The rise and rise of SARS-CoV-2 Omicron variants

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20 July 2022

The "let it rip" perspective adopted by the ruling elite internationally, except for China, has allowed the SARS-CoV-2 virus devastating humanity to evolve into myriads of variants with enhanced capabilities to evade the human immune system and vaccination programs. The human body has been allowed to become a virtual Petri dish for the proliferation of a plethora of new variants.

According to analysis published in *Nature* magazine, SARS-CoV-2 virus mutates at a relatively slow rate, as its genome contains a self-repair mechanism due to an error-correcting enzyme rare in RNA viruses. It mutates at about half the rate of the influenza virus and one-quarter that of HIV, yet COVID-19 has mutated into numerous new forms, producing successive waves of the pandemic in just over two years.

Omicron was first detected in Botswana and South Africa in November 2021. The new variant had 50 amino-acid mutations compared to the original virus, 30 of them to its spike protein. The virus uses the spike protein to fuse to the host cell and gain entry. Scientists have centered their research on the spike protein as this is the key to the virus's infectivity.

Three sub-variants, dubbed BA.1, BA.2 and BA.3, are all thought to have arisen in South Africa around the same time, indicating that the virus had some time to evolve significantly before being detected.

The BA.1 variant had several mutations in common with the Delta variant and other variants of concern, but also showed many unique features.

Despite its first emerging in South Africa, scientists think BA.1 originated somewhere else, as yet unknown. It is thought it probably arose in a rural area where there was no surveillance of SARS-CoV-2, eventually making its way to South Africa's Gauteng province, where it was subsequently detected. Johannesburg, the province's capital with its sprawling township community and an international airport, gave the new variant unlimited opportunity to take hold and spread internationally.

BA.1 very rapidly displaced the Delta variant and spread around the world due to its enhanced infectivity. In less than one month, the variant had spread to 77 countries in Africa, Europe, Africa, North and South America.

"A lot of us were expecting the next weird variant to be a child of Delta, and this [BA.1] is a bit of a wild card," says Professor of Evolution and Genomics at the University of Oxford Aris Katzourakis.

Evolutionary biologist and biostatistician at the Catholic University of Leuven in Belgium Tom Wenseleers suspected that BA.1 was able to infect people who were immune to Delta due to vaccination or earlier infection.

This was a devastating blow to all the advocates of a vaccine-only and herd immunity approach to suppressing the pandemic.

The ability of a respiratory virus to evade the body's immune system was a well-known feature of viruses such as influenza and was an entirely predictable evolutionary path for SARS-CoV-2.

Mathematical epidemiologist at the London School of Hygiene and Tropical Medicine Adam Kucharski told *Nature*, "The easiest way for the virus to cause new epidemics is to evade immunity over time. That's similar to what we see with the seasonal coronaviruses."

There are four species of seasonal coronaviruses known to infect humans—HCoV-NL63, HCoV-229E, HCoV-OC43 and HCoV-HKU1—are all known to cause reinfection and produce seasonal outbreaks.

Omicron's genetic characteristics

Studies began to emerge that Omicron BA.1 was able to proliferate at an enhanced rate. Associate Professor of School of Public Health Michael Chan Chi-wai and his team in Hong Kong found that BA.1 multiplies 70 times faster than the Delta variant and the original SARS-CoV-2 strain. This meant that BA.1 was probably even more infective than the measles virus, the most infective virus known to humanity thus far.

SARS-CoV-2's spike protein is made up of 1,273 amino acids. Its receptor binding domain is the section of the protein that binds to the human angiotensin-converting enzyme 2 (ACE2) receptors. This area, comprising of amino acids 319–541, is the site of 15 mutations, half of the spike mutations found in BA.1.

BA.1 has three mutations like Delta that enable immune escape—that is, the ability of the infecting organism to evade the host's immune system. It has another 11 mutations, one of which is thought to increase ACE2 binding and thus access to the host cell by a factor of 1,000.

Another significant area in the spike protein is known as the furin cleavage site, an area between the two main parts of the protein known as S1 and S2. The furrow in between is particularly significant because mutations in this region can enhance the virus's infectivity.

BA.1 shares a mutation in position 681 with the Alpha and Delta variants that make the virus more transmissible, but it also has a mutation in position 655 near the furin cleavage site, now under investigation.

A report published in *Cell Host & Microbe*, led by School of Medicine at Mount Sinai New York scientist Alba Escalera in an in-vitro study, found that the "substitution S:655Y, represented in the gamma and omicron VOCs (variants of concern), enhances viral replication and spike protein cleavage."

The N-terminal domain area of the spike protein, known as the antigenic supersite, is considered to be important in antibody recognition and attack. Mutations in this area are known to make immune escape more likely. Omicron has four consecutive mutations in positions 142–145. One of these, at position 142, it shares with Delta.

Taken together, these mutations enabled the latest version of SARS CoV-2 to proliferate across the planet.

The emergence of BA.2

The origin of the BA.2 variant remains unclear, but it was first detected in November 2021 in the Philippines, almost simultaneously with BA.1. By late January it had been detected in 40 countries, with Denmark having recorded most cases, followed by India, Sweden and Singapore.

BA.2 was dubbed the "stealth" variant, as conventional surveillance for the SARS-CoV-2 virus could not distinguish between Delta and BA.2.

Professor of Computational Systems Biology and Director at UCL Genetics Institute in London Francois Balloux said: "BA.1 and BA.2 are about 20 mutations apart. Interestingly, the two Omicron sub-lineages are sister clades (group of organisms that include a common ancestor) that split from each other several months ago, and are not derived from each other. Both carry roughly comparable mutations relative to the ancestral SARS-CoV-2 strain."

A study conducted at Tokyo University comparing BA.1 and BA.2 concluded that BA.2 was so different that it should be designated by the World Health Organisation (WHO) as a full-fledged variant with a new Greek letter. The researchers, led by Kei Sato, explained, "Based on our findings, we propose that BA.2 should be recognized as a unique variant of concern, and this SARS-CoV-2 variant should be monitored in depth."

Co-founder of the World Health Network Yaneer Bar-Yam, in an interview with the WSWS, said the description of BA.2 as a sub-variant of Omicron was likely incorrect. "BA.2 is different enough from BA.1 that it should be given its own designation—its own Greek letter—according to the current numbering scheme. But that's politically not very comfortable because people are declaring this to be over and having a new Greek letter would raise questions that require us to re-evaluate what's going on."

According to Sato: "The remarkable diversification of Omicron probably occurred around Gauteng Province and that all Omicron lineages emerged there … Although BA.1 spread worldwide earlier than BA.2, since January 2022, the lineage frequency of BA.2 has increased and exceeded that of BA.1 in multiple countries, such as the Philippines, India, Denmark, Singapore, Austria, and South Africa."

Sato's team concluded that BA.2 had a 1.4 times higher reproduction number compared to BA.1.

Jiahui Chen, Visiting Assistant Professor at the Department of Mathematics, Michigan State University, and his team, in a preprint published in May determined that BA.2 has 32 mutations in common with BA.1, but BA.2 has 28 distinct ones.

BA.3 has a total of 34 mutations with 21 shared with other variants, but failed to take off, with only several hundred cases.

More subvariants: BA.4 and BA.5

BA.4 was first detected in January in Limpopo state, South Africa, while BA.5 was found in February in KwaZulu-Natal state, South Africa. The two variants spread very rapidly across the country, and by the end of April BA.4 made up 35 percent of cases in South Africa, while BA.5 was in 20 percent of those infected.

The two variants are causing the current surge in cases internationally. According to *Nature*, genetically scientists consider them to be more closely related to the BA.2 variant, but they have their own unique mutations.

Dr. Eric Topol, founder and director of the Scripps Research Translational Institute, described BA.5 as the "worst version of the virus that we've seen. It takes immune escape, already extensive, to the next level."

Significantly, computational epidemiologist at the University of Bern Christian Althaus commented to *Nature* that the "rise of BA.4 and BA.5 seems to stem … from their capacity to infect people who were immune to earlier forms of Omicron and other variants."

Althaus considers that the extent of the surge will be determined by the history of an area's COVID-19 waves and vaccination rates.

"It might be 5 per cent in some countries and 30 per cent in others. It all depends on their immunity profile," he says.

A preprint paper "Virological characteristics of the novel SARS-CoV-2 Omicron variants including BA.2.12.1, BA.4 and BA.5," published in May, outlined that BA.4 and BA.5 both have reproduction numbers higher than BA.2, that is, they are more contagious.

The research led by Izumi Kimura and his team, from the Division of Systems Virology at the Institute of Medical Science at the University of Tokyo, found that their "experiments revealed that the immunity induced by BA.1 and BA.2 infections is less effective against BA.4/5. Cell culture experiments showed that BA.2.12.1 and BA.4/5 replicate more efficiently in human alveolar epithelial cells [cells on the lungs surface] than BA.2, and particularly, BA.4/5 is more fusogenic [able to fuse with human cells] than BA.2. Furthermore, infection experiments using hamsters indicated that BA.4/5 is more pathogenic than BA.2."

They predict that BA.4/5 will potentially be a greater threat to global health than BA.2.

BA.4/5 have identical spike proteins but have several different mutations on the rest of the virus that are not considered significant in terms of the virus's infectivity and lethality.

The variants BA.4/5 have the L452R mutation that they share with Delta, which is thought to make the virus more contagious and may help it evade destruction by the immune system. They possess the F486V mutation, located near where the spike protein binds with its host cell, and is thought to assist with any immune response. Both mutations are considered important in facilitating the virus's evasion of the immune system.

How and where did Omicron develop?

There has been considerable research into the emergence of Omicron and the proliferation of its variants.

It is significant that all the Omicron variants emerged in South Africa, which, along with the rest of the African continent has been largely abandoned by the global imperialist powers, allowing it to become a source of successive waves of pathogenic organisms. The recently emergence of monkeypox virus onto the international scene highlights this.

Where and how the Omicron variants emerged is very important and will give insights into the evolution of the SARS-CoV-2 virus and how to combat its rise.

Scientist from the Institute of Infectious diseases and Molecular Medicine at the University of Cape Town in South Africa Darren Martin and his team published a research paper preprint, "Selection analysis identifies unusual clustered mutational changes in Omicron lineage BA.1 that finds the likely impact Spike function."

They wrote, "Given the evident epidemic growth advantages of Omicron over all previously known SARS-CoV-2 lineages, it is crucial to determine both how such complex and highly adaptive mutation constellations were assembled within the Omicron S-gene, and why, despite unprecedented global genomic surveillance efforts, the early stages of this assembly process went completely undetected."

Three contending theories have emerged. One possibility is that

although millions of SARS-CoV-2 genomes have been sequenced internationally, scientists simply missed the initial mutations that eventually evolved into Omicron. Another theory is that the variant evolved in one person with a long-term infection, and thus escaped detection until the mutations were far along. The third is that the strain arose in an unknown animal host, such as mice or rats. and then reinfected humans. Computational biologist at the University of Basel in Switzerland Richard Neher told *Nature* that whichever theory a researcher favors "often comes down to gut feeling rather than any sort of principled argument."

Even though SARS-CoV-2 is one of the most studied organisms on the planet, the Omicron variants developed completely undetected into organisms that have threatened mankind.

While scientists have submitted 7.5 million sequenced genomes to the publicly available GISAID genome database, South Africa has sequenced less than 1 percent of its known cases, while from Tanzania to Zimbabwe and Mozambique only 1,000 sequences have been submitted, an even tinier fraction.

Darren Martin calls for the sequencing of SARS-CoV-2 genomes in the very low surveillance areas to obtain a more complete picture. "It is possible that the three sublineages of Omicron each separately arrived in South Africa from a region with limited sequencing capacity," he told *Nature*.

Some scientists have called this theory "extremely implausible." Bioinformatician at the University of KwaZulu-Natal in Durban and at Stellenbosch University's Centre for Epidemic Response and Innovation, Tulio de Oliveira, said that earlier stages of Omicron would have been detected when infected people traveled to an area with higher levels of genomic surveillance.

A second theory states that the virus was able to rapidly evolve in a person with a compromised immune system where the virus can continue to live for an extended period. Such people are relatively common in Africa due to the high prevalence of the HIV virus. There are approximately 23.8 million people with HIV living on the continent and about a million people a year die of the disease, unable to receive adequate medical support.

Scientists consider such people to be likely receptacles of fast-paced viral evolution. These infections can persist for as long as five months.

"There, the virus can multiply for weeks or months, and different types of mutation can emerge to dodge the body's immune system." Chronic infections give the virus "the opportunity to play cat and mouse with the immune system", computational evolutionary biologist at Temple University in Philadelphia, Pennsylvania, Sergei Pond told *Nature*.

A paper published on virological.org, "Preliminary genomic characterisation of an emergent SARS-CoV-2 lineage in the UK defined by a novel set of spike mutations," in December 2020, identified immune compromised patients whose virus genome sequencing of SARS-CoV-2 infections revealed "unusually large numbers of nucleotide changes and deletion mutations…"

"The virus has to change to stick around," says Ben Murrell, interdisciplinary virologist at the Karolinska Institute in Stockholm. According to *Nature,* the receptor-binding domain, where many of Omicron's mutations are concentrated, is an easy target for antibodies, and probably comes under pressure to change in a long-term infection.

Angela Rasmussen, a virologist at the University of Saskatchewan Vaccine and Infectious Disease Organization in Saskatoon, Canada, considers this scenario as unlikely as none of the cases studied so far had the level of mutation displayed in Omicron. "It seems like a lot of mutations for just one person," she said.

Another consideration posed by scientists is that Omicron's properties could have come from a number of mutations working in concert. Two mutations found in Omicron N501Y together with Q498R combine to enhance Omicron's ability to bind the ACE2 protein by about 20 times.

Martin and his team think that about 12 Omicron mutations in three clusters work together to overcome the deleterious effect of any single mutation.

The scientists think these mutation clusters enable the virus to evolve more rapidly than if they obtained the mutations one by one.

Martin and his team argued, "We further propose that the mutations in each of the three clusters therefore cooperatively interact to both mitigate their individual fitness costs, and adaptively alter the function of Spike."

Rasmussen thinks that multiple immune-compromised people were involved, or Omicron may have evolved in a person with a long-term infection who spent some time in the population before detection. "There are a lot of open questions," Rasmussen told *Nature*.

SARS-CoV-2 is a promiscuous virus and is known to infect several animal species including leopards, hyenas, hippopotamuses, ferrets and hamsters. Omicron's spike protein is known to be able to bind to the ACE2 protein of turkeys, chickens and mice.

According to a study led by research scientist Neil Bate from the Department of Molecular & Cell Biology, University of Leicester, "We show Q498H, and Q498R plus N501Y, enable variants to bind to rat ACE2 with high affinity. These mutations are now emerging in CoV-2 variants, such as the Omicron variant, where they would be expected to drive increased human-to-human and cross-species transmission."

A scientific paper published in the *Journal of Genetics and Genomics*, "Evidence for a mouse origin of the SARS-CoV-2 Omicron variant," found mutations in the Omicron genome that were adapted to evolve in mice and not humans. They found that, in human hosts, G (Guanine) to U (Uracil) substitutions tend to occur in RNA viruses at a higher rate than C (Cytosine) to A (Adenine) switches do, but Omicron does not show this pattern.

This theory would require that a mutation would occur in an infected person, enabling the virus to jump into a rat, then another mutated virus to jump back into humans, occurring for all the Omicron variants. The chances of this occurring is very low, as each mutation is in itself a very rare event.

Some conclusions about Omicron and public health

The fact that SARS-CoV-2 has been able to emerge and differentiate into Omicron and its variants disproves definitively the complacent nostrums trotted out with the emergence of Omicron. At its most crass, Australian Chief Medical Officer Paul Kelly said at a press conference in December 2021 that if Omicron was more transmissible, but less severe, and there were mass infections, that this would be his "number one Christmas present."

The evolution of Omicron and the resulting mass wave of infections shows that the SARS-CoV-2 virus can evolve to meet the increasingly limited mitigation measures governments set in place and it can continue to devastate humanity indefinitely.

The public health policies adopted by capitalist governments around the world, besides China, do not even deserve the name of "herd immunity," since they have nothing to do with either immunity or preserving the "herd," i.e., the human race.

The financial aristocracy initially seized on the pandemic as a means of enriching itself, through gigantic corporate bailouts. Then the back-to-work drive began, since workers had to produce the surplus value required to pay for the bailouts. The back-to-school campaign was a necessary corollary, since parents with school children had to be sent back to their workplaces.

In the course of these events, the ruling class began to understand the positive value of the pandemic, from its parasitic standpoint, since the virus disproportionately killed the old and weak, those who could no longer work and generate profits. The longer the pandemic continues, the less would be “wasted” on pensions, health care and other benefits for those who were no longer able to contribute to the “economy,” i.e., to increasing the wealth of the corporate oligarchy.

The working class is thus compelled to deal with two plagues, not one. The first is the mounting infectivity and lethality of a virus that has been given free rein to mutate without limit, and find the ideal genetic form to attack the entire human race. The second is the parasitism and incompetence of a capitalist class that is single-mindedly focused on the increase in its own wealth, no matter how deadly the consequences, in terms of war, mass suffering, poverty and sheer social dysfunction, for humanity as a whole.