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#### Correspondence

Prof. Dr. Jay Shah, Dept. of Surgery, Patan Hospital, Patan Academy of Health Sciences, Lalitpur, Kathmandu, Nepal  
Email: drjaywufei@gmail.com  
drjaywufei@hotmail.com

#### Peer Reviewers

Prof. Dr. Gehanath Baral, Nobel Medical College, Biratnagar, Nepal

Prof. Dr. Ganesh Dangal, Kathmandu Model Hospital, Kathmandu, Nepal

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## Breakthrough infection after COVID-19 vaccination: A threat for Nepal due to SARS-CoV-2 variants circulating in 2nd wave ravaging India

Jay Shah<sup>1</sup>✉, Priscilla Samson<sup>2</sup>, Nabees MS Pradhan<sup>3</sup>, Shreekrishna Maharjan<sup>4</sup>, Ashis Shrestha<sup>5</sup>, Jenifei Shah<sup>6</sup>, Jesifei Shah<sup>7</sup>, Sarala KC<sup>8</sup>

<sup>1</sup>Prof. Surgery, <sup>3</sup>Prof. Orthopaedics and Trauma surgery, <sup>4</sup>Assoc. Prof. Biochemistry and Molecular Lab Medicine, <sup>5</sup>Asst. Prof. General Practice and Emergency Medicine, Patan Hospital, School of Medicine; <sup>2</sup>Assoc. Prof., <sup>8</sup>Prof. & Nursing Dean, School of Nursing and Midwifery; Patan Academy of Health Sciences, Lalitpur, Kathmandu, Nepal. <sup>6,7</sup>Intern Doctor, Ruijin Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

### Abstract

After a year of the COVID-19 pandemic, the meta-analysis in Dec 2020 did not support its reinfections. Now it is clear that not only reinfection following earlier exposure is a reality, but also breakthrough infections after vaccinations have been increasingly reported. A breakthrough infection means that the infection has broken through the protection provided by the vaccine. The course of the disease, strict observation for preventive measures, together with safe vaccines is necessary for long-term solutions. The effectiveness of the vaccine, durability of immunity, the role of the virus variants, the incidence and severity of breakthrough infections are the challenges in real life. A breakthrough infection is the detection of SARS-CoV-2 RNA or antigen in the respiratory specimen  $\geq 14$  days after inoculation of a vaccine. A breakthrough infection of 0.04 to 13% has been reported in the literature. Nepal began vaccine rollout in late Jan 2021. Nearly 3 million population has been vaccinated by two vaccines, the Covishield (AstraZeneca, from India) and Vero Cell (Sinopharm, China). Only minor 'Adverse Event Following Immunization' after the initial vaccine rollout has been reported. There is a lack of reports on the breakthrough infection for these vaccines in the local population. Analysis of the data on breakthrough infection from the vaccine rollouts in Nepal is awaited.

**Keywords:** breakthrough infection, COVID-19 vaccine, Nepal, SARS-CoV-2 variants, 2nd wave

## Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection was thought not to cause re-infection<sup>1</sup>, and has been proven otherwise as COVID-19<sup>2,3</sup> which hit Nepal in mid-Jan 2020<sup>4</sup> prompting the government to adopt preventive measures and lockdown<sup>5,6</sup>, is known now to cause re-infection as well as breakthrough infection<sup>7-11</sup> after vaccination<sup>12</sup>. A breakthrough infection depends on the protective efficacy of the vaccine, window period of immunity or decline of immunity, and specificity against variant. The reported incidence of breakthrough infection ranges from 0.04% to 13%<sup>13-23</sup> but most reports favor a lower rate. This has important consideration for the prevention and control of the ongoing pandemic following vaccine rollouts in Nepal. The published data on the breakthrough infection in the local population is still in waiting. This review discusses the issues of breakthrough infection in light of the equitable distribution and vaccination coverage, the emerging virus variants, future planning to prevent and control the ongoing COVID-19 pandemic.

## Method

The terms 'breakthrough infection, SARS-CoV-2, COVID-19, COVID19' were used to search the repository of published data on PubMed, Google Scholar, NepJol, and Google. Google was used also to find the relevant web page on vaccination and breakthrough infection of COVID-19. All article types from Jan 2020 till 23 May 2021 were included in this review.

## Discussion

### Breakthrough infection of COVID-19

After a year, the meta-analysis published in Dec 2020 did not support the possibility of COVID-19 re-infections following recovery of initial infection from SARS-CoV-2.<sup>1</sup> Exactly a year earlier on 31 Dec 2019, China informed the World Health Organization (WHO) local

office, of pneumonia of unknown etiology emerging in Wuhan in Hubei province, and quickly shared the genome sequence which led to the naming of the disease now known all over the world as COVID-19 (Coronavirus disease 2019), which emerged due to new strain of RNA viruses- the SARS-CoV-2. It was subsequently declared by WHO an outbreak of 'public health emergency of international concern' on 30 Jan 2020. Later the outbreak was upgraded to a 'pandemic' by WHO on 11 Mar 2020.<sup>2,3</sup> In Nepal, the 1st imported case of COVID-19 was reported on 13 Jan 2020.<sup>4</sup> There was a gradual increase in the number of cases, and the government followed the recommended preventive measures of quarantine, isolation, and lockdown.<sup>5,6</sup> A clear understanding of the course of the COVID-19, the durability of immunity, the incidence, and severity of reinfection, the breakthrough infection after vaccination, and the role of virus variants are important for the prevention and control of the ongoing pandemic.<sup>7-11</sup> A breakthrough infection depends on the protective efficacy of vaccine (for a particular antigen), vaccine protection window (infection acquired before the immunity is built up or waning of immunity), and specificity of vaccine (against variant).

A breakthrough infection of COVID-19 means that the virus has broken through the protection provided by the vaccine and has caused the infection with or without symptoms. It differs from the term re-infection which refers to the infection following exposure to the initial infection. Thus, a breakthrough infection, as per the Centers for Disease Control and Prevention (CDC) of America, is defined as the detection of SARS-CoV-2 RNA or antigen in a respiratory specimen  $\geq 14$  d after full vaccination.<sup>12</sup>

The efficacy of vaccines shown in clinical trials is based on the degree to which they can prevent infection and is put to scrutiny for their effectiveness in the real world after the mass vaccine rollout.<sup>13</sup> In the real world, the breakthrough infection after COVID-19 vaccination is higher than those reported during clinical trials. For example, positive tests

for SARS-CoV-2 after vaccination was found in 0.97% to 1.19% among health care workers in California, higher than (0.05%) reported during the clinical trials.<sup>14</sup> Regular testing for asymptomatic and symptomatic persons, the local community infection, and differences in the demographics of trial participants from the real world data are some of the possible explanations for a higher rate of breakthrough infection than trials during the development of vaccines.

In a skilled nursing facility, a higher rate of 4% (22) breakthrough infection among fully vaccinated residents and the staff, and 23% (145) infection among partially vaccinated persons were reported.<sup>15</sup> A majority i.e., 14 (64%) of those 22 fully vaccinated had only an asymptomatic infection, while three had mild nonspecific symptoms, two mild specific symptoms, and three developed pneumonia. A total of 4 out of 22 required hospitalization, and one died.<sup>15</sup> This shows that serious breakthrough infection occurs only in a very small number of cases after vaccination. From a public health perspective, the COVID-19 vaccine served the purpose of infection prevention and control. However, it also emphasizes the need for measures of workplace safety like the use of personal protective equipment (PPE) in the high-risk area, and adherence to protective measures of restrictions, isolation, quarantine, and testing.<sup>5,6,16</sup> Timeline of the diagnostic workup, clinical course, and virological confirmation of UK variant causing mild breakthrough infection in a healthcare professional working in the isolation area of a designated COVID-19 hospital in Shaanxi Province was reported by the CDC China on 17 Mar 2021.<sup>17</sup> The CDC China emphasized the adherence to general infection prevention and control measures, to follow good clinical practices and adequate and proper use of PPE during procedures to prevent breakthrough infection.

In Nepal, there is a need for studies on breakthrough infection after the COVID-19 vaccination. This is also necessary to help in the plan for further public health measures of prevention and control of the pandemic.

### **The variants of concern (VOCs) and breakthrough infection of COVID-19**

Studies show emerging variants are related to the increased rate of breakthrough infections.<sup>18</sup> The variants may be behind the breakthrough infections, as reported in 6 cases from Kerala, India, in which 4 patients had UK variant B.1.1.7, and 2 had E484K and S477N mutations in spike protein associated with possible immune escape.<sup>19,20</sup> Indian Council of Medical Research (ICMR) revealed that vaccines reduce the risk of hospitalization, but there could be a large number of people who may have a mild infection and do not go for testing for the breakthrough infection. The ICMR estimates a 4.5% breakthrough infection in India and lacks a record for deaths.<sup>21</sup> The ICMR report of a very "smaller number" of 0.04% (i.e. 2-4/10,000) breakthrough infections to have occurred in India is seen otherwise from the findings of small-scale studies published in a peer-reviewed journal.<sup>22</sup> In this small study of 123 employees in a hospital in Delhi, out of 113 vaccinated (Covaxin 28, Covishield 85), 107 (94.7%) individuals who had completed both doses, 15 (13.3%) developed symptomatic breakthrough infections in >14 d after 2nd dose. Out of these 15-breakthrough infections, only one required hospitalization, and the rest of the 14 only showed mild disease. This study reported overall infection after any dose of vaccine in 19 (16.9%). However, employees were tested selectively when they developed symptoms. Thus, asymptomatic infections may have been missed which is of concern because they could further spread the virus.<sup>23</sup> The NYC Department of Health and Mental Hygiene (DOHMH) in a preliminary analysis has suggested that the B.1.526 variant does not lead to more severe disease or increased risk for breakthrough infection.<sup>24</sup>

There have been three specific VOCs for COVID-19: the B.1.1.7 (the UK variant, already identified in >80 countries), the B.1.351 (the South Africa, SA variant, already identified in >41 countries), and the P.1 (Brazil) variant. Similar to B.1.351 and P.1, the UK variant is

more transmissible and more severe than previous variants. Reportedly, the SA variant has a 6-fold reduction in the neutralization by sera from vaccinated individuals and may render vaccines less effective, increasing the chance of breakthrough infection.<sup>25</sup>

Given the environment of vaccine hesitancy, it may be of help to add to the definition of breakthrough infection provided by CDC America which requires a positive polymerase-chain-reaction (PCR) test from the respiratory tract specimen. The addition of further evidence of a lower respiratory tract infection, for example, radiographic abnormalities or low oxygen saturation on pulse oximetry will help narrow down the breakthrough infection. This will further help to increase the public's trust in vaccines and also not get scared of breakthrough infection.<sup>26</sup>

### The risk of VOCs of the SARS-Cov-2

European CDC put the probability of the infection and community spread of variants as very high due to their increased transmissibility, hospitalization, and death. The center also emphasizes non-pharmaceutical interventions (NPIs) as important roles.<sup>27</sup>

Despite the extraordinary success of COVID-19 vaccine development, the effectiveness against the new variants is uncertain and so is the breakthrough infection rate. The available data suggests that vaccines retain the ability to prevent hospitalizations and deaths, even for antigenic variations. This makes the global approach of vaccine deployment, surveillance, and tracking even more important.<sup>28</sup>

Emerging variants of SARS-CoV-2 are of clinical concern. A cohort of 417 persons who had received the second dose of BNT162b2 (Pfizer–BioNTech) or mRNA-1273 (Moderna) vaccine at least 2 w previously, identified 2 women with vaccine breakthrough infection. Both women tested positive for SARS-CoV-2 by PCR testing. Viral sequencing revealed variants of likely clinical importance, the E484K in 1 woman and three mutations (T95I, del142–

144, and D614G) in both. These observations indicate a potential risk of illness after successful vaccination and subsequent infection with the virus variant. This also means there is a need for continued efforts to prevent and diagnose infection and to characterize the variants in vaccinated persons.<sup>18</sup>

In a yearlong, from Dec 2020 to Mar 2021, a study on post-vaccine infections found 189(0.8%) out of 22,729 healthcare personnel, after one dose of an mRNA vaccine had a breakthrough infection. Among 189 infections, 26(13.8%) occurred  $\geq 14$  d after the 2nd dose (fully vaccinated). Further analysis revealed higher infection in early and incomplete vaccination in 49(25.9%)  $< 14$  d of 2nd dose (partially vaccinated), and 114(60.3%)  $< 14$  d of 1st dose (early infection). Univariate analysis showed breakthrough infection in partially and fully vaccinated were more likely (than early post-vaccination) to be infected with variants B.1.427/B.1.429. The higher rate of infection before vaccine-derived full immunity requires continued infection control measures of social distancing and masking, particularly in the early days. Also, surveillance for VOCs is necessary for early planning and control for a surge in infection in the future.<sup>16</sup>

An Israeli study reported reduced neutralization of variants B.1.1.7 (UK) and B.1.351 (SA) after the Pfizer vaccine, and higher breakthrough infection due to these variants.<sup>29</sup> Qatar reported (as of 31 Mar 2021) a breakthrough infection in 6689 (1st dose) and 1616 (2nd dose) after Pfizer BNT162b2 vaccine, and that the vaccine was effective despite the VOCs B.1.1.7 (UK) and B.1.351 (SA), but 20% points lower effectiveness for SA variant than reported from Israel and the USA.<sup>30</sup>

The CDC America revealed (15 Apr 2021) 5,800 breakthrough infections among 77 million vaccinated persons, 1/3<sup>rd</sup> (29%) was asymptomatic, 396(6.8%) required hospitalization, and 74(1.3%) died from COVID-19. Interestingly 2/3<sup>rd</sup> (65%) of infections occurred in women, though this may

be due to the tendency among women to get tested. All ages were affected, but 40% occurred in >60 y, and possibly more infection due to VOCs B.1.351 (SA variant).<sup>12,31</sup> Further analysis of hospitalized or fatal COVID-19 vaccine breakthrough cases of 1,949 reported to CDC as of 17 May 2021 (out of 123 million fully vaccinated) found that 980(50%) were female, 1,539(79%) people ≥65 y, 354(18%) asymptomatic infections, 1811(93%) hospitalizations (of which 443 i.e., 25% asymptomatic or not related to COVID-19) and 353(18%) died (of which 63 i.e., 18% were asymptomatic or not related to COVID-19).<sup>12</sup> However, CDC also acknowledges that the number of breakthrough infections reported to CDC is an undercount of all SARS-CoV-2 infections among fully vaccinated persons.

The adequate vaccine coverage of 70% among adults, though important, still require further consideration for decreased immunity over time, transmission by children and adolescents, use of vaccines for the pregnant and immunocompromised, need of booster are still uncertain which is further compounded by unequal distribution and shortages to cover 70% of world populations.<sup>32</sup>

### The COVID-19 situation and VOCs in Nepal

In Nepal, three variants of the viruses circulating in the country were confirmed by the Ministry of Health and Population on 18 May 2021.<sup>33</sup> The variants were detected from the 35 samples following the gene sequencing in 35 samples by the Council of Scientific and Industrial Research Institute of Genomics and Integrative Biology in India, a WHO-recognized center. The variants included 'B.1.617.2' in 34 samples and 'B.1.617.1' in one sample. This double variant was first detected in Maharashtra, India, in Oct 2020. And on Tue, May 2021, the B.167.2, with higher transmissibility and reduced neutralization causing the uncontrollable 2nd wave in India. Earlier in Jan 2021, the UK variant 'B.1.1.7' was identified in three samples from Nepal sent for sequencing to Hong Kong.<sup>33</sup> On the same day, on 18 May 2021, Nepal recorded 8,203 new cases and 196 deaths.<sup>34</sup> Following the

devastation in India, the effect of the ongoing 2nd wave of COVID-19 has affected and paralyzed Nepal with a lockdown in the Kathmandu valley and most of the provinces in the country.

In Nepal, the 2nd wave of COVID-19 followed the devastating effect of variants in India. This required yet another lockdown, seriously impacting the country and overwhelming the health care facilities as case positivity rate increased to >50% and demand for healthcare increased which lead to acute shortage of oxygen, beds, ICU care, and ventilator support all over Nepal.<sup>35</sup>

The ongoing 2nd lockdown in Nepal was implemented from 0600 on Thu 29 Apr 2021, in Kathmandu valley (and outside provinces with different local measures) for the fear of VOCs infections from across the open border with India where the 2nd wave ravaged the country.<sup>36,37</sup> As of 25 May 2021 the 2nd lockdown is still in effect. Earlier, Nepal had experienced its 1st partial lockdown on 18 Mar 2020 followed by a countrywide lockdown on 24 Mar 2020.<sup>38</sup>

Vaccine rollout in Nepal started on 27 Jan 2021 with the administration of Covishield targeting health care workers and high-risk groups.<sup>39,40</sup> Only minor Adverse Event Following Immunization (AEFI) were reported.<sup>40</sup> The 2nd dose expected after 4 w was delayed by a further 8 w due to lag in delivery of a further 1 million doses Nepal had paid to Serum Institute of India.<sup>41</sup> The Vero Cell (from China, Sinopharm)<sup>39</sup> rollout in Nepal, 1st phase 1st dose, was completed by Apr 7-28 and rollout 2nd dose<sup>42</sup> was scheduled from 16-25 May 2021.

The situation during 2nd wave in Nepal is serious. In key information for travelers to Nepal, a level-4 advisory of a very high level of COVID-19 risk was issued by CDC USA because of the ongoing 2nd wave. The advisory warned that even fully vaccinated travelers may be at risk for getting and spreading COVID-19 variants and should avoid all travel to Nepal.<sup>43</sup>

The WHO director-general Tedros has denounced inequities in COVID-19 vaccine access and distribution around the world.<sup>44</sup> Tedros emphasized that vaccines remain out of reach in low-income countries, marking the first anniversary of the COVAX dose-sharing facility on 23 Apr 2021. He urged wealthier countries to be more responsible and share the excess vaccine doses to help vaccinate health workers in low-income countries. Vaccine availability remains a serious issue as out of 900 million doses >81% have gone to high- or upper-middle-income countries, and only 0.3% to low-income countries even after the setup of the ACT (Access to COVID-19 Tools) Accelerator a year ago.<sup>44,45</sup> The WHO Coronavirus (COVID-19) dashboard shows a grave situation worldwide with 3.48 million deaths out of 167.42 million confirmed cases, mortality of 2.1%, as of 25 May 2021.<sup>46</sup> This has now become obvious that "If the world doesn't share the vaccine, the virus will take on the world".<sup>39,47</sup>

From low daily cases of 152 on 1 Apr 2021, the spike reached over 8,000/d since 5 May 2021, a grave situation for a relatively small population of 29.5 million in Nepal. An unprecedented >45% positive rate of COVID-19 RT-PCR tests show how serious community infection is in Nepal. The health facilities in Kathmandu and provinces are overwhelmed and forced to turn away patients due to a shortage of beds and resources, the availability of oxygen, and trained human resource to operate ventilators and ICU care across the country. Since the 2nd lockdown in effect from 29 Apr 2021, the surge of cases is seen in villages where people lack access to testing and specialized care forcing them not to seek health service until severely sick. This reflects the fact of underreporting of cases or deaths from the government record which may not reflect the actual data.<sup>48</sup> Some patients do not even make it on time and succumb on the way to the hospital.

The prohibitory measures including lockdown in almost all districts, closer to 22 entry points along the open and porous Nepal-India border, suspension of domestic and international

flights have affected the daily lives. The 13 entry points which remain open, lack sufficient capacity for screening, contact tracing, or public health measures of safety, adding to the gravity of the situation because vulnerable populations are forced to adopt negative strategies for their very survival.<sup>45</sup>

The international passenger flights remain suspended until May 31 midnight.<sup>48</sup> The further vaccine rollout to cover the population across the country remains unknown given the continued lockdown, and concrete plan from the government to acquire vaccine.

### Rollouts of COVID-19 vaccines in Nepal

The vaccine rollout began on 27 Jan 2021, with Covishield grant assistance from India. The 1st dose in the 1st phase was provided to a priority group of frontline health workers, security personnel, sanitation workers, elderly people living in care homes, prisoners, and extended to media persons.<sup>41</sup> The 1st phase was completed on 5 Mar 2021 with 438,000 persons receiving the 1st dose.

Nepal has one of the highest (97%) willingness to accept the COVID-19 vaccine. This was reflected in a survey among low- and middle-income countries (LMICs) in Asia, Africa, and South America, and two higher-income countries (Russia and the United States). In general, LMIC had high acceptance (80%) compared to the USA (65%) and Russia (30%).<sup>49</sup>

On vaccine availability, the government had decided to buy 2 million doses of the vaccine from the Serum Institute of India at \$4 per dose and the first consignment of 1 million doses arrived on 21 Feb 2021. For the 2nd phase (7-15 Mar 2021), 348,000 doses of Covishield were provided under the WHO-backed COVAX facility. Citizens >65 y were included in the 2nd phase, and around 1.3 million people across the country got the jabs. The final tally stands at 438,000 people receiving the 1st dose of Covishield but only 370,000 received the 2nd dose (20-24 Apr 2021) across the country, Table 1.<sup>41</sup>

China Sinopharm's Vero Cell (BBIBP-CorV) under grant assistance of 800,000 doses arrived in Nepal on 29 Mar 2021. The persons working in postal and telephone services, public transports, water supply, tourism sector, paramedics in the production of and sales distribution of medicines, electricity supply, storage and transportation of consumer goods as well as health workers who missed out in the 1st phase (started on 27 Jan 2021 with Covishield) got the Chinese jabs. The jabs were made available from Dhulikhel Hospital, Barhabise Hospital of Sindhupalchok, and district hospitals in Nuwakot, Rasuwa as well as various hospitals in 3-districts of Kathmandu valley.<sup>41</sup> The rollout of the 2nd dose (16-24 May 2021) of the Chinese Vero Cell administration was streamlined from the ward

offices (the lowest local administrative unit), public facilities, schools, and health facilities not catering to COVID-19 patients because of the ongoing lockdown during the 2nd wave.

The vaccine diplomacy of India has left Nepal in the lurch because of the 1 million Covishield it gifted in Jan 2021, nearly half of it was used in 1st phase targeting health care workers and high-risk groups. Because of the Indian ban the people >65 y who got Covishield in extended vaccine rollout of 1st phase, had to wait for their second dose as Nepal did not receive further 1 million doses it had paid to Serum Institute of India. Nepal already received the first batch of 348,000 doses of Covishield under COVAX on 7 Mar 2021, and another 1.92 million was expected by the end of May 2021.<sup>50</sup>

**Table 1. The status of COVID-19 vaccine rollout in Nepal, as of 15 May 2021 (modified from<sup>41</sup>)**

| Vaccine         |  | Received         | Used               |                  |
|-----------------|--|------------------|--------------------|------------------|
| Grant, India    | Covishield*                            | 1,000,000        | 1st phase 1st dose | 438,000          |
| Purchase, India | Astrazenica,                           | 1,000,000        | 2nd phase          | 1,300,000        |
| Covax           | ChAdOx1 nCoV- 19                       | 438,000          | 1st phase 1st dose | 370,000          |
| Grant, China    | Vero Cell,<br>Sinopharm,<br>BBIBP-CorV | 800,000          | 1st phase 1st dose | 289,000          |
| <b>Total</b>    |  | <b>3,148,000</b> |                    | <b>2,397,000</b> |

\*From 1 million dose grant only half was delivered, and the purchased quantity is yet to be fulfilled<sup>50</sup>

So far, Nepal has received a total of 3,148,000 and administered 2,397,000 and remaining to administer 751,000 doses, Table 1.<sup>41</sup>

There is a lack of scientific published data, as of yet, on breakthrough infection rate and the outcome after the vaccination drive from the vaccines made available from India (Serum Institute manufactured AstraZeneca's Covishield) and China (Sinopharm's Vero Cell, BBIBP-CorV).

### Future vaccine strategies

As per a survey across LMIC, Nepal has one of the highest (97%) willingness to accept a COVID-19 vaccine. Thus, an efficient and equitable vaccine availability and distribution will help in immunization on a global scale.<sup>49</sup>

From identification of the virus to COVID-19 vaccines within a year is an important achievement. The ongoing pandemic has impacted the normality of the world with 3,478,956 deaths globally as of 24 May 2021 based on data Worldometer.<sup>51</sup> This also highlights the inadequacy of rich and poor nations alike, with lockdowns and human lives lost across the globe, rich and powerful countries including, for example, the USA has reported the highest death toll of 604,087 and Europe of 1,061,517 deaths.<sup>51</sup>

Based on SARS-CoV-2 evolution, a yearly revision of the vaccine sequence may be needed to include emerging mutations. The slow progress on vaccine coverage globally may require an extension of dosing schedules from 4 w to 12 w (or up to 16 w) between the 1st and 2nd dose to maximize the number of protected individuals and break the chain of

transmissions. However, this may increase the chance of breakthrough infection, especially in the elderly because of non-protective levels of antibodies during the window period before the 2nd dose.<sup>52</sup> Pfizer's chief executive officer, Albert Bourla, predicted the likely need for a third dose at 6-12 mo, and then annual revaccination.<sup>53</sup>

There is still a lot to be discovered and to be proved in the case of COVID-19 because the new findings keep adding up together with the recurring waves of infection, the emerging variants, the global vaccine coverage, and individual country's mitigation strategies to prevent and control the ongoing pandemic.

The WHO calls for solidarity against the COVID-19 pandemic and advises reducing the existing huge gap between countries around the globe for affordable vaccine access. The situation is aggravated due to stockpiling of vaccines by high-income countries and unethical, inequitable distribution of the vaccine. Doing away with vaccine nationalism and opting for an equitable vaccine distribution is an important humanitarian need to control the pandemic because 'no one is safe until everyone is safe'.<sup>54</sup>

The UNICEF has called on world leaders to: "1. Ensure equitable access to vaccines between countries by providing vaccines, sharing knowledge and expertise, and fully funding the Access to COVID-19 Tools (ACT) Accelerator, which is working to provide equitable access to and implementation of COVID-19 diagnostics, therapeutics, and vaccines; 2. Ensure equitable access to vaccines within countries by ensuring all sectors of the population are included in national distribution and vaccination programs, regardless of who they are or where they live, including stigmatized and marginalized communities for whom access to healthcare might not be straightforward; 3. Support countries financially, politically, and technically to ensure that curbing COVID-19 is not a standalone goal and instead is one important element of a broader health strategy, implemented alongside communities

to bring longer-term improvements to people's health and access to healthcare."<sup>54</sup>

The WHO has time and again emphasized ensuring fair and equitable access to vaccines, and ensure every country receives them and can roll out to protect their people, starting with the most vulnerable. A safe and effective vaccine is a game-changer. Yet, being vaccinated is not full proof and requires precautionary measures of wearing masks, cleaning hands, ensuring good ventilation indoors, physically distancing, and avoiding crowds because the evidence is still emerging as to how much vaccines protect against SARS-CoV-2 infection and transmission. It's the vaccination and not the vaccines that will stop the pandemic.<sup>55</sup>

Recently (16 May 2021), Nepal's Foreign Minister Pradeep Gyawali mentioned the government's plan to secure vaccines.<sup>56</sup> So far, Nepal has received 1 million doses of Covishield as a grant from India, another 1 million doses (from a purchase of 2 million), plus 100,000 doses for the Nepal Army. China gifted 800,000 Vero Cell vaccines.<sup>56</sup> Nepal also received 348,000 doses of Covishield under the COVAX. A further plan to buy 5 million doses from India did not materialize. Talks with Sinopharm to buy 2 million doses of Vero Cell for delivery by June 2021 are underway. Also, the Russian Sputnik vaccine has been approved for emergency use and Nepal has asked for 8 million doses, 4 million right away but it's unlikely the demand will be met because Russia is not producing enough. The diplomatic channels have been activated to convince the Americans to provide Nepal some of the vaccine doses from its stockpile of 60 million AstraZeneca. Additionally, Nepal is also 'knocking on COVAX's door' as per Gyawali.<sup>56</sup>

The vaccines should be available for everyone who could benefit from them to contribute to the control of the pandemic. The world needs to come to terms that no country is safe until every country is safe.

## Conclusion

Vaccination access, equitable distribution, and distribution around the world for prevention and control of SARS-CoV-2 Coronavirus disease (COVID-19) remain a problem with less than 1% vaccination coverage in low-income countries. If further delay in vaccination occurs there is a high chance for loss of protective window leading to breakthrough infection. The evidence shows re-infection following earlier exposure to COVID-19 occurs in a small percentage. The breakthrough infection has been reported in a small percentage of people after vaccination. The durability of immunity, incidence, and severity of breakthrough infection, and the role of new variants are emerging challenges in real-life scenarios. Nepal has safely vaccinated nearly 3 million population with Covishield (AstraZeneca, in India) and Vero Cell (Sinopharm, China). Further analysis of the data on breakthrough infection after vaccination and the effectiveness of these vaccines in the local population is awaited.

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### Author Contribution

Concept, design, planning: ALL; Literature review: JS; Draft manuscript: JS; Revision of draft: JS, NP, PS, JEN, JES; Final manuscript: ALL; Accountability of the work: ALL.

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