Original Article

Pattern of Adverse Drug Reactions — An Observational Study in A Tertiary Care Teaching Hospital

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ABSTRACT

Introduction: *ADR is defined as "A response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or the modifications of physiological function". It is the undesirable effect of medicine that occurs beyond its known therapeutic effects. This study aimed to analyze the pattern of adverse drug reactions among the study respondents.* ***Methods and 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.* ***Result:*** *Out of 600 patients, adverse drug reaction was detected in 16 (2.70%) patients. Among the three departments, the highest number of patients with ADR was detected in the pediatrics department (56.3%). Steven Johnson syndrome was the most common ADR (4, 25.0%), followed by each drug-induced rash and hypersensitivity (3, 18.8%). 4 (25.0%) were mild in severity, 9 (56.3%) were moderate and 3 (18.7%) were severe, and the predominant body system affected by ADRs was dermatology (8, 50%). Positive de-challenge was observed in 14 (87.5%) cases with ADR and positive re-challenge was observed in 2 (12.5%) cases.*

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Moreover, 62.5% of ADRs were developed by oral route. ***Conclusion:*** *The most frequently experienced ADR is Steven Johnson's Syndrome, which predominantly occurs through the oral route. The prominent department is the pediatric department, and a majority of the cases are moderate in severity. Moreover, dermatology is the most commonly affected body system. This study also states that a vast number of ADR cases recover after withdrawing the offending drug.*

Keywords: *Adverse drug reaction, Steven Johnsons Syndrome, Dermatology, Toxic epidermal necrolysis*

INTRODUCTION

An adverse drug reaction (ADR) is a common clinical problem while treating a patient. Adverse drug reaction (ADR) is the undesirable effect of medicine that occurs beyond its known therapeutic effects and is one of the main reasons for iatrogenic disease [1,2]. In the US 106,000 hospital patients died from ADRs in 1994, which was fourth to sixth leading cause of death after heart disease, cancer, and stroke [3]. Previous reports have suggested that 7–11.2% of ADRs result in hospitalization [4,5]. Incidence of adverse drug reactions in hospitalized patients (USA) was 6.7% with a fatality rate of 0.32% [3]. Another study done in the United States found death rates were 19.18% [6]. It is estimated that only 10% of serious ADRs and 2-4% of non-serious ADRs are reported [7]. The incidence of suspected ADR in India was 13% [8]. In Bangladesh, a real scenario of ADR is ambiguous as enough reports were not received to understand the real country situation regarding the safety of the medicine used. Being densely populated country detection and reporting of ADR is low. ADRs have become a public agenda worldwide only after the medical catastrophe of thalidomide, a medicine that caused more than 10000 cases of phocomelia [9]. As a response to this disaster, 120 countries have their national pharmacovigilance system for reporting ADRs. All of them report the collected data to the WHO Collaborating Centre, which is also named the Uppsala Monitoring Centre, established in 1978 [10]. Certainly, community pharmacies play a pivotal role in the healthcare system due to their extensive geographical coverage and accessibility without the need for scheduled appointments. The ease of access for patients seeking healthcare services makes these pharmacies a crucial component of the healthcare network. Given that community pharmacies cater to individuals with and without prescriptions, they become integral in ensuring the safe use of medications [11]. Adverse drug reactions (ADRs) stemming from both immune and nonimmune mechanisms represent a significant global contributor to morbidity and mortality. These reactions stand out as the foremost iatrogenic illnesses, impacting 5 to 15 percent of therapeutic drug courses and posing a substantial risk to patient health worldwide [12, 13]. Dermatologic symptoms frequently accompany drug reactions, arising from the metabolic and immunologic activities affecting the skin. Among these manifestations, morbilliform rashes stand out as the most common dermatologic response to drug exposure. Typically, an erythematous, maculopapular rash emerges within one to three weeks after the administration of the drug, initially appearing on the trunk and subsequently spreading to the limbs. Urticaria, commonly associated with Type I allergic reactions, may also manifest in Type III or pseudoallergic reactions. It presents an additional facet of drug-related dermatologic responses. However, severe nonallergic hypersensitivity cutaneous reactions, such as erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis, represent more critical conditions. Rapid identification of

these bullous skin diseases is imperative due to their association with significant morbidity and mortality [14]. So, this study aimed to assess the pattern of adverse drug reactions.

OBJECTIVES

General Objective

- To evaluate the pattern of adverse drug reactions.

Specific Objectives

- To see the age and gender distribution of the respondents.
- To know the educational status of the patients.
- To assess the distribution of the study patients by ADR Detection.
- To know the clinical manifestations of adverse drug reactions.
- To analyze the severity of ADR.
- To recognize the de-challenge and re-challenge output of ADRs.
- To observe the involved route.

METHODS & MATERIALS

This observational study was conducted at the Department of Pharmacology, Dhaka Medical College, Bangladesh, from July 2019 to June 2020. All the patients admitted to the medicine, dermatology, and pediatric ward of Dhaka Medical College Hospital fulfilling the inclusion and exclusion criteria were considered as the study population. A total of 600 patients were selected by purposive sampling technique. The scale of severity as mild, moderate and severe was done following the national guideline on the pharmacovigilance system in Bangladesh (NGPSB, 2017). [15]

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.

Data were collected in a specially designed data collection form. A prescription audit was done to find out the patient's record which includes confirmed clinical diagnosis, patient profile, clinical history, medication charts, laboratory data, and other relevant data were reviewed and necessary data were collected according to the objectives of the study. Collected data were analyzed using descriptive statistics. Continuous data were expressed as mean ± SD (standard deviation) and the nominal data were expressed as percentages. Analysis of data was carried out by using a statistical package for social science (SPSS) 22.0 for Windows. Ethical clearance was taken from the Ethical Review Committee (ERC) of the same institute. Informed written consent was obtained from the participants.

RESULTS

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 our patients was 27.8 ± 21.4 years **[Table I].**

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	

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

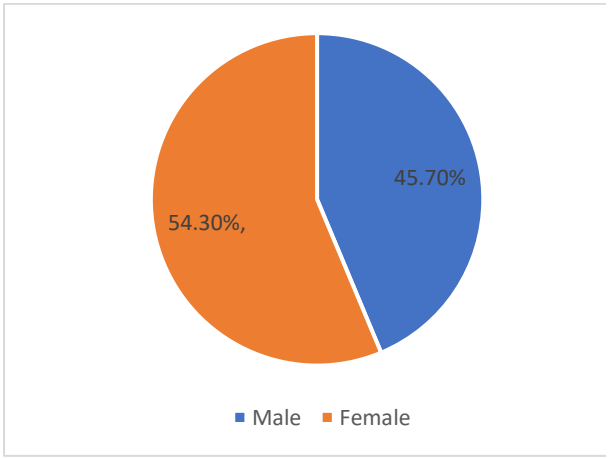


Figure 1: Gender distribution of respondents (N=600)

In this series, there were 9 (56.3%) female subjects and 7 (43.7%) male subjects among the 16 detected cases of ADR **[Figure 2].**

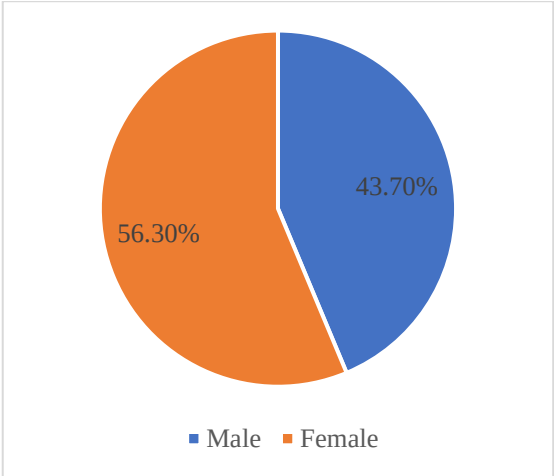
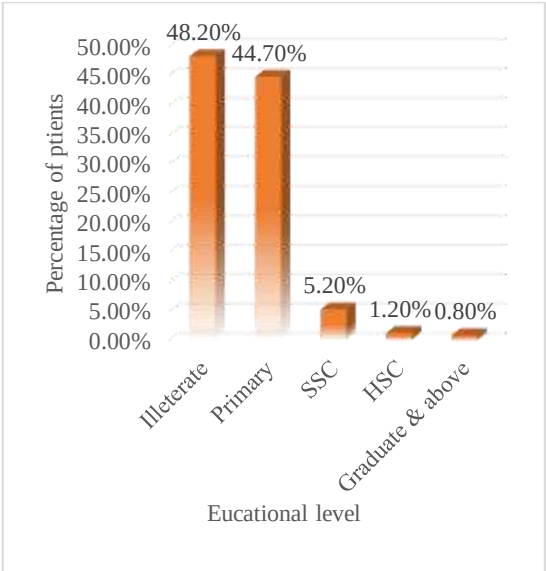


Figure 2: Gender distribution of ADR detected cases (n=16)

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 3]**.



SSC; Secondary School Certificate, HSC; Higher Secondary Certificate

Figure 3: Educational status of the participants (N=600)

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 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

Out of 600 patients, adverse drug reaction was detected in 16 (2.70%) patients, and 584 (97.30%) patients did not develop any adverse drug reaction **[Table III]**.

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

There was no significant difference ($P<0.05$) in the detection of ADRs in different departments of Dhaka Medical College Hospital. Among the three departments, the highest number of patients with ADR was detected in the pediatrics department (56.3%), followed by the dermatology department (31.3%), and were lowest (12.5%) in the medicine department **[Table IV]**.

Table IV: Distribution of the study patients by department basis ADR detection (N=600)

Department	ADR		Total (n=600) No. (%)	p-value
	Yes (n=16) No. (%)	No (n=584) No. (%)		
Pediatrics	9(56.3%)	193(33.0%)	202(33.7%)	0.101^{ns}
Dermatology/skin	5(31.3%)	196(33.6%)	201(33.5%)	
Medicine	2(12.5%)	195(33.4%)	197(32.8%)	
Total	16(100%)	584(100%)	600(100%)	

A chi-square test was done, ns= not significant

Steven Johnson syndrome was the most common ADR (4, 25.0%), followed by each drug-induced rash and hypersensitivity (3, 18.8%), then each of toxic epidermal necrolysis (TEN) and bullous drug reaction (2, 12.5%). A few patients also presented with drug-induced vasculitis and gum bleeding **[Table V].**

Table V: Distribution of the study patients by clinical manifestations of adverse drug reaction (n=16)

Clinical manifestations	n	%
Steven Johnson's syndrome	4	25.0
Drug-induced rash	3	18.8
Hypersensitivity/ Drug allergy	3	18.8
Toxic epidermal	2	12.5

necrolysis (TEN)		
Bullous drug reaction	2	12.5
Drug induced vasculitis	1	6.3
Gum bleeding with diarrhea	1	6.3
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 VI].**

Table VI: 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

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

Table VII: 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 study positive de-challenge was observed in 14 (87.5%) cases with ADR and positive re-challenge was observed in 2 (12.5%) cases with ADR **[Table VIII].**

Table VIII: Distribution of the ADR by de-challenge/or re-challenge (n=16)

ADR management	n	%
*Positive de-challenge	14	87.5
Positive re-challenge	2	12.5
Total	16	100.0

*Positive de-challenge: is an improvement of the reaction after discontinuation of the medicine. (NGPSB, 2017).

* Positive re-challenge: is a recurrence of the reaction that had subsided with the prior de-challenge (NGPSB, 2017).

Among 16 patients, 12 patients (75%) needed hospitalization due to ADR and 4 patients (25%) developed ADRs after hospital admission **[Table IX].**

Table IX: Distribution of ADR patients according to time of occurrence (n=16)

Admissions	n	%
Before admission	12	75.0
After admission	4	25.0
Total	16	100.0

It was observed that, 62.5% ADRs developed by oral route and 37.5% by parenteral route **[Figure 4].**

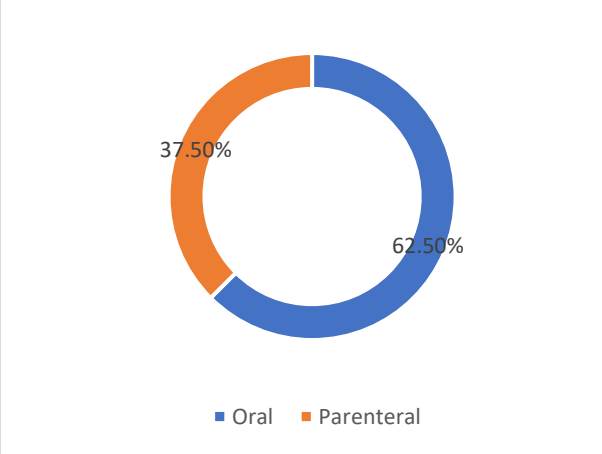


Figure 4: Pie diagram showing the route involved in ADRs.

DISCUSSION

Among the three departments, the highest number of patients with ADR was detected in the pediatrics department (56.3%), followed by the dermatology department (31.3%), and were lowest (12.5%) in the medicine department in this study. This reflects that adverse drug reaction is more common in the pediatric age group. As they have immature physiology and developmental disabilities that impair their ability to communicate and self-administer medications [16]. In this study, the demographic profile showed that female (54.3%) patients were higher than male (45.7%). In this series, there were 9 (56.3%) female subjects and 7 (43.7%) male subjects among the 16 detected cases of ADR. Similar findings were found in the study done by James and Rani, et al, which showed female (60%) and male (40%) [17]. 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% [18]. In the current study, the department basis detection of ADR was 56.3% in pediatrics, 31.3% in Dermatology, and 12.5% in the medicine department. Which was not too far from the study done by Begum, et al. [19]. Another study done by Parvin, et al., where found ADR in the dermatology department was 9% [20]. In this current study majority of adverse drug reactions were Steven Johnson's Syndrome (25%) followed by each drug-induced rash and hypersensitivity (3, 18.8%), then each toxic epidermal necrolysis (TEN) and bullous drug reaction (2, 12.5%). A few patients also presented with drug-induced vasculitis and gum bleeding. In this study, the highest route of adverse drug reaction occurrence was oral (62.5%). These results are near to the findings of Misra, et al., in which the predominant route 80% was per oral and 20% was parenteral [21]. In this series, it was found that 12 (75%) adverse drug reactions occurred before admission and 4 (25%) ADRs occurred during the hospital stay. Another study was done by Arulmani, et al., where they found 58(3.4%) ADR-related admissions and 63(3.7%) ADR occurs during hospital stay which is not comparable to the present study [22]. In this study severity assessment by ADR severity grading scale showed 56.3% ADR as moderate and 25% as mild which is a similar finding to the study done by Begum, et al., where 31.6% mild and 42.1% were moderate eases [19]. 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 et al, where skin and appendage disorders were the most commonly reported disorders (26%) followed closely by the body as a whole (25%) [23]. In the present study suspected drug was withdrawn (de-challenge) from the prescription after the occurrence of adverse drug reaction in the majority of cases 14 (87.5%), In 2 (12.5%) cases rechallenge was performed. These results are near to the findings of Venkatasubbaiah, et al., in which that de-challenge was performed in most of the cases 149 (58.7%) and rechallenge was done in 9 (3.5%) cases [24].

LIMITATIONS OF THE STUDY

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community. Moreover, outdoor patients of ADR were not included in this study.

CONCLUSION

The most frequently experienced ADR is Steven Johnson's Syndrome, which predominantly occurs through the oral route. The prominent department is the pediatric department, and the majority of the cases are moderate in severity. Moreover, dermatology is the most commonly affected body system. This study also states that a vast number of ADR cases recover after withdrawing the offending drug.

RECOMMENDATION

There is no known way to prevent the development of ADRs due to medicines but to reduce incidence we can take steps to indiscriminate use of drugs should be prohibited, The culprit drug should be distinguished from others as early as possible by determining the timing of administration and onset of drug reaction. Therefore, with the help of study, we should strengthen the program of pharmacovigilance to ensure the safe use of medicines in the community. Moreover, further studies should be conducted involving a large sample size and multiple centers.

FUNDING

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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. *Pirmohamed M, Park BK. Adverse drug reactions: back to the future. British journal of clinical pharmacology. 2003 May;55(5):486.*
3. *Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. Jama. 1998 Apr 15;279(15):1200-5.*
4. *Al Hamid A, Ghaleb M, Aljadhey H, Aslanpour Z. A systematic review of hospitalization resulting from medicine-related problems in adult patients. British journal of clinical pharmacology. 2014 Aug;78(2):202-17.*
5. *Kongkaew C, Hann M, Mandal J, Williams SD, Metcalfe D, Noyce PR, Ashcroft DM. Risk factors for hospital admissions associated with adverse drug events. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2013 Aug;33(8):827-37.*
6. *Bond CA, Raehl CL. Adverse drug reactions in United States hospitals. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2006 May;26(5):601-8.*
7. *Gov, UK, 2019.Yellow card: please help to reverse the decline in reporting of suspected adverse drug reactions. Drug Safety Update, pp1-4.*
8. *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.*
9. *Mellin GW, Katzenstein M. The saga of thalidomide: neuropathy to embryopathy, with case reports of congenital anomalies. New England Journal of Medicine. 1962 Dec 6;267(23):1184-93.*
10. *Uppsala Monitoring Centre (UMC) News, Public Services, 2014. Two South Asian Countries Join the WHO Program. Published on 23rd December 2014*
11. *Leone R, Moretti U, D'Incau P, Conforti A, Magro L, Lora R, Velo G. Effect of pharmacist involvement on patient reporting of adverse drug reactions: first Italian study. Drug safety. 2013 Apr;36:267-76.*

12. *Grammer LC, Greenberger PA. Patterson's allergic diseases. Lippincott Williams & Wilkins; 2012 Feb 3.*
13. *Jick H. Adverse drug reactions: the magnitude of the problem. Journal of Allergy and Clinical Immunology. 1984 Oct 1;74(4):555-7.*
14. *Riedl MA, Casillas AM. Adverse drug reactions: types and treatment options. American family physician. 2003 Nov 1;68(9):1781-91.*
15. *Khan MW. Pharmacovigilance system in Bangladesh: a regulatory perspective. Journal of Pharmaceutical Research Science & Technology [ISSN: 2583-3332]. 2019;3(1):1-6.*
16. *Priyadharsini R, Surendiran A, Adithan C, Sreenivasan S, Sahoo FK. A study of adverse drug reactions in pediatric patients. Journal of Pharmacology and Pharmacotherapeutics. 2011 Dec;2(4):277-80.*
17. *James JE, Rani JA. A prospective study of adverse drug reactions in a tertiary care hospital in South India. Asian J Pharm Clin Res. 2020;13(1):89-92.*
18. *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;40(1):37.*
19. *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.*
20. *Parvin M, Mateti UV, Noronha TM. Evaluation of adverse drug reactions in dermatology department of a charitable hospital in India. Libyan Journal of Medical Sciences. 2019 Jul 1;3(3):77-82.*
21. *Misra D, Bose M, Parida S, Das S, Mishra S, Mishra SS. Adverse drug reaction reporting in a tertiary care teaching hospital in eastern India: a retrospective study.*
22. *Arulmani R, Rajendran SD, Suresh B. Adverse drug reaction monitoring in a secondary care hospital in South India. British journal of clinical pharmacology. 2008 Feb;65(2):210-6.*
23. *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.*
24. *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.*