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Review Article

Omicron Genomics: New Pandemic Phase, are we Better Prepared?

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Abstract

The mind-numbing cases of COVID-19 and repetitive waves of its infection worldwide with massive progression of genetic mutations and virulence abilities had dire consequences on human health, scarcity of healthcare facilities, job crisis, diminished supplies of food and essentials and high rate of morbidity and mortality among young population. This time the storm may not take lives but also livelihoods. Successive shutting barriers between the nations may not just be the answer to tackling the maniac virus. Quality of life and livelihood in many nations have been severely impacted after lockdowns, more so in developing countries. Many areas across the world face acute and chronic food scarcity. Due to the increased lethality of omicron variants of SARS-CoV-2 and growing concern over its devastating effects, it is necessary to identify the potential consequences and develop a powerful strategy to combat the upcoming challenges. Here, I addressed the pandemic challenges, pathogenicity, social-health inequalities, bitter consequences and possible solutions to fight future pandemic bursts.

Keywords: Pandemic; Omicron; SARS-Cov2; Covid-19 Epidemic; Challenges; Inequalities

Introduction

On 26th November 2021, a new mutated variant B.1.1.529 of SARS-CoV2 was reported as a global health threat, originating in South Africa and Botswana. The variant was named on the Greek alphabet O, Omicron on the recommendation of WHO's Technical Advisory Group on Virus Evolution (TAG-VE). Constant vigilance and tracking were required to monitor and evaluate the constant evolution and circulation of the deadly virus. The TAG-VE, established in June 2020, has been under the constant pressure of the mutations emerging from the virus and thus, continues with regular meetings. The team discussed analysing the impact of newly emerging variants such as delta, Omicron and other mutated forms for their impact on severity, ease of transmission, etc [1]. The global situation of corona epidemic is worth to consider for preventing future outbreaks (Figure 1a).

Further, the variant is classified as a variant of concern (VOC) or variant of interest (VOI) according to the guidelines provided by the WHO (https://www.who.int/news/item/28-11-2021-update-on-omicron). South African researchers highlighted many aspects of Omicron, and its other aspects are under clinical investigation. The microscopic structure of the variant was veiled until the appearance got its space under a paper entitled "First photo of Omicron from the Bambino Gesu research group". The structure was given by the State University of Milan researchers and published on Ansa.com. Professor C.F Perno and Professor C.Alteri, with the help of their team Valentino Costabile, Rossana Scutari, and Luna Colagrossi. The structure revealed some interesting mutations in the spike protein of the omicron variant that have a high tendency to infect human lung cells because of their increased affinity for the ACE2 receptors (Figure 1b).

Pathogenic determinants of Omicron variants

Omicron got classified as a variance of concern due to many mutations in the Spike gene [2,3]. Immunological and clinical data related to transmissibility and severity of the variant is not yet available to provide definitive evidence. However, we can infer from the known data and research about the mutations of the variant to extrapolate initial indications on transmissibility, brutality, and immune dodging [4]. Many mutations are present in the receptor-binding and N-terminal domains and play a major role in ACE2 binding and subsequent pathogenesis. The deletion mutations of the Omicron at position S:H69- and S:V70-, coincides with the deletions exhibited by Alpha and Eta variants. The 69/70 deletions are the basis of detecting the variant in the S-assay. However, the deletions found in another variant may be confusing. A 3-aa insertion at position 214 is also present in the spike protein. Many mutations present at the furin cleavage site may be associated with increased transmissibility and infection [5].

Importantly, the Omicron variant has a high mutational landscape, including A67V, T95I, G142D, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493K, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, and L981F in the spike protein variant [6]. It also exhibited some common pathogenic muta-

tions with alpha or delta variants, including deletions at H69-V70 and Y144, and point substitutions at G142D, T478K, N501Y, D614G, and P681H (Figure 1c). The combination of mutations exhibited by the omicron variant may increase the binding affinity to ACE2 [7]. In addition, deletions of 3 amino acids at particular sites of ORF1 have some speculations that the mutation aids in innate immune dodging. The ability to dodge innate immunity is due to cells degraded by viral components [8]. Importantly, the immune evasion properties of this variation, together with a concomitant reduction in virulence, are caused by a significant antigenic alteration within the spike protein and a novel endocytic entry mechanism [9].

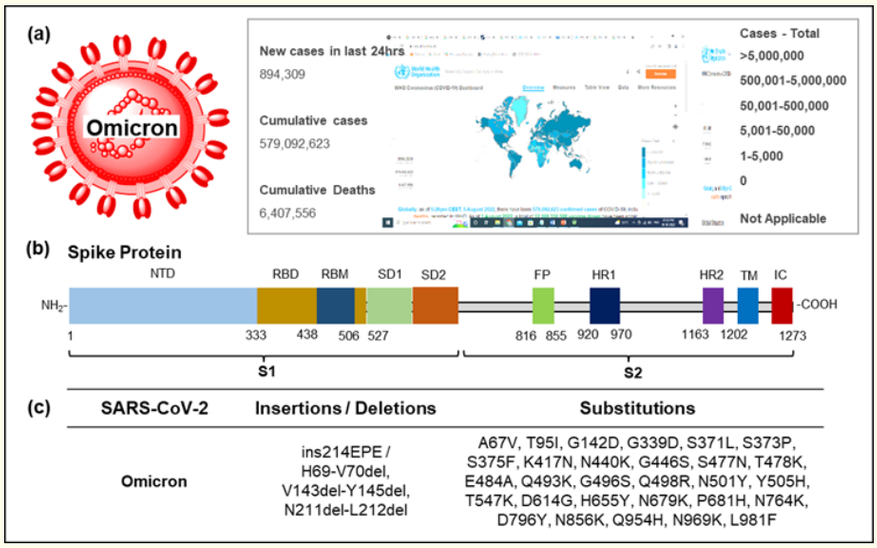

Figure 1: Surveillance of Omicron: a) Global corona epidemic status- As of 5:26 p.m. CEST on August 5, 2022, there were 579,092,623 confirmed cases of COVID-19 worldwide, including 6,407,556 fatalities, reported to WHO. b) Domain architecture of SARS-CoV-2 spike protein- A crown-like structure called a "corona" is produced on the surface of the virion by the spike glycoprotein projections, which are composed of the S1 and S2 subunits. The primary receptor-binding domain (RBD) is represented by subunit S1, and the virus-cell membrane fusion process is carried out by subunit S2. c) Pathogenic determinants of Omicron- The report suggests many important residues that potentially have a pathogenic function in the omicron variation, including the deletion of Y144 and H69-V70, as well as the replacements of G142D, T478K, N501Y, D614G, and P681H. FP- Fusion peptide, HR1/2- Heptad repeat-1/2, IC- Intracellular domain, NTD- N-terminal domain, RBD-Receptor-binding domain, RBM- Receptor-binding motif, SD1/2- Subdomain-1/2, TM- Transmembrane region.

Current pandemic challenges from life to livelihood

The world is under a question mark and constant threat. The challenging threat may be not just surviving this time but also extending to livelihood. Whether we stay together or perish together was what the UN Secretary General António Guterres meant while addressing the pandemic. Covid-19 waves following each other with mutations push the world under a great threat [10-12]. As the world economy is completely interconnected, the pandemic shook the economy badly with the virus's rapid spread. The pandemic was described as the worst global crisis since WWII by the international labor organization (ILO). Bold and compelling steps are needed to halt the pandemic this time and save societies from economic devastation and overcome economic and financial stability. The world is facing the worst health and economic crisis unlike any we have seen in the past century, taking lives and livelihoods. Local businesses, investments and MNEs have been affected badly, resulting in financial repercussions [13]. As followed by economic vulnerabilities, global food insecurity is also a major issue faced due to the pandemic. With reduced incomes and disturbed supply chains, chronic and acute food crises were heightened. Many factors contributed to the overall deaths due to hunger in almost every country; the effect was expected to continue (https://www.worldbank.org/en/topic/agriculture/brief/food-security-and-covid-19). The world is shaken by the loss of lives and the fear of living with the threat of losing the near and dear ones any time sooner. Countries worldwide imposed tight rules to stop the variant from crossing the borders.

Bitter face of precautionary travel restrictions

The first sequenced omicron case was reported from Botswana on November 11, 2021, and a few days later, another sequenced case was reported from Hong Kong by a traveller from South Africa (https://www.gisaid.org/hcov19-variants/). Australian authorities Health minister Natasha Fyles ensured that the patient was kept in the most secure quarantine facility at Howard Springs. As reported in Switzerland, the whole world is taking the utmost precautious steps; the government reconsidered its entry restrictions to keep a check on the spread. Overpopulated countries like India also came forward in taking measures against international travel. The new guidelines generated recently restrict all the travellers, irrespective of their vaccination status, to undergo COVID-19 testing on arrival mandatorily. Many countries are demanding a complete

travel ban. Israel, for example, has suspended all aviation into its borders after the detection of its first Omicron infection. The case was reported on Friday, just a month after it opened aviation facilities. Similarly, Morocco has also claimed to block all the incoming flights for at least two weeks to curb the spread of this new strain. South Africa's president Cyril Ramaphos claimed the omicron variant as a tocsin for vaccine inequality globally. He also criticized banning South Africa and sister countries from travel, resulting in economic distress.

WHO has pleaded with countries worldwide to uplift the ban on South African countries as apprehension over the variant of concern. Matshidiso Moeti, Africa's regional director of WHO, urged countries to respect and follow Science and international health regulations against travel restrictions. He stated in a worrisome tone, indicating that the restriction may slightly reduce the spread of COVID-19 but may impose a heavy burden on lives and livelihoods". He warned the countries of the economic crisis the world would be pushed into in his statement. He demanded the restrictions if implemented, should not be pointlessly offensive or intrusive and should have a scientific ground according to the International Health Regulations.

Omicron guided optimism and menace

Many people question whether the immunity conferred by Omicron may offer for cross-variant protection and bring about the end of the pandemic. The Omicron variation often causes milder symptoms than other VOC, especially in vaccinated persons, and is highly transmissible. A new study published in Nature, however, demonstrates that Omicron very slightly increases cross-variant neutralisation and the amount of humoral immune response in uninfected people [14]. In contrast, Omicron breakthrough infections in those who had received the vaccine led to high titres of antibodies that neutralise all VOC. This shows that whereas Omicron infection serves as a "booster" in those who have had vaccinations, it offers little protection from other VOC in those who have not [15].

However, the researchers discovered that infection with a pre-Omicron variation had a 15.1 percent efficacy in preventing symptomatic reinfection with either subvariant and a 28.3 percent effectiveness in preventing reinfection with either BA.4 or BA.5. Stronger defence was provided by prior Omicron infection: it was 76.1 percent effective in avoiding symptomatic reinfection and 79.7 percent effective in preventing BA.4 and BA.5 reinfection [16]. The researchers note that this result is consistent with other studies and is likely brought on by the estimates` large confidence intervals, despite the fact that it is contradictory to show higher protection against any reinfection than symptomatic reinfection.

Prevention of spillover is the ultimate solution

Every viral pandemic that has occurred since the turn of the twentieth century has likely been caused by spillover events, in which a disease that begins in animals leaps into humans [17]. In addition, an August 2021 review of disease outbreaks over the previous four centuries shows that, partly as a result of human-induced environmental changes, the chance of pandemics increasing several-fold year in the future decades [18]. However, a lot of the global initiatives launched in response to the COVID-19 pandemic to strengthen global defences against upcoming epidemics continue to fall short in giving spillover prevention first priority. The danger of spillover increases when there are more chances for interactions between animals and people, such as in the wildlife trade, in animal agriculture, or when forests are removed for mining, farming, or roadways. Infected animals are more prone to shed viruses under circumstances where they are more likely to do so, such as when they are improperly nourished or kept in crowded conditions.

In order to effectively limit the danger of spillover, a worldwide approach should concentrate on four steps, according to decades of study in the fields of epidemiology, ecology, and genetics [19]. First, it's important to safeguard tropical and subtropical forests. Studies suggest that the main worldwide driver of newly developing contagious diseases of zoonotic origin may be changes in land use, particularly in tropical and subtropical forests [20]. Species that can coexist with humans and frequently have viruses that can infect humans are among the wildlife that survives forest clearing or degradation [21]. Climate change is further exacerbated by the destruction of trees. By driving creatures like bats towards locations where many humans reside from formerly favourable environments, this may help with spillover effects [22]. Second, both locally and internationally, there has to be rigorous regulation or a prohibition on the sale and trading of live wild animals that are dangerous to the public's health. Restrictions on commercial markets and trade in urban and peri-urban areas must not violate the rights and requirements of Indigenous peoples and local communities, who frequently depend on animals for their food security, way of life, and cultural activities. Numerous nations, like Brazil, Canada, and the United States, already have various hunting regulations based on the community.

Third, while dealing with domesticated animals, biosecurity needs to be strengthened. This might be accomplished, among other things, by improving veterinarian care, illness surveillance for animals, animal housing and feeding practises, and quarantines to stop the spread of pathogens. Animals raised for food have a higher risk of contracting and transmitting infections when they are ill. Additionally, almost 80% of cattle diseases may infect a variety of hosts, including people and wildlife [23]. Fourth, it is important to enhance people's health and financial stability, especially in areas where infectious diseases are prone to spreading. Malnourished individuals and those with untreated HIV infections are two examples of individuals who may be more vulnerable to zoonotic viruses than others. Pathogens can change before spreading to others, especially in immunosuppressed people like these [24].

Social and health-related inequalities should not be avoided

Social and health-related inequities have come to light as a result of the Covid-19 epidemic and its economic and social effects [25,26]. New disparities have emerged both within and across countries as a result of the pandemic and our reaction to it [27]. However, one may logically assume that we now have the means to resolve inequities linked to pandemics given the availability of very effective vaccinations. However, well-known social science fundamental cause theory predicts that those with more resources would compete to profit the most from vaccinations, leaving enormous groups of underprivileged people vulnerable [28]. While other potentially life-saving precautionary measures have been dispersed unevenly. Due to the high infectiousness of the disease and the speed at which mutations produce new variations, any activity that increases inequality by lagging behind disadvantaged people and nations puts everyone-rich and poor-at danger. It's time to make sure this benefit that can save lives is distributed fairly.

The spread of a pandemic and the tactics taken to combat it, such as social isolation, total lockdowns, and the production and distribution of vaccines, are prime examples of how social context cannot be separated from medical phenomena. We must make sure that pricing, availability, and acceptance of vaccinations are independent of the resources available to people and nations in order to support their equal distribution [29]. This is only feasible if we can increase public awareness of the vaccine's health-protective effects, if all citizens are treated equally by the international community, and only if political decision-making processes regarding vaccine distribution strategies are made independent of established power structures [30]. By doing this, we will achieve less inequities, healthier populations, and strengthened faith in political institutions, which is a crucial component of contemporary democracies.

Concluding Remarks

According to the WHO and others, the rapid spread of the omicron variant of the coronavirus, with its subsequent short-term immune boost, could signal the end of the pandemic. However, researchers warn that the environment remains unstable and difficult to model. Different countries have different vaccination approaches, types and coverage, as well as different rates of disease and recovery, leaving a diverse immunological landscape. Therefore, the pandemic is still unpredictable and challenging to anticipate, experts believe Omicron won't be the last version. Infectious disease modeler Graham Medley predicts that this strain will not be the last and that the next strain will have unique characteristics. Amidst this challenge, a combination prevention approach of vaccination and public health measures is expected to remain an effective strategy. However, "There is so little understanding of what's going on, and that's true, even for scientists," said the Child Health Research Foundation director in Dacca, Bangladesh. Although shutting the barriers is intended to buy some time against the virus, the consequences are yet to be faced, and many challenges ahead are waiting.

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Conflicts of Interest

The authors declare no conflict of interest.

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