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Pharmacovigilance Study of Antibiotics in a Tertiary Care Hospital

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ABSTRACT

Background: Antibioticsare currently the most commonly prescribed drugs in hospitals, worldwide. Detecting ADRs and establishing preventive measures is essential for patient safety.
Methods: A prospective, Cross-sectional, Observational study was conducted at inpatient and outpatient Department of Medicine in tertiary health care centre. 96 patient's relevant medical history were obtained from ADR forms (CDSCO forms) and patients files from 1 October 2022 to 31 December 2022.
Results: A total of 96ADR forms and patients' files were collected, analysed and assessed on WHO causality assessment scale. It was observed that male patients 58(60.41%) predominated over females 38 (39.58%) in ADR occurrence. Age wise distribution of the ADRs revealed that the Middle-aged patients were more accounted 41 (42.70 %), followed by geriatric28 (29.16 %), and Adult 23 (23.95 %). ADRs reported with Beta-Lactams were 37(38.54%) followed by Aminoglycosides19 (19.79%), and Quinolones 15(15.62%). GIT 29(30.20%) was the most affected organ system by Adverse Drug Reactions. The most common ADR was Abdominal pain 13(13.54%), Dyspnoea, Diarrhoea, Rashes 08 (8.33%), Vomiting, allergic reactions 6 (6.25%) and Cough. Severity assessment showed that out of 96 ADRs, mild reactions were high followed by moderate and severe reaction.
Conclusion: This study concluded the spontaneous reporting of Adverse Drug Reactions to antibiotics and other drugs, proper documentation and periodic reporting to regional pharmacovigilance centres should be promoted to ensure drug safety.

Key Words: *Antibiotics, Adverse Drug Reactions, Beta-Lactams, Aminoglycosides*

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INTRODUCTION

WHO defines ADR as ''any response to a drug which is noxious and unintended, and occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function" Early detection, evaluation, monitoring and reporting of ADR are essential to make drug treatment safe, efficacious and cost effective [1].

Adverse drug monitoring and spontaneous reporting are important in recognizing adverse reactions in local population. Adverse reactions are recognized hazards of drug therapy. Adverse drug reactions (ADRs) are main causes for mortality and morbidity in both hospitalized and ambulatory patients. The current epidemiological studies have revealed that the ADRs are the fourth to sixth leading cause of death [2].

Detecting ADRs and establishing preventive measures is essential for patient safety. Therefore, the importance of pharmacovigilance (PV) must be emphasized.Furthermore, efficient spontaneous reporting system is necessary to uncover ADRs [3].

According to a study conducted by Novotny *et al*., the most troublesome classes of drugs contributing to Adverse Drug Reactions were antibiotics [4]. Antibiotics are currently the most commonly prescribed drugs in hospitals, worldwide [5]. But, excessive and inappropriate use of antibiotics renders its major limitation i.e., increased drug resistance [6]. Antibiotic resistance occurs when an antibiotic is no longer effective at killing or limiting the growth of bacteria. The rational use of antibiotics is a major health need. Prevention of ADRs is possible by proper monitoring, which fortified the national directive to institutionalize a pharmacovigilance centre in every medical college in the country [7]. It is extremely important that institutions and hospitals have an antibiotic policy and ensure that the best choices are made by individual prescribers.

Although a number of studies on ADRs caused by various drugs have been conducted, only few have focused specifically on antibiotics. Main aim of the study was to monitor the safety (adverse drug reactions) of antibiotics commonly prescribed in medicine unit of tertiary care hospital for a period of 3 months, establish most common antibiotics that give maximum ADRs, determine the list of most commonly affected organ system and assess the causality and severity of ADRs.

MATERIALS AND METHODS

This Prospective, Observational, non-interventional study was carried out in the inpatient and outpatient Medicine department of tertiary care hospital from 1 October 2022 to 31 December 2022. The study was initiated after the approval of the study protocol by Institutional Ethics Committee.

All patients of either sex and of any age who developed ADR were included in the study. Pregnant and lactating womenwere excluded from the study.

Data about demographic details and drug administration, dosage, frequency, date of onset of reaction and the patient's relevant medical history were obtained from ADR forms (CDSCO forms) and patients files.

The causality was assessed by using Naranjo causality assessment scale and the severity was assessed by using the Hartwig and Siegel severity assessment scale according to the recommendation by the WHO Uppsala Monitoring Centre.

RESULTS AND OBSERVATIONS

Data analysis revealed that male patients 58(60.41%) predominated over females 38 (39.58%) in ADR occurrence. **[Figure-1]**

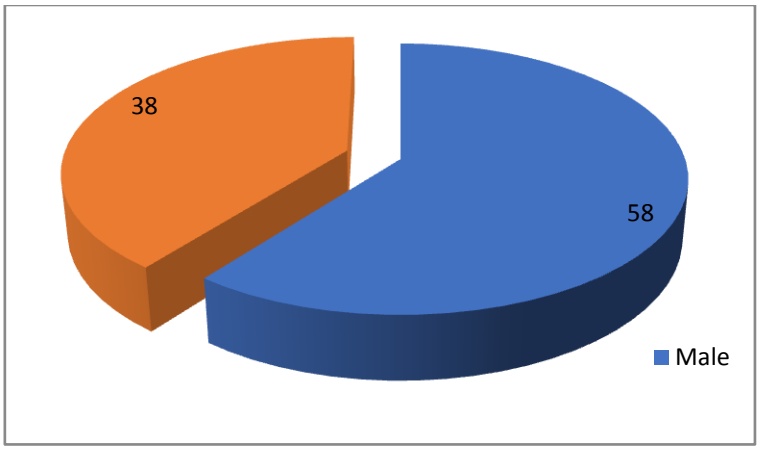


Figure 1: Gender-wise ADRs distribution.

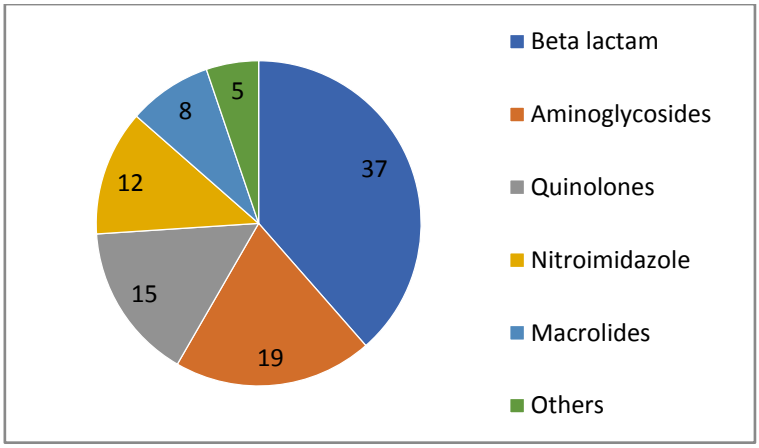
[Table 1] shows the age wise distribution of the ADRs and revealed that the Middle-aged patients were more accounted 41 (42.70 %), followed by geriatric28 (29.16 %), and Adult 23 (23.95 %).

Table 1: Age wise distribution of ADRs (n=96)

Age group (years)	Number of ADR (%)
Children 0-18	04 (04.16 %)
Adult 19-45	23 (23.95 %)
Geriatrics>65	28 (29.16 %)

During the study period, a total of 96 ADRs related to antibiotics were collected, analysed and assessed on WHO causality assessment scale.

Out of 96 patients, 37 patients received Beta-Lactams antibiotics, 19 received Aminoglycosides, 15 received Quinolones, 12 received Nitroimidazole, 8 received Macrolides and 5 were on other antibioticdrugs. **[Figure 2]**



[Figure 2]

ADRs reported with Beta-Lactams were (Ceftriaxone, Amoxicillin/Clavulanic acid, Cefotaxime, Tazobactam) 37(38.54%) followed by Aminoglycosides (Amikacin, Gentamicin, Streptomycin, 19(19.79%), Quinolones (Ofloxacin, Levofloxacin)15(15.62%), Nitroimidazole 12 (12.5%), Macrolides (Azithromycin) 8 (8.33 %) and others 5 (5.20 %).

Table 2: ADRs due to various therapeutic classes of antibiotics

Antibiotics	Number of ADRs (%)
Beta lactams	**37 (38.54 %)**
Ceftriaxone	15 (15.62 %)
Amoxicillin/Clavulanic acid	07 (07.29 %)
Etoperidone	08 (08.33 %)
Cefotaxime	03 (03.12 %)
Tazobactam	02 (02.08 %)
Cefuroxime	01 (01.04 %)
Cefixime	01 (01.04 %)
Aminoglycosides	**19 (19.79 %)**
Amikacin	11 (11.45 %)
Gentamicin	07 (07.29 %)
Streptomycin	01 (01.04 %)
Quinolones	**15 (15.62 %)**
Ofloxacin	07 (07.29 %)
Levofloxacin	03 (03.12 %)
Ciprofloxacin	05 (05.20 %)
Metronidazole	**12 (12.50 %)**
Macrolides	08 (08.33 %)
Azithromycin	07 (07.29 %)
Clarithromycin	01 (01.04 %)
Others	**05 (05.20 %)**
Fungal antibiotic - Fluconazole	03 (03.12 %)
Clindamycin	02 (02.08 %)

GIT 29(30.20%) was the most affected organ system by Adverse Drug Reactions due to antibiotics followed by the Skin 21 (21.87%), Respiratory system18(18.75%), CVS 08 (08.33%), CNS 10(10.41%), Musculo-skeletal system 7(7.29%) and Urinary System 3 (3.12%). [**Figure 3]**

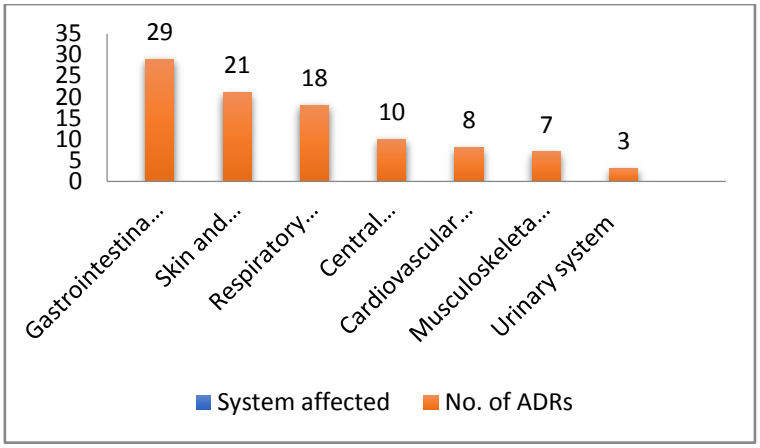


Figure 3: Organ systems affected by adverse drug reaction

The most common ADR was Abdominal pain 13(13.54%), Dyspnoea, Diarrhoea, Rashes 08 (8.33%), Vomiting, allergic reactions 6 (6.25%), Cough, Tingling sensations 05 (5.20%), Hypotension4 (4.16%), Joint pain, sore throat 03 (3.12%), Dizziness, Pain at injection site, burning micturition, headache, Nasal blockade, Fatigue 02 (2.08%), Vertigo, change in stool colour, constipation, restlessness, anxiety, difficulty in passing urine 01(1.04%). **[Table 3]**

Table 3: Types of various adverse drug reactions

Types of ADRs	NO of ADRs (%)
Vomiting	06
Loose stools/diarrhoea	08
Rashes	08
Dizziness	02
Joint pain	03
Allergic reaction/itching /swelling	06
Abdominal pain	13
Change in stool colour	01
Tingling sensation	05
Pain at the site of injection	02
Constipation	01
Dyspnoea	08
Hallucination	01
Vertigo	01
Decreased appetite	01
Burning micturition	02
Tinnitus	02
Nocturia	01
Restlessness	01
Headache	02
Body ache	02
Hypotension	04
Fatigue	02
Ulcers in mouth	01
Pruritus	01
Cough	05
Sore throat	03
Anxiety	01
Nasal blockage	02
Difficulty in passing urine	01

Severity assessment was carried out using Hartwig and Siegel scale and found that out of 96 ADRs, mild reactions were high followed by moderate and severe reaction**. [Table 4]**

Table 4: Severity assessment of adverse drug reaction

Severity of ADRs	No of ADRs (%)
Mild	**83**
Moderate	**13**
Severe	**00**

Causality was assessed by Naranjo algorithm scale and causality was definite in 9 (9.33 %), probable in 37 (38.54 %) and possible in 50 (52.08 %) **[Figure 4].**

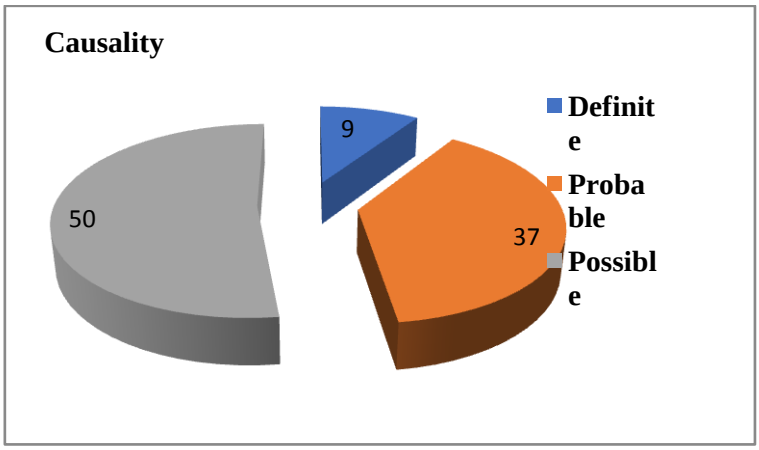


Figure 4: Causality assessment of adverse drug reactions

DISCUSSION

Adverse drug reactions (ADRs) are important cause of mortality and morbidity in both hospitalized and ambulatory patients. So, there is a need to study ADRs seriously to create awareness about ADRs among patients to motivate health care professionals in the hospital to report ADRs and to minimize the risk. Early detection, evaluation and monitoring of ADR are essential to reduce harm to patients and thus improve public health [1] [8].

Over the study period, it was found that there is a male sex predominance for ADRs with antibiotics than female. The similar study which was conducted shows the same predominance of ADRs in the study population. The predominance of male sex in occurrence of ADRs with antibiotics was more which may be due to larger number of male populations enrolled into the study when compared to females [9] [11] [12].

Incidence of ADR is higher among middle-aged patients followed by geriatric patients, adults and paediatrics. Similar study shows the same predominance of middle-aged patients. The result implied that the middle-aged patients were more prone to antibiotic ADRs. The reason for such findings might be changes in pharmacokinetic and pharmacodynamics parameters in various age groups and the presence of comorbid illnesses and multiple drugs along with infectious diseases [13].

The beta lactam, aminoglycosides and fluoroquinolones were the most used antibiotic classes, so that the reported ADRs were also more in these drug classes. The cephalosporins were the most used antibiotic class in this study. A study conducted by Stav Reva et al, also revealed the predominance of cephalosporinses the main cause for ADRs [9] [10].

Gastro-intestinal tract was the main organ system affected followed by Cutaneous and Respiratory manifestations. Other studies also found the predominance of the gastrointestinal system followed by the skin in ADR occurrence [13] [14].

Severity assessment revealed that out of 96 ADRs mild ADRs were high followed by moderate and severe ADRs. Another similar study conducted showed same prevalence of severity assessment in their study population [15].

The causality assessment of ADRs was done using the Naranjo scale in which no reactions were found to be unlikely and majority were possible with a smaller number of probable and definite reactions. These data correlate with the study of Starve et al, Jimmy Jose et al, Priyadarshini et al, where the causality was possible in most of the ADRs [9] [16] [17].

CONCLUSIONS

The health system should promote the spontaneous reporting of Adverse Drug Reactions to antibiotics and other drugs, proper documentation and periodic reporting to regional pharmacovigilance centres to ensure drug safety. Our study revealed the occurrence of mild to moderate ADRs and none of them were serious or lethal.

Although it would be prudent to initially focus on the more serious ADRs, yet it is important to consider even so called non- serious ADRs as they can have a significant impact on the patient's quality of life. Pharmacovigilance needs to be enforced in our country for better and safe use of drugs. More awareness is required among the health fraternity to recognize and report ADRs due to antibiotics.

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