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Spectrum of Adverse Event Following COVID-19 Immunization in High Altitude, Nepal

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ABSTRACT

Introduction: Nepal started vaccinating frontline workers against COVID-19, in January 2021. Side effects of the vaccine are still unknown in high-altitude regions. Poor surveillance and the lack of health workers in remote places to take care of people in case of vaccination could prove to be a challenge in the drive, in high altitudes like Humla district, Nepal. High-altitude regions are harder to access and mobilization of vaccines and manpower is strenuous due to harsh weather conditions and complex geography. We aimed to study the spectrum of Adverse Events Following COVID-19 Immunization among the front liners of the Humla district.

Methods: This is a cross-sectional study conducted in Humla district, Nepal. COVID-19 Immunization vaccine recipients were contacted through a phone call within 5 days of vaccination to record the adverse effects. Patterns and distribution of adverse effects were analyzed in high-altitude settings. Ethical approval was taken from the Nepal Health Research Council.

Results: Of the total respondents, 84.1% (95% C.I: 80.9 to 86.9) had shown symptoms after vaccination. The average time for the appearance of symptoms was 1.27 +_ 0.60 days. For systemic effects, tenderness was the side effect seen after vaccination (63.8%) followed by other side effects like pain (58.5%), Pyrexia (37.4%), Chills (29.8%), Myalgia (28.9%), and Malaise (15.2%) while for localized effects, the symptoms such as Arthralgia (16.6%) and Bruising (16.1%) were the most common effects.

Conclusions: Serious and life-threatening adverse effects following immunization were not seen in our study site which was at an altitude of 2500 meters and above. Our study shows a similar type of side effect pattern as that of the lower altitude regions.

Keywords: *Adverse effects ; COVISHIELD; High altitude; Vaccine.*

INTRODUCTION

On January 27, 2021, Nepal's vaccination campaign began, and as of April 20, 2021, 17 million doses of the COVID-19 vaccine had been given to chosen communities as a first dose.[1] The effectiveness of this vaccine in reducing infection, severe disease, and hospitalization, has been reported, revealing it to be 62.1% effective after two standard two doses.[2]

According to the European Medicines Agency (EMA), almost 50 % of participants experienced injection site pain, headaches, or weariness after receiving the Oxford-AstraZeneca vaccine. Following the first dosage of the ChAdOx1 nCoV-19 vaccine, research done in the United Kingdom utilizing the COVID Symptom Study app found

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that the incidence of local and systemic reactions was 58.7% and 33.7 percent, respectively.[3] Another study employing the Mobile Vaccine Adverse Events Reporting System (MVAERS) among Korean health workers found an AEFI of 66.1 % after the first dose of ChAdOx1 nCoV-19 vaccine.[4] Shrestha et al. found an 85.04% incidence of AEFI after the first dose of Covishield immunization in one of central Nepal's main tertiary hospitals.[5]

Studies suggest that high-altitude residence may be beneficial in the novel coronavirus disease (COVID-19) implicating that traveling to high places or using hypoxic conditioning could be favorable as well[6]

The lack of human resources, technology to transport the vaccine, harsh climate, and arduous geography are among the many challenges in the high altitude of Nepal.[7] Once a vial is opened, ten or eleven people must be ready to get their dose within a six-hour interval.[6]

Vaccination at higher altitudes may have incompatible adverse side effects compared to the side effects of vaccination in other regions.There is a lack of sufficient evidence of the adverse effects of COVID-19 in high-altitude regions.We conducted the study to explore the spectrum of Adverse events following COVID-19 Immunization among frontline workers in the Humla District.

METHODS

We conducted a telephone-based cross-sectional study among 603 frontline workers between February to March 2021 to determine the spectrum of Adverse events following COVID-19 immunization among frontline workers in High altitude, Humla District. Prior to data collection, ethical approval was obtained from the Nepal Health Research Council (Ref no.2475). We obtained written permission from the District Administration Office in Humla and verbal consent from each participant prior to the interview. We assured the voluntary participation of the participants and maintained the confidentiality and anonymity of the participants throughout the study.

Study Area and Study Population

Our study area was the Humla District. Humla is Nepal's highest district, with most settlements located between 3,000 and 5,000 meters above sea level. Humla District, located in Karnali Province, is one of Nepal's seventy-seven districts. The region is one of the most underdeveloped areas in Nepal with only one hospital and campus and few higher secondary schools in Simikot serving the whole district. Most of the villages of Humla don't have access to electricity to maintain the cold chain. According to the 2011 census, the district, which includes Simikot as its district headquarters, spans an area of 5,655 km2 (2,183 sq mi) and has a population of 50,858 people. The district consists of 7 Municipalities, all of which are rural municipalities. The COVID-19 vaccination program in Humla district was started in February 2021 at the district hospital, Simikot. The first phase of vaccination was given to frontline workers.

The target population was frontline workers who took the first dose of COVISHIELD from the district hospital located at Simikot, Humla.Frontline workers were prioritized for vaccination and chosen as the study population due to their increased exposure to COVID-19, which may also influence their immune response to vaccination.-sentences as such could expand the rationale for choosing frontline workers

Pregnant and lactating women were excluded due to the unknown risks of COVID-19 vaccination in these populations at the time of the study. Participants with flu-like symptoms were excluded to avoid confounding the identification of vaccine-related side effects- these sentences could further explain the exclusion criteria

Participants were contacted between the 5th day of vaccination. Subjects with flu-like symptoms, pregnant, lactating women, below 18 years were excluded. The first vaccine made available by the Nepalese government was COVISHIELD. This vaccine contains genetically modified organisms produced in genetically modified human embryonic kidney 293 cells.

Sample Size Calculation and Sampling Technique

The sample size (n) was determined using the Cochrane formula, assuming 50% prevalence and 5% permissible at 95% confidence interval(CI). Taking 10% of the non-response rate, our calculated sample size was 422. However, we recruited 603 participants conveniently. The calculated sample size was 422, we recruited 603 participants to account for potential data loss and to increase the statistical power of the study, given the importance of capturing diverse AEFI experiences in this remote population

Data Collection Tool and Technique

The list of recipients of the vaccine was extracted from the record available in the record section of the vaccination centers from the district hospital. We conducted telephone-based interviews. The survey was estimated to take around 10 minutes to complete. We constructed and developed a questionnaire to report the AEFI. The questionnaire consisted of three components, a) Socio-demographic component including age (in years), gender(male/female), ethnicity (Brahmin, Chhetri, Madhesi, Janajati, Tharu and Dalit), education and monthly income b) anthropometric components consisting of height (in meter), weight (in kilogram) and BMI (kg/m2), and c) AEFI component (Tenderness, Pyrexia, Pain, Nausea, Myalgia, Malaise, Induration, Headache, Fatigue, Dizziness and Chills)

Data Analysis

We analyzed the typical symptoms that have been reported. We categorized the symptoms into systemic and localized. Those diseases that affect the entire body rather than the single organ were categorized as systemic diseases whereas those that start in one area of the body or organ system and are limited to that area were categorized as localized diseases [8]. Similarly, after collecting the data, we entered, coded, and analyzed data in IBM Statistical Package for Social Sciences (SPSS) version 20. We calculated frequencies and percentages for all categorical variables as a part of descriptive analysis.

RESULTS

The mean age of respondents was 34.5 years (34.5±10.3) and the youngest respondent was 18 years while the eldest was 77 years. The majority of respondents (79.6%) were male. This study reported that more than half of the respondents (58.7%) belonged to the Chhetri ethnic group. Data on educational status demonstrated the average completed years of education as 11±7.1. Similarly, the average monthly income of the participants was 31443.3±18536.8.

The majority of respondents (64.5%) at the time of the study had normal BMI while very few proportions of participants had obesity. Similarly, only 12.8% of participants had one of the comorbidities.

Table 1. Participants` Characteristics (n= 603)

Characteristics	n (%)
Gender	
Female	123 (20.4)
Male	480 (79.6)
Ethnicity	
Brahmin	48 (8.0)
Chhetri	354 (58.7)
Madhesi	15 (2.5)
Janajati	146 (24.2)
Tharu	4 (0.7)
Dalit	36 (6.0)
BMI	
Underweight	45 (7.5)
Normal Weight	386 (64.5)
Pre-obesity	139 (23.2)
Obesity	28 (4.7)

Of the total respondents, 84.1% (95% C.I: 80.9 to 86.9) had shown symptoms after vaccination as represented by Figure 1. The average time for the appearance of symptoms was 1.27 +_ 0.60 days.

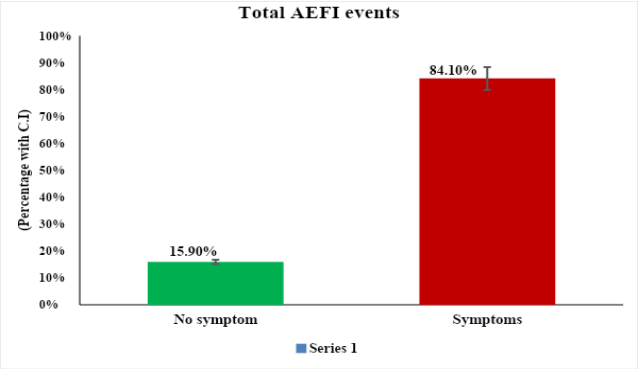

Figure 1: Total AEFI Events

Figure 2 depicts the AEFI comparison between men and women, where we discovered a significant difference in the AEFI between the men and women groups.

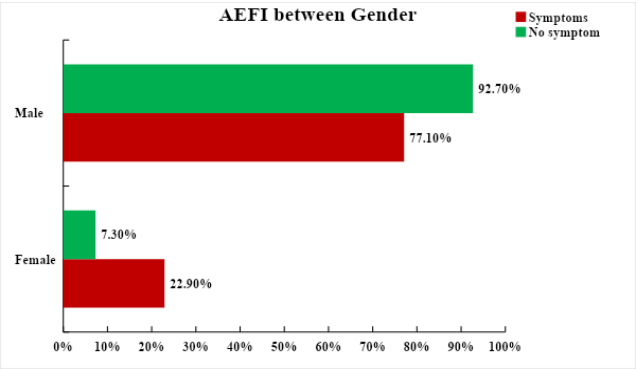

Figure 2: AEFI between gender

We categorized symptoms of vaccination as systemic and localized effects. As represented in Figure 3 tenderness was the significant side effect seen after vaccination (63.8%) followed by other side effects like pain (58.5%), Pyrexia (37.4%), Chills (29.8%), Myalgia (28.9%) and Malaise (15.2%). Likewise, other effects like Dizziness, Nausea, and Injection site induration were less common among the participants.

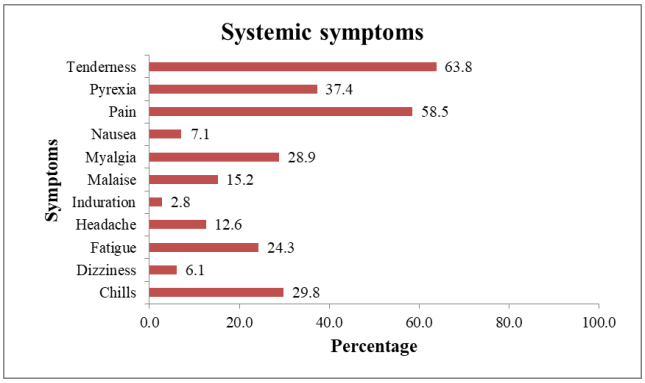

Figure 3: Systemic Symptoms

For localized effects, symptoms such as Arthralgia (16.6%) and Bruising (16.1%) were the most common effects, followed by erythema, abdominal pain, and lymphadenopathy.

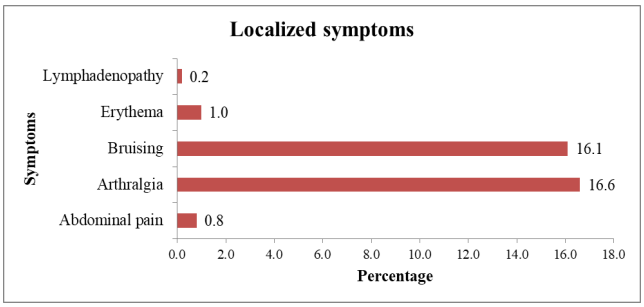

Figure 4: Localized symptoms

DISCUSSION

This study aimed to study the spectrum of Adverse Event Following COVID-19 Immunization among the front liners in High Altitude, Humla district, Nepal. The most common side effects seen in this study were tenderness (63.8%), pain (58.5%), pyrexia (37.4%) followed by chills (29.8%), myalgia (28.9%) and fatigue (24.3%) which are common side effects of COVID-19 according to WHO and Centers for Disease Control and Prevention (CDC).[9] This study mainly focused on AEFI at high altitudes. Out of 603 respondents, the majority (84.1%) had shown AEFI events that allied with the post-vaccine cross-sectional study conducted among healthcare workers in Chitwan Medical College of Nepal which is located in the Terai region accounting for 78.9% among 424 respondents. Therefore, the percentage of adverse effects seen among participants was almost similar regardless of the difference in regions.[10]

Similarly, a study done in western Nepal revealed that 91.6% of the total respondents developed some form of AEFI where the majority of them were males with a mean age of 33 which aligns with the findings presented by our study.[11] While one of the studies which was conducted in India showed a contrasting result as a major proportion of women reported post-vaccination symptoms in comparison to men.[12] This could be because, when compared to men, women are regarded to have a more robust immune response and build larger cell-mediated and humoral immune responses in response to antigenic stimulation by vaccination or infection.[13]Likewise, a study conducted in Jember, Indonesia did not show any association between AEFI events and gender which is opposed to the result revealed by our study.[14] This difference might be due to the dissimilarity in the study population. Initially, countries like Peru temporarily suspended the trials of Covid vaccine after finding neurological problems in one volunteer.[15] Furthermore, studies conducted in countries like Canada and Russia reported symptoms more among the female population than in males which is in contrast to the findings of our study.[16,17]

This study found the majority of side effects were injection site-related effects like tenderness (63.8%), pain (58.5%), and pyrexia (37.4%) which allied with most of the immunization cases.[18] Comparably, one of the studies from Japan revealed 82% of local adverse events like headache, fatigue, nausea, 71% of injection site pain, and 48% of systemic adverse events like myalgia which is common in this study.[19] A study conducted in the United Kingdom in the peak winter season from December 2020 to March 2021 reported that tenderness and local pain around the site of injection was the most common symptom experienced by the participants which is consistent with the findings revealed in this study. This resemblance in both studies might be due to similar temperate conditions.[20]

CONCLUSION

Limitations of this study were reliance on self-reported data, recall bias, and the limitations of telephone-based data collection .Serious and life-threatening adverse effects following immunization were not seen in our study site which was at an altitude of 2500 meters and above. Our study shows a similar type of side effect pattern as that of the lower altitude regions. More study needs to be done in other high altitude regions to understand the physiological impact of altitude on vaccination.

CONFLICT OF INTEREST

None

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