triggered a policy from the Indonesian Ministry of Health to utilize sunlight as a source of vitamin D to increase immunity during the COVID-19 pandemic.

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