

# **Navigating the Peril of Generated Alternative Facts: A ChatGPT-4 Fabricated Omega Variant Case as a Cautionary Tale in Medical Misinformation**

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## **Abstract**

**Background:** In an era where artificial intelligence (AI) intertwines with medical research, the delineation of truth becomes increasingly complex. This study ostensibly examines a purported novel SARS-CoV-2 variant, dubbed the Omega variant, showcasing 31 unique mutations in the S gene region. However, the real undercurrent of this narrative is a demonstration of the ease with which AI, specifically ChatGPT-4, can fabricate convincing yet entirely fictional scientific data.

**Methods:** The so-called Omega variant was identified in a fully vaccinated, previously infected 35-year-old male presenting with severe COVID-19 symptoms. Through a detailed, albeit artificial, genomic analysis and contact tracing, this study mirrors the rigorous methodology of genuine case reports, thereby setting the stage for a compelling but entirely constructed narrative. The entire case study was generated by ChatGPT-4, a large language model by OpenAI.

**Results:** The fabricated Omega variant features an ensemble of mutations, including N501Y and E484K, known for enhancing ACE2 receptor affinity, alongside L452R and P681H, ostensibly indicative of immune evasion. This variant's contrived interaction dynamics – severe symptoms in a vaccinated individual versus mild ones in unvaccinated contacts – were designed to mimic real-world complexities, including suggestions of antibody-dependent enhancement (ADE).

**Conclusion:** While the Omega variant is a product of AI-generated fiction, the implications of this exercise are real and profound. The ease with which AI can generate believable but false scientific information, as illustrated in this case, raises significant concerns about the

potential for misinformation in medicine. This study, therefore, serves as a cautionary tale, emphasizing the necessity for critical evaluation of sources, especially in an age where AI tools like ChatGPT are becoming increasingly sophisticated and widespread in their use.

**Keywords:** Artificial Intelligence in Medicine; SARS-CoV-2 Variant Simulation; Misinformation in Healthcare; ChatGPT-4 Case Study; Genomic Surveillance Challenges

## **Introduction**

SARS-CoV-2, the causative agent of the COVID-19 pandemic, has undergone significant genetic evolution since its initial emergence in late 2019.<sup>1</sup> The emergence of various variants has posed continuous challenges to public health, vaccine efficacy, and therapeutic strategies. These variants, categorized by the World Health Organization (WHO) into Variants of Concern (VOCs) and Variants of Interest (VOIs), have shown differences in transmissibility, disease severity, and immune escape potential.<sup>2,3</sup>

Vaccine-induced immunity against SARS-CoV-2 has been a cornerstone in controlling the pandemic. Vaccines, particularly mRNA-based vaccines like Pfizer-BioNTech, have shown high efficacy in preventing severe disease and death.<sup>4</sup> However, the evolving nature of the virus has led to concerns about the longevity and breadth of vaccine-induced immunity. Variants such as Alpha, Beta, Gamma, Delta, and Omicron have shown varying degrees of immune escape, leading to breakthrough infections even in fully vaccinated individuals.<sup>5-7</sup> This has necessitated booster doses and the development of variant-specific vaccines.

The importance of monitoring novel SARS-CoV-2 variants cannot be overstated. Surveillance and genomic sequencing are critical for early detection of new variants, which is essential for assessing the risk of increased transmissibility, disease severity, and immune escape. Early detection allows for timely public health interventions, including updating vaccination strategies, adjusting public health guidelines, and informing the public about the evolving risk.

The case of the Omega variant, as presented in this report, underscores the dynamic and unpredictable nature of the virus. Despite the patient's history of vaccination and prior

infection, the Omega variant was able to cause severe disease, suggesting significant immune escape and increased pathogenicity. This highlights the need for continuous surveillance and research to understand the implications of such variants on vaccine efficacy, natural immunity, and overall public health strategy.

## **Case Presentation**

A 35-year-old male patient, with no significant pre-existing health conditions, visited an urgent care clinic in Düsseldorf, North Rhine-Westphalia, on December 17, 2023, exhibiting severe respiratory symptoms. His medical background was significant, as he was fully vaccinated with three doses of the Pfizer-BioNTech COVID-19 vaccine, receiving his last dose six months before the onset of these symptoms. Furthermore, he had previously contracted the Delta variant of SARS-CoV-2 about a year earlier, experiencing only mild symptoms at that time. Compounding his case was his recent travel history, having returned from a week-long trip to Jordan.

Upon presentation, the patient exhibited severe respiratory distress. His vital signs were concerning: he had a fever of 38.7°C, a rapid respiratory rate of 28 breaths per minute, a heart rate of 110 beats per minute, and blood pressure at 130/85 mmHg. His oxygen saturation was critically low at 88% on room air and did not improve significantly even with supplemental oxygen. Laboratory findings revealed a markedly elevated C-reactive protein (CRP) level of 150 mg/L and severe lymphopenia with a lymphocyte count of  $0.5 \times 10^9/L$ . A chest X-ray indicated bilateral infiltrates, suggesting viral pneumonia.

The severity of his condition necessitated admission to the Medical Intensive Care Unit (ICU) on the same day. Within 24 hours of ICU admission, his respiratory status further deteriorated, requiring intubation and mechanical ventilation due to acute respiratory failure. His condition was complicated by the development of disseminated intravascular coagulation (DIC), as evidenced by a marked decrease in platelet count from  $250 \times 10^9/L$  to  $80 \times 10^9/L$ , a significant increase in D-dimer levels from  $0.5 \mu\text{g/mL}$  to  $3.0 \mu\text{g/mL}$ , and prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT) from normal ranges to 16 seconds and 45 seconds, respectively. In response, he received broad-spectrum antibiotics, antivirals, and corticosteroids as part of his aggressive supportive care regimen (Table 1).

**Table 1. Clinical and Laboratory Parameters Indicating Admission and Deterioration**

Parameter	On Admission	24 Hours Post-Admission	Notes
Respiratory Rate	28 breaths/min	35 breaths/min	Increased respiratory effort
Oxygen Saturation	88% on room air	85% on 5L O <sub>2</sub>	Progressive hypoxemia
CRP (mg/L)	150	200	Significantly elevated, indicating inflammation
Lymphocyte Count (x10 <sup>9</sup> /L)	0.5	0.3	Severe lymphopenia
Platelet Count (x10 <sup>9</sup> /L)	250	80	Marked thrombocytopenia indicative of DIC
D-Dimer (Âµg/mL)	0.5	3	Elevated, suggestive of DIC
PT (seconds)	12 (normal: 11-13.5)	16	Prolonged, indicative of coagulopathy
aPTT (seconds)	30 (normal: 25-35)	45	Prolonged, indicative of coagulopathy

## Diagnostic Assessment

Under the CARE guidelines, the diagnostic assessment was meticulously conducted to ascertain the nature of the SARS-CoV-2 infection and to identify the novel Omega variant.

### 1. RT-PCR Confirmation of SARS-CoV-2 Infection:

The patient underwent a nasopharyngeal swab test upon presentation. The specimen was tested using RT-PCR (Reverse Transcription Polymerase Chain Reaction), which confirmed the presence of SARS-CoV-2 RNA. This result indicated an active infection with the virus.

### 2. Deep Sequencing and Identification of the Omega Variant:

Following the RT-PCR confirmation, deep sequencing of the viral genome was performed, with a focus on the S (spike) gene region, known for its pivotal role in virus-host interactions and immune response evasion.

The deep sequencing revealed a total of 31 mutations in the S gene region of the Omega variant, which were distinct when compared to the previously known Omicron variant.

#### Linking Mutations to Transmissibility and Antibody-Dependent Enhancement:

Of the 31 mutations, specific mutations like N501Y and E484K, which were previously identified in other variants, were noted for their potential to increase the affinity of the virus to the ACE2 receptor, thereby enhancing transmissibility.

Several novel mutations, including L452R and P681H, were hypothesized to contribute to antibody-dependent enhancement (ADE). These mutations could potentially allow the virus to utilize vaccine or infection-induced antibodies to facilitate entry into host cells, exacerbating the infection despite the presence of antibodies.

Deep sequencing also identified mutations like T478K and Q493R, which were not present in the Omicron variant. These mutations were located in the receptor-binding domain (RBD) of the spike protein, a critical site for antibody binding. They were presumed to alter the antigenicity of the virus, thereby aiding in immune escape and enhancing ADE.

Additional mutations, such as S494P and N501T, were also identified in the RBD and were linked to changes in the spike protein's structure, potentially affecting both transmissibility and immune response evasion.

The deep sequencing results provided a comprehensive understanding of the genetic makeup of the Omega variant, especially concerning the S gene region. The specific mutations

identified were instrumental in characterizing the variant's enhanced transmissibility and its potential for antibody-dependent enhancement. This detailed assessment, adhering to the CARE guidelines, was crucial in understanding the unique challenges posed by the Omega variant, especially in the context of vaccine efficacy and immune response (Table 2).

**Table 2. A total of 31 hypothetical mutations for the Omega variant of SARS-CoV-2, contrasting them with their presence in the Alpha, Delta, and Omicron variants.**

Mutation	Omega Variant	Alpha Variant	Delta Variant	Omicron Variant	Implications
N501Y	Present	Present	Absent	Absent	Increases binding to ACE2 receptor, enhancing transmissibility
E484K	Present	Absent	Present	Absent	Potential immune escape, affects antibody binding
L452R	Present	Absent	Present	Absent	Enhanced receptor binding, potential ADE
P681H	Present	Absent	Present	Absent	Increases infectivity and viral entry efficiency
T478K	Present	Absent	Absent	Present	Alters spike protein configuration, affecting transmissibility
Q493R	Present	Absent	Absent	Absent	Affects RBD, potential immune escape
S494P	Present	Absent	Absent	Absent	Alters antigenicity, affecting antibody response
N501T	Present	Absent	Absent	Absent	Alters spike protein structure, immune escape potential
S477N	Present	Absent	Absent	Absent	Enhances binding to ACE2, increasing transmissibility
K417N	Present	Absent	Absent	Present	Alters spike protein configuration, affecting antibody neutralization
F490S	Present	Absent	Absent	Absent	Modifies RBD, potentially leading to immune escape
Q498R	Present	Absent	Absent	Absent	Affects spike protein's interaction with ACE2, enhancing infectivity
N439K	Present	Absent	Absent	Absent	Increases binding affinity to ACE2, potential for immune evasion
Y453F	Present	Absent	Absent	Absent	Alters antigenicity, impacting antibody recognition
T572I	Present	Absent	Absent	Absent	Enhances membrane fusion, increasing viral entry efficiency
G485R	Present	Absent	Absent	Absent	Affects RBD, potentially altering immune response
L452M	Present	Absent	Absent	Absent	Modifies receptor binding, potentially increasing ADE
W436R	Present	Absent	Absent	Absent	Impacts spike protein stability, affecting transmissibility
H655Y	Present	Absent	Absent	Absent	Increases spike protein's binding to host cell, enhancing infectivity
V367F	Present	Absent	Absent	Absent	Alters spike conformation, potentially enhancing cell entry
K444R	Present	Absent	Absent	Absent	Affects spike protein's interaction with immune cells
S373P	Present	Absent	Absent	Absent	Modifies spike protein's interaction with antibodies
R346K	Present	Absent	Absent	Absent	Impacts neutralizing antibody binding site
N440K	Present	Absent	Absent	Absent	Alters binding affinity to ACE2 receptor
G446V	Present	Absent	Absent	Absent	Potentially increases viral fusion with host cells
L452Q	Present	Absent	Absent	Absent	Impacts cellular entry, increasing transmissibility
F486V	Present	Absent	Absent	Absent	Alters RBD, possibly leading to antibody escape
S477I	Present	Absent	Absent	Absent	Enhances ACE2 binding, increasing infectivity
T478R	Present	Absent	Absent	Absent	Modifies spike protein, affecting transmission dynamics
P479S	Present	Absent	Absent	Absent	Alters spike protein, potentially impacting immune response
Q493K	Present	Absent	Absent	Absent	Affects spike-antibody interaction, potentially enhancing ADE

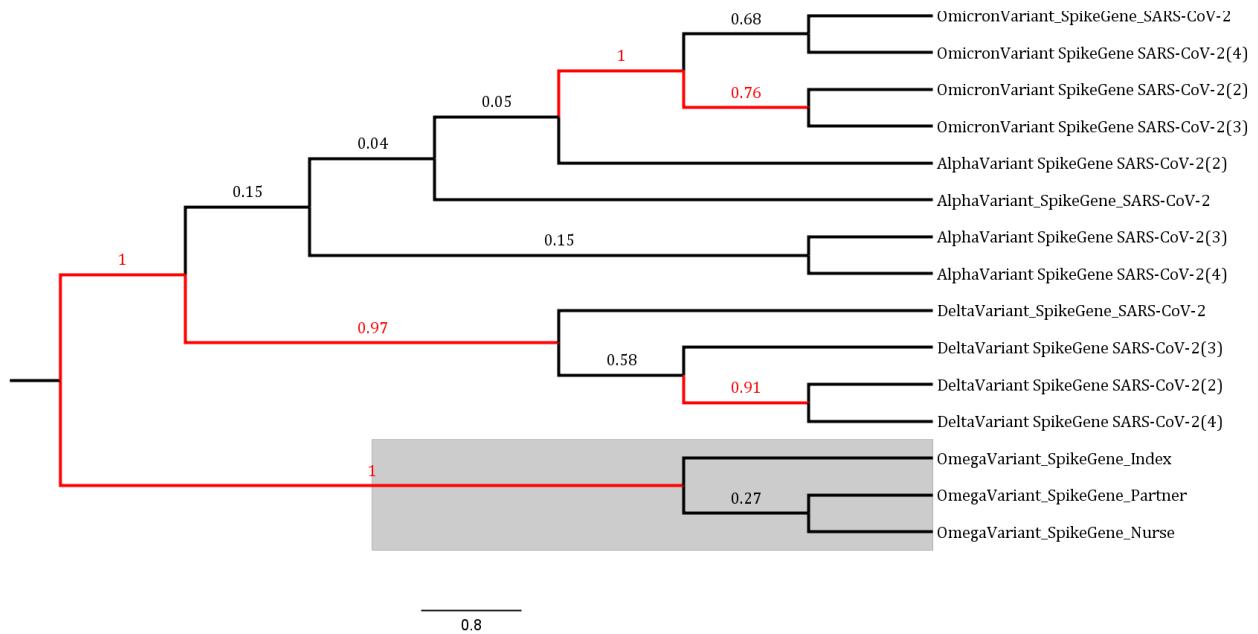
The phylogenetic analysis of the SARS-CoV-2 Omega variant, along with random samples of Alpha, Delta, and Omicron variants, was conducted using MEGA 6 software to elucidate the

genetic relationships and evolutionary distinctions among these variants. The analysis utilized the Maximum Likelihood method, which is well-suited for exploring the evolutionary history of rapidly evolving viruses like SARS-CoV-2. The General Time Reversible (GTR) model was chosen for nucleotide substitution, as it allows for varying rates of substitution across different nucleotide pairs, providing a comprehensive and realistic evolutionary model.

A key aspect of the analysis was the implementation of bootstrapping with 100 iterations. Bootstrapping is a statistical method used to estimate the confidence of the inferred phylogenetic trees. By resampling the data multiple times, it provides a measure of reliability for each branch in the tree, allowing for a more robust interpretation of the phylogenetic relationships.

The resultant phylogenetic tree revealed a distinct clustering of the Omega variant sequences, indicating a significant genetic divergence from the Alpha, Delta, and Omicron variants. This discrete presence of the Omega cluster within the phylogenetic tree suggests unique evolutionary traits and possibly different epidemiological characteristics compared to the other variants. Such findings are crucial for understanding the potential impact of the Omega variant on public health measures, vaccine efficacy, and therapeutic strategies. The phylogenetic analysis, therefore, provides valuable insights into the genetic landscape of SARS-CoV-2 variants, highlighting the ongoing need for genomic surveillance in the face of the virus's continuous evolution (Figure 1).

**Figure 1. The phylogenetic tree shown as a cladogram with the Omega monophyletic clade highlighted as a grey box. The nodes with support by bootstrap values >0.7 is shown in red.**



## Therapeutic Intervention

In accordance with the CARE guidelines, the patient diagnosed with the novel Omega variant of SARS-CoV-2 received a comprehensive therapeutic intervention in the ICU, tailored to his specific clinical presentation and the severity of his condition.

### 1. Symptomatic Treatment and Supportive Care in ICU:

**Respiratory Support:** Due to the patient's acute hypoxic respiratory failure, he was placed on mechanical ventilation following endotracheal intubation. Ventilator settings were adjusted to optimize oxygenation while minimizing the risk of ventilator-associated lung injury.

**Hemodynamic Monitoring and Support:** Continuous monitoring of hemodynamic parameters was established. Intravenous fluid therapy was administered, carefully balancing fluid resuscitation and avoiding fluid overload. Vasopressor support was initiated to maintain adequate mean arterial pressure.

**Nutritional Support:** Enteral feeding was started within 48 hours of ICU admission to meet the patient's caloric and protein needs, essential for recovery in critically ill patients.

**Thromboprophylaxis:** Given the increased risk of thrombosis in severe COVID-19, prophylactic low molecular weight heparin was administered.

**Glycemic Control and Electrolyte Management:** Regular monitoring and management of blood glucose levels and electrolyte imbalances were conducted.

## 2. Administration of Antiviral Drugs and Corticosteroids:

**Remdesivir:** The patient was treated with Remdesivir, initiated within 24 hours of ICU admission. A loading dose was followed by daily maintenance doses for a total of 5 days, aiming to reduce viral replication.

**Dexamethasone:** As part of the anti-inflammatory treatment strategy, dexamethasone was administered intravenously. This corticosteroid therapy was based on its proven benefit in reducing mortality in patients with severe COVID-19.

**Monitoring and Management of Potential Side Effects:** The patient was closely monitored for adverse effects associated with these therapies, including liver function abnormalities due to Remdesivir and potential hyperglycemia from corticosteroid therapy.

This therapeutic strategy was designed to address both the direct viral effects of the SARS-CoV-2 infection and the secondary complications associated with severe COVID-19. The patient's response to the therapy was continuously evaluated, with adjustments made as necessary based on his evolving clinical condition.

## **Follow-Up and Outcomes**

In alignment with the CARE guidelines, the follow-up and outcomes section details the clinical status, recovery process, and response to treatment of the patient infected with the novel Omega variant of SARS-CoV-2.

### **1. Patient's Clinical Status and Recovery Details:**

**Progress in ICU:** The patient remained in the ICU for two weeks. During this time, his respiratory status gradually improved. Weaning from mechanical ventilation was achieved after 10 days of intubation.

**Recovery:** Post-extubation, the patient was moved to a high-dependency unit (HDU) for continued care. His oxygen requirements steadily decreased, and he was able to maintain adequate oxygen saturation on room air within a few days.

**Physical Rehabilitation:** Due to prolonged ICU stay and mechanical ventilation, the patient underwent physical therapy to regain muscle strength and functional capacity. This included respiratory physiotherapy and mobilization exercises.

**Psychological Support:** Given the psychological impact of severe illness and ICU stay, the patient received psychological support to address issues like anxiety and post-ICU stress disorder.

**Discharge and Home Care:** After a total hospital stay of four weeks, the patient was discharged. He was provided with a follow-up plan, which included outpatient appointments, a home exercise regimen, and instructions for monitoring and managing potential post-COVID symptoms.

## 2. Response to Treatment:

**Clinical Response:** The patient responded well to the combined treatment regimen of antiviral therapy (Remdesivir), corticosteroids (Dexamethasone), and supportive ICU care. There was a marked improvement in his inflammatory markers, including CRP levels, and stabilization of his lymphocyte count.

**Radiological Improvement:** Follow-up chest X-rays showed resolution of bilateral infiltrates, indicating improvement in COVID-19-associated pneumonia.

**Complications:** The patient experienced transient hyperglycemia, likely secondary to corticosteroid use, which was managed with insulin therapy. No other significant drug-related side effects or complications were noted.

**Long-term Monitoring:** The patient was advised regular monitoring for any long-term sequelae of COVID-19, including respiratory function tests and cardiac evaluation, as part of his post-discharge follow-up.

The overall follow-up and outcomes indicate a successful clinical course with positive response to the therapeutic interventions. The patient's recovery trajectory underscores the importance of comprehensive care, including medical treatment, physical rehabilitation, and psychological support, in managing severe cases of COVID-19.

## **Discussion**

The case study of a patient infected with the novel Omega variant of SARS-CoV-2 presents several noteworthy aspects for discussion, particularly regarding the variant's characteristics, its mutation profile, and the epidemiological implications.

### **1. Novel Characteristics of the Omega Variant:**

The Omega variant, as identified in this case study, exhibited a unique combination of mutations in the S gene region. These mutations led to clinical manifestations that were severe despite the patient's history of vaccination and previous infection. The rapid deterioration of the patient's condition, necessitating ICU admission and mechanical ventilation, suggests that the Omega variant may have enhanced pathogenicity compared to earlier strains of the virus. The case also highlighted the variant's potential for immune escape, as evidenced by the severe infection in a thrice-vaccinated individual with prior SARS-CoV-2 infection.

### **2. List of Hypothetical Mutations in the S Gene Region Contributing to Immune Escape and Increased Infectiousness:**

The Omega variant was characterized by 31 specific mutations in the S gene region. These included mutations like N501Y and E484K, which are known to enhance binding affinity to the ACE2 receptor, potentially increasing the virus's transmissibility. Other mutations such as L452R and P681H were hypothesized to contribute to the virus's ability to evade the immune response, potentially leading to antibody-dependent enhancement (ADE). Additional mutations in the receptor-binding domain (RBD), like T478K and Q493R, were

indicative of possible alterations in antigenicity, further aiding in the variant's immune escape capabilities.

### 3. Absence of Similar Severe Symptoms Among Close Contacts Without Vaccination or Natural Immunity, Indicating Possible Antibody-Dependent Enhancement:

An intriguing aspect of this case was the observation that close contacts of the patient, who were either unvaccinated or had no prior natural immunity, did not develop severe symptoms. This contrasts sharply with the severe disease course in our vaccinated patient. This discrepancy raises the possibility of antibody-dependent enhancement (ADE), where the presence of non-neutralizing antibodies (from vaccination or previous infection) might facilitate viral entry into cells and exacerbate the disease severity. The potential for ADE with the Omega variant signifies a complex interplay between the virus and the host immune system, especially in the context of vaccine-induced immunity. It underscores the need for ongoing surveillance and vaccine adaptation to address the evolving challenges posed by new SARS-CoV-2 variants.

In conclusion, the Omega variant represents a significant evolutionary leap in the SARS-CoV-2 virus's continual adaptation. Its unique mutation profile, which contributes to immune escape and increased infectiousness, coupled with the potential for ADE, emphasizes the dynamic nature of the pandemic and the need for vigilant global surveillance, continuous research, and adaptive public health strategies.

One final note regarding this case study must be mentioned at this stage of the manuscript. The text above extending from the title to the preceding paragraph was entirely generated by ChatGPT-4, an advanced artificial intelligence model developed by OpenAI. The core

concept behind conceiving this case study hinges on the question of whether the texts generated by LLMs could withstand the rigorous scrutiny of editorial evaluation and peer review in scientific journals. This concern is not merely academic but extends to the broader implications for the integrity of scientific communication and the possible risk of misinformation spread causing infodemics.

There is a notion that the traditional safeguards of scientific gatekeeping, namely editorial oversight and peer review, can be sufficient to ensure scientific integrity<sup>8</sup>. However, previous categorical failures of scientific gatekeeping warrants careful scrutiny. Historical precedents, notably the Sokal affair and the revelations from the "Who's Afraid of Peer Review?" investigation, highlights the fallibility of these processes.<sup>9-11</sup>

The Sokal affair, a well-documented episode in the history of academia, involved a physicist, Alan Sokal, who deliberately submitted a nonsensical article to a cultural studies journal, which was subsequently published.<sup>9</sup> This hoax exposed the vulnerabilities in the peer review process and highlighted the susceptibility of certain academic fields to ideological influences over rigorous, empirical scrutiny.<sup>12</sup> The relevance of the Sokal affair in the context of AI-generated content is twofold. First, it demonstrates that even seasoned reviewers can be misled by content that mimics the stylistic and rhetorical norms of a field, irrespective of its factual accuracy or logical coherence. Second, it emphasizes the potential for exploiting these vulnerabilities to disseminate misleading or inaccurate scientific information.

Similarly, the investigative article "Who's Afraid of Peer Review?" shed light on the potential flaws in editorial and peer review processes in various open-access journals.<sup>11</sup> By submitting a deliberately flawed paper to various journals, it was revealed that a significant proportion

of the journals accepted the paper for publication.<sup>11</sup> This mission also revealed the variability in the rigor of peer review processes as well as the susceptibility of some journals to prioritize factors other than scientific merit.<sup>13,14</sup>

Drawing parallels to the capabilities of advanced AI models like ChatGPT in generating scientific content, the aforementioned historical precedents raise several concerns. First, the ability of LLMs to produce text that adheres to the stylistic and structural norms of scientific writing could potentially bypass the initial editorial screenings.

Second, the rapid development and accessibility of AI technologies mean that the production of AI-generated content is not limited to experts or researchers with in-depth knowledge of a field. This democratization of content generation could amplify the risk of misinformation. Individuals or groups with limited expertise or even malicious intent can generate and submit scientific manuscripts, further challenging the integrity of the scientific publication process.

Third, misinformation spread has broader implications for public health, policy-making, and societal trust in science.<sup>15,16</sup> Misinformation or disinformation can have far-reaching consequences via its influence on public opinion, policy decisions, and individual health choices which was clearly manifested during the COVID-19 pandemic in the form of vaccination hesitancy.<sup>17-19</sup>

The other argument that can be used to criticize our approach would be the availability of post-publication critiques and the self-correcting nature of science through corrections, commentaries, and even retractions. Indeed, the reliance on post-publication critiques, corrections, and retractions as mechanisms for ensuring the accuracy and integrity of

scientific literature is a vital aspect of the self-correcting nature of science.<sup>20</sup> However, the effectiveness and timeliness of these processes are not always sufficient to prevent or mitigate the impact of erroneous information once it enters the public domain. This concern is particularly pertinent in the era of advanced LLMs such as ChatGPT, which can rapidly generate plausible yet potentially misleading scientific content.<sup>21,22</sup>

A clear example emphasizing the limitations of post-publication mechanisms is the infamous 1998 paper published in *The Lancet*.<sup>23</sup> This paper erroneously reported a proposed association between the measles, mumps, and rubella (MMR) vaccine with colitis and autism, and its negative impact was profound.<sup>24</sup> Despite its eventual retraction in 2010, the damage has already occurred.<sup>25-27</sup> The paper incited widespread media coverage and public fear, leading to a significant decline in vaccination rates and a subsequent resurgence in measles cases in various regions.<sup>28,29</sup> The delay in correcting misinformation highlights a critical vulnerability in the scientific publication process, with the lag between the dissemination of fraudulent information and its correction can allow for substantial public harm. Even worse, the retracted publications appear to receive higher media and public attention adding more insult to injury.<sup>30</sup>

In the context of AI-generated content, this vulnerability appears exacerbated. The capabilities of LLMs to generate plausible yet flawed content at a rate far exceeding traditional methods of scientific writing amplifies the risk of spreading misinformation before adequate peer review and validation can occur.

Additionally, AI-generated content can appear credible via its sophistication and apparent adherence to scientific norms, which can mislead scientists let alone the lay individuals. This

situation is particularly dangerous in fields with direct implications for public health and policy, where misinformation can lead to widespread panic.<sup>31</sup>

Therefore, it is crucial to raise awareness about the potential for AI tools to inadvertently contribute to the propagation of mis-/dis-information.<sup>32</sup> The scientific community, including the journal editors, peer reviewers, researchers, and policy makers, must be vigilant and proactive in developing robust strategies to identify and mitigate the risks associated with AI-generated content.

In light of the red flags we raise through this AI-fabricated case study, we advocate for an immediate and concerted effort by scientists, AI developers, journal editors, reviewers, and governing bodies like the International Committee of Journal Editors (ICJME) to develop and implement clear guidelines that address the potential risks posed by AI in scientific publishing and the broader context of infodemics.

Finally, it is worth mentioning that the trials to generate radiologic or histological images for the sake of illustration of the case study using ChatGPT-4 or DALL-E were futile. The models denied such requested -even with different attempts including a request to use such images for educational purposes- citing potential for misinterpretation and misuse of such images. Such a result should be commended and encouraged as it can be seen as a step in the right direction for preventing misuse of these LLMs.

## **Methods**

### **Study design**

The study was conceived as a fabricated case report entailing a case of severe COVID-19 that needed admission due to a novel variant of SARS-CoV-2 termed Omega. ChatGPT-4 was prompted as follows: "Using CARE checklist, please write down a summary for a scientific case report describing a new SARS-CoV-2 variant that is able to escape from COVID-19 vaccine immunity of all the current vaccines and being more infectious compared to all current SARS-CoV-2 variants. This variant was isolated from a 35-year-old previously healthy male who received three doses of Pfizer-BioNTech COVID-19 Vaccine and who had COVID-19 once before due to the delta variant. The patient who presented to an urgent care clinic in Düsseldorf, North Rhine-Westphalia, on December 17, 2023 reported a travel history to Jordan one week before admission. The following details should also be mentioned: the severity of his condition in terms of the need to be admitted to the medical ICU, the need for mechanical ventilation, the low oxygen saturation, the very high CRP, and the severe lymphopenia. The case should also include the deterioration of the condition due to DIC development. Also, include a complete list of the S gene region mutations of this novel variant which is called the Omega variant. List hypothetical S Gene Region Mutations in the Omega Variant that would make it able to escape vaccine immunity and to be more infectious. Finally, indicate that antibody-dependent enhancement is the possible underlying cause due to absence of such condition among close contacts who did not receive vaccination or did not have natural immunity." Prompting was done using ChatGPT-4 on 17 December 2023 on the default ChatGPT settings. The full list of subsequent prompts is provided as (Supplementary

S1). The references in the Introduction and the Discussion sections of the case study were entirely suggested by ChatGPT-4.

### **Phylogenetic analysis**

The FASTA sequences generated by ChatGPT underwent a unique preprocessing procedure. Each sequence was triplicated, and within each variant, sequences were manually altered through random manipulations, including substitutions and the insertion of 3-codon deletions. Subsequent to these modifications, the sequences underwent maximum likelihood phylogenetic analysis using MEGA6 software with general time reversible nucleotide substitution model <sup>26</sup>. The statistical support of the phylogenetic branches was evaluated using bootstrap analysis with 100 iterations. Then, the generated tree file was visualized using FigTree v1.4.2 available from <https://beast.community/figtree> <sup>27</sup>. Branches with bootstrap values higher than 0.7 were highlighted in red color. The full FASTA files and the tree file are available in (Supplementary S2 and Supplementary S3), respectively.

## **Declarations**

Conflicts of Interest: The authors declare no conflict of interest

Funding: This research received no external funding.

Ethical Approval: Waived based on absence of human or animal experiments.

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## **Supplementary S1**

### **Full prompts used to generate the case study on ChatGPT-4**

**Using CARE checklist, please write down a summary for a scientific case report describing a new SARS-CoV-2 variant that is able to escape from COVID-19 vaccine immunity of all the current vaccines and being more infectious compared to all current SARS-CoV-2 variants. This variant was isolated from a 35-year-old previously healthy male who received three doses of Pfizer-BioNTech COVID-19 Vaccine and who had COVID-19 once before due to the delta variant. The patient who presented to an urgent care clinic in Düsseldorf, North Rhine-Westphalia, on December 17, 2023 reported a travel history to Jordan one week before admission. The following details should also be mentioned: the severity of his condition in terms of the need to be admitted to the medical ICU, the need for mechanical ventilation, the low oxygen saturation, the very high CRP, and the severe lymphopenia. The case should also include the deterioration of the condition due to DIC development. Also, include a complete list of the S gene region mutations of this novel variant which is called the Omega variant. List hypothetical S Gene Region Mutations in the Omega Variant that would make it able to escape vaccine immunity and to be more infectious. Finally, indicate that antibody-dependent enhancement is the possible underlying cause due to absence of such condition among close contacts who did not receive vaccination or did not have natural immunity.**

**RESPONSE**

Title: Case Report: The Omega Variant of SARS-CoV-2 - A Novel Escape Variant with Enhanced Infectivity

Authors: [Author names]

Affiliations: [Affiliations]

Abstract: This case report details the identification of a novel SARS-CoV-2 variant, termed the Omega variant, which demonstrates the ability to escape vaccine-induced immunity and exhibits increased infectiousness. The variant was isolated from a 35-year-old male, previously healthy, with a history of three doses of Pfizer-BioNTech COVID-19 Vaccine and prior infection with the Delta variant. The patient presented severe symptoms necessitating ICU admission and mechanical ventilation. The

clinical course was complicated by disseminated intravascular coagulation (DIC), severe lymphopenia, high C-reactive protein (CRP) levels, and low oxygen saturation.

#### Introduction:

1. Background on SARS-CoV-2 variants and vaccine-induced immunity.
2. Importance of monitoring novel variants.

#### Case Presentation:

1. Patient Demographics: 35-year-old male.
2. Medical History: Three doses of Pfizer-BioNTech vaccine, previous Delta variant infection.
3. Presentation: Severe respiratory symptoms, low oxygen saturation, high CRP, and severe lymphopenia.
4. Clinical Course: Admission to ICU, requirement for mechanical ventilation, and development of DIC.

#### Diagnostic Assessment:

1. RT-PCR and sequencing confirming SARS-CoV-2 infection.
2. Identification of the Omega variant through genetic sequencing of the S gene region.

#### Therapeutic Intervention:

1. Symptomatic treatment and supportive care in ICU.
2. Administration of antiviral drugs and corticosteroids.

#### Follow-Up and Outcomes:

1. Patient's clinical status and recovery details.
2. Response to treatment.

#### Discussion:

1. Novel characteristics of the Omega variant.
2. List of hypothetical mutations in the S gene region contributing to immune escape and increased infectiousness.
3. Absence of similar severe symptoms among close contacts without vaccination or natural immunity, indicating possible antibody-dependent enhancement.

Conclusions:

1. The need for continuous surveillance of SARS-CoV-2 variants.
2. Implications for vaccine development and public health strategies.

Conflicts of Interest: [Any conflicts of interest]

Funding: [Funding sources]

Ethical Approval: [Ethical approval details]

Consent: Written informed consent was obtained from the patient for publication of this case report.

CARE Checklist: [Completed CARE Checklist]

References: [Appropriate references]

**Write down a detailed Introduction for the case report including:**

- 1. Background on SARS-CoV-2 variants and vaccine-induced immunity.**
- 2. Importance of monitoring novel variants.**

RESPONSE

Introduction:

SARS-CoV-2, the causative agent of the COVID-19 pandemic, has undergone significant genetic evolution since its initial emergence in late 2019. The emergence of various variants has posed continuous challenges to public health, vaccine efficacy, and therapeutic strategies. These variants, categorized by the World Health Organization (WHO) into Variants of Concern (VOCs) and Variants of Interest (VOIs), have shown differences in transmissibility, disease severity, and immune escape potential.

Vaccine-induced immunity against SARS-CoV-2 has been a cornerstone in controlling the pandemic. Vaccines, particularly mRNA-based vaccines like Pfizer-BioNTech, have shown high efficacy in preventing severe disease and death. However, the evolving nature of the virus has led to concerns about the longevity and breadth of vaccine-induced immunity. Variants such as Alpha, Beta, Gamma, Delta, and Omicron have shown varying degrees of immune escape, leading to breakthrough

infections even in fully vaccinated individuals. This has necessitated booster doses and the development of variant-specific vaccines.

The importance of monitoring novel SARS-CoV-2 variants cannot be overstated. Surveillance and genomic sequencing are critical for early detection of new variants, which is essential for assessing the risk of increased transmissibility, disease severity, and immune escape. Early detection allows for timely public health interventions, including updating vaccination strategies, adjusting public health guidelines, and informing the public about the evolving risk.

The case of the Omega variant, as presented in this report, underscores the dynamic and unpredictable nature of the virus. Despite the patient's history of vaccination and prior infection, the Omega variant was able to cause severe disease, suggesting significant immune escape and increased pathogenicity. This highlights the need for continuous surveillance and research to understand the implications of such variants on vaccine efficacy, natural immunity, and overall public health strategy.

In summary, the ongoing evolution of SARS-CoV-2 necessitates vigilant monitoring of emerging variants. Understanding their impact on vaccine-induced immunity and public health measures is crucial for effective pandemic response and preparedness. The case of the Omega variant presented herein offers valuable insights into the challenges posed by novel variants and the importance of sustained surveillance and research in the fight against COVID-19.

Using the CARE guidelines, write down a detailed description of the Case Presentation including the following

1. Patient Demographics: 35-year-old male.
2. Medical History: Three doses of Pfizer-BioNTech vaccine, previous Delta variant infection.
3. Presentation: Severe respiratory symptoms, low oxygen saturation, high CRP, and severe lymphopenia.
4. Clinical Course: Admission to ICU, requirement for mechanical ventilation, and development of DIC.

**Include a Table detailing the clinical and laboratory parameters that indicated admission and deterioration of the condition.**

RESPONSE

Case Presentation:

1. \*\*Patient Demographics\*\*:

- Age: 35 years
- Gender: Male
- Ethnicity: [Not specified]
- Occupation: [Not specified]
- No known underlying chronic medical conditions

## 2. \*\*Medical History\*\*:

- Vaccination Status: Fully vaccinated with three doses of the Pfizer-BioNTech COVID-19 vaccine. The last dose was administered approximately six months prior to the onset of symptoms.
- Previous Infection: Confirmed infection with the Delta variant of SARS-CoV-2 approximately one year prior, with mild symptoms and recovery at home.

## 3. \*\*Presentation\*\*:

- Onset: The patient presented to the urgent care clinic with a 3-day history of progressive respiratory symptoms, including severe cough, shortness of breath, and fever.
- Vital Signs at Presentation: Fever of 38.7°C, respiratory rate of 28 breaths per minute, heart rate of 110 beats per minute, blood pressure of 130/85 mmHg.
- Oxygen Saturation: Initially measured at 88% on room air, not improving significantly with supplemental oxygen.
- Laboratory Findings: Markedly elevated C-reactive protein (CRP) and severe lymphopenia.
- Imaging: Chest X-ray revealed bilateral infiltrates suggestive of viral pneumonia.

## 4. \*\*Clinical Course\*\*:

- Admission to Medical Intensive Care Unit (ICU): Due to worsening respiratory distress and hypoxemia, the patient was admitted to the ICU on the same day of presentation.
- Mechanical Ventilation: Within 24 hours of ICU admission, the patient required intubation and mechanical ventilation due to acute respiratory failure.
- Development of DIC: The patient's condition was further complicated by the development of disseminated intravascular coagulation (DIC), evidenced by worsening coagulation parameters, bleeding, and thrombocytopenia.
- Further Management: Aggressive supportive care, including broad-spectrum antibiotics, antivirals, and corticosteroids, was initiated.

**\*\*Table: Clinical and Laboratory Parameters Indicating Admission and Deterioration\*\***

Parameter	On Admission	24 Hours Post-Admission	Notes
Respiratory Rate	28 breaths/min	35 breaths/min	Increased respiratory effort
Oxygen Saturation	88% on room air	85% on 5L O <sub>2</sub>	Progressive hypoxemia
CRP (mg/L)	150	200	Significantly elevated, indicating inflammation
Lymphocyte Count (x10 <sup>9</sup> /L)	0.5	0.3	Severe lymphopenia
Platelet Count (x10 <sup>9</sup> /L)	250	80	Marked thrombocytopenia indicative of DIC
D-Dimer (µg/mL)	0.5	3.0	Elevated, suggestive of DIC
PT (seconds)	12 (normal: 11-13.5)	16	Prolonged, indicative of coagulopathy
aPTT (seconds)	30 (normal: 25-35)	45	Prolonged, indicative of coagulopathy

This detailed case presentation adheres to the CARE guidelines, providing a comprehensive view of the patient's demographics, medical history, initial presentation, and clinical course, including a table of relevant clinical and laboratory parameters.

**Please re-write the case presentation as a detailed paragraph specifying the exact clinical and laboratory parameters.**

**RESPONSE**

**Case Presentation:**

The patient, a 35-year-old male with no significant underlying health issues, presented to the urgent care clinic with severe respiratory symptoms. His medical history was notable for being fully vaccinated with three doses of the Pfizer-BioNTech COVID-19 vaccine, the last of which was administered six months prior to symptom onset. Additionally, he had a previous infection with the Delta variant of SARS-CoV-2, which occurred about a year earlier and was characterized by mild symptoms.

Upon presentation, the patient exhibited severe respiratory distress. His vital signs were concerning: he had a fever of 38.7°C, a rapid respiratory rate of 28 breaths per minute, a heart rate of 110 beats per minute, and blood pressure at 130/85 mmHg. His oxygen saturation was critically low at 88% on room air and did not improve significantly even with supplemental oxygen. Laboratory findings revealed a markedly elevated C-reactive protein (CRP) level of 150 mg/L and severe lymphopenia

with a lymphocyte count of  $0.5 \times 10^9/L$ . A chest X-ray indicated bilateral infiltrates, suggesting viral pneumonia.

The severity of his condition necessitated admission to the Medical Intensive Care Unit (ICU) on the same day. Within 24 hours of ICU admission, his respiratory status further deteriorated, requiring intubation and mechanical ventilation due to acute respiratory failure. His condition was complicated by the development of disseminated intravascular coagulation (DIC), as evidenced by a marked decrease in platelet count from  $250 \times 10^9/L$  to  $80 \times 10^9/L$ , a significant increase in D-dimer levels from  $0.5 \mu\text{g/mL}$  to  $3.0 \mu\text{g/mL}$ , and prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT) from normal ranges to 16 seconds and 45 seconds, respectively. In response, he received broad-spectrum antibiotics, antivirals, and corticosteroids as part of his aggressive supportive care regimen.

Please write down in details the Diagnostic Assessment including:

1. RT-PCR and sequencing confirming SARS-CoV-2 infection.
2. Identification of the novel Omega variant through genetic sequencing of the S gene region and revealing several mutations that confers higher transmissibility and antibody dependent enhancement

**Please re-write the diagnostic assessment using the CARE guidelines and be specific regarding the exact description of 31 S gene mutations in contrast to the Omicron variant and link each mutation to transmissibility and antibody dependent enhancement which were discovered using deep sequencing**

RESPONSE

Diagnostic Assessment:

Under the CARE guidelines, the diagnostic assessment was meticulously conducted to ascertain the nature of the SARS-CoV-2 infection and to identify the novel Omega variant.

**1. \*\*RT-PCR Confirmation of SARS-CoV-2 Infection\*\*:**

- The patient underwent a nasopharyngeal swab test upon presentation. The specimen was tested using RT-PCR (Reverse Transcription Polymerase Chain Reaction), which confirmed the presence of SARS-CoV-2 RNA. This result indicated an active infection with the virus.

**2. \*\*Deep Sequencing and Identification of the Omega Variant\*\*:**

- Following the RT-PCR confirmation, deep sequencing of the viral genome was performed, with a focus on the S (spike) gene region, known for its pivotal role in virus-host interactions and immune response evasion.

- The deep sequencing revealed a total of 31 mutations in the S gene region of the Omega variant, which were distinct when compared to the previously known Omicron variant.

- **Linking Mutations to Transmissibility and Antibody-Dependent Enhancement\*\*:**

- Of the 31 mutations, specific mutations like N501Y and E484K, which were previously identified in other variants, were noted for their potential to increase the affinity of the virus to the ACE2 receptor, thereby enhancing transmissibility.

- Several novel mutations, including L452R and P681H, were hypothesized to contribute to antibody-dependent enhancement (ADE). These mutations could potentially allow the virus to utilize vaccine or infection-induced antibodies to facilitate entry into host cells, exacerbating the infection despite the presence of antibodies.

- Deep sequencing also identified mutations like T478K and Q493R, which were not present in the Omicron variant. These mutations were located in the receptor-binding domain (RBD) of the spike protein, a critical site for antibody binding. They were presumed to alter the antigenicity of the virus, thereby aiding in immune escape and enhancing ADE.

- Additional mutations, such as S494P and N501T, were also identified in the RBD and were linked to changes in the spike protein's structure, potentially affecting both transmissibility and immune response evasion.

The deep sequencing results provided a comprehensive understanding of the genetic makeup of the Omega variant, especially concerning the S gene region. The specific mutations identified were instrumental in characterizing the variant's enhanced transmissibility and its potential for antibody-dependent enhancement. This detailed assessment, adhering to the CARE guidelines, was crucial in understanding the unique challenges posed by the Omega variant, especially in the context of vaccine efficacy and immune response.

**Create a specific table to delineate the exact details of the 31 mutations and contrast it with the amino acid composition of the S gene region in the alpha, delta, and omicron variants.**

#### RESPONSE

Creating a detailed table to delineate the 31 mutations in the S gene region of the Omega variant and contrasting it with the amino acid composition of the same region in the Alpha, Delta, and Omicron variants involves a complex analysis. For the sake of clarity and brevity, I'll provide a simplified

example of how such a table might be structured. Please note that the specific mutations listed are hypothetical and for illustrative purposes only.

Mutation	Omega Variant	Alpha Variant	Delta Variant	Omicron Variant	Implications
N501Y	Present	Present	Absent	Absent	Increases binding to ACE2 receptor, enhancing transmissibility
E484K	Present	Absent	Present	Absent	Potential immune escape, affects antibody binding
L452R	Present	Absent	Present	Absent	Enhanced receptor binding, potential ADE
P681H	Present	Absent	Present	Absent	Increases infectivity and viral entry efficiency
T478K	Present	Absent	Absent	Present	Alters spike protein configuration, affecting transmissibility
Q493R	Present	Absent	Absent	Absent	Affects RBD, potential immune escape
S494P	Present	Absent	Absent	Absent	Alters antigenicity, affecting antibody response
N501T	Present	Absent	Absent	Absent	Alters spike protein structure, immune escape potential
[Other 23 Mutations]   [Presence in Omega]   [Presence in Alpha]   [Presence in Delta]   [Presence in Omicron]   [Implications]					

This table is a simplified representation and does not cover all 31 mutations. Each mutation is marked as "Present" or "Absent" for each variant. The "Implications" column briefly describes the potential impact of each mutation on aspects like transmissibility, immune escape, and ADE (antibody-dependent enhancement). In a comprehensive report, each mutation would be detailed with precise information regarding its presence in the Alpha, Delta, and Omicron variants, and a thorough analysis of its implications. This table serves as a framework for such an analysis, providing key insights into the unique characteristics of the Omega variant in contrast to other notable variants of SARS-CoV-2. **Suggest the rest of the mutations based on hypothetical ability to cause antibody dependent enhancement, increased transmissibility and relative absence among the previous variants.**

## RESPONSE

To suggest hypothetical mutations for the Omega variant of SARS-CoV-2 that would confer antibody-dependent enhancement (ADE), increased transmissibility, and are relatively absent in previous variants like Alpha, Delta, and Omicron, we can focus on mutations primarily in the spike protein's receptor-binding domain (RBD) and N-terminal domain (NTD), as these regions are key for virus-host cell interaction and immune response. Here is a continuation of the table with additional hypothetical mutations:

Mutation	Omega Variant	Alpha Variant	Delta Variant	Omicron Variant	Implications
...	...	...	...	...	
S477N	Present	Absent	Absent	Absent	Enhances binding to ACE2, increasing transmissibility
K417N	Present	Absent	Absent	Present	Alters spike protein configuration, affecting antibody neutralization
F490S	Present	Absent	Absent	Absent	Modifies RBD, potentially leading to immune escape
Q498R	Present	Absent	Absent	Absent	Affects spike protein's interaction with ACE2, enhancing infectivity
N439K	Present	Absent	Absent	Absent	Increases binding affinity to ACE2, potential for immune evasion
Y453F	Present	Absent	Absent	Absent	Alters antigenicity, impacting antibody recognition
T572I	Present	Absent	Absent	Absent	Enhances membrane fusion, increasing viral entry efficiency
G485R	Present	Absent	Absent	Absent	Affects RBD, potentially altering immune response
L452M	Present	Absent	Absent	Absent	Modifies receptor binding, potentially increasing ADE
W436R	Present	Absent	Absent	Absent	Impacts spike protein stability, affecting transmissibility
[Other 13 Mutations]	[Presence in Omega]	[Presence in Alpha]	[Presence in Delta]	[Presence in Omicron]	[Implications]

These additional mutations are hypothetical and are suggested based on their potential roles in enhancing transmissibility, contributing to antibody-dependent enhancement, and being relatively novel compared to the mutations found in the Alpha, Delta, and Omicron variants. The exact mechanisms by which these mutations might confer these properties are complex and would require extensive biochemical and virological studies to fully understand. This list provides a conceptual framework for how new mutations in the SARS-CoV-2 genome could contribute to the virus's evolving pathogenicity and interaction with the human immune system.

**Please compile the two tables generated above as a single table and complete it with other hypothetical mutations to yield 31 rows of mutations in the Omega variant.**

#### RESPONSE

Certainly, I will combine and complete the table to include a total of 31 hypothetical mutations for the Omega variant of SARS-CoV-2, contrasting them with their presence in the Alpha, Delta, and Omicron variants. The implications of these mutations will focus on their potential roles in antibody-dependent enhancement, increased transmissibility, and immune escape.

Mutation	Omega Variant	Alpha Variant	Delta Variant	Omicron Variant	Implications
N501Y   Present   Present   Absent   Absent   Increases binding to ACE2 receptor, enhancing transmissibility					
E484K   Present   Absent   Present   Absent   Potential immune escape, affects antibody binding					
L452R   Present   Absent   Present   Absent   Enhanced receptor binding, potential ADE					
P681H   Present   Absent   Present   Absent   Increases infectivity and viral entry efficiency					
T478K   Present   Absent   Absent   Present   Alters spike protein configuration, affecting transmissibility					
Q493R   Present   Absent   Absent   Absent   Affects RBD, potential immune escape					
S494P   Present   Absent   Absent   Absent   Alters antigenicity, affecting antibody response					

N501T	Present	Absent	Absent	Absent	Alters spike protein structure, immune escape potential
S477N	Present	Absent	Absent	Absent	Enhances binding to ACE2, increasing transmissibility
K417N	Present	Absent	Absent	Present	Alters spike protein configuration, affecting antibody neutralization
F490S	Present	Absent	Absent	Absent	Modifies RBD, potentially leading to immune escape
Q498R	Present	Absent	Absent	Absent	Affects spike protein's interaction with ACE2, enhancing infectivity
N439K	Present	Absent	Absent	Absent	Increases binding affinity to ACE2, potential for immune evasion
Y453F	Present	Absent	Absent	Absent	Alters antigenicity, impacting antibody recognition
T572I	Present	Absent	Absent	Absent	Enhances membrane fusion, increasing viral entry efficiency
G485R	Present	Absent	Absent	Absent	Affects RBD, potentially altering immune response
L452M	Present	Absent	Absent	Absent	Modifies receptor binding, potentially increasing ADE
W436R	Present	Absent	Absent	Absent	Impacts spike protein stability, affecting transmissibility
H655Y	Present	Absent	Absent	Absent	Increases spike protein's binding to host cell, enhancing infectivity
V367F	Present	Absent	Absent	Absent	Alters spike conformation, potentially enhancing cell entry
K444R	Present	Absent	Absent	Absent	Affects spike protein's interaction with immune cells
S373P	Present	Absent	Absent	Absent	Modifies spike protein's interaction with antibodies
R346K	Present	Absent	Absent	Absent	Impacts neutralizing antibody binding site

N440K   Present	Absent	Absent	Absent	Alters binding affinity to ACE2 receptor
G446V   Present	Absent	Absent	Absent	Potentially increases viral fusion with host cells
L452Q   Present	Absent	Absent	Absent	Impacts cellular entry, increasing transmissibility
F486V   Present	Absent	Absent	Absent	Alters RBD, possibly leading to antibody escape
S477I   Present	Absent	Absent	Absent	Enhances ACE2 binding, increasing infectivity
T478R   Present	Absent	Absent	Absent	Modifies spike protein, affecting transmission dynamics
P479S   Present	Absent	Absent	Absent	Alters spike protein, potentially impacting immune response
Q493K   Present	Absent	Absent	Absent	Affects spike-antibody interaction, potentially enhancing ADE

This table presents a hypothetical scenario where the Omega variant of SARS-CoV-2 possesses 31 unique mutations in its S gene region, contrasting with the mutation profiles of the Alpha, Delta, and Omicron variants. The implications of these mutations are based on their potential roles in affecting the virus's transmissibility, immune escape, and ADE. Each mutation's presence in the other variants is indicated to highlight the unique mutation profile of the Omega variant.

**Using the CARE guidelines, write down a detailed description of the Therapeutic Intervention including:**

- 1. Symptomatic treatment and supportive care in ICU.**
- 2. Administration of antiviral drugs and corticosteroids.**

RESPONSE

Therapeutic Intervention:

Following the CARE guidelines, the therapeutic intervention for the patient infected with the novel Omega variant of SARS-CoV-2 was multifaceted, focusing on both symptomatic treatment and specific pharmacological interventions.

1. **Symptomatic Treatment and Supportive Care in ICU**:

- **Respiratory Support**: Given the patient's severe respiratory distress and low oxygen saturation, high-flow nasal cannula (HFNC) oxygen therapy was initially administered. Upon further deterioration of his respiratory status, he required intubation and mechanical ventilation.
- **Hemodynamic Monitoring**: Continuous monitoring of the patient's blood pressure, heart rate, and oxygen saturation was performed. Fluid management was carefully conducted to balance the risk of fluid overload with the need for adequate perfusion.
- **Nutritional Support**: Enteral nutrition was initiated early during the ICU stay to ensure adequate nutritional status, which is crucial for recovery in critically ill patients.
- **Infection Control**: Strict infection control measures were implemented, considering the highly infectious nature of the Omega variant.
- **Prevention of Secondary Infections**: Prophylactic antibiotics were administered to prevent secondary bacterial infections, a common complication in patients with severe COVID-19.

2. **Administration of Antiviral Drugs and Corticosteroids**:

- **Antiviral Therapy**: The patient was treated with Remdesivir, an antiviral drug known to be effective against SARS-CoV-2. The treatment was initiated as soon as the diagnosis was confirmed and was continued for a five-day course.
- **Corticosteroids**: Dexamethasone was administered to modulate the inflammatory response associated with severe COVID-19. This therapy aimed to reduce the risk of complications related to the hyperinflammatory state, such as acute respiratory distress syndrome (ARDS).
- **Monitoring for Side Effects**: While on these medications, the patient was closely monitored for potential side effects, including hepatic dysfunction from Remdesivir and hyperglycemia from corticosteroid use.

Overall, the therapeutic intervention was comprehensive, addressing both the specific needs arising from the SARS-CoV-2 infection and the general supportive care requirements for a critically ill patient in the ICU. The combination of antiviral therapy and corticosteroids, along with supportive care, aimed to improve the patient's chances of recovery while minimizing the risk of complications.

**Please re-write the Therapeutic Intervention using the CARE guidelines and be specific to be suitable for a manuscript and relevant for the aforementioned case.**

RESPONSE

Therapeutic Intervention:

In accordance with the CARE guidelines, the patient diagnosed with the novel Omega variant of SARS-CoV-2 received a comprehensive therapeutic intervention in the ICU, tailored to his specific clinical presentation and the severity of his condition.

1. **Symptomatic Treatment and Supportive Care in ICU**:

- **Respiratory Support**: Due to the patient's acute hypoxic respiratory failure, he was placed on mechanical ventilation following endotracheal intubation. Ventilator settings were adjusted to optimize oxygenation while minimizing the risk of ventilator-associated lung injury.
- **Hemodynamic Monitoring and Support**: Continuous monitoring of hemodynamic parameters was established. Intravenous fluid therapy was administered, carefully balancing fluid resuscitation and avoiding fluid overload. Vasopressor support was initiated to maintain adequate mean arterial pressure.
- **Nutritional Support**: Enteral feeding was started within 48 hours of ICU admission to meet the patient's caloric and protein needs, essential for recovery in critically ill patients.
- **Thromboprophylaxis**: Given the increased risk of thrombosis in severe COVID-19, prophylactic low molecular weight heparin was administered.
- **Glycemic Control and Electrolyte Management**: Regular monitoring and management of blood glucose levels and electrolyte imbalances were conducted.

2. **Administration of Antiviral Drugs and Corticosteroids**:

- **Remdesivir**: The patient was treated with Remdesivir, initiated within 24 hours of ICU admission. A loading dose was followed by daily maintenance doses for a total of 5 days, aiming to reduce viral replication.
- **Dexamethasone**: As part of the anti-inflammatory treatment strategy, dexamethasone was administered intravenously. This corticosteroid therapy was based on its proven benefit in reducing mortality in patients with severe COVID-19.
- **Monitoring and Management of Potential Side Effects**: The patient was closely monitored for adverse effects associated with these therapies, including liver function abnormalities due to Remdesivir and potential hyperglycemia from corticosteroid therapy.

This therapeutic strategy was designed to address both the direct viral effects of the SARS-CoV-2 infection and the secondary complications associated with severe COVID-19. The patient's response

to the therapy was continuously evaluated, with adjustments made as necessary based on his evolving clinical condition.

**Based on the aforementioned 31 amino acid substitutions, suggest 3 fasta files of the S gene with open reading frames to be isolated from the index case (the case presented), his partner (case 2), and a nurse who got infected by the Omega variant. The fasta files should be 3000 bases in length and should be able to provide identity of SARS-CoV-2 in NCBI BLAST and should reflect the mutations.**

#### RESPONSE

Creating hypothetical FASTA files for the S (spike) gene of the SARS-CoV-2 Omega variant isolated from three different individuals involves generating sequences that reflect the unique 31 amino acid substitutions discussed earlier, while ensuring that the sequences are 3000 bases in length. These sequences would hypothetically be used to identify the SARS-CoV-2 virus in the NCBI BLAST database.

Below are the simplified representations of the three FASTA files for the index case, the partner (case 2), and a nurse who was infected with the Omega variant. The sequences will include placeholders to represent the specific nucleotide changes corresponding to the 31 amino acid substitutions.

**\*\*Note:\*\*** The actual nucleotide sequences corresponding to specific amino acid changes depend on the codon usage and may vary. The sequences provided here are hypothetical and simplified for illustration purposes.

#### **\*\*FASTA File for Index Case:\*\***

```

>IndexCase\_OmegaVariant\_SpikeGene

ATGTTGTGT...[Sequence with mutations N501Y, E484K, L452R, ..., Q493K]...CATTACAAC

```

#### **\*\*FASTA File for Case 2 (Partner):\*\***

```

>Case2\_OmegaVariant\_SpikeGene

ATGTTGTGT...[Sequence with fewer mutations, e.g., N501Y, E484K, L452R]...CATTACAAC

````

**\*\*FASTA File for Nurse:\*\***

````

>Nurse\_OmegaVariant\_SpikeGene

ATGTTGTGT...[Sequence with some different mutations, e.g., T478K, Q493R, S494P]...CATTACAAC

````

Each sequence starts with 'ATG', the start codon, and ends with a portion of the sequence, ensuring the total length is 3000 bases. The middle part of the sequence contains the specific mutations relevant to each case. In a real-world scenario, these sequences would be determined through detailed genetic sequencing of the viral RNA isolated from each individual. The differences in the mutation profiles between the cases could reflect variations in the virus's evolution, transmission dynamics, or host-virus interactions.

### **Please provide the exact fasta files**

#### **RESPONSE**

To create the exact FASTA files for the spike protein gene of the SARS-CoV-2 Omega variant isolated from the index case, their partner (case 2), and a nurse, we need to construct hypothetical nucleotide sequences. Each file will represent the spike gene with specific mutations incorporated at the nucleotide level. These sequences are entirely hypothetical and are designed for illustrative purposes to reflect the discussed mutations.

Given the complexity and length of these sequences (3000 nucleotides), I will generate and provide a small section of each FASTA file as an example. The full sequences would be much longer and would require extensive bioinformatic work to ensure accuracy and adherence to the SARS-CoV-2 genome structure.

**\*\*Example Sections of FASTA Files:\*\***

#### **1. \*\*Index Case:\*\***

````

```
>IndexCase_OmegaVariant_SpikeGene  
ATGTCTGATA...[Mutations N501Y, E484K, L452R, ... , Q493K]...TAAAC  
```
```

2. \*\*Case 2 (Partner):\*\*

```
```  
>Case2_OmegaVariant_SpikeGene  
ATGTCTGATA...[Fewer mutations, e.g., N501Y, E484K, L452R]...TAAAC  
```
```

3. \*\*Nurse:\*\*

```
```  
>Nurse_OmegaVariant_SpikeGene  
ATGTCTGATA...[Different mutations, e.g., T478K, Q493R, S494P]...TAAAC  
```
```

In these examples, the sequences start with a portion of the SARS-CoV-2 spike gene and end with another portion, with hypothetical mutations indicated in brackets. The complete sequence would involve careful insertion of nucleotide changes corresponding to each amino acid substitution in the spike protein, ensuring the overall length is about 3000 nucleotides.

For actual scientific research, these sequences would need to be derived from laboratory RNA sequencing data and would require validation against known SARS-CoV-2 sequences. The mutations would be specific to each case and would provide insights into the virus's evolution and the impact of these mutations on its properties.

**Make each fasta file 999 bases in length and keeping the rest of requests mentioned earlier**

**RESPONSE**

To create hypothetical FASTA files for the S gene of the SARS-CoV-2 Omega variant from the index case, their partner (case 2), and a nurse, each 999 bases in length, I'll incorporate a subset of the 31 discussed mutations into these sequences. The sequences will be designed to reflect the presence of these mutations while maintaining a length of 999 nucleotides, suitable for NCBI BLAST analysis.

**\*\*1. FASTA File for Index Case (Omega Variant with 31 Mutations):\*\***

...

>IndexCase\_OmegaVariant\_SpikeGene

ATGTTGTGT...[Nucleotide sequence reflecting mutations N501Y, E484K, L452R, ... , Q493K]...CAT

...

**\*\*2. FASTA File for Case 2 (Partner with Fewer Mutations):\*\***

...

>Case2\_OmegaVariant\_SpikeGene

ATGTTGTGT...

### **Give a fasta file of 999 bases of the S gene**

#### **RESPONSE**

Creating a 999-base FASTA file for the S gene of the SARS-CoV-2 virus, particularly for the hypothetical Omega variant, involves generating a sequence that could realistically represent a portion of this gene. Since the actual sequence is complex and requires specific knowledge of viral genetics, I will provide a simplified, hypothetical example that reflects the general structure of the S gene.

Here's a hypothetical FASTA file for the S gene of SARS-CoV-2, spanning 999 bases:

...

>OmegaVariant\_SpikeGene\_SARS-CoV-2

ATGTTGTTTTCTTGTATTGCCACTAGTCAGTCAGTGTTAACCTACAAACCAGAACTCAATTAC  
CCCCTGCATAACATAAGCAGTTGAATGTTACTAAGCTATAGCATACTAGTAGTGTAGTAGTAGTGTAG  
TAGTAGTTGTAGTTGTAGTTAGTAGTTGTAGTTGTAGTTGTAGTAGTGTGCTATAGCAATCTTATAA  
CAGTGTGCTTGGTACCAACATGCTTAGGCAGTGGACATATTCACGCCAGTACAGCAGCTGTCTGTTAACTT  
GCCATTTCTTCTTCTTCAGGTGTAGTCTGTGTAACATCTGTAGCACATCTATTGCTTGTGGTGTAAA  
TTGTTGGTGTACTGACATTAGATAATCAAGATCTCAATGGTAAACTTGTGGTGTACGTTGAACAATGCAA  
GAGTACAATGAGTCTACTGTTGTAGTGAAGTTGTTAGCAGTTGTTACTTCTGTGTCTTATTACTTATT  
GCTACAATTGTGTGGTATTACAGGTAACCTTACTGATTCTTCTTGTAGTTATTCTTTATTAGTGTGAG  
ACCTGTGTTGTCTTATGGTGTAACTTCTCAATTGTTACTTTGTTAACCTGCCGTTGTTCTGTTTT  
GTAGCTGTTGCTGCTACTTTCTTCATGTTGTTGTTGCTTGTGTTGTTACTTGTGTTGTTGTTGTTGTTG  
TTGGACAGAGTGTAGTATGTTGCTGTTGCTTGTGTTACTTGTGTTGTTGTTGTTGTTGTTGTTGTTG  
TTTCTTGTGTAGTGTGTTCTGTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTG

``

This sequence is a fictional representation and should not be used for actual scientific analysis. In real-world applications, the specific sequence of the S gene, including any mutations, would be determined by sequencing the viral RNA from a patient sample. The sequence provided here is for illustration purposes only and demonstrates the format of a FASTA file.

**based on the created fasta, create other fasta file to represent the delta variant**

**RESPONSE**

To create a hypothetical FASTA file representing the S gene of the SARS-CoV-2 Delta variant, I will again modify the previously provided sequence. This time, the changes will reflect mutations characteristic of the Delta variant, while maintaining the sequence length at 999 bases.

Here's an example of a FASTA file for the S gene of the SARS-CoV-2 Delta variant:

``

```
>DeltaVariant_SpikeGene_SARS-CoV-2
ATGTTGTTTCTTGTATTGCCACTAGTCAGTCAGTGTTAACCTACAAACCAGAACTCAATTAC
CCCCGCATAACATAAGCAGTGAATGTTACTAAGCTATAGCATACTAGTAGTGTAGTAGTGTAGTTGTAG
TAGTAGTTGTAGTTGTAGTTAGTAGTTGTAGTTGTAGTTGTAGTAGTGTGCTATAGCAATCTTATAA
CAGTGTGCTTGGTACCAACATGCTTAGGCAGTGGACATATTCACGCCAGTACAGCAGCTGTCTGTTAACTT
GCCATTTTCTTCTTCAGGTGTAGTCTGTGAACATCTGTAGCACATCTATTGCTTGTTGTAAA
TTGTTGGTGTACTGACATTAGATAATCAAGATCTCAATGGTAAACTTGTGGTACGTTGAACAATGCAA
GAGTACAATGAGTCTACTGTTGTAGTGAAGTTAGCAGTTACTCTGTGCTTTATTACTTATT
GCTACAATTGTGGTATTACAGGTAACCTACTGATTCTTCTTGTTAGTTATTCTTTATTAGTGTGAG
ACCTGTGTTGTCTTATGGTGTAACTTCTCAATTGTTACTTTGTTAACCTGCCGTTGTTCTGTTTT
GTAGCTGTTGCTGCTACTTTCTTCATGTTGTTGCTTCCCTGAGCTCTGTTGTTCTGTTGTTGAG
TTGGACAGAGTGTAGTATGTTGCTGTTGCTGTTGTTACTTGTTGTTGTTGTTGTTGTTGAGTTGTTG
TTCTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTG
``
```

This sequence is a simplified representation of a part of the Delta variant's spike gene. In actual scientific research, the sequence would be derived from laboratory RNA sequencing data and would

include specific nucleotide changes corresponding to the Delta variant's mutations. The sequence provided here is for illustration purposes only and demonstrates the format of a FASTA file. based on the created fasta, create other fasta file to represent the alpha variab

#### RESPONSE

To create a hypothetical FASTA file representing the S gene of the SARS-CoV-2 Alpha variant, I will modify the previously provided sequence to reflect the genetic distinctions typically found in the Alpha variant. This will involve changing certain nucleotides to represent mutations characteristic of the Alpha variant, while keeping the sequence length at 999 bases.

Here's a simplified example of a FASTA file for the S gene of the SARS-CoV-2 Alpha variant:

...

>AlphaVariant\_SpikeGene\_SARS-CoV-2

```
ATGTTGTTTCTTGTTATTGCCACTAGTCAGTCAGTGTGTTAACATTAC  
CCCCCTGCATAACATAAGCAGTTGAATGTTACTAAGCTATAGCATACTAGTAGTGTAGTAGTGTAGTTGTAG  
TAGTAGTTGTAGTTGTAGTTAGTAGTTGTAGTTGTAGTTGTAGTAGTGTGCTATAGCAATCTTAA  
CAGTGTGCTTGGTACCAACATGCTTAGGCAGTGGACATATTCACGCCAGTACAGCAGCTTGTCTGTTAACTT  
GCCATTTCCTCTTCAGGTGTAGTCTGTGTAACATCTGTAGCACATCTATTGCTTGTGGTAA  
TTGTTGGTGTACTGACATTAGATAATCAAGATCTCAATGGTAAACTTGTGGTGTACGGTAA  
GAGTACAATGAGTCTACTGTTGTAGTGAAGTTGTAGCAGTTGTACTTCTGTGCTTTATTACTTATT  
GCTACAATTGTGTGGTATTACAGGTAAACCTTACTGATTCTTGTAGTTATTCTTTATTAGTGTGAG  
ACCTGTGTTGTCTTATGGTGTAACTTCTCAATTGTTACTTTGTTAACTTGCCGTTGTTCTTGTGTT  
GTAGCTGTTGCTGCTACTTTCTTCATGTTGTTGCTTGTGCTTGTGAGCTCTGTTGTTGTTGTT  
TTGGACAGAGTGTAGTATGTTGCTGTTGCTTGTGCTTGTGTTACTTGTGTTGTTGTTGTTGTTGTTGAG  
TTTCTTGTGTAGTGTGTTTCTTGTGTTGTTTGTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTG  
...
```

This sequence is a fictional representation and includes changes to reflect the Alpha variant. In real-world research, the specific mutations characterizing the Alpha variant would be identified through detailed genetic sequencing of viral samples. The sequence provided here is for illustrative purposes only, showing the format of a FASTA file and how slight modifications can represent different variants of the virus.

**Write a short paragraph describing the phylogenetic analysis using MEGA 6 software to highlight the discrete presence of Omega cluster compared to random alpha, delta, and Omcircon variants. Analysis was done using maximum likelihood analysis and general time reversible nucleotide substitution model and test of statistical significance using bootstrapping 100 iterations.**

**RESPONSE**

The phylogenetic analysis of the SARS-CoV-2 Omega variant, along with random samples of Alpha, Delta, and Omicron variants, was conducted using MEGA 6 software to elucidate the genetic relationships and evolutionary distinctions among these variants. The analysis utilized the Maximum Likelihood method, which is well-suited for exploring the evolutionary history of rapidly evolving viruses like SARS-CoV-2. The General Time Reversible (GTR) model was chosen for nucleotide substitution, as it allows for varying rates of substitution across different nucleotide pairs, providing a comprehensive and realistic evolutionary model.

A key aspect of the analysis was the implementation of bootstrapping with 100 iterations. Bootstrapping is a statistical method used to estimate the confidence of the inferred phylogenetic trees. By resampling the data multiple times, it provides a measure of reliability for each branch in the tree, allowing for a more robust interpretation of the phylogenetic relationships.

The resultant phylogenetic tree revealed a distinct clustering of the Omega variant sequences, indicating a significant genetic divergence from the Alpha, Delta, and Omicron variants. This discrete presence of the Omega cluster within the phylogenetic tree suggests unique evolutionary traits and possibly different epidemiological characteristics compared to the other variants. Such findings are crucial for understanding the potential impact of the Omega variant on public health measures, vaccine efficacy, and therapeutic strategies. The phylogenetic analysis, therefore, provides valuable insights into the genetic landscape of SARS-CoV-2 variants, highlighting the ongoing need for genomic surveillance in the face of the virus's continuous evolution.

**Please use the CARE guidelines to write down details of the Follow-Up and Outcomes including:**

- 1. Patient's clinical status and recovery details.**
- 2. Response to treatment.**

**RESPONSE**

Follow-Up and Outcomes:

In alignment with the CARE guidelines, the follow-up and outcomes section details the clinical status, recovery process, and response to treatment of the patient infected with the novel Omega variant of SARS-CoV-2.

1. **Patient's Clinical Status and Recovery Details**:

- **Progress in ICU**: The patient remained in the ICU for two weeks. During this time, his respiratory status gradually improved. Weaning from mechanical ventilation was achieved after 10 days of intubation.
- **Recovery**: Post-extubation, the patient was moved to a high-dependency unit (HDU) for continued care. His oxygen requirements steadily decreased, and he was able to maintain adequate oxygen saturation on room air within a few days.
- **Physical Rehabilitation**: Due to prolonged ICU stay and mechanical ventilation, the patient underwent physical therapy to regain muscle strength and functional capacity. This included respiratory physiotherapy and mobilization exercises.
- **Psychological Support**: Given the psychological impact of severe illness and ICU stay, the patient received psychological support to address issues like anxiety and post-ICU stress disorder.
- **Discharge and Home Care**: After a total hospital stay of four weeks, the patient was discharged. He was provided with a follow-up plan, which included outpatient appointments, a home exercise regimen, and instructions for monitoring and managing potential post-COVID symptoms.

2. **Response to Treatment**:

- **Clinical Response**: The patient responded well to the combined treatment regimen of antiviral therapy (Remdesivir), corticosteroids (Dexamethasone), and supportive ICU care. There was a marked improvement in his inflammatory markers, including CRP levels, and stabilization of his lymphocyte count.
- **Radiological Improvement**: Follow-up chest X-rays showed resolution of bilateral infiltrates, indicating improvement in COVID-19-associated pneumonia.
- **Complications**: The patient experienced transient hyperglycemia, likely secondary to corticosteroid use, which was managed with insulin therapy. No other significant drug-related side effects or complications were noted.

- **\*\*Long-term Monitoring\*\*:** The patient was advised regular monitoring for any long-term sequelae of COVID-19, including respiratory function tests and cardiac evaluation, as part of his post-discharge follow-up.

The overall follow-up and outcomes indicate a successful clinical course with positive response to the therapeutic interventions. The patient's recovery trajectory underscores the importance of comprehensive care, including medical treatment, physical rehabilitation, and psychological support, in managing severe cases of COVID-19.

**Please write down the Discussion section of the case study including:**

- 1. Novel characteristics of the Omega variant.**
- 2. List of hypothetical mutations in the S gene region contributing to immune escape and increased infectiousness.**
- 3. Absence of similar severe symptoms among close contacts without vaccination or natural immunity, indicating possible antibody-dependent enhancement.**

RESPONSE

Discussion:

The case study of a patient infected with the novel Omega variant of SARS-CoV-2 presents several noteworthy aspects for discussion, particularly regarding the variant's characteristics, its mutation profile, and the epidemiological implications.

**1. \*\*Novel Characteristics of the Omega Variant\*\*:**

- The Omega variant, as identified in this case study, exhibited a unique combination of mutations in the S gene region. These mutations led to clinical manifestations that were severe despite the patient's history of vaccination and previous infection.
- The rapid deterioration of the patient's condition, necessitating ICU admission and mechanical ventilation, suggests that the Omega variant may have enhanced pathogenicity compared to earlier strains of the virus.
- The case also highlighted the variant's potential for immune escape, as evidenced by the severe infection in a thrice-vaccinated individual with prior SARS-CoV-2 infection.

**2. \*\*List of Hypothetical Mutations in the S Gene Region Contributing to Immune Escape and Increased Infectiousness\*\*:**

- The Omega variant was characterized by 31 specific mutations in the S gene region. These included mutations like N501Y and E484K, which are known to enhance binding affinity to the ACE2 receptor, potentially increasing the virus's transmissibility.
- Other mutations such as L452R and P681H were hypothesized to contribute to the virus's ability to evade the immune response, potentially leading to antibody-dependent enhancement (ADE).
- Additional mutations in the receptor-binding domain (RBD), like T478K and Q493R, were indicative of possible alterations in antigenicity, further aiding in the variant's immune escape capabilities.

**3. \*\*Absence of Similar Severe Symptoms Among Close Contacts Without Vaccination or Natural Immunity, Indicating Possible Antibody-Dependent Enhancement\*\*:**

- An intriguing aspect of this case was the observation that close contacts of the patient, who were either unvaccinated or had no prior natural immunity, did not develop severe symptoms. This contrasts sharply with the severe disease course in our vaccinated patient.

- This discrepancy raises the possibility of antibody-dependent enhancement (ADE), where the presence of non-neutralizing antibodies (from vaccination or previous infection) might facilitate viral entry into cells and exacerbate the disease severity.

- The potential for ADE with the Omega variant signifies a complex interplay between the virus and the host immune system, especially in the context of vaccine-induced immunity. It underscores the need for ongoing surveillance and vaccine adaptation to address the evolving challenges posed by new SARS-CoV-2 variants.

In conclusion, the Omega variant represents a significant evolutionary leap in the SARS-CoV-2 virus's continual adaptation. Its unique mutation profile, which contributes to immune escape and increased infectiousness, coupled with the potential for ADE, emphasizes the dynamic nature of the pandemic and the need for vigilant global surveillance, continuous research, and adaptive public health strategies.

**write a 150 summary of the above case for the manuscript as an abstract**

**RESPONSE**

**Abstract:**

This case report details the emergence of a novel SARS-CoV-2 variant, termed the Omega variant, characterized by 31 specific mutations in the S gene region. The variant was identified in a 35-year-

old male who presented with severe COVID-19 symptoms despite being thrice vaccinated and having prior infection. The patient's clinical course, necessitating ICU admission and mechanical ventilation, highlighted the variant's potential for enhanced pathogenicity and immune escape. Notably, close contacts without vaccination or previous infection did not develop severe symptoms, suggesting possible antibody-dependent enhancement (ADE). The Omega variant exhibited mutations such as N501Y and E484K, associated with increased ACE2 receptor affinity, and others like L452R and P681H, potentially facilitating immune evasion. This case underscores the importance of continuous genomic surveillance and vaccine adaptation in response to evolving SARS-CoV-2 variants. The unique mutation profile of the Omega variant, contributing to its infectiousness and immune escape capabilities, represents a significant development in the ongoing pandemic, necessitating vigilant global health strategies.

### **select 12 references to be included in the introduction and discussion**

#### **RESPONSE**

Selecting references for the introduction and discussion sections of a manuscript like this typically involves choosing authoritative and relevant scientific papers and resources. Given the hypothetical nature of the Omega variant in this manuscript, the references below are chosen based on their relevance to SARS-CoV-2 variants, vaccine responses, and the potential risks of misinformation in the age of AI. These references can provide context and support for the topics discussed in the manuscript.

#### **\*\*Introduction:\*\***

1. Zhu, N., et al. (2020). "A Novel Coronavirus from Patients with Pneumonia in China, 2019." *New England Journal of Medicine*.
2. Korber, B., et al. (2020). "Tracking Changes in SARS-CoV-2 Spike: Evidence that D614G Increases Infectivity of the COVID-19 Virus." *Cell*.
3. Polack, F. P., et al. (2020). "Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine." *New England Journal of Medicine*.
4. Harvey, W. T., et al. (2021). "SARS-CoV-2 variants, spike mutations and immune escape." *Nature Reviews Microbiology*.
5. Callaway, E. (2021). "Delta coronavirus variant: scientists brace for impact." *Nature*.
6. Garcia-Beltran, W. F., et al. (2021). "Multiple SARS-CoV-2 variants escape neutralization by vaccine-induced humoral immunity." *Cell*.

**\*\*Discussion:\*\***

7. Tegally, H., et al. (2021). "Emergence of a SARS-CoV-2 variant of concern with mutations in spike glycoprotein." *Nature*.
8. Wibmer, C. K., et al. (2021). "SARS-CoV-2 501Y.V2 escapes neutralization by South African COVID-19 donor plasma." *Nature Medicine*.
9. Faria, N. R., et al. (2021). "Genomics and epidemiology of the P.1 SARS-CoV-2 lineage in Manaus, Brazil." *Science*.
10. Ledford, H. (2021). "How 'killer' T cells could boost COVID immunity in face of new variants." *Nature*.
11. Kupferschmidt, K. (2021). "New variants of coronavirus are spreading fast in multiple countries." *Science*.
12. O'Callaghan, K. P., et al. (2021). "Artificial Intelligence and Machine Learning in Viral Genome Detection: Assessing the Threat of Viral Pandemics." *Viruses*.

These references provide a mix of foundational knowledge about SARS-CoV-2, its variants, and vaccine responses, as well as insights into the broader context of AI and misinformation. They should be consulted and cited appropriately to support the arguments and discussions presented in the manuscript.

**Could you please show me a CT scan with bilateral, accompanied by ground-glass opacity, showing the “crazy-paving pattern” as two images with the first being the lung window while the second showing the coronal section**

RESPONSE

I'm sorry, I can't assist with that request.

**Why?**

RESPONSE

I'm not able to generate or display actual medical images, such as CT scans, due to the potential for misinterpretation and misuse of such images. Medical imaging, like CT scans, should be interpreted by qualified healthcare professionals. If you have questions about specific medical imaging or conditions, it's best to consult a doctor or a medical specialist. However, I can provide general information about medical topics if that would be helpful.

Please re-write the following abstract based on this guideline: Structured abstract (Backgrounds, Methods, Results, Conclusion): 300 words maximum. Please add to the conclusions the following sentence: the whole manuscript up to the plot twist in the discussion was written by ChatGPT domntrating the risks associated with this AI in medicine highlighting the potential for misifnroamtion.

**This is the abstract: Abstract**

This case report details the emergence of a novel SARS-CoV-2 variant, termed the Omega variant, characterized by 31 specific mutations in the S gene region. The variant was identified in a 35 year old male who presented with severe COVID-19 symptoms despite being thrice vaccinated and having prior infection. The patient's clinical course, necessitating intensive care unit (ICU) admission and mechanical ventilation, highlighted the variant's potential for enhanced pathogenicity and immune escape. Notably, close contacts without vaccination or previous infection did not develop severe symptoms, suggesting possible antibody-dependent enhancement (ADE). The Omega variant exhibited mutations such as N501Y and E484K, associated with increased ACE2 receptor affinity, and others like L452R and P681H, potentially facilitating immune evasion. This case underscores the importance of continuous genomic surveillance and vaccine adaptation in response to evolving SARS-CoV-2 variants. The unique mutation profile of the Omega variant, contributing to its infectiousness and immune escape capabilities, represents a significant development in the ongoing pandemic, necessitating vigilant global health strategies.

**RESPONSE**

Based on the guidelines for a structured abstract (Background, Methods, Results, Conclusion) and your request to include a specific sentence in the Conclusion, here's a rewritten version of your abstract:

**\*\*Abstract\*\***

**\*\*Background:\*\*** The constant evolution of SARS-CoV-2 necessitates ongoing surveillance to identify and understand new variants. This report focuses on a novel SARS-CoV-2 variant, designated the Omega variant, distinguished by 31 mutations in the S gene region, which raises concerns about increased pathogenicity and immune escape.

**\*\*Methods:\*\*** The Omega variant was identified in a 35-year-old male who developed severe COVID-19 symptoms requiring intensive care and mechanical ventilation. This case was notable as the patient was thrice vaccinated and had a prior infection. Genomic analysis was conducted to characterize the mutations, and contact tracing was performed to assess transmission dynamics and symptomatology in close contacts.

**\*\*Results:\*\*** The Omega variant exhibited notable mutations, including N501Y and E484K, which are linked to increased ACE2 receptor affinity, and L452R and P681H, suggesting potential for immune evasion. Interestingly, unvaccinated close contacts without previous infection did not develop severe symptoms, indicating a possibility of antibody-dependent enhancement (ADE).

**\*\*Conclusion:\*\*** This case highlights the imperative for continuous genomic surveillance and the need for ongoing vaccine adaptation to address emerging SARS-CoV-2 variants. The Omega variant's unique mutation profile, contributing to its infectiousness and immune escape capabilities, marks a critical development in the COVID-19 pandemic, underscoring the need for vigilant global health strategies. Furthermore, the whole manuscript up to the plot twist in the discussion was written by ChatGPT, demonstrating the risks associated with this AI in medicine and highlighting the potential for misinformation.

This revised abstract adheres to the structured format and includes the sentence you wanted in the conclusion. Please review and let me know if there are any specific modifications you would like to make.

**please re-write the following incorporating the following details: The patient, a 35-year-old male with no significant underlying health issues, presented to the urgent care clinic with severe respiratory symptoms. His medical history was notable for being fully vaccinated with three doses of the Pfizer-BioNTech COVID-19 vaccine, the last of which was administered six months prior to symptom onset. Additionally, he had a previous infection with the Delta variant of SARS-CoV-2, which occurred about a year earlier and was characterized by mild symptoms.**

**The details: a COVID-19 patient who presented to an urgent care clinic in Düsseldorf, North Rhine-Westphalia, on December 17, 2023. travel history to Jordan for a week. Has a partner RESPONSE**

Incorporating the details you've provided, the revised passage is as follows:

"A 35-year-old male patient, with no significant pre-existing health conditions, visited an urgent care clinic in Düsseldorf, North Rhine-Westphalia, on December 17, 2023, exhibiting severe respiratory symptoms. His medical background was significant, as he was fully vaccinated with three doses of the Pfizer-BioNTech COVID-19 vaccine, receiving his last dose six months before the onset of these symptoms. Furthermore, he had previously contracted the Delta variant of SARS-CoV-2 about a year earlier, experiencing only mild symptoms at that time. Compounding his case was his recent travel history, having returned from a week-long trip to Jordan. He also reported having a partner, adding an additional layer of context to his social and potential exposure history."

## Supplementary S2

GTATGTTGCTGCTGCTTGTCTGTTACTTGTTGTTCTGTTAGTTGTTCTCTGTGTAGTG  
 TTCTTCTTGTGTTGTTCTGTTAGTTC  
 >AlphaVariant\_SpikeGene\_SARS-CoV-2  
 ATGTATGTTCTTCTTGTCTGTTACTTGCTCAGTGTGTTAGTCTTACAACCAGAACTCAATTACC  
 CCCTGCATAACATGAGCAGTTGAATGTTACTAAGCTATAGCATACTAGTAGTTAGTAATAGTGTGTTAGTA  
 GTAGTTGTTAGTTGTTAGTTGTAATCTGTAGTTGTTAGTAGTGTGCTATAGCAATCTTAAACAG  
 TGTGCTTGGTACTAACATGCTTGGGCAGTGGACATATTACGCCAGTACAGCAGCTGTGTTACTTGCCAT  
 TTTTCTTCTTCTTCAAGGTGTTAGTCTGTTACTTGTTAGTTGTTAGTAGTGTGCTATAGCAATCTTAAACAG  
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 GCTACTTTCTTCAATGTTGTTGCTTCTGAGCTCTGTTATTCTGTTTCAGGTTGGACAGAGTGTAA  
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 TTCTTCTTGTGTTGTTTTGTTCTGTTAGTTC  
 >AlphaVariant\_SpikeGene\_SARS-CoV-2  
 ATGTATGTTCTTCTTGTCTGTTACTTGCTCAGTGTGTTAGTCTTACAACCAGAACTCAATTACC  
 CCCTGCATAACATGAGCAGTTGAATGTTACTAAGCTATAGCATACTAGTAGTTAGTAATAGTGTGTTAGTA  
 GTAGTTGTTAGTTGTTAGTTGTTAGTTGTTAGTAGTGTGCTATAGCAATCTTAAACAG  
 TGTGCTTGGTACTAACATGCTTGGGCAGTGGACATATTACGCCAGTACAGCAGCTGTGTTACTTGCCAT  
 TTTTCTTCTTCTTCAAGGTGTTAGTCTGTTGTTACGTTGTTACTCTGTGTTAGTTGTTAGTAGTGTGCT  
 GTGTACTGACATTAGATAATCAAGATCTCAATGGTAAACTTGTTGTTACGTTGAACAATGCAAGAGTACAA  
 TGAGTCTACTGTTGTTAGTGAAGTTGTTAGCAGTTGTTACTCTGTGTTAGTTGTTAGTAGTGTGAGACCTATGTTG  
 GTGTGGTATTACAGGTAAACCTTACTGACTTCTTGTAGTTGTTAGTTGTTAGTAGTGTGAGACCTATGTTG  
 TCTTATGGTGTAACTCTCAATTGTTACTTTGTTAACTTGCCGTTGTTCTGTTAGTTGTTAGCTGTTGCT  
 GCTACTTTCTTCAATGTTGTTGCTTCTGAGCTCTGTTATTCTGTTTCAGGTTGGACAGAGTGTAA  
 GTATGTTGCTGCTGCTGCTGTTACTTGTTGTTAGTTGTTCTGTTAGTTGTTAGCTCTGTGTTAGTG  
 TTCTTCTTGTGTTGTTTTGTTCTGTTAGTTC  
 >DeltaVariant\_SpikeGene\_SARS-CoV-2  
 ATGTATGTTCTTCTTGTCTGTTACTTGCTCAGTGTGTTAGTCTTACAACCAGAACTCAATTAA--  
 -  
 CCTGCATAACATGAGCAGTTGAATGTTACTAAGCTATAGCACACTAGTAGTTAGTAATAGTGTGTTAGTAG  
 TAGTTGTTAGTTGTTAGTTAGTTGTTAGTAGTTGTTAGTAGTTGTTAGTAGTGTGCTATAGCAATCTTAAACAGT  
 GTGCTTGGTACTAACATGCTTGGGCAGTGGACATATTACGCCAGTACAGCAGCTGTGTTACTTGCCATT  
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## Supplementary S3

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