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LETTER

Preparatory phase for clinical trials of COVID-19 vaccine in Nepal

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ABSTRACT

Public health data suggested a rapid rise in COVID-19-confirmed cases in Nepal along with increased deaths. There has been a wide variation in clinical outcomes of this disease. Control of this pandemic depends on the availability of vaccines or drugs for SARS-CoV-2. Thus, viral and human genetics/genomics and immunology are necessary to understand whether these factors will affect clinical trials of vaccines in Nepal.

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Coronavirus (CoV) was first isolated in 1937 from an infectious bronchitis virus in birds and reported in 1960 from humans. It belongs to *coronaviridae* family and the beta-coronavirus subfamily. The virus appears as a Solar Crown in electron microscope, hence named 'corona'. It is a large enveloped virus containing single stranded, positive-sense RNA with genomic length of 27–32 kb.[1] The viral envelope consists of at least three structural proteins: The membrane protein (M) and the envelope protein (E) are involved in virus assembly, whereas the spike protein (S) mediates virus entry into host cells.[2] CoVs cause disease in both humans and animals. More than 80% of infections were known to be zoonotic. Seven types of human CoVs, viz., HCoV-OC43, HCoV-HKU1, HCoV-229E, HCoV-NL63, SARS-CoV, MERS-CoV, and SARS-CoV-2, have been reported.[1,2]

The entire world is suffering from the coronavirus disease 2019 (COVID-19) pandemic caused by Severe Acute Respiratory Syndrome CoV-2 (SARS-CoV-2) which has infected over 14 million people worldwide with more than a half-million deaths.[3,4] No animal host has been confirmed as a vector of SARS-CoV-2 although it supposedly originated from wild animals.[1,2] While the history of SARS-CoV-2 is short, scientists are still learning about its pathogenesis, clinical manifestations, and transmission dynamics.

Despite Nepal Government's official lockdown, the COVID-19-positive cases are increasing due to a large number of Nepalese migrant returnees from India who were living there for their livelihood and other purposes. India also has experienced a rapid growth of COVID-19 cases,[5,6] so migrant Nepalese from India lead to an unprecedented surge in the virus contagion in Nepal. Most of the people in quarantines and those suspected and confirmed COVID-19 cases were in bordering areas of Nepal. Through July 2020, over 17,000 cases have been confirmed by real-time polymerase chain reaction (RT-PCR) and 40 deaths due to COVID-19.[3–6] Most infected patients who died were 40–50 years old and had co-morbidities, such as renal diseases, tuberculosis, diabetes, and cancer. According to Nepal's Ministry of Health and Population of Nepal, over 99% of patients have been asymptomatic, while the rest showed mild symptoms and required no ICU and ventilator facility except for a few cases.[6] Its clinical presentation is different from other highly affected countries where severity followed by death is relatively high.[6] Such a variation might be due to the diverse travel history and strain variation in SARS-CoV-2. The majority of patients have recovered from infection. It is important to note that there are ninefold more males with COVID-19 positive than females; males were migrant workers in community, which may be the reason for this higher number of male positive cases. There is no clear scientific evidence why COVID-19 infection has such varied clinical presentation in Nepal.

This pandemic has created the need for a common global platform to develop vaccines and drugs. Provision of mandatory quarantine should be effective, but adversely affects the overall economy of people and countries.[7] Therefore, a safe and effective vaccine against COVID-19 is the answer to this major public health crisis. Many biotechnology companies worldwide are working to develop vaccines.[8] After testing immunogenicity, stability, and toxicity, if found to be suitable, the vaccine would receive quality approvals such as Good Clinical Practice (GCP), Good Manufacturing Practices (GMP).[9] Currently, 23 candidate vaccines are in clinical trials to evaluate their safety and immunogenicity and few candidates are entering phase III trial soon.[10,11] A passive vaccination strategy using hyperimmune human serum can be employed in sick patients.[12] Once vaccine is successfully developed and licensed, its use will be

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mainstreamed in general population for prevention of disease. Nevertheless, there might be a risk of reduced effectiveness in some variants of SARS-CoV-2 due to potential mutations evolved with time. Thus, even after the vaccine development, there may be a challenge in its effectiveness in Nepal due to the diversity of SARS-CoV-2 (yet to be defined) as well as the physiology and immune response of Nepalese people. Other associated factors include availability and accessibility of vaccine, health policy and system, average age of people; precautions maintained in quarantine and per capita income also influence disease prevention.[9] Thus, the ongoing pandemic has highlighted the urgency that the Government of Nepal should invest in research on strengthening of molecular diagnostic facilities and training of human resources to generate more data on viral genomics, human genetics, and immune responses. This will further enable our understanding on whether a COVID-19 vaccine can be effectively used in Nepal and to develop a procedure for a fair application of vaccine into population at higher risk across the country.

Contributions

GPG, YS, SPD, and BDP conceptualized and developed the outline for this manuscript. GPG, YS, SPD, and KP developed the first draft. YS, GPG, SL, RS, DKP, AM, KP, PP SPD, and BDP contributed to data acquisition and further review of the manuscript. The authors read and approved the final manuscript.

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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