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Immunization Strategies for Prevention of COVID-19 Infection: Regional and Global Analysis

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Abstract: ***Covid-19, affected socio-economic aspects across the world and has proved destructive. Millions of people affected and died due to severity of the pandemic. Several precautionary measures to stop spread of infection has been initiated, however, the entire world is struggling to mitigate its impact and transmission of infection. Experts advocated immunization as an effective mode to control the pandemic but there are challenges of universal access of vaccines particularly among the low income countries. Therefore, in the present study an attempt is made to analyse the spread of coronavirus and impact of vaccination on transmission of infection. Also it is tried to assess challenges of universal vaccination and possible strategy for equitable access of vaccine to combat spread of infection. It is found that intensity of vaccination is helpful to reduce spread of the covid-19 disease.***

Keywords: Covid-19, Vaccination, Immunization Strategies, Vaccine Equity, Vaccine Accessibility

1. Introduction

The whole world is struggling with the outburst of COVID-19, which is responsible for millions of infection cases and deaths. The uncontrolled spread of coronavirus resulted in global disaster and health emergency in many countries. European countries, USA, Brazil, and India are the worst effected economies; however, every country is fighting with Covid-19 infection. Second wave of infection was more deadly across the world and several efforts are taken to find prevention strategies for COVID-19 spread such as isolation, contentment zones, sanitization, social distancing and more. Despite the preventive efforts the transmission of coronavirus infection is continuously rising over the time. Researchers are working to find effective vaccines to curb spread of the infection and some vaccines have been developed and immunization has been begun in most of the countries. According to WHO vaccination is a highly effective method for preventing certain infectious diseases and are in general fairly safe and serious adverse reactions are uncommon, though vaccines rarely protect 100% of the recipients, so all additional precautions against infection should be carefully considered. After Spanish flu and Bubonic plague, Covid-19 is found the deadliest contagious disease which is attributed to its structure due to RNA virus. Studies show that RNA viruses have a higher mutation rate than DNA viruses (1,2). However, it is also observed that DNA viruses can evolve rapidly and they may have mutation rates close to those of RNA viruses (3). Therefore, experts argued that higher mutation of the coronavirus needs intensified efforts to curb the coronavirus' spread as mutations can tweak the building blocks of proteins (4).

Transmission cycle of coronavirus infection is observed in waves since it was first observed in China and adversely affected all nations; many European countries, India, Brazil USA and several other have passed through second and third wave also. The uncontrolled spread of the Covid-19 can be stopped effectively by vaccination of the population across the world. Therefore, immunization process is started and larger share of population of countries like USA and European countries have been vaccinated. Consequently the infection rate of coronavirus transmission is sharply declined in these countries. On the other hand, Asian, African and Latin American countries are struggling for immunization due to non-availability of the vaccines and hence non-immunization of the potential population may escalate infection rate.

The paper aims to present a comparative status of spread of coronavirus and pre-vaccine and post vaccine scenario of infection pattern with case studies and will assess the need of fast vaccination to achieve the herd immunity. It is also attempted to analyse the obstacles faced by the developing and under developed countries in procuring vaccines as they are struggling shortage of vaccines which can affect the immunization process and may be a threat to curb coronavirus infection.

2. Methodology

In the present study, the analysis is based on the data available in public domain like World Health Organization (WHO) and Our World in Data etc (5). We have considered 200 countries including India to analysis the impact of vaccination on coronavirus transmission. Number of new cases, total confirmed cases, total vaccination per hundred, vaccination of population per hundred and the test data is adopted from the above mentioned source. The analysis and inferences will be helpful to make future roadmap to tackle the transmission of coronavirus infection. The data analyzed span the period from 22 January 2020 to 14 May 2021. It was observed a significant growth followed by gradual slow down and 'saturation' in the infection spread, which indicates the influence of factors like Covid-19 management strategies and vaccination in certain countries. However, the involuntary situation pertaining to the covid-19 spread data is beyond the scope of the present paper. A few case studies

of vaccination are also discussed and analysed for comparative assessment of vaccination impact on coronavirus infection.

3. Results

3.1 Global Status of Covid-19 Spread and concern of developing economies

Since, novel coronavirus first case was reported in December 2019, it has spread exponentially around the world and has become a source of severe morbidity and mortality due to progressive pneumonia (6, 7). Observed data demonstrates that the infection load was severe in Europe, the USA, India, Brazil and in certain other parts of the world. Study shows that while some countries can be better described by exponential growth; many other countries are more accurately described by a power law (8). It was found that the growth dynamics of the pandemic followed more power law which indicates more advanced transmission of infection (8). Evidently, coronavirus infection is highly contagious which needs to contain transmission across the nations and particularly in the developing countries as they have no proper health infrastructure and resources. There were more than 168 million infected cases and about 3.5 million deaths across the world by the end of May 2021. USA (33 million), India (26 million), Brazil (16 (million), France (5.6 million) and Turkey (5.1 million) were the top infected countries while Asia (49 million) was on top with infected cases followed by Europe (46 million), North America, (39 million), South America (27 million), Africa (5 million) and Oceania (0.07 million). Global infection load of the corona is depicted in Figure-1.

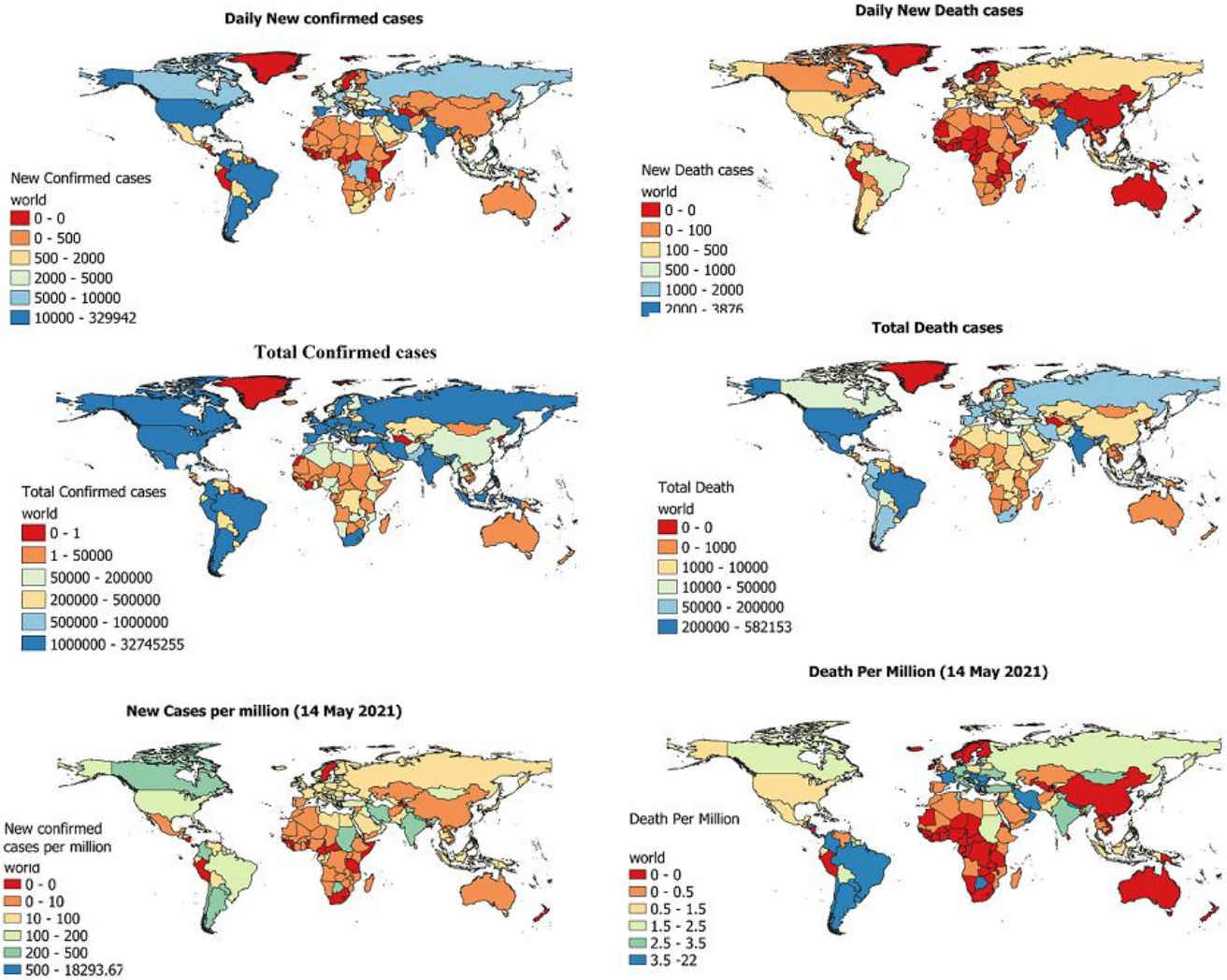


Figure 1: Global analysis of Daily New Confirmed cases, total confirmed cases, Daily New death cases, total death cases, per million new confirmed cases and per million death cases. The data is considered of 14 May 2021. The data is adopted from WHO and Our World in Data.

3.2. Status of vaccination distribution

For reduction in spread of coronavirus, about a dozen of vaccines have approved or under approval process for general and emergency use of in many countries. About 2 billion of doses had been administrated world-wide. Country-wise analysis shows that Israel, UAE, Bahrain, and USA have made significant progress in immunization and vaccinated more than 50% of the population, while many other countries are in process to vaccinate their citizen.

India, China, Russia, Brazil have vaccinated 10-30% of their citizen. However, many other countries have vaccinated comparatively very less or yet to start and available data shows there is low vaccination in the African countries (Figure 2).

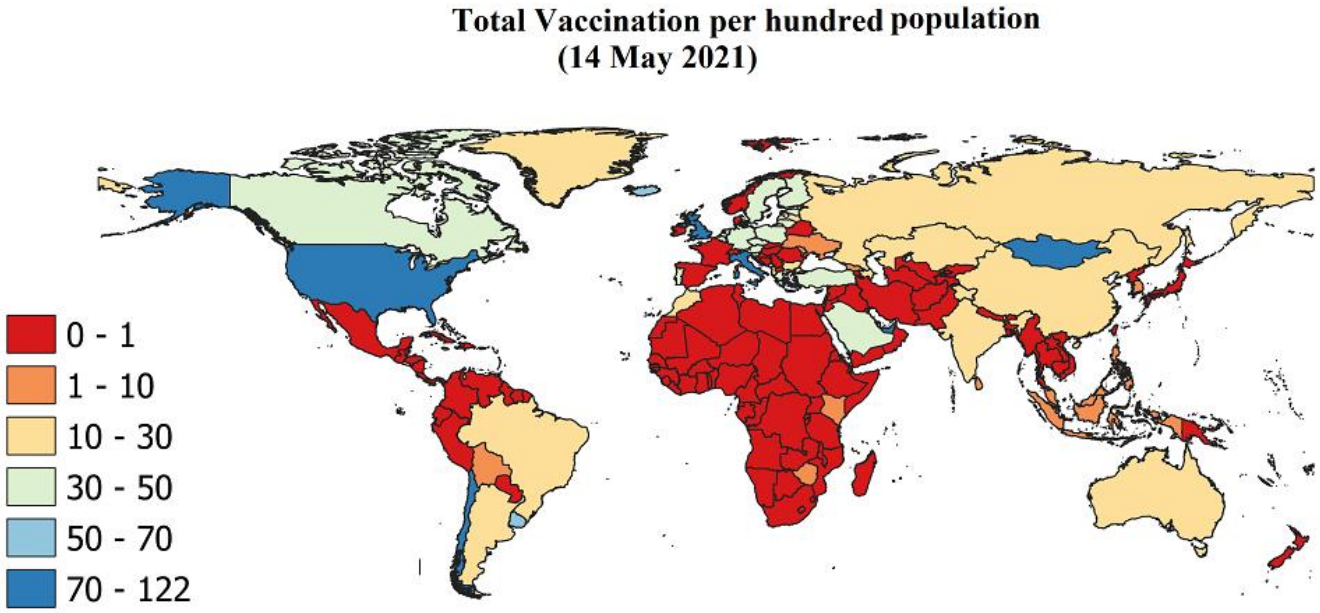


Figure 2: Total vaccination per hundred population for low income countries, lower and upper middle level countries and high income countries. The data is adopted from WHO and Our World in Data.

Similarly, the continent-wise analysis of vaccination shows that the North American countries and European countries have made significant progress in vaccination of their citizens; the total vaccination per 100 population is more than 50%, while the vaccination in Asian and African countries is very poor; which is less than 20% (Figure 3. The average vaccination in world is about 18% received at least one dose of the vaccine (Figure 3).

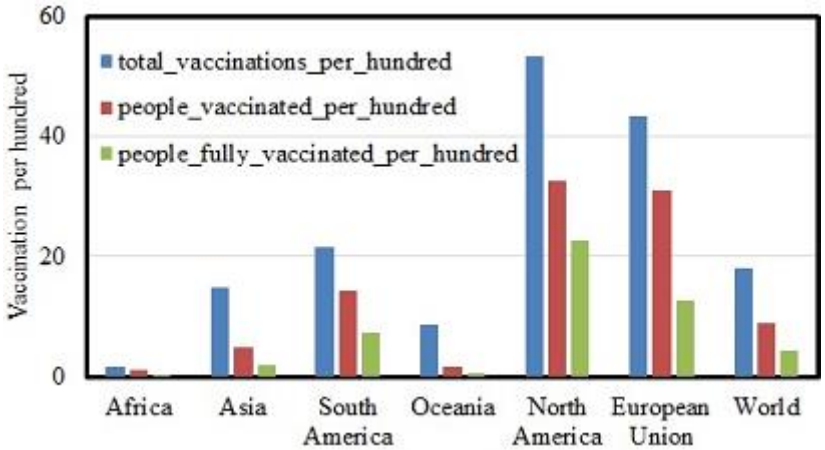


Figure 3: Region-wise Status of Vaccination per hundred population. The data is adopted from WHO and Our World in Data.

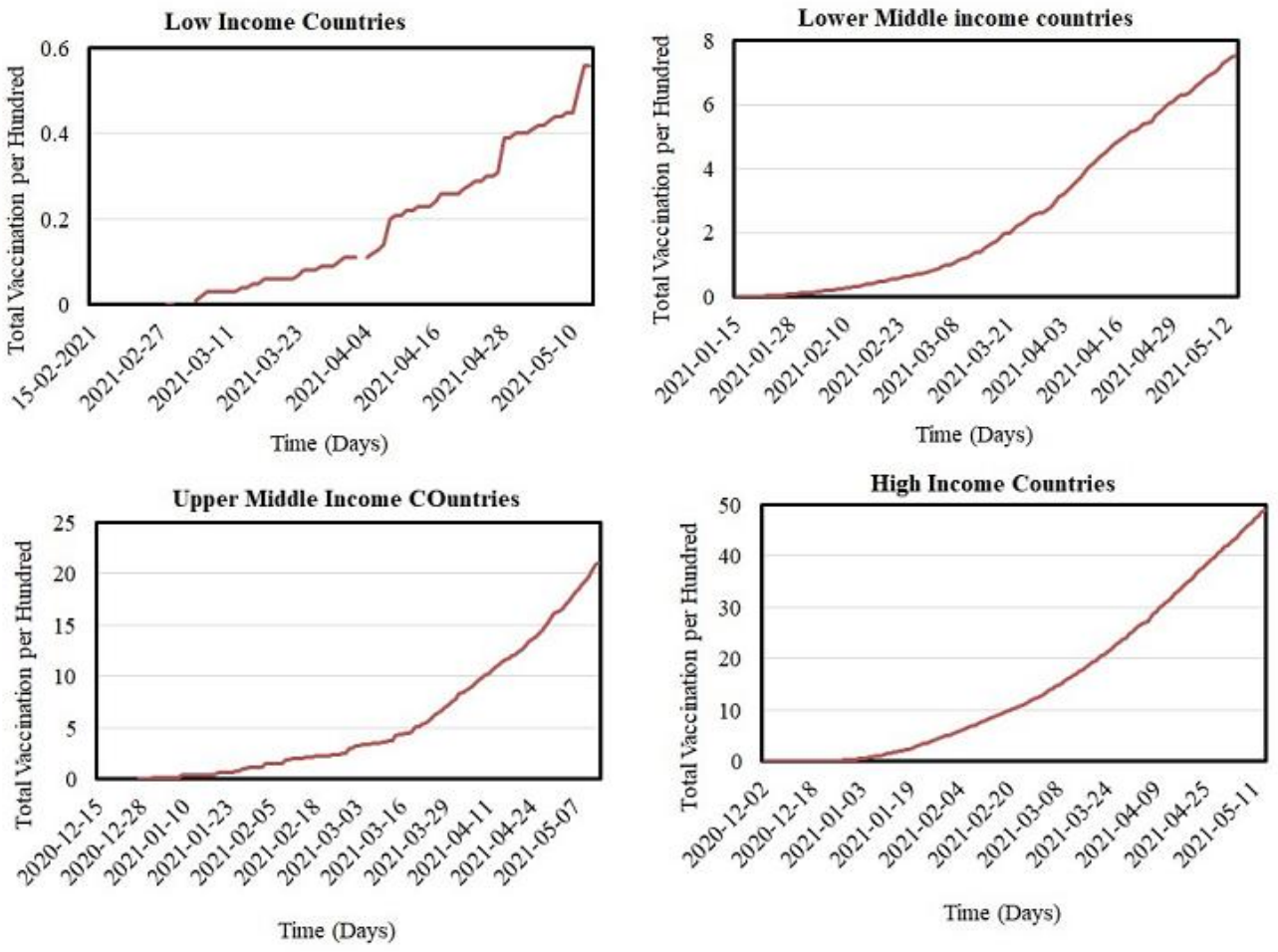


Figure 4: Pattern of economy-wise vaccination per hundred population. The data is adopted from WHO and Our World in Data

In terms of income, the vaccination is very high in the high income countries which is more than 50% in terms of total vaccination per 100 population. Similarly, the total vaccination of upper middle income countries is about 20% of the population. While the vaccination in lower middle income countries are about 8%. The vaccination in low income countries is the lowest among the lower middle income, upper middle income and high income countries, and less than 1 per hundred population (Figure 4).

3.3 Impact of Vaccination of Covid-19 Infection

The Covid-19 pandemic has marked unprecedented global societal and economic disruptive impact that necessitates developing efficacious strategies to control COVID-19 infection and to develop urgently needed vaccines (9). Though every country is trying with suitable strategy to control the infection but it could not be possible to stop absolutely infection of coronavirus. The introduction of vaccines can be a key game changer to mitigate economic, social and health consequences of the coronavirus in the year ahead. However, studies suggest that access to these vaccines is likely to be highly uneven across countries. This uneven access of vaccine the global economy plunks to lose about US$9.2 trillion if governments fail to ensure developing economy access to COVID-19 vaccines (10). Subsequently, the COVID-19 pandemic requires global roll-out of vaccines that can protect against the infection of disease. Literature suggests that contagious disease immunization entail herd immunity (11). On the other hand, the transmission of the virus can be lessened by means of physical distancing, face coverings, and testing and tracing and potentially with alternative therapeutics. Moreover, the risk of outbreaks and disruption to economic and social life will probably remain until effective vaccines are administered to large portions of the global population to prevent hospitalisation of severe disease and preferably achieve herd immunity to halt transmission of the virus (12).

The share of population to be immunized in order to attain herd immunity may vary from disease to disease. Coronavirus infection is a contagious disease and study shows that under certain conditions, the number of contaminated surfaces grows logistically, corresponding to possible rapid transmission of infection. In such a surface network, pathogen can be transmitted great distances quickly—as far as people move (13). Theoretically, to reduce infection rate and impact of infection at least 50 percent population needs to be vaccinated to curb fast infection of the disease. This is derived from the assumption that any biological growth follows logistic pattern of growth with inflection point of (K/2), where K represents the total population size. Therefore, half of the population of every country should be vaccinated within 2-3 months to contain the Covid-19 infection and gradually above 84 percent of the total population in the next 2-3 months. The rationale behind

to vaccinate within time span of 2-3 months lies as life span of antibody falls in this range (14). Also fast immunization of the potential population is imperative because the mutation of SARS-CoV-2 is faster and of doubling time comparatively higher. If the time span increases in that case the vaccine may not be effective due to mutation of the virus and sustainability of antibodies developed in the population.

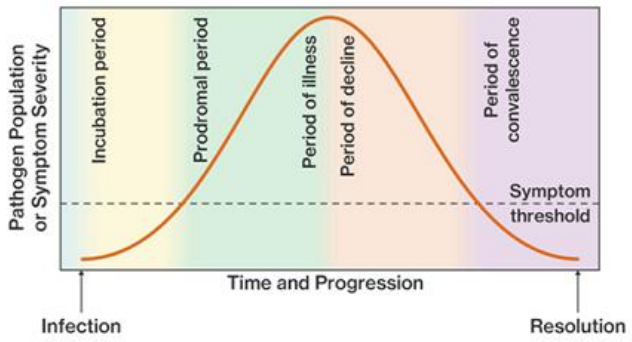
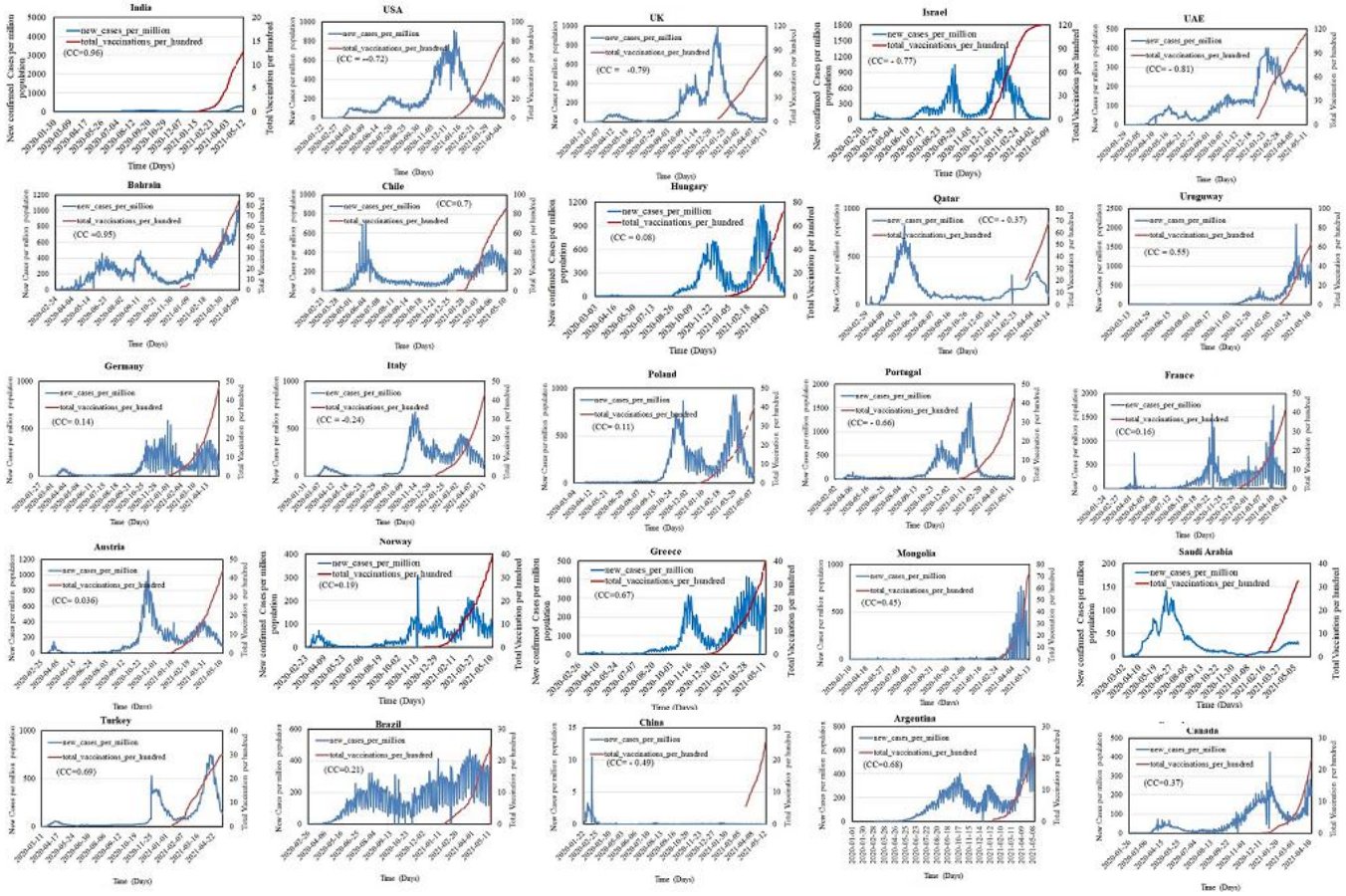


Figure 5: Diseases spread through five stages: incubation period, prodromal period, period of illness, period of decline, and period of convalescence. Here, we assume these categories correspond to five stages of innovation diffusion namely Innovators (2.5%), Early adopters (13.5%), Early majority (34%), Late majority (34%) & Laggards (16%).
Source:
https://www.coursehero.com/sg/microbiology/stages-of-disease/; Retrieved on 14.06.2021

Therefore, for achieving herd immunity and to manage spread of coronavirus infection 84% population may be required to develop antibody altogether, whether natural exposure to coronavirus or through immunization process, to restrain further spread of Covid-19. The observed data shows that after vaccination process the number of infected cases is declining and infection is found inversely proportional to the number of vaccinated population. The transmission of infection is found significantly declined in those countries where vaccination of population reached more than 50% (Figure 5).

Data indicate that the vaccination programme has been effective in reduction of new cases of the coronavirus. Israel, UAE, Bahrin, UK, USA etc. have started their vaccination program in wide range and soon completed vaccination more than 50% and the results shows that there is declining trend in new confirmed cases as well as declining trend in new death cases also. The relationship between new per million infected cases and vaccination is significant, and high vaccination reduces the new confirmed cases (Figure 6). Similar results have also shown in the reduction of new death cases with increase in vaccination (Figure 7). Figure 6 illustrates the pattern of infection pre and post immunization and reveals that post immunization process the rate of infection decline in the targeted countries, while Figure 7 reveals the rate of death cases decline in the high vaccinated countries.



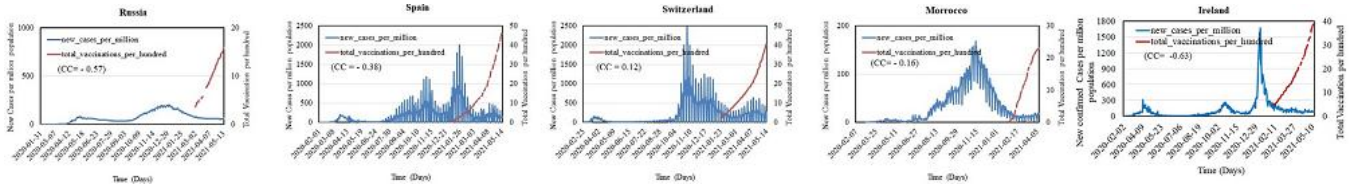


Figure 6: New cases per million population (blue line, left y axis) and Total vaccination per hundred population. Here, we have considered the countries of total vaccination are more than 20%. The data is adopted from WHO and Our World in Data.

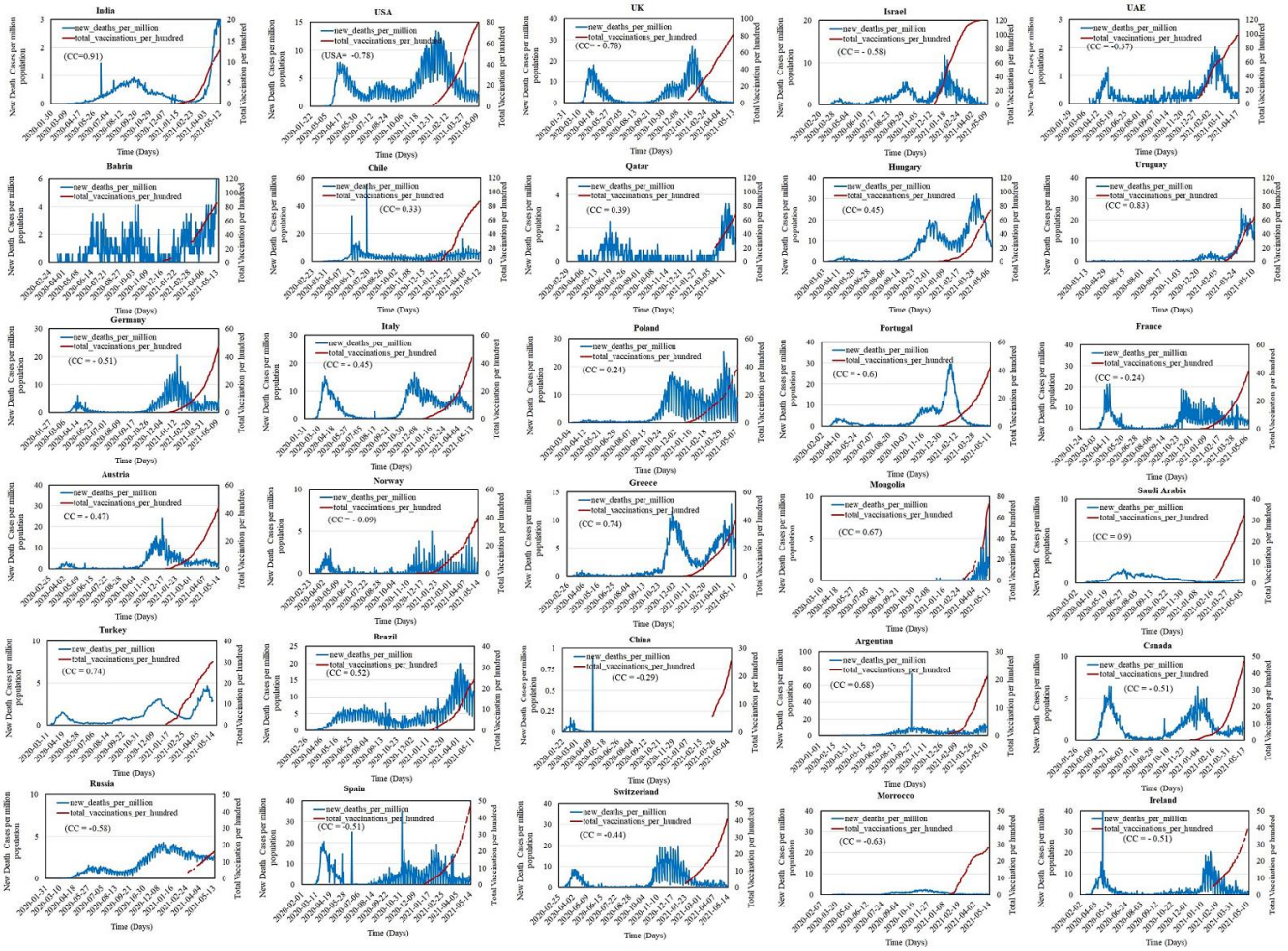


Figure 7: New Daily Death cases per million (left y axis, blue line) and total vaccination per hundred (red line, right y axis) of major countries. The data is adopted from WHO and Our World in Data

3.4 Challenges of Universal Accessibility of Vaccines

In many developed and developing countries mandatory vaccination has begun from beginning of the year 2021. The countries with high coverage for mandatory vaccinations have strong public health systems that are robustly responding to the COVID-19 pandemic and people in these countries with mandatory vaccinations are likely to be more risk averse and comply with pandemic control measures (15,16). Therefore, many European countries and the USA, Russia, India, Brazil, China and more are making efforts to develop effective vaccine. Some companies have developed Covid-19 vaccines in a very short time span that normally takes several years and to inoculate enough people for global vaccine immunity the world now needs more doses of COVID-19 vaccines than it has done for any other vaccine in history (17,18). Many manufactures are coming in the market to produce Covid-19 vaccines; - Moderna-USA; Pfizer-BioNTech- Multinational; Sputnik Light/Sputnik V-Russia; Oxford AstraZeneca-Multinational, BBIBP CorV-USA, CoronaVac-Brazil & Turkey, Novavax-UK & South Africa, Johnson & Johnson-Multinational, Covishield & Covaxin- India, Sinovac-China and Convidecia-Multinational. However, immunization of the whole population in a short period, more than 7 billion population (World Bank), is a mammoth task due to regional and economic diversity. Due to higher demand of vaccine, it is also observed that the competition of vaccination has led inequality among the countries; particularly between developed, developing and low income countries. Low and least income countries are not prepared for diagnostics of Covid-19, as these countries neither have capacity to manufacture vaccines and infrastructure as compared to developed economies. African and sub-Saharan countries may be deprived of Covid-19 vaccination programme as these countries have scarcity of resources and required infrastructure. The United Nations' sustainable Goal-3 focuses for good health and well-being for all. The goal can

be achieved if countries abandon an approach of vaccine nationalism and think for supporting the global response. For this there is a need to develop a mechanism of 'Vaccine Equity' which is crucial to stop rapid spread of Covid-19 infections between countries. Status of vaccination is presented in Figures 2. The vaccine equity will enhance possibility of universal access of vaccines and will provide an opportunity to ensure vaccination to those countries that have inadequate resources (Figure 3, Figure 4).

3.5 Framework for Covid-19 Vaccine Equity

Covid-19, pandemic has brought several challenges such as social, economical and psychological disruption across the countries. In the beginning of the disease there were several uncertainties among the policy makers and the governments to tackle the spread of coronavirus infection, diagnostic tests, and improved therapies. The major concern of the respective governments was to protect public health and socio-economic well being. Accordingly, many governments invested huge amount to develop vaccine. As a result, several companies from developed countries including India and China developed promising vaccines and expanded infrastructure to scale up production of vaccines. The procurement and management of Covid-19, vaccines have considerable implications when planning for the equitable allocation is concerned. Since, certain vaccines have been developed, now issue of fair allocation of Covid-19 vaccines is a critical issue and how these challenges can be minimised. Uneven allocation of Covid-19 vaccinations in middle and lower countries may hit the vaccination programmes in these countries. The skew distribution of vaccines on national and global level can create gaps in vaccines access and will adversely affect immunization strategy. Therefore, massive vaccination campaigns would therefore require billions of doses to satisfy global demand by prioritization strategies. High vulnerability groups such as health workers and indispensable professionals are the first to receive a vaccine, followed by age groups older than 65 years (19). Supply chain management can be another vital issue for different platforms and strategic alliances between pharmaceuticals and institutions Hence, amplify SARS-CoV-2 vaccine production sites worldwide and maximize the production of vaccines on large scale to meet global demand will be the decisive factors (20). To ease the bottleneck of vaccination WHO (WHO Concept for fair access and equitable allocation of COVID-19 health products) (21, 22) categorises target groups as (i) frontline workers in health and social care settings (ii) people over the age of 65 years and (iii) people under the age of 65 years who have underlying conditions that put them at a higher risk of death. For ensuring universal and timely accessibility of vaccines deliverables should be derived hassle free mechanism as follows.

3.5.1. Development & Production

- Adapting clinical and health Research guidelines
- Authorization by regulatory Agency for safety and transparency
- Scaling up of Production
- Trouble-free Licensing for optimization/voluntary Licensing

3.5.2. Affordability

- Public and Pool funding for Covid-19 vaccines programmes
- Minimization of profit and optimization of Resources
- Supply chain management

3.5.3. Universal Accessibility

- Equal Concern irrespective of nationality
- Strong & efficient Supply Chain for distribution
- Prioritization of severity of infection

Thus, right approach and network among the stakeholders, efficient and transparent strategy will enhance outcome of vaccine equity by promoting fairness and transparency to mitigate health inequalities. Also WHO should devise a buffer pool of vaccines which could be supplied to those countries particularly least income countries in case of emergency. Therefore, universal accessibility and affordability will be the key driver for equitable distribution of vaccine.

3.6.1 Case study-1: Israel

Israel was first country to show that the vaccination have nationwide effect. Israel initiated the national vaccination campaign on December, 2020, with Pfizer–BioNTech's mRNA COVID-19 vaccine BNT162b2. The Ministry of Health of Israel recommended the two doses of vaccine in the interval of 21- days. After vaccination of more than three-months of adults, the need of ventilators among covid-19 patients and was found that number of new cases declined dramatically (23). Israel delivered vaccine to the 62% of the population with at least one dose and 58% of the population are fully vaccinated till 14 May 2021. While about 88% of the population with age 50 years and above have received two doses of the vaccine (Figure 8). With this high coverage of vaccination, the number of infectious cases declined by prioritisation of the target groups of population, allocation and documentation of eligible individuals, strong and effective cooperation between government and community-based health funds with advance information technology are the major factors for rapid roll out of the vaccination. To study the impact of vaccine, the Ministry of Health used the aggregate data from the national SARS-CoV-2 surveillance and vaccination programme dataset to compare the impact of vaccine between vaccinated and unvaccinated population. This experience provides the importance and motivation for high vaccine coverage to protect the population against covid-19 infection. More such post vaccination studies are required to strength vaccination programme, social desirability and social adoptability. There is need of timely reporting of vaccine effectiveness against Covid-19 variants in different age group of the population. The empirical data suggests that numbers of infectious cases are inversely proportional to the number of vaccination (Figure 6 and Figure 8).

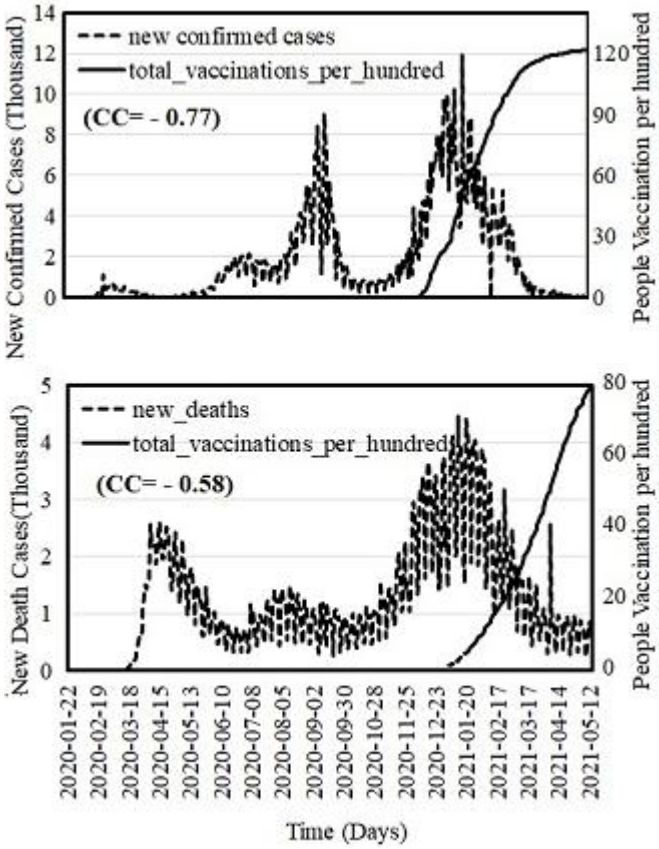


Figure 8: New confirmed cases (dash line, left y axis), daily New death cases (dash line, left y axis) and people vaccination per hundred population (solid line, right y axis) for Israel. of Israel for the period 22 January 2020 to 14 May 2021. The data is adopted from WHO and Our World in Data

3.6.2. Case Study-2: United States of America (USA)

USA has started nation-wise vaccination program in December 2020 to control the spread of coronavirus infection with recommendation of Pfizer - BioNTech, Moderna and Johnson & Johnson vaccines. Initially, the vaccination was started with prioritization of healthcare workers, long-term care residents and high-risk individuals resulted rapid decline in Covid-19 hospitalisations and death among these groups.

As the vaccination started in December 2020, about 46% of population has covered with one dose and 36% of population in US has covered with two dose of vaccine (fully vaccinated) by 14 May 2021. The total vaccination has covered about 80% population having one dose or two doses (Figure 9).

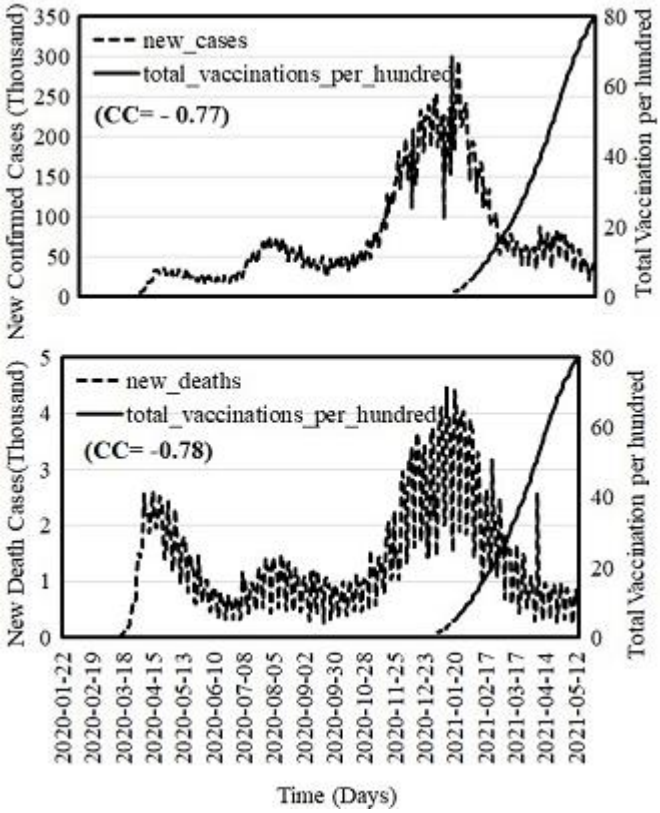


Figure 9: New confirmed cases (dash line, left y axis, top panel), New Death cases (dash line, left y axis, bottom panel) and Total vaccination per hundred (right y axis, solid line) for USA. The data is adopted from WHO and Our World in Data.

The rapid roll out of vaccination across the USA has shown positive results; the number of new confirmed cases and number of death cases have fallen considerably. In the case of USA also, the vaccination has positive impact to reduce infectious cases and found inverse association between number of vaccination and number of cases. Vaccination also reduces number of death which can be linked to the number of infectious cases.

3.6.3 Case study-3: United Kingdom (UK)

The UK has approved three vaccines Pfizer-BioNTech jab, AstraZeneca and Moderna for vaccination of population. The vaccination was started on 03 January 2021 and vaccinated about 53% of the population with one dose and 28% of the population fully vaccinated up to 14 May 2021. While the total vaccination has reached about 80% resulted reduction in number of new cases and number of death in the UK. In the UK, the confirmed cases have fallen 95% among the age over 80 years, while the death has fallen about 93% in this age group. The confirmed cases have fallen by 91% in the age group 18 to 69 while death case fallen 87% in this group (Figure 10). Thus, in the case of UK, the vaccination has reached to herd immunity, as theoretically to reach herd immunity, it is estimated that at least 55% of population need to be vaccinated to fight against novel covid-19. With maximum 85% of the population will need vaccination depend on the country infection rate.

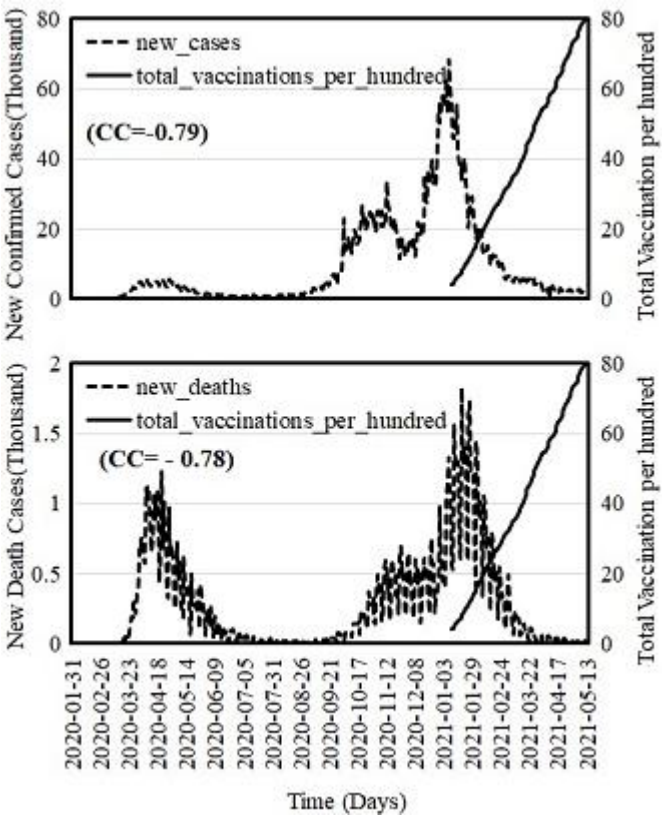


Figure 10: New confirmed cases (dash line, left y axis, top panel), New Death cases (dash line, left y axis, bottom panel) and Total vaccination per hundred (right y axis, solid line) for UK. The data is adopted from WHO and Our World in Data.

3.6.4. Case Study-4: India

India was also severely affected by the coronavirus infection responsible for minions of infected cases and thousands of deaths. India has large population so vaccination to all the population is very difficult that requires huge resources. Despite criticalities, India developed its own effective vaccine i.e. Covaxin manufactured by Bharat Biotech and Covishield, developed by Oxford, is being manufactured by Sirum Institute of India. India has started its vaccination program on 16 January 2021 in 2957 vaccination centres with two vaccines Covishield and Covaxin which are developed by India. Later DCGI approved Russia's Sputnik V vaccine also for emergency use in India. The first phase of vaccination covered health workers and frontline workers including police force, paramilitary forces, sanitation workers and disaster management volunteers. By end of the March 2021, 14 million healthcare and frontline workers had been vaccinated.

In the second phase of vaccination, the vaccine rollout covered all the residents above the age 45. On 19 April it was announced the next phase of vaccination to cover the population of age 18 and above from 1 May 2021. In the period of four months, the total vaccination covered about 13% of the population, 10% population has taken at least one dose and 2.88% of the population is fully vaccinated by 14 May 2021. Total 19.85 crore doses have been vaccinated with 15.52 crore of one dose and 4.33 crore vaccinated with second dose up to 25 May 2021 (Figure 11). There is still need minimum 50% vaccination to reach herd immunity. The empirical data illustrates that vaccination in India has positive impact on infection rate and need to speed up vaccination process to reach larger population to reduce infection rate.

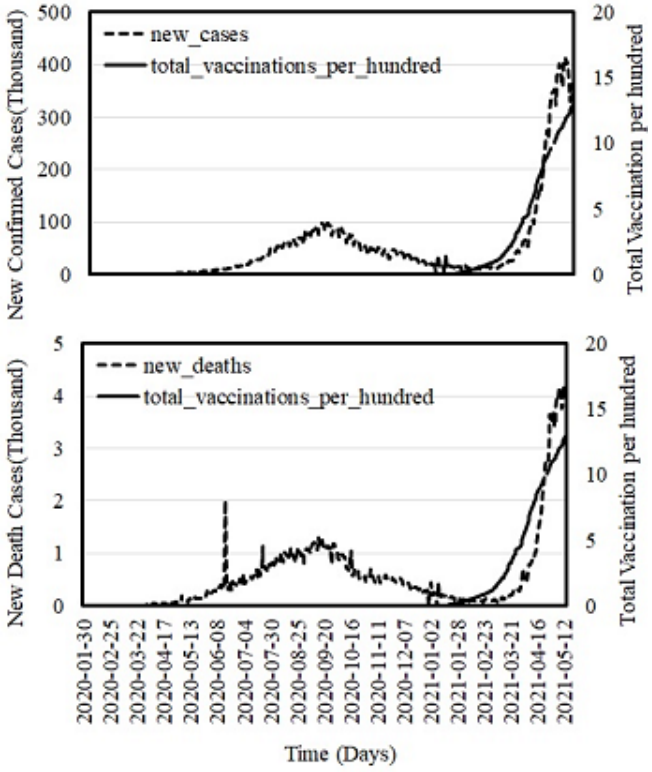


Figure 11: New confirmed cases (dash line, left y axis, top panel), New Death cases (dash line, left y axis, bottom panel) and Total vaccination per hundred (right y axis, solid line). The data is adopted from WHO and Our World in Data.

4. Discussion and Conclusions

From the inception of the covid-19 pandemic led global adversity resulting in societal and economic set back. Analyzing severity and different aspects of covid-19 infection is imperative for future strategy. As the infection continues to spread, the effective reproduction of infected cases become lower over time. Rapid deployment of vaccines against COVID-19 and efficient and effective vaccination strategies should be directed by explicit objectives (24). The ECDC also put forwarded arguing that in an initial phase maximum health gains would be obtained by vaccinating groups at highest risk of severe COVID-19, any vaccination strategy could only be assessed against its objectives, and would therefore need to be adapted to the evolving circumstances (25). Therefore, the setting up prioritisation of target groups and clear measurable goals for COVID-19 vaccination strategies is of crucial importance. It is because the initial objective of the vaccination strategy is to exit emergency status; the vaccination of all older adults is the most efficient and effective approach (26). Efficient and suitable vaccination will help to stop fast mutation of the virus and chances of new variants can be minimised because new variants can replace the existing variants and may be more risky.

Vaccination strategy should be based on targeting groups and intensity of the infection; may vary from country to

country. Mechanism of vaccinates should be intended universal access, de-licensing, and universal nationalism. It is reported that governments in high-income countries representing 16% of the global population have secured at least 70% of doses available in 2021 from five leading vaccine candidates (27). This protectionism approach will hit the success of vaccination and poor countries will not be able to achieve vaccination. So, vaccine equity will provide a rational approach for vaccination and will reduce infection load uniformly across the countries and uninterrupted chain of vaccination. Studies suggested that the U.S. COVID-19 vaccination program has the potential to substantially reduce the burden of disease in the United States by preventing illness in fully vaccinated people and interrupting chains of transmission (28). Since, most countries are lacking the capacity to rapidly produce vaccines, pressure on global supply chains will increase in order to scale up production and meet the global demand. Therefore, it is imperative that manufacturers and governments should share data, knowledge and technology with a larger group of other manufacturers to produce more COVID-19 vaccines. This will make the vaccination process more effective and efficient. In addition, genome sequencing, sustainability of antibodies and sero survey strategy should be adopted.

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Author Contribution

The contributions of N.K. are in conceptualization, investigation, analysis, review, writing, and editing the manuscript. The contributions of S.N. are in conceptualization, methodology, formal analysis, writing, review and editing of manuscript, visualization.

Declaration of conflict interest

The authors declare no conflict of interest.

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