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Sars Cov-2 Variants – Meta – Analysis

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Abstract

Background of the Study: SARS-COV-2 refers to severe acute respiratory syndrome coronavirus 2. It belongs to family Coronaviridae, subfamily Coronavirinae and β genera. Coronaviruses are crown-shaped particles with spikes protruding from their surface. The SARS-CoV-2 genome is a 29.9 kb positive-sense single-stranded RNA molecule containing 14 ORFs encoding four structural and 16 non-structural ones. Proteins (nsp 1-16). Structural proteins include spike protein (S), envelope protein (E), membrane protein (M) and nucleoprotein (N). Non-structural proteins are involved in viral RNA replication and gene expression, forming an RNA synthesis complex in which nsp12 functions as an RNA-dependent RNA polymerase. Unlike other RNA viruses, coronaviruses have RNA proofreading machinery to correct genetic mutations due to nsp14 3′-5′ exonuclease activity. However, it has been estimated that SARS-CoV-2 undergoes 3 × 10–6 mutations per nucleotide per replication cycle

Aims & Objective: The aim of this study is to review the spread of current variants of SARS-CoV-viruses. 1. To look at the disease profile of different variants of SARS CoV-2 Virus. 2. To look at the current variants of SARS CoV-2 Virus prevalent in different parts of the world.

Methods: A Meta analysis method is used to study about corona virus and its variants. Data was collected from various publications in indexed journals, recent editions of textbooks, website of CDC, NCDC, WHO. Follow by Prisma, at first stage of the search, 280 articles were found, and after reviewing the titles of the articles, 120 duplicate and overlapping articles were deleted and 160 articles remained. In total, 60 articles were removed due to noncompliance with the criteria, the extract of 40 potentially related articles were reviewed, and 50 articles were excluded due to lack of access to the full text articles. Finally, 10 appropriate papers were selected to enter the meta-analysis stage.

Results: SARS-CoV-2 spike mutations can increase transmissibility and immune escape, while some recurrent mutations may reduce disease severity. It also finds limited cross-protection across related coronaviruses, evidence of recombination in SARS-CoV, and stronger ACE2 binding that may help explain faster spread. SARS-CoV was detected in 329 of 436 patients, or 75%, and human metapneumovirus in 41 of 335 patients, or 12%; other respiratory pathogens were rare. The macaque experiment further showed all 4 infected macaques shed virus, and 3 of 4 developed lung damage similar to human SARS.

Conclusion: COVID-19, a novel coronavirus first detected in Wuhan in December 2019, caused a global pandemic and prompted widespread public-health measures and vaccine development. The outbreak reduced active cases through vaccination but exposed major gaps in pandemic preparedness, prompting calls for stronger long-term readiness.

Keywords: SARS, Cov-2, Variants

INTRODUCTION

SARS-COV-2 refers to severe acute respiratory syndrome coronavirus 2. It belongs to family Coronaviridae, subfamily Coronavirinae and β genera. Coronaviruses are crown-shaped particles with spikes protruding from their surface. The SARS-CoV-2 genome is a 29.9 kb positive-sense single-stranded RNA molecule containing 14 ORFs encoding four structural and 16 non-structural ones. Proteins (nsp 1-16). Structural proteins include spike protein (S), envelope protein (E), membrane protein (M) and nucleoprotein (N). Non-structural proteins are involved in viral RNA replication and gene expression, forming an RNA synthesis complex in which nsp12 functions as an RNA-dependent RNA polymerase. Unlike other RNA viruses, coronaviruses have RNA proofreading machinery to correct genetic mutations due to nsp14 3′-5′ exonuclease activity. However, it has been estimated that SARS-CoV-2 undergoes 3 × 10–6 mutations per nucleotide per replication cycle.

RNA viruses divide into five branches. Certain groups in a particular branch may be related and/or share functionality with viruses classified in a different branch. Branch 1 contains the leviviruses and their eukaryotic relatives (e.g., mitoviruses, narnaviruses, ourmiaviruses); Branch 2 represents several families of +RNA viruses (from eukaryotes) (e.g.p. the orders Picornavirales and Nidovirales and the families Caliciviridae, Potyviridae, Astroviridae and Solemoviridae) and various dsRNA viruses (e.g. partitiviruses and picobirnaviruses); In branch 3 there are certain +RNA viruses such as the alphavirus and offlavivirus supergroups, the nodaviruses, tombusviruses and many new and small groups; In branch 4 are dsRNA viruses such as cystoviruses, reoviruses and totiviruses; Branch 5 consists of RNA viruses. The main differences between SARS-CoV and MERS-CoV lie in the sequence of the SARS-CoV-2-S gene, three short insertions in the N-terminal domain, and changes in four out of five key residues in the receptor binding motif. (11) Genome organizations and gene expression are similar in all coronaviruses. ORF1a/b, located at the 5′ end, encodes 16 nonstructural proteins (NSPs) (named NSP1–NSP16); other ORFs at the 3′ end code for structural proteins, including S, envelope (E), membrane (M), and nucleocapsid (N) proteins.

AIMS & OBJECTIVES:

The aim of this study is to review the spread of current variants of SARS-CoV-2 viruses.

1. To look at the disease profile of different variants of SARS CoV-2 Virus.
2. To look at the current variants of SARS CoV-2 Virus prevalent in different parts of the world.

METHODS

TYPE OF STUDY: - A Meta analysis of corona virus and its variants related articles published in various indexed journals.

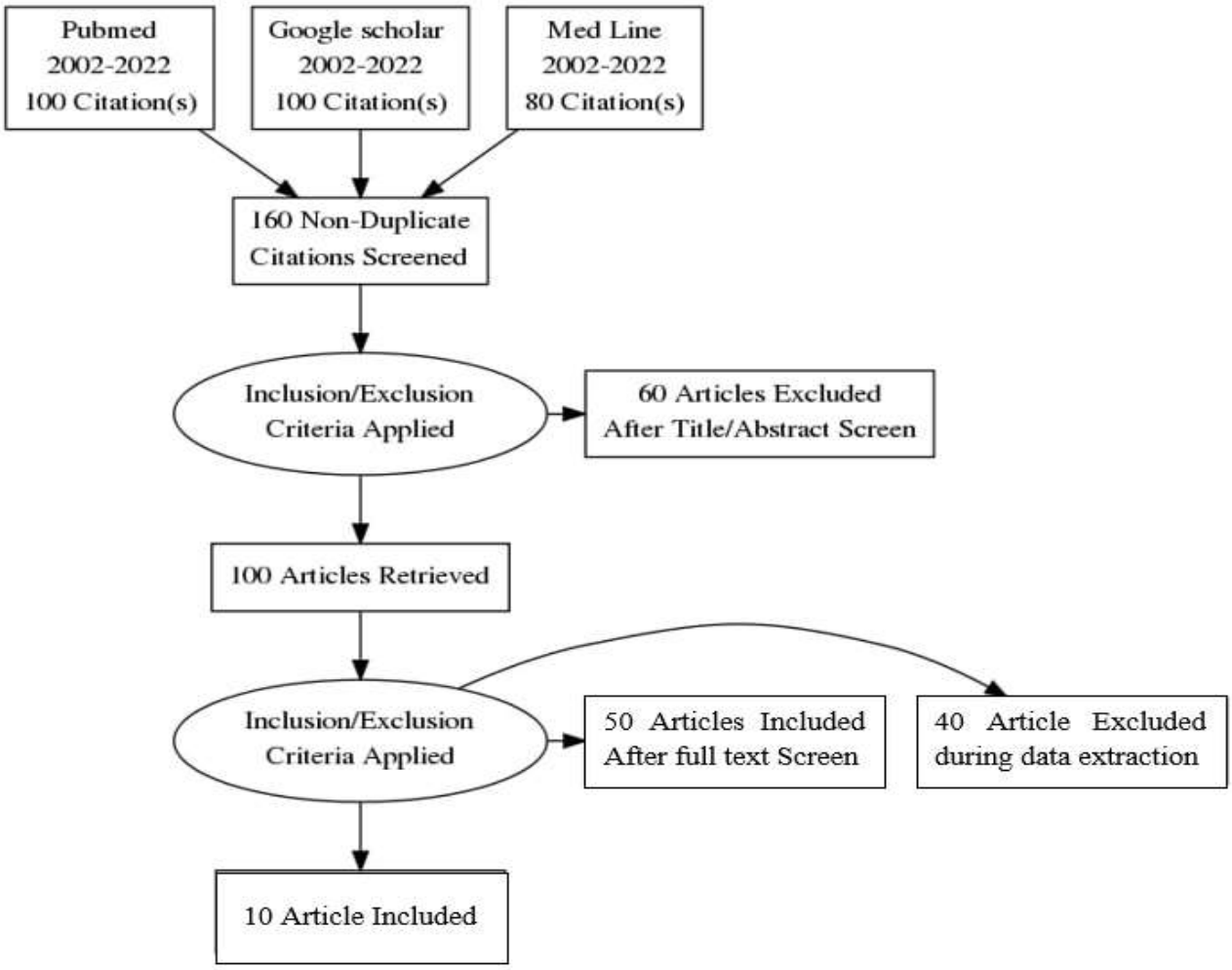
DATA TYPE: - Data for this meta-analysis will be collected from following sources.

- Data from various publications in indexed journals.

- Data from recent editions of textbooks.
- Data from website of CDC, NCDC, WHO.

TIME FRAME: - All the studies in the indexed journal from year 2003 to 2022

SEARCH STRATEGY: - This meta-analysis followed the PRISMA guidelines. Articles were searched on Pubmed, Google scholar, Web of Science, Science Direct and scopus sing term related to covid, variants, MERS, pandemic, SARS 2003. Boolean AND, OR, and NOT were used.



RESULTS

Table No. 1 Effects of SARS-CoV-2 Variants in different Countries/Cities

S.No	AUTHOR	YEAR	COUNTARY/CITY	STUDY FINDING
01.	Jalen Sin	2022	Canada	Mutations in the spike protein of SARS-CoV-2 variants confer increased transmissibility and resistance to antibody,mediated neutralisation. Recurrent attenuating mutations such as P323L, L37F, G251V, and

	gh et al.,	0-2021		Q27stop have also been identified and are thought to reduce disease severity. Attenuating mutations suggest that SARSCoV2 is evolving to be less pathogenic in humans.
02.	Jie Cui et al.,	2919	China, USA	Anti-SARS CoV strategies only Worked against WIV1, not SHC014. Furthermore, n HKU3 related strains with a much wider geographical distribution and RBD truncations. Similarly, anti-S antibodies against MERS, CoV were ineffective in protecting against infection with a pseudovirus containing the bat MERSr-CoV S.
03.	Shuo Su et al.,	2016	China, USA	SARSCoV may have recombinated with alpha- and gamma CoV lineages. Based on the Sequence of the SARS CoV- TOR2 strain, many specific breakpoints and a large number of smaller recombinant regions have been identified in the RNAdependent RNA polymerase (RDRP, nsp12 gene) at the following locations: nucleotides 13 392-13 610, 15 259-15 342, and 15 974-16 108.
04.	Bin Chen et al.,	2020	China	SARS-CoV-2 has a stronger and faster ability to spread than many known viruses. The affinity of the human ACE2 protein for the RBD of the new coronavirus is 10 to 20 times higher than that of the SARS virus, which probably explains why SARS-CoV-2 spreads faster. For COVID-19, the candidates mainly include drugs that target protein S, nonstructural proteins (3CLpro, PLpro, Helicase, and RdRp) and blockers of viral RNA synthesis
05.	Lia van der Hoek et al.,	2007	Netherlands	For COVID-19, the candidates mainly include drugs that target protein S, nonstructural proteins (3CLpro, PLpro, Helicase, and RdRp), and blockers of viral RNA synthesis. Only HCoV-NL63 has been linked to a specific respiratory disease in children, namely croup.
06.	Sandro M. Hirabara et al.,	2022	Canada	It addressed the following critical issues related to VOCs: a) characteristics of SARS-CoV-2 VOCs with mutations in the S gene; b) possible evasion of variants of neutralizing antibodies generated by vaccination, previous infection or immunotherapies; c) potential risk of new pandemic waves triggered by the variants worldwide; and d) prospects for future studies and actions aimed at preventing or reducing the impact of new variants during the current COVID-19 pandemic.
07.	William T. Harve	2021	UK	We summarize the literature on mutations in the spike protein of SARS-CoV-2, the primary antigen, focus on their impact on antigenicity and contextualize them in protein structure, and discuss them in the context of observed mutation frequencies in global sequence data sets.

	y et al.,			
08.	Thomas G. Ksiazek et al.,	2003	England	A novel coronavirus was isolated in patients who met the SARS case definition. Cytopathologic features were observed in Vero E6 cells inoculated with a throat swab specimen. Electron microscopic examination revealed ultrastructural features characteristic of coronaviruses. Immunohistochemical and immunofluorescence staining showed reactivity with group I coronavirus polyclonal antibodies. Consensus coronavirus primers designed to amplify a fragment of the polymerase gene by reverse transcription polymerase chain reaction (RT-PCR) were used to obtain a sequence that uniquely identifies the isolate as a single coronavirus only distantly related to previously sequenced coronaviruses.
09.	David S. Hui, MD et al.,	2016	Hongkong, China	Bats appear to be the common natural source of both SARS-CoV and MERS-CoV. The clinical features are similar, but MERS progresses to respiratory failure much faster than SARS. Although the estimated pandemic potential of MERS-CoV is lower than that of SARS-CoV, the mortality rate from MERS is much higher and is likely related to older age and comorbid conditions in sporadic cases. It is also important to be alert to the emergence and any mutation of other groups of circulating SARS-like CoVs in bat populations that could pose a threat to human health.
10.	Thijs Kuiken et al.,	2003	Hong Kong	SARS-CoV infection was diagnosed in 329 (75%) of 436 patients who met the SARS case definition; human metapneumovirus was diagnosed in 41 (12%) of 335, and other respiratory pathogens were diagnosed only sporadically. SARS-CoV was therefore the most likely causative agent of SARS. All four SARS-CoV-infected macaques shed SARS-CoV through their nose, mouth and throat two days after infection. Three of four macaques developed diffuse alveolar damage similar to that seen in SARS patients, and were characterized by epithelial necrosis, serosanguineous exudate, hyaline membrane formation, type 2 pneumocyte hyperplasia, and the presence of syncytia. SARS-CoV was detected in pneumonic areas by virus isolation and RT-PCR and localized to alveolar epithelial cells and syncytia by immunohistochemistry and transmission electron microscopy.

DISCUSSION

The global COVID-19 pandemic has rapidly evolved from a health crisis to an economic crisis, affecting the entire world population but disproportionately affecting certain groups. It has rapidly reduced and widened pervasive inequalities, with immediate and lasting implications for the RCRC's humanitarian mandate and principled advocacy. Since the rapid spread of the SARS-CoV-2 pandemic, many variants have emerged, including alpha, beta, gamma, delta. However, the conclusion regarding disease severity of these virus variants is more consistent. Accordingly, we look for studies in the relevant area and record their clinical data. A meta-analysis was used to combine information from different studies. Comparing the results of different studies, we found that the alpha variant had a higher risk of disease severity than the wild-type viruses. The alpha variants showed a significantly higher risk of hospitalization and ICU admissions but a lower risk of mortality than the wild-type. Global outbreak with more than 8,000 patients

in more than 30 countries and a mortality rate of 9.2%. The disease is an infectious disease dominated by SARS and is etiologically related to the novel coronavirus. However, SARS is a lower respiratory disease and upper respiratory symptoms are rare and mild. The result suggests that the pulmonary fibrosis seen in these fatal cases may be related to SARS rather than pre-existing lung injury. The second year of covid-19 pandemic has been admitted by variants of concern SARS CoV-2 lineages that has driven resurgent waves of the disease often more severe than the earlier waves. We find that variants with partial immune escape do not. This research advanced our understanding of the danger posed by different variants. Both WHO and US CENTRE of disease control and pandemic designate certain strain as VOC.

CONCLUSION

There are hundreds of coronaviruses, most of which circulate in animals. Only seven of these viruses infect humans, and four of them cause cold symptoms. But three times in the past 20 years, a coronavirus has jumped from animals to humans, causing serious illnesses. The world and China have seen a rapid spread of COVID-19, a novel and occasionally fatal respiratory disease that is thought to have started in a live animal market in China. In December 2019, Wuhan, China, reported finding the novel coronavirus for the first time. In China, tens of thousands of individuals contracted the disease, and it was widely contagious over most of that nation. New coronavirus infections were initially linked to travel from Wuhan, but now the virus has taken hold in 177 countries and territories around the world in a fast-spreading pandemic. Public health officials in the United States and around the world are working to contain the spread of the virus through public health measures such as social distancing, contact tracing, testing, quarantines and travel restrictions. Scientists are working to find drugs to treat the disease and to develop a vaccine. On January 30, the World Health Organization declared the outbreak of the new coronavirus a “public health emergency of international concern”. On March 11, 2020, the World Health Organization declared the COVID-19 epidemic a pandemic following the continued spread of the disease outside of China. The bulk of the population has received one of the many anti-virus vaccines that are currently available. Globally, there are currently very few COVID cases that are active. Due to greater vaccination and immunization during the outbreak, the recovery percentage is significantly higher than it was the previous year. There have been demands for the world to be more ready for the upcoming pandemic in the wake of COVID19.The shortcomings of earlier attempts and the demand for a more comprehensive and long-lasting strategy to preparedness have been placed into stark relief by COVID-19. COVID-19 has highlighted the limitations of previous efforts and the need for a more ambitious and long-term approach to preparedness.

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REFERENCES

1. Su, S. et al. Epidemiology, genetic recombination, and pathogenesis of coronaviruses. Trends Microbiol. 24, 490–502 (2016).
2. Cheng A, Zhang W, Xie Y, Jiang W, Arnold E, Sarafanos SG et al (2005) Expression, purifcation, and

characterization of SARS coronavirus RNA polymerase. Virology 335(2):165–176
3. Ferron F, Subissi L, Silveira De Morais AT, Le NTT, Sevajol M, Gluais L et al (2018) Structural and molecular basis of mismatch correction and ribavirin excision from coronavirus RNA. Proc Natl Acad Sci 115(2):E162–E171
4. Sender R, Bar-On YM, Gleizer S, Bernshtein B, Flamholz A, Phillips R et al (2021) The total number and mass of SARSCoV-2 virions. Proc Natl Acad Sci 118:2
5. Conaviruses. Trends Microbiol. 24, 490–502 (2016). 2. Wolf, Y. I. et al. Origins and evolution of the global RNA virome. mBio 9, e02329- 18 (2018).
6. Kuhn, J. H. et al. Classify viruses—the gain is worth the pain. Nature 566, 318–320 (2019).
7. Van der Hoek, L. Human coronaviruses: what do they cause? Antivir. Ther. 12, 651–658 (2007).
8. Zhong, N. S. et al. Epidemiology and cause of severe acute respiratory syndrome (SARS) in Guangdong, People's Republic of China, in February, 2003. Lancet 362, 1353–1358 (2003).
9. Zaki, A. M. et al. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. N. Engl. J. Med. 367, 1814–1820 (2012)
10. Drexler, J. F., Corman, V. M. & Drosten, C. Ecology, evolution and classification of bat coronaviruses in the aftermath of SARS. Antivir. Res. 101, 45–56 (2014)
11. Zhou, P. et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 579, 270–273 (2020).
12. Ou, X. et al. Characterization of spike glycoprotein of SARS-CoV-2 on virus entry and its immune cross-reactivity with SARS-CoV. Nat. Commun. 11, 1620 (2020)
13. Graham RL, Baric RS. Recombination, reservoirs, and the modular spike: mechanisms of coronavirus cross-species transmission. J Virol. 2010;84(7):3134-3146.
14. Su S, Wong G, Shi W, et al. Epidemiology, genetic recombination, and pathogenesis of coronaviruses. Trends Microbiol. 2016;24(6): 490-502.
15. Lee N, Hui D, Wu A, et al. A major outbreak of severe acute respiratory syndrome in Hong Kong. N Engl J Med. 2003;348(20): 1986-1994.
16. Graham RL, Baric RS. Recombination, reservoirs, and the modular spike: mechanisms of coronavirus cross-species transmission. J Virol. 2010;84(7):3134-3146.
17. Su S, Wong G, Shi W, et al. Epidemiology, genetic recombination, and pathogenesis of coronaviruses. Trends Microbiol. 2016;24(6): 490-502.
18. Lee N, Hui D, Wu A, et al. A major outbreak of severe acute respiratory syndrome in Hong Kong. N Engl J Med. 2003;348(20): 1986-1994.
19. Li W, Shi Z, Yu M, et al. Bats are natural reservoirs of SARS like coronavirus. Science 2005;310:676-679.
20. Lau SK, Woo PC, Lj K, et al. Severe acute respiratory syndrome coronavirus-like virus in china horseshoe bats. Proc Natl Acad Sci USA 2005;102:14040-14045.
21. Tsang KW, Ho PL, Ooi GC, et al. A cluster of cases of severe acute respiratory syndrome in Hong Kong. N Engl J Med. 2003;348(20): 1977-1985.
22. Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus AD, Fouchier RA. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. N Engl J Med. 2012;367(19):1814-1820.
23. Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020; 579(7798):270-273.

24. Ye Q, Lu D, Shang S, et al. Crosstalk between coronavirus disease 2019 and cardiovascular disease and its treatment. ESC Heart Fail. 2020;7(6):3464-3472.
25. Han X, Ye Q. Kidney involvement in COVID-19 and its treatments. J Med Virol. 2021;93(3):1387-1395.
26. Tian D, Ye Q. Hepatic complications of COVID-19 and its treatment. J Med Virol. 2020;92(10):1818-1824.
27. Ye Q, Wang B. The mechanism and treatment of gastrointestinal symptoms in patients With COVID-19. Am J Physiol Gastrointestinal liver Physiol. 2020;319(2):G245-G252
28. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med. 2020. https://doi.org/10.1056/NEJMoa2001316.
29. CDC. 2019 Novel coronavirus, Wuhan, China. 2020. https://www.cdc.gov/ coronavirus/2019-nCoV/summary.html. Accessed 1 Feb 2020.
30. Zhou P, Yang XL, Wang, XG, Hu B, Zhang L, Zhang W, et al. Discovery of a novel coronavirus associated with the recent pneumonia outbreak in humans and its potential bat origin. bioRxiv. 2020; doi: https://doi.org/10. 1101/2020.01.22.914952