UNRAVELING THE ENIGMA: AN EXTENSIVE ANALYSIS OF THE UNPREDICTABLE HEALTH RISK OF "COVID-19: JN.1"

By

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A thesis submitted to the School of Pharmacy in partial fulfillment of the requirements for the degree of Bachelor in Pharmacy

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Declaration

It is hereby declared that

1. The thesis that was turned in is our own, original work that we did while earning a degree from Brac University.
2. The thesis does not include any previously published or third-party written content, unless properly cited through complete and correct referencing.
3. Nothing in the thesis has been submitted or accepted for credit toward any other degree or certificate from a university or other organization.
4. I have acknowledged all main sources of help.

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Approval

The thesis titled "Unraveling the Enigma: An Extensive Analysis of the Unpredictable Health Risk of "Covid-19: JN.1" submitted by Mahmud Al Maruf (20146030) has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelors of Pharmacy.

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Ethics Statement

This study does not involve any human and animal trial.

Abstract/ Executive Summary

"Covid-19: JN.1" is a mysterious illness that casts doubt on our understanding of illness since it poses an unknown risk to health. This thesis proposes to explain “Covid-19: JN.1”s complexity by taking a close look at it (possible symptoms, causes, transmission, prevention, treatment). The goal is to comprehensively investigate “Covid-19: JN.1” in order to contribute to public health, disease management, and global health security. The research's findings and suggestions are meant to provide the global health community with more adaptability and strength against “Covid-19: JN.1”

Dedication

Dedicated to my parents

Acknowledgement

First and foremost, I want to thank God for all of his blessings, which have been granted to me in an attempt to give me the power and persistence to finish this project.

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List of Acronyms

SARS-CoV-2- Severe Acute Respiratory Syndrome Coronavirus 2

SPSS- Statistical Package for the Social Sciences

WHO- World Health Organization

CDC- Centers for Disease Control and Prevention

ACE2- Angiotensin-converting enzyme 2

RBD- Receptor Binding Domain

TNF- Tumor necrosis factor

IL-1β- Interleukin-1 beta

CD T-cells- Cytotoxic T cells

Chapter 1:

Introduction

People worry about getting sick because new pathogens have the potential to emerge and generate issues for global health systems. The emergence of COVID-19 in late 2019 has dramatically altered the global health situation, eliciting unprecedented responses from medical groups, governments, and the general public. As the world dealt with repeated waves of the epidemic, a slew of varieties emerged, each posing distinct challenges. Among these, the recently found "COVID-19: JN.1" variant has caused significant concern due to its unknown health hazards and potential public health consequences [1].

The research provided in this thesis has several key objectives. First, it looks at the different kinds of covid variants and its general structure and the general treatment of those variants. Second it defines the molecular and genetic aspects of COVID-19: JN.1, emphasizing how these features set it apart from earlier variants. Third, it investigates the epidemiological trends related to this variety, such as transmission rates, morbidity, and mortality. Fourth, it evaluates the efficacy of current vaccinations and therapeutic interventions against COVID-19: JN.1. Finally, this thesis assesses the variant's socioeconomic impact, taking into account the future direction and limitations.

This investigation uses a multidisciplinary approach to provide useful insights into the continuing battle against COVID-19. By fully understanding the unanticipated health risk offered by COVID-19: JN.1, we can better prepare for future difficulties and strengthen our resilience to emerging infectious diseases.

1.2. Aim of this project

The aim of this thesis is to conduct a thorough investigation of the complex environment surrounding Covid-19 variation JN.1, deconstructing its distinguishing characteristics, transmission processes, and consequences for illness outcomes. This work looks into the fields of epidemiology, virology, and clinical medicine to solve the riddles of the health hazards associated with this variation, providing insights that may enhance decision making and intervention efforts at both the local and global levels.

1.3. Objectives of this study

The objective of this study are-

- To know the characteristics, transmission processes, and consequences of Covid-19 JN.1.
- To provide an intensive idea about different types of Covid (alpha, beta, delta, omicron).
- To provide a future direction and limitations about the Covid-19 JN.1.

Chapter 2:

Methodology

This study takes a mixed-methods approach to thoroughly examine the health concerns linked with the Covid-19 variation JN.1. Quantitative data, such as incidence, prevalence, and mortality rates, will be obtained from national and international health databases and hospital records, while clinical symptoms and outcomes will be evaluated using retrospective patient medical records. Statistical analyses such as logistic regression and survival analysis will be carried out using SPSS and Qualitative data will be collected through semi-structured interviews with doctors and patients, as well as focus group discussions with community members, to investigate attitudes and experiences. Thematic and content analyses will be carried out using NVivo. Ethical considerations, such as informed permission and data anonymization, will be strictly adhered to, and relevant institutional review boards will provide ethical approval.

Chapter 3:

Different variants of Covid 19

SARS-CoV-2 causes COVID-19 and is continually evolving. The World Health Organization (WHO) labels new coronavirus variations after Greek letters, beginning with the Alpha variety, which appeared in 2020. From the beginning of the outbreak, several notable variations have been found, such as Alpha, Beta, Delta, and Omicron. The details of covid variants has been shown on Figure 1 [31].

3.1. Alpha:

Alpha (B.1.1.7) is the first widely publicized variety. Alpha was initially found in the United Kingdom (UK) in November 2020. The infections increased dramatically in December that year. It rapidly spread over the whole world and became the most common variety in the United States (US). So the CDC designated it as a variant of concern [26]. The more aggressive Delta version eventually supplanted Alpha.Some alterations to Alpha's spike protein were suggested to increase its infectiousness. This variant was thought to be 30–50% more infectious than the initial SARS-CoV-2 strain [2]. According to studies, the Alpha lineage was more likely to infect humans and was more deadly than the original virus [27].

3.2. Beta:

Beta (B.1.351) was first found in South Africa in late 2020 [30]. After that this variation of Covid 19 has spread to other countries. Experts have expressed alarm about its many alterations and ability to elude antibodies. Beta was rarely found in the United States. The CDC reported

that Beta (B.1.351) was apparently 50% more infectious than the initial Covid 19 variants [28]. The researchers reported that Beta was more dangerous than all other variations that cause more people being hospitalized and finally leading to death [3].

3.3. Delta:

Delta (B.1.617.2) was first found in India in late 2020. The outbreak of this variant quickly spread around the world, resulting in the most dominant Covid 19 variant until Omicron replaced its position in December 2021 [3]. This variant caused more than twice as many infections as earlier versions, with estimates ranging from 77% to 85% more infectious in the continents than Alpha variant [4]. In the USA, in June 2021, after a continuous drop in COVID-19 cases and hospitalizations, Delta's arrival coincided with a sudden threat. Even in the most immunized areas, increases occurred in the autumn of 2021 [25]. This led specialists to advise patients to seek booster doses for this specific variant [24]. This variant of Covid-19 causes more severe sickness than other variations in those who were not immunized. The research data reported from Scotland and Canada, both mentioned by CDC, indicated that Delta was a higher probability to end up in hospitalization for the unvaccinated.

3.4. Omicron:

Omicron and its sub variants have been the prevalent SARS-CoV-2 strains in the United States (US) for about two years. The major Omicron strain (BA.1) is not anymore in existence, These sub variants account for the majority of Covid-19 cases in the world. The variant was initially detected in Botswana and South Africa in late November of 2021. Then the variant quickly spread to neighboring nations. By middle December of 2021, Omicron led to cases per day in the United States to approach one million [5]. By 2022, it had produced a variety of sub variants, where the sub variants have been found to be highly dangerous disease propagators

[6]. The original Omicron strain was more transferable than Delta's. One explanation is that over 30 of Omicron's mutations exist on the virus's spike protein, which bonds to the cells of humans, and some of them have been reported to increase the risk of disease [9].

Figure 1: Covid-19 Variants [31]

Chapter 4:

Covid-19 JN.1

The World Health Organization (WHO) has recently listed a new coronavirus variant, JN.1, to the list of "variants of interest". JN.1 has been considered to be the second highest level of surveillance. The variant was first discovered in the 12 nations in September while the highest proportions have been seen in the United States, United Kingdom, Canada, France, Singapore and Sweden. According to the UK Health Security Agency, JN.1 was found in around 7% of the positive covid-19 tests analyzed [9]. JN.1 was responsible for only 3% of illnesses in early November, but now accounts for more than 27%, according to the WHO. According to statistics from the US Centers for Disease Control and Prevention (CDC), JN.1 is the most rapidly expanding variant in the country, accounting for 14-28% of new cases [10].

4.1. Epidemiology of JN.1

The JN.1 starts with the appearance of its parent lineage BA.2.86 in mid-2023; BA.2.86 originated from the considerably earlier (2022) omicron subvariant BA.2..

Chronic infections that might go untreated for months (or even years in certain cases) are likely to contribute to the formation of these step-change variations.
In chronically infected humans, the virus silently tests and eventually keeps several changes that allow it to overcome immunity and live. For BA.2.86, this led to more than 30 mutations of the spike protein [15].

BA.2.86 and now JN.1 seem to behave differently in invitro experiments by two different approaches. The first addresses how the pathogen escapes immunization. JN.1 carried over nearly thirty mutations in its spike protein gene. It also acquired a unique mutation, L455S, that limits the ability of antibodies to adhere to the viruses and prevent infections [15].
The second stage includes changes to JN.1 entrance and multiplication in our body's cells. Without getting into the biochemical information, recent significant lab-based investigations in the US and EU found that BA.2.86 reaches lung cells in the same way that pre-omicron variants like delta do. In contrast, early research undertaken by Australia's Kirby Institution utilizing a variety of techniques revealed replication traits more closely associated with the omicron family [17].

Further research to address these various cell entry findings is essential since it has consequences for where the virus might want to multiply in the human body, perhaps affecting

the severity of the disease and propagation. Whichever happens, these data demonstrate that JN.1 (and SARS-CoV-2 in general) can not only circumvent the human immune system, but also develop new ways to invade tissues and disseminate successfully. We intend to investigate more how this occurs in people and how it influences clinical results.

4.2. Genetic Mutation of JN.1

The COVID-19: JN.1 variation marks a substantial development in the genomic landscape of SARS-CoV-2, the virus that causes COVID-19. Genetic mutations are an essential component of viral evolution, and SARS-CoV-2 has exhibited an extraordinary ability to change, resulting in the formation of new variations with distinct properties. The JN.1 variation is no exception, with a number of alterations that require critical scrutiny.

4.2.1. Spike Protein Mutations:

The spike (S) protein of SARS-CoV-2 is required for viral entrance into host cells, making it a prime target for vaccines and therapeutic antibodies. The JN.1 variant contains numerous significant mutations in the spike protein, which may modify its binding affinity to the ACE2 receptor and potentially increase transmissibility. Other variants have specific mutations such as N501Y, E484K, and K417N, which are associated with enhanced binding affinity and immune evasion. In JN.1, the combination of these mutations may pose similar issues [6].

4.2.2. Receptor Binding Domain (RBD) Mutations:

Mutations in the spike protein's receptor-binding domain have a substantial impact on the virus's capacity to infect host cells and avoid the immune response. The JN.1 variation has changes in the RBD that may influence how the virus interacts with the immune system, potentially resulting in decreased vaccination efficacy and increased reinfection rates [9].

4.3. Implications of Genetic Mutations:

4.3.1. Increased Transmissibility:

The transmission of a virus between people is a complex multiscale process that includes both within- and outside-host mechanisms. Numerous investigations have revealed the higher transmissibility of the dominant JN1 mutations. Some of these have addressed virus characteristics associated with within-host processes, such as viral load, the ability to initiate infection with a low dose of inoculate, and the affinity of the virus spike receptor binding domain (RBD) for the host's angiotensin-converting enzyme 2 (ACE2). Other research has looked at virus properties that affect outside-host processes, such as the stability of virus variations in aerosols and their persistence on surfaces [26].

4.3.2. Impact on Disease Severity:

While certain modifications may weaken the virus, others may increase virulence, potentially leading to more serious illness outcomes. The precise impact on illness severity requires additional epidemiological and clinical research.

4.3.3. Immune Evasion:

Changes in the spike protein and other areas of the virus can enable it to avoid neutralizing antibodies produced by previous infection or immunization. This could result in more breakthrough infections and the requirement for new immunizations or booster doses.

4.3.4. Diagnostic and Therapeutic Challenges:

Genetic differences can impair the performance of diagnostic tests, resulting in false negatives. Furthermore, antiviral and monoclonal antibody therapy may be less effective against new variations, prompting the development of novel therapeutic approaches.

4.4. Transmission and spread

The transmission and dissemination of the COVID-19: JN.1 variation are significant areas of concern, given the variant's ability to change the path of the pandemic. Understanding the mechanisms and circumstances that contribute to its spread is critical for developing effective public health interventions.

4.4.1. Airborne Transmission:

JN.1, like other SARS-CoV-2 variations, spreads predominantly through respiratory droplets produced by an infected individual coughing, sneezing, talking, or breathing. The version may also be capable of airborne transmission via tiny aerosol particles, which can remain in the air for long periods of time, particularly in poorly ventilated areas [21].

4.4.2. Surface Transmission:

Although less prevalent, the virus can be transmitted by touching surfaces contaminated with viral particles and then touching the face, especially the eyes, nose, or mouth. The specific role of surface transmission in the JN.1 version is unknown, however it is thought to be similar to other varieties [23].

4.4.3. Close Contact: Close and sustained contact with an infected person raises the risk of transmission. The JN.1 variety may have alterations that increase its capacity to spread between individuals in close contact, but additional research is required to prove this [22].

4.5. Disease Pathogenesis

COVID-19 variant According to the China CDC, the severity of symptoms caused by JN.1 is not significantly different from that of the EG.5 variant. The JN.1 variant is responsible for an increasing number of infections on the Chinese mainland, although the majority of cases are asymptomatic or mild, according to Peng Zhibin, a respiratory disease expert with the Chinese Center for Disease Control and Prevention.

It causes a severe inflammatory response, known as a "cytokine storm." High levels of pro-inflammatory cytokines, including IL-6, IL-1β, TNF-α, are present. These cytokines lead to severe inflammation, tissue damage, and systemic symptoms associated with severe COVID-19 infections [25]. The immunological response also involves the activation of macrophages and neutrophils, which may lead to tissue damage and inflammation.

The imbalance between innate and adaptive immunity is critical in the evolution of COVID-19. Mild instances are frequently accompanied by a significant adaptive immunological response, including the activation of CD8+ T-cells and plasmablasts [25]. However, in severe cases, innate immune responses predominate, as seen by the production of inflammatory cytokines and a decrease in CD4+ and CD8+ T-cells, resulting in lymphopenia and T-cell exhaustion. Immune dysregulation leads to a lengthy pro-inflammatory state that can last weeks.

Chapter 5:

Treatment of different variants of covid

Alpha:

Pfizer, Moderna, and Johnson & Johnson all said their vaccines were effective in preventing severe disease and hospitalization in Alpha cases [22].

Beta:

South Africa discontinued distributing the AstraZeneca-Oxford vaccine (which is not available in the United States) in early 2021 because clinical testing revealed that it did not give enough protection against mild and moderate illness caused by the Beta strain. Pfizer-BioNTech, Moderna, and Johnson & Johnson also found lower levels of beta protection [24].

Delta:

In the United States, all three vaccinations were deemed extremely effective in preventing serious disease, hospitalization, and death from Delta [24]. No vaccination is completely effective, and Delta produced breakthrough infections in some fully vaccinated individuals. Infected vaccinated persons might also transfer the virus to others, however they were most likely only contagious for a brief period of time. Delta has caused the CDC to advocate "layered prevention strategies" for both vaccinated and unvaccinated individuals. That is, in addition to getting their immunizations, people were urged to follow techniques like washing their hands, wearing masks, and keeping a physical distance from one another, especially when indoors in areas where there was significant or high transmission.

Omicron:

According to the CDC, while breakthrough infections in vaccinated persons are predicted, maintaining up to date on immunizations is the best way to guard against Omicron. Scientists are testing the efficacy of a new updated COVID-19 booster for the autumn of 2023 against

EG.5 and BA.2.86 [24]. Currently, the CDC expects the revised vaccination to be beneficial in lowering severe sickness and hospitalization caused by the two most recent sub variants.

5.1. Treatment of new variant JN1

Antiviral therapy is recommended to people with light to serious sickness who are not in the hospital but are at risk of developing severe disease or being hospitalized, as with other versions.

The very first course of therapy is Paxlovid, an antiviral medicine that reduces the amount of the viral infection causing COVID-19 in the body, preventing symptoms from intensifying. Despite the fact that the infections are constantly mutating, research suggests the treatment remains effective. There's plenty of studies being done in this field, including the search for innovative antiviral medicines.

A frequently asked question is, "Why would I consume Paxlovid, particularly if I just suffer from a minor illness like COVID?" I want to underline that it is still an important area of research with mixed results, but recent research reveals that there might be an advantage to lowering the chance of having long-COVID, or post-COVID disorders, particularly in people over the age of 50 and those with prior medical conditions [12].

It is critical to remember that some people continue to have a higher chance of acquiring more severe COVID. Paxlovid is beneficial and recommended for people over 50, as well as those with underlying medical conditions such as hypertension or diabetes, who are at risk of COVID-19 problems and hospitalization.

Updated COVID-19 vaccinations, which have just been introduced, are likely to improve protection against JN.1. These vaccinations are intended to improve protection against the most recent strains, particularly JN.1. It is critical to have an updated vaccine to maintain optimal protection, especially since immunity from previous immunizations fades over time.

Chapter 6:

Future direction and limitations

JN.1 is an important variant of Covid-19. First, as a pathogen, it is a distinctively novel variation of SARS-CoV (the COVID virus) that is rapidly replacing other circulating strains

[15]. It is also crucial for what it indicates about COVID's evolution. Normally, SARS-CoV-2 mutations appear to be very similar to what came before, with only a few changes giving the virus a considerable advantage over its parent.

But, variations seem to appear out of nowhere with significantly distinct characteristics than what was before there as was the case with the omicron (B.1.1.529) two years ago [22]. This has crucial implications for sickness and transmission.

It was unclear whether the "step-change" development would ever happen another time, since the ongoing success of the progressively developing omicron variants.

JN.1 is so unique and causes such an increase in new infections that many are wondering if the WHO might acknowledge it as a subsequent variety of concern, replete with its own Greek character. By any case, with JN.1, we've entered the next phase of this epidemic.

Chapter 7:

Conclusion

To summarize, the advent of the JN.1 variety, a descendent of the BA.2.86 variant, presents additional obstacles in the fight against COVID-19. While JN.1 has similar symptoms and severity to prior omicron variations, its increased transmissibility and capacity to elude

immunity underline the need for comprehensive public health interventions. Vaccination, especially with the newest formulations, is an important strategy in preventing serious illness. Furthermore, antiviral medications such as Paxlovid remain effective, emphasizing the significance of prompt intervention. With growing case rates projected in the coming weeks, preventive measures such as immunization, testing, and availability to antiviral drugs are critical for reducing the effect of this variation and slowing the spread of COVID-19.

References

1. What to know about JN.1, the latest Omicron variant. (2024, January 9). *Johns Hopkins Bloomberg School of Public Health.*

2. Katella, K. (2024, January 31). *3 things to know about JN.1, the new coronavirus strain*. Yale Medicine.
3. *JN.1 variant shows no notable changes in pathogenicity: China CDC*. (n.d.).
4. Woo, A., & Woo, A. (2024, February 2). What to know about the COVID-19 JN.1 variant. *NewYork-Presbyterian*.
5. Hoffman, M. (2024, January 10). COVID-19 variant JN.1: What you need to know about its global takeover - Health Policy Watch. *Health Policy Watch*.
6. Katella, K. (2023, September 1). *Omicron, Delta, Alpha, and more: What to know about the coronavirus variants*. Yale Medicine.
7. Borczuk, A. C., & Yantiss, R. K. (2022). The pathogenesis of coronavirus-19 disease. Journal of Biomedical Science, 29(1).
8. Parasher, A. (2020). COVID-19: Current understanding of its Pathophysiology, Clinical presentation and Treatment. Postgraduate Medical Journal, 97(1147), 312–320.
9. Katella, K. (2024, January 31). 3 things to know about JN.1, the new coronavirus strain. Yale Medicine.
10. *What you need to know about JN.1, the latest COVID variant*. (2024, January 12). The Hub.
11. Looi, M. (2023). Covid-19: WHO adds JN.1 as new variant of interest. *BMJ*, p2975.
12. Yameny, A. (2023). Short Communication: The COVID-19 JN.1 variant diagnosed in Egypt. *Journal of Medical and Life Science*, *5*(4), 318–321.
13. Satapathy, P., Kumar, P., Mehta, V., Suresh, V., Khare, A., Rustagi, S., Daulati, M. N., Neyazi, M., Najafi, E., & Neyazi, A. (2024). Global spread of COVID-19's JN.1 variant: Implications and public health responses. *New Microbes and New Infections*, *57*, 101225.

14. Altamimi, I., Alabdulkarim, I. M., Alhumimidi, A. S., Albabtain, M. A., & Temsah, M. (2024). Navigating Novel Uncertainties of COVID-19: The Rise of the JN.1 Variant. *Cureus*.
15. Chong, C., Wee, L. E., Jin, X., Zhang, M., Malek, M. I. A., Ong, B., Lye, D., Chiew, C. J., & Tan, K. B. (2024). Risks of SARS-CoV-2 JN.1 infection and COVID-19 associated emergency-department (ED) visits/hospitalizations following updated boosters and prior infection: a population-based cohort study. *Clinical Infectious Diseases*.
16. Paciello, I., Maccari, G., Pierleoni, G., Perrone, F., Realini, G., Troisi, M., Anichini, G., Cusi, M. G., Rappuoli, R., & Andreano, E. (2024). SARS-CoV-2 JN.1 variant evasion of IGHV3-53/3-66 B cell germlines. *Science Immunology*, *9*(98).
17. Tsai, S., Lu, C., Bau, D., Chiu, Y., Yen, Y., Hsu, Y., Fu, C., Kuo, S., Lo, Y., Chiu, H., Juan, Y., Tsai, F., & Yang, J. (2020). Approaches towards fighting the COVID-19 pandemic (Review). *International Journal of Molecular Medicine*, *47*(1), 3–22.
18. MacIntyre, C. R. (2020). Global spread of COVID-19 and pandemic potential. *Global Biosecurity*, *1*(3).
19. Iqbal, M. M., Abid, I., Hussain, S., Shahzad, N., Waqas, M. S., & Iqbal, M. J. (2020). The effects of regional climatic conditions on the spread of COVID-19 at global scale. *The Science of the Total Environment*, *739*, 140101.
20. Jain, V., & Singh, L. (2020). Global Spread and Socio-Economic Determinants of COVID-19 Pandemic. *SSRN Electronic Journal*.
21. World Health Organization: WHO. (2020, January 10). *Coronavirus*.
22. Wikipedia contributors. (2024, September 12). *COVID-19*. Wikipedia.
23. *About COVID-19*. (2024, June 13). COVID-19.

24. Khan, M., Adil, S. F., Alkhathlan, H. Z., Tahir, M. N., Saif, S., Khan, M., & Khan, S. T. (2020). COVID-19: A Global Challenge with Old History, Epidemiology and Progress So Far. *Molecules*, *26*(1), 39.
25. Lyngse, Frederik Plesner, et al. "Increased Transmissibility of SARS-CoV-2 Lineage B.1.1.7 by Age and Viral Load." *Nature Communications*, vol. 12, no. 1, Dec. 2021.
26. Arav, Yehuda, et al. "Is the Increased Transmissibility of SARS-CoV-2 Variants Driven by within or Outside-Host Processes?" *Mathematics*, vol. 10, no. 19, Sept. 2022, p. 3422.
27. Ciotti, Marco, et al. "The COVID-19 Pandemic." Critical Reviews in Clinical Laboratory Sciences, vol. 57, no. 6, July 2020, pp. 365–88.
28. Yuki, Koichi, et al. "COVID-19 pathophysiology: A review." Clinical Immunology, vol. 215, Apr. 2020, p. 108427.
29. Daniel, John. "Education and the COVID-19 pandemic." Prospects, vol. 49, no. 1–2, Apr. 2020, pp. 91–96.
30. Haynes, Barton F., et al. "Prospects for a safe COVID-19 vaccine." Science Translational Medicine, vol. 12, no. 568, Nov. 2020.
31. Homage Malaysia. "COVID-19 Variants: Everything You Need to Know - Homage Malaysia." Homage Malaysia, 4 Jan. 2023, www.homage.com.