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FACTORS which WILL DETERMINE THE FATE OF COVID-19

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Conflict of interest

I declare that I have no conflict of interest

Abstract

The aim of this research is to show the result of struggle between the international community and COVID-19 after administration of vaccines which based on current fundamental factors. Covid19 has caused real threat to the entire world in the past 2 years. Nearly 5 million have been dead since its occurrence and many countries have been severely hit economically during imposing mandatory lockdown which led to paralyzing of all life facilities. Global efforts have been united to find a safe and effective vaccine against COVID-19 to prevent the devastating consequences if the virus left untreated. Many pharmaceutical companies have managed to produce different types of vaccines based on different known technology such as Pfizer, AstraZeneca, Moderna, Jonson and Johnson, Sinopharm.

There are many factors which will determine the fate of pandemic among them:

1. High mutation rate of SARS-COV-2 due to lack of error correcting process(proofreading) which means the virus capacity to proofread and remove mismatching nucleotides during genome replication and transcription.
2. sustainability of the antibodies induced by vaccine and evaluation the period of its effectiveness.
3. Inequalities in distributing of vaccines worldwide which made many low- income and developing countries unable to vaccinate their people while some developed countries started to give a booster dose at least 6 months after completion of primary vaccine series.
4. Impact of misleading rumors of using COVID-19 vaccines.

Introduction

Corona viruses are group that belong to the coronaviridae family in the order Nidovirales 1. COVID-19 is caused by a novel coronavirus called SARS -COV-2. The most common symptoms were fever, dry cough, loss of smell and taste and fatigue 2. More severe symptoms include shortness of breath, reduce consciousness, neurological complications such as stroke, brain inflammation, cardiac problem, lever dysfunction and systemic hyperinflammation with multiorgan failure and death 3. 80% of patients recover from the disease without need to hospital admission. About 15 % have serious illness which require oxygen, while 5 % become critically ill and need intensive care 4. Aging people with underlying chronic disease are at

higher risk of developing serious or critical illness and death. Some healthy adults without known serious chronic illness may be vulnerable to severe complications and or death by COVID-19.

In general, clinical outcomes of the disease range from spontaneous viral clearance and severe illness or death specially among elderly people with underlying conditions. Symptoms of new Omicron variant were the same as a common cold, including headaches, sore throat, runny nose, fatigue and sneezing. No cough or loss of smell and taste had been reported for first person infected with Omicron variant, according to Angeque Coetzee, chair of south African Medical Association 5.

SARS-COV-2 is single strand positive sense RNA- virus that replicate inside host cell by hijacking cell machinery. RNA viruses, like SARS-COV-2, can mutate in larger extent than DNA viruses because RNA polymerase that copies the virus genome generally lacks proofreading skills, which makes RNA viruses prone to high mutation rate- up to a million times greater than the DNA- containing cells of their host.

Mutations happen in the genetic material responsible of spike protein production which consist of 1300 amino acid. Spikes attach to host respiratory angiotensin converting enzyme receptors within respiratory system which enables virus to penetrate inside the cell more easily and this in turn would facilitate virus to replicate and create thousands of copies of virion to transmit and infect neighboring cells in short period of time.

It's worth to note that there are thousands of different types of COVID-19 circulating across the world because viruses can mutate all time, but some of such mutations can cause significant genetic changes in bases sequences of RNA which in turn lead to changes in type of spike glycoprotein. Immune system produces antibodies against many parts in the spike protein of virus either by natural infection or vaccines, so if some of these antibodies don't work against some mutational changes in some places, the other will remain active, because virus cannot change every single epitope on its surface by which antibodies recognize virus, if virus did this so spike protein will lose its function. Influenza viruses evolve more rapid than SARS-COV-2 since it compromise of 8 RNA segments which facilitate mutation with different strains, therefore influenza vaccine must match strain circulates to provide right protection.

Five variants of SARS-CoV-2 have been recorded by WHO: the Alpha variant (formerly called the UK variant and officially referred to as B.1.1.7). The Beta variant (formerly called the south Africa variant and officially referred to as B.1.351). The Gamma variant (formerly called the Brazil variant and officially referred to as P.1) and the Delta variant (formerly called the India variant and officially referred to as B.1.617.2). Delta variant causes more infection and transmit

faster than first original form of COVID-19. SARS-CoV-2 Omicron variant (B.1.1.529) has first emerged in South Africa on 24 November 2021.

WHO designated it a variant of concern and named it Omicron on 26 November, 2021. Approximately 60 mutations occurred in this new variant which included 32 mutations in the spike protein, main antigenic targeted by antibodies generated after Covid-19 infection or vaccination. Such high number of mutations need a long period to evolve inside person who has weakened immunity system like HIV infection, without killing its host and survives by necessary supportive treatment. More than 20% of south Africa population suffering from HIV and effective therapy are not available for millions of them due to shortage of access to health institutions. Immunocompromised population In South Africa without proper therapy against HIV may increase the risk of emerging new more transmissible and infectious SARS-CoV-2 strains.

Scientist are concerned that significant mutations in spike protein targeted by vaccines may give the virus the possibility to evade immune system and update of available vaccines be inevitable. COVID-19 vaccines and boosters are still effective against Omicron variant at preventing severe illness and death as in the beginning of pandemic, but its easily transmissible will very likely cause more fatalities and hospitalizations according to European center for disease prevention and control 6. It's very important to accelerate the vaccination rate, in all countries and encourage hesitant individuals to administer it in order to prevent such consequences. COVID-19 vaccines have succeeded to protect people against different virus variants, but Pfizer has begun to modify vaccine to meet changes in genome sequences of omicron variant to prevent escaping from host immunity system and provide more protection.

High risk group of people are vaccinated yearly against influenza virus, when scientists predict which version of virus variants will dominate, because virus has the capability to induce mutation in high rate compare with DNA viruses. Titer of antibody produced by influenza vaccines reduces with time, this has raised concern that SARS COV2 will take the same track as we know both viruses belong to the same family (RNA viruses), but influenza virus has higher mutations rate than SARS-COV-2 because genome composes of eight segmented RNA which give influenza virus this privilege while COVID-19 composes of single strand RNA.

Clinical trials have been conducted to show how long dose antibody last in the blood after vaccination and this is the main issue that scientists have raised concerns about. Most vaccines consist of two doses with 3-4 weeks apart, but interval has been prolonged to 6 weeks in most countries to allow more people to be vaccinated. There is two term which are very important in vaccination industry: efficacy and effectiveness: Efficacy mean the ability of vaccine to prevent disease in comparing with placebo group under ideal and controlled circumstances while

effectiveness refers to performance of vaccines in real world. Moderna COVID-19 vaccine has high efficacy with 94% while Pfizer-BioNTech with 95%.

Real- world data shows that Pfizer and Moderna vaccines are effective at reducing the risk of COVID-19, including severe illness by 90% or more in those who are fully vaccinated, while Johnson and Johnson vaccine was 66.3% in clinical trials, People with underlying disease, those who are taking medication are often not included in clinical trials. There are important factors which determine the effectiveness of vaccine such as age, underlying chronic disease, how vaccine is stored and administered. It's not necessary for vaccine to have high effectiveness in order to be useful, influenza vaccine has 40-60% effectiveness but it saves thousands of lives every year.

Sustainability of antibodies

Activation of acquired immune system occurs by offending antigen as natural infection or by vaccine. B cells act as antigen presenting cells when they internalize antigen and presented piece of antigen on MHC II molecules to present antigen to helper T cells. By this process activation of B-cells occurs in germinal centers of secondary lymph organs such as spleen and lymph nodes. Activated B cells begin to differentiate into memory B cells or plasma cells that produce antibodies 7. After differentiation, memory B cells relocate to the periphery of the body where they be more likely to encounter antigen in the event of a future exposure. Differentiating through T cells independent antigen process takes place anywhere in the body8and results in short-lived plasma cells that secrete IgM antibodies 9.

Activation of B cells by T cell-dependent processes are subdivided into primary and secondary response: The presence of T cell at the time of initial contact of B cell with antigen is called primary response which produces short-lived plasma cells that remain in the extramedullary regions of lymph nodes, while secondary response results in producing longer-lived plasma cells that secrete IgG and IgA, and frequently travel to the bone marrow 9. Activation of memory B cells occurs by detection and binding of same antigen shared by parent B cell. The efficiency of memory B cells is the basis for vaccines and booster shots 10. Memory B cells can be very long-lived, studies have shown memory B cells for smallpox persisting at least 60 years after vaccination and Hepatitis B virus vaccination or infection confer such long-lasting immunity.

Plasma cells develop into one of two types of cells: short-lived plasma cells (SLPC or blasmablast) or long-lived plasma cells (LLPC). Lifespan of plasma cell play a key role in determination of how long dose immunity last after infection. Long-lived plasma cells provide long-term protection through releasing antibodies for decades or even continue whole life of individual.11,12. It's important to note that long-lived plasma cells unlike B cells don't need antigen restimulation to create antibody. Continuous production of antibodies is a result of

constant replenishment of short-lived plasma cells by memory B cells re-stimulation, as it was thought. Some studies have shown continuous production of antibodies by long-lived plasma cells in the absence of antigen and depletion of B cells as it occurs with monoclonal antibody treatment 13,14,15. Long -lived plasma cells in the bone marrow are still the main source of antibodies independently of B cells 16. The long-term Survival of (LLPC) is dependent on specific environment in the bone marrow, the plasma cell survival niche 17.

Long-lived plasma cells secrete high affinity class switched antibodies för months, years or a lifetime which are in bone marrow while short -lived plasma cells are formed in the extrafollicular site of secondary lymphoid organs with low affinity IgM antibodies. There are many factors which may determine the durability of antibodies among them:

The life span of plasma cells and memory B cells play a key role in the concept of how long dose immunity continue against any antigen, and this depends on type of signal such as cytokine received from T helper cells during activation of B cells against specific virus like TNF – alfa (tumor necrosis factor-alpha) which can play pro- apoptotic role (promote survival of cell) by inducing the expression of anti – apoptotic gene such as Bcl -2 (B cell lymphoma -2) which result in inhibition of apoptosis 18. Long survival of memory B cell in response to some vaccination or infection is due to therefore in part for presence of anti – apoptosis gene. Immunity response to specific virus determines by the ratio between anti – apoptotic and pro – apoptotic protein which lead to whether a cell lives or dies. If the ration is in favor of anti – apoptotic process, it will result in long survival of cell and vice versa. Genetic process governs immunity response against offending virus which explain in part the difference in survival rate of plasma cells and memory cell. Inhibition of P53 (tumor suppressor gene) by many viruses' protein such as HBV (Hepatitis B virus) protein 19 has been shown to induce anti – apoptotic process, since p53 cannot induce its transcriptional transactivation activity (expression of proapoptotic protein) in the apoptosis. This may give us explanation why nearly all newborns who become infected with the HBV develop lifelong hepatitis B and 10% of adults develop a chronic infection that can lead to cirrhosis and liver cancer (hepatocellular carcinoma). The integration of HBV-DNA into host genome confers this risk. The nature of HBV genetic makeup gives it the ability to persist, in different percentage in both children and adults, in the body for whole life and this is also may explain long lasting immunity which generated either by natural infection or by vaccine. B cells which differentiate into long- lived plasma cells and long-lasting Memory B cells may occur due to presence of anti-apoptotic protein in virus gene during T helper- dependent activation of B cell. Memory B cells activated through the same antigen shared by parent B cells (both act as antigen presenting cell), this can in turn stimulate expression of anti-apoptosis genes in memory B cells. The nature of virus gene may determine

the response of immune system cells regarding durability of immunity. SARS-COV-2 lacks in part this privilege to maintain durable immunity.

Booster shot

Booster shot is defined as extra administration of a vaccine after primer dose. It's needed to increase immunity against that antigen to same protective level which has declined over time.There are several ways to evaluate the need for a booster dose after a primary vaccination:

1. Through measuring the level of antibodies against a disease after a time has passed since administration of vaccine, if it declines with time so the need for a booster dose is necessary and justified.

2. Detection of immunological responses to primary vaccine: If it was rapid, there is no sufficient time for the body to create memory against the disease and number of memory cells will not be high for a long period of time20.

3. Memory B and T cells count against antigen can be measured after passing a certain time following administration of vaccine.

4. By screening the prevalence of the disease in vaccinated populations.

According to the criteria above, there are some vaccines such as Tetanus need a booster shot every 10 year21 while hepatitis A and B vaccine is effective for entire life. It's worth to note that administration of booster dose with the presence of already high amount of antibody could develop to Arthur's reaction which is type III hypersensitivity induced by high level of IgG antibodies causing inflammation which is often self-resolved after a few days. It's important to increase time between primary dose and booster dose22.

COVID-19 is a novel disease which became pandemic in short time, international efforts have been gathered to find safe and effective vaccine against it, so many famous pharmaceutical companies such as Pfizer- BioNTech, AstraZeneca, Moderna, Johnson and Johnson, Sputnik Russia, Sinopharm-China and other have conducted clinical trials in 3 phases. FDA in USA and other domestic health authorities in other countries have authorized COVID-19 vaccines for emergency use after reviewing their clinical trials data.

Vaccines have contributed to declining the infection and mortality rate in many countries which resulted in easing most of healthy restrictions imposed during pandemic surge. Pfizer-BioNTech, Moderna, AstraZeneca, Sputnik and Sinopharm vaccines have been given in two doses, while Janssen and Janssen given in one dose. Many developing countries have not been vaccinated their populations due to unfairness in distribution of vaccines.

Israel was one of first countries which started to vaccinate their people early and removed all precautionary measures against Covid-19 after decline of infection and mortality rate following vaccination. Delta variant changed situation dramatically due to increasing of infections number among vaccinated people which indicated breakthrough infection which justified giving a booster shot.

Pfizer-BioNTech has conducted clinical trials to show the effectiveness, side effect and benefit of the booster dose after at least 6 months of completion of full vaccination which indicated higher antibodies titer that boost immune protection. The most important issue facing the effectiveness of vaccine is the declining of antibody titer over time which could results in reinfection of vaccinated population according to Pfizer experts.

Pfizer asked FDA to allow a booster shot of its COVID-19 vaccine to be available for everyone 18 years age and older to boost immunity response and getting more protection against delta variant. FDA amended the emergency use authorizations for both Moderna and Pfizer-BioNTech COVID19 vaccines authorizing use of a single booster dose for all individual 18 years of age and older after completion of primary vaccination with any FDA- approved COVID-19 vaccines.

Before that a single booster dose of Moderna and Pfizer-BioNTech COVID-19 vaccines was authorized for administration to individuals:

- 65 years of age and older.
- 18 through 64 years of age who are at high risk of severe COVID-19.
- 18 through 64 years of age with frequent occupational exposure to COVID-19.

Inequalities in distribution of vaccine worldwide

In the beginning of pandemic crisis, there has been fear that developed countries which manufactured COVID-19 vaccines would seize most of doses for their needs. These fears were justified when just 5% of Africans populations have been fully vaccinated while high-and upper middle income countries have vaccinated their populations by 75%. In Latin America and Caribbean countries approximately 37% have been fully vaccinated against COVID-19.

WHO has planned that 70% of the global populations will be vaccinated in the mid of 2022, but in the current unequal distribution, this goal is not possible, and this can pose a big problem which require cooperation of international community to find comprehensive strategies for fighting COVID-19.

UN secretary has considered unfair distribution of COVID-19 vaccines across globe as immoral issue. This has raised questions about obligation of developed countries by human rights principles in the presence huge difference in the rate of vaccination between countries. All individuals regardless of who they are or where they live must have equitable access to vaccine if we want world without pandemic, otherwise world could not beat the pandemic.

The mutations of SAR-COV-2 occur in unvaccinated communities which could threat global efforts to get rid of pandemic in short time, therefore unless there is equivalent distribution of Covid-19 vaccines, no country will be in safe side even if it manages to vaccinate entire its citizens.

COVID-19 has caused economical disasters alongside healthy crisis globally and many communities are still suffering from pandemic consequences, it will take many years for international economic to be recovered at condition all countries have the same access to COVID19 vaccines.

COVID-19 Vaccines Global Access, abbreviated as COVAX, is a worldwide initiative aimed to accelerate the development and manufacturing of COVID-19 vaccines and guarantee fair and equitable access for every country. COVAX is co-led by the coalition for Epidemic Preparedness Innovations (CEPI), Gavi and WHO, alongside key delivery partner UNICEF. WHO can only achieve its target if the countries and companies that control vaccine supply put contracts for COVAX and the African Vaccine Acquisition Trust- or AVAT- fist for delivery and donated doses. To bring the pandemic under control, the world must use the tools properly and share them fairly.

Increase communities' immunity, protect health-care system, enable deteriorated economies to recover again, and reduce the risk of new variants emerging, all these targets can be achieved by equitable access to vaccines which will speed up the end of pandemic.

Impact of misleading rumors of using COVID-19 vaccine

One of the most important factors which has obstacle the termination of pandemic is misguiding rumors about the hazards of using vaccine against COVID-19. Some people without scientific basis are still spreading unjustified and unreasonable allegations among them:

1 The time needed to conduct Clinical trials for efficacy and safety purposes of COVIOD-19 vaccine was short.
2 Messenger RNA vaccine such as Pfizer-BioNTech and Moderna may interfere with genetic material of recipients.

3 COVID-19 vaccines may cause dangerous disease in future such as infertility.

4 Natural immunity (Herd immunity) is better than vaccination.

By scientific concrete evidence we will disprove all these allegations. As it's known that any vaccine must pass three phases of clinical development trails to ensure efficacy and safety:

Phase 1: vaccine is given to small group of healthy volunteers to make ensure immune response and monitoring possible side effects.

Phase 2: After successful clinical trials in phase 1, larger group of people will be involved to establish efficacy in treating and preventing the condition, to make sure appropriate dosing level and to make comparison with placebo group.

Phase 3: Thousands of participants are participated to demonstrate the safety and efficacy of the vaccine, confirm effective dose, identify side effects. The virus must be circulated during the trails to determine if the vaccine is effective to protect against the virus or disease.

In the case of Covid-19 vaccines Phase I and phase II clinical trials were combined to help speed up the process, safety and immunogenicity were measured which were cornerstone in determining if the vaccine to be licensed. International efforts and big funding have accelerated and shortened the time to manufacture a safe and effective vaccine to about 10 months. vaccine effectiveness and possible new side effect continue to be monitored in real-world after delivering of vaccines to recipient.

Are vaccines interfering with genetic material of recipients?

People were affected by misinformation that vaccines such as Pfizer-BioNTech and Moderna interfere with DNA of host cells which in turn would change genetic characteristics of recipients. It was one of most important rumors which results in decreasing vaccination rate worldwide and many people have lost their life due to misleading information. ordinary individuals should not be blamed when they see some doctors and social figures who have contrary opinion are involving in debate that vaccines may pose danger on their lives in future due to this interference. m RNA-based vaccine is a technology depends on entering part of genetic material into the cell in the form of mRNA- molecules responsible for spike protein production which can temporarily produce this protein. mRNA is large molecule that cannot enter the cell on its own. The lipid nanoparticles help the mRNA molecule to be taken up by cells. mRNA is not integrated into DNA and in addition mRNA molecules beak down rapidly. Within first day's most of protein is

produced but some protein has been found after 10 days. m RNA vaccine does its job inside cytoplasm of cells and not in nucleus of cell where DNA is located and therefore there is not integration between them.

The myth that COVID-19 vaccines cause infertility

This is other misinformation spreads in social media that administration of COVID-19 vaccines can cause male infertility and erectile dysfunction without any concrete evidence that supports this allegation. The true is that SARS-COV-2, the virus that causes COVID-19, poses a risk for both disorders especially those who had a severe case. A study of 45 men which was conducted at the university of Miami on vaccine safety showed that the Pfizer and mRNA vaccines appear safe for male reproductive23.

Several viruses, including Ebola, Zika, herpes simplex, Epstein-Barr, human papilloma. HIV and mumps have been known to cause temporary or permanent fertility issues, and orchitis, a painful inflammation or swelling of the testes.

To preserve male fertility and sexual function against complication of disease, its necessary to get COVID-19 vaccines. All misleading rumors which spread fear among people that vaccines could bring about infertility have unscientific backgrounds.

In the entire history of vaccines, no side effect has been occurred more than 2 months after administration of vaccine, therefore it's not true that vaccine will cause unknown side effect after 10 to 15 years or more.

Is herd immunity better than vaccination to reach community immunity?

Skeptics to vaccination have argued that herd immunity is the best way to defeat pandemic by reaching community immunity by natural infection. This allegation is not acceptable and unreasonable for the following important causes:

1. Risk groups such as elderly people with underlying conditions, immunocompromised and organ transplant patients could die from complications of COVID-19.
2. In order to reach 80% of community immunity we need long time while short time is required by vaccination.
3. Overstrain of public health institutions due to high number of infectious people who need hospitalization and admission to intensive care units.
4. Allowing the pandemic to spread in community and causes high mortality and morbidity rate is against human rights and not moral issue.

5. Devastating economic and social consequences of pandemic pose a real threat to many countries if last for a long period of time.
6. Thanks to vaccination, many pandemics in the past decades have been stopped or eradicated such as Polio, measles, smallpox, Rubella, mumps and other, which saved millions of lives worldwide.

Conclusion

COVID-19 is still threating international community despite presence of a safe and effective vaccines which be produced by famous and credentials pharmaceutical companies. Mutations of COVID-19 pose a future obstacle when potential significant change in base sequence of mRNA could lead to emergence of new strains of COVID-19 which resist available current vaccines. We acknowledge that update of current vaccines will not take more time to adapt changes in structural of genetic material of virus as it occurs with influenza virus. SARS-COV-2 can mutate in unvaccinated population which shed light the importance of free access to vaccines for everybody in the world. The first step to prevent spreading of COVID-19 and recurrence of high infection and mortality rate again as in the beginning is understanding that this pandemic is a common threat for all communities and no nation will be in safe side if there is no fair distribution of vaccines globally.

There is no in the present time equitable free access to vaccine for all countries while 50 state have failed to achieve the goal applied by world health organization to vaccinate 10% of their populations in the end of September 2021. Most of these states located in Africa continent which are classified as poor and low- income countries, there just 4.4% of population get vaccinated according to world health organization. In addition to difficulties in getting vaccines, these countries are suffering from fragile infrastructure health sector which obstacle the storage process of vaccines. Many of more vaccinated countries belong to middle or high- income which purchased directly from manufactured companies.

World health organization aspired to vaccinate 40% of world population in the end of 2021. Misleading rumors against COVID-19 are still one of main factors which hinder increased rate of vaccination worldwide. There was deficit in scientific debates or programs in social media or states-run media which expose these unbased allegation. Success of COVID-19 vaccines in decreasing mortality rate across world helps skeptics from taking vaccine to change their mind and a lot of people deserted these allegations and took required doses. It’s important to impose hard juridical measures against those who without scientific evidence try to spread unguided information against administration of COVID-19 vaccines in social media and debates which

affect negatively people towards boycott of vaccination. A lot of people have lost their lives or suffering from severe COVID-19 complications since they believed such rumors and did not take vaccines.

Sustainability of antibody following completely of vaccine series pose hornstone in prediction of how world will seem after delivering of COVID-19 vaccines. As documented scientific fact that antibodies, after completion of a 2-dose m RNA primary series, declined over time and the need for booster shot become necessary for all individuals of 18 years of age and older according to FDA authorization. Before that a booster shot was authorized to some category of population as mentioned above. We should answer the most important following question regarding COVID-19 and its vaccine:

1- Why has antibody level declined following SARS-COV2 infection or vaccination?

2- Why dose immunity last for a long period of time after vaccination or natural infection in some viruses?

3-What is the fate of SARS-COV-2 following scheduled booster shot for all individuals?

Durability of immunity depends on many factors such as nature of antigen, types of signals such as cytokines received from T help cells, integration of genetic material of virus or bacteria with host DNA, presence of anti-apoptotic gene that interfere with genetic makeup of immune system cells. Declining of antibodies following natural infection or vaccination over time indicate that ability of plasma cells and memory B cells to maintain stable and effective antibody level, diminished due to shortness of their lifespan.

Replenishment of plasma cells requires restimulation of memory B cells to maintain protective level of antibodies which explain the need for booster dose in the setting of COVID-19. Long-term immunity against Virus can be due to forming long- lived plasma cells which resides bone marrow to continuously produce antibodies without restimulation of memory B cells. Immunological response can also play a role in determining sustainability of immunity, rapid stimulation to antigen results in adequate time to create memory against antigen and subsequently memory cells will not be in sufficient number to create immunity for entire life or for a long period of time.

Memory B cells against specific antigen at some point can lose their function or undergo apoptosis (programmed cell death) at certain point. Long survival memory B cells is hypothesized due to expression of anti-apoptosis genes on their surface cell. Presence of anti-apoptotic genes in virus genetic makeup may play a role in long- lasting immunity due integration of genetic material of virus with Host immune cells, characteristic that COVID-19 does not have since virus cannot enter nucleus of cell. We must take in consideration that high

mutated strains may emerge which can escape immunity which obstacle the global efforts to curb pandemic.

The researcher has concluded that:

1. Immunity produced by COVID-19 vaccine declines through time according to confirmed clinical trials data, individuals may need regular or multiple booster dose in the future to maintain immune response. This explanation based on the antibody titer against SARS=COV-2 decreased after several months following the second dose of the Pfizer-BioNTech vaccine.

2. SARS-COV-2 will not disappear like other zoonosis pandemics therefore, vaccination and booster shot will remain the best way to protect our communities against it which render virus less detrimental and decrease its spreading which in turn may prevent emergence of new mutation, the condition by which COVID-19 may convert to endemic.

3. More infectious and transmissible strains of SARS-COV-2 may emerge in unvaccinated populations due to unequitable distribution of vaccines. This poses a tremendous obstacle facing world health organization efforts to combat the pandemic. Ensure free access to vaccines for everybody is the optimal option to protect against sever COVID-19 and emergence of its dangerous strains.

4. Modify COVID-19 vaccines is possible to face emergence of highly mutated coronavirus variant which resist to existing vaccines, but Booster shot is required to protective antibody level in order to combat Omicron variant and prevent its spread. Modified vaccine which will be produced by Pfizer can also be used against it.

More studies are needed to evaluate the sustainability of immune response after booster shot.

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