SPECIAL REPORT

COVID-19 VACCINES
Adverse Events Following Immunization
Surveillance Report
December 2021: A Year of Vaccinovigilance

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ABSTRACT

This is a periodic report issued by the Iraqi Varmacovogilence Centre at the Ministry of Health in Iraq to show the Adverse Events Following Immunization (AEFI) reported to the national database of adverse events. Iraq database of adverse events which is called VigiFlow is subsequently shared with the global database (VigiBase).

This report included all cases of suspected adverse events due to temporal association with the vaccines referred to our centre from early March until 10th December 2021. The three deployed vaccines as part of the mass vaccination campaign in Iraq are *Pfizer BioNTech*, *AstraZeneca and Sinopharm*. Like any other medicinal product, vaccines are not free of adverse events that necessitate continuous and thorough study of the benefit-risk balance against COVID-19 disease or death prevention. According to WHO, AEFI includes any untoward medical occurrence that follows immunization and has a temporal association with the administration of the vaccine and not necessarily causality association.

BACKGROUND

Iraq has developed an AEFI surveillance plan as a part of the national deployment and vaccination plan (NDVP) that includes various pharmacovigilance (PV) activities related to the spontaneous AEFI reports received from the vaccinees.

We are receiving and documenting AEFI by many routes through this surveillance plan. These routes are continuously re-evaluated and evolved with time. The primary data sources we received are through a liaison person at each vaccine station who is well-trained to fill pre-designed forms to report any adverse events and then submit these forms to the Iraqi pharmacovigilence centre (IPC) either as a paper-based or online e-Report. The second source is an online self-assessment form designed to be filled by the beneficiaries themselves. Beneficiaries can access these forms either through the WhatsApp number of the IPC or through the vaccination platform website run by the extended program on immunization (EPI). Information received via both is validated and entered into the national database (The VigiFlow).

Reports of serious AEFIs shall reach the national database within 24 hours. Only serious cases will require further investigations and causality assessment based on the WHO seriousness criteria. Serious AEFI are those that cause: death, hospitalization, significant disability, life-threatening state, or congenital anomaly/ birth defect, or is a part of a cluster or a part of a group of events with an unexpectedly high rate or severity, or a suspected signal.

The IPC worked in collaboration with the EPI program at the Public Health Directorate and the relevant departments in all Iraqi Health Directorates. These parties are trained efficiently to do their allocated duties accurately. Our work is under continuous evaluation and reassessment depending on the feedback received from the stakeholders.

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Total Administered Doses (1st + 2nd doses)
12,268,671

Fully Vaccinated Individuals
4,723,133

Total AEFI Reports
9761

Non-serious Cases
9651 (99%)

Serious Cases
110 (1%)

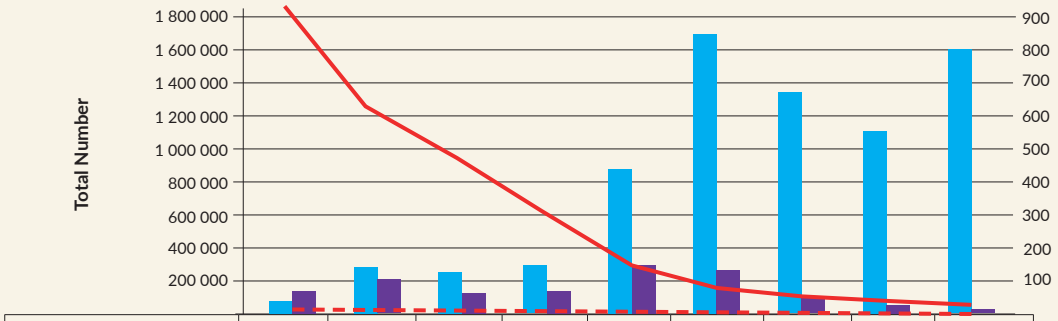
Reporting Data Analysis:

A. Summary

Table 1 | General summary of the reported cases

	Pfizer	AstraZeneca	Sinopharm	Total
	Count (%)***	Count (%)***	Count (%)***	Count (%)
All reported cases	6534 (67%)	2026 (20.7%)	1201 (12.3%)	9761
Number of doses administered	8,693,288 (70.9%)	1,066,323 (8.7%)	2,509,060 (20.4%)	12,268,671
Non-serious cases*	6459 (67%)	2000 (20.7%)	1192 (12.3%)	9651 (99%)
Serious cases**	75 (68%)	26 (24%)	9 (8%)	110 (1%)
Total reporting rate per 100,000 administered dose	75	190	48	80
Serious reporting rate per 100,000 administered dose	0.9	2.4	0.4	0.9
Number of AEs per patient	3.14	2.65	2.17	2.68

Source: VigiFlow (Dataset date: 8/12/2021, MedDRA version: 24.0)
* Non-serious cases mean mild, expected local and systemic AEFIs.
** Serious cases are those that meet the WHO seriousness criteria
***The percentages are in relation to the total of all vaccines

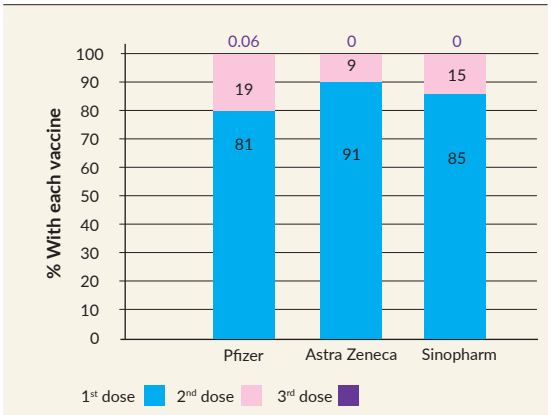


	March	April	May	June	July	August	September	October	November
Monthly administered doses	56,985	294,695	243,247	301,136	870,715	1,666,384	1,330,556	1,132,431	1,589,292
New COVID infection	151,836	214,275	131,883	148,822	280,695	261,551	115,153	51,945	25,924
Reposting rate	932	619	489	310	143	82	56	47	20
Serious AEFI reporting rate	15.8	11.9	6.6	4.3	0.9	0.5	0.4	0.4	0.4

Source: VigiFlow (Dataset date: 8/12/2021, MedDRA version: 24.0)
Reporting rate is calculated as number of AEFI cases per 100000 administered dose for all the administered vaccines doses
The AEFI cases were distributed over the months based on the date of onset

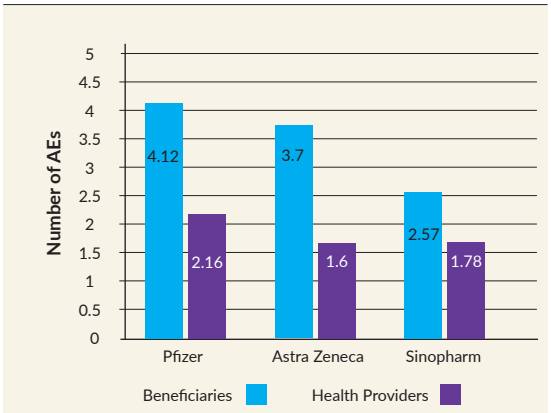
Figure 1 | Monthly distribution of the administered doses of the vaccine, new COVID infection, adverse, and serious AEFI reporting rates.

	Pfizer	Astra Zeneca	Sinopharm
Vaccine Doses	8,6933,288	1,066,323	2,509,060
AEFI reports	6534	2026	1201



Source: VigiFlow (Dataset date: 8/12/2021, MedDRA version: 24.0)

Figure 2 | Percentage of AEFIs reports according to the number of doses for each type of the vaccine



Source: VigiFlow (Dataset date: 8/12/2021, MedDRA version: 24.0)

Figure 3 | Average number of AEFIs per report according to source of data

Table 2 | Reporter qualification of the AEFI cases

Reporter Qualification	Count	Percentage
Physician	586	6%
Pharmacist	5,669	58.2%
Other Health Professional	1,342	13.7%
Beneficiaries/Non Health Professional	2,151	22.1%

Data Source: VigiFlow (Dataset date: 10/12/2021)

B. Demographic data

Table 3 | Gender and age groups distribution of the reports

Patient Sex	Count	Percentage
Female	3985	41.7 %
Male	5422	57.3 %
Gender unspecified	138	1.4 %
Age Group	**Count**	**Percentage**
12 - 17 years	51	0.5%
18 - 44 years	5,857	61.4%
45 - 64 years	2,593	27.2%
65 - 74 years	428	4.5%
≥ 75 years	84	0.9%
Unknown	493	5.2%

Note: Age represents the age at the time of vaccination. Some case reports records may be the missing date of birth

Data Source: Vigilyze (Dataset date: 8/12/2021, MedDRA version: 24.0)

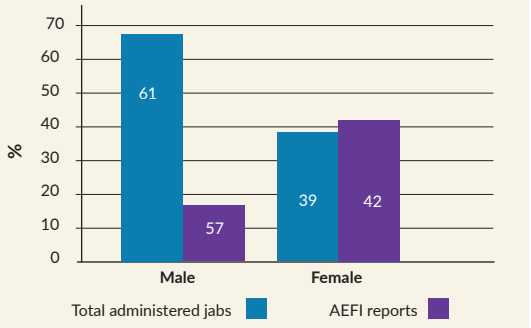


Figure 4 | Distribution of total administered doses and reported AEFI according to gender

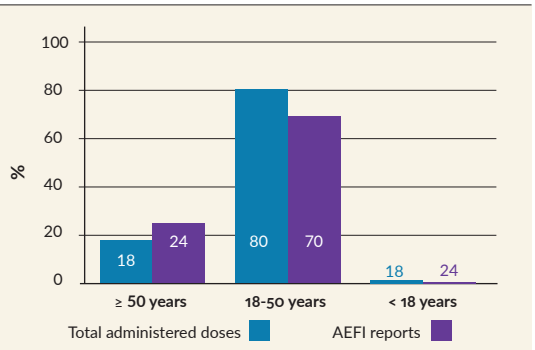


Figure 5 | Distribution of total administered doses and reported AEFI according to age

C. Adverse Events Following Immunization

Table 4 | Number of most widely reported adverse event following immunization for each vaccine type until December 8th 2021

Preferred Term *	Pfizer	Astra Zeneca	Sinopharm	Total**	
	Count	Count	Count	Count	(%)
Pyrexia / Chills	3,855	1,407	647	5,924	62.1%
Vaccination site pain	2,464	486	297	3269	35.1%
Lethargy/Fatigue	2,215	527	360	3106	32.8%
Headache	1,560	495	245	2312	24.2%
Arthralgia/Myalgia	1,447	509	215	2182	22.9%
Nausea / Vomiting	637	177	93	913	9.6%
Dyspnea/ Cough	421	93	62	580	6.1%
Rash/ Pruritus/ Erythema	281	52	36	374	3.8%
Abdominal pain	213	72	25	311	3.3%
Diarrhoea	201	63	34	302	3.2%
Chest pain	217	56	15	291	3.0%
Injection site reactions/ allergy/ swelling	195	69	64	288	3.0%
Dizziness/ Vertigo/ Somnolence	197	19	20	241	2.5%
Lymphadenopathy	130	10	4	144	1.5%
Oropharyngeal pain	93	7	8	108	1.1%
Tachycardia/ Palpitation	66	11	13	90	0.9%
Rhinorrhea/ Nasal congestion	65	4	15	84	0.9%
Hypoaesthesia	57	9	6	73	0.8%
Decreased appetite	44	9	3	56	0.6%
Hypertension	38	12	4	55	0.6%
Influenza-like illness	27	11	4	43	0.5%
Hypotension	30	12	1	43	0.5%
Syncope / Loss of consciousness	42	7	1	53	0.5%
Hyperhidrosis	22	7	11	40	0.4%
Extensive swelling of vaccinated limb	20	9	1	30	0.3%
Renal pain	21	4	3	29	0.3%
Anosmia	20	2	2	24	0.3%
Ocular Hyperemia / Eye pain	19	2	1	23	0.2%
Insomnia	17	0	3	20	0.2%
Ageusia	9	5	0	14	0.1%
COVID-19	9	1	3	13	0.1%

Data Source: VigiLyze (Dataset date: 08/12/2021, MedDRA version: 24.0)

*Preferred Terms (PTs), are distinct descriptors (single medical concept) for a symptom, sign, disease diagnosis, therapeutic indication, investigation, surgical or medical procedure, and medical social or family history characteristic.

Some PTs which were used interchangeably, were grouped together in one category for easier display. For this table, the top 60 PTs were included

** Total number may be slightly higher than the sum of the three vaccines due to a very small number of reports with an unidentified vaccine type

DISCUSSION

The majority of the reported AEFIs (about 70%) involved people less than 50 years in line with the vaccination age distribution and the established global demographic safety profile in the pre-marketing studies and the post-marketing surveillance data.[1-3] Strong immune response of people of this age group and their increase awareness about reporting adverse events of the vaccines might explain this result.

A higher female to male ratio is a consistent trend in the spontaneous reporting systems

D. Serious, rare cases and Adverse Events of Special Interest

Table 5 | Serious cases demographic, patient and vaccine details

	Pfyzer	Astra Zeneca	Sinopharm	Total
Number of cases	75 (68%)	26 (24%)	9 (8%)	110 (1.1%)
Age groups				
12 - 17 years	2 (2.7%)	0 (0%)	0 (0%)	2 (2%)
18 - 44 years	41 (55%)	14 (54%)	4 (45%)	59 (54%)
45 - 64 years	19 (25%)	4 (15%)	5 (55%)	28 (25%)
65 - 74 years	6 (8%)	6 (23%)	0 (0%)	12 (11%)
≥ 75 years	1 (1.3%)	2 (8%)	0 (0%)	3 (3%)
Unknown	6 (8%)	0 (0%)	0 (0%)	6 (5%)
Gender				
Female	29 (38%)	11 (42%)	6 (66.7%)	46 (42%)
Male	43 (58%)	15 (58%)	3 (33.3%)	61 (55%)
Unknown	3 (4%)	0 (0%)	0 (0%)	3 (3%)
Vaccination info				
1st Dose	70	23	7	100
2nd Dose	5	3	2	10
Median time: days to onset (range)	3.3 (30-0)	10 (73-0)	12.3 (90-0)	5.6 (90-0)
Median time: days to onset (range) with first dose	3.2 (30-0)	11.4 (73-0)	13.4 (90-0)	5.5 (90-0)
Median time: days to onset (range) with second dose	6.4 (25-0)	3.3 (10-0)	8.5 (17-0)	5.8 (25-0)
Seriousness Criteria				
Death	4	3	1	8
Hospitalization	30	13	4	47
Life-threatening	17	8	1	26
Disability	14	3	2	19
Other important medical events	26	7	3	36

Data Source: Vigilyze (Dataset date: 15/12/2021)

worldwide.[4-6] However, in Iraq, most AEFI cases (57%) were reported by males; the percentage reached up to 62 % among those reported by the beneficiaries themselves. Of note, 61 % of the vaccinated persons were men, and 39 % were women. Gender differences in AEFI cases could be due to differences in vaccination rate, tendency to report adverse events, or a real gender effect. Data need more analysis to unveil the exact causes.

The surveillance system in Iraq has comprised mainly of pharmacists as safety responsible persons. Hence, most of the cases (58.2 %) were reported by them, and physicians reported only 6 %. A relatively large number of the reports came directly from the beneficiaries, 22.1 %, and those were characterized by a higher number of adverse events per a report.

The top reported AEFIs to our centre were consistent with those reported by clinical trials.[1-3] Pyrexia, fatigue, vaccination site pain, headache, arthralgia were the top reported adverse events after vaccination. We noticed a progressive decline in the reported AEFI with time in this report. This may be because people and health care providers have become more aware of the adverse events of the vaccine and their treatment and more confident that they are non-dangerous.

Confusion might occur once symptoms develop after vaccination, whether due to mild covid infection or adverse events of the vaccine itself. This is because the pandemic is still ongoing, vaccines are not totally preventing

infection, especially after only one dose, and most AEFIs are reported after the first dose.

The majority of the reported adverse events were from people who received the Pfizer vaccine, followed by Astra Zeneca; the least was from those who received the Sinopharm vaccine. These data need careful interpretation, considering some confounding factors and the considerable difference in the number of doses given from each type.

We have received 110 cases with serious AEFIs. Around 60% of them had occurred in males and were distributed throughout the different age groups. Thirty-two per cent of them happened in those 50 years and above, the age group that received only 18% of the administered vaccines. The challenge in notifying serious adverse events is to find whether they are a mere temporal association with the administration of the vaccine or a result of it. In our series, all serious adverse events were investigated thoroughly, and only a small number of serious adverse events were probably linked to vaccination.

CONCLUSION

The adverse events profile of the vaccines in Iraq is in line with the global data analysis. The serious reported cases are few, and most of the vaccinees who experienced these adverse events have recovered or are recovering. The temporally associated death cases following immunization are among the fewest in the world reported so far. None of the death cases was proven to be caused directly by the vaccine. Finally, considering the ever-increasing risk of COVID-19 infection and the emerging strains, the threat of the pandemic still exceeds the risk of using the vaccines in mass vaccinations. This conclusion is based on the local safety data in the Iraqi database analysis, the global regulatory authorities benefits/risk assessment and the global effectiveness data.

REFERENCES

1. Wu Q, Dudley MZ, Chen X, Bai X, Dong K, Zhuang T, Salmon D, Yu H. Evaluation of the safety profile of COVID-19 vaccines: a rapid review. *BMC Med*. 2021;19(1):173. doi: 10.1186/s12916-021-02059-5. PMID: 34315454; PMCID: PMC8315897.
2. PfizerBioNTech. Comirnaty 30 micrograms/dose concentrate for dispersion for injection Summary of product characteristics. European Medicines Agency 2021. URL: https://www.ema.europa.eu/en/documents/product-information/comirnaty-epar-product-information_en.pdf. Accessed on 30 December 2021.
3. AstraZeneca AB. ChAdOx1-S [recombinant] suspension for injection Summary of product characteristics. European Medicines Agency 2021. URL: https://www.ema.europa.eu/en/documents/product-information/vaxzevria-previously-covid-19-vaccine-astrazeneca-epar-product-information_en.pdf. Accessed on 30 December 2021.
4. Watson S, Caster O, Rochon PA, Ruijter H. Aggregated evidence from globally collected individual case reports during half a century. *E Clinical Medicine*. Published: October 25, 2019. DOI: https://doi.org/10.1016/j.eclinm.2019.10.001.
5. Kim HJ, Jeong HE, Bae JH, Baek YH, Shin JY. Characteristics and trends of spontaneous reporting of therapeutic ineffectiveness in South Korea from 2000 to 2016. **PLoS One**. 2019;14(2):e0212905. Published 2019 Feb 28. Doi:10.1371/journal.pone.0212905
6. Marques J, Ribeiro-Vaz I, Pereira AC, Polónia J. A survey of spontaneous reporting of adverse drug reactions in 10 years of activity in a pharmacovigilance centre in Portugal. *Int J Pharm Pract*. 2014 Aug;22(4):275-82. Doi: 10.1111/ijpp.12078. Epub 2013 Nov 5. PMID: 24188533.

Disclaimer

The ICSRs were not clinically reviewed. To assess whether the data support the hypothesis of an association between COVID-19 vaccines and an increased risk of a certain outcome, additional information is required (e.g. quantitative disproportionality measures, and qualitative, clinical reviews of the data). When comparing different COVID-19 vaccines, it is important to keep in mind that observed differences might be caused by biases intrinsic to spontaneous reporting systems.

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