RESEARCH ARTICLE

Pattern of adverse drug reaction reporting by community pharmacists: A Community Pharmacovigilance Study in Eastern Nepal

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Abstract

Background: Adverse drug reactions (ADRs) are common causes of mortality and morbidity globally. This study was aimed to know the pattern of ADRs and to assess its causality, severity and preventability in a sub-metropolitan city reported by community pharmacist. **Methods:** A cross-sectional community-based study was conducted among 200 patients in Dharan, a sub-metropolitan city in Eastern Nepal. Fifteen community retail pharmacies representing various part of the city were selected for the study. The pharmacists from the selected pharmacies were provided one-day training on pharmacovigilance and ADR reporting prior to the study. A self-designed ADR reporting form was distributed to the pharmacists to collect the sociodemographic details and suspected ADRs, the causality, severity and preventability assessment of the ADRs were conducted. The descriptive statistics were used to analyze the data using Microsoft Excel 2010. **Results:** A total of 332 ADRs were observed in 200 patients out of which majority were male (53.5%) and aged 18-25 years (29%). The most common ADR was nausea and vomiting (27.7%) followed by abdominal discomfort (19.3%). Antibiotics (28%) were responsible for most of the ADRs followed by non-steroidal anti-inflammatory drugs (25.5%). Diclofenac (12%) was the most common drug responsible for the ADRs followed by Cefixime (11%) and Amoxicillin (9.5%). On causality assessment, most of the ADRs were "possible" (72.5%). All ADRs were "mild" on severity assessment and "possibly-preventable" on preventability assessment respectively. **Conclusions:** The most common ADR was nausea and vomiting. Diclofenac was the most common drug class causing ADRs. Strategies targeting appropriate and cautious use of this class of drugs among the patients may benefit in reducing the number of ADRs. Strengthening of pharmacovigilance program involving community pharmacists might improve safe use of medicines in the community.

Keywords: Adverse Drug Reactions; Causality; Community Pharmacists; Nepal

INTRODUCTION

Adverse drug reaction (ADR) are responses to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for modification of physiological function [1]. ADRs are considered as the fifth leading cause of death globally and are also one of the commonest cause of morbidity in most of the countries across the world [2, 3]. Prompt ADR reporting is crucial in ensuring drug safety. Pharmacovigilance provides information about ADRs in the general population and plays an important role in rational use of drugs and patient safety [4]. Despite its start in 2004, pharmacovigilance program was

started in 2004 in Nepal; however, it is still in preliminary stage even after 16 year of its start.

Community pharmacists supply medicines in accordance with a prescription and also sell them without a prescription [5]. They are the easily accessible health care professional to the public in Nepal and are frequently the primary contact person also for medical suggestions. Some drug retailers even examine and prescribe medicines to the patients [6]. Nepal is a country with large ethnic variability, variable disease distribution and practicing several different systems of medicine ranging from ancient, traditional to the modern and scientific systems of medicine. Self-medication is highly prevalent in Nepal [7, 8]. The utilization of complementary and alternative therapy is also high here [9, 10]. Patients often add herbal medicines to medications prescribed by their physicians without informing the physician which may result in drug-drug interaction and adverse drug reactions [11].

Community pharmacists can play an important role toward reducing the prevalence of ADRs and drug-drug interactions and providing information and instruction about appropriate drug use. In a number of countries the pharmacist plays an important role in the reporting of suspected ADRs [12]. Pharmacovigilance is hospital-centered in Nepal. The community pharmacists can play a substantial role in pharmacovigilance in addition to their responsibilities regarding drug dispensing. Data on ADR reporting by community pharmacist is scarce in Nepal. ADR reporting has not been reported in a community setting. This study was aimed to know the pattern of ADR and to assess its causality, severity and preventability in a sub-metropolitan city reported by community pharmacist.

METHODS

Study setting: The study was conducted in 15 community pharmacies representing various areas of the city Dharan. According to the Nepal 2011 census it had a total population of 1.41 million. At the time of the data collection the city had 251 community pharmacies.

Type of Study and its duration: A descriptive cross sectional study was conducted from June to September, 2018.

Study Population: Patients visiting community pharmacies with the complain of ADR

Inclusion and Exclusion criteria: Patient aged 18 years, having ADR and visiting the community pharmacies and giving consent to participate were enrolled in the study. Pregnant and lactating women, patients taking multiple drugs, patients with psychiatric disorder, cancers, HIV/AIDS and tuberculosis were excluded from the study.

Study sampling: Convenience sampling method was used.

Data collection instruments: The following instruments in this study.

1. ADR reporting form: A self-designed ADR reporting form was used to collect the data (Appendix 1) which was adapted from previous literature [13]. It consisted of sociodemographic information, details of suspected drug, description of ADR, medical history and action taken by pharmacists on ADRs.

2. Modified Hartwig and Siegel scale: It was used for severity assessment [14].

3. Naranjo Algorithm: It was used for assessment of probability of ADRs [15]. It comprises of 10 questions that are answered "Yes", "No", or "Do not know". Different scores (-1, 0, +1 or +2) are assigned to each answer. Total scores range from -4 to +13. The ADR were categorized into "definite" (score ≥ 9, "probable" (score 5 to 8), "possible" (score 1 to 4) and "doubtful" (score <1).

4. Schumock and Thornton scale: It was used for preventability assessment of ADRs [16]. It had three sections: preventable, probably preventable and non-preventable. Section A consisted of five questions and section B four questions. All the answers were categorized as "Yes" or "No". ADRs were "definitely preventable" if answer was "yes" to one or more questions in section A. If answers were all negative then we proceeded to section B. ADRs were "probably preventable" if answer was "yes" to one or more questions in section B. If answers were all negative then we proceeded to section C and in Section C, the ADRs were non-preventable.

Data Collection method: The purpose and protocols of this study were thoroughly explained to every participant and verbal consent were taken. The community pharmacists were given one day hand-on training by experts prior to data collection regarding filling of the form. The training module included introduction, importance and method of ADR reporting, information about our research and its data collection tools. After the end of the study, the forms were collected from the pharmacists and were checked for completeness and then coded. A pilot testing of the data collection tools was carried out by administering it to ten patients and they were not included in the final data analysis. Any information that can potentially expose recognition of a particular study respondent such as respondent's name was excluded from the data collection tools. No incentive was given to the pharmacists and the study participants.

Ethical approval: Ethical approval was obtained from the National Health Research Council, Kathmandu Nepal.

Statistical analysis: Decoding of the data was done and the data were entered into Microsoft Excel 2010. Descriptive statistics like frequency, mean, standard deviation and percentage were calculated using SPSS version 16. The data were presented as table and graphs.

RESULTS

A total of 332 ADRs were reported in 200 patients from the community pharmacists. Out of 200 patients, majority were male (53.5%), aged 18-25 years (29%), married (78.5%) and literate (89.5%) (**Table 1**). The details of the community pharmacists is given in the **Appendix 1.**

Table 1: Sociodemographic characteristics of the patients (n=200)

Variables		Frequency	Percentage
Gender	Male	107	53.5
	Female	93	46.5
Age group (years)	18 – 25	58	29.0
	26 – 35	51	25.5

	36 – 45	56	28
	46 – 55	26	13
	>55	9	4.5
Marital status	Married	157	78.5
	Unmarried	43	21.5
Educational level	Illiterate	21	10.5
	Literate	179	89.5
Occupation	Business	54	27.0
	Student	12	6.0
	Housewife	24	12.0
	Farmer	39	19.5
	Job	57	28.5
	Unemployed	14	7.0

Appendix 1. Details of the Community pharmacists (n=15)

Variables		Frequency	Percentage
Gender	Male	13	86.67
	Female	2	13.33
Educational level	Diploma	12	80
	Bachelor and above	3	20
Profession	Pharmacist	3	20
	Assistant pharmacist	12	80

Classes of medicines suspected for ADR: Most of the ADRs (28%) were caused by antibiotics followed by non-steroidal anti-inflammatory drugs (NSAIDs) (25.5%) (**Figure 1**).
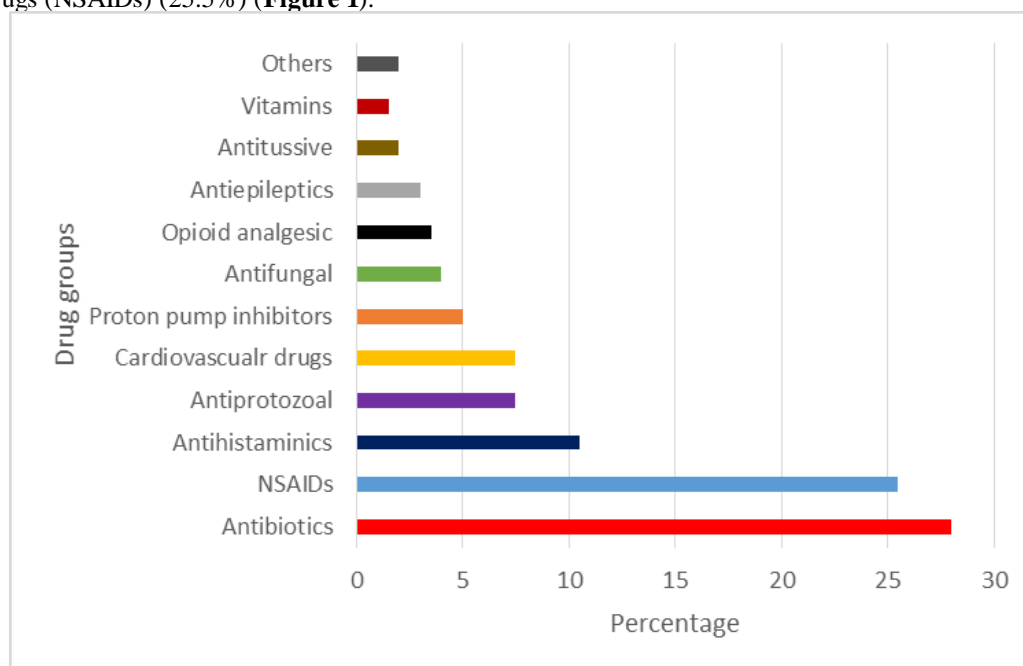
**Figure 1: List of the drug group suspected for adverse drug reactions (n=200)**

Top ten medicines causing ADR: Diclofenac (12%) was the most common drug for ADR in the study participants followed by Cefixime (11%) and Amoxicillin (9.5%) (**Table 2**).

Table 2: List of the drugs causing the ADRs (n=200)

Drugs	ATC classification	Frequency	Percentage
Diclofenac	M01AB05	24	12
Cefixime	J01DD08	22	11
Amoxicillin	J01CA04	19	9.5
Cetirizine	R06AE07	16	8
Ibuprofen	M01AE01	16	8
Metronidazole	J01XD01	15	7.5
Amlodipine	C08CA01	9	4.5
Bromhexine	R05CB03	7	3.5
Pantoprazole	A02BC02	7	3.5
Pregabalin	N03AX16	6	3

Others	-	59	29.5

System affected by ADR: Gastrointestinal system (70.2%) was most commonly affected by ADRs followed by central nervous system (12.3%) and dermatological system (11.7%) (**Figure 2**).
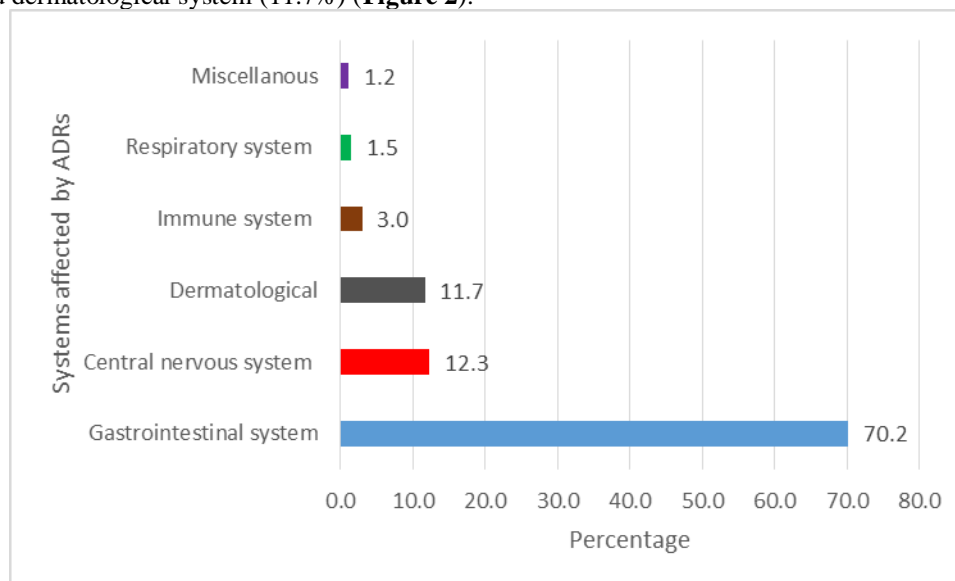
Figure 2: System affected by the adverse drug reactions (n=332)

Common ADRs caused by medicines: Nausea and vomiting (27.7%) was the commonest ADR followed by abdominal discomfort (19.3%) and diarrhea (9.9%) (**Table 3**).

Table 3: List of the adverse drug reactions (n=332)

Drugs	Frequency	Percentage
Nausea and Vomiting	92	27.7
Abdominal Discomfort	64	19.3
Diarrhea	33	9.9
Rashes	28	8.4
Drowsiness	27	8.1
Constipation	20	6.0
Metallic Taste	14	4.2
Headache	14	4.2
Itching	11	3.3
Ankle edema	10	3.0
Anorexia	5	1.5
Sore Throat	5	1.5
Dry Mouth	5	1.5
Others	4	1.2

Causality, severity and preventability assessment of ADR: On causality assessment, most of the ADRs were "possible" (72.5%) and "probable (27.5%)". None of the ADRs were "definite". All ADRs were "mild" on severity assessment. Out of 332 ADRs, definitely-preventable and probably preventable were 61% and 19% respectively on preventability assessment. Ten percent of the ADR could not be assessed for preventability due to incomplete data.

Management of ADR and its outcome: Out of 200 patients, 71 (35.5%) needed a pharmacological treatment for the ADRs and 179 (89.5%) patients recovered from the ADRs. The offending drug were withdrawn in 89 (44.5%) patients and dose reduced in 12 (6%) patients for the management of the ADRs (**Table 4**).

Table 4: Management of the adverse drug reaction and its outcome (n=200)

Variables		Frequency	Percentage
Treatment	Pharmacological	71	35.5
	Non-pharmacological	95	47.5
	Unknown	34	17
Outcome	Recovered	179	89.5
	Unknown	21	10.5
Actions taken	Drugs withdrawn	89	44.5
	Dose reduced	12	6
	Dose not changed	80	40
	Unknown	19	9.5

DISCUSSION

The study highlights the pattern of ADRs and its causality, severity and preventability assessment in a community setting

reported by community pharmacists. Majority of the patients were male in our study and this was comparable to a report by Palaian et al [17]. In general ADRs are more common in females [18]. Access to healthcare for men and women is different in different countries [19]. In our part of the world, male have more access to the healthcare compared to female [20]. Most of the patients belonged to age group of more than 35 years. In contrast, Palaian et al had reported most of the patients belonged to 20-40 years of age [17]. Majority of the ADRs were caused by antibiotics and it was in consistent with the other reports [17]. This may be due to use of antibiotics without prescription to treat common cold and other seasonal viral infections for which the patients do not go to the hospital [21]. They usually contact the community pharmacists and take various antibiotics. This signifies inappropriate use of antibiotics in the community which may have negative effect on antibiotic resistance and its spread. They must be informed about irrational use of the antibiotics through appropriate educational interventions.

In our study Diclofenac sodium was responsible for the most of the ADRs. This was inconsistent with other reports in which Ibuprofen+Paracetamol was the most common drug responsible for ADRs [17]. The difference may be due to high prevalence of self-medication among people in community and their past experience regarding various analgesics. NSAIDs are among the most frequently used medicines in a community setting and thus may cause the incidence of ADRs to occur at higher rate [22]. Gastrointestinal system was the most affected system by the ADRs in the study. In contrast to this finding, dermatological system was the most commonly affected in other study [17]. Nausea and vomiting was the most common ADRs reported in our study. Itching was the most common ADR reported in other study [17]. Proper instructions by the community pharmacists to take NSAIDs after food which may minimize the incidence of ADRs. One third of the patients required pharmacological treatment for the ADRs. A lower percentage of the patients required pharmacological treatment in other study [17]. The community pharmacists can educate the patients on how to take medicines properly and can have significant impact on the incidence of ADR in community [23].

The causality assessment is used to establish a probable relationship between medication and ADRs [24]. Most of the ADRs were "possible" on causality assessment and similar findings was also reported by Palaian et al [17]. Due to co-morbidities and polypharmacy, ADR could not be attributed to a single drug [24]. Most of the ADRs were mild on severity assessment and similar findings were reported elsewhere [17]. In this study, 90% of the total ADRs were preventable and similar findings were reported in other study [17]. More than half of the all ADRs are preventable with appropriate care [25].

ADR reporting is an ongoing and continuous process. The success of pharmacovigilance program depends upon the active involvement of the all healthcare professionals including community pharmacists [26]. Emphasizing the national and regional pharmacovigilance program can be beneficial for improving the current situation of ADR reporting in a community setting. Community pharmacists can have an important role in ADR reporting among patients in the community setting. Jeddah Declaration on patient safety 2019 also emphasizes promotion of medication safety in community

pharmacies [27]. Pharmacists working in the community should be encouraged to share their knowledge and experience regarding pharmacovigilance and ADR reporting. Data from hospital settings facilitated the development and improvement in medication safety programmes, many of which were successful. Community pharmacists should be educated regarding ADR reporting in the community who can ultimately help to improve patient safety. Considering the need to create awareness and to promote the reporting of ADR amongst community pharmacists, our study provides the baseline data.

The study has some limitations. The findings of present study cannot be generalized to entire country as it was conducted in a single city; however, since the condition of healthcare sector and pharmacovigilance practice is similar across the country so it is likely that results are similar in other community setting as well. Being a cross-sectional study, long term effects of ADRs could not be traced. Future longitudinal studies may address these aspects of ADRs. The outcomes of treatment interventions like re-challenge and de-challenge were not measured in this study as it was conducted at community setting and therefore none of the ADRs were categorized as definite. Association between ADRs and the independent variables were not conducted.

CONCLUSIONS
The present study concluded that the most common drug responsible for ADRs in the community patients were Diclofenac and Cefixime. Gastrointestinal system was most commonly affected by the ADRs. The preventability assessment showed that all of the ADR observed among the community patients were non-preventable. Most of the ADRs were probable and mild. The findings of this study might make the healthcare policy makers aware about the current situation regarding pharmacovigilance system who may take adequate steps for formulating appropriate strategies to prevent the patients from untoward effects of improper use of drugs. Upon strengthening the community based pharmacovigilance system there can be more rational use of medicines in community. Education programs on pharmacovigilance should be formulated and implemented to community pharmacists which would further increase the reporting of ADRs.

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Appendix 1 (ADR reporting form)

Adverse drug reaction reporting form

Patients' code.. Age:................. Gender: Male/Female

S.N.	Suspected drug(s)	Concomitant drug	Starting date	Stopping date	Indication

Brief description of the reaction...
....
....
....

Outcome of the reactions: recovered/No recovered/Unknown

Treatment of the reaction: Medical/Non-medical/Unknown

Actions taken: drug withdrawn/dose reduced/dose not changed/unknown

_____

Details of the reporter:

Name:....................... Qualification:...................................

Mobile:.......................

Signature and date....................................