

Vaccine Development Amidst Covid-19 Pandemic and Explorations for its Cure: Which Side of the Divide are we on? A Perspective Research Work

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ABSTRACT

With the continuous effects of COVID-19 pandemic on various aspects of human, material as well as economic endeavours across the globe, intensive research for a lasting cure to the disease include quest for development of effective drugs and vaccines. This paper is a synopsis of the global COVID-vaccination efforts. It reviewed and constellated materials on COVID-19 vaccine production, its distribution, administration and overall impact on the control of the COVID-19 pandemic and highlights lessons learnt. Information on candidate COVID-19 vaccines recommended for Emergency Use Authorization (EUA) were obtained from various media sources and search engines (Google scholar, PubMed, Electronic and print media, Newsletters). The results were analyzed using descriptive statistics. We observed the urgency posed by COVID-19 pandemic, did not allow for thorough clinical trials for all the currently available vaccines before their widespread public consumption and there is asymmetrical vaccine distribution and uptake between the low and moderate income countries. The unmet COVID-19 vaccine needs in Africa have been inadequate for several reasons. The vaccines have nevertheless shown immense efficacy and effectiveness. Whether there will be sustained effectiveness and resilience of these vaccines to mutant newer strains of the corona virus in the future remains unknown. With the little evidence of mutant strains, episodic waves of infections and benefit of a lead time, the gap in the global vaccine distribution and administration needs to be more ambitious and focused in terms of international collaborations and media risk communication to improve supply and uptake of vaccines particularly in Africa..

Keywords: Control, COVID-19, Coronavirus, Vaccines

INTRODUCTION

The first case of COVID-19 was reported by the authorities in Wuhan city, China in late December 2019. A reoccurring feature from suspect and confirmed cases investigated by the Chinese government authorities showed that majority of these cases had had contact with a wholesale market in Wuhan. Many of the initial patients were regular visitors to the market, or store owners as well as market employees. There was subsequent global wide spread of the disease even before the local and international health organizations could fully establish in

depth information about the cause, modes of transmission, treatment and control^{1,2}.

As at June 30th 2020, about 10.2 million people across the globe had already been infected with over 500,000 deaths. Globally, there was over 163, 000 new cases and 3, 946 deaths over the previous 24 hours. As shown in Table one the highest infection rate was in the Americas with over 5 million infections and followed by Europe (2.6 million) and Eastern Mediterranean (1.0 Million). CDC, WHO, Johns Hopkins.

Table 1: Global burden of COVID-19 burden by region as at 30th June, 2020

Region	Cases	Deaths
Globally	10,185,374	503 862 deaths (3 946)
Americas	5,136,705	247 129 deaths (2 338)
Europe	2,692,086	197 254 deaths (416)
EasternMediterranean	1,058,055	24 423 deaths (535)
SouthEastAsia	784,931	21 593 deaths (515)
Africa	297,290	6 010 deaths (131)
WesternPacific	215,566	7 440 deaths (11)

(WHO Situation Report 162)³

The spread of the coronavirus have been through successive waves at alarming rates. By the end of June 2021, a year afterwards, the total global estimate of infections is over 180.4 million with total death toll of at least 3.9 million people. Evidence shows that America, Europe and South East Asia recorded the highest rates of infections of 71.8 million, 55.7 million, and 34.6 million respectively while the lowest infections estimates were observed in Africa (3.9 million) and Western Pacific (3.5 million).

Several infection prevention and control measures that included pharmaceutical medications ranging from antimalarials (Hydroxy-chloroquine), antifungal (Itraconazole), antifilarial (Ivermectin), antidiabetic (Metformin), antihypertensive (Calcium Channel

Blockers, Angiotensin II Converting Enzyme Inhibitors), anticancer (Tocilizumab), and antiviral (Remdesivir). As of October 22, 2020, remdesivir, an antiviral agent, was the only drug fully approved for treatment of COVID-19. It is indicated for treatment of COVID-19 disease in hospitalized adults and children aged 12 years and older who weigh at least 40 kg.

The non-pharmaceutical preparations include an array of food supplements such as selenium, calcium). There have been policies and protocols, COVID-19 prevention and treatment measures at global scale have been deployed with no prospect of cure in view. Early enough, there was concurrent attention on the production of vaccines to complement control measures. These aimed at boosting immunity and reducing transmission rates through herd

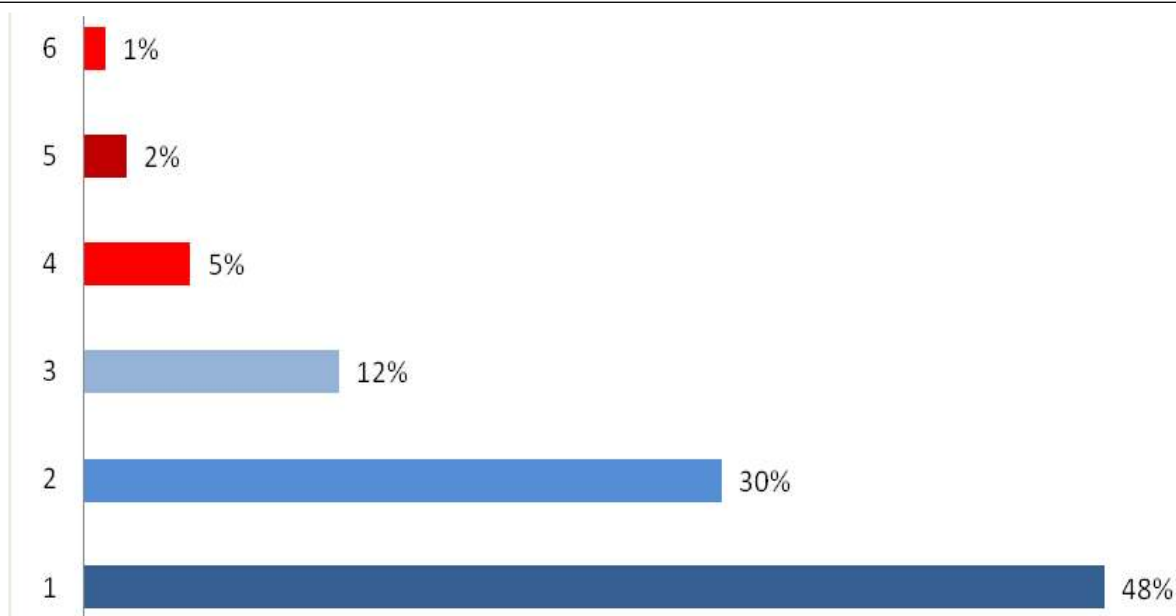


Figure1: Global COVID-19 infections and deaths as at 27th June 2021 (WHO: COVID-19 Weekly Epidemiological update, 46th Edition)⁴

Key: 1- Americas (1,887,725;48%), 2-Europe (1,181,135; 30%), 3- South-East Asia (484,397; 12%), 4- Eastern Mediterranean (215,325; 5%), 5- Africa (94,323; 2%), 6-Western Pacific (53, 826;1%), N= 3,916,771

immunity.

At present, several vaccines branded by different pharmaceutical companies have passed through accelerated clinical trials and competitive processes and are being administered across the globe^{5,6}.

Stages in Vaccine Production

Before a vaccine is approved and licensed for human administration it has to go through a systematic and highly regulated process.⁸⁻¹¹ The degree of scrutiny over a vaccine is intensified as the vaccine approaches the final stages of licensure for human use and is usually more rigorous than the process for other drugs. This is due to the high sensitive nature of vaccines and the possible adverse effect from wrongly constituted or contaminated vaccines. Generally, the following stages are involved in vaccine production.

a. Exploratory stage: This stage is laboratory based and may last between 2 to 4 years⁸. The main activity of this stage is the identification of the actual constituent of the

antigen potent enough to challenge and elicit immunological response to protect the host against the identified disease. The constituent could be natural or synthetic antigenic substances: either viruses or virus-like particles, bacteria or bacteria-like particles, weakened microbial toxins or some pathogenic substances, and Pre-Clinical Stage: This stage involves researches using cell line cultures and animal inoculation.

Ascertaining the safety of the candidate vaccine on in-vitro human cells, tissues and laboratory animals is accompanied with determining the potency of its immunogenicity. The most suitable route of administration of the candidate vaccine is established with a safe starting dose. Subsequent safe doses for the next phase of trial may be constituted here. Challenge studies may also be carried out at this stage whereby animals are vaccinated and then deliberately infected with the virulent pathogens to establish the preliminary potency of the vaccine under development. This stage normally lasts for 1 to 2 years and several vaccine trials often fail to progress

beyond this stage⁹.

b. Institutional Review Board Approval: If a candidate vaccine passes through the above stage then the body of researchers involved in the study or their sponsors would apply for ethical approval from licensed and accredited institutional review board with sufficient and convincing information on the safety and non-maleficence of the candidate vaccine on humans. The possibility of serious long and short adverse drug reactions and associated complications following administration of the vaccine are all checklisted before ethical approval is granted for the clinical trials¹⁰.

c. Phase I Clinical Trial: This stage involves studies with human subjects of a smaller number of 10 to 30 volunteers. The aim of this stage is to ascertain how humans would react to the vaccine in real life situations and its safety. This stage also helps to establish the type and extent of immune protection the vaccine would produce; those administering the trial vaccine, those being administered the vaccine and as well as those receiving the placebo are not blindfolded. All findings are properly documented and examined to determine whether or otherwise to proceed to the next phase of trial. If the vaccine is primarily meant for children, it is first of all tested in adults and it is not until efficacy and safety is established is the trial dovetailed to children¹¹.

At the end of phase I clinical trial which normally last from several months to a year, the following questions could be sufficiently answered such as: what is the dose and frequency of administration of the vaccine?, what are the actual side effects or problems associated with the vaccine?, and how does the vaccine generally affects those who it has been administered?¹²

d. Phase II Clinical Trial: This stage is premised on satisfactory results of the candidate vaccine in phase I clinical trial and it involves a larger number of participants of several hundreds of thousands. This trial marks transition from a controlled clinical trial to a field evaluation of a vaccine among the target population and it typically lasts from several months to 2 years. This phase looks again at vaccine preparation as a whole, the optimal dose and the exact schedule of administration amidst

other socio-demographic variables such as gender, age, occupation, race, alcohol and cigarette consumption among others. Data obtained is usually subjected to statistical analyses and conclusions are drawn about the potency, efficacy, and duration of action, immunogenicity and other immune-physiological characteristics of the candidate vaccine. Phase II trials may also be able to pick very rare but serious side/adverse effects that could not be identified in phase I trials due to the relatively low sample size.¹³

Under phase II clinical trial, human challenge can be carried out and is generally referred to as IIa where participant who have been immunized with the candidate vaccine are intentionally infected with the pathogen the vaccine is meant to protect against. Participants are observed to establish the preliminary efficacy of the vaccine. The utility of human challenge process lies in its pivotal role in shortening the duration of production of candidate vaccine where the catastrophe caused by a pathogen calls for an urgent and accelerated vaccine production.¹³ It is also reserved for diseases that could effectively be managed with a lasting cure.

Phase III Clinical trial: When a candidate vaccine has successfully passed phase II clinical trial it is then subjected to phase III clinical trial. The main objective of this phase of trial is to establish the safety and efficacy of active ingredient of a formulations i.e. vaccine. The tests are carried out on a large population of people involving several countries. It involves the collection of serological data from a significant section of the vaccinated both at the pre- and post-vaccination periods and also from those classified as vaccine failures. Either experimental or observational research approach can be adopted to gather information; however the most reliable approach is the prospective randomized double-blinded controlled study in which confounders and mediators that could influence the study outcome are made constant. Nested cohort studies, longitudinal prospective cohort studies, retrospective otherwise known as historical cohort are a few research designs that can be used for population-based vaccination interventions or pre-exposure cohort studies for a population at risk. Case-controlled studies,

observational studies and uncontrolled open population studies are other alternative approaches to this phase of trial.¹⁴

This phase of trial establishes immunological correlates of protection as its end points after administering both the candidate vaccine and placebo into the study populations. Information on antibody sero-conversion, antibody titre, duration of memory, the number and duration of booster doses are all established in phase III trial and follow-up of the entire population is required up to post-licensure period of vaccine commercialization. The sample size should be sufficiently large enough in order to establish the probability of occurrence of very rare serious adverse events of 1/100, 1/1000, 1/10,000, 1/100,000 and even more. All the severe adverse events are properly documented concerning every vaccine including all the socio-demographic parameters of the subjects and associated environmental factors as well.¹⁴

Phase III clinical trial outcome gives a guide on the fate of the candidate vaccine as to whether there is need to modify the vaccine composition to address any documented severe adverse events, their direct association with the vaccine; how successful management of these severe adverse reactions or how life threatening it could be; and whether the vaccine should be suspended temporarily or permanently. This phase of trial lasts few months, few years and when successful, manufacturers tend to apply to the regulatory agencies for marketing and wide-scale unrestricted public administration.¹⁵⁻¹⁷

Phase IV Clinical Trial: This is also called post-licensure studies and surveillance, and it is usually observational cohort or case control studies where there is no more standardization of subjects, evaluations, immunizations as well as laboratory procedures. This phase of trial tries to gather further information that could not be obtained during phases I to III clinical trials. These include: vaccines and other drug interactions; optimum activity in specific age groups; gender differences; vaccine changing strains; efficacy in immune-compromised subjects, elderly as well as patients with specific diseases; and ability to sustain long term efficacy and safety.¹⁹

Post marketing surveillance helps manufacturers to know whether a new antigenic strain has evolved that has rendered the candidate vaccine ineffective. A mechanism of pharmaco-vigilance is instituted at this stage by the national drug regulatory bodies to gather all relevant information on adverse reactions associated with the new vaccine. Persons in the communities under surveillance are expected to report such cases for proper documentation and publication upon confirmation.¹⁸⁻²⁰

By 30th June 2021, exactly one year and a half since announcement of a novel Coronavirus causing disease (COVID-19), several COVID-19 vaccines were already in circulation. Some of the vaccines were administered within less than a year of the outbreak of this disease.^{21,22} The vaccines presently in circulation or at the final stage of clinical trial Pre-licensure are:

- a. Abdala Vaccine. Abdala is produced by Cuba's Centre for Genetic Engineering and Biotechnology. Cuban government announced arrival of this vaccine to the world on 22nd June 2021. It is a three-shot vaccine with efficacy of 92% on COVID 19 disease. There are no available reports about the successes of the clinical trials of this vaccine as data from clinical trials is still being analysed, and also no reports of its efficacy rates on the various variants of SARS CoV 2 across the globe¹².
- b. Soberana 2 Vaccine. Soberana is produced by Cuba's state-run Biopharma Company BioCubaFarma. By its second shots of the recommended three doses, the efficacy of Soberana is 62%. Just as Abdala, there are no available reports about the successes of its clinical trials as results are being awaited from analysis of concluded trials; neither are there available records about its efficacy on the various SARS CoV 2 variants round the globe²³.

In March 2021, the Cuban health authorities commenced vaccination of health officials with the two locally produced vaccines Abdala and Soberana 2 even before the results of clinical trial were out due to the rapid spread in the country. Government intends to vaccinate at least 1.7 million of the entire 2.1 million inhabitants of Havana by August 2021

where the infection is most severe, and eventually to vaccinate the entire 11.2 million people of the island. Cuba is at present working on at least five other vaccines which are at different stages of development.

- c. **Sputnik V Vaccine.** In August 2020, Russia's National Research Centre for Epidemiology and Microbiology gave approval for the use of Sputnik vaccine with the demonstration of the first dose publicly administered to the daughter of the Russian president Vladimir Putin. The vaccine had barely completed Phase II clinical trial and yet to commence phase III clinical trial. Sputnik was deemed efficacious at 92% after its second shot²⁴.

The vaccine uses a variant of human Adenovirus as a vector to carry the mRNA of SARS CoV 2 and the company has offered to share one of their vector human Adenovirus variant with AstraZeneca to shore up efficacy of her vaccine. Russia's Gamaleya Research Institute is marketing the vaccine worldwide and countries like India, Brazil, China, Hungary, Republic of Korea alongside some other 50 countries have already placed order for supply of the vaccine.²⁵

A recent publication from Lancet describing the phase III clinical trial of Sputnik vaccine and its pronouncement of its efficacy at 91.6% have generated more debate. First, the mode of data gathering and analysis by Lancet appeared unclear and less comprehensive; and second, the result of phase II clinical trial that would have given birth to phase III, if comprehensive, was carried out on only 38 volunteers within Russia. This number is too small to draw statistical inferences and this contributes to the reason the scientific research world view Sputnik vaccine with uncertainty.²⁶

- d. **Moderna.** Preliminary data released on the 16th of November, 2020 showed that Moderna COVID-19 vaccine has an efficacy of 94.5%. It was subsequently authorized for emergency use by FDA on 19th December, 2020. It is also an mRNA vaccine that is stable at 36-46°F. The Moderna vaccines can

thus be preserved in temperatures of domestic refrigerators for up to 30 days while storage of up to 6 months would require temperatures of -4°F. Findings from its II and III clinical trials in children aged 12 to 17 years, as documented in May 2021, showed equivalent immunological immune response and protection as earlier observed in adults. The vaccine is said to be 93% effective at preventing COVID-19 after a single dose but two doses are recommended to be given 28 days apart.

Moderna on the average has 95% efficacy rate, and is reported to prevent severe disease, hospitalizations and death in 100% of cases. Reports of its efficacious characteristics have been documented in the UK, South African and Latin American variants and evidence show reduction in the virulence of the newer Delta variant.^{27,28}

- e. **Pfizer-BioNTech.** This COVID-19 vaccine is a mRNA strand which was authorized for emergency use by the American Food and Drug Administration (FDA) on the 11th December, 2020. The vaccine consisting of mRNA, which codes for the virus spike protein, is encapsulated in a lipid nano-particle as a vehicle to prevent enzymatic degradation of the genetic material by tissue enzymes if injected in naked form. The host cells churn out the spike proteins when injected and on recognizing the viral antigens, the body's immune system is triggered and immunity is mounted against the virulent SARS-CoV 2 wild type. The vaccine is said to have recorded a 95% efficacy in its phase III clinical trial and is stored at -94°F creating some logistic challenges of transport and storage around the developing world.²⁹ Records have shown that it has 100% efficacy against severe hospitalized COVID-19 cases and potentially aversion of death given in two doses, 21 days apart for optimum effect. The vaccine is reputed to be effective against the UK, South African and Latin American variants, however with reduced efficacy; it is also preventive against the Delta variant.³⁰
- f. **AstraZeneca-University of Oxford (ADZ1222).** AstraZeneca and University of Oxford announced an

interim report on the efficacy of their COVID-19 vaccine on the 23rd of November, 2020. Analysis of data from clinical trials in subjects from both Brazil and UK showed that ADZ1222 demonstrated an efficacy of up to 90% reducing severity of the disease and also preventing hospitalizations. Half dose of a full single dose regimen was found to produce 90% efficacy; in another study, a full two dose regimen given one month apart produced 62% efficacy rate. With the two combined, the average efficacy was found to be 70%. The vaccine can comfortably be stored at the temperature of domestic refrigerator of 36-46°F for up to six months.³¹

ADZ1222 uses a replication-deficient variant of a virus in a weakened version of a common cold virus. In this instance, Adenovirus version, associated with infections in chimpanzees. The genetic material of the spike protein is retained to induce infected cells of the host produce the spike proteins after vaccinations; this stimulates cells of immune system to attack the virulent SARS CoV 2 virus and eventually halting the infection.^{31,32}

AstraZeneca vaccine is said to have 76% efficacy against symptomatic COVID-19 infection, 100% protection against severe infections and death, and uniquely 85% efficacious in those 65 years and above with symptomatic COVID-19. The vaccine is however reported to be associated with blood clots and so far, up to 222 cases of blood clot have been reported out of the 34 million vaccinations carried out (0.00007%). Administration of the vaccine has been suspended in several countries due to these alleged associated coagulopathies which are chiefly pulmonary embolism, deep vein thrombosis and thrombocytopenia.

AstraZeneca is given in two equal doses 28 days apart and is reputed to be efficacious against the Brazilian and UK variant but of little effect against the South African type.³¹⁻³³

f. Johnson and Johnson. On the 15th of November, Johnson & Johnson announced that it had commenced her second global phase III COVID-19

vaccine clinical trial with an ambitious target of enrolling 60,000 volunteers worldwide. The vaccine has an advantage of a single dose regime with impressive subject tolerability. The ENSEMBLE is said to produce 66% efficacy at a single shot 28 days post vaccination and 100% efficacy at preventing severe disease, hospitalizations or death after 49 days.³⁴

Johnson & Johnson uses inactivated common cold virus preferably an Adenovirus variant as a vector, and the vaccine has been linked with cerebral venous sinus thrombosis (CVST) and thrombocytopenia. In all, of the 7 million vaccine doses administered so far, only six cases of CVST cases have been reported. The vaccine is given as a single dose and is reputed to be effective against the South African, Brazilian, UK and Latin American variants but with less efficacy against the first two. A new side effect that has evolved to be associated with Johnson & Johnson vaccine is Guillain-Baare syndrome which is a severe neurological autoimmune disease, though also in a very tiny segment of the recipients of the vaccine. And it may be transient in most cases.³⁴⁻³⁶

g. Sinovac Biotech. This China-based COVID-19 vaccine has been subjected to phase III clinical trials in several countries across the globe with different findings among races and groups. In Brazil, it recorded 50.38% efficacy, 65% in Indonesia and 91.25% in Turkey. This vaccine is an inactivated type that uses inactivated SARS CoV 2 viruses; a second clinical trial in Brazil recorded 78% efficacy rate in mild cases but a 100% protection against severe cases, hospitalizations and deaths. As of now, there are not yet available reports on the level of efficacy of Sinovac on the various SARS CoV 2 virus variants.^{37,38}

h. Novavax Vaccine. NVX-CoV2373 vaccine produced by Novavax is the first indigenous COVID-19 vaccine from India. It was unveiled to the whole world by the company on 28th January, 2021 with a documented efficacy of 89.3%. It uses recombinant nanoparticle technology, a full length perfusion spike

protein is made and conjugated with saponin-based matrix-M adjuvant constituting the main active ingredients of the vaccine.

Novavax is stable at temperatures of 2-8°C and is documented to be effective against the South African and UK variants. Reports on Brazilian and Latin American variants are not yet conclusive.^{39,40}

- i. CanSino Biologics. This vaccine was developed in Pakistan in collaboration with the Chinese military. The vaccine is a single dose regime and is reputed to have an efficacy of 65.7% when administered to prevent clinical disease. A phase III clinical trial conducted on 30,000 volunteers showed 90.98% efficacy. Mexico and Malaysia have already placed orders for the supply of this vaccine. The efficacy of the vaccine keeps dropping over a time period of months raising doubts about the actual efficacy of the vaccine. It has been reported that the efficacy of Cansino can drop to 50% over a period of six months following vaccination.⁴²

Cansino uses SARS CoV 2 virus antigen incorporated into an Adenovirus vector as the biological active ingredients. Findings have shown that a single shot of this vaccine will not confer immunity on host beyond six months hence necessitating multiple booster doses. Also, its efficacy on the various SARS CoV 2 variants is not yet known.

- j. Bharat Biotech COVAXIN. This vaccine produced by Bharat Biotech has gone through phase III clinical trial and has shown a 100% efficacy against severe COVID-19 disease with measurable drop in hospitalizations and deaths. Bharat developed COVAXIN by obtaining seed strains of SARS CoV 2 from Indian Council of Medical Research (ICMR) National Institute of Virology and introducing it to 25,800 volunteers recruited into its phase III study. Participants were aged 18-98 years; 10% were above 60 years. The active biological ingredient consists of a whole virion inactivated vero cell combined with an adjuvant to enhance its potency. Already, several million doses of the vaccine have been administered

in India alongside other countries with a proven efficacy of 78% against mild, moderate and severe disease. It is reputed to have a 100% efficacy against hospitalization and death. There are no available records of COVAXIN efficacy rate on the various SARS CoV 2 variants across the globe.^{43,44}

Covid-19 Vaccination In Nigeria

Nigeria received 4 million doses of AstraZeneca COVID-19 vaccine in March, 2021 which has since been exhausted on her over 200 million people. The country received another delivery of close to 4 million doses of the vaccine from the global vaccine sharing scheme COVAX by July ending; another 3.92 million doses of Pfizer/Biotech or Moderna vaccines from COVAX is expected by August ending; and another 3.577 million doses of Pfizer/Biotech or Moderna towards end of year with additional 29.85 million doses of Johnson & Johnson from African Union on the way. So far, Nigeria has administered 3,938,945 doses of COVID-19 vaccine as at 3rd August 2021 with documentation on disease burden at 175, 264 confirmed cases and 2,163 deaths. The rate of spread and transmissibility of the virus in the country has substantially been slowed down with the commencement of vaccination. There are no documented cases of SARS-Cov-2 infections among the fully vaccinated persons⁴⁵⁻⁴⁷

Global Vaccination Campaigns

The ongoing COVID-19 immunization exercise is the largest global immunization campaign in human history. The speed at which vaccines were reeled out with limited clinical trial conclusions about the efficacy, potency, adverse side effects of the various COVID-19 candidate vaccines clearly depicts COVID-19 induced urgency upon the whole wide world. On weighing the odds against the benefits, WHO quickly issued Emergency Use Authorization (EUR) for any vaccine that showed any promise based on consideration of more grave consequences of not having any vaccination at all versus any adverse effects the vaccines could cause.⁴⁸

It appears the entire world population of 7.8 billion people was recruited into a clinical trial for the first time. Global

report especially from the most affected countries such as Italy, USA, Britain, Brazil, Spain, Mexico and India have shown a dramatic reduction in new COVID-19 cases since the commencement of the worldwide COVID-19 immunization campaign. Studies however show fewer cases of fully immunized individuals being infected with the disease and significant reduction in COVID-19 infection among adults especially the elderly in these countries.⁴⁸⁻⁵⁰

With the current 41 million doses of vaccines administered a day globally, it would require at least 6 months for 75% of the world population to be fully vaccinated and hence establish herd immunity. There is concern about the inequity distribution of the COVID-19 vaccines across regions with more of the vaccines disproportionately going to the high income nations 20 times more compared to supplies to Africa and poor regions of India and China, Bangladesh, Iran, Syria. Vaccine distributions have been generally protracted as well.⁵⁰

SARS-Cov 2 Variants, Immunization & Its Challenges

A strong lesson learnt from the challenges of reportage on vaccination and its effects from countries is that stigma is a strong social factor that can affect immunization efforts. To prevent stigmatization, WHO had thereby grouped and renamed the SARS-Cov 2 variants to give them more scientific identity and hence detach their association with any country or region of the world, and encourage reportage of variants from regions and countries. The variants are presently grouped into: variants of interest (B.1.427, B.1.429, B.1.525, B.1.526, B.1.617.1, B.1.617.3); variants of concern (B.1.7, B.1.351, B.1.351.2, B.1.351.3), B.1.617.2, AY.1, AY.2, AY.3, P.1, P.1.1, P.1.1.2; and variants of high consequence which none has presently been detected.

This effort de-emphasizes nomenclature associated with country (UK, California, USA, Brazil, South Africa among others) or pharmaceuticals specific branding of COVID-19 variants. For instance, formally termed Indian variant, the most virulent strain currently causing

epidemic spikes across the globe has been changed to the delta variant.

As well, although, most of the vaccines approved for emergency use have substantial suppressive impact on the virulent delta strain in humans if the vaccines are given on time, there has been limited time span to test for sustained efficacy of the present vaccines in humans over a long term. Garnering from the episodic waves of COVID-19 and the high mutation rate of antigenic composition of Corona virus, there are concerns of reversal of achieved gains in vaccine development due a likelihood of unresponsiveness of highly mutant strains to currently available vaccines.

Precision medicine, computational modeling and predictions are viable tools to deploy to have insight into the sustainability of the vaccines. While the current vaccines appear to have slowed the spread of COVID-19, more research is needed to position ahead of time drugs and vaccines that would neutralize completely new variants that will enter our biosphere.^{48,51-53}

CONCLUSION

COVID-19 pandemic definitely tested and triggered emergency preparedness and response beyond medical input on a global scale. While research continues for effective measures, drugs and vaccines, due diligence to ethical considerations, Good Manufacturing/Medical Practices (GMP) must continue to have the upper hand in ensuring the bio-safety of adopted measures on a global scale.

In spite of the challenges, the efficaciousness of the vaccines in humans is a welcome development however further research must be encouraged over the 80 candidate vaccines at various stages of development and clinical trials across the globe to improve on the duration of potency of the COVID-19 vaccines against newer variants. As we do not know the long term potency and efficacy of all the vaccines presently on display, we should be prepared to scientifically offer a solution to the puzzle: "If we wake up one day and all these vaccines fail to act on a newly emerged highly virulent mutant, what is

then the way forward?”.

Recommendations

1. With the limited time frame to subject COVID-19 vaccines to full experimentation and clinical trials, there are still possibilities of medium or long term adverse effects not presently documented ensuing for which high level pharmaco-vigilance and migration efforts need to be prepared in this regard to especially in more remote or landlocked settings.

2. The wide gaps (0.5% in L&MIC and 80% in HIC respectively) in the distribution of the COVID-19 vaccine and its administration need to be bridged through a more unified international collaboration to ensure cohesive vaccination efforts and reduce migration related re-infection of cleared zones as was experienced in Australia. Nigeria and many African countries remain the least vaccinated and hence may constitute a major hurdle towards early global control of the disease.

Declaration

We declare that we have no conflict of interest.

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