Yemeni Journal of Medical and Health Research

Analysis of Reported Adverse Events Following COVID-19 Vaccination to Yemeni National Pharmacovigilance Center

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DOI: https://doi.org/10.47372/yjmhr.2026(15).2.5

Abstract

Introduction: The COVID-19 pandemic has significantly impacted Yemen, a country already facing severe humanitarian challenges. The introduction of COVID-19 vaccines prompted the need to monitor adverse events following immunization (AEFIs) to ensure safety and efficacy. Therefore, this study aimed to identify the types and outcomes of adverse events that the Yemeni National Pharmacovigilance Center received after the COVID-19 immunization during 2022.

Methods: This observational descriptive cross-sectional study analyzed the secondary data from the Yemeni National Pharmacovigilance Center of reported AEFIs during 2022. By using AEFI reporting form, data about AEFIs types and outcomes were collected and entered into the Vigibase database. Data were categorized as serious or non-serious based on World Health Organization (WHO) criteria.

Results: A total of 205AEFIs reports were received. Two thirds (66.8%) of reports of male recipients and 77.0% of the received reports for vaccine recipients aged between 18-44 years. The majority (73.2%) of reported AEFIs related to Janssen COVID-19 vaccine NRVV Ad26 (JNJ 78436735) and the most commonly reported adverse events were fever (69.6%), headache (30.4%), and arthralgia (23.0%). Serious adverse events were rare, comprising only 3.4% of total reports.

Conclusion: The number of reported AEFI post COVID-19 vaccinations was very low related to the total vaccinated population and the identified adverse events are more or less similar to the typical symptoms of most previous vaccines, and most of them were tolerated. Ongoing efforts to improve surveillance and reporting mechanisms are essential to enhance the understanding and management of vaccine-related adverse events.

Keywords: COVID-19, Vaccination, Adverse Events, Yemen, Pharmacovigilance.

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تحليل الآثار الجانبية المبلغ عنها بعد التطعيم ضد كوفيد-19 للمركز الوطني لليقظة الدوائية اليمني

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ملخص الدراسة

المقدمة : أثّرت جائحة كوفيد-19 بشكل كبير على اليمن، البلد الذي يواجه بالفعل تحديات إنسانية جسيمة. وقد أستدعى إدخال لقاحات كوفيد-19وحصول المواطنين عليها ضرورة رصد الآثار الجانبية التي تلي التطعيم لضمان سلامتها وفعاليتها. لذلك، هدفت هذه الدراسة إلى تحديد أنواع ونتائج الآثار الجانبية التي تلقاها المركز الوطني لليقظة الدوائية اليمني بعد التطعيم ضد كوفيد-19 خلال2022.

المنهجية: أجريت دراسة مقطع العرضي وصفية لتحليل بيانات الآثار الجانبية التي تلي الحصول على لقاحات كوفيد 19 المُبلّغ عنها إلى المركز الوطني اليمني للتيقظ الدوائي خلال عام 2022. وباستخدام نموذج الإبلاغ عن الآثار الجانبية. تم جمع البيانات حول أنواع الآثار الجانبية ونتائجها، وتحليلهامن خلال قاعدة بيانات Vigibase. وصُنفت الآثار الجانبية على أنها خطيرة أو غير خطيرة بناءً على معايير منظمة الصحة العالمية.

النتائج: تم استلام 205 بلاغ عن الآثار الجانبية التي تلت الحصول على لقاحات كوفيد 19. ثلثا هذه البلاغات (66.8%) كانت لمتلقين لقاح ذكور، و77.0% من البلاغات كانت لمتلقين تتراوح أعمارهم بين 18 و44 عاماً. وكانت غالبية (73.2من الآثار الجانبية المبلغ عنها مرتبطة بلقاح كوفيد-19 نوع جانسن NRVV Ad26 (JNJ 78436735)، وكانت أكثر الآثار الجانبية المبلغ عنها شيوعاً هي الحمى (69.6%)، والصداع (30.4%)، وآلام المفاصل (23.0%). أما الآثار الجانبية الخطيرة فكانت نادرة، حيث شكلت 3.4% فقط من إجمالي البلاغات.

الخلاصة: كان عدد الآثار الجانبية المُبلغ عنها بعد تلقي لقاحات كوفيد-19 منخفضاً جداً مقارنةً بإجمالي عدد السكان المُلقحين، وكان نمط هذه الآثار الجانبية مُشابهاً تقريباً للأعراض التي تلي معظم اللقاحات السابقة، وأنَمعظم هذه الآثار ممكن تحمُّلها. تُعد الجهود المُستمرة لتحسين آليات المراقبة والإبلاغ ضرورية لتعزيز فهم وإدارة الآثار الجانبية المُتعلقة باللقاحات.

كلمات مفتاحية: كوفيد-19، التطعيم، الآثار الجانبية، اليمن، التيقظ الدوائي، أسترازينيكا، الصحة العامة.

مدير المركز الوطني للتيقظ والسلامة الدوائية

Introduction

The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, has had far-reaching implications globally since its emergence in late 2019. The virus's rapid spread led to unprecedented health, social, and economic challenges, impacting populations worldwide [1].

Yemen, a country already grappling with humanitarian crises, faced additional complexities in responding to the pandemic [2]. As the first cases of COVID-19 emerged in Yemen, the country's fragile healthcare system and limited resources were quickly overwhelmed. The initial confirmed case of COVID-19 in Yemen was reported in Hadhramaut, the southern province, on the 10thof April 2020, marking the beginning of a protracted battle against the virus with the subsequent implementation of public health measures, including lockdowns, social distancing, and mask mandates, aimed to mitigate the spread of the virus and protect vulnerable populations [3].

In the face of these obstacles, the international scientific community came together to produce and distribute COVID-19 vaccinations at a never-before-seen speed [4]. On April 20, 2021, Yemen launched a large vaccination campaign against COVID-19 with AstraZeneca's COVID-19 vaccine NRVV Ad (ChAdOx1 nCoV-19), a significant step in the nation's pandemic response[5]. The objective of the vaccination campaign was to create herd immunity, lower the number of COVID-19 cases in Yemen, and immunize a sizable section of the populace [6].

However, like with any immunization program, it became crucial to track and evaluate adverse events that were reported to the Yemeni National Pharmacovigilance Center after receiving the COVID-19 vaccination. To guarantee the effectiveness and long-term viability of the immunization program, it was crucial to comprehend the safety profile of COVID-19 vaccinations in the Yemeni population [7], a procedure aimed to examine the unfavorable incidents documented throughout this critical period, shedding light on the impact of COVID-19 vaccination on public health in Yemen and guiding future immunization strategies in the country.

The purpose of this retrospective study is to examine the types and outcomes of adverse events that the Yemeni National Pharmacovigilance Center received after the COVID-19 immunization. The results of this study may help Yemen's continuing vaccination efforts by enhancing the monitoring and management of adverse events associated with the COVID-19 vaccination.

Methods

Study design and setting

This is an observational descriptive cross-sectional study based on secondary analysis of AEFIs reports following COVID-19 vaccination received by the Yemeni National Pharmacovigilance Center belonged to the Supreme Board of Drugs and Medical Appliances (SBDMA).

The Yemeni National Pharmacovigilance Center was

established in 2019 and became a member of the Heath Gulf Council. In 2022 it became a full member of the WHO Program for International Drug Monitoring.

Target population

All individuals in the Internationally Recognized Government (IRG) areas eligible to receive any types of the available COVID-19 vaccines provided by the Ministry of Public Health and Population (MoPHP), the Expanded Program on Immunization (EPI).

Sampling and Sampling technique

A universal sampling includeed all received reports of the adverse events following COVID-19 vaccinations recorded by the AEFIs responsible staffs in all health care facilities providing the immunization services at IRG areas were used. Passive AEFIs reports sent directly to the Pharmacovigilance Center during 2022.

Data collection

Vigibase is the WHO global database of adverse event reports for medicines and vaccines. AEFI reporting form was distributed thoroughly as a paper to all health care facilities providing the COVID-19 vaccines services and it is also available electronically. Through this form, data about AEFIs types and outcomes were collected. AEFIs types were categorized as serious or non-serious. According to the WHO, an AEFI is defined as 'serious' if it meets one or more of the following criteria: results in death; is life-threatening; requires inpatient hospitalization or prolongation of an existing hospitalization; results in persistent or significant disability/ incapacity; is a congenital anomaly/ birth defect; and/or is a medically important event or reaction [8].

Statistical analysis

Data of each AEFIs report completeness and consistency were checked and verified and then entered into the Vigibase database that managed by Uppsala monitoring center (UMC, Uppsala, Sweden) manually.

Ethical consideration

Permission was given from the (MoPHP), Primary Health Care Sector and EPI based on an official letter from the Yemeni Council of Medical Specialization-Aden. There were no other ethical issues involved in the conduct of this study. Informed consent was not necessary because only anonymized routine record-based data were analyzed retro-spectively.

Results

The total received AEFIs reports during 2022 was 205. Table 1 shows that, all vaccinated individuals were Yemeni, two thirds (66.8%) of AEFIs reports were of male and 33.2% of female vaccinated individuals. From the 205 reports, only 74 have age data. Of this 74 reports, 57 (77.0%), 13 (17.6%) and 04 (5.4%) aged between 18–44, 45–64, and 65 years and above respectively. The Table also shows that around three quarters (73.2%) of reported AEFIs linked to Janssen COVID-19 vaccine NRVV Ad26 (JNJ 78436735), 22.4% related to Astra Zeneca COVID-19 vaccine NRVV Ad (ChAdOx1 nCoV-19) and only 4.4% of Sinovac COVID-19 vaccine inact (Vero) CZ02.

Table 1: Reported AEFIs by Sex, Age, Type of COVID-19 Vaccines (n=205)

Variable	No.	%
Sex		
Male	137	66.8
Female	68	33.2
Age Group (n=74)		
18 - 44 years	57	77.0
45 - 64 years	13	17.6
≥ 65 years	04	5.4
Type of Vaccine (n=205)		
Janssen (JNJ 78436735)	150	73.2
AstraZeneca (ChAdOx1 nCoV-19)	46	22.4
Sinovac (inact (Vero) CZ02)	09	4.4

General disorders and site conditions were the most commonly reported adverse events post the administration of the three vaccines followed by musculoskeletal and connective tissue disorders and nervous system disorders as shown in Table 2.

Table 2: Reported AEFIs according to System Organ Class (SOC), (n=205)

Types of reported AEFIs by SOC	Janssen (n=150)		AstraZeneca (n=46)		Sinovac (n=09)		Total (n=205)	
	No.	%	No.	%	No.	%	No.	%
General disorders and administrationsite conditions	127	84.7	37	80.4	5	55.6	169	82.4
Musculoskeletal and connective tissue disorders	68	45.3	20	43.5	3	33.3	91	44.4
Nervous system disorders	55	36.7	19	4.3	2	22.2	76	37.1
Gastrointestinal disorders	22	14.7	3	6.5	2	22.2	27	13.2
Respiratory, thoracic and mediastinal disorders	11	7.3	4	8.7	1	11.1	16	7.8
Skin and subcutaneous tissue disorders	8	5.3	2	4.3	1	11.1	11	5.4
Others	5	3.3	0	0.0	2	22.2	7	3.4

From Table 3, it is clear that, fever is the most commonly reported adverse event post all COVID – 19 vaccines used (69.3%) and followed by headache (30.7%), arthralgia (23.4%), general body pain (14.1%), myalgia (13.2%), injection site pain (10.7%) and lethargy (10.2%). Table 3 also shows that, dizziness, nausea, chills, dyspnea, malaise, vomiting and diarrhea were the reported adverse events within 8.3%, 8.3%, 7.8%, 3.9%, 3.9%, 3.9% and 3.4% of the received reports respectively. Only 7 of the 205 (3.4%) reported adverse events were considered as serious events. Of them, death, prolonged hospitalization and disabling/ incapacitating were reported each by two of the received reports.

Table 3: Reported Non Serious and Serious AEFIs (n=205)

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Types of reported AEFIs	Janssen (n=150)		AstraZeneca (n=46)		Sinovac (n=09)		Total (n=205)	
	No.	%	No.	%	No.	%	No.	%
Non serious events								
Fever	106	70.7	30	65.2	6	66.7	142	69.3
Headache	46	30.7	16	34.8	1	11.1	63	30.7
Arthralgia	35	23.3	12	26.1	1	11.1	48	23.4
General body pain	20	13.3	8	17.4	1	11.1	29	14.1
Myalgia	17	11.3	9	19.6	1	11.1	27	13.2
Injection site pain	15	10.0	6	13.0	1	11.1	22	10.7
Lethargy	15	10.0	4	8.7	2	22.2	21	10.2
Dizziness	12	8.0	4	8.7	1	11.1	17	8.3
Nausea	13	8.7	3	6.5	1	11.1	17	8.3
Chills	11	7.3	3	6.5	1	11.1	16	7.8
Dyspnea	4	2.7	3	6.5	1	11.1	8	3.9
Malaise	5	3.3	2	4.3	1	11.1	8	3.9
Vomiting	4	2.7	3	6.5	1	11.1	8	3.9
Diarrhea	3	2.0	2	4.3	2	22.2	7	3.4
Serious events								
Death	0		2		0		2	
Prolonged hospitalization	1		1		0		2	
Disabling/incapacitating	0		2		0		2	
Other medically important condition	0		0		1		0	

Discussion

Ever since the start of vaccine production, people have expressed worries about their administration's hazards and risks. There is a great variation in people's confidence in vaccines that relies on several factors, including awareness about vaccines, the possible associated risks, experiences, religious, or political aspects, in addition to social and economic status [9]. Vaccine reluctance represents a serious health threat worldwide. Like any other vaccines, hesitancy can hinder the successful control of the spread of the COVID-19 pandemic [10]. A systematic review at 2023 by Hanna *et al*. found that common barriers to receive COVID-19 vaccines in Lebanon included both the fear of potential long-term and short-term adverse events [11].

This study based on the statistics from the Yemeni National Pharmacovigilance Center that gave a thorough understanding of the distribution of adverse events that have been recorded after receiving the COVID-19 vaccines, revealing that between January and December 2022, of a total of 468,156 people were fully vaccinated with Janssen, AstraZeneca or Sinovac vaccines in IRG areas of

Yemen[12], a total of 205 case reports of them were received to the Pharmacovigilance Program representing a reporting rate of 0.44case reports per 1000 of fully vaccinated people.

Observations of the current study on AEFIs with all three COVID-19 vaccines used in IRG areas of Yemen showed a higher reporting rate of AEFIs among males (66.8%) than females (33.2%). These results were in contrast with findings from the Saudi Arabian retrospective cross-sectional study conducted by El-Shitany *et al*. [13] which showed a significant increase in the number of female participants who reported different side effects after they receive the vaccine (58.0%) compared to males (28.1%) and of the Lebanon study by Zeitoun *et al.* [14] that showed a higher reporting rate of AEFIs among females (61.7%) than males (39.3%), as well as in a Vietnamese study [15].

The higher percentage (77.0%) of reported AEFIs in this study were among vaccine recipients aging between 18 and 44 years compared to reported AEFIs (17.6%) and (5.4%) among those aging between 45 and 64 years and those aging ≥ 65 years respectively. Similarly, Tran *et al*. in Vietnam found a decrease of AEFI reporting following vaccination with AstraZeneca with the increase of age; the lowest incidence was in people aging more than 60years [15]. Likewise, in Afghanistan, Azimi *et al*. reported a higher prevalence of AstraZeneca adverse reactions in participants aging 40 years or less as compared to those aging more than 40 years [16].

The analysis of this study revealed that the most common adverse events for COVID-19 vaccines were fever, headache, arthralgia, general body pain, Myalgia, injection site pain and lethargy. The findings of Beatty *et al*. in USA[17] and of Zeitoun *et al.* in Lebanon [14] showed that injection site pain, fatigue, general body pain, headache, and fever were the most common reported adverse events whereas a study by El-Shitany *et al*. showed that injection site pain, headache, fatigue, and fever were the main symptoms among Saudi residents [13].

In the present study, AEFIs were more frequently reported following the JanssenCOVID-19 vaccine, while in Al Khames Aga *et al*. study done at 2021 on Iraqi and Jordanian participants [18] and in Lebanon study by Zeitoun *et al*.at 2023[14], the higher incidence of AEFIs were associated with the AstraZeneca vaccine.

A very low rate (3.4%) of reported serious AEFIs in this study were subsequently assessed by the Serious AEFI Special Committee and the final decision revealed that they are not related to COVID-19 vaccines. This committee was appointed in April 2021 through a ministerial decision (603/1) by the MoPHP to evaluate serious AEFIs with COVID-19 vaccines. Low rates of serious AEFIs were also found in the Lebanon study [14].

Limitations

Despite the valuable findings from this study, there were many limitations such as underreporting, emphasis on short-term impacts, and population representation challenges.

Conclusion

In general, the number of reported AEFI post COVID-19 vaccinations was very low related to the total number of persons (468,156) who were fully vaccinated during 2022 and the side effects that were identified are more or less similar to the typical symptoms of most previous vaccines, and most of them are tolerated. Although our analysis provides valuable insights of the symptoms reported, it is crucial to acknowledge the limitations in data quality. Efforts should focus on improving surveillance methods to enhance the accuracy and representativeness of AEFI reporting.

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