Original Article

Antibiotic Related Adverse Drug Reactions — A Descriptive Analysis

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ABSTRACT

Introduction: *Adverse drug reaction (ADR) is the undesirable effect of medicine that occurs beyond its known therapeutic effects. It is a common clinical problem while treating a patient. In many cases, antibiotics have been reported to be major causes of ADRs. This study aimed to assess the adverse drug reactions that are related to antibiotics.* ***Methods & Materials:*** *This observational study was conducted at the Department of Pharmacology, Dhaka Medical College, Bangladesh, from July 2019 to June 2020. A total of 600 patients were selected by purposive sampling technique as per inclusion and exclusion criteria. Collected data were analyzed using descriptive statistics. Analysis of data was carried out by using a statistical package for social science (SPSS) 22.0 for Windows.* ***Results:*** *Out of 600 patients, adverse drug reaction was detected in 16 (2.7%) patients, and among these 16 patients, 11 (68.80%) patients developed ADR by antibiotics. Among the 11 antibiotic-related ADR patients, 4 (36.37%) occurred due to cotrimoxazole, 3(27.28%)*

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vancomycin, 2 (18.18%) ciprofloxacin, 1 (9.09%) ceftriaxone, and 1 (9.09%) amikacin. The predominant body system affected by ADRs was dermatology (8, 50%). It was observed that 81.3% of ADR cases were prescribed with polypharmacy. ***Conclusion:*** *This study concludes that some antibiotics especially cotrimoxazole possess several adverse reactions. Therefore, they must be routinely encountered and anticipated. Moreover, when possible, the physician should employ the fewest number of antibiotics necessary and choose those least likely to interact with other drugs.*

Keywords: *Antibiotic, Adverse drug reaction, Polypharmacy, Efficacy, Safety*

INTRODUCTION

Worldwide the safety of medicines has been a major issue involving health care delivery systems. Both in developed and developing nation adverse drug reaction (ADR) cause a huge burden accounting for considerable morbidity and mortality[1]. Effectiveness and safety are the two primary concerns regarding a medication. While the effectiveness of a drug can be measured through comparative cases, the same cannot be easily quantified for safety[2]. Medicines can treat or prevent illness and diseases. However, sometimes medicines can cause problems. These issues are referred to as adverse drug reactions (ADRs). Anyone can experience an adverse drug reaction, but individuals who take more than 3 or 4 medications daily are at a higher risk. In a study carried out at an Indian tertiary care hospital, antibiotics accounted for 40.9% of ADRs[3]. Similarly, an Australian tertiary center found that antibiotics were associated with 25% of ADRs.. Furthermore, previous studies have shown that 26.88% of ADRs are considered severe and that 99.47% require additional medical intervention. Several South Korean reports have identified antibiotics as a leading cause of ADRs[4,5]. Antibiotics have been identified as significant contributors to ADRs. In a study focusing solely on outpatients, sulfonamides, followed by penicillin, were reported as the most frequent causative antibiotics. Prior reports have shown that quinolones, ciprofloxacin in particular, are another common causative antibiotic. This study shows that penicillin and quinolones were responsible for the majority of ADRs[6,7]. Anaphylaxis is an acute hypersensitivity reaction and can be caused by antibiotics. Anaphylaxis can result in immediate urticaria, laryngospasm, bronchospasm, hypotension, and death. In the critical care setting, these reactions may be masked by underlying conditions or other therapies[8]. Bangladesh submitted its first batch of adverse reaction case reports to Vigi Base through Vigi Flow in December 2014 and became the latest 120th member country of the WHO pharmacovigilance program[9]. Within very few reports published in scientific journals, one reported a case of fetal toxic epidermal necrosis due to levofloxacin[10]. *Nahar, et al*., studied the adverse effects of two antitubercular drug regimens. Another study conducted at Khulna Medical College revealed ADR caused 25% fatality. Drugs like carbamazepine and co-trimoxazole were the most vulnerable drugs[11]. A study conducted in a South Indian tertiary referral hospital revealed that 0.7% of total admissions were drug-related and 1.8% fatal ADRs[12]. This study aimed to asses the adverse drug reactions that are related to antibiotics.

OBJECTIVE

General Objective

- To observe the antibiotic-related adverse drug reactions.

Specific Objectives

- To see the age and gender distribution of the respondents.
- To know the education status of the study subjects.
- To observe the distribution of the study patients by department.
- To assess the severity of the study subjects.
- To see the impact of polypharmacy on ADRs.
- To analyze the affected body system by ADRs.

METHODS & MATERIALS

This observational study was carried out at the Department of Pharmacology, Dhaka Medical College, Bangladesh, spanning from July 2019 to June 2020. The study included all patients admitted to the medicine, dermatology, and pediatric wards of Dhaka Medical College Hospital who met the inclusion and exclusion criteria. A total of 600 patients were chosen using purposive sampling techniques.

Inclusion Criteria: patients who are admitted to medicine, dermatology, and pediatric wards of Dhaka Medical College Hospital, patients who were diagnosed as ADR on admission or later after admission, patients of both genders and ages < 80 years, patients who were willing to give consent.

Exclusion Criteria: patients who were not willing to give consent, patients who developed an ADR due to poisoning of drugs (Accidental or intentional), blood or blood products, and vaccines, ADRs due to alternate systems of medicines like homeopathy, Ayurvedic, Unani, etc. were excluded from the study. Data were gathered using a specially crafted data collection form. A prescription audit was conducted to retrieve patient records, encompassing confirmed clinical diagnoses, patient profiles, clinical histories, medication charts, laboratory results, and other pertinent information, aligned with the study objectives. Analyzing the collected data utilized descriptive statistics, with continuous data presented as mean ± SD (standard deviation) and nominal data as percentages. Statistical analysis was performed using the Statistical Package for Social Science (SPSS) version 22.0 for Windows. Ethical clearance was obtained from the institution's Ethical Review Committee (ERC), and informed written consent was acquired from all participants.

RESULTS

Table I: Distribution of respondents by their age in years (*n*=600)

Age group (years)	*n*	%	Mean±SD (range)
<10	215	35.8	27.8±21.4 (0.60 – 80) years
11-20	30	5.0	
21-30	65	10.8	
31-40	96	16.0	
41-50	88	14.7	
51-60	80	13.3	
61-70	18	3.0	
71-80	8	1.3	
Total	600	100.0	

In this series, the highest number of the respondents (215, 35.8%) were in the age group <10 years, followed by the age group 31-40 years (96, 16.0%), and the lowest number of respondents (8, 1.3%) were in the age group 71-80 years. The mean age of the patients was 27.8 ± 21.4 years. [**Table I**]

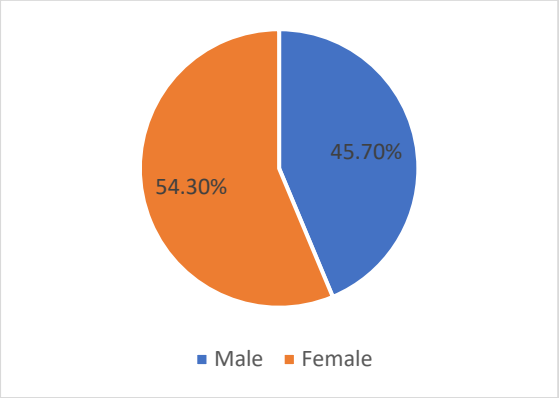
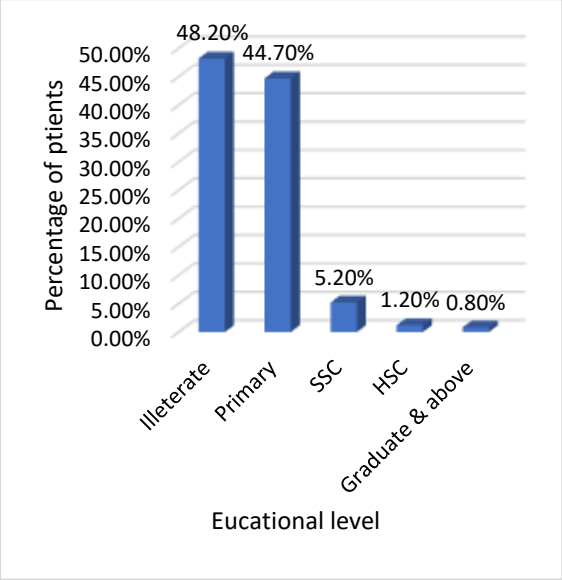


Figure 1: Gender distribution of respondents (*n*=600)

It was observed that the ratio of female to male was 1:1.2. Males were 274 (45.7%) and females were 326 (54.3%) in number. [**Figure 1**]



SSC; Secondary School Certificate, HSC; Higher Secondary Certificate.

Figure 2: Educational status of the participants (*n*=600)

Among 600 patients, 289 (48.2%) patients were illiterate, 268(44.7%) patients were educated by primary education, 31(5.2%) patients were SSC, 7 (1.2%) patients were HSC and 5 (0.8%) patients were graduate and above. [**Figure 2**]

Table II: Distribution of the study patients by department (*n*=600)

Department	*n*	%
Pediatrics	202	33.7
Medicine	197	32.8
Skin/ Dermatology	201	33.5
Total	600	100.0

In this study, 202 (33.70%) patients were from the pediatrics department, 201 (33.5%) patients were from the dermatology department and 197 (32.8%) patients were from the medicine department. [**Table II**]

Table III: Distribution of the study patients by ADR Detection (*n*=600)

Detection of ADR	*n*	%
Yes	16	2.7
No	584	97.3
Total	600	100.0

Out of 600 patients, adverse drug reaction was detected in 16 (2.7%) patients, and 584 (97.3%) patients did not develop any adverse drug reaction. [**Table III**]

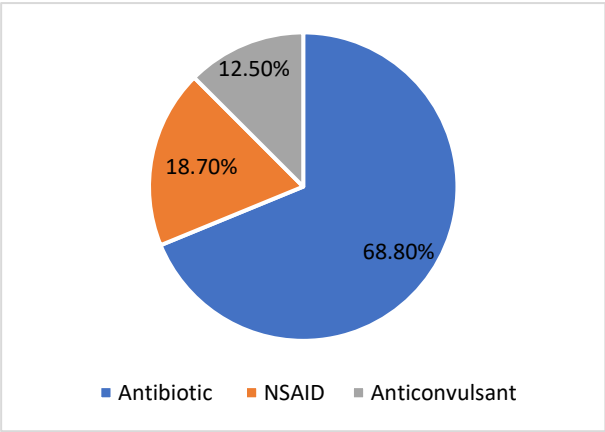


Figure 3: Distribution of patients according to group of drugs involved (*n*=16)

Among 16 patients, 11 (68.80%) patients developed ADR by antibiotics, 3 (18.70%) patients by NSAIDs, and 2 (12.50%) patients by anti-convulsant. [**Figure 3**]

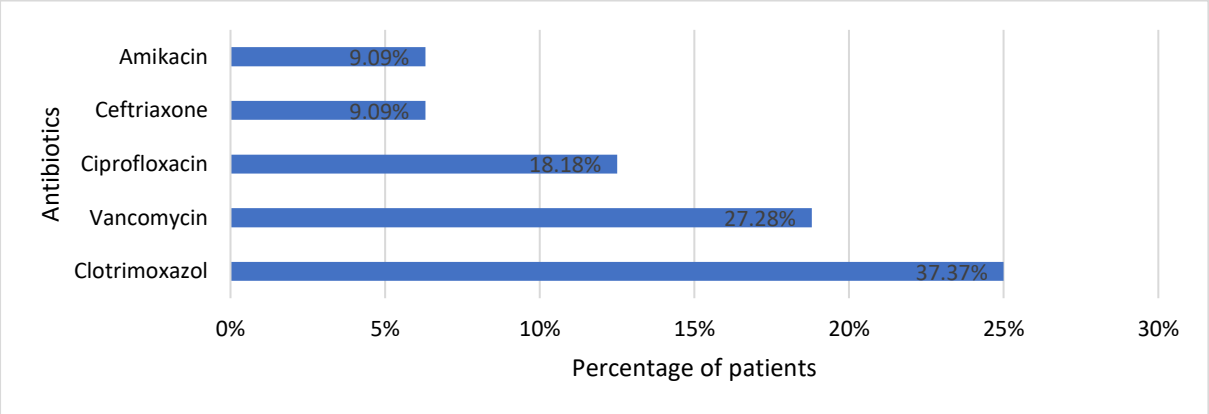


Figure 4: Distribution of patients with ADR according to antibiotic involved (*n*=11)

Among the 11 antibiotic-related ADR patients, 4 (36.37%) were due to cotrimoxazole, 3(27.28%) vancomycin, 2 (18.18%) ciprofloxacin, 1 (9.09%) ceftriaxone, and 1 (9.09%) amikacin. [**Figure 4**]

Table IV: Distribution of ADR patients according to severity (*n*=16)

Severity	*n*	%
Mild	4	25.0
Moderate	9	56.3
Severe	3	18.7
Total	16	100.0

Among 16 ADR cases 4 (25.0%) ADR cases were mild, 9 (56.3%) were moderate and 3 (18.7%) were severe. [**Table IV**]

Table V: Distribution of the study patients by characterizations of the system affected with ADR (*n*=16)

Organ system involved	n	%
Dermatological	8	50.0
Body as a whole	6	37.4
GIT	1	6.3
Vascular	1	6.3
Total	16	100.0

In this series, the predominant body systems affected by ADRs were dermatology (8, 50%) followed by the body as a whole (6, 37.4%), GIT (1, 6.3%), and vascular (1, 6.3%). [**Table V**]

Table VI: Distribution of the ADR according to polypharmacy (*n*=16)

Polypharmacy	*n*	%
Yes	13	81.3
No	3	18.7
Total	16	100.0

It was observed that 81.3% of ADR cases were prescribed with polypharmacy and 18.7% without polypharmacy. [**Table VI**].

DISCUSSION

In this series, the prominent age group was 0-10 years (35.8%). The generated results exhibited similarity with the study done by Chowdhury, et al. in which the majority (40%) of patients were in age group 0-15 years[14]. This reflects that adverse drug reaction is more common in the pediatric age group. Due to their underdeveloped physiology and developmental challenges that hinder their ability to communicate and manage medications on their own. In this study, the demographic profile showed that female (54.3%) patients were higher than male (45.7%). Similar findings were found in the study done by James and Rani, et al, which showed female (60%) and male (40%)[15]. In the present study detection of ADR was 2.7%. Similar findings were found in the study done by *Gor* and *Desai et al.*, in which the detection of ADR was 3%[16]. Antimicrobial agents (68.8%) were the most common suspected drugs causing ADRs in our study. The second most causative agent was NSAIDs (18.7%). A similar finding was found in to study conducted by *Begum, et al.* where antibiotics were the most common cause of ADRs (42.9%), and (33.3%) were due to NSAIDs[17]. Another study done by *Venkatasubbaiah, et al.,* presented most of the adverse drug reactions were due to antibiotics (24.01%)[18]. In our study co-trimoxazole was the most vulnerable drug 4(25%). According to the Uppsala Monitoring Centre, they received a total of 119301 reports of co-trimoxazole. Out of which 6811 reports were obtained from the year 2020. Occurrence of ADR by antimicrobials may be due to the availability of drugs without prescription[19]. In Bangladesh, the local pharmacy shop dispenses antimicrobials without prescriptions to patients and this may lead to more occurrences of ADRs due to antimicrobials. In this study suspected drug-wise distribution had shown that, among the 11 antibiotic-related ADR patients, 4 (36.37%) were due to cotrimoxazole, 3(27.28%) vancomycin, 2 (18.18%) ciprofloxacin, 1 (9.09%) ceftriaxone, and 1 (9.09%) amikacin. This observation was not consistent with the study conducted in India. Whereas ceftriaxone (27) resulted in a higher proportion of ADRs. However, *IY Jung et al* showed that 44 (3.4%) patients experienced serious ADRs in their study. Penicillin and quinolones were the most frequently reported drugs causing ADRs (both at 16.0%), followed by third-generation cephalosporins at 14.9%[20].

In this study the body system frequently affected was dermatological (50%) followed by the body as a whole (37.4), GIT (6.3%), and vascular (6.3%). This result is also similar to the study done by Hariraj and Aziz, where skin and appendage dis-

orders were the most commonly reported disorders (26%) followed closely by the body as a whole (25%)[21]. Another study done by Nahar, et al., found that the system most frequently involved is dermatological and the reaction type was hypersensitivity (67%) which correlates with our study[22]. ADRs are more likely with multiple drug therapies, and with each additional medication a patient takes, the risk of an ADR episode increases by 1.14 times, which in turn directly extends the length of the hospital stay[23]. Polypharmacy (81.3%) was the premier significant risk factor for ADRs identified in our study. This was not similar to the study done by *Mudigubba, et al*., which showed 18.1% of patients developed ADRs due to polypharmacy[24]. Comparatively, it is less than the study conducted in elderly patients 70%[25].

Limitations of the Study:

The study was carried out in a single hospital with a limited sample size, so the findings may not reflect the entire population. Additionally, outpatients experiencing ADRs were not included in this study.

Conclusion:

This study concludes that some antibiotics especially cotrimoxazole possess several adverse reactions. Therefore, they must be routinely encountered and anticipated. The multiplicity of medications and underlying conditions in hospitalized patients affect the presentation and management of adverse reactions.

Recommendation:

This study warrants further research for the development of possible intervention strategies to reduce the burden of adverse drug reactions caused by antibiotics. Moreover, further studies should be conducted involving a large sample size and multiple centers. When possible, the physician should employ the fewest number of antibiotics necessary and choose those least likely to interact with other drugs.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. *Pirmohamed M, James S, Meakin S, Green C, Scott AK, Walley TJ, Farrar K, Park BK, Breckenridge AM. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients. Bmj. 2004 Jul 1;329(7456):15-9.*
2. *Gupta P, Udupa A. Adverse drug reaction reporting and pharmacovigilance: Knowledge, attitudes and perceptions amongst resident doctors. Journal of pharmaceutical sciences and research. 2011 Feb 1;3(2):1064.*
3. *Geer MI, Koul PA, Tanki SA, Shah MY. Frequency, types, severity, preventability and costs of Adverse Drug Reactions at a tertiary care hospital. Journal of pharmacological and toxicological methods. 2016 Sep 1;81:323-34.*
4. *Trubiano JA, Cairns KA, Evans JA, Ding A, Nguyen T, Dooley MJ, Cheng AC. The prevalence and impact of antimicrobial allergies and adverse drug reactions at an Australian tertiary centre. BMC infectious diseases. 2015 Dec;15:1-5.*
5. *Sharma S, Khajuria V, Mahajan V, Gillani Z, Richa V, Tandon V. Adverse drug reactions profile of antimicrobials: A 3-year experience, from a tertiary care teaching hospital of India. Indian Journal of Medical Microbiology. 2015;33(3):393.*
6. *Macy E, KY TP. Self-reported antibiotic allergy incidence and prevalence: age and sex effects. The American journal of medicine. 2009 Aug 1;122(8):778-e1.*

7. *Basko-Plluska JL, Thyssen JP, Schalock PC. Cutaneous and systemic hypersensitivity reactions to metallic implants. Derm. 2011 Apr 1;22(2):65-79.*
8. *Granowitz EV, Brown RB. Antibiotic adverse reactions and drug interactions. Critical care clinics. 2008 Apr 1;24(2):421-42.*
9. *Uppsala Monitoring Centre (UMC) News, Public Services, 2014. Two South Asian Countries Join the WHO Program. Published on 23rd December 2o14*
10. *Begum ZA, Sultana S, Umar BU, Ferdous AH, Uddin MK, Islam SH. Study of adverse drug reactions in out-patient departments of a teaching hospital. ||| Bangladesh Journal of Pharmacology|||. 2012 Jun 11;7(2):104-7.*
11. *Nahar, N., Khan, T. H., Banu, L.A., Khan, M. I., and Hossain, A.M., 2014. Perception of medical practitioner regarding adverse drug reactions reporting and pharmacovigilance. Journal of Shaheed Suhrawardy Medical College, 6(1), pp18-22*
12. *Kalaiselvan V, Thota P, Singh GN. Pharmacovigilance Programme of India: Recent developments and future perspectives. Indian journal of pharmacology. 2016 Nov 1;48(6):624-8.*
13. *Chowdhury FR, Mohammed FR, Alam MZ, Nur ZA, Hoque MA, Uddin MM, Bakar MA. Etiology and outcome of patients admitted in a tertiary level hospital with adverse drug reaction (ADR). J Dhaka Med Coll. 2008;17:17-21.*
14. *James JE, Rani JA. A prospective study of adverse drug reactions in a tertiary care hospital in South India. Asian J Pharm Clin Res. 2019;13(1):89-92.*
15. *Gor AP, Desai SV. Adverse drug reactions (ADR) in the inpatients of medicine department of a rural tertiary care teaching hospital and influence of pharmacovigilance in reporting ADR. Indian journal of pharmacology. 2008 Jan 1;40(1):37-40.*
16. *Begum ZA, Sultana S, Umar BU, Ferdous AH, Uddin MK, Islam SH. Study of adverse drug reactions in out-patient departments of a teaching hospital. ||| Bangladesh Journal of Pharmacology|||. 2012 Jun 11;7(2):104-7.*
17. *Venkatasubbaiah M, Reddy PD, Satyanarayana SV. Analysis and reporting of adverse drug reactions at a tertiary care teaching hospital. Alexandria journal of medicine. 2018;54(4):597-603.*
18. *Uppsala Monitoring Centre (UMC), WHO program members. Members of the WHO program for International Drug 2020.*
19. *Jung IY, Kim JJ, Lee SJ, Kim J, Seong H, Jeong W, Choi H, Jeong SJ, Ku NS, Han SH, Choi JY. Antibiotic-related adverse drug reactions at a Tertiary Care Hospital in South Korea. BioMed research international. 2017 Dec 31;2017.*
20. *Hariraj V, Aziz Z. Direct patient reporting of adverse drug reactions: An analysis of spontaneous reports submitted to Malaysian pharmacovigilance centre. Tropical Journal of Pharmaceutical Research. 2018 Oct 5;17(8):1673-9.*
21. *Nahar N, Karim A, Paul P, Khan TH. Response of reporting adverse drug reactions among medical practitioners. Bangladesh Med J. 2011;40(2):13-8.*
22. *Kumar BN, Nayak K, Singh H, Dulhani N, Singh P, Tewari P. A pharmacovigilance study in medicine department of tertiary care hospital in Chhattisgarh (Jagdalpur), India. Journal of young pharmacists. 2010 Jan 1;2(1):95-100.*
23. *Mudigubba MK, Rajashekarachari Y, Dahiya S. Evaluation of predisposing factors associated with suspected adverse drug reactions of hospitalized patients. Journal of Young Pharmacists. 2018;10(2):202.*
24. *Ahmed B, Nanji K, Mujeeb R, Patel MJ. Effects of polypharmacy on adverse drug reactions among geriatric outpatients at a tertiary care hospital in Karachi: a prospective cohort study. PloS one. 2014 Nov 17;9(11):e112133.*