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Commentary

COVID-19 vaccination campaign in Nepal, emerging UK variant and futuristic vaccination strategies to combat the ongoing pandemic

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ABSTRACT

With the emergence of the new variants of concern (VOC) of the SARS-CoV-2, the efficacy of certain vaccines against them requires further research and considerations for future scenarios of COVID-19 vaccination. The vaccines' lack of efficacy against VOC will pose at risk to the vaccinated population and is a public health threat. In this commentary, we discuss Nepal's recent experiences and expectations regarding the confirmation of VOC B.1.1.7 from the United Kingdom in the country.

1. Introduction

The first case of COVID-19 reported in Nepal was on January 13, 2020, in a 32-years-old man who had returned to Nepal from Wuhan, China [1,2]. The Government of Nepal announced an immediate countrywide lockdown after the single case itself. The second case was reported only after two months, i.e., in March 2020. However, despite the countrywide lockdown, travel restriction and border closures, the cases of COVID-19 started to rise from April 2020 and peaked during September–October 2020 [3]. Most of the cases of COVID-19 were asymptomatic and involved young males [4]. As of March 11, the cases of COVID-19 have crossed 274,000, with around 3000 deaths [5].

Meanwhile, on January 18, 2021, the Ministry of Health and Population, Nepal (MoHP-Nepal) confirmed three cases of the United Kingdom (UK) variant of concern (VOC) B.1.1.7 of SARS-CoV-2. The cases were confirmed in individuals who had arrived in Nepal from the UK four weeks back. Public health experts are concerned about the

encroachment of this new virus VOC and the probability of its spread in Nepal as its approach towards containing COVID-19 has been lackadaisical. Nepal shares a border with two populous countries, India and China, and has an open border with India; hence, getting more of the VOC is higher [6]. Rapid vaccination against SARS-CoV-2 for the general population is needed to contain the spread of new variants of COVID-19 across the country.

The success of the COVID-19 vaccination largely depends on Nepal's ability to acquire COVID-19 vaccines from different countries and manage its logistics, distribution, and delivery [7]. Among various COVID-19 vaccines approved for mass rollout, Nepal's Government has started vaccination of front-liners with 1 million doses of COVID-19 AstraZeneca vaccines AZD1222 (Covishield®) donated by India's Government under the Vaccine Maitri initiative [8]. The vaccination against COVID-19 was planned to be completed in two phases. The two doses of Covishield® of AstraZeneca are recommended to be administered 4–12 weeks apart. The first phase of vaccination aimed at frontline medical

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workers, sanitation workers, ambulance drivers and security officers began on January 27, 2021, across all the 77 districts of Nepal. In the first phase of the COVID-19 vaccination drive, about 184,857 people received the doses and were concluded on February 6, 2021 [9–11].

The remaining COVID-19 vaccines following the completion of the first phase of vaccination were administered to the officials and staff of diplomatic missions and journalists since February 8, 2021. The second phase of the vaccination drive has begun from February 14, 2021, and estimated to be continued till February 20, 2021, targeting the district-based government employees, public corporations' employees, banks and financial institutions, journalists, people's representatives, staffs of local levels and security personnel deputed at border security posts. The Government has planned to vaccinate 72% of the total of 28.16 million people in the country. However, by the end of the first phase of vaccination, only 3% of the prioritised people were vaccinated. Since 28% of the country's population comprises those below 14 years of age, the vaccine would not be administered in them as it is not indicated to be administered below the age of 18. The vaccines provided by India is anticipated to be enough to administer to about 430,000 people.

Nepal is expected to get around 500,000 vaccines as humanitarian aid from China shortly [12]. Additionally, under the provision of the World Health Organization's COVAX facility, Nepal is to receive around 2.25 million doses of COVID-19 vaccines by late February 2021. These vaccines will be sufficient to vaccinate 3.3% people (around one million) of Nepal's total population. The Government is also planning to procure more COVID-19 vaccines doses to administer to the public with a strategic approach [10,11,13,14].

The steps taken by the Government of Nepal on the supply and distribution of the vaccine is commendable. Though 72% of the population is enough to achieve herd immunity, achieving this target is an uphill task for a resource crunch country like Nepal and management of COVID-19 in Nepal is further complicated by the newer variants such as the UK variant (B.1.1.7) [9,11], belonging to B.1.1.7 lineage [13,14]. COVID-19 is still in its full swing with its second wave and the SARS-CoV-2 variants, including SARS-CoV-2 variants B.1.1.7 in the UK, B.1.351 in South Africa and other mutant viruses [15]. The UK variant is believed to express an increased transmissibility rate of more than 70% compared to the existing pandemic SARS-CoV-2 previous lineages. It spread rapidly due to a single mutation in the viral spike's amino acid protein [13,14]. A study recently reported that the SARS-CoV-2 B.1.1.7 variant is refractory and relatively resistant to neutralisation by most monoclonal antibodies, modestly more resistant to convalescent plasma and vaccine sera [16]. However, one study revealed that SARS-CoV-2 infection and vaccine-induced antibodies, using the messenger RNA vaccine, mRNA-1273, effectively neutralised the SARS-CoV-2 B.1.1.7 UK variant supports the findings that vaccine-induced immune responses can provide adequate protection against COVID-19 despite emerging UK variant virus [17]. The more significant variants of the SARS-CoV-2 protein could facilitate new SARS-CoV-2 mutants to escape vaccine-induced antibodies and create vaccination problems. Investigating SARS-CoV-2 S protein mutations in details would help understand the emerging virus variants better and pave ways to find solutions to combat COVID-19 and its different variants [13]. If looked upon the scenario until now, vaccines' inoculation has failed to meet the precedent statistics, which raised doubts about completion of the COVID-19 vaccination drive as planned by the Nepal government. Also, the Covishield® vaccine is not to be administered to people below 18 years of age, and there are specific percentages of people ranging from 14 to 18 years. The Government should take steps to procure enough doses of COVID-19 vaccines suitable for administration to this younger age-group.

Due to the resource and cost problem, the Government of Nepal has reduced the daily testing range for COVID-19, which led to a lackadaisical attitude among people towards COVID-19 safety measures. In such a scenario, the appearance of different variants of SARS-CoV-2 seems to be a possible threat, and we can get more of such variant as the virus

mutates and spread. Such a situation may be worrisome and challenging as it could affect the efficacy of developed COVID-19 vaccines. So, the primary strategy should be to vaccinate as much of the target population as possible to achieve herd immunity and get some immunity. The country's diagnostic capacity needs to be upgraded and promote a healthy and hygienic environment and resourceful hospitals for treatment.

2. Challenges in COVID-19 vaccination drive

The expiry date of the unopened multidose vial of the COVID-19 vaccine is six months from the manufacture date [18]. Within six months, the vaccines need to be shipped from the manufacturing companies to countries worldwide, completing each country's required legal formalities. Accordingly, the logistics, distribution, and delivery systems in the vaccine recipient country must be planned and made ready alongside. The distribution and storage facilities at different levels within the receiving country must be arranged systematically. The adequate supply of the COVID-19 vaccines from central to regional and regional to local vaccine delivery outlets such as community hospitals, ward offices, and primary health posts is a challenging job.

Additionally, throughout all these channels, the cold chain must be maintained for COVID-19 vaccines to be effective and fit for administration. The Cold Chain section of Nepal's Logistics Management division manages the storage, distribution, and transportation of the routine vaccines [19]. The vaccines usually are provided through UNICEF and Gavi to the country, and 11 antigens under the National Immunization Schedule of Nepal is available free of cost to the public [20,21]. Amidst COVID-19, the country's logistic arrangement seems to be less disrupted and the vaccination programs halted for a short period during the early phase of COVID-19 in Nepal has been providing the vaccination services continuously taking the necessary precautions [22]. Likewise, the first phase of vaccination against COVID-19 was completed so far without any significant problems [23]. That might be because of efficient vaccine delivery and logistics system within the country and support by USAID-JSI.

Furthermore, there is a plan for the second dose administration (booster dose) three months after the first dose to provide more protection than administering the second dose at a 1-month interval. There have been discussions regarding the effectiveness of the first dose of the COVID-19 vaccines for a longer duration before administering the second dose. However, completing the first and second dose of vaccinations is necessary to get fully immunised against the infection cannot be denied. Suppose Covishield® and other COVID-19 vaccines' effectiveness is proven to be for more days than the estimated four to twelve weeks in any time soon. In that case, there is a high chance that more people will be vaccinated in the first phase itself, which will also aid in achieving herd immunity sooner.

Moreover, if it is not the case, then the first and second doses of vaccines must be administered within six months of the vaccines' manufacture. That requires proactive approaches and a robust logistics and distribution system, and a cadre of healthcare workers at a different level to meticulously monitor and handle the vaccines' supply, distribution, and administration throughout the country. The healthcare systems have been burdened because of the pandemic, and the healthcare providers' workload is increased, but the health institutes are under-resourced. So, there remains a high chance of vaccine expiry for the second dose, especially in under-resourced and marginalised countries that are not manufacturing the vaccine in their own countries and cannot effectively mobilise human resources.

As WHO Director-General quoted "The world is on the brink of catastrophic moral failure due to unfair COVID-19 vaccine rollouts and the price of this failure will be paid with lives in the world's poorest countries, the availability of vaccines in the lower and lower-middle-income countries is a big deal. There seems to be inequity in vaccine distribution around the globe. Although WHO and UN emphasise the

“health for all” campaign worldwide, people in low and middle-income countries have received a tiny fraction of the required doses of COVID-19 vaccines. Also, at the international level, Nepal needs to tie up with other developing countries and work alongside the WHO in advocating adequate distribution to lower-income countries. It is a right and equity issues, and multilateral institutions need to ensure that LICs get the fair share of vaccines’ global supply. Nepal must use its bilateral ties and diplomacy and get vaccines from China and India as a priority either in donation or through purchase. Furthermore, the Government should plan to mobilise the healthcare financing and government budget allocated for some development projects or non-essential projects for the time being to adjust funds required for buying COVID-19 vaccines.

3. Conclusions

Definitively, genomic surveillance should be improved in all the countries [24–27], including Nepal. That is necessary to warrant early detection of SARS-CoV-2 VOC, to understand the actual geographical and temporal distribution of VOC in the territories [28], to analyse its actual impact, including transmission, morbidity and mortality, and the efficacy of the available vaccines against such VOC [8,29]. Currently, multiple countries have begun their national COVID-19 vaccination programs using only one type of vaccine [30]. Given the mentioned considerations, using different vaccines from various biotechnological approaches (e.g., mRNA, viral vectors, inactivated virus) would be suitable for distinct epidemiological scenarios [31,32]. Finally, even in developed countries, the current dilemma is the lack of enough vaccines to supply the governments for their application. A significant increase in vaccine production, new alliances and support from the public and private sectors are needed in a global effort to increase and achieve massive vaccinations against COVID-19. The occurrence of various mutants of SARS-CoV-2 is an alarming situation and provide us with evidence that the vaccination programs against COVID-19 should be strengthened and speed up. Hence, Nepal needs to work on logistics, distribution and delivery system for vaccination. Alongside Nepal need to use diplomatic, official, and other endeavour/approaches to secure its people’s required vaccines.

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CRedit authorship contribution statement

Ranjit Sah: Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Asmita Priyadarshini Khatiwada:** Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Sunil Shrestha:** Data curation, Writing – review & editing. **K.C. Bhuvan:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – review & editing. **Ruchi Tiwari:** Writing – review & editing. **Ranjan K. Mohapatra:** Writing – review & editing. **Kuldeep Dhama:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Alfonso J. Rodriguez-Morales:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial

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