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Adverse Events following AstraZeneca COVID-19 Vaccine in Saudi Arabia: A Cross-Sectional Study among Healthcare and Nonhealthcare Workers

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Keywords
Coronavirus disease · Safety · AstraZeneca COVID-19 vaccine

Abstract
Introduction: Many COVID-19 vaccines have been emerging with different efficacy and safety profiles. So far, very little attention has been paid to severity and reactogenicity of COVID-19 vaccine among healthcare workers. Thus, the aim of this study is to investigate the side effects associated with the first dose of AstraZeneca COVID-19 vaccine among healthcare workers (HCWs) and nonhealthcare workers (non-HCWs). ***Method:*** This is an observational cross-sectional study conducted at King Abdullah bin AbdulAziz University Hospital, Saudi Arabia, between February 28 and March 12, 2021. The major outcomes were the reported side effects of day 1, day 2, and day 3 after vaccination among HCWs and non-HCWs. Other outcomes included the onset and the duration of the reactions or the side effects that were reported. ***Results:*** A total of 526 participants completed the survey with 173 (32.8%) HCWs and the remaining majority were non-HCWs. Some of the most frequently reported side effects among the participants on the first day were muscle aches (49%), followed by fever (42%) and headache (40%). HCWs experienced more muscle aches, headache, sore throat, and abdominal pain, which were statically significant, compared to non-HCWs. The mean onset of symptoms was 16 (±15.3) h in the HCW arm compared with 12.2 (±10.2) h in non-HCWs ($p = 0.0024$). Furthermore, the mean duration of symptoms in the HCW group was 37 (±19) h compared with 32.3 (±13) h in the non-HCW group ($p = 0.067$). ***Conclusion:*** The reported side effects were common but not pressing in both groups. HCW respondents appeared to have more COVID-19 vaccine-associated symptoms.

Introduction

The coronavirus disease (COVID-19) pandemic, which started in 2019 in China, continues to spread, despite multiple lockdowns and prolonged control measures implemented in most countries [1]. Health care workers (HCWs) are at risk for COVID-19 infection, and reports have described cases in HCWs since early in the outbreak [2]. Besides the high mortality risk, several studies found that COVID-19 has a negative impact on the psychological and well-being of HCWs [3, 4].

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Table 1. Baseline characteristics of survey participants

Individual characteristics	HCW (n = 173)	Non-HCW (n = 353)	p value
Age, mean (SD), years	37 (9)	41 (14)	0.84
BMI, mean (SD)	27 (8)	27 (6.9)	1
Male gender, *n* (%)	83 (46.82)	161 (51.2)	0.60
Previous COVID-19 infection, *n* (%)	14 (8)	22 (6.2)	0.46
Healthy, *n* (%)	135 (78.03)	295 (83.56)	0.60
Comorbidities, *n* (%)			
Lung disease	15 (8.67)	15 (4.24)	0.04
Hypertension	13 (7.51)	32 (9.06)	0.62
Diabetes mellitus	8 (4.62)	29 (8.21)	0.14
Heart disease	2 (1.15)	11 (3.11)	0.23
Immune disease	2 (1.15)	2 (0.56)	0.60

BMI, body mass index; HCW, healthcare worker.

Since the beginning of the COVID-19 pandemic, major efforts have been executed to develop an effective and safe vaccine [5]. In December 2020, several vaccine candidates were shown to be safe and efficacious in trials, and mass vaccination (in combination with existing control measures) is seen as one of the central elements to controlling the pandemic [1, 6, 7].

Vaccines mainly act by simulating a natural infection and thereby promoting development of a humoral and cellular immune response aimed at defending the host against a specific pathogen [8]. The majority of the known aftereffects were mild in terms of severity such as headache, pain at the injection site, muscle pain, and fever [9, 10]. There are some serious adverse events reported in COVID-19 vaccine trials, and several European countries withdrew the AstraZeneca vaccine over its alleged link to blood clots [11].

A recent cross-sectional study that was conducted among HCWs in Saudi Arabia showed that 12% of HCWs were not willing to receive COVID-19 vaccine. Among those, almost half were hesitant to receive the vaccine due to concern about adverse events [12]. Up to our knowledge, there is no study investigating the adverse events among HCWs and non-HCWs in Saudi Arabia. In this study, we report the adverse events following the first dose of AstraZeneca vaccine among HCWs and non-HCWs.

Materials and Methods

A cross-sectional study was directed at King Abdullah Bin AbdulAziz University Hospital (KAAUH) in Riyadh, Saudi Arabia. A survey was distributed to all individuals who received AstraZeneca vaccine between February 28 and March 12, 2021, at day 3 after vaccine. Two pharmacy interns approached all individuals who received the COVID-19 vaccine by hospital phone on day 3 after vaccination. A description to the study and its objective was provided to all individuals. We included all individuals who got the vaccine in the study period.

Structured Survey

The structured survey consists of 2 parts. The first part of the survey included information about the demographic data of the participant such as age, weight, height, gender, ethnicity, and comorbid conditions. The second part of the survey included information about the specific symptoms that were experienced by each participant after getting the COVID-19 vaccine. Ten symptoms were listed in the survey including fever, sore throat, muscle pain, eye muscle pain, new loss of smell or taste, shortness of breath, headache, numbness, palpitation, and abdominal pain. Participants were inquired about the side effects they experienced during days 1, 2, and 3 after the vaccinations. Also, the participant may add any other symptoms that were not listed in the abovementioned options. In addition to that, the participants were required to describe the severity of each symptom in the first 3 days after getting the vaccine. The scale of severity ranged from no symptoms to severe symptoms. Participants were also asked about the average time their symptoms started and the duration the symptoms persisted. Additionally, participants were asked whether using a pain killer resolved the symptoms that can be managed by the pain killers. Once the participant completed the survey, the data were uploaded and saved into a secure Excel spreadsheet.

Statistical Analysis

Categorical data were presented as frequencies and percentages and compared using the χ^2 test or Fisher's exact test as appropriate. Continuous data were presented as mean with standard deviation or median with interquartile range and compared using the t test for normally distributed data or Mann-Whitney U test for nonnormally distributed data. The data were analyzed using IBM SPSS Statistics (Version 26) predictive analytics software. Significance was assumed for a p value <0.05.

Table 2. Side effects to COVID-19 vaccine reported within 3 days following the first dose

Side effect, *n* (%)	HCW (*n* = 173)	Non-HCW (*n* = 353)	*p* value
Day 1 after vaccination			
Muscle pain	111 (64)	151 (43)	0.000
Headache	86 (49.7)	124 (35)	0.002
Fever	69 (40)	152 (43)	0.511
Numbness	20 (12)	25 (7)	0.097
Eye muscle pain	18 (10)	15 (4)	0.012
Gastrointestinal symptoms	16 (9)	6 (2)	0.000
Sore throat	14 (8)	8 (2.3)	0.004
Palpitation	12 (7)	13 (4)	0.126
Smell/taste loss	4 (3.2)	3 (0.8)	0.225
Shortness of breath	6 (3.5)	17 (4.8)	0.651
Day 2 after vaccination			
Muscle pain	96 (56)	119 (34)	0.000
Headache	64 (37)	90 (26)	0.008
Fever	59 (34)	105 (30)	0.318
Numbness	15 (9)	12 (3)	0.019
Eye muscle pain	16 (9)	16 (5)	0.029
Gastrointestinal symptoms	12 (7)	9 (3)	0.030
Sore throat	14 (8)	4 (1)	0.000
Palpitation	11 (6)	9 (3)	0.049
Smell/taste loss	6 (4)	1 (0.3)	0.006
Shortness of breath	3 (2)	12 (3)	0.405
Day 3 after vaccination			
Muscle pain	44 (25)	52 (15)	0.004
Headache	29 (17)	44 (13)	0.182
Fever	12 (7)	37 (11)	0.205
Numbness	7 (4)	6 (2)	0.134
Eye muscle pain	5 (3)	7 (2)	0.541
Gastrointestinal symptoms	8 (5)	8 (2)	0.176
Sore throat	11 (6)	0 (0)	0.000
Palpitation	6 (4)	8 (2)	0.404
Smell/taste loss	2 (1)	0 (0)	0.108
Shortness of breath	4 (2)	7 (2)	0.757

HCW, healthcare worker.

Results

The study included 528 participants who were willing to participate in the study. Thirty-three percent (173/528) of them were HCWs while the remaining were non-HCWs. The mean age of HCWs was 37 years compared to 41 years in non-HCWs. Approximately 80% of participants were healthy in both groups, and the distribution of comorbidities was balanced except for lung disease which was more predominant among HCWs. Fourteen (8%) in HCWs and 22 (6.2%) in non-HCWs had a previous COVID-19 infection. The baseline characteristics of the participants are presented in Table 1.

The most reported side effects by participants on the first day were muscle aches (49%), followed by fever (42%) and headache (40%). HCWs experienced more muscle aches, headache, sore throat, and abdominal pain which were statistically significant compared to non-HCWs. Participant responses about the side effects they experienced during days 1, 2, and 3 after the vaccinations are presented in Table 2. Additionally, a summary on the occurrence and severity of adverse events reported by HCWs and non-HCWs is shown in Figure 1.

Approximately 78% of HCWs used analgesics to alleviate the adverse events compared to 71.9% of non-HCWs. Among those who used analgesics, 85% of HCWs reported a symptom relief compared to 91% of non-HCWs. The mean onset of symptoms was 16 h in the HCW group compared with 12.2 h in the non-HCW group ($p = 0.0024$). Furthermore, the mean duration of

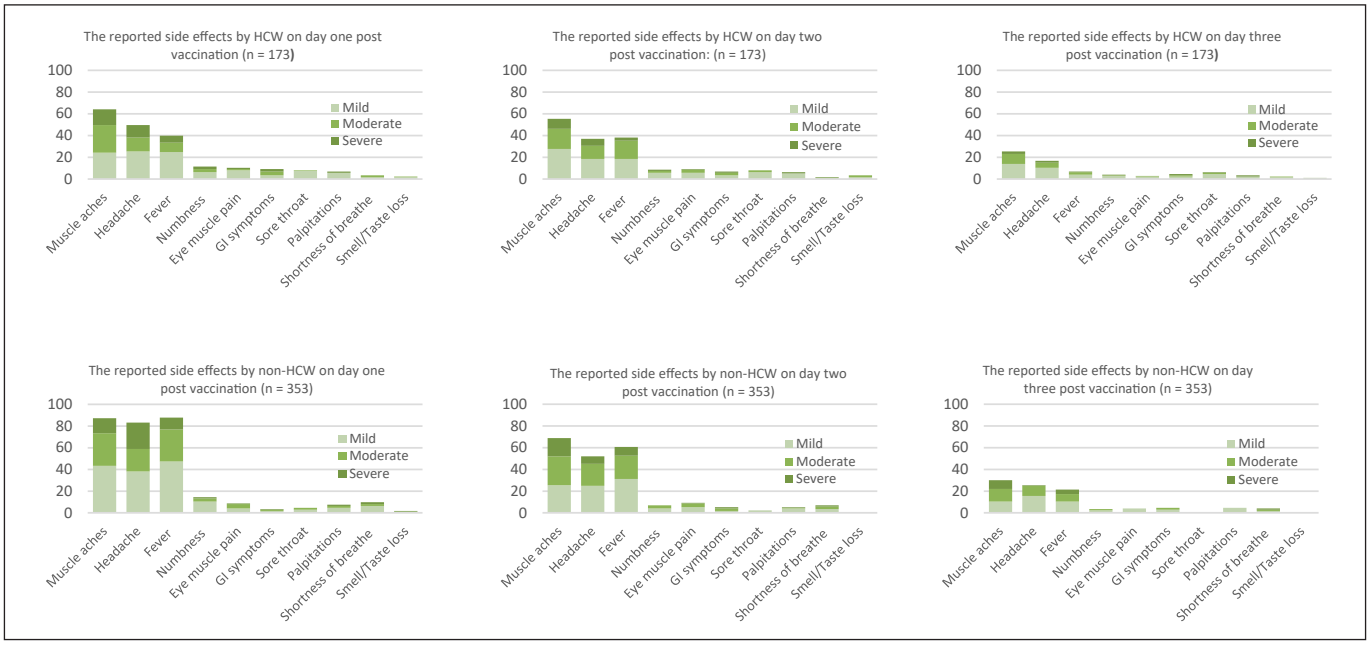

Fig. 1. The differences in reported side effects between HCWs and non-HCWs during the first 3-day period after vaccine. HCWs, healthcare workers.

Table 3. Onset and duration of the side effects and whether symptoms were resolved by pain killers

	HCW (n = 173)	Non-HCW (n = 353)	p value
Onset of side effect, mean ± SD, h	16 (15.38)	12.2 (10.2)	0.002
Duration of side effect, mean ± SD, h	37 (19.5)	32.32 (13.6)	0.067
Symptoms relieve on painkillers, n (%)			
No	6 (3.46)	7 (1.98)	0.371
Yes	115 (66.47)	233 (66)	1
Not taken	38 (21.96)	99 (28.04)	0.405
Maybe	14 (8.09)	12 (3.39)	0.030

HCW, healthcare worker.

symptoms in the HCW group was 37 h compared with 32.3 h in the non-HCW group (p = 0.067). Results on the duration of symptoms and need for analgesics for symptom relief are illustrated in Table 3.

Discussion/Conclusion

The present study was designed to determine if there is a difference in the adverse events following AstraZeneca COVID-19 vaccine among HCWs and non-HCWs. The vast majority of individuals were healthy in both groups, and the distribution of comorbidities was balanced except for lung disease, which was more predominant among HCWs.

In our study, there have been no reports of severe complications linked to the AstraZeneca vaccine in a single center in Saudi Arabia for both groups. The adverse events and severity was more predominant in the HCW group compared to the non-HCW group following the first dose of AstraZeneca vaccine. The most reported adverse events on the first day were muscle pain (49%), followed by fever (42%) and headache (40%). HCWs experienced more muscle pain, headache, sore throat, and gastrointestinal symptoms, which were statistically significant, compared to non-HCWs. On the second and

third day, the reported side effects as well as the severity of the side effects decreased among all participates. This result is consistent with other COVID-19 vaccines in which the highest percentage of adverse events were noticed in the first day and then decreased markedly through the seventh day [13].

In March, a study reported findings in 5 HCWs who were 32–54 years of age and presented with thrombosis 7–10 days after receiving the first dose of AstraZeneca vaccine [14]. Therefore, the use of AstraZeneca vaccine was withheld temporarily in some European countries due to the serious thromboembolic events [11, 15]. A recent study assessed the clinical and laboratory features of 11 patients in whom thrombosis had developed after receiving AstraZeneca vaccine. Of those, 9 were women, with a median age of 36 years, beginning 5–16 days after vaccination [16]. The problem with spontaneous reports of suspected thromboembolic events to AstraZeneca vaccine is difficult to distinguish a causal effect from a coincidence because the COVID-19 infection is associated with blood clotting as well [15, 16]. The serious adverse event started with simple symptoms like headache and fatigue and continued beyond 3 days. Therefore, AstraZeneca vaccine can result in the rare development of thrombotic events, and this highlights the importance of educating the recipients about reporting any persistent symptoms after vaccination and the healthcare workers pay more attention to childbearing women.

This study did not show any significant difference between HCWs and non-HCWs regarding the duration of adverse events. Both groups behaved similarly, and all the adverse events subsided with time as shown in Figure 1. This observed finding may be explained by the high utilization of analgesics in both groups. This finding further supports the benefits of prophylaxis paracetamol which was used in phase 1/2 of AstraZeneca vaccine and showed a significant reduction in adverse events including pain, muscle ache, and headache [17].

The difference in side effects between HCW and non-HCW groups might be due to the psychosocial factor. As reported in a cross-sectional study in Saudi Arabia, 37% of HCWs were not sure to uptake the COVID-19 vaccine and preferred to wait, and 11% said "no" to uptake the vaccine [12]. HCWs may be more sensitive to symptoms due to their medical education (e.g., knowledge or higher education) than non-HCWs. Another suggested factor is the possibility of previous asymptomatic infection among HCWs which leads to a stronger immune response.

The current study has some limitations. First, it was conducted in a single center with convenience sampling which may limit the generalizability of the findings. Participants were liable for recall bias when responding to the survey on the third day after receiving the vaccine, thus influencing accurate retrieving of events. Using the subjective scale to determine the severity of symptoms, for example, mild, moderate, or severe, rather than using an objective criterion may have created variation in participants' responses.

Statement of Ethics

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the KAAUH Institutional Review Board (IRB Log #: H-01-R-059). All subjects have given written informed consent.

Conflict of Interest Statement

The authors declare no conflicts of interest.

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Author Contributions

Ahlam Alghamdi and Afrah Alkazemi contributed to conceptualization; Isra Alghamdi and Ghada Alwarafi contributed to data curation; Abdulrahman Alissa contributed to project administration; Abdulrahman Alissa and Afrah Alkazemi contributed to writing – original draft; Ahlam Alghamdi and Hadeel Alwagas contributed to writing – review and editing. All authors have read and agreed to the published version of the manuscript.

Data Availability Statement

The data relating to this study are available from the corresponding author upon reasonable request.

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