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Pharmacovigilance Data as a Trigger to Identify Antimicrobial Adverse Effects: A Study Using Reports from Basra Pharmacovigilance Centre

Abstract

Background: pharmacovigilance is the science and activities related to detecting, evaluating, understanding, and preventing adverse effects and ensuring that medicines are used safely and effectively. Antimicrobials have played an important role in the treatment and cure of diseases; however, irrational prescribing may lead to differing types of adverse drug reactions (ADRs)

Aim of Study: This study aims to summarize and analyze data from Basra from the pharmacovigilance center in Basrah concerning antibiotic use-related ADR.

Method: This study is a retrospective cohort study of antibiotic use in 2022-2023. The study population consists of patients who received antibiotics during the study period. The outcome of interest is the incidence of adverse events associated with antibiotic use.

Results: Penicillin and third-generation cephalosporin were the most frequent causes of ADRs, and both accounted for 29% of the reported cases followed by glycopeptide, and vancomycin about 24%. Skin and subcutaneous tissue disorders were the most common clinical manifestation, occurring in 80 cases (75%), followed by difficulty in breathing (8.5%) and with remaining (16%) miscellaneous symptoms like hypotension, urticaria, headache, and GIT disorders

Conclusion: Penicillin and third-generation cephalosporins are the most common causative antibiotics for ADRs and skin manifestations were the most frequently experienced symptom. Inappropriate antibiotic prescriptions were common and associated with increased risks of adverse drug events and higher attributable healthcare expenditure and increase need for education programs for rational use of antibiotics.

1. Introduction

Pharmacovigilance is the science and activities related to detecting, evaluating, understanding, and preventing adverse effects or other drug-related problems. Pharmacovigilance is an essential component of drug safety and helps ensure that medicines are used safely and effectively [1]. It involves collecting and analyzing data on adverse effects or other drug-related problems and developing and implementing strategies to prevent these problems from occurring in the future. The ultimate goal of pharmacovigilance is to ensure that patients receive the best possible care and that medicines are used in a safe and effective way. The aim is to promote the safety and effective use of medicines through the early detection and evaluation of drug safety risks [2]. The pharmacovigilance system is essentially based in spontaneous reports of Adverse Drug Reactions (ADR). ADR can be associated with severe outcomes and significant mortality, besides, most of them are deemed to be preventable events. Globally, antibiotics are among the most widely prescribed medications and their extensive use is linked to antibiotic-associated ADR [3].

Antibiotics are essential drugs in the fight against bacterial infections, but they are not without risks. These drugs can cause adverse reactions that range from mild to severe, and their improper use can lead to the development of antibiotic-resistant bacteria [4]. Pharmacovigilance is the science and activities related to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problems. In this graduation project, we will explore the importance of pharmacovigilance for antibiotics and its impact on patient safety. We will discuss the current strategies and systems in place to monitor and manage adverse reactions to antibiotics. Finally, we will propose recommendations for improving pharmacovigilance practices for antibiotics to ensure they’re safe and effective use in clinical practice.

Drug safety is an essential aspect of healthcare that aims to ensure the safe and effective use of medications. The safety of drugs is assessed through various methods, including preclinical and clinical trials, post-marketing surveillance, and adverse event reporting [5].

Adverse drug events (ADEs) refer to any negative or unintended side effects that occur when taking a medication. These effects can range from mild to severe and can impact a patient's health, quality of life, and ability to function [6].

It is crucial to report any suspected ADEs to healthcare professionals or regulatory agencies, such as the US Food and Drug Administration (FDA). Reporting ADEs helps to identify potential safety concerns with medications, as well as the need for additional research, labeling changes, or patient education [7].

Patients, caregivers, and healthcare professionals can report ADEs to the FDA through the MedWatch program. This program collects and analyzes reports

Antibiotic safety monitors

Antibiotic drug safety monitoring is a process of continuously monitoring and evaluating the safety and effectiveness of antibiotics. This is done to make sure that the drugs are not causing serious side effects or promoting bacterial resistance. The monitoring can involve various techniques, such as clinical studies, post-marketing surveillance, and adverse event reporting systems [8].

Agencies such as the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have established regulations and guidelines for antibiotic drug safety monitoring. These guidelines detail the requirements for drug manufacturers to submit safety data and report adverse events as part of drug approval and post-marketing surveillance [9].

Overall, antibiotic drug safety monitoring is crucial to ensure that antibiotics are safe and effective for use in treating bacterial infections.

Aim of Study:

This study aims to summarize and analyze data from Basra from the pharmacovigilance center in Basrah concerning antibiotic use-related ADR.

2. Methods

2.1. Study design

This study is a retrospective cohort study of antibiotic use in 2022-2023. The study population consists of patients who received antibiotics during the study period. The outcome of interest is the incidence of adverse events associated with antibiotic use.

2.2. Data collection

To collect data, we accessed electronic medical records from hospitals and clinics in the study area. We collected information on patient demographics, diagnosis, antibiotic prescribing practices, and the occurrence of adverse events associated with antibiotic use.

2.3. Data analysis

The data were analyzed using SPSS software. We used descriptive statistics to summarize patient demographics, antibiotic use, and adverse events. We also conducted bivariate and multivariable analyses to examine the association between antibiotics and the occurrence of adverse events.

2.4. Ethical considerations

Ethical approval was obtained from our institution's ethics committee before the study began.

3. Results

Table 3.1: Demographic data for patients included in the study

parameter	No. (%)
Patient age (years)	
0-10	13 (12.3%)
11-20	35 (33%)
21-30	12 (11.3%)
31-40	21 (19.8%)
41-50	18 (17%)
51-60	1 (0.9%)
More than 60	6 (5.7%)
Gender	
Male	56 (52.8%)
Female	50 (47.2%)
Hospital	
Maternal and children hospital	50 (47%)
Al-Mawani hospital	20 (19%)
Al-Sader hospital	14 (13%)
Al-Fayhaa hospital	12 (11%)
Basra Teaching hospital	10 (9%)

Duration of hospital residence	
1-2 days	88 (83%)
3-4 days	7 (6.6%)
5-6 days	5 (4.7%)
More than one week	6 (5.7%)
No of antibiotics were taken at the same time	
Single	65 (61.3%)
Two	38 (35.8%)
Three	3 (2.8%)
Duration of hospital stay	
1-2 days	88 (83%)
3-4 days	7 (6.6%)
5-6 day	5 (4.7%)
More than 1 week	6 (5.7%)
The severity of the reported adverse effect	
Mild	105 (99.1%)
Severe	1 (0.9%)

Table3.2: Type of antibiotic-associated with adverse effect

Type	No (%)
Penicillin	31 (29%)
cephalosporin	31 (29%)
Vancomycin	26 (24%)
Quinolone	7 (6.6%)
Macrolide	4 (3.7%)
Aminoglycoside	4 (3.7%)
Tetracyclines	2 (1.8%)
Other (tinidazole)	1 (0.9%)

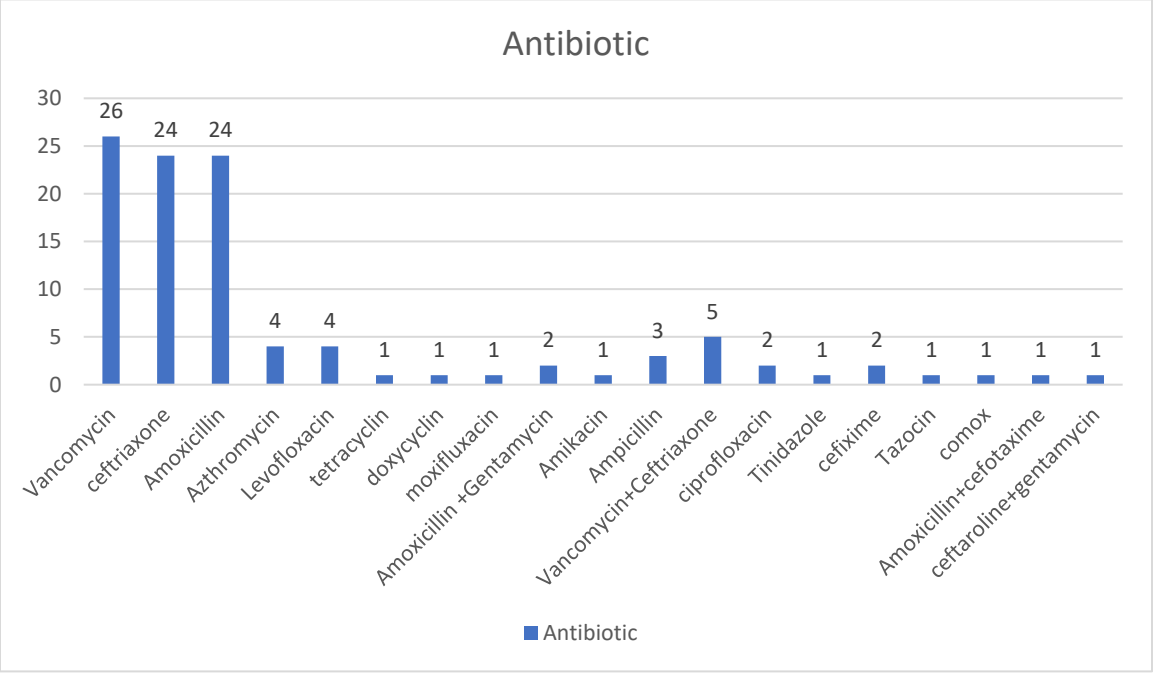

Figure 3.1: Type of antibiotics associated with adverse effects

Table 3.3: Type of reported adverse effect

Type of ADR	Severity of ADR	No. (%)
Skin rash	Mild	80 (75.5%)
Difficulty in breath	Mild	9 (8.5%)
Other (hypotension, urticaria, headache, GIT symptoms)	Mild	17 (16%)

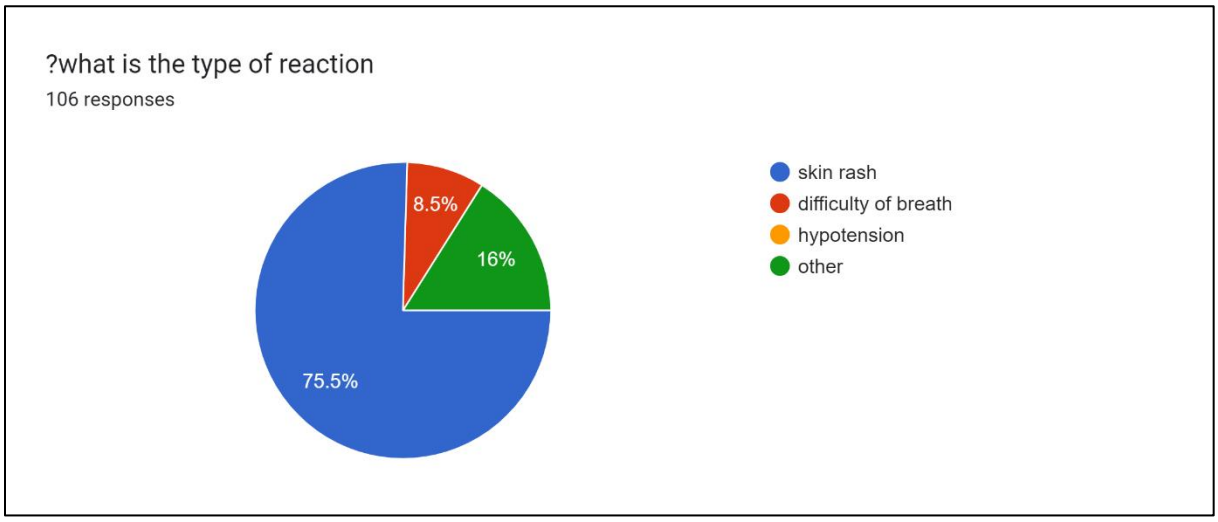

Figure 3.2: Type of ADR

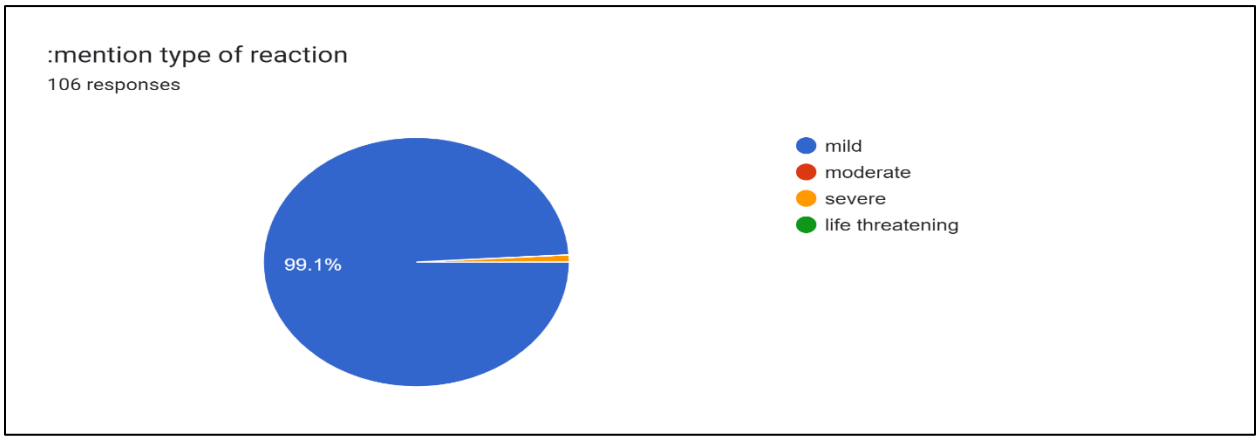

Figure 3.3: Severity of adverse effect

Table 3.4: Management of the reported ADR

Response to ADR	**Number**	**Percent**
Discontinue medication	72	69%
Continue a medication	31	30%
Pharmacological Intervention	**Number**	**Percent**
Administration of hydrocortisone	6	5.8%
Administration of diphenhydramine	1	1%
Both of hydrocortisone and diphenhydramine	41	39.8%
Other	55	53.4%

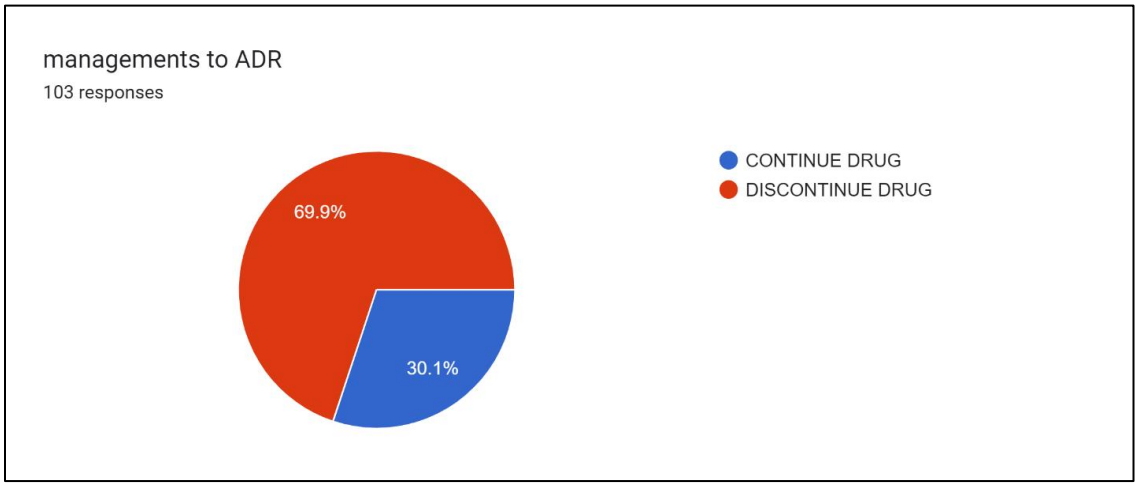

Figure 3.4: Medical Intervention regarding ADR

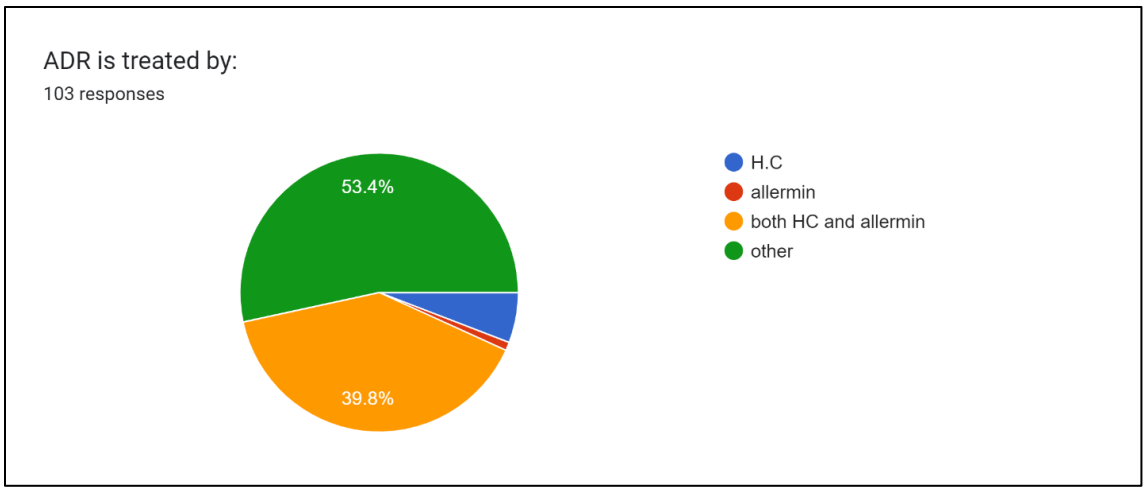

Figure 3.5: Medical Response to ADR

4. Discussion

The World Health Organization (WHO) defines Pharmacovigilance as the science and activities relating to the detection, assessment, understanding, and prevention of adverse drug effects. The aim is to promote the safety and effective use of medicines through the early detection and evaluation of drug safety risks [10].

Globally, antibiotics are among the most widely prescribed medications, and their extensive use is linked to antibiotic-associated ADR. Antibiotics relatively have a good safety profile, however, excess or misuse of antibiotics administration increases the incidence for the occurrence of adverse effects as well as increases in antibiotic resistance. The adverse effects of antibiotics range from mild skin reactions to severe life-threatening anaphylaxis reactions.

This study aims to summarize data from Basra from the pharmacovigilance center in Basrah concerning antibiotic use-related ADR and analyze the reports received from Basra hospitals' exclusive usage of antibiotics.

This study includes a random sample of 106 reports of antibiotics' adverse effects, about 56 (52.8%) male and 50 (47.2%) female as shown in demographic data [Table 1]. Most reports received from Basrah Hospital for Maternal and Pediatrics about (with age groups from (11-20) years and (31-40) years are the highest number of reports about 33% and 20% respectively. This could be explained by excess and inappropriate administration of antibiotics in children due to their high vulnerability to various types of infection make them at higher risk of adverse effects.

This result agrees with other studies that found a high prevalence of antibiotic use among hospitalized pediatric patients. Many prescriptions were inappropriate, with dosage and duration of treatment as the most frequent errors. Inappropriate antibiotics were associated with an increased risk of several adverse drug events, including *Clostridioides difficile* infection and severe allergic reactions among children [11]. Patients who were prescribed three or more antibiotics per prescription, and had short Hospitalization time were more likely to experience prescribing errors [12]. These results are concerning, as overuse and inappropriate use of antibiotics are major factors in the development of antibiotic-resistant microorganisms.

In the present study, most reports of adverse effects were recorded for penicillin and cephalosporin (about 30% of all ADR of antibiotics) as shown in Table 2. These results could be explained by the fact that Penicillins and cephalosporins are the class of drugs that remain a highly valuable group of antibiotics in primary care. They are considered among the safest of antibiotics generally effective at eradicating common bacterial infections and are relatively inexpensive and therefore widely used to treat skin, ear, sinus, and upper respiratory tract infections [13]. Adverse effects of pencillins and cephalosporins range from diarrhea, urticaria, erythema, increased incidence of infection, and hypersensitivity reaction. Hypersensitivity is, however, its most important adverse reaction resulting in nausea, vomiting, pruritus, urticaria, wheezing, laryngeal edema, and cardiovascular collapse [14]. Even penicillins allergy is more common than cephalosporins, however, there is a cross-sensitivity between them. It is commonly taught that approximately 10% of patients who are allergic to penicillin will have an adverse reaction to cephalosporins. However, within the medical literature, this quoted cross-allergy risk of 10% has been questioned [15].

The second antibiotic with highly reported adverse effects is vancomycin about 29% of reports [Table2]. Vancomycin is effective against *Gram-positive* bacteria especially methicillin-resistant *Staphylococcus aureus* (MRSA), ampicillin-resistant *enterococci* , and *Gram-positive* organisms in patients allergic to penicillin [16]. The main adverse reactions of vancomycin include hypersensitivity reactions, nephrotoxicity, ototoxicity, and so on. The most common manifestations of hypersensitivity reaction are hypersensitivity macular cutaneous rashes (Red Man syndrome) and anaphylaxis which usually occurs after intravenous administration [17]. Therefore, vancomycin should be considered as a last resort in the case of ineffective use of other agents.

In the present study, a lower number of ADR reports include other types of antibiotics like azithromycin, ciprofloxacin, tetracycline, doxycycline, and gentamycin [figure 1]. This may be explained by a low administration rate of these antimicrobials especially oral ones in hospitalized patients and lower hypersensitivity reactions than B-lactam antibiotics.

In Table 3, the most likely symptom of ADR is skin rash (about 80, 75.5%) followed by difficulties in breathing (8, 7.5%) with remaining (17, 16%) miscellaneous symptoms like hypotension, urticaria, headache, and GIT disorders. Skin manifestations are the most common ADR of antibiotics and penicillin, third-generation cephalosporins, and glycopeptides were the most common causative antibiotics for skin and subcutaneous-related ADRs. Similar results were seen in other studies where cutaneous ADR is the predominant effect of antibiotics [18, 19].

Regarding the severity of the reported ADR, most symptoms were mild 99% and less than 1% were severe as shown in Table 3. The medical intervention for most reported cases (about 70%) was discontinuation of antibiotics and 30% continue the medication with or without administration of antiallergic drugs like corticosteroids alone or in combination with antihistamines. Continuation of causative antibiotics based on the severity of ADR and the medical status of the patients. In the present study, most ADRs were mild and the continuation of antibiotics was reasonable when appropriate intervention and monitoring is done especially in cases where alternative antibiotics were not available.

Finally, Pharmacovigilance reports give an important information about the common ADR of medications and appropriate responses to it, to ensure the safety of medicine. Pharmacists play crucial roles in health systems in maintaining the rational and safe use of medicines since they are drug experts who are specifically trained in this field. Effective use of pharmacists' workforce will improve the outcome of pharmacotherapy as well as decrease global health costs.

5. Conclusion

Penicillin and third-generation cephalosporins are the most common causative antibiotics for ADRs and skin manifestations were the most frequently experienced symptom. Inappropriate antibiotic prescriptions were common and associated with increased risks of adverse drug events and higher attributable healthcare expenditures. These findings highlight the individual- and national-level consequences of inappropriate antibiotic prescribing and further support the implementation of outpatient antibiotic stewardship programs.

6. Recommendation

1. A large sample size study is required for more detail information.

2. Educational programs are required for the medical staff regarding the rational use of antibiotics and proper response to the possible ADR.

3. Education about the importance of pharmacovigilance and encouraging the pharmacists to take their role in patient care and reporting adverse drug reactions in the official pharmacovigilance center.

4. pharmacists can utilize pharmacovigilance systems interfaced with electronic health records to monitor the performance of the drugs they fill and also identify adverse drug reactions earlier than non-pharmacists, thereby reducing high healthcare costs.

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