



Community-Based Approach to Clinical Trials: Insights and Challenges from COVID-19 Vaccine Trials in Nepal

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SUMMARY

Vaccine trials in Nepal are not a new phenomenon. However, following the COVID-19 pandemic, there were several vaccine trials for COVID-19 vaccines in Nepal. Unlike previous trials, COVID-19 vaccine studies required swift and large-scale enrollment from communities. These trials aimed to recruit healthy individuals to evaluate the safety and efficacy of the vaccines in preventing the targeted disease.

In clinical trials other than vaccines, researchers can enroll patients with specific medical conditions with their consent from the hospital. In contrast, vaccine trials require researchers to recruit healthy volunteers primarily found in community settings. Recruiting healthy individuals from these communities is challenging because it involves navigating various layers of community stakeholders who must be supportive and grant permission for participation. Therefore, community-wide engagements crucial for the success of vaccine trials.

Communities need to be fully informed and positively engaged, despite potential negative influences from media and misconceptions about the trials. Despite these challenges, effective community interventions and engagement resulted in the successful enrollment of up to 4,600 participants across three trial centers within just two months.

Conducting the clinical trial in Nepal with a community-based approach has been enriching and effective. This strategy facilitated smooth implementation and deepened connections with the local population. Engaging with community leaders, stakeholders, and members helped overcome challenges such as participant recruitment and adverse event management. The active involvement of community members in various trial stages fostered trust, cooperation, and empowerment. This experience underscored the importance of community engagement, cultural sensitivity, and collaboration in achieving successful and sustainable clinical research, inspiring us for future endeavors.

Key Words: Vaccine trial, clinical trial, community-based approach, COVID-19, Nepal.

INTRODUCTION

A clinical trial is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Interventions include but are not restricted to drugs, cells and other biological products, surgical

procedures, radiological procedures, devices, behavioral treatments, process-of-care changes, preventive care, etc. (1,2) The definition indicates that a Vaccine Trial is a specific type of clinical trial. Vaccine trials aim to determine the safety, effectiveness, and potential side effects of a new vaccine. These trials follow rigorous protocols to ensure that the vaccine provides

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adequate protection against a particular disease and is safe for public use. Therefore, it can be said that all vaccine trials are clinical trials.

In general, health-related interventions/trials encompass a wide range of measures such as drugs, vaccines, surgical procedures, devices, behavioral treatments, educational programs, dietary interventions, quality improvement interventions, and process-of-care changes. These interventions aim to bring about modifications in health-related outcomes. Typically, the implementation of most of these interventions/trials occurs within a hospital-based setting. Hospitals, acting as central hubs for healthcare, have multidisciplinary teams of medical experts, including physicians, nurses, paramedics, lab technicians, and more. (3) This setting also provides the necessary infrastructure for executing clinical trials. Moreover, hospitals attract patients from diverse backgrounds and demographics, serving as a valuable asset in clinical trials. This diversity allows researchers the opportunity to examine the impact of interventions across a broad spectrum of populations. (4)

In the areas of clinical trials, the trials related to drugs, procedures, or any equipment are typically focused on evaluating the safety and efficacy of the products in patients with specific medical conditions. These trials are conducted in hospital settings, where individuals with the targeted health conditions seek medical care. Patients visit the hospital, where researchers enroll them in the study after obtaining their consent. (5) In contrast, vaccine trials are often carried out in a healthy population, frequently within university and community settings. In a university setting, the researcher typically posts a trial notice on university website or notice board, and interested students voluntarily enroll themselves in the trial after expressing their interest. Similarly, in community settings, the researchers use IEC brochures and other media to inform and enroll the participants in the trial. (6) toxicity, safety, and pharmacokinetics of the drug decide whether it goes for the clinical trial. Clinical trial of a drug is executed in four different phases (phase I, II, III, and IV)

COVID-19 VACCINE TRIALS IN NEPAL

Several vaccine trials have been conducted in Nepal, primarily by the Institute of Medicine TU, Kathmandu University and its collaborators, as well as by the Society for Local Integrated Development Nepal (SOLID Nepal) and its partners. SOLID Nepal, a national NGO focused on health, carried out two vaccine trials, enrolling 1,200 and 4,600 healthy volunteers, respectively within a very limited span of time.

The selection criteria required participants to be unvaccinated and free from prior COVID-19 infection, making it challenging to find a large enough pool of

eligible participants in urban areas, where many had already received COVID-19 vaccinations. As a result, the trials had to be conducted in rural and community settings, where a more diverse participant pool could meet the specific enrollment criteria outlined in the protocol. Therefore, SOLID Nepal opted to conduct the vaccine trials in rural areas, partnering with local organizations that had longstanding relationships with the community. New trial sites were also established near these communities, leading to the expansion of vaccine trial sites to the Chitwan, Jhapa, and Sunsari districts of Nepal. This expansion marked a significant milestone in the field of clinical trials in the country.

Experience in community and the challenges

Since vaccine trials were a new initiative in Nepal, local organizations and bodies lacked sufficient knowledge in this area, making it challenging to find suitable partners and community mobilizers. Even explaining the concept to local authorities was a challenging task. Acknowledging the sensitivity of conducting trials in regions with limited education and information, SOLID Nepal established partnerships with three local organizations in the selected districts. The main goal of this collaboration was to engage local community actors in raising awareness and informing potential participants about the clinical trial process. Social mobilizers were recruited and trained on the vaccine trial, the overall project, and their specific roles and responsibilities. Additionally, the established sites were prepared for vaccination, and the necessary human resources were trained accordingly.

Participants recruitment

Upon project initiation, the study faced the massive challenge of finding participants meeting the criteria set by the study protocol. Many participants were disqualified during screening at the vaccination sites due to non-compliance with the inclusion criteria specified in the protocol. Additionally, even though the participants met the criteria, the hesitancy to participate in the clinical trial was prevalent in the community. A high number of participants refused vaccination even after signing the informed consent, which we respected the decision made by the participants.

However, an alternative approach was adopted to address the challenge of screening failure at the vaccination site, involving the preliminary screening conducted within the community by organizing a health camp. This approach aimed to identify and bring the participants who fulfilled the inclusion criteria to the designated vaccination sites. This approach was successfully implemented and proved efficient in managing the participants. Also, the implementation of this approach not only facilitated the identification of eligible participants but also played a crucial role

in addressing health issues within the community and helped uncover health problems among individuals who were previously unaware, enabling early management of these issues. Identified individuals were promptly referred to hospitals or health centers for further medical attention. Through effective mobilization via health camps and strong coordination between the trial sites and partner organizations, the recombinant two-component COVID-19 vaccine (Recov) trial successfully enrolled 4,607 participants, including 314 specifically in the immunogenicity group. Similarly, another trial for the recombinant COVID-19 vaccine (Sf9 cell) successfully enrolled 1,269 participants.

Follow-up, monitoring and reporting

Following the enrollment, the trained social mobilizers maintained regular contact with participants daily, conducting thorough follow-ups to monitor any solicited or unsolicited events. In case of any events, the social mobilizers promptly communicated with physicians at the sites, ensuring necessary and immediate management while prioritizing the participants' health. After administering three consecutive doses of vaccines spaced 21 days apart, the follow-up process was extended for up to six months for vaccinated participants. Any instances of Severe Adverse Events (SAEs) were promptly addressed and reported to the sponsor, the Ethical Review Board of Nepal Health Research Council (NHRC), and the Department of Drug Administration (DDA). Moreover, detailed information regarding each SAE was presented to the Data Safety and Monitoring Board (DSMB) to determine its relation to the study vaccine. The decisions of the DSMB were then submitted to the sponsor, NHRC, and DDA respectively, ensuring a comprehensive and transparent approach to safety monitoring in the study.

Management of severe adverse events (SAEs)

Serious Adverse Events (SAEs) are critical occurrences that encompass severe side effects, hospitalization, persistent disability or incapacity, congenital anomaly/birth defects, life-threatening situations, or even death. Given the size of this trial, management of the SAE cases was also a challenging task. For the immediate response and management of any kind of SAE, our three site hospitals had standby medical staff to address such emergencies and a robust referral system was in place as per the requirement. All participants and their social mobilizers were strictly instructed to seek the nearest medical support and notify site investigators in the event of SAEs immediately. All SAE cases were thoroughly examined and tested to identify their relation with the study vaccine and the reports were thoroughly discussed in the DSMB meetings. The social mobilizers and communities collaborated extensively to report and address any adverse events experienced by the participants. The trial projects received strong

support in the management of these issues.

Media management

Another challenge we faced was media reporting. Some reputable outlets claimed that marginalized communities were being targeted in the clinical trials, despite these articles being groundless. This caused significant rumors within the communities, leading to fear among participants and eroding trust in our study team from local representatives. To address the situation and rebuild trust, we held meetings with local representatives, community members, and participants. Similarly, media advocacy was conducted to clarify the process of clinical trials. The trial projects organized workshops and meetings with journalists to clarify the issues surrounding clinical trials. Over time, the media recognized that clinical trials ultimately benefit people and began advocating for them. From this experience, we learned the importance of proactive communication with the media to prevent misinformation and minimize misunderstandings.

Endpoint collection

The collection of endpoint cases was another important yet challenging issue in this trial as there was a provision for self-antigen test in the protocol. However, a substantial number of participants faced difficulties in conducting these tests on their own. To address this, social mobilizers underwent training and were actively involved in administering the antigen tests. The process of collecting endpoint cases involved regular communication initiated by social mobilizers who closely monitored participants for any indications of COVID-19 infection. Additionally, participants were instructed to promptly reach out to social mobilizers if they experienced any symptoms associated with COVID-19. Ultimately, a total of 210 potential endpoint cases were identified across three different sites. This extraordinary achievement was made possible solely through our strong community engagement.

Hindrances from the law enforcement agency

Despite the significant success of community participation in the trial, the social mobilizers faced various hurdles from law enforcement agencies at the community level. To facilitate endpoint collection, our team set up mobile health camps at the community level. These camps included home visits where antigen tests were conducted, medical check-ups were performed, and medications were dispensed. If an antigen test was positive, the swabs were collected for polymerase chain reaction (PCR) for further analysis. However, during one operation, two of our social mobilizers were detained by local armed forces. Despite our attempts to explain the situation, we struggled to convince the authorities, leading to the detention of our mobilizers and the seizure of our vehicle.



LESSONS LEARNT

Conducting the clinical trial in Nepal using a community-based approach has been an enriching and multifaceted experience. The utilization of a community-centric strategy has not only facilitated the smooth implementation of the trial but has also fostered a deeper connection with the local population. Engaging with the community has proven instrumental in overcoming various challenges, from participant recruitment to management of adverse events. The collaborative efforts with local leaders, stakeholders, healthcare practitioners, and community members have enhanced the trial's credibility and acceptance. This approach has allowed us to build trust within the community, leading to a higher level of participant cooperation and enthusiasm.

The active involvement of community members in various stages of the trial, including the dissemination of information, participant monitoring and follow-up and feedback collection, has not only contributed to the trial's success but has also empowered the local community. This empowerment is reflected in the sense of ownership and pride expressed by community members who see themselves as integral contributors to advancing medical knowledge.

In conclusion, the experience of conducting the clinical trial in Nepal using a community approach has been holistic and rewarding. It has highlighted the importance of community engagement, cultural sensitivity, and collaborative partnerships in ensuring the success and sustainability of clinical research endeavors in diverse settings.

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