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International Journal of Family & Community Medicine

Short Communication

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The evolution and global impact of Covid-19 and Omicron: the way forward?

Abstract

Coronaviruses are a family of pathogenic viruses that including MERS, SARS, and SARS-Cov-2, and are known to cause respiratory and other illnesses in man and animals. The SARS-CoV-2 virus, responsible for the COVID-19 virus is a monopleiotropic clade of the coronavirus family first reported in Wuhan, China in December 2019 where it was found to cause a previously unreported form of viral pneumonia. The virus readily spreads by airborne microdroplet infection, and within a month of its report to the WHO in December 2019 was found in the USA and other countries and was declared a pandemic by the WHO within the first few months of its discovery and emergence. Numerous mutations of the virus with variations in infectivity and pathogenicity began to appear within the first year, including the current Delta and Omicron, both of which are more contagious than their SARS-CoV-2 progenitor strain. Omicron, while approximately five-fold more transmissible than Delta, may infect both vaccinated and unvaccinated people, and is now responsible for the majority of currently infected people but to date has resulted in only mild and non-life-threatening outcomes. Due to the greater infectivity and the mild illness attributed to the Omicron, it may be an important development in terminating the continued spread of the pandemic.

Keywords: RNA Coronaviruses, COVID-19, epigenetic variants, Omicron

Volume 6 Issue 1 - 2022

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Received: January 12, 2022 | **Published:** January 20, 2022

Preface

The global impact of the Covid-19 pandemic on the health and healthcare delivery of the world populations has been extraordinary. Throughout the course of history, pandemics occur about once every one hundred years, while epidemics occur somewhere around the globe about three times as often and each time a sometimes novel but different infectious entity may been identified as the causal agent and public health measures were soon implemented to ultimately contain the infectious agent.[1] The adverse impact on human health and survival in affected populations may be variable, but typically epidemics and pandemics effect those individuals with comorbidities and advancing age more severely than in otherwise younger, more healthy individuals.[2,3] On Dec 31, 2019 the novel coronavirus, now known as SARS-CoV-2, was identified as the cause of an outbreak of viral pneumonia of unknown origin in Hubei Province, Wuhan, China, having infected over 200 people and causing several deaths in first known identification of the previously unidentified illness.[1-5]

The illness was later named coronavirus disease 2019 (COVID-19), which soon spread globally in a seemingly exponential manner. The World Health Organization (WHO) determined the novel virus to be the origin of a pandemic within the first few months of its emergence. During the first three months after COVID- 19 emerged, nearly one million people became infected and 50,000 mostly older individuals had succumbed due to complications of the illness. By six months into the outbreak the number of cases worldwide exceeded ten million and there were more than 500,000 deaths. To date, there have been over 60 million cases and 800,000 deaths from COVID-19 just in the United States.[6] One of the most troubling observations about COVID-19, similar to other viral respiratory illnesses, is that asymptomatic silent transmission can occur from infected people before they are aware they have been exposed to the virus, and before they may have developed any symptoms of illness. Moreover, once an individual has become infected, the virus may infect multiple organs and tissues including brain, cardiovascular, pulmonary, and other organs in its newfound host.[6] The NIH National Institute of Allergy and Infectious Diseases (NIAID) COVID-19 research efforts were developed based upon earlier ongoing research on coronaviruses, including Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS) both of which caused similar but less severe illness than the SARS-CoV-2 virus now recognized to be causing the COVID-19 pandemic. Containment of the pandemic has presented previously unknown challenges, linked to the nature of the illness, the modes of transmission, the development of mutant strains, and the variable immune responses of infected or immunized individuals. Numerous epigenetic COVID variants have now emerged, most recently the Delta and the Omicron, which although more contagious, have been shown to variations in the magnitude of serious illness and especially for the Omicron, few if any deaths at the time of this writing including those individuals that presented with the age-associated comorbidities that complicated recovery in previously prevalent and more virulent covid strains.

Introduction

The SARS-CoV-2 was first reported from an outbreak in Hubei Province, Wuhan, China in late Dec 2019, where it had caused a previously unknown respiratory illness in over 200 individuals and numerous deaths in the weeks preceding the report to the WHO and their subsequent announcement and warning to the International community.[4] Within three months the illness had spread to multiple countries, which led the World Health Organization (WHO) to declare it a pandemic in less than four months from its original report. The illness was determined to be caused by a newly emerging member of the coronavirus family, cornoaviridiae, in the complex molecular form of a previously unknown variant of the virus.[2] The new coronavirus variant was found to have a unique RNA genome that exhibited a larger molecular footprint and more aggressive spike proteins than other members of the corona virus species. As with many infectious illnesses, older members of the population, especially those over age 60 or 70 years and more frequently presenting with cardiovascular,

respiratory, obesity, diabetes or other comorbidities were soon found to have a greater risk for more serious coronavirus illness and thus more likely to succumb to the combined effects of the viral infection and their comorbidities.[1,3]

Vaccine development

Early in the course of the emerging pandemic, the US Government incentivized and coordinated efforts with private enterprise to develop and implement operation 'Warp Speed' a novel program to discover more about the virus and to initiate the development of a useful vaccine in record time. Several novel vaccines were developed using mRNA and other technologies under operation Warp Speed during the first year, including multiple clinical trials undertaken within the same year. Within less than one year from the time of discovery to vaccine delivery, scientific advancement enabled three of the novel vaccines to receive emergency use authorizations (EUA) from the FDA all within the first year of the pandemic. Beginning in late 2020, the same year of inaugurating Warp Speed Immunization programs were initiated in multiple countries, historically marking the shortest time frame for the development of a new vaccine yet observed for any previous vaccine and enabling the implementation of vaccination programs throughout much of the Globe. It soon became apparent however that the immune responses to vaccination were transient in nature, as some individuals who had been considered to have been 'fully vaccinated' with any of the recommended COVID-19 vaccination protocols developed breakthrough infections. Further studies revealed that the newly generated circulating antibody levels initially peaked during the first month of exposure or immunization but declined to near non-protective levels within the first 6 to 8 months following vaccination. The transient nature of the antibody response is a common observation not only among coronaviruses but has been observed in other unrelated viruses as well and which has posed a significant problem in attempting to develop more long-lasting vaccines for those viruses.[10] Unlike some of the common 'childhood viruses' an immunization with the covid vaccines has not yet provided evidence of a fully effective lifelong immunity after first exposure.

Development of mRNA vaccines

The mechanism of vaccine development for mRNA vaccines represents a novel approach to vaccine development, in that it mobilizes the protein biosynthetic process of the host cells to produce copies of the molecular fragment obtained from the viral epitope and may be accomplished in less time than traditional methods of vaccine development. This is in contrast to inactivated viral entities used in traditional vaccine development to generate the immune response, which often can produce long lasting immunity, as can natural immunity. Upon delivery of an mRNA 'vaccine' material, containing only an epitope fragment of the virus that can encode a target antigen, host cells will accept the biological mRNA fragment and translate it into an antigenic protein in situ, thereby utilizing the cell's own protein biosynthetic machinery to generate an immune response. The individual's immune system will then mount a robust adaptive immune response against the target antigenic protein generated from the cell's newly acquired mRNA. However, because the spike protein that contains the epitopes introduced in COVID-19 vaccines are prone to mutate over time, the molecular characteristics of the antibodies produced from the original vaccination may no longer recognize a newly emerged viral clade that has amended its original epitope configuration, which may indeed be the case with the Omicron variant. In antibody generation, the broader the array of epitopes in the presenting antigenic substance, the broader would be the expected spectrum of the resulting antibodies produced. Thus, this may account for the more robust immune responses which typically follow natural immunity from prior virus exposure than those generated from mRNA vaccines.[16-19]

Viral transmission

Coronavirus transmission occurs primarily via microdroplet infection, similar to that of other respiratory viruses, and contaminated microdroplets were found to remain viable on exposed surfaces for several hours after release by an infected host, including surfaces that could easily become contaminated with the microdroplets with normal air movements released by innocent virus releasing passersby.[2,11] As is common among viruses, many including the coronaviruses are disseminated and transmitted via the airborne microdroplet mechanism. This airborne characteristic poses a great and virtually insurmountable problem to public health workers in attempting to devise effective control strategies, including both indoor confinements and outside close environments by physical containment, protective clothing, and chemical antiseptic agents alone. The airborne microdroplets can sometimes be carried considerable distances, contaminating objects and surfaces along the way, possibly distant from their point of respiratory origin. While social distancing helps in the immediate spray of the respiratory microdroplets between nearby individuals, the airborne movements may carry the virus-laden droplets in all directions, thus contaminating a broader swath where others may enter. Masking is also partially beneficial depending on the efficacy of the type of mask applied, especially in slowing the microdroplet spread from a potential asymptomatic carrier to an unsuspecting individual recipient who may enter an invisible but contagious swath.

Immunity to COVID-19

Lifelong immunity is a unique and valuable characteristic of many of the 'childhood viruses,' induced as outlined below. While most of the so-called 'childhood viruses can induce a lifelong immunity, the coronaviruses appear to be a notable exception in that the limited immunity gained via prior exposure or immunization to COVID-19 appears to be elicit only a transient response. Experience has now demonstrated that the coronavirus immune response typically lasts less than one year, and thus enabling a re-infection albeit it of lesser magnitude and intensity to occur upon re-exposure to a covid virus of the same or different substrain.[6,9]

The development of the immune response to a viral infection includes both the plasma-based humeral response and elements of the bone marrow. During the development of the normal response to a novel virus, the immune system triggers the maturation of clones of short-lived plasma blasts and a population of longer lasting antibody producing plasma memory cells (B cells and T cells). This newly acquired immune memory becomes encoded and may last for decades or longer via the actions of both the plasma B cells and additional memory cells of the bone marrow. As the patient clears the viral infection, longer lasting B cells typically continue the to support the humeral response in the event of a re-exposure to reinfection, but producing a lower level of circulating antibody concentrations than were observed during the active phase of the infection.[6] The bone marrow develops the formation of bone marrow plasma cells (BMPCs) that function as a second arm of the long-term immunoreactive elements of the immune responses and which also contributes to the long-term immune-protective phenomena of viral infections via stablishing an embedded code to reactivate an immune response should re-exposure occur. The somewhat sluggish nature of the coronavirus immune responses where the viral replication in

Citation: Tulp OL, Einstein GP. The evolution and global impact of Covid-19 and Omicron: the way forward? *Int J Fam Commun Med.* 2022;6(1):11–13. DOI: 10.15406/ijfcm.2022.06.00255

vivo occurs more rapidly than the lagging immune recovery presents a special case however if one is to fully prevent covid reinfection, as the challenge to emerging reinfection occurs more rapidly than the immune system can respond in the most effective manner.[2,12,13]

The immunogenic epitopes of covid vaccines are located primarily on the spike proteins that interact with the ACE2 receptor sites in the host. In contrast, natural immunity from prior exposure to the live virus encompasses the entire virus, and thus is likely to generate a broader based immune response due to the multiple epitopes encountered by the innate immune response of the host, thereby emphasizing the added protective benefits of natural vs. vaccine induced immunity. As occurs with many viruses, coronaviruses have also demonstrated a propensity to undergo epigenetic mutations, where the infectivity and contagion may undergo changes in pathophysiologic sequela following infection. The extent of acquired immunity to a previous or emerging variant remains unclear.

The Omicron clade

Most recently the emergence of the Omicron variant has quickly become the most prevalent variant in numerous geographic locations, displacing earlier variants in the virosphere. Although Omicron has now been shown to be up to five-fold more highly transmissible than the Delta and other previous forms of the virus, it has resulted in less severe illness and few if any deaths at this time.[12,13] Studies indicate that a periodic booster vaccine containing one or more of the epitopes is likely to keep the immune system sufficiently engaged however, and able to produce adequate numbers and availability of circulating antibodies to minimize the impact and magnitude of reinfection, and to thus become readily available should re-exposure to an active viral threat occur. Re-exposure is more likely to occur during an active pandemic where local airflow in common spaces and a potentially contaminated environment cannot be easily fully neutralized 100% of the time since critical spaces may need to be reutilized on a continuing basis, especially in active healthcare and other private and public environments.

Conclusion

In conclusion, the current pandemic has evolved from a less pathogenic strain of the coronavirus and has now presented the greatest global challenge to public health measures that has been imposed in the past century. When smallpox was prevalent, it was observed that farm workers who had been exposed to cowpox, a related virus, were immune to smallpox, leading to the concept of developing an attenuated but cross-reactive nonpathogenic form of the infectious agent to vaccinate people to protect them from the pathogenic form. This practice has resulted in the virtual extinction of the smallpox virus. Now comes the less pathogenic epigenetic Omicron variant of the covid-19 virus, which while although having a larger genome and being more highly contagious than other variants, poses a lesser risk for serious infection and has resulted in lower rates of hospitalization and few if any documented deaths than other COVID-19 variants, including those individuals who present with comorbidities.[15] The pandemic has now attributed to over 312 million individuals becoming stricken with the virus, and over 5.5 million deaths world-wide, with no immediate end in sight.[15] Should infection with the less pathogenic Omicron variant prove to be able to provide adequate natural protection from more pathogenic variants of covid-19, and it along with booster vaccines could facilitate the culmination of the pandemic and ease the global impact on the healthcare and financial burdens that the current pandemic. Only time may dictate if this may enable global populations to return toward a state of normalcy.

Acknowledgments

The authors want to thank the sponsoring institutions for the Institutional resources to complete this Editorial Perspective.

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Citation: Tulp OL, Einstein GP. The evolution and global impact of Covid-19 and Omicron: the way forward? *Int J Fam Commun Med.* 2022;6(1):11–13. DOI: 10.15406/ijfcm.2022.06.00255