

Adverse Drug Reaction Pattern to Commonly used Antibiotics in a Tertiary Care Hospital: A Prospective Observational StudyRanjit Debbarma¹, Mrigendra Kumar², Jeetendra Kumar³¹PGT (Final Year), Department of Pharmacology, Jawaharlal Nehru Medical College & Hospital, Bhagalpur, Bihar²Associate Professor, Department of Pharmacology, Jawaharlal Nehru Medical College & Hospital, Bhagalpur, Bihar³Associate Professor and HOD, Department of Pharmacology, Jawaharlal Nehru Medical College & Hospital, Bhagalpur, Bihar

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Corresponding Author: Dr. Mrigendra Kumar

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Abstract:**Background:** Drugs play a significant role in prophylaxis, diagnosis, and treatment of each and every disease. They are beneficial to the patients at the same time; they also result in unwanted and harmful effects which are called adverse drug reactions (ADRs). The aim of this study was to evaluate and analyse adverse drug reactions to antibiotics in patients of a tertiary care hospital at Bhagalpur, Bihar.**Methods:** This prospective observational study was carried out in Department of Pharmacology, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar from January 2022 to December 2022. Patients were collected from various department of OPD and hospital ward of JLNMC, Bhagalpur, Bihar.**Results:** A total number of 138 ADRs were selected during this study period. 98 were males and 40 were females. Maximum number of patients were from General Medicine department followed by General Surgery followed by Dermatology. Most of the reactions were mild (77.4%). Gastrointestinal system was the most commonly affected organ. In majority of the ADRs the suspected drug was withdrawn (60.8%). The association between a drug and ADR was evaluated using the Naranjo scale. In order to prevent or reduce harm to patients and thus improve public health, mechanisms for evaluating and monitoring public health, evaluating and monitoring the safety of medicines in medical use are vital.**Conclusion:** Antibiotics are most commonly prescribed drugs so its monitoring regarding ADRs may benefit the clinicians in early identification and management of ADRs so that quality of life of patient can be safeguarded at an earliest.**Keywords:** Antibiotics, ADR, Naranjo scale.This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.**Introduction**

World Health Organisation (WHO) defines adverse drug reaction (ADR) as “any response to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease or for the modification of physiologic function.” Adverse drug reaction is the 7th most common cause of death with 6.5% of admissions in National Health Service (NHS) hospitals is due to ADRs.(1) Sometimes, ADR-related costs may exceed the cost of the treatment of disease.(2) Antibiotics are considered to be the commonly used drugs in hospital setting due to higher prevalence of infectious diseases especially in India. These are observed to be the main culprit of ADRs.(3,4) 3.2-40.9% of ADRs are reported due to antibiotics as per various studies conducted in Indian

population.(5-8) This may be because of self-medication, over-the-counter use, and irrational prescription. Also excessive and irrational use of antibiotics may cause antibiotic resistance.(9) Thus, the rational use of antibiotics is a major health need.

Phatak et al rightly said that “drugs are double edged weapons”, so ADR monitoring is one of the crucial part during the treatment period of patient.(10) Uppsala monitoring centre, Sweden in collaboration with WHO was first established in the year 1971 with its important role in maintaining the international database of ADRs. In order to prevent and monitor ADRs, pharmacovigilance centers are being established in tertiary care centres in India. Establishing an antibiotic policy in every institution and ensuring that the best choice

among antibiotics should be prescribed by physicians can also prevent ADRs.

Material and Methods

This prospective observational study was conducted in a Department of Pharmacology, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar from January 2022 to December 2022. ADRs were collected from different departments like General medicine, Dermatology, Paediatrics, Orthopaedics, Pulmonology and general surgery. All patients of either sex and of any age who developed an ADR during the study period were included in the study. Pregnant women and nursing mothers were excluded.

Demographic data like patient initials age, sex, marital status, medical history, surgery history,

allergies, herbal and cosmetic use had been recorded on the case record form. The prescription given to the patient including the drug prescribed, dose, frequency and duration of the treatment was noted on the case record form.

The type of reactions, causality and severity were assessed using Rawlins and Thomson, Naranjo and modified Hartwig scale respectively.

Results

During the study period, 138 ADRs were reported. Of these 98 (63.7%) were males and 40 (36.3%) were females (Table 1). The number of adults who experienced ADRs were 113 (81.8%) and children below 12 years were 25 (18.2%) (Table 2).

Table 1 : Distribution of ADR's based on gender of the patient

| Sex | No. of patients | Percentage |
|--------|-----------------|------------|
| Male | 98 | 63.7% |
| Female | 40 | 36.3% |
| Total | 138 | 100.0% |

Table 2 : Distribution of ADR's based on the age group of patients

| Age group | No. of patients | Percentage |
|-----------|-----------------|------------|
| Adult | 113 | 81.8% |
| Children | 25 | 18.2% |
| Total | 138 | 100.0% |

As shown in Table 3, the maximum number of ADRs were received from General Medicine department-56, followed by Dermatology -28, Paediatrics -21, Orthopaedics -18, Pulmonology - 9 and General Surgery-6. The most commonly affected organ system was Gastrointestinal system -72(52.2%) followed by skin-57 (41.4%), Respiratory system-6 (4.3%) and urinary system-3 (2.1%). This is depicted in Table 4.

Table 3 : Number of ADR's received from different departments

| Name of Departments | No. of patients |
|---------------------|-----------------|
| General Medicine | 56 |
| Dermatology | 28 |
| Pediatrics | 21 |
| Orthopaedics | 18 |
| Pulmonology | 9 |
| General Surgery | 6 |

Table 4 : Distribution of organ system affected due to ADR'S

| Organ system | No. of patients | Percentage |
|-------------------------|-----------------|------------|
| Gastrointestinal system | 72 | 52.2% |
| Skin | 57 | 41.4% |
| Respiratory System | 6 | 4.3% |
| Urinary System | 3 | 2.1% |

Table 5 shows that Piperacillin-31(22.4%) is causing the highest no. of ADRs i.e. followed by Ceftriaxone - 26(18.8%) and Cefotaxime-17(12.3%). Combination of Amoxicillin with Clavulanic acid showed 16(11.6%) of ADRs. Ofloxacin -15(10.8%) and Amikacin showed 9(6.5%) of ADRs.

Table 5: Antibiotics causing ADR'S

| Drugs | No. of ADR'S | Percentage |
|----------------------------|--------------|------------|
| Piperacillin | 31 | 22.4% |
| Ceftriaxone | 26 | 18.8% |
| Cefotaxime | 17 | 12.3% |
| Amoxicillin+Clavulanicacid | 16 | 11.6% |
| Ofloxacin | 15 | 10.8% |
| Amikacin | 9 | 6.5% |
| Norfloxacin | 7 | 5.0% |
| Gentamicin | 6 | 4.3% |
| Azithromycin | 4 | 2.8% |
| Erythromycin | 4 | 2.8% |
| Doxycycline | 3 | 2.1% |

Majority of the reactions were Type A Augmented reactions as shown in Table 6.

Severity of reported ADRs were assessed using the Modified and Siegel scale (Table 7). Most of the ADRs were mild (101) (73.1%), 28(20.28%), were moderate and only a few 9 (6.3%) were severe. In this study, ADRs were assessed based on Naranjo's Casualty assessment scale. Most of the reported

ADRs were possible-119(86.23%) and some were probable-19(13.76%) (Table 8).

From this study it was found that there was a recovery from ADRs in total of 132 (95.6%) patients, although 0% had fatal ADRs . Unknown outcome was 0%. 6(4.3%) cases were recovering (Table 9).

Table 6: Type of reaction (Classification according to Rawlin & Thomson)

| Category | No. of ADR'S | Percentage |
|----------|--------------|------------|
| Type A | 108 | 78.2% |
| Type B | 30 | 21.8% |

Table 7: Level of Severity of reported ADR'S (Using the modified Hartwig & Siegel scale)

| Level of Severity | No. of ADR'S | Percentage |
|-------------------|--------------|------------|
| Mild | 101 | 73.1% |
| Moderate | 28 | 20.28% |
| Severe | 9 | 6.5% |

Table 8: Causality assessment (According to Naranjo's Scale)

| Causality parameters | No. of ADR'S | Percentage |
|----------------------|--------------|------------|
| Definite | 0 | 0% |
| Probable | 19 | 13.76% |
| Possible | 119 | 86.23% |
| Unlikely | 0 | 0% |

Table 9: Outcome

| Parameters | No. of ADR'S | Percentage |
|------------|--------------|------------|
| Fatal | 0 | 0% |
| Recovering | 6 | 4.3% |
| Recovered | 132 | 95.6% |
| Unknown | 0 | 0% |

Discussion

Treatment of infections always includes antibiotics. As the drug resistance incidence is on the raise, there is a huge need for taking steps to promote rational use of antibiotics. Antibiotics are the most commonly used and misused drugs by patients and prescribers.(11) This study tried to find out the pattern of Adverse drug reactions of antibiotic drug class in the post marketing surveillance studies. Antibiotics are used for treatment and prophylaxis of various infectious conditions and are considered

as safer drugs when used rationally. Antibiotics are considered as the second most prescribed drugs in the world, only next to the drugs indicated for cardiovascular diseases.(12) The males in our study extra numbered the females. In our study, it shows that Piperacillin has maximum number of ADRs. Usually Piperacillin is used in combination with Tazobactam. All reported adverse effects are those which could occur with Piperacillin alone. Adverse effects with Piperacillin being diarrhea, nausea, vomiting, abdominal pain and

dermatological reactions. These reactions are mild but occur commonly. Piperacilin is effective against many infections. As It is the most frequently used antibiotics adverse effects observed also would have been maximum in this study. The second group of drugs causing ADRs in this study was the 3rd generation Cephalosporins, Ceftriaxone and Cefotaxime. The most common system associated with ADRs to Cephalosprins were the Skin and Gastrointestinal system. The finding is consistent with many studies that have reported high percentage of dermatological manifestations.(13) Maculopapular rash was most commonly reported due to amoxicillin which was in conformity with the findings of Ghosh .et.al. In our study there was one patient of Stevens Johnson syndrome due to Amoxicillin- Clavulanic acid combination similar to the findings by salvo et.al.(14) From the above findings, ADRs to beta lactum antibiotics were maximum and the skin and its appendages followed by gastrointestinal system were involved. (15).Patterns of organ system involvement and of signs and symptoms were quite similar, with gastrointestinal effects predominating(nausea, Vomiting, diarrhea or abdominal pain), followed by effects on the Central nervous system(dizziness, headache or insomnia). In regard to the reported adverse effects of Flouroquinolones, bodyaches along with muscle and joint pains were also observed in a few number of patients on Ciprofloxacin.

Difficulty in hearing, vertigo and tinnitus were reported from patients prescribed with Gentamycin and Amikacin. A woman was given Gentamycin and developed myoclonus, involuntary muscle jerks and spasm. One child showed abnormal kidney function tests treated with Amikacin. (16)(17).

Adverse reactions to Macrolide antibiotics were few in comparison with the other antibiotics. The adverse effects were also mild being Gastrointestinal reactions occurring with both Erythromycin and Azithromycin. Macrolides are considered to be one of the safest anti-infective groups in clinical use, with severe adverse reactions being rare. Erythematous rash and allergic reactions were seen in a few patients. In one study, an erythematous rash in sun exposed parts of the body had been reported taking Doxycycline for Malaria prophylaxis. It was also found that doxycycline did not cause a significantly higher percentage of all skin events, when compared with other antimicrobials.

Analysis of the type of reported ADRs according to Rawlin and Thompson showed Type A predominance. This result coincides with the study conducted by Oshikoyo et. al and Starveva et.al.(18) Type A reactions are dose related and preventable. Type B reactions comprise

approximately 21% and include hypersensitivity reactions.(19)

Conclusion

Monitoring of adverse drug reactions is an ongoing, ceaseless and continuing process. Since newer and newer drugs hit the market, the need for pharmacovigilance grows more. Monitoring of the adverse effects of newer drugs and potentially risky drugs is mandatory. This study concluded that the spontaneous reporting of adverse drug reactions of antibiotics is good in our hospital setting.

The health system should promote the spontaneous reporting of adverse drug reactions to antibiotics and other drugs, proper documentation and periodic reporting to pharmacovigilance centre to ensure drug safety.

The active involvement of a well trained clinical pharmacist for detecting the adverse drug reactions and delivering the awareness classes for the health care professionals regarding the need of reporting the incident could improve in all hospitals.

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