Pak. j. life soc. Sci. (2025), 23(1): 9158-9164 E-ISSN: 2221-7630;P-ISSN: 1727-4915

Pakistan Journal of Life and Social Sciences

www.pjlss.edu.pk

https://doi.org/10.57239/PJLSS-2025-23.1.00718

RESEARCH ARTICLE

The Pattern of Pharmacovigilance Reports of Antibiotics Submitted to the Iraqi Pharmacovigilance Center before and After Covid-19

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ARTICLE INFO

Received: Apr 21, 2025

Accepted: Jun 16, 2025

Keywords

Antibiotics
Pharmacovigilance
COVID-19
Adverse Drug Reactions ADRs

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ABSTRACT

Introduction antibiotics had been heavily used in the COVID-19 period naturally leading to increase the occurrence of adverse drug reactions. Objectives To assess the changing reporting pattern 6 months before and after the first case of COVID-19 in Iraq. Methods A retrospective analysis of the data reported to the Iraqi Centre of Pharmacovigilance was conducted to assess if any change in the pattern of the reported antibiotics has occurred among different antibiotics for the period from Sep 2019 till Sep 2020. Descriptive statistics were conducted for data analysis, and the chi-square test has been utilized to assess differences in ADR severity between the comparative groups. Results The majority of patients were aged 18-44, with a slight increase in the 45-64 age group in 2020. A shifted has been seen from ceftriaxone in the first 6 months to azithromycin in the second 6 months. Gastrointestinal disorders emerged as the most common ADR in 2020, while skin and subcutaneous tissue reactions predominated in 2019. A significant increase in serious ADRs was observed in 2020 compared to 2019. Conclusion This study focused the attention on the dynamic nature of antimicrobial use and ADRs profiles. The increased prevalence of serious ADRs 6 months after COVID-19 underlines the need for more governmental and non- governmental support to the Iraqi Centre of Pharmacovigilance to implement antibiotic stewardship programs to minimize the risk of AB ADRs.

INTRODUCTION

General overview

Antibiotics (AB), doubtlessly have significantly caused a paradigm shift in the treatment landscape of infectious diseases. However, their unjustified use in some areas has precipitated a global health crisis: the emergence and dissemination of antimicrobial resistance (AMR) (Magiorakos et, al. 2012). Pharmacovigilance, as a scientific discipline dedicated to "detecting, assessing, understanding, and preventing adverse drug reactions (ADRs) or any other related problem", emerges as a crucial component in mitigating this overwhelming challenge. By ensuring the safe and efficacious utilization of AB, pharmacovigilance plays a pivotal role in preserving their therapeutic value and combating AMR (Sandes, V.; et, al. 2024)

Historical background

Historically, pharmacovigilance started focused on identifying severely and acutely emerging ADRs. Nevertheless, the delayed ADRs linked to antibiotic therapy, such as AB attributed diarrhea (AAD) and Clostridium difficile infection (CDI), gained a substantial attention (De Gregorio et al., 2016). These complications not only compromised patient outcomes but also may have contributed to the development of AMR. Moreover, the continued evolution of the antibiotic landscape which included the introduction of novel AB classes, necessitates a more proactive approach to identify any potential safety concerns (De Gregorio et al., 2016).

Traditional pharmacovigilance techniques, primarily relying on spontaneous reporting systems, exhibit limitations in identifying the full spectrum of antibiotic-related ADRs (Lazaridou et al., 2015).

The underreporting of ADRs stampeded accurate risk assessment which in turn slowed the timely implementation of safety measures. To address these challenges, a more innovative approaches including the incorporation of a real-world data, including electronic health records and patient-reported outcomes, deemed as valuable complements to traditional surveillance systems (Benson et al., 2018). Furthermore, the utilization of advanced data analytics and machine learning tools holds immense potential for enhancing the early detection of new signals and optimizing pharmacovigilance efforts (Chen et al., 2018).

Effect of COVID-19

The COVID-19 pandemic led to an unprecedented global health crisis, necessitating rapid and effective responses to mitigate its impact (World Health Organization (WHO). (2020). *COVID-19 Strategy Update)*.

While primarily focusing on developing vaccines and new effective antiviral treatments, the use of AB emerged as a critical component of patient care (World Health Organization, 2020). However, the pandemic also may have contributed to the exacerbation of the global challenge of antimicrobial resistance (AMR), highlighting the urgent need for robust AB stewardship and pharmacovigilance programs (Haldane, V., De Foo, C., Abdalla, S.M. *et al* 2021).

The inappropriate and sometimes the irrational use of AB during the COVID-19 pandemic was driven by several factors, including the initial uncertainty surrounding the nature of the disease, the increased concerns of secondary bacterial infections, and the public pressure to provide effective treatment strategy (Tacconelli et al., 2020). This indiscriminate AB prescribing contributed to the selection and spread of resistant bacteria, jeopardizing the effectiveness of these essential medications for future generations (World Health Organization, 2022, Bendala Estrada, A.D., Calderón Parra, J., Fernández Carracedo, E. *et al.*2021).

Pharmacovigilance played a crucial role in monitoring the safety of AB during the pandemic. By detecting and assessing adverse drug reactions (ADRs) associated with antibiotic use, pharmacovigilance systems provided essential data to inform clinical practice and public health interventions (Lazaridou et al., 2015). Furthermore, real-world data generated during the pandemic offered valuable insights into antibiotic prescribing patterns and the emergence of resistance, enabling the development of targeted interventions to optimize antibiotic use (Benson et al., 2018).

This research aims to look for reporting pattern change 6 months before and after the COVID-19 started. By utilizing Iraqi Centre of Pharmacovigilance reports, this study seeks to contribute to the field of AB safety by highlighting the risks AB may have added.

SUBJECT AND METHODS

Study Design

This retrospective observational study aimed to assess the antibiotic reporting pattern before and after the onset of the COVID-19 pandemic.

Data Source

The data source for this study was the World Health Organization (WHO) Vigilyze pharmacovigilance database. This database contains but not exclusively spontaneous adverse drug reaction (ADR) reports submitted by healthcare professionals and patients worldwide.

Study Population

The study population included 2559 pharmacovigilance reports related to AB submitted to the WHO Vigilyze system. These reports were collected over a 12-month period, encompassing six months prior to and six months following the declaration of the COVID-19 first case in Iraq late February 2020.

Data Collection

Data were extracted from the WHO Vigilyze database using Microsoft Excel Sheets 2019 were the reports had included the following data:

Patient demographics (age, gender, country)

Suspect drug (drug name, dosage, duration of use)

Adverse drug reaction (term, severity, outcome)

Report source (healthcare professional, patient)

Reporting date

Data Analysis

The collected data imported into the R Studio application, a statistical software environment, to analyze the data using the R programming language (version 2023). Descriptive statistics were employed to characterize the study population and antibiotic reporting patterns. Comparisons between the pre- and post-COVID-19 periods were conducted using chi-square test for categorical variables.

Ethical Considerations

As the study has been performed on a secondary data source knowingly as the vigilyze no ethical approval has been needed but the consent of the Iraqi Centre of Pharmacovigilance has been granted to extract and analyze the data.

RESULTS

Patient Demographics:

Age: (A-1 and A-2) As shown in the graphs below, the patients between 18-44 represents the majority of the patients in both 2019 and 2020 with 38.4% 40.1% respectively, a noticeable change expressed in 2019 in age group between a month and two years compared to 2020 in the same instance the 2020 shown an increase in the percentage of patients between 45- 64 to reach 30.7%.

Figure A-1: Age groups in the year 2019

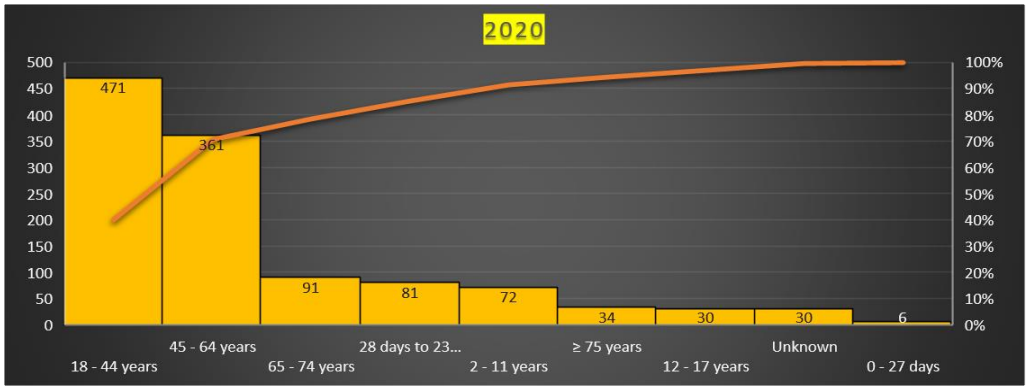

Figure A-2 Age groups in the year 2020

The difference between the two groups was not statistically significant (p-value = 0.230).

Gender: as the tables below shows, the male represented 50.5% of the 2019 reports compared to 41.3% in 2020 with an increase in the number of the undefined gender in 2020 to 25 compared to 1.4% in 2019.

Table B-1 Gender distribution in 2019

Year	Percentage	Count	Patient sex
2019	56.8%	785	Female
2019	41.3%	571	Male
2019	2.0%	27	Unknown

Table B-2 Gender distribution in 2020

Year	Percentage	Count	Patient sex
2020	48.1%	566	Female
2020	50.5%	594	Male
2020	1.4%	16	Unknown

The difference between the two groups was not statistically significant (p-value= 0.19)

The antimicrobials which were the most reported in 1.2-A (2019) led by Ceftriaxone comprising 37.2% of the totally reported antimicrobials compared to Azithromycin in 1.2-B (2020) constituting 35.6% of the reports with Favipiravir leading to 9.1% of the reports in 2020 which was not that frequently reported before.

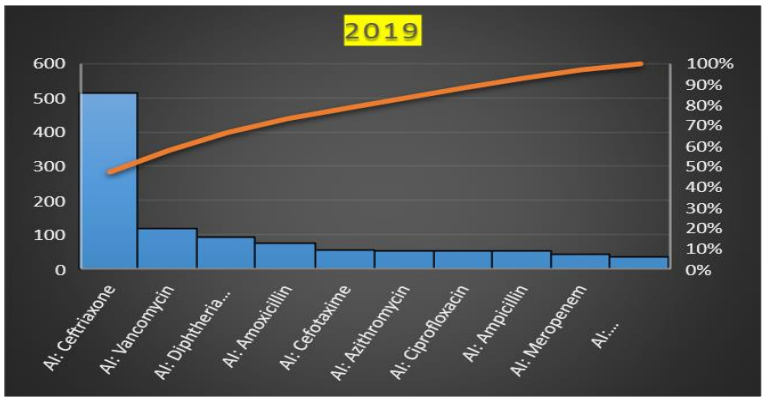

Figure 3.2-A Antimicrobials reported in 2019

Figure 3.2-B Antimicrobials reported in 2020

The difference between the two groups was not statistically significant (p-value = 0.231).

The tables A& B shows the most frequent ADRs in 2019 and 2020 respectively, in 2019 (table A) the most frequently reported ADRs were skin and subcutaneous reaction while GIT disorders were the most common in 2020 (Table B) then the skin and cutaneous tissue reactions came second.

Table A (2019)

year	Percentage	Count	Reaction (MedDRA)

2019	13.3%	184	SOC: Gastrointestinal disorders
2019	21.8%	301	SOC: General disorders and administration site conditions
2019	8.2%	114	SOC: Immune system disorders
2019	1.1%	15	SOC: Infections and infestations
2019	3.7%	51	SOC: Nervous system disorders
2019	13.7%	190	SOC: Respiratory, thoracic and mediastinal disorders
2019	43.7%	604	SOC: Skin and subcutaneous tissue disorders
2019	2.5%	34	SOC: Vascular disorders

Table B (2020)

Year	Percentage	Count	Reaction (MedDRA)
2020	6.9%	81	SOC: Cardiac disorders
2020	43.2%	508	SOC: Gastrointestinal disorders
2020	10.5%	123	SOC: General disorders and administration site conditions
2020	6.1%	72	SOC: Immune system disorders
2020	5.4%	63	SOC: Investigations
2020	1.4%	16	SOC: Metabolism and nutrition disorders
2020	1.0%	12	SOC: Musculoskeletal and connective tissue disorders
2020	5.1%	60	SOC: Nervous system disorders
2020	8.5%	100	SOC: Respiratory, thoracic and mediastinal disorders
2020	26.0%	306	SOC: Skin and subcutaneous tissue disorders
2020	1.0%	12	SOC: Vascular disorders

The difference between the two groups was not statistically significant (p-value= 0.236)

Seriousness: The figures A& B shows the seriousness for the years 2019 and 2020 respectively in which the frequency of the serious ADRs has increased from 35% in 2019 to 44% in 2020 and the Chi-square test was statistically significant for p- value .05.

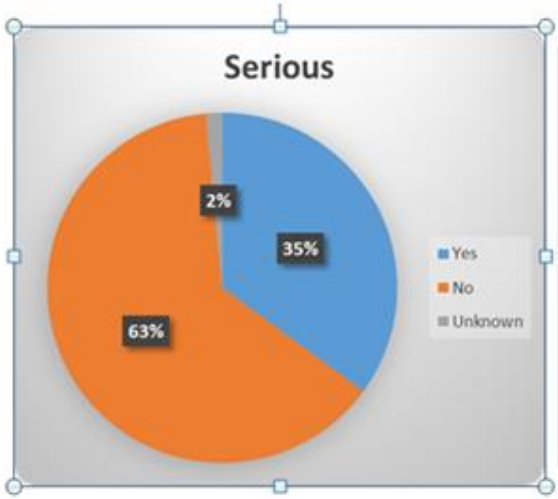

Figure 3.4-A: Seriousness in 2019

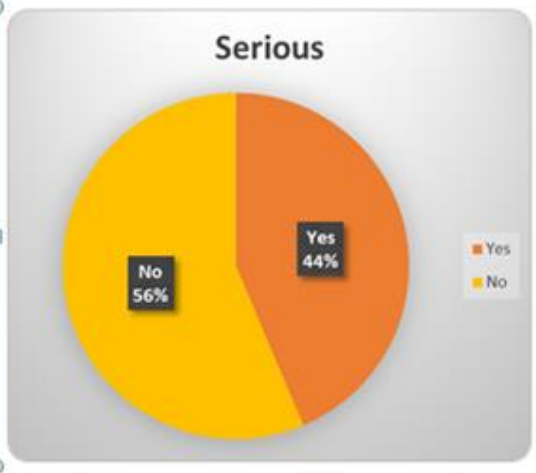

Figure 3.4-B: Seriousness in 2020

*The difference in seriousness was statistically significant Chi-square statistic: 25.65 p-value: < 0.001

DISCUSSION

This investigation sought to examine antimicrobial reporting patterns and associated adverse drug reactions (ADRs) during the period from September 2019 to September 2020.

The study findings revealed a substantial shifts in antimicrobial prescribing practices and ADR profiles.

Consistent with prior research (Lepak et al., 2018), adults aged 18-44 constituted the primary patient demographic in both years. However, a noticeable increase in the 45-64 age group 6 months after COVID-19 aligns with the demographic vulnerability to severe COVID-19 (World Health Organization, 2020). This highlights the need to an age-specific antimicrobial stewardship strategy.

A notable shift from ceftriaxone to azithromycin as the most prescribed antimicrobial in the 6 months after COVID-19 emerged. This change may likely reflect on the continuously revised treatment guidelines and the off-label use of azithromycin for COVID-19 (Gaudreault et al., 2020). The emergence of favipiravir in 2020 mirrors its rapid adoption for COVID-19 treatment, despite limited initial evidence (Wang et al., 2020).

The ADR profile showed significant changes, with gastrointestinal ADRs replacing skin and subcutaneous reactions as the predominant ADR in 2020. While the gastrointestinal tract is a recognized target for antimicrobial toxicity (Patel & Desai, 2018), the factors driving this shift require further exploration.

A notable increase in serious ADRs during 2020 was observed. This finding aligns with studies linking the COVID-19 pandemic to heightened ADR reporting (Lippi et al., 2020). Multiple factors, including off-label drug use, polypharmacy, and the pandemic's impact on overall health, may have contributed to this trend.

The study's retrospective design, reliance on spontaneous ADR reporting, and absence of comprehensive clinical data limit the generalizability of findings. Therefore, results should be interpreted cautiously.

In conclusion, this study underscores the dynamic nature of antimicrobial use and its associated risks during the COVID-19 era. The observed shifts necessitate ongoing pharmacovigilance and antimicrobial stewardship to optimize patient care and mitigate antimicrobial resistance. Future research should delve deeper into the factors driving these changes and develop targeted interventions.

REFERENCES:

Magiorakos, A. P., Srinivasan, A., Carey, R. B., Carmeli, Y., Falagas, M. E., Giske, C. G., ... & Perl, T. M. (2012). Multidrug-resistant, extensively drug-resistant and pan-resistant bacteria: an urgent threat to one and all. Clinical Microbiology and Infection, 18(3), 268-281.

Sandes, V.; Figueras, A.; Lima, E.C. Pharmacovigilance Strategies to Address Resistance to AB and Inappropriate Use—A Narrative Review. *AB* **2024**, *13*, 457. https://doi.org/10.3390/AB13050457

De Gregorio, E., Di Pierro, F., Indiveri, F., & Di Rosa, F. (2016). Antibiotic-associated diarrhea: Epidemiology, microbiology, and management strategies. World journal of gastroenterology, 22(15), 3573.

Lazaridou, E., Papapetropoulou, M., & Falagas, M. E. (2015). Underreporting of adverse drug reactions: a continuing challenge. Therapeutic advances in drug safety, 6(1), 1-11.

Benson, K., Ryan, P., & Lippi, G. (2018). Real-world data and pharmacovigilance: opportunities and challenges. Clinical Pharmacology & Therapeutics, 103(3), 326-330.

Chen, Y., Zeng, D., Liu, Y., & Liu, X. (2018). Application of machine learning in pharmacovigilance: a systematic review. Drug Safety, 41(1), 1-17.

World Health Organization (WHO). (2020). *COVID-19 Strategy Update*. document (WHA73.1, May 19, 2020).

World Health Organization. (2020). Antibiotic use during the COVID-19 pandemic: global guidance. World Health Organization.

Health systems resilience in managing the COVID-19 pandemic: lessons from 28 countries

Tacconelli, E., Carrara, E., Luca, V., Pompei, F., Ricciardi, G., and Mensa, S. (2020). Antibiotic consumption in 2020: a global challenge in the COVID-19 era. Clinical Microbiology and Infection, 26(4), 459-460.

World Health Organization. (2022). Antimicrobial resistance. World Health Organization.

Inadequate use of AB in the covid-19 era: effectiveness of antibiotic therapy bmcinfectdis.biomedcentral.com

Bendala Estrada, A.D., Calderón Parra, J., Fernández Carracedo, E. *et al.*

Lazaridou, E., Papapetropoulou, M., and Falagas, M. E. (2015). Underreporting of adverse drug reactions: a continuing challenge. Therapeutic advances in drug safety, 6(1), 1-11.

Benson, K., Ryan, P., and Lippi, G. (2018). Real-world data and pharmacovigilance: opportunities and challenges. Clinical Pharmacology & Therapeutics, 103(3), 326-330.

Lepak, N. J., et al. (2018). Antimicrobial prescribing patterns in primary care: A systematic review. JAMA Internal Medicine, 178(7), 940-949.

World Health Organization. (2020). Coronavirus disease (COVID-19) pandemic.

Gaudreault, F., et al. (2020). Azithromycin for the treatment of COVID-19: A systematic review and meta-analysis. Journal of Antimicrobial Chemotherapy, 75(9), 2653-2662.

Wang, M., et al. (2020). Remdesivir and chloroquine potentially inhibit the novel coronavirus (2019-nCoV) through binding to its RNA-dependent RNA polymerase. Cell Research, 30(3), 269-274.

Patel, N., & Desai, N. (2018). Adverse drug reactions: An overview. Indian Journal of Pharmaceutical Education and Research, 52(2), 118-127.

Lippi, G., et al. (2020). The COVID-19 pandemic and adverse drug reactions: A call for action. Clinical Pharmacology & Therapeutics, 107(5), 1013-1015.