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Viral Chronicles: The Ever-Evolving Saga of COVID-19

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Abstract

Coronaviruses, belonging to the family of RNA viruses, have recently captured global attention owing to their remarkable ability to infect a diverse array of species, ranging from animals to humans. These viral agents, recognized by their characteristic crown-like morphology when observed through electron microscopy, have a historical association with zoonotic diseases. Previous examples include Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV). The term "Corona" itself, emblematic of this distinctive morphology, was coined by pioneering virologists June Almeida and David Tyrrell, underscoring the profound impact these viruses have had on scientific understanding and public health. Leading the charge within this viral lineage is the newly identified coronavirus SARS-CoV-2, which serves as the causative agent behind the current COVID-19 pandemic. Its emergence has ushered in a new era of global health crisis, characterized by unprecedented transmission rates and severe respiratory complications. As the virus continues to evolve and adapt, understanding the intricacies of its emergence and mutation becomes paramount. This paper embarks on a comprehensive exploration of the multifaceted aspects surrounding COVID-19, delving into its zoonotic origins, intricate genomic architecture, mechanisms of replication, and the formidable challenge posed by viral mutations. By unraveling the evolutionary trajectory of SARS-CoV-2, we aim to decipher the underlying mechanisms driving its pathogenicity and transmissibility, thus laying the groundwork for informed public health interventions. Zoonotic spillover events, often facilitated by human-animal interactions, serve as the genesis for novel coronavirus outbreaks. Understanding the dynamics of cross-species transmission is essential for predicting and preempting future pandemics. Moreover, genomic surveillance plays a pivotal role in monitoring viral evolution, detecting emerging variants, and informing vaccine development strategies. In this endeavor, we aim to contribute to the collective knowledge base surrounding COVID-19, leveraging insights from virology, epidemiology, and molecular biology. By synthesizing the latest scientific evidence and empirical observations, we strive to elucidate the underlying mechanisms driving the emergence and mutation of SARS-CoV-2, thereby empowering public health authorities and policymakers to mount effective responses to the ongoing pandemic. In essence, this paper represents a holistic exploration of the evolutionary dynamics of COVID-19, underscoring the urgent need for interdisciplinary collaboration and evidence-based interventions in the global fight against emerging infectious diseases.

Keywords: Zoonotic disease, Coronavirus, Respiratory syndrome, Replication mechanism, Mutation

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INTRODUCTION [1–3]

The emergence of COVID-19 represents a significant milestone in the history of pandemics, marking the fifth such global health crisis since the influenza pandemic of 1918. Tracing its origins to Wuhan, China, SARS-CoV-2 swiftly spread across borders, infecting millions and claiming countless lives. Acknowledged as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses, this microorganism has presented unparalleled obstacles to global public health infrastructures. Notably, SARS-CoV-2 exhibits remarkable resilience, surviving on various surfaces for extended periods and demonstrating sensitivity to environmental factors such as heat and ultraviolet radiation. Moreover, the dynamic nature of SARS-CoV-2 is exemplified by the emergence of multiple variants, each with distinct genetic signatures and biological properties. Variants such as Alpha, Beta, Gamma, Delta, Eta, Iota, Kappa, Lambda, and Mu have raised concerns regarding their transmissibility, virulence, and potential to evade immune responses. Of particular interest is the spike protein, which undergoes frequent mutations, accounting for a substantial proportion of genetic diversity observed in SARS-CoV-2. These mutations not only influence viral infectivity and pathogenesis but also pose challenges for diagnostic testing and vaccine efficacy.

HISTORY [4–6]

The onset of the COVID-19 pandemic can be pinpointed to December 2019, when instances of pneumonia with unidentified causes were communicated to the China office of the World Health Organization. History of Pandemic caused by other viruses before COVID-19 shown in figure F1.Investigations revealed a novel coronavirus as the causative agent, with bats identified as the probable reservoir. The role of wet markets in facilitating interspecies transmission underscored the complex interplay between human activities and emerging infectious diseases. Subsequent genomic analyses confirmed the zoonotic origin of SARS-CoV-2, with genetic similarities to coronaviruses found in bats and other wildlife. The rapid escalation of COVID-19 prompted the WHO to declare it a pandemic on January 30, 2020, reflecting its unprecedented global impact and urgency for coordinated action. Efforts to contain the spread of the virus were met with myriad challenges, including issues of misinformation, resource constraints, and disparities in healthcare infrastructure. Despite these challenges, the scientific community rallied together to accelerate research efforts, leading to the development of diagnostic tests, therapeutics, and vaccines in record time. In summary, the COVID-19 pandemic underscores the interdependence of global health and the crucial need for readiness and collaboration in combating emerging infectious diseases. As the world continues to grapple with the evolving threat posed by SARS-CoV-2 and its variants, concerted efforts must be made to prioritize scientific inquiry, equity in healthcare delivery, and international cooperation to safeguard public health and mitigate future pandemics.

EPIDEMIOLOGY [7–9]

The epidemiological progression of the COVID-19 outbreak can be delineated into distinct phases. The initial phase, marked by the local outbreak traced back to exposure at a food wholesale market, served as a pivotal moment in the emergence of the pandemic. Subsequently, the second phase commenced on January 13, characterized by the rapid expansion of infections, primarily within hospital settings and through intrafamilial transmission. This phase heralded a significant shift in the trajectory of the outbreak, highlighting the insidious nature of the virus's spread. The third phase, which commenced on January 26, witnessed a concerning surge in cluster cases, signifying a critical juncture in the evolution of the pandemic.

Manifestation-Focused Monitoring

Vigilant symptom tracking serves as a cornerstone for the timely identification and control of diseases, aiding substantially in early detection and containment initiatives. These encompass a multifaceted approach, including rigorous symptomatic screenings at key points of entry such as airports and train stations. Additionally, community-based fever monitoring initiatives serve as frontline defenses against undetected transmission. Home observation protocols targeting recent travelers to Hubei Province enable early identification of potential cases, facilitating timely intervention and isolation. Furthermore, the testing of hospitalized patients with compatible symptoms ensures swift diagnosis and appropriate management, thereby mitigating further spread within healthcare settings.

Contact-Based Surveillance

Contact-based surveillance mechanisms serve as a cornerstone of proactive outbreak control strategies. By systematically identifying and testing individuals with close contact history to confirmed cases, irrespective of symptomatology, health authorities can effectively preempt secondary transmission chains. This targeted approach enables the early detection of asymptomatic or presymptomatic cases, minimizing the risk of undetected spread within the community. Through meticulous contact tracing efforts and prompt isolation of contacts, public health agencies can curtail the onward transmission of the virus, thereby mitigating the impact of the pandemic.

ETIOLOGY [10–14]

The term “Corona” originates from the Latin word “coronam,” meaning crown, aptly describing the crown-like appearance of Coronaviruses due to the presence of spike glycoproteins on their surface. Coronaviruses belong to the group of positive-stranded RNA (+ssRNA) viruses and constitute the largest group within the Nidovirales order, encompassing families such as Coronaviridae, Arteriviridae, Roniviridae, and Mesoniviridae. Coronaviruses typically enter the body through respiratory droplets or direct contact with an infected person. Once inside a host, the virus attaches to specific receptors on the surface of cells, typically in the respiratory tract. The virus then enters the cell, where it hijacks the cell's machinery to replicate its genetic material and produce new viral particles. Visualizing Corona: A Diagrammatic Representation of Coronavirus Structure shown in Figure 2.

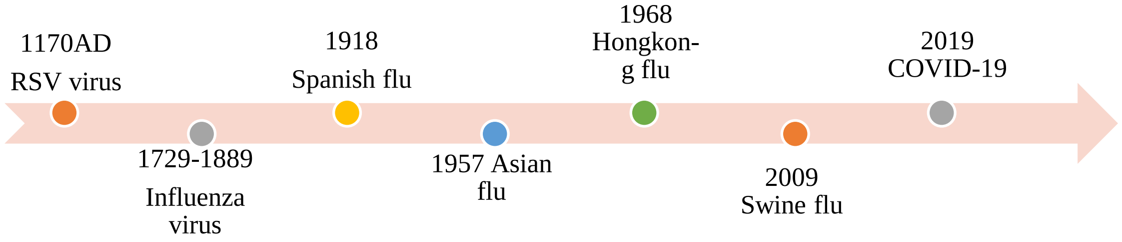


Figure 1. History of Pandemic caused by other viruses before COVID-19.

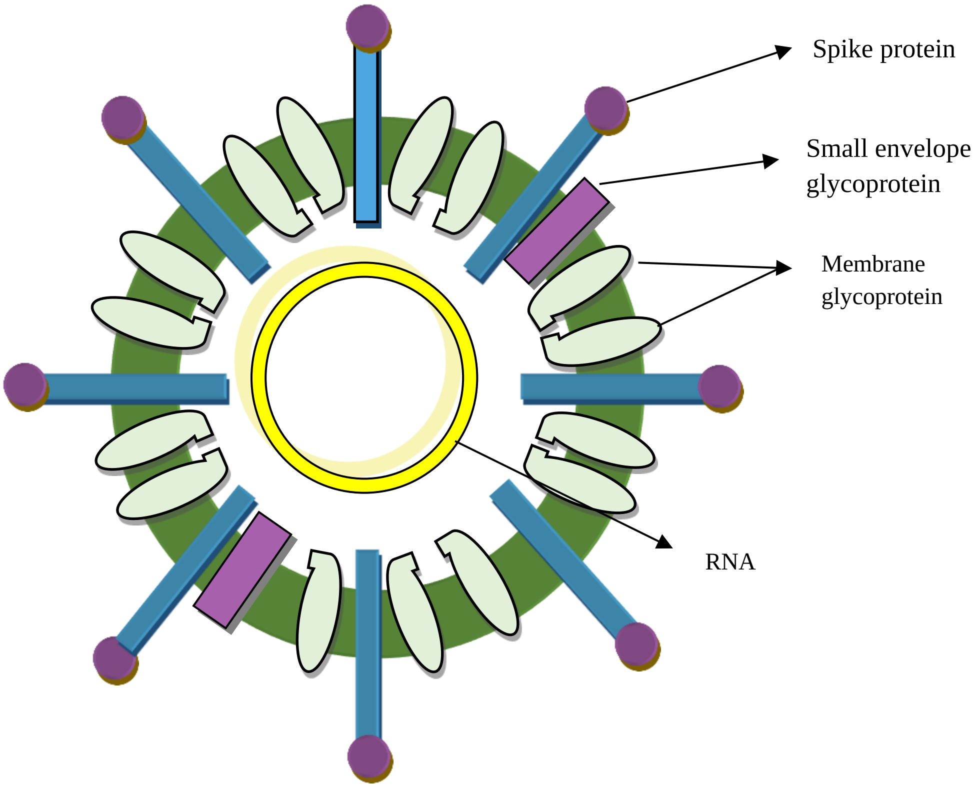


Figure 2. Visualizing Corona: A Diagrammatic Representation of Coronavirus Structure.

Common Human Coronaviruses

The immune system responds to the viral infection by mounting an inflammatory response, which can cause symptoms such as fever, cough, and difficulty breathing. In some cases, particularly with more pathogenic strains like SARS-CoV, MERS-CoV, and SARS-CoV-2, the immune response can become dysregulated, leading to severe lung inflammation and organ damage

Alternative Pathogenic Human Coronaviruses

Pathogenic human Coronaviruses, including SARS-CoV, MERS-CoV, and SARS-CoV-2, exhibit distinctive structural proteins and high mutation rates, facilitating altered variants. Zoonotic transmission, influenced by intermediate hosts like civet cats and dromedary camels, and environmental factors, emphasizes the importance of comprehensive prevention and control strategies aligning with One Health principles. These viruses have garnered significant attention due to their high mortality rates, reaching up to 10% and 35% for SARS-CoV and MERS-CoV, respectively.

SARS-CoV-2 VARIANT CLASSIFICATION [15–20]

The U.S. Department of Health and Human Services (HHS) has introduced a specialized task force, termed the SARS-CoV-2 Variant Assessment Team (SVAT), dedicated to swiftly evaluating emerging viral strains. This team classifies the variants into four tiers: Variants for Enhanced Monitoring (VEM), Variants of Emerging Interest (VEI), Variants of Public Health Significance (VPS), and Variants of Epidemiological Attention (VEA). New variants are associated with heightened transmissibility, leading to increased infectivity and potentially elevated rates of re-infection.

Variant Being Monitored (VBM)

Alpha (B.1.1.7)

The Alpha variant, first identified in the United Kingdom, exhibits a significantly higher transmissibility rate of approximately 50% compared to the wild-type virus. Studies by the COVID-19 Genomics UK (COG-UK) Consortium have identified over 4,000 mutations in its spike protein, with notable changes such as the N501Y mutation, enhancing infectiousness. This mutation alters the receptor-binding motif (RBM) within the receptor-binding domain (RBD), resulting in increased infectivity due to enhanced binding to the human ACE2 receptor.

Beta (B.1.351)

First detected in the Nelson Mandela Bay, the Beta variant carries several mutations, including the concerning mutations K417N, E484K, and N501Y, which may impact viral infectivity and immune evasion.

Gamma (P.1)

Initially identified in travelers from Amazonas and Brazil, the Gamma variant has exhibited higher infectivity rates than the Alpha and Beta variants. With 10 mutations in its spike protein and additional mutations in other genomic regions, it poses a significant public health concern.

Variant of Interest (VOI)

Eta (B.1.525)

Emerging from diverse regions such as the United Kingdom and Nigeria, the Eta variant, also identified as lineage B.1.525, has sparked scientific interest due to its unique genetic makeup. Although its exact implications for transmission, severity, and immune evasion are still under investigation, the Eta variant carries mutations such as E484K and Q677H in the spike protein, which have been associated with altered viral properties. While not yet elevated to the level of VOC, ongoing monitoring and research are essential to assess its potential impact on the global pandemic landscape.

Iota (B.1.526)

The Iota variant, initially detected in New York City, United States, has been classified as a Variant of Interest (VOI). With mutations such as E484K and S477N in the spike protein, the Iota variant has raised concerns regarding potential changes in transmissibility, disease severity, and immune evasion. While further studies are warranted to elucidate its clinical significance and epidemiological implications, its VOI designation underscores the need for continued vigilance and surveillance to monitor its spread and impact.

Kappa (B.1.617.1)

The Kappa variant, first identified in India alongside the Delta variant, has been labeled as a Variant of Interest (VOI). Featuring mutations such as L452R and E484Q in the spike protein, the Kappa variant has prompted heightened scrutiny due to its potential implications for viral properties and disease dynamics. While its exact significance is still under investigation, ongoing surveillance and analysis are imperative to assess its emergence and potential impact on global COVID-19 dynamics.

Variant of Concern (VOC)

Variant of Concern (VOC) denotes a subset of SARS-CoV-2 variants that have garnered considerable attention from public health authorities due to their heightened transmissibility, severity, or potential to evade immune responses.

Delta (B.1.617.2)

First detected in India in December 2020, the Delta variant is approximately 60% more transmissible than other variants. With 13 mutations in its genome, it has become the predominant variant globally, contributing to surges in cases worldwide.

Omicron (B.1.1.529)

Emerging from South Africa in November 2021, the Omicron variant is characterized by a remarkable diversity of mutations, particularly in the spike protein. With over 50 mutations, including significant alterations in key viral proteins, Omicron poses significant challenges to global containment efforts due to its potential for increased transmissibility and immune evasion.

Epsilon (B.1.427 and B.1.429)

The Epsilon variant was first identified in California, United States. While initially categorized as a Variant of Interest (VOI) due to its potential impact on public health, it later transitioned to a Variant of Concern (VOC). The Epsilon variant is characterized by mutations such as L452R in the spike protein, which may confer increased transmissibility and potential immune escape. While further research is ongoing to understand its impact on vaccine efficacy and disease severity, its designation as a VOC underscores the need for continued surveillance and mitigation efforts

Lack of VOHC-Classified SARS-CoV-2 Variants:

To date, there have been no SARS-CoV-2 variants designated as Variants of High Consequence (VOHC), underscoring the current absence of identified strains with extreme implications shown in Table 1.The schematic overview of mutations in spike in Alpha and Delta variants shown in Figure 3.

TRANSMISSION [24–27]

COVID-19 spreads primarily through close contact between individuals, typically within a distance of 6 feet. Key modes of transmission include:

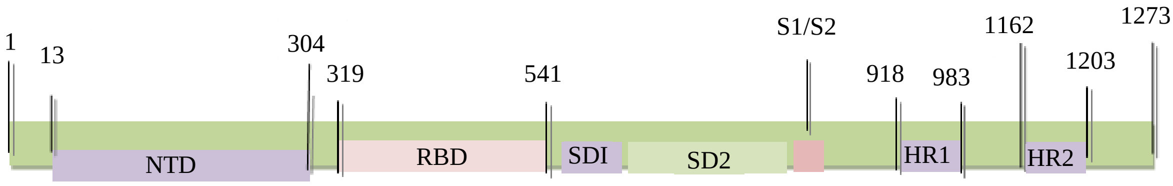
Hand-to-Surface Transmission: COVID-19 can spread via contaminated surfaces, where individuals may contract the virus by touching objects or surfaces harboring viral particles and subsequently touching their face, particularly the mouth, nose, or eyes.

Respiratory Droplets: Respiratory droplets of varying sizes are produced during respiratory activities.

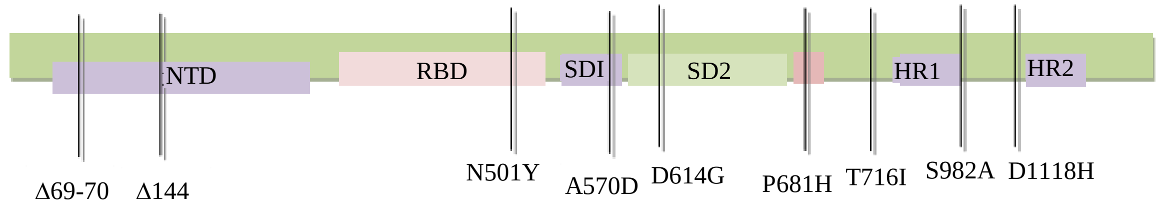
Larger droplets (>5 μm) settle quickly, while smaller droplets can remain suspended in the air for longer periods and travel greater distances.

Table 1. Summary of variants of SARS-CoV-2 classified by SARS-CoV-2 Interagency Group (SIG) [21–23]

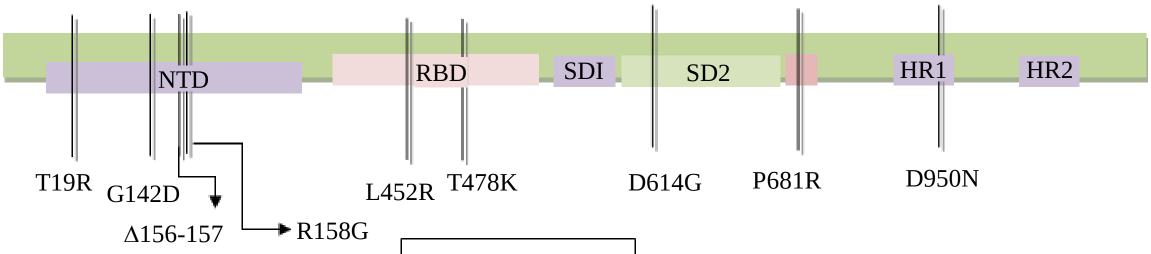
	Variant Classification		
Variant Being Monitored (VBM)	***Variant of Interest (VOI)***	***Variant of Concern (VOC)***	***Variant of High Consequence (VOHC)***
• Alpha (B.1.1.7 and Q lineages) • Beta (B.1.351 and descendent lineages) • Gamma (P.1 and descendent lineages) • Epsilon (B.1.427 and B.1.429) • Eta (B.1.525) • Iota (B.1.526) • Kappa (B.1.617.1) • 1.617.3 • Mu (B.1.621, B.1.621.1) • Zeta (P.2)	• Eta(B.1.525) • Iota (B.1.526) • Kappa (B.1.617.1)	• Delta (B.1.617.2 and AY lineages) • Omicron (B.1.1.529 and BA lineages) • Epsilon (B.1.427 and B.1.429)	• No variant



(A) Wild-type



(B) Alfa variant



(C) Delta variant

Figure 3. The schematic overview of mutations in spike in Alpha and Delta variants.

Environmental Factors: Humidity and temperature play roles in virus transmission, with optimal humidity levels ranging between 50 to 80%.

Airborne Transmission: SARS-CoV-2 has the potential to spread through aerosols, particularly in poorly ventilated indoor environments. Utilizing interventions like mask-wearing and enhancing indoor air circulation can effectively reduce the risk associated with this mode of transmission. The survival times of COVID-19 on various surfaces are as follows: On cardboard, the virus can persist for up to 1 day, while on copper surfaces, it remains viable for about 4 hours. Plastic surfaces can harbor the virus for up to 2-3 days, and similarly, stainless steel surfaces also retain infectious virus particles for the same duration. These findings underscore the importance of regular surface disinfection and hygiene practices to minimize the risk of transmission

SIGNS AND SYMPTOMS [28–32]

Fever: Elevated body temperature, often a prominent early symptom of COVID-19 infection.

Cough: Persistent coughing, which can be dry or produce phlegm, is a common respiratory symptom.

Fatigue: Generalized weakness, tiredness, and lethargy, often accompanying other symptoms.

Dyspnea: Shortness of breath or difficulty breathing, indicating compromised respiratory function.

Breathlessness: Difficulty breathing, especially evident during physical exertion, suggesting potential respiratory complications.

Stomach Discomfort: Feeling unwell or queasy in the abdomen, often coupled with an inclination to vomit.

Emesis: Forceful expulsion of stomach contents through the mouth, possibly prompted by stomach discomfort or other gastrointestinal issues.

Diarrhea: Frequent loose or watery bowel movements, which can occur in COVID-19 cases with gastrointestinal involvement.

DIAGNOSIS AND TREATMENT [33–36]

Diagnosis

Genetic Analysis

The primary diagnostic method for identifying COVID-19 entails genetic analysis, aiming to detect specific sequences of the SARS-CoV-2 virus. This can be performed using a variety of specimens, including nasopharyngeal swabs, oropharyngeal swabs, saliva, and bronchoalveolar lavage fluid.

Immunological Assays

Immunological assays, including enzyme-linked immunosorbent assays (ELISA) and lateral flow assays, detect the presence of specific antibodies against SARS-CoV-2, aiding in both diagnosis and surveillance of COVID-19. They are typically conducted by healthcare professionals and processed in laboratories.

Antigen Tests:

Antigen tests, sometimes referred to as rapid COVID-19 tests, detect specific proteins from the virus. While antigen tests provide quick results, they are less sensitive than PCR tests and may require confirmation with a PCR test, especially in asymptomatic individuals.

Viral Cultivation

Within laboratory environments, techniques for viral cultivation are utilized to isolate and cultivate the SARS-CoV-2 virus from samples obtained from patients, enabling subsequent research endeavors and the advancement of therapeutic strategies. These tests can help identify past infections but are not typically used for diagnosing acute cases.

Treatment

Symptomatic Management

Treatment for COVID-19 primarily involves managing symptoms. This could involve prioritizing adequate rest, maintaining hydration levels, and employing over-the-counter remedies to alleviate symptoms like fever, coughing, and bodily discomfort.

Oxygen Therapy

Patients with severe respiratory symptoms may require supplemental oxygen therapy to maintain adequate oxygen levels in the blood. This can be administered through nasal prongs, masks, or mechanical ventilation in severe cases.

Immunomodulatory Therapies

Immunomodulatory agents like tocilizumab and baricitinib are being investigated for their potential to regulate the immune response in COVID-19 patients, potentially reducing inflammation and preventing cytokine storm.

Host-Directed Therapies:

Host-directed therapies focus on targeting host factors essential for viral replication, such as protease inhibitors and interferons. These treatments aim to disrupt viral propagation within host cells, limiting disease progression.

Combination Therapies

Combination therapies involving a blend of antiviral drugs, immunomodulators, and monoclonal antibodies are being explored to maximize treatment efficacy and address potential viral resistance. These synergistic approaches offer promise in combating COVID-19 from multiple angles.

Steroids

Corticosteroids, such as dexamethasone, may be prescribed for patients with severe COVID-19 to reduce inflammation and improve clinical outcomes.

Supportive Care

In addition to specific antiviral treatments, patients with COVID-19 may require supportive care, including fluid management, nutritional support, and monitoring for complications such as secondary infections and organ dysfunction.

CONCLUSION [37, 38]

In the unfolding narrative of the COVID-19 pandemic, the emergence of mutated strains underscores the relentless adaptability of the virus. With each mutation potentially heightening its infectiousness and severity, the imperative for stringent preventive measures remains paramount. Social distancing, diligent hand hygiene, and universal mask-wearing persist as our stalwart defenses against viral transmission. Yet, in the absence of a definitive cure, the pursuit of effective treatments persists. Antiviral agents like Remdesivir, Ritonavir, Chloroquine, and Hydroxy-Chloroquine, while undergoing rigorous clinical evaluation, offer glimpses of promise in mitigating the impact of COVID-19. These ongoing trials, coupled with a deeper understanding of viral mutations, hold the potential to unveil novel treatment modalities and therapeutic avenues. Amidst the global race to contain and combat the virus, the imperative for robust research and surveillance cannot be overstated. The relentless scrutiny of viral variants, coupled with proactive measures to curb their proliferation, represents our collective endeavor to avert future pandemics. As we navigate the ever-evolving saga of COVID-19, vigilance, resilience, and scientific innovation stand as our steadfast allies in confronting this formidable adversary and safeguarding global health.

REFERENCES

1. Liu YC, Kuo RL, Shih SR. COVID-19: The first documented coronavirus pandemic in history. Biomedical journal. 2020 Aug 1;43(4):328-33.
2. Khan M, Adil SF, Alkhathlan HZ, Tahir MN, Saif S, Khan M, Khan ST. COVID-19: a global challenge with old history, epidemiology and progress so far. Molecules. 2020 Dec 23;26(1):39.

3. Pan L, Wang J, Wang X, Ji JS, Ye D, Shen J, Li L, Liu H, Zhang L, Shi X, Wang L. Prevention and control of coronavirus disease 2019 (COVID-19) in public places. Environmental Pollution. 2022 Jan 1;292:118273.
4. He X, He C, Hong W, Zhang K, Wei X. The challenges of COVID-19 Delta variant: prevention and vaccine development. MedComm. 2021 Dec;2(4):846-54.
5. Hadj Hassine I. Covid-19 vaccines and variants of concern: a review. Reviews in medical virology. 2022 Jul;32(4):e2313.
6. Plante JA, Mitchell BM, Plante KS, Debbink K, Weaver SC, Menachery VD. The variant gambit: COVID-19's next move. Cell host & microbe. 2021 Apr 14;29(4):508-15.
7. Sohrabi C, Alsafi Z, O'neill N, Khan M, Kerwan A, Al-Jabir A, Iosifidis C, Agha R. World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). International journal of surgery. 2020 Apr 1;76:71-6.
8. Weiss SR, Navas-Martin S. Coronavirus pathogenesis and the emerging pathogen severe acute respiratory syndrome coronavirus. Microbiology and molecular biology reviews. 2005 Dec;69(4):635-64.
9. Rajnik M, Cascella M, Cuomo A, Dulebohn SC, Di Napoli R. Features, evaluation, and treatment of coronavirus (COVID-19). Uniformed Services University Of The Health Sciences. 2021 Mar 1.
10. Chang L, Yan Y, Wang L. Coronavirus disease 2019: coronaviruses and blood safety. Transfusion medicine reviews. 2020 Apr 1;34(2):75-80.
11. Sohrabi C, Alsafi Z, O'neill N, Khan M, Kerwan A, Al-Jabir A, Iosifidis C, Agha R. World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). International journal of surgery. 2020 Apr 1;76:71-6.
12. Zhou D, Zhang P, Bao C, Zhang Y, Zhu N. Emerging understanding of etiology and epidemiology of the novel coronavirus (COVID-19) infection in Wuhan, China.
13. Ganesh A. Epidemiology of Covid–19: An epidemic into a pandemic. Journal of Dental Research and Dental Prospects. 2022;1(01).
14. Khan M, Adil SF, Alkhathlan HZ, Tahir MN, Saif S, Khan M, Khan ST. COVID-19: a global challenge with old history, epidemiology and progress so far. Molecules. 2020 Dec 23;26(1):39.
15. Nkwoemeka NE, Okwelogu IS, Chiedozie AP. A scoping review on epidemiology, etiology, transmission, clinical presentation, treatment and management of Coronavirus Disease (COVID-19). European journal of biology and medical science research. 2020 Apr;8(2):45-54.
16. Cascella M, Rajnik M, Aleem A, Dulebohn SC, Di Napoli R. Features, evaluation, and treatment of coronavirus (COVID-19). Statpearls [internet]. 2023 Aug 18.
17. Yavari M, Sanei M, Avakian A. Pathophysiology of Covid-19. Int. Jr. Infect Dis & Epidemlgy. 2022;3(2):40-3.
18. Ornell F, Moura HF, Scherer JN, Pechansky F, Kessler FH, von Diemen L. The COVID-19 pandemic and its impact on substance use: Implications for prevention and treatment. Psychiatry research. 2020 Jul 1;289:113096.
19. Jamil S, Mark N, Carlos G, Cruz CS, Gross JE, Pasnick S. Diagnosis and management of COVID-19 disease. American journal of respiratory and critical care medicine. 2020 May 15;201(10):P19-20.
20. Bhimraj A, Morgan RL, Shumaker AH, Baden L, Chi-Chung Cheng V, Edwards KM, Gandhi RT, Gallagher JC, Muller WJ, O'Horo JC, Shoham S. Lessons learned from coronavirus disease 2019 (COVID-19) therapies: critical perspectives from the infectious diseases society of America (IDSA) COVID-19 treatment guideline panel. Clinical Infectious Diseases. 2022 May 1;74(9):1691-5.
21. Gottlieb RL, Vaca CE, Paredes R, Mera J, Webb BJ, Perez G, Oguchi G, Ryan P, Nielsen BU, Brown M, Hidalgo A. Early remdesivir to prevent progression to severe Covid-19 in outpatients. New England Journal of Medicine. 2022 Jan 27;386(4):305-15.
22. Shumaker AH, Bhimraj A. Pharmacologic treatment and management of Coronavirus Disease 2019. Infectious Disease Clinics. 2022 Jun 1;36(2):349-64..
23. Schwartz DA, Avvad-Portari E, Babál P, Baldewijns M, Blomberg M, Bouachba A, Camacho J, Collardeau-Frachon S, Colson A, Dehaene I, Ferreres JC. Placental tissue destruction and insufficiency from COVID-19 causes stillbirth and neonatal death from hypoxic-ischemic injury: a

study of 68 cases with SARS-CoV-2 placentitis from 12 countries. Archives of pathology & laboratory medicine. 2022 Jun 1;146(6):660-76.

24. Balwan WK, Saba N. Tracking the Coronavirus: Variant of Concern (VOC). Shodhsamhita, VIII (12-VI). 2022.
25. Ong SW, Chiew CJ, Ang LW, Mak TM, Cui L, Toh MP, Lim YD, Lee PH, Lee TH, Chia PY, Maurer-Stroh S. Clinical and virological features of SARS-CoV-2 variants of concern: a retrospective cohort study comparing B. 1.1. 7 (Alpha), B. 1.315 (Beta), and B. 1.617. 2 (Delta).
26. Jungnick S, Hobmaier B, Mautner L, Hoyos M, Haase M, Baiker A, Lahne H, Eberle U, Wimmer C, Hepner S, Sprenger A. In vitro rapid antigen test performance with the SARS-CoV-2 variants of concern B. 1.1. 7 (Alpha), B. 1.351 (Beta), P. 1 (Gamma), and B. 1.617. 2 (Delta). Microorganisms. 2021 Sep 16;9(9):1967.
27. Wise J. Covid-19: New coronavirus variant is identified in UK.
28. Wibmer CK, Ayres F, Hermanus T, Madzivhandila M, Kgagudi P, Oosthuysen B, Lambson BE, De Oliveira T, Vermeulen M, Van der Berg K, Rossouw T. SARS-CoV-2 501Y. V2 escapes neutralization by South African COVID-19 donor plasma. Nature medicine. 2021 Apr;27(4): 622-5.
29. Davies NG, Abbott S, Barnard RC, Jarvis CI, Kucharski AJ, Munday JD, Pearson CA, Russell TW, Tully DC, Washburne AD, Wenseleers T. Estimated transmissibility and impact of SARS-CoV-2 lineage B. 1.1. 7 in England. Science. 2021 Apr 9;372(6538):eabg3055.
30. Lythgoe KA, Hall M, Ferretti L, de Cesare M, MacIntyre-Cockett G, Trebes A, Andersson M, Otecko N, Wise EL, Moore N, Lynch J. SARS-CoV-2 within-host diversity and transmission. Science. 2021 Apr 16;372(6539):eabg0821.
31. O'Toole Á, Hill V, Pybus OG, Watts A, Bogoch II, Khan K, Messina JP, COVID T, Network BU, Tegally H, Lessells RR. Tracking the international spread of SARS-CoV-2 lineages B. 1.1. 7 and B. 1.351/501Y-V2 with grinch. Wellcome Open Research. 2021;6.
32. Corum J, Zimmer C. Inside the B. 1.1. 7 Coronavirus Variant. The New York Times. 2021 Jan 18;18.
33. da Silva JF, Esteves RJ, Siza C, Soares EP, Ramos TC, Campelo EC, da Costa CF, de Alencar LC, Cavalcante RP, Florêncio CR, Mattos TP. Cluster of SARS-coV-2 gamma variant infections, parintins, Brazil, march 2021. Emerging infectious diseases. 2022 Jan;28(1):262.
34. Naveca FG, Nascimento V, Souza V, Corado AD, Nascimento F, Silva G, Mejía MC, Brandão MJ, Costa Á, Duarte D, Pessoa K. Spread of Gamma (P. 1) sub-lineages carrying Spike mutations close to the furin cleavage site and deletions in the N-terminal domain drives ongoing transmission of SARS-CoV-2 in Amazonas, Brazil. Microbiology Spectrum. 2022 Feb 23;10(1):e02366-21.
35. Papanikolaou V, Chrysovergis A, Ragos V, Tsiambas E, Katsinis S, Manoli A, Papouliakos S, Roukas D, Mastronikolis S, Peschos D, Batistatou A. From delta to Omicron: S1-RBD/S2 mutation/deletion equilibrium in SARS-CoV-2 defined variants. Gene. 2022 Mar 10;814:146134.
36. Del Rio C, Malani PN, Omer SB. Confronting the delta variant of SARS-CoV-2, summer 2021. Jama. 2021 Sep 21;326(11):1001-2.
37. Hageman JR, Alcocer Alkureishi L. Omicron: A Variant of Concern?. Pediatric Annals. 2022 Jan 1;51(1):e1-.
38. Tian D, Sun Y, Xu H, Ye Q. The emergence and epidemic characteristics of the highly mutated SARS-CoV-2 Omicron variant. Journal of medical virology. 2022 Jun;94(6):2376-83.