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Analysis of COVID-19 Vaccine Adverse Drug Reactions Reported Among Sultan Qaboos University Hospital Staff

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Abstract

Objectives: The aim of this study was to report any suspected adverse drug reactions (ADRs) experienced by all vaccinated staff and students. **Methods:** This study conducted during COVID-19 vaccination campaign that took place in a tertiary teaching hospital in Muscat from 29/Aug/2021 to 12/Sep/2021. An online survey was generated, and sent to all staff and students via email and through their mobile phones. An announcement at the hospital website with a link to the survey was made. Data analysis with descriptive statistics was done via STATA software. **Results:** In this study, 8,421 individuals reported being vaccinated with a total of 11,468 doses administered. A total of 8,014 patients' doses received the Pfizer-Biotech vaccine while 3,454 patients' doses received the Oxford-AstraZeneca brand. There were a total of 3,275 (38.8%) responses to the survey distributed. A total of 741 individuals (22.6%) experienced an ADR after taking the vaccine and 67% (n = 498) were females (P<0.001). Majority of the ADRs reported were fever and chills (19.7%) followed by localized pain at the injection site (18.8%). Other ADRs were reported such as hair loss (0.5%) and one patient reported a clot in the right leg.

Most responders (27%) considered their ADRs as mild while 25% of the responders considered them as severe. **Conclusion:** In the study cohort, there were mild symptoms of COVID-19 vaccines, and females had more risk of ADRs compared to males. It is crucial to observe for long term ADRs to the vaccines and a follow-up monitoring should be done to subjects to preclude any unwanted effects.

Keywords: Pfizer-BioNTech (BNT162b2), Oxford-AstraZeneca (ChAdOx1 nCoV-19), COVID-19 vaccines, COVID-19, Adverse Drug Reactions.

Advances in Knowledge

- This study found Adverse Drug reactions in a long-term follow up, and has described some adverse drug reactions that were not previously documented in the literature due to COVID-19 vaccines.

Application to Patient Care

- Health care providers should be aware of other unreported adverse drug reactions, and should be vigilant upon monitoring patients while receiving COVID-19 vaccination.

Introduction

Both COVID-19 vaccines that are available in Oman; the Pfizer-BioNTech (BNT162b2) and the Oxford-AstraZeneca (ChAdOx1 nCoV-19) received an Emergency Use Authorization by the Food & Drug Administration (FDA) and UK's Medicines and Healthcare products Regulatory Agency (MHRA) as they have shown acceptable efficacy and safety profile in patients in the first and second phases of the clinical trial.¹⁻⁵ Given that the vaccine is relatively new, there were no long term adverse drug reactions (ADRs) reported or studied. In clinical trials,¹⁻³ the most common ADRs reported were; injection site pain, headache and fatigue for both vaccines. On the other hand, some serious ADRs have been observed in both vaccines.⁶ In the Oxford-AstraZeneca (ChAdOx1 nCoV-19) vaccine trial, 0.7% serious ADRs were reported in the vaccine group, while in the Pfizer-BioNTech (BNT162b2) vaccine trial, 0.6% of serious ADRs have been reported.^{6,7}

COVID-19 vaccination campaigns were held across the globe, to ensure proper eradication of the virus. Sultan Qaboos University Hospital (SQUH) started the vaccination process to cover initially health care providers, who have direct contact with admitted patients with COVID-19 virus. Eventually the vaccination campaign covered all hospital staff, followed by the university staff and students.

The aim of this study was to evaluate ADRs outside the context of clinical trials and provide more context on the long term possible ADRs at Sultan Qaboos University (SQU), Muscat, Oman.

Methods

This was an observational retrospective study that was conducted after COVID-19 vaccination campaign (29/Aug/2021 to 12/Sep/2021) that took place at SQU, Muscat, Oman. All the staff were scheduled for vaccination including students. The dates were announced earlier ahead of the campaign start date. All individuals were asked to fill a form with information requested by the infection control team such as age, contact number, any known allergies, etc. After the approval from the Medical Research Ethics Committee (MREC # 2499, 8th/July/2021) at the College of Medicine & Health Sciences at SQU, a list was provided of all vaccinated individuals with all their details by the Infection Control team. The study included all individuals above 12 years old who received the 1st or 2nd dose of the vaccine at SQUH.

Using an online google form, a short survey was generated in Arabic and English. There were a maximum of 14 questions that were easy and fast to fill. It took around 2 minutes or less to fill the survey. Questions were mainly related to ADRs experienced after the vaccination either after the 1st dose or 2nd dose or both doses. There were also questions related to the recovery from the ADR, outcomes, as well as the effect of the ADR on going back to work.

The survey was sent via the university email to all staff/students. Moreover, it was announced on the hospital website where a QR scan code and link to the survey was also accessible. There was also an initiative for free text messages by Omantel (Oman Telecommunication Company) to all vaccinated staff with a direct link to the survey. A lot of emphasis was done by all

pharmacists in sending the survey link through different clinical groups and reminding healthcare professionals to complete the survey. The survey was voluntary and not compulsory.

Descriptive statistics were used to describe the data. For categorical variables, frequencies and percentages were reported. Differences between groups were analyzed using Pearson's χ^2 tests (or Fisher's exact tests for cells <5). For continuous variables, mean and standard deviation were used to present the data. An *a priori* two-tailed level of significance was set at the 0.05 level. Statistical analyses were conducted using STATA version 16.1 (STATA Corporation, College Station, TX, USA).

Results

Between 3rd January 2021 to 25th July 2021, a total of 11,468 doses of COVID-19 vaccines were administered corresponding to 8,421 individuals (>12 years old). There were a total 8,014 individuals who received the Pfizer-BioNTech (BNT162b2) where 80% ($n=6414$) received only the 1st dose and 1600 participants received the second dose. On the other hand, a total of 3,454 Individuals who received Oxford-AstraZeneca (ChAdOx1 nCoV-19) and 1909 individuals (55%) were for the 1st dose while 15.7% ($n=1545$) were for the second dose.

Among the 8,421 subjects who were vaccinated, only 39% ($n = 3275$) responded to the survey distributed in which there were significantly more females than males (57% *versus* 43%). Majority of responses were filled by adults whereas 49% were by participants aged 12 to 30 years old followed by 29% aged 31-40. Only 19% of the responses were from those aged 41 to 50 years while the elderly contributed to only 1% of the responses. Among all responses 22.6% (741/3276) were individuals who experienced an ADR. Sixty five percent of the participants who responded received the Pfizer-BioNTech (BNT162b2) and 38% received Oxford-AstraZeneca (ChAdOx1 nCoV-19).

Around 39% of individuals who completed the survey were health care providers who work at the hospital, 19% were students and 9% were university staff. There were a total of 35% of individuals that were categorized as others.

The reported adverse effects were very similar. An average of 14.5% of all reports were fever and shivering, localized pain at the injection site, fatigue, restlessness and headaches. This is followed by dizziness (7.7%) and muscle cramps (6.5%). There were 31 (0.95%) individuals who experienced tinnitus and hearing loss. (Figure 1)

The results showed that there was a significant increase in ADR incidents in females ($P<0.001$) compared to males. (Figure 2)

Among the two types of vaccine brands, there was a significant differences in ADR distribution amongst males and females. ADRs were also significantly more prevalent in the Oxford-AstraZeneca (ChAdOx1 nCoV-19) compared to the Pfizer-BioNTech (BNT162b2) brand as shown in Figure 3, in fever and shivering ($P<0.001$), localized pain and swelling ($P=0.013$), Fatigue and restlessness ($P<0.001$), and headache ($P<0.001$).

There were also other ADRs that were reported which are not listed in the distributed survey. There were 61 reports on body pain which included muscular and bone pain. Other reports included chest tightness ($n=15$), irregular cycle ($n=12$), flu like symptoms ($n=15$), swollen lymph nodes ($n=5$), loss of appetite ($n=7$), palpitations ($n=5$), loss of smell ($n=5$), hypotension ($n=5$), insomnia ($n=4$), hair loss ($n=4$) and neuropathic pain on the fingertips ($n=3$).

Discussion

There are very limited data regarding the long term side effects of the COVID-19 vaccines. This is due to the emergency use authorization by both the MHRA and the FDA, and due to them being released only about 2 years ago. In this retrospective study on SQUH COVID-19 vaccination campaign, investigation of the rate of adverse effects from two types of COVID-19 vaccines; the Pfizer-BioNTech (BNT162b2) and the Oxford-AstraZeneca (ChAdOx1 nCoV-19). There are currently only scant reports of long term side effects and that the number of participants enrolled in these clinical trials was very low.⁸

The majority of the participants who experienced an ADR received the Pfizer-BioNtech (BNT162b2) vaccine (65%), and this was due to the abundant availability of this type of vaccine initially in our institution. Most of the responders in our study were females (57%), and they also

reported higher incidence of adverse events (67%) compared to males, this is in line with two other published reports by Dutta S *et al* (2021) and David *et al* (2021) where they had also higher adverse effects in females compared to males.^{9, 10}

In this cohort, there was no difference in age distribution among persons who have experienced an ADR, however this may be due to having a small number of participants who are above 50 years (6%) while the majority of our participants are aged 12-30 years old (46%). In a study of a cohort that included all age categories, David *et al* (2021), did not observe any age difference in the development of ADRs between younger participants compared to the elderly (80 years and above).¹⁰ Higashino T *et al* (2022), did observe that vaccine recipients aged 30-69 years old had significantly more ADRs when compared to those aged 18-29 years old.¹¹

In this study, ADRs were mostly of fever and shivering (19.7%), localized pain and swelling (18.8%), fatigue and restlessness (18.6%) followed by headache (16.8%). In those four most common ADRs, they were more pronounced in individuals who received the Oxford-AstraZeneca (ChAdOx1 nCoV-19) than those who received the Pfizer brand while, dizziness and drowsiness were experienced in 7.7% and it was mostly by Pfizer-BioNtech (BNT162b2) vaccine participants than the Oxford brand.

There were no serious adverse effects reported in our cohort, such as pulmonary embolism, myocarditis, thrombosis or stroke, unlike the incidents reported by Klein N *et al*.¹² This could be due to either under reporting, small sample size, or the incidence did not occur in the first place.

In the literature, thrombotic events were documented in relation to the Oxford-AstraZeneca (ChAdOx1 nCoV-19) vaccine more than other vaccines, in which some cases were fatal.^{8, 13} A case study published by SQUH did report an extensive deep vein thrombosis and pulmonary thromboembolism by the Pfizer-BioNTech (BNT162b2) vaccine in a 59-year old patient.¹⁴ The occurrence of thrombosis was not proven as a direct association with the vaccines, however, further studies are warranted to corroborate this association.

In the Arab population, as described by Hatmal *et al* (2022),¹⁵ the most commonly reported adverse drug reaction were tiredness (59%), followed by injection site pain and swelling (58%), where those reactions had multiple risk factors, including age, gender, health status of participant, smoking status, type of COVID-19 vaccine and number of doses. These two reactions, were also the most common in this study. Those two adverse drug reactions are very common in most vaccinations, not necessarily COVID-19 vaccination.¹⁶

Recovery of the side effects caused by the different types of vaccines took 1-3 days in 48% of our responders in the cohort, and 7% recovered on the same day. Responders that required to seek medical attention after experiencing an ADR from the vaccines were 5.5%. About 9% of participants required time off work for the day following the vaccination day, and 11.6% reported to work but were still not feeling well. Although a high percentage did not feel well after a vaccination, time taken as sick leave due to COVID-19 infection is much longer.

This study, is the first one to report such ADRs on COVID-19 vaccines in our institution and Oman at large. As with any other retrospective study, there are limitations that are inherent in this type of design. There were some missing questions in the survey sent to participants with one major question missed that was related to the brand of vaccine received by responders who did not experience an ADR. This affected the interpretation of the results and could be misleading if not properly interpreted. Additionally, the questionnaire sent was non-compulsory, hence the low rate of response by the participants. Those that did not experience any untoward side effects might not seem interested to fill any forms. Moreover, the study did not have a specific scale for severity and therefore severity was more subjective to symptoms and responders' own opinion rather than an objective measurement.

Conclusion

In summary, this observational retrospective study did demonstrate the most common side effects experienced by both COVID-19 vaccines used at our institution in Oman; Oxford-AstraZeneca (ChAdOx1 nCoV-19) and Pfizer-BioNTech (BNT162b2). In this cohort, only mild symptoms were experienced, and females had more risk of ADRs compared to males. It is crucial to observe for long term ADRs to the vaccines and a follow-up monitoring should be

done to subjects to preclude any unwanted effects. Furthermore, spreading awareness to this type of vaccine is specifically recommended to enhance better uptake of the vaccine.

Conflicts of Interest

The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements) except for the sponsorship in providing free text messages to all SQU staff and students who have received the vaccines, or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this article.

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Authors' Contribution

BHAB, IMAR did the study conception and design. HBW provided the data. Further data collection was done by BHAB, IMAR. BHAB, IMAR and ISAZ did the analysis and interpretation of results. BHAB, IMAR drafted the manuscript. BHAB, IMAR, ISAZ reviewed the results. and approved the final version of the manuscript. All authors approved the final version of the manuscript.

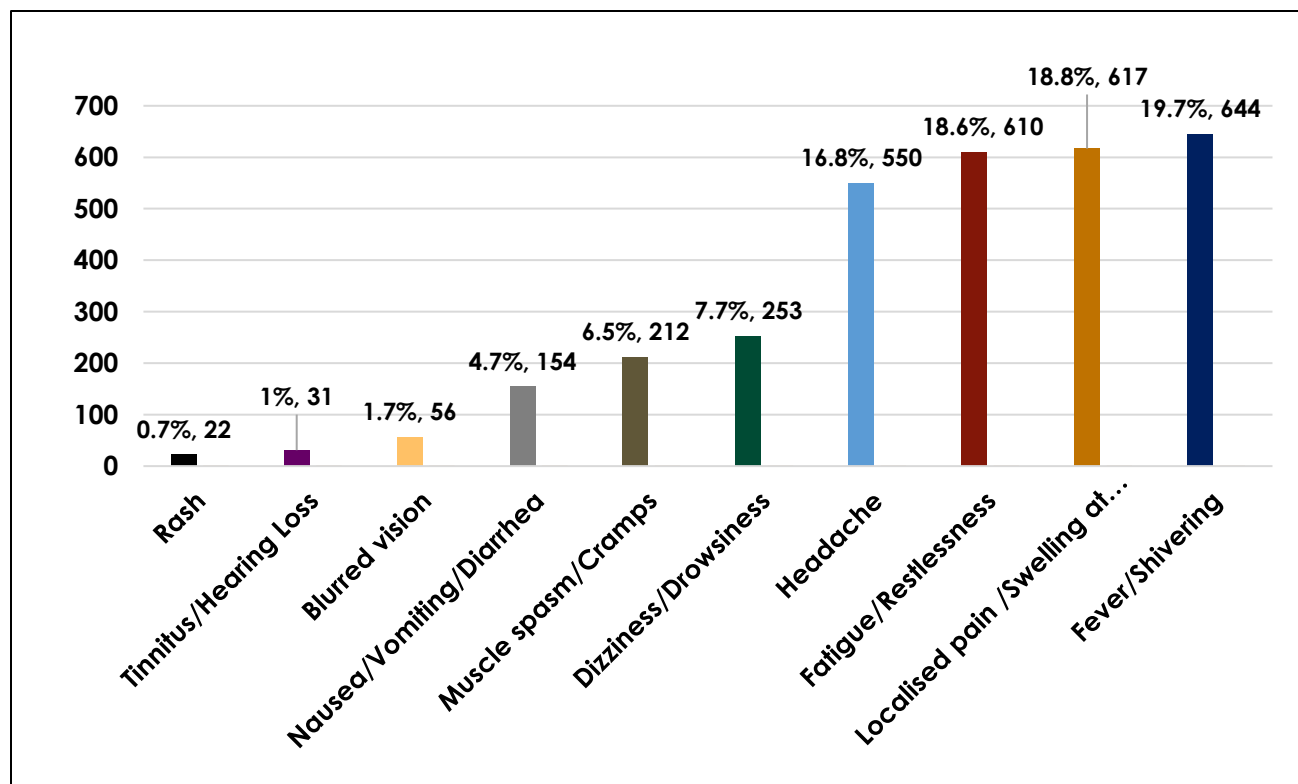
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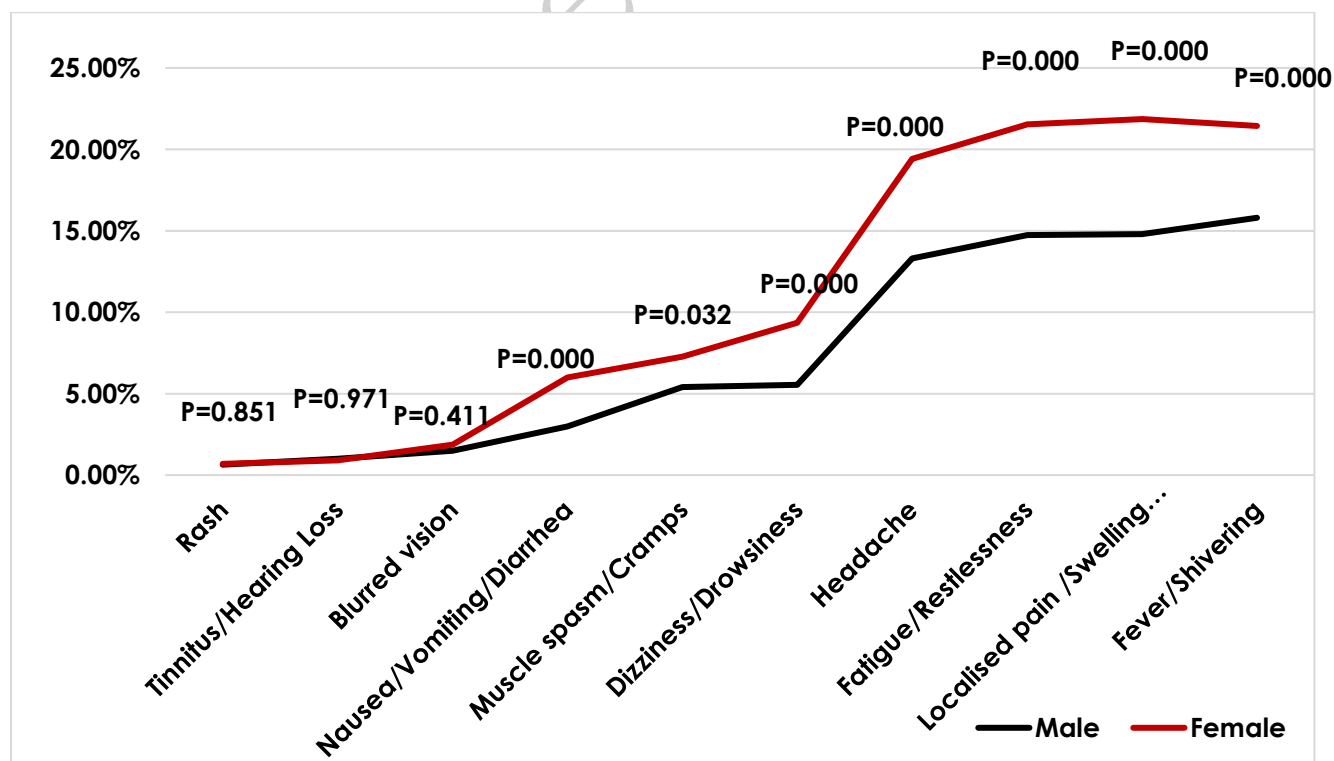
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305 **Figure 1:** ADRs experienced by responders

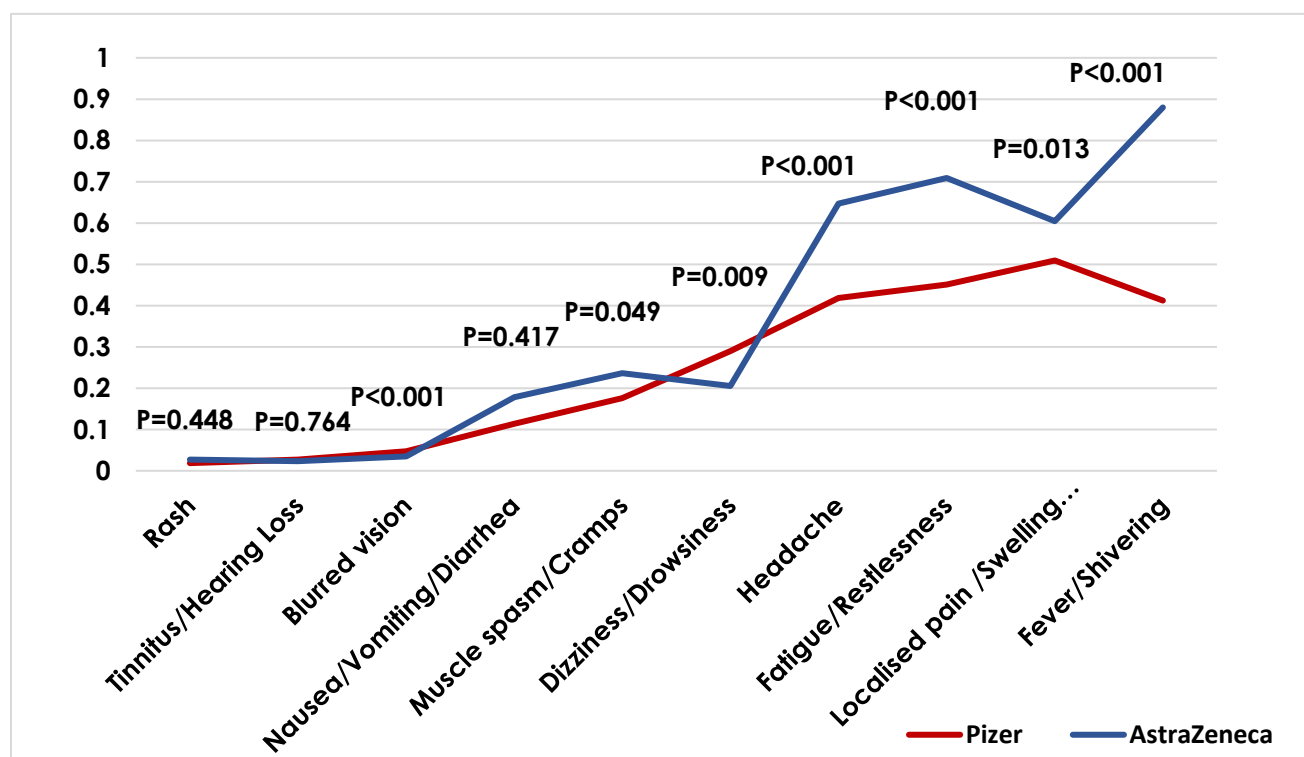


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308 **Figure 2:** Gender distribution among experienced ADRs (kindly keep it colored)



310 **Figure 3:** Vaccine brand distribution among experienced ADRs (kindly keep it colored)