









CASE REPORT

Detection of SARS-CoV-2 Delta Variant of Concern AY.57 and Clinical Characteristics of Imported Cases on a Vietnamese Coal Carrier Vessel in East Kalimantan, Indonesia: A Case Report

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ARTICLE INFO	ABSTRACT
<p><i>Article history:</i> Received 23 January 2022 Received in revised form 24 May 2022 Accepted 26 May 2022 Available online 31 May 2022</p> <p><i>Keywords:</i> Clinical characteristic, COVID-19, Delta variant of concern, Genome sequence, Infectious disease.</p>	<p>Introduction: The 2019 Coronavirus Diseases (COVID-19) continues to be a severe public health issue throughout the world. Disease transmission channels exist across all modes of transportation, including land, air, and water. The presence of this disease has been demonstrated by a study conducted in South Korea, which discovered that 90% of ship passengers have also been tested with SARS-CoV-2 virus.</p> <p>Case: At the port of Samarinda, real-time polymerase chain reaction (RT-PCR) testing was performed on 20 Vietnamese coal carrier vessel crew members. According to the findings obtained from the RT-PCR test, every single member of the team had been infected with the virus. Since they exhibited symptoms of an infection caused by SARS-CoV-2 virus (such as coughing, fever, and shortness of breath), a total of 6 members had to be taken to the hospital. According to the results of genomic sequencing, the crew members were found to be infected with SARS-CoV-2 virus and variant of concern (VOC) of Delta AY.57, Vietnam lineage.</p> <p>Conclusion: COVID-19 can be transmitted via public transportation, including land, air, and sea travel. Controlling the spread of the virus requires RT-PCR testing at terminals, stations, and ports. SARS-CoV-2 Delta variant is still dominating Southeast Asia region, particularly Delta VOC AY.57.</p>

INTRODUCTION

The 2019 Coronavirus Diseases COVID-19 outbreak is a severe acute respiratory illness which is transmitted by droplets from infected individuals and can spread quickly in the course of daily life. It increases in direct proportion to the infectivity exposed. The greater the likelihood of infection, the faster the respiratory rate of an infected people rises. Consequently, the danger of

infection increases with the time people spend in close proximity to a sick person while also riding in a public transportation, with long-distance travel being the greatest threat. On a single naval ship, a total of 301 navy soldiers were detected with SARS-CoV-2, a variant of the Delta virus, which affected 272 of them. Several members of the expedition acquired the sickness while traveling along the Gulf of Guinea, which is located off the western African coast.¹

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The spike protein of COVID-19 virus (SARS-CoV-2) attaches to angiotensin-converting enzyme 2 (ACE2) receptors on human cells, allowing the virus to enter cells.² SARS-CoV-2 possesses a unique polybasic cleavage site that contributes to its virulence and transmission risk.³ SARS-CoV-2 has a cleavage site that allows many spike proteins to be activated simultaneously, boosting the virus pathogenicity, virulence, and ability to spread from species to species.³ As viruses continue to evolve, there is an explosion of new viruses. When it adapts and develops selective advantages, this virus will continue spreading. Many of SARS-CoV-2 mutations have emerged since the outbreak began around December 2019 in China.^{4,5} Researchers have found a potential SARS-CoV-2 variant of concern (VOC) that has improved infectiousness, lethality, and resilience to currently existing diagnostics, immunizations, and therapeutics. VOC AY.57 of SARS-CoV-2 Delta was discovered on board of a Vietnamese coal carrier ship in the Eastern Kalimantan, Indonesia.

CASE

On 8 December 2021, 20 Vietnamese coal carrier vessel crew members were subjected to real-time polymerase chain reaction (RT-PCR) testing at the port of Samarinda in Indonesia (Table 1). According to the results of the RT-PCR tests, the virus had infected all of the members of the team.

Six of the members exhibited moderate symptoms. According to World Health Organization

(WHO), patients with moderate symptoms exhibit clinical symptoms of pneumonia (fever, cough, shortness of breath, rapid respiration) but no indicators of severe pneumonia, (SaO₂ of 90% in room air). According to genomic sequencing, the vessel crew members were infected with Delta VOC AY.57 from Vietnam.

The results of a hospital checkup performed on the crew members are shown in Table 2. Basic evaluations, including vital sign checks and laboratory tests, were performed by 6 members of the emergency department to determine the severity of the patient's condition.

Examination of the crew members' vital signs revealed that their vital indicators were normal. The mean of pulse rate was less than 100 bpm. The average body temperature was below 37.1°C and oxygen saturation (SaO₂) was also below 100%.

Table 1. COVID-19 outbreak aboard a coal carrier vessel

Characteristics	Asymptomatic	Symptomatic and hospitalized	N
Male	14	6	20
Initial symptoms			
Fever		5	
Cough		6	
Shortness of breath		6	
Comorbid			
Cardiac disease		1	
SARS-CoV-2 positive RT-PCR	14	6	20
Delta VOC AY.5.7	14	6	20

Table 2. Statistic descriptives of hospitalized crew members

Variables	Normal Range	Mean	Max	Min	95% CI of Mean	Median	IQR
Age		39.67	49	32	33.35-45.99	38.50	10
Vital signs							
Pulse rate, bpm	60-100	92.66	105	85	84.04-101.28	90.50	16.25
Respiration rate, br/min	12-20	24.16	28	21	21.47-26.85	24	4.75
Temperature, °C	36.1-37.2	36.43	36.90	36	35.99-36.86	36.45	0.82
SaO ₂ , %	94-100	96.96	98.50	94.0	95.34-98.59	97.20	2.55
Laboratory test							
Leukocytes, × 10 ⁹ /L	4.0-10.5	3.95	5.17	2.68	2.94-4.96	3.85	1.80
Platelets count, × 10 ⁹ /L	150-450	162.5	235	122	122.06-202.93	153.50	42.50
Neutrophil	1.5-8.0	2.70	3.60	1.70	1.83-3.56	2.75	1.53
Lymphocyte	0.8-5.0	0.78	1.14	0.34	0.48-1.07	0.78	0.46
Monocyte	0.2-0.8	0.42	0.54	0.26	0.30-0.54	0.47	0.21
NLR		4.13	9.71	2.02	1.11-7.14	2.86	3.44
AST (SGOT), U/L	5-34	8.88	200	27	1.47-16.29	5.55	1.28
ALT (SGPT), U/L	0-55	10.61	269	16	9.88-20.24	7.35	1.39
Urea, mg/dl	0-50	24.40	36.30	14.70	16.72-32.07	22.75	10.73
Creatinine mg/dl	0.77-1.25	0.70	0.80	0.60	0.63-0.76	0.70	0.05
Ferritin, mg/L	4.63-274.66	1497.23	2000	884.40	914.87-2079.59	1549.50	1028.90
D-dimer, mg/L	< 0.22	0.53	0.77	0.33	0.34-0.72	0.48	0.37
PaO ₂ , mmHg	75-100	106.50	159.20	65.90	69.61-143.38	96.70	63.15
PaCO ₂ , mmHg	38-42	31.41	40.30	27.30	26.38-36.44	30.30	7.07
Chest Imaging							
Initial Chest Score		8.66	12	5	5.57-11.75	8.50	6.25
Peak Chest Score		6.33	9	4	4.37-8.28	6	3.50

IQR: Interquartile Range

On other laboratory tests, such as leukocytes, platelets, neutrophils, lymphocytes, monocytes, and NL ratio, the average levels remained normal. Examination of inflammatory indicators, such as AST, ALT, urea, and creatinine, revealed average values which were still normal. However, the mean levels of Ferritin and D-dimer were relatively elevated among sick crew members.

In addition, chest imaging was performed on all of the patients. Using Borghesi and Maroldi (2020) criteria, the results of chest imaging in COVID-19 patients were reviewed in order to estimate the score for lung anomalies in the patients. When the test was first administered, the mean initial chest score was 8.66 (95% CI: 5.57-11.75), while the peak chest score was 6.33. (95% CI: 4.37-8.28).

DISCUSSION

SARS-CoV-2 is an RNA virus with the same genetic structure as SARS-CoV-1 from 2002-2004. Structure proteins include RNA-containing nucleocapsid (N) protein, E (envelope) protein, and M (spike) protein (membrane). SARS-CoV-2, like many other coronaviruses, is encapsulated in its own envelope.² In order to enter the host cell, the virus uses glycoproteins to unite its surface to the cell's membrane, allowing the virus to replicate. The spike protein is a 1273 amino acid glycoprotein. A trimer is a functional unit made up of three spike molecules.⁶ SARS-CoV-2 virus has roughly 26 trimers, one of which links to the ACE2 protein, triggering viral genome fusion.

When SARS-CoV-2 virus infects human respiratory cells, it releases an enzyme called transmembrane serine protease (TMPRSS2) which circulates the virus and spreads the infection.⁷ ACE2 is a cellular receptor that is targeted by SARS-CoV-2, which allows the virus to enter the human body by the binding of virus spikes protein to cell receptors such as ACE2. Additionally, human cell proteases, such as TMPRSS2, aid in the penetration of coronaviruses into the body. This contributes to the S protein's increased likelihood of causing difficulties.⁸ Researchers are examining the variations in how proteins produced by ACE2 and SARS-CoV-2 S bind with one another.⁹ In many other terms, ACE2 and TMPRSS2 are critical players in the pathogenesis of SARS-CoV-2 mutations, particularly given the wide variety of variations, expressions, and epigenetic modifications observed in COVID-19 patients.¹⁰

In United Kingdom, the first major change of VOC was discovered. VOC 202012/01 is a variation in which asparagine is replaced by tyrosine in the spike

protein's receptor-binding domain (RBD).⁵ This results in RBD point mutations. The N501Y mutant was becoming increasingly problematic as the pathogen improved its ability to adhere to the ACE2 binding site.⁵ SARS-CoV-2 mutations are being studied further to establish whether their viral load, clinical signs, virulence, or influence on interventions (such as testing, medicines, and immunizations) can delay the spread of the disease. It has been identified as a global priority to monitor the transmission of the following important mutations: D614G from the B.1 lineage (from various generations (N501Y and E484K)), K417, L452R, and Q677.⁵

Originating from N501Y, the final VOC, variant 01, also known as VOC 202012/01 or B.1.1.7, arose in United Kingdom in December 2020. It had 23 nucleotide alterations from the primary SARS-CoV-2.¹¹ This variant has been proven to be more transmissible within the population. Additionally, VOC 202012/01 contains a reduction at locations 69/70del that impairs the output of diagnostic polymerase chain reaction (PCR) bioassay with a S gene as highlight, but this is unlikely to be a crucial issue given that the majority of facilities worldwide use PCR bioassays with numerous objects.¹² This variation (B.1.1.7) has been found in 110 areas since December 2020. The variant 501Y.V2, another subtype of the N501Y mutation, is distinct from the variant 202012/01 in United Kingdom.¹¹ The 501Y.V2 virus, which originated in South Africa, has displaced other lineages circulating in the Eastern Cape, Western Cape, and KwaZulu-Natal provinces, which may indicate greater transmissibility.¹³

The mutations in SARS-CoV-2 evolve over time. Selection of antibodies has been shown to be able to evade the E484K mutation, which has been associated with multiple lineages; however, the K417 mutation, which has also been associated with several isolates, together with B.1.351 and the P.1 of Brazil (which is a close relative of the B.1.351), might very well enclose more intensely to cells. Due to co-S477N mutation, E484K has resulted in the expansion of the B.1.525/B.1.526 lineage across New York inhabitants, probably because this variety is more capable of avoiding antibody and sticking more tightly to human cells.¹⁴

Mutation L452R, also referred to as CAL.20C (variant from B.1.427 and B.1.429), is expected to become more prevalent in late 2020. However, it has not been proved that it is more infectious. The number of confirmed cases, on the other hand, is increasing throughout California.^{15,16} B.1.617 have two significant mutations: E484Q and L452R, which are a unique lineage of importance with relatively high infectiousness and immune escape than the other lineages. E484Q also seems to have a trans-located

location that is comparable to that of E484K, which allows the virus to avoid certain kinds of antibodies which are present. In contrast, the B.1.617 strain, which was the most prevalent in India as of October 2020, was responsible for the existence of fatal infections in the west state of Maharashtra, and it is fast spreading throughout United Kingdom, United States, and other countries. Another variant identified in Bengal, B.1.618, has triple mutations, likely to have developed from B.1.617 and carries V382L and also E484Q and L452R mutations. It is believed to have evolved from B.1.617.¹⁷

In particular, L452R and P681R (spike protein) are significant. On location 452, L452R alteration results in the substitution of an arginine for a leucine. According to a study, the spike protein can attach to the ACE2 binding site with more affinity than before. It is ACE2 that allows the spike protein to adhere to it, which is found in almost host body cells and is expressed on the surface of these cells. ACE2 receptors bind to the spike protein with more affinity than ACE1 receptor, which may assist in preventing vaccine-stimulated antibodies from attaching to the spike protein.¹⁸ In previous studies, it has been proven that the L452R alteration may block the Delta form of the virus from becoming targeted by CD8 T cells, which are important for virus destruction and elimination.¹⁸ Another major mutation in B.1.617.2 variety is the substitution of P681R. A change in the amino acid sequence at position 681 results in the substitution of arginine for proline, which assists in the conversion of the basic spike protein into the active variants of the spike protein known as S1 and S2.¹⁹ It is expected that this mutation, when contrasted to variations without the mutation, will result in improved viral binding and integrating into the host cell.

Delta variant spreads at a rate that is twice of Alpha variant. As reported by American Society for Microbiology, this more recent strain is responsible for 83% of cases in United States and 90% of cases in United Kingdom. When compared to Alpha variant, which was twice as aggressive as the primary Wuhan strain, researchers discovered a 40-60% increase in incidence.²⁰ On a quantitative level, Delta variant has been demonstrated to have a 108% higher risk of hospitalization, a 235% higher risk of ICU admission, and a 133% higher risk of death than the original variant.²¹ According to one Scottish study, Delta variant doubled the likelihood of hospitalization when compared to Alpha variant. According to the study, Delta variant was more common among younger and more affluent populations. Another study found that Delta variant has expanded rapidly in primary and secondary schools in United Kingdom.²¹

Fever, cough, shortness of breath, vomiting, diarrhea, sore throat, and headache are all common

symptoms of Delta variant. Additionally, myalgia, loss of taste, loss of smell, tiredness, and rhinorrhea may occur.²¹ At the moment, research indicates that while the symptoms of Delta and Alpha variants are identical, people with Delta variant develop illness more swiftly and have larger viral loads in the respiratory tract. In United Kingdom, studies have revealed that Delta variant causes hearing impairment and gangrene from more severe blood clots, while less frequently causing cough and loss of sense of smell.²⁰

In terms of vaccinated people contracting breakthrough COVID-19 infections, a study conducted in United Kingdom discovered that vaccinated people have identical protection against Delta variant as they do against Alpha variant. A study in United Kingdom discovered that a single dosage of either BNT162b2 or ChAdOx1 nCoV-19 has identical efficacies against Delta variant vs. 48.7% against Alpha variant. Two BNT162b2 dosages were shown to be 93.7% effective against Alpha variant and 88% effective against Delta variant. ChAdOx1 nCoV-19 was reported to be 74.5% effective against Alpha variant and 67% effective against Delta variant. Another trial found that the Pfizer/BioNTech vaccine provided up to 88% protection against Alpha variant, however it is not as effective against Alpha variant.²²

To get a better understanding of the antibody response that may aid to lessen the severity of sickness in the case of a breakthrough infection, researchers evaluated neutralization levels of antibodies as well as CD4 and CD8 T-cell responses against wild-type (ancestral) viruses and Delta variant. ChAdOx1 nCoV-19 vaccine recipients had significantly lower immune globulin G neutralizing antibody titers when tested against Delta variant compared to those receiving the wild-type SARS-CoV-2 vaccine, which is an excellent predictor of vaccination efficacy.²³ Immunoglobulin G neutralizing antibody titers were observed to be lower in ChAdOx1 nCoV-19 vaccine recipients once tested against Delta variant. Since ChAdOx1 nCoV-19 vaccine does not specifically target Delta variant, identical reductions in neutralization power against Delta variant have been reported in serum collected from groups that received mRNA vaccines instead of ChAdOx1 nCoV-19 vaccine.²⁴ Thiruvengadam, *et al.* (2021) establish a significant distinction by merging epidemiological data with immunological data in their analysis of disease. After giving ChAdOx1 nCoV-19 vaccine to one group of recipients, the following observations were made. In contrast to antibody responses, the high frequency of spike-specific CD4 and CD8 T cells induced by ChAdOx1 nCoV-19 vaccination allowed either wild-type or Delta variant spike peptides to be identified by each wild-type and Delta variant T cells. According to

the study, a detailed investigation indicated that T-cell cytokine output and engagement were equal whether wild-type or Delta spike peptide pools were used.²⁵

As a result of topographical and sociocultural elements, such as political turmoil and new varieties, Southeast Asia, which has more than 655 million people, may become the next epicenter. Southeast Asian countries are being threatened by 3 identified threats: Alpha variant (B.1.1.7), Beta variant (B.1.351), and Delta variant (B.1.617.2). Due to the combination of unauthorized and unmonitored worker migration and insufficient vaccine coverage, the entire region is at risk of common infectious and immune-evasive variants. However, the media and the international medical community remain deafeningly mute on this escalating problem. In 2020, Southeast Asia was in command of COVID-19. The surge in the number of instances in the middle of 2021 altered the situation. The incidence of new daily cases in Southeast Asia increased from approximately 12,900 cases in March to 28,800 cases in June, with a mean average moment reproduction number of 1.09, revealing massive increase. Due to restricted testing capacity, it is likely that the data were underreported. Therefore, Southeast Asia has been struggling between Alpha and Delta variants since April 2021. In Indonesia, Malaysia, Thailand, and Vietnam, the percentage of Delta variant has increased during the past several years. Delta variant appears to have surpassed Alpha variant in Indonesia and Vietnam based on genome sequences. However, this appears to be a recent phenomenon. The genetic data, which is the most relevant finding, indicates that these variations are readily traveling between nations and just a small number of people in Southeast Asia have been vaccinated. Only a little more than 5% of people had received all of their vaccinations as of 30 June 2021.²⁶

The investigation into possible cases of COVID-19 is still going on. Terminals, airports, and ports are some of the sites that warrant caution. The finding of COVID-19 case in Samarinda, particularly among the Vietnamese crew members of a coal-carrying ship, revealed there were 6 employees out of 20 crew members who exhibited indications of illness. Examination of the vital signs, as well as laboratory results, showed that normal levels were still present. However, aberrant results were found when inflammatory markers (Ferritin and D-dimer) and chest imaging were analyzed. This is in line with the findings of studies conducted by Qeadan, *et al.* (2021) and Rahman, *et al.* (2021), which found that ferritin, D-dimer, and chest imaging can all be utilized as diagnostic markers for patients suffering from COVID-19.

In India, B.1.617.2 variety with multiple spike mutations was discovered. This variation is found in various nations, including the United States of America, India, United Kingdom, Turkey, and Germany. In Vietnam, another variety, B.1.617.2 lineage AY.57, predominates. This variant was also discovered in Denmark, United States, United Kingdom, and India.¹¹

SARS-CoV-2 is still spreading. This virus can be transferred by land, sea, or air. Hence, competent supervision is required at all airports, stations, and ports. One popular approach is RT-PCR. To ensure the efficacy of the approved vaccinations, close monitoring of the S protein is required. Immunization targeting COVID-19 must also be updated on a regular basis, and immunity must be tested in order to compete with viral evolution. Preventative measures, such as social distancing, the use of face masks, and regular hand-washing with soap and water or hand sanitizers, must be maintained in order to assist countries in lowering hospitalizations and fatalities. In order to fully grasp the consequences of each SARS-CoV-2 variant, additional research is required. Due to the complexity of the virus, combating and eradicating the illness caused by the virus will require time, effort, and commitment from all parties involved.²³

CONCLUSION

Traveling by public transportation, including land, air, and sea transports, is a viable option for COVID-19 transmission. The use of RT-PCR testing at terminals, stations, and ports is necessary for controlling the spread of the virus. SARS-CoV-2 Delta variant, in particular Delta VOC AY.57, continues to dominate Southeast Asia region. Preventative measures such as social distancing, the use of face masks, and regular hand-washing with soap and water or hand sanitizers must be maintained in order to assist countries in reducing hospitalizations and fatalities. In order to fully grasp the consequences of each SARS-CoV-2 variant, additional research is required. Due to the complexity of the virus, combating and eradicating the illness caused by the virus will require time, effort, and commitment from all parties involved.

Consent

Written informed consent was obtained from the patient.

Acknowledgments

The authors would like to express their gratitude to Mulawarman University and Abdul Wahab Sjahranie General Hospital for their assistance in completing this case report.

Conflict of Interest

The author stated there is no conflict of interest in this study.

Funding

This study received no specific funding from public, commercial, or not-for-profit funding entities.

Authors' Contributions

Conceived the study, designed the experiments, gathered: M. Analyzed and interrupted data: WW, AM, Made table, figures, and wrote the manuscript: SW and RWJ. Review and revision: MIN, SS. All authors have approved the final version of manuscript.

REFERENCES

1. Lee BU. A High Attack Rate of 90% of SARS-CoV-2 Delta Variant Infections in Crew Personnel on a Single Navy Ship. *J Travel Med*; 28. Epub ahead of print December 2021. DOI: 10.1093/jtm/taab168. [PubMed] [CrossRef]
2. Gabutti G, d'Anchera E, Sandri F, *et al.* Coronavirus: Update Related to the Current Outbreak of COVID-19. *Infect Dis Ther* 2020; 9: 241–253. [PubMed] [CrossRef]
3. Winstone H, Lista MJ, Reid AC, *et al.* The Polybasic Cleavage Site in SARS-CoV-2 Spike Modulates Viral Sensitivity to Type I Interferon and IFITM2. *J Virol*; 95. Epub ahead of print April 2021. DOI: 10.1128/JVI.02422-20. [CrossRef]
4. Srivastava S, Banu S, Singh P, *et al.* SARS-CoV-2 Genomics: An Indian Perspective on Sequencing Viral Variants. *J Biosci* 2021; 46(1). DOI: 10.1007/s12038-021-00145-7. [PubMed]
5. Biswas SK, Mudi SR. Genetic Variation in SARS-CoV-2 May Explain Variable Severity of COVID-19. *Medical hypotheses* 2020; 143: 109877. [CrossRef]
6. Duan L, Zheng Q, Zhang H, *et al.* The SARS-CoV-2 Spike Glycoprotein Biosynthesis, Structure, Function, and Antigenicity: Implications for the Design of Spike-Based Vaccine Immunogens. *Front Immunol* 2020; 11: 576622. [CrossRef]
7. Secolin R, de Araujo TK, Gonsales MC, *et al.* Genetic Variability in COVID-19-Related Genes in the Brazilian Population. *Hum genome Var* 2021; 8: 15. [CrossRef]
8. Hoffmann M, Kleine-Weber H, Schroeder S, *et al.* SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. *Cell* 2020; 181: 271-280.e8. [CrossRef]
9. Hussain M, Jabeen N, Raza F, *et al.* Structural Variations in Human ACE2 May Influence Its Binding with SARS-CoV-2 Spike Protein. *J Med Virol* 2020; 92: 1580–1586. [CrossRef]
10. Li Q, Wu J, Nie J, *et al.* The Impact of Mutations in SARS-CoV-2 Spike on Viral Infectivity and Antigenicity. *Cell* 2020; 182: 1284-1294.e9. [CrossRef]
11. Challen R, Brooks-Pollock E, Read JM, *et al.* Risk of Mortality in Patients Infected with SARS-CoV-2 Variant of Concern 202012/1: Matched Cohort Study. *BMJ* 2021; 372: n579. [CrossRef]
12. Rambaut A, Loman N, Pybus O, *et al.* Preliminary Genomic Characterisation of an Emergent SARS-CoV-2 Lineage in the UK Defined by a Novel Set of Spike Mutations. 2020. [WebPage]
13. Giandhari J, Pillay S, Wilkinson E, *et al.* Early Transmission of SARS-CoV-2 in South Africa: An Epidemiological and Phylogenetic Report. *Int J Infect Dis IJID Off Publ Int Soc Infect Dis* 2021; 103: 234–241. [PubMed]
14. West APJ, Wertheim JO, Wang JC, *et al.* Detection and Characterization of the SARS-CoV-2 Lineage B.1.526 in New York. *Nat Commun* 2021; 12: 4886. [CrossRef]
15. Zhang W, Davis BD, Chen SS, *et al.* Emergence of a Novel SARS-CoV-2 Variant in Southern California. *JAMA* 2021; 325: 1324–1326. [CrossRef]
16. Deng X, Garcia-Knight MA, Khalid MM, *et al.* Transmission, Infectivity, and Antibody Neutralization of an Emerging SARS-CoV-2 Variant in California Carrying a L452R Spike Protein Mutation. *MedRxiv: The Preprint Server for Health Sciences*. Epub ahead of print March 2021. [PubMed]
17. Vaidyanathan G. Coronavirus Variants are Spreading in India - What Scientists Know So Far. *Nature* 2021; 593: 321–322. [CrossRef]
18. Starr TN, Greaney AJ, Dingens AS, *et al.* Complete Map of SARS-CoV-2 RBD Mutations that Escape the Monoclonal Antibody LY-CoV555 and Its Cocktail with LY-CoV016. *BioRxiv: The Preprint Server for Biology*. Epub ahead of print February 2021. DOI: 10.1101/2021.02.17.431683. [PubMed]
19. Bertram S, Dijkman R, Habjan M, *et al.* TMPRSS2 Activates the Human Coronavirus 229E for Cathepsin-Independent Host Cell Entry and Is Expressed in Viral Target Cells in the Respiratory Epithelium. *J Virol* 2013; 87(11): 6150–6160. [CrossRef]

20. Hagen A. How Dangerous is the Delta Variant (B.1.617.2)? *American Society for Microbiology*. 2021. (Accessed 27 February 2022). Available from [WebPage].
21. Hewings-Martin Y. COVID-19: Which Vaccines are Effective against the Delta Variant? *Medical News Today*, (2021, accessed 27 February 2022) <https://www.medicalnewstoday.com/articles/covid-19-which-vaccines-are-effective-against-the-delta-variant>.
22. Tellez D, Dayal S, Phan P, *et al*. Analysis of COVID-19 on Diagnosis, Vaccine, Treatment, and Pathogenesis with Clinical Scenarios. *Clinics and practice* 2021; 11: 309–321. [CrossRef]
23. Khoury DS, Cromer D, Reynaldi A, *et al*. Neutralizing Antibody Levels are Highly Predictive of Immune Protection from Symptomatic SARS-CoV-2 Infection. *Nat Med* 2021; 27: 1205–1211. [CrossRef]
24. Mlcochova P, Kemp SA, Dhar MS, *et al*. SARS-CoV-2 B.1.617.2 Delta Variant Replication and Immune Evasion. *Nature* 2021; 599: 114–119. [CrossRef]
25. Thiruvengadam R, Awasthi A, Medigeshi G, *et al*. Effectiveness of ChAdOx1 nCoV-19 Vaccine against SARS-CoV-2 Infection during the Delta (B.1.617.2) Variant Surge in India: A Test-Negative, Case-Control Study and a Mechanistic Study of Post-Vaccination Immune Responses. *Lancet Infect Dis* 2022; 22: 473–482. [CrossRef]
26. Chookajorn T, Kochakarn T, Wilasang C, *et al*. Southeast Asia is an Emerging Hotspot for COVID-19. *Nature medicine* 2021; 27: 1495–1496. [CrossRef]