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A Comparative Study on Covid-19 Corona Virus Variants: Alpha, Beta, Gamma, Delta: Review Paper

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Abstract: ***Here in this review paper we basically discuss about the two covid-19 originate hypothesis, one is zoonotic spill-over hypothesis and another is lab leak hypothesis. This lab leak hypothesis recently on news due to substantial evidence found by USA. There are other lab leak phenomenon happen in past like 1977 Russian flu, most critics believe in that time it was also a lab escape phenomenon. Our review paper is also focused on various covid variants, till now and there comparative study. Here in this paper, we attempt to find cause of the COVID origination, and also represent a comparative study of various SARS-COV-2 variants. We also discussed how it seems in near future whether pandemic will end soon or we have to adopt to live with the virus?***

Keywords: Zoonotic Spillover hypothesis, Lab leak hypothesis, Alpha variant, Beta variant, Gamma variant, Delta variant, comparative study, pandemic, Covid-19, SARS-COV-2, Wuhan Institute of Virology, Wuhan Sea food market

I. INTRODUCTION

Corona virus is a group of viruses from the family Coronaviridae and order Nidovirales, which infers to enveloped, positive-strand RNA viruses which infect vertebrates and invertebrates. Coronaviruses constitute the subfamily Orthocoronavirinae, that can cause mild to lethal respiratory tract infections in birds and mammals. The genome size of corona virus is as large as 27-32kbp. The virus is characterized with Spike(S) protein which gives a crown-like appearance (as in electron micrographs) due to the presence of spike like protrusions and thus gaining the name, coronavirus.

The corona virus in animals is as old as in the 1920s, when the chicken had an acute respiratory infection, reported in North America (the virus was then called IBV). In 1940, two new variants of corona virus was reported to cause murine encephalitis (JMV) and hepatitis (MHV) in mice. No human infection cases were reported until 1960s, when the corona virus was responsible for a substantial proportion of upper respiratory tract infections in children. In 1961-1962, two unique human corona viruses were collected and cultivated, viz, B814 and 229E, which caused common cold like symptoms and got inactivated by ether. An severe acute respiratory syndrome (SARS) outbreak emerged in China along with 4 other countries, in 2003, during which the SARS-COV (Severe Acute Respiratory Syndrome- associated coronavirus) was first identified. Other human corona virus identified till date includes, HCoV NL63 in 2003, HCoV HKU1 in 2004, MERS-CoV in 2012, and SARS-CoV-2 in 2019.

II. COVID-19 PANDEMIC: THE ORIGIN

The novel coronavirus identified in 2019, that engulfed the human population worldwide causing the COVID-19 pandemic is officially known as SARS-COV2. This is the third serious Coronavirus outbreak in less than 20 years, after SARS in 2002-2004 and MERS in 2012-2013. Unlike the other human strains of Coronavirus, the deadly SARS-COV2 has varying degrees of severity, from flu-like symptoms to death. This pandemic, started in late 2019 and still continuing 2021 has caused deaths in millions globally and with severe after effects even after recovery, but the questions related to the origin of the SARS-COV2 and its early transmission event from animal to human remains unanswered. Some hypothetical theories are being considered as the source of this SARS-COV2 outbreak.

The most commonly believed hypothesis suggests that the SARS-COV2 is a zoonotic virus, a virus that is transmitted between animals and people. On the basis of the sequence homology of Cov-19 have been isolated from these animals and the viral nucleic acids of the virus isolated from SARS-CoV-2 infected patients bats, snakes and pangolins have been cited as potential carriers of the disease. The outbreak began in Wuhan city, in the Hubei province of China and the first COVID-19 cases were reported in December 2019. It is initially suspected that the virus came from wild animals sold in the Huanan Seafood Market. Although the transmission of coronaviruses from animals to humans is rare, but studies suggest that it might have spread from bats or the pangolins that were being sold in the market illegally. The new coronavirus had spread rapidly in many parts of the world and on March 11, 2020, the World Health Organization (WHO) declared COVID-19 a pandemic. However, it still remains unclear exactly how the virus first spread to humans from animals.

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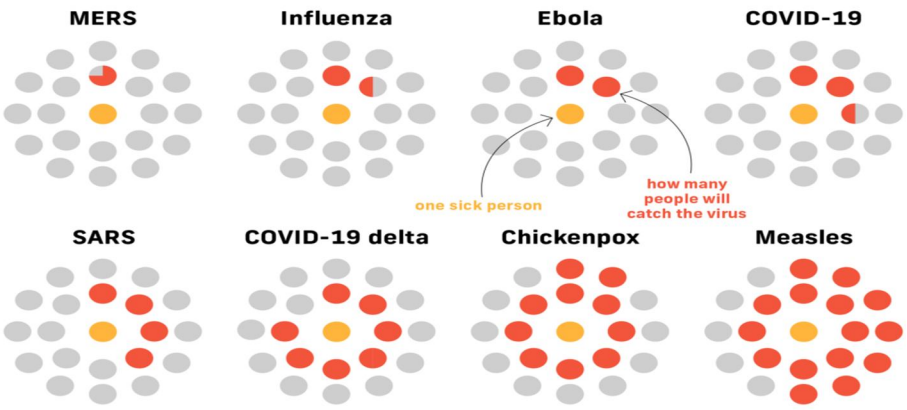
Another hypothesis on the origin of the COVID-19, proposes the lab leak theory, which suggests that the virus has been accidently escaped from the Wuhan Institute of Virology (WIV). Researchers in WIV were known to work with such contagious viruses and a purposeful genetic modification of a coronavirus that gave rise to a deadly, more infectious and human-transmissible variant. This type of genetic modification is called gain-of-function, as new traits are acquired. The newly developed virus had infected one of the researchers who went to the Wuhan market a week before the outbreak and leaked among the common people in the market. The SARS-COV2 thus escaped the lab and soon declared as "variant of concern" by WHO.

III. SARS-COV2 VARIANTS: ALL YOU NEED TO KNOW ABOUT THE DIFFERENT VARIANTS

All the viruses, including the SARS-COV2 undergo mutations repeatedly making them weaker or even or more dangerous. The SARS-COV2, in this case is continuously evolving and being more transmissible with each mutation, posing a threat to mankind. Four variants of SARS-COV2 have been declared as "variant of concern" by the WHO so far, which cause COVID19.



CDC (MERS), The Lancet (SARS, measles), Univ. of Mich (Covid-19, ebola), JHU (chickenpox)
NPR/Tom Wenseleers(COVID-19 delta)

A. The Alpha Variant

Alpha Variant or the lineage B.1.1.7 is the first SARS-COV2 variant , that was identified in November, 2020 in the United Kingdom, which began to spread rapidly by mid-December. The Alpha variant can be substitute by 23 mutations: 14 non-synonymous mutations, 3 deletions, and 6 synonymous mutations. This VOC-202012/01 (Variant of Concern-202012/01) had been detected with mutations targeting the spike protein at three independent genomic loci that are highly predictive of B.1.1.7 - HV69/70del, Y144del, and A570D.

As a consequence of the mutation, the transmissibility of the virus increased by about 50% (according to CDC) as compared to the wild strain making it more infectious and with severe effects.

In February, 2021, a E484K mutation, which is also present in Beta and Gamma variants, has been reported in UK.

There is no impact on susceptibility to EUA monoclonal antibody treatments with minimal impact on neutralization by convalescent and post-vaccination sera.

B. The Beta Variant

Beta variant (B.1.351, B.1.351.2, B.1.351.3) of SARS-COV2 was first reported in South Africa, in December,2020. Like in Alpha variant, there are three mutations of particular interest in the spike region of the B.1.351 genome: K417N, E484K , N501Y. These mutations acquired the virus with efficacy to attach to human cells more easily as compared to the previous variants. The two mutations; E484K , N501Y, occurred within the RBM of the receptor-binding domain (RBD). Apart from these there are five less concerned spike mutations are detected so far: L18F , D80A , D215G , R246I , A701.

A significantly reduced susceptibility to the combination of bamlanivimab and etesevimab monoclonal antibody treatment has been observed.

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C. The Gamma Variant

Gamma variant (P.1, P.1.1, P.1.2), another variant causing COVID 19, was detected in NIID, Japan in January, 2021. This variant has 17 amino acid substitutions, out of which ten are in the spike protein. These three spike protein mutations are of concern: N501Y, E484K and K417T. The P.1 also has two distinct sub-variants: 28-AM-1 and 28-AM-2, both of which carry the K417T, E484K, N501Y mutations. According to a research article in Science Journal, P.1 infected people have a greater chance of transmissibility and death than B.1.1.28 infected ones. Gamma variant caused widespread infection in early 2021 and is currently considered as a "variant of concern". Significantly reduced susceptibility has been observed to the combination of bamlanivimab and etesevimab monoclonal antibody treatment, but in the other hand EUA monoclonal antibody treatments are available.

D. The Delta Variant

SARS-COV2 Delta Variant (B.1.617.2, AY.1, AY.2, AY.3, AY.4, AY.5, AY.6, AY.7, AY.8, AY.9, AY.10, AY.11, AY.12) or Indian variant was first detected in India in late 2020. It was declared as a "variant of concern" in June,2021 and is the cause for Second Wave of India and Third Wave in UK and South Africa. By July,2021 an increase in number of cases have been noticed in Asia, the United States, and Australia. The B.1.617.2 genome has 13 mutations, four of them in the spike protein and of particular concern: D614G, T478K , L452R , P681R.

The D614G mutation has made it highly transmissible. The Reproductive number(R0) for COVID 19 was about 1.5-3.5 on average which suggests the virus being highly infectious. The Delta variant is however even more infectious with an average R0 value of 7, that is, each infected person can infect seven more people. With such high R0 value the Delta variant of SARS-COV2 can be considered as contagious as chicken pox.

L452R mutation confers stronger affinity of the spike protein for the human ACE2 receptor making is easier to attach to human cells. It also provides the virus with decreased recognition capability in the human immune system. P681R can increase cell infectivity by cleaving the S precursor protein to the active S1/S2 configuration.

A potential reduction in neutralization by some EUA monoclonal antibody treatments and in neutralization by post-vaccination sera is noticed. Delta variant with K417N corresponds to lineages AY.1 and AY.2 and is commonly known as the "Delta plus" or "Nepal variant". This K417N mutation is also present in the Beta variant. According to reports, as of late July, 2021, the AY.3 variant accounted for approximately 15% of cases in the United States.

Apart from the four mentioned Variants Of Concern (VOC), there is a list of Variants of Interest (VOI) declared by the WHO:

- Eta
- Iota
- Kappa
- Lambda
- Zeta
- Theta
- Epsilon

WHO renames SARS-CoV-2 variants

From alpha to lambda

Variants of concern

WHO label		Lineage	First documented samples
α	Alpha	B.1.1.7	UK Sep. 2020
β	Beta	B.1.351	South Africa May 2020
γ	Gamma	P.1	Brazil Nov. 2020
δ	Delta	B.1.617.2	India Oct. 2020

Variants of interest

ε	Epsilon	B.1.427/ B.1.429	USA Mar. 2020
ζ	Zeta	P.2	Brazil Apr. 2020
η	Eta	B.1.525	*Multiple* Dec. 2020
θ	Theta	P.3	Philippines Jan. 2021
ι	Iota	B.1.526	USA Nov. 2020
κ	Kappa	B.1.617.1	India Oct. 2020
λ	Lambda	C.37	Peru Aug. 2020

Virus variants in Asia threaten the whole world.

IV. CONCLUSION

Period of confusion is natural as we learnt what waves of the alpha, bet, gamma, delta variant under the country's modest-at-best safety protocols look like, we have seen how swiftly the next wave can be expected one ends. People are tired of good behavior, they are exhausted of self abnegating to protect others whom they realize as refusing to protect themselves, even if that's not an accurate understanding of why people are yet to be vaccinated. The situation we are all in is extremely complicated but the best ways to keep yourself and others safe is following the govt. protocols.

Our intensive study found out that there were mainly four variant Alpha variant, Beta variant, gamma and Delta variant. Among them delta variant was the deadliest of all. It has a R0 value of around 7. Our observation also found out Vaccine may reduce the mortality rate but people have to maintain SOPS to remain safe and secure. Due to mutation may be some variants are not as deadly as delta variant still in near future, if we do not follow the SOPs may be there will be more "variant of concern".

1) *Comment:* The path of endemic COVID-19 will also depend on how much the virus itself continues to mutate, delta variant has already derailed the reopening of universities, schools, colleges, it also stalled the world economy, especially Indian economy badly suffer due to the outbreak of delta variant causes major impact on India. And with so much with the mutation world still vulnerable to infection, the virus has many, many opportunities to luck into new variants that may yet enhances its ability to spread and reinfect. The positive news is that virus is unlikely to evolve so much that it sets our immune system back to zero. According to Sarah Cobey, an evolutionary Biologist at Chicago University, " Our immune response is so complex, it's basically impossible to escape them all". Here let's say, antibodies that quickly neutralize SARS-COV-2 do indeed drop over time, as it happens against most of the pathogens, but reserves of B cells & T cells that recognize the virus lie in wait. As for example our immunity against infection may abate first, but the protection against severe illness and death are much more durable. it is mentionable that Vaccine against respiratory viruses rarely protect against full infection because they are better at inducing immunity in the lungs than in the nose, where respiratory viruses gain first footstep. The variants like beta, gamma, delta, that erode some protection from vaccines. Better vaccines and better treatments might reduce the risk of COVID-19 but if we do not follow the SOPS then it will be a calamity. This experience may also aware people to take all respiratory viruses more seriously, leading to lasting changes in their lifestyle like mask wearing and ventilation. Endemic COVID-19 means finding a new way of life to live with this virus, as may we have to live with this virus.
2) *Conflict of Interest:* The authors reports no conflicts of interest to disclose.

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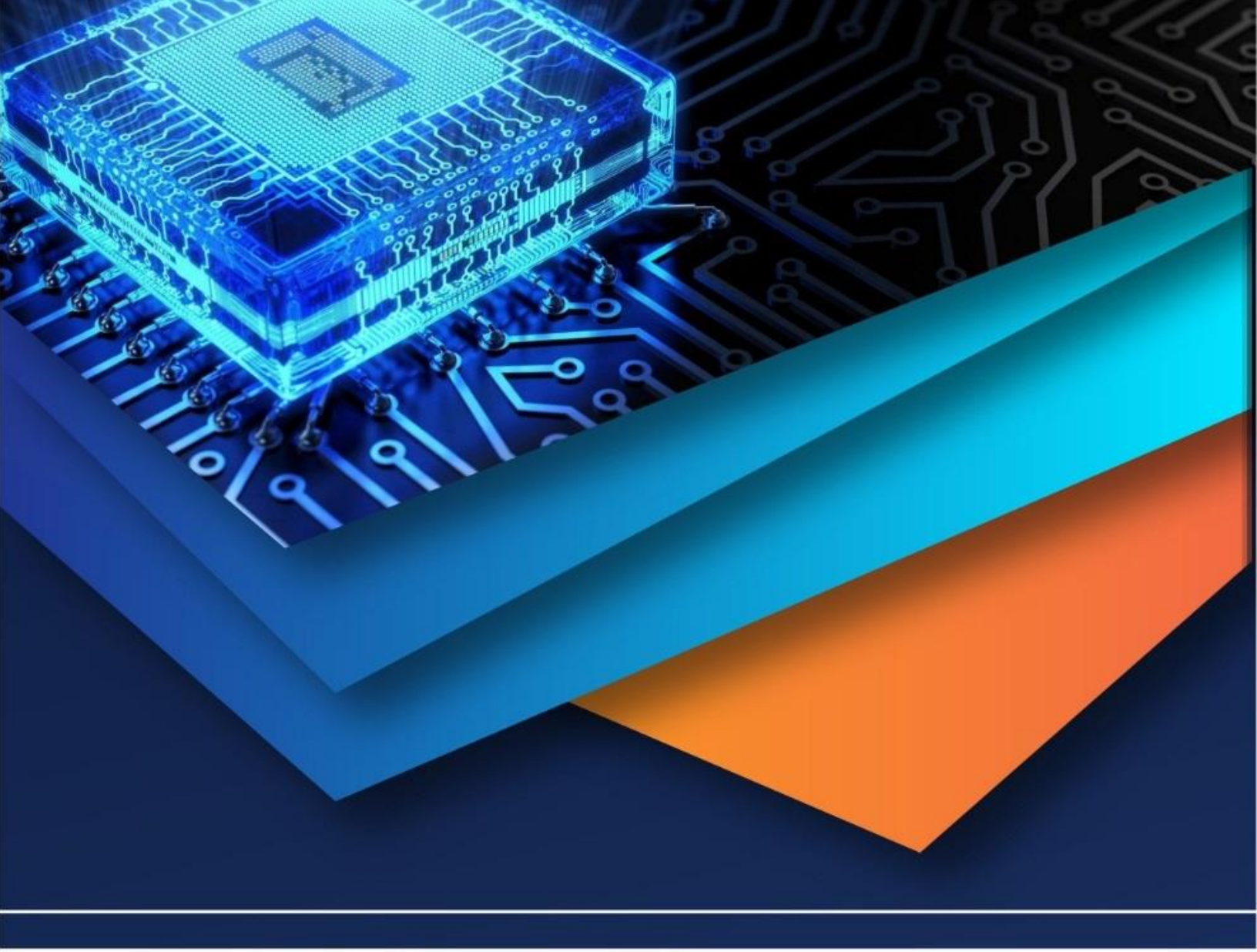

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