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Health-care Professionals' Knowledge and Perception of Adverse Drug Reaction Reporting and Pharmacovigilance in a Tertiary Care Teaching Hospital of Nepal

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Abstract

Background: Underreporting of adverse drug reactions (ADRs) is common globally, and Nepal is not an exception to this. Health-care professionals (HCPs) play a vital role in reporting ADR during routine practice. Lack of knowledge and awareness about pharmacovigilance and reporting ADRs among HCPs may contribute to underreporting. **Objective:** The objective of this study was to evaluate the knowledge and perception of HCPs regarding ADR reporting and pharmacovigilance in a tertiary care teaching hospital in, Nepal. **Methods:** A descriptive cross-sectional study was conducted. A questionnaire was distributed to 215 HCPs (medical doctors, nurses, and pharmacists) between March and September 2018. Knowledge and perception regarding ADR reporting and pharmacovigilance were studied. Data were analyzed using IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp, Armonk, New York). **Results:** The HCPs included 75 medical doctors, 126 nurses, and 14 pharmacists. Majority of the participants were female (67%), and the majority of participants were not aware of pharmacovigilance. Among the participants, pharmacists were found to have better knowledge regarding pharmacovigilance. However, other HCPs (doctors and nurses) strongly agreed about the necessity of having adequate knowledge about pharmacovigilance. Out of 215, 57.7% agreed that the important benefit of reporting ADR was to identify safe drugs and improve patient safety. The main reasons for not reporting were – ADR reporting was not widely promoted by relevant authorities (47%), followed by not knowing where and how to report ADR (34.9%). However, other HCPs (doctors and nurses) strongly agreed about the necessity of having adequate knowledge about pharmacovigilance. **Conclusions:** The knowledge of HCPs on ADR reporting and pharmacovigilance was poor. Despite a low knowledge of ADR reporting and pharmacovigilance among HCPs, there was a positive perception that ADR reporting is necessary and ADR monitoring system should be established in the hospital. This study also highlights a need for future intervention studies focusing on educating HCPs about ADR and pharmacovigilance.

Keywords

adverse drug reaction reporting systems, health-care professionals' knowledge, Nepal, perception, pharmacovigilance

Introduction

According to the World Health Organization (WHO), an adverse drug reaction (ADR) is defined as "a response to a drug which is harmful and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease or for the modification of body functions."[1] Pharmacovigilance is defined as "the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problems."[2] ADRs are an important cause for morbidity and mortality and can impose a considerable financial burden.[3-6] In Nepal, most patients do not have health insurance, and the Government of Nepal (GoN) provides a partial financial subsidy to deprived citizens of 1,00,000 NPR (≈909 USD) for medical treatment of major health problems.[7] The major health problems are defined as cancer, cardiovascular diseases, renal diseases, sickle cell anemia, Parkinson's disease, head and spinal injury. Therefore, the majority of Nepalese patients have to spend out of their pocket for the medical treatment of major health problems.[8,9] There is no provision of support from

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GoN for the medical treatment of ADRs. Correct reporting of ADR would be cost-effective by reducing ADRs occurrence, thus reducing medical visits and hospital admissions.[7]

ADR reporting is important to ensure patient safety. Medical doctors, nurses, and pharmacists are key health-care professionals (HCPs) responsible for reporting ADR and the practice of reporting directly influences the outcome.[10] National pharmacovigilance centers play a significant role in drug safety.[11] Nepal became a member of the WHO Program for International Drug Monitoring in 2006. The Department of Drug Administration (DDA) was nominated as the national pharmacovigilance center.[12] Twelve regional pharmacovigilance centers (RPCs) were established under DDA in different institutions of Nepal.[12,13] However, underreporting of ADR is widely prevalent in Nepal.[14-16] In the context of Nepal, it is not mandatory for HCPs working at different hospitals to report ADR to either regional pharmacovigilance center or national pharmacovigilance center.

Among the different causative factors of ADR among individuals an important one is genetic variation. As Nepal is a multiethnic, multicultural, and a multilingual nation, there is significant genetic variation among the population.[17] These variations can be expressed as both pharmacodynamic and pharmacokinetic variations and increase the possibility of ADR. Thus, it is of the utmost importance to report ADR. As Nepal is a developing nation, many Nepalese are living below the poverty line, with lack of safe drinking water, under unhygienic conditions, and with poor governance of health facilities needing special attention for reducing ADRs.[18]

Post-marketing surveillance and ADR reporting not being mandatory can affect reporting rates. Whether it is a country with voluntary reporting of ADR like India[19] or developed nations of Europe like France, Italy and Sweden, the prevalence of underreporting is a known problem.[20] The study by Rabbur and Emmerton in 2005 made an international comparison between eight developed countries, with respect to ADR reporting systems and reporting rates. The study found that voluntary reporting caused a low rate of ADR reports.[21] It was found that the chief reasons for underreporting were either due to governmental limitations or because of the absence of practice.[22,23] This highlights the importance of making mandatory ADR reporting systems.

The main emphasis of a spontaneous reporting system is to identify serious unidentified ADR.[24] Underreporting is a noteworthy disadvantage of spontaneous reporting.[25] HCPs play an important role in spontaneous reporting of ADR and management of drug therapy. Widely used spontaneous reporting system by HCPs can be applied to all drugs[26] and can cover the entire population with ease of practice and at low cost.[12,20] Many studies have shown the importance of reporting ADR which enhances patient safety.[27,28] The mainstay of a proficient pharmacovigilance framework[29-31] is a commitment by HCPs to ADR reporting. Among HCPs, pharmacists play an important role in strengthening pharmacovigilance.[32,33]

Rationale, Aims, and Objectives

In many countries, underreporting of ADR by HCPs is a problem due to lack of awareness and knowledge about the guidelines to be followed to identify and report possible ADR.[34-36] Universal College of Medical Sciences Teaching Hospital (UCMSTH) is the tertiary care teaching hospital of the Universal College of Medical Sciences. The institution offers undergraduate and graduate courses. Pharmacovigilance is taught in the medical and pharmacy curriculum but excluded from the nursing course. The institution lacks RPC. This study was conducted to assess HCPs' knowledge and perception regarding ADR reporting and pharmacovigilance in a tertiary care teaching hospital in Nepal.

Methods

The study used a descriptive, cross-sectional research design.

Study Site

UCMSTH which was established in 1988 is a 790-bedded tertiary care teaching hospital situated at Ranigaun, Bhairahawa, Province No. 5, Nepal.

Study Period

The data collection was conducted for 6 months from March to September 2018.

Study Population and Sampling

All the medical doctors, nurses, and pharmacists working in the hospital and willing to participate in the study were included.

For calculating sample size, we assumed the knowledge and perception of HCPs on ADR reporting and pharmacovigilance to be 50% to get maximum possible size using a single proportion of size less than 10,000 as follows:

$$N = \frac{N'}{1 + N'(0.05)^2} = \frac{465}{1 + 465(0.05)^2} = 215,$$

where N' = total number of HCPs within inclusion criteria in our study, N = sample size, and 0.05 is the marginal error.

Sampling Technique

We assumed that there would be variation in knowledge and perception of ADR reporting and pharmacovigilance among HCPs. Study participants were recruited using stratified random sampling technique with proportion allocation as shown below:

Health-care professionals in UCMS	Total no. in hospital	% of the sample taken	Number selected
Medical doctors	165	35	75
Nurses	275	59	126
Pharmacists	25	6	14
Total	465	100%	215

Questionnaire and Pilot Testing

A questionnaire was developed based on previously published studies[31,37-41] by the researchers after extensive literature review. The prepared questionnaire was also critically examined by a panel of experts with backgrounds in regulation, clinical pharmacy, pharmacovigilance, academia, statistics, and regulatory affairs. The primary investigator interviewed respondents using a structured questionnaire having three parts:

1. socio-demographic information
2. questions related to knowledge (15 questions)
3. questions related to perception (10 questions)

To test the validity and reliability, the questionnaire was pilot-tested by administering it to a sample of 22 (10% of sample size) HCPs. The overall Cronbach's alpha value was 0.724. The results of the pilot study were not included in the main study. Respondents were also asked to provide two important suggestions to strengthen ADR reporting and pharmacovigilance. The questionnaire was then administered to selected HCPs after obtaining their informed consent. Any explanation required in understanding the questionnaires was provided.

Statistical Analysis

The data were systematically checked for errors and analyzed using IBM SPSS for Windows, Version 21.0 (IBM Corp, Armonk, New York). The knowledge of HCPs was presented in percentage and number as shown in different tables below. The perception was studied based on the degree of agreement of the respondents with a set of statements based on the Likert scale. The chi-square test was performed to compare the knowledge of different subgroups of HCPs at a significance level of $P < 0.05$.

Results

Demographics

Table 1 shows the sociodemographic characteristics of the participants. A total number of 215 HCPs comprising 75 medical doctors, 126 nurses, and 14 pharmacists participated. Among the participants, the majority were female (N = 144, 67%). Majority of the participants (N = 188, 87.4%) were in the age group of 20 to 29 years. Very few participants (9.3%) had attended a pharmacovigilance course.

Table 1. Sociodemographic Characteristics of the Participants.

Characteristics	n (%)
Gender	
Male	71 (33.0)
Female	144 (67.0)
Age, y	
20-29	188 (87.4)
30-39	26 (12.1)
40-49	1 (0.5)
Profession	
Medical doctor	75 (34.9)
Nursing	126 (58.6)
Pharmacists	14 (6.5)
Working experience (in years)	
<2	126 (58.6)
2-5	62 (28.8)
5-10	23 (10.7)
>10	4 (1.9)
Attended pharmacovigilance course	
Yes	20 (9.3)
No	195 (90.7)
Qualifications	
Diploma	73 (34.0)
Undergraduate	137 (63.7)
Postgraduate	5 (2.3)

Knowledge Regarding ADR Reporting and Pharmacovigilance

Table 2 shows participants' responses to the 15 questions investigating knowledge of HCPs regarding pharmacovigilance. Out of 215 participants, the correct response on the definition of ADR and pharmacovigilance was given by 131 (60.4%) and 115 (53.5%) of HCPs respectively. Only 68 respondents (31.6%) were able to respond to the question about the identification of rare ADR during the fourth phase of the clinical trial. It was found that only 127 (59.1%) knew about the spontaneous reporting system for ADR. Interestingly, 176 (81.9%) of HCPs believed that ADR monitoring center should be established in every hospital. Only 22 participants

Table 2. Knowledge Regarding ADR Reporting and Pharmacovigilance.

	Correct responses given by HCPs				
	Medical doctors	Nurses	Pharmacists	Total	
Questions	n = 75	n = 126	n = 14	N = 215	*P**
ADR definition	51 (68.0%)	69 (54.8%)	11 (78.6%)	131 (60.9%)	.067
Pharmacovigilance definition	44 (58.7%)	58 (46%)	13 (92.9%)	115 (53.5%)	.002
Important purpose of pharmacovigilance	48 (64.0%)	76 (60.3%)	13 (92.9%)	137 (63.7%)	.056
Rare ADRs can be identified in which of the phase of clinical trial	26 (34.7%)	30 (23.8%)	12 (85.7%)	68 (31.6%)	0
Which method is commonly employed to monitor ADR of new drugs	42 (56.0%)	74 (58.7%)	11 (78.6%)	127 (59.1%)	.286
Opinion on establishing ADR monitoring center in hospital	58 (77.3%)	105 (83.3%)	13 (92.9%)	176 (81.9%)	.307
Are you aware of the UK yellow card scheme for collecting information on ADR	4 (5.3%)	8 (6.3%)	10 (71.4%)	22 (10.2%)	0
Do you know about existence of national pharmacovigilance program in Nepal	14 (18.7%)	18 (14.3%)	9 (64.3%)	41 (19.1%)	0
Type-A ADR augmented definition	57 (76.0%)	54 (42.9%)	10 (71.4%)	121 (56.3%)	0
Regulatory body responsible for monitoring ADR	53 (70.7%)	57 (45.2%)	13 (92.9 %)	123 (57.2%)	0
Causality assessment definition	39 (52.0%)	31 (24.6%)	12 (85.7%)	82 (38.1%)	0
Scale commonly used to establish causality of ADR	27 (36.0%)	14 (11.1%)	9 (64.3%)	50 (23.3%)	0
Responsible professionals for reporting ADR	50 (66.7%)	87 (69.0%)	11 (78.6%)	148 (68.8%)	.915
Kind of ADR to be reported	61 (81.3%)	65 (51.6%)	13 (92.9%)	139 (64.7%)	0
Information required for ADR case report	57 (76.0%)	115 (91.3%)	13 (92.9%)	185 (86.0%)	.034

Note. ADRs = adverse drug reactions; HCPs = health-care professionals.
*$P < .015$ is statistically significant.

(10.2%) were aware of the UK yellow card scheme for collecting the information on ADR. More than half of the participants were not aware of the existence of national pharmacovigilance program in Nepal. Medical doctors (n = 57, 76.0%) were better able to differentiate the type of ADR than nurses and pharmacists. Majority of the HCPs were not aware of causality assessment. Most of the participants (n = 185, 86.0%) knew about the information to be included in an ADR reporting form.

Perceptions About ADR Reporting and Pharmacovigilance

Table 3 shows the perceptions of HCPs regarding pharmacovigilance and ADR reporting where the majority of the HCPs responded *agree* (52.54%) on the given statements followed by *strongly agree* (39.24%).

Table 4 shows the perception of HCPs on the importance of reporting ADR. Out of 215, 57.7% (n = 124) agreed that the importance of reporting ADR was to identify safe drugs and improve patient safety.

Table 5 shows the factors that discouraged reporting of ADR by HCPs. The main reasons for not reporting were ADR reporting was not widely promoted by relevant authorities (n = 101, 47%) followed by not knowing where and how to report ADR (n = 75, 34.9%). The other reasons were a lack of information (n = 37, 17.2%) and not having enough time (n = 2, 0.9%).

The suggestions which were provided by HCPs were listed as follows:

- RPC should be established in the hospital
- Pharmacovigilance should be taught to HCPs

Table 3. HCPs' Perception of ADR Reporting and Pharmacovigilance.

Statements	*Strongly disagree* n (%)	*Disagree* n (%)	*Neutral* n (%)	*Agree* n (%)	*Strongly agree* n (%)
Reporting of ADR is necessary	1 (0.5)	2 (0.9)	8 (3.7)	63 (29.3)	141 (65.6)
Information on how to report ADR should be taught to students	0	0	1 (0.5)	123 (57.2)	91 (42.3)
Health-care profession has important responsibility to report ADR	0	2 (0.9)	2 (0.9)	164 (76.3)	47 (21.9)
Any ADR should be reported spontaneously	0	5 (2.3)	23 (10.7)	136 (63.3)	51 (23.7)
Patients should be counseled about ADR every time their medications are dispensed	1 (0.5)	2 (0.9)	11 (5.1)	138 (64.2)	62 (28.8)
Female patient should be asked if she is pregnant when dispensing medications	2 (0.9)	0	3 (1.4)	48 (22.3)	162 (75.3)
The topic of pharmacovigilance should be included as a core topic in the curriculum	1 (0.5)	2 (0.9)	14 (6.5)	131 (60.9)	67 (31.2)
Concerned authorities are not working actively to improve ADR reporting in Nepal	5 (2.3)	2 (0.9)	52 (24.2)	86 (40)	70 (32.6)
Total score	10 (0.6%)	15 (0.9%)	114 (6.7%)	889 (52.5%)	664 (39.2%)

Note. HCPs = health-care professionals; ADR = adverse drug reaction.

Table 4. HCPs' Perception of the Importance of Reporting ADR.

Profession	Participant response to the most important reason for reporting ADR			
	To identify safe drugs and improve patient safety	To calculate incidence of ADR	To identify predisposing factors.	To identify previously unrecognized ADR
Medical doctors	41 (54.7%)	6 (8.0%)	21 (28.0%)	7 (9.3%)
Nursing	75 (59.5%)	29 (23.0%)	13 (10.3%)	9 (7.1%)
Pharmacy	8 (57.1%)	3 (21.4%)	0	3 (21.4%)
Total	124 (57.7%)	38 (17.7%)	34 (15.8%)	19 (8.8%)

Note. HCPs = health-care professionals; ADR = adverse drug reaction.

Table 5. Factors That Discouraged Reporting of ADR by HCPs.

Profession	Participant response to the discouraging factors for reporting ADR			
	Lack of information provided by the patient	Don't have enough time	Don't know where and how to report	Not widely promoted by relevant authorities
Medical doctors	11 (29.7%)	1 (50.0%)	16 (21.3%)	47 (46.5%)
Nursing	20 (15.9%)	1 (0.8%)	56 (44.4%)	49 (38.9%)
Pharmacy	6 (42.9%)	0	3 (21.4%)	5 (35.7%)
Total	37 (17.2%)	2 (0.9%)	75 (34.9%)	101 (47%)

Note. ADR = adverse drug reaction; HCPs = health-care professionals.

- Concerned authorities should promote awareness about the National Pharmacovigilance Center and program
- Training on pharmacovigilance should be provided to the HCPs during and after their professional study

Discussion

There are a limited number of studies[14,41,42] which have evaluated the pharmacovigilance knowledge and reporting behavior of various HCPs in Nepal. But this study was the first one conducted in Province No. 5 of Nepal evaluating the knowledge and perceptions of HCPs working at UCMSTH regarding pharmacovigilance and ADR reporting.

In this study, majority of nurses were involved followed by doctors and pharmacists. This finding is similar to that reported in another study.[43] In our study, the majority of participants were female. The findings of this study are similar to the study conducted by Santosh et al[41] where the author included HCPs working at four RPCs. This may be due to the higher number of female health practitioners working in Nepal. Another reason might be due to the participation of a higher number of nurses in this study. While examining the age group of the participants, mostly younger and less experienced HCPs were seen. Most participants had graduate qualifications such as Bachelor of Medicine and Bachelor of Surgery (MBBS), Bachelor of Science in Nursing (BSc Nursing), and Bachelor in Pharmacy (BPharm). Work experience of most participants was also found to be less than 2 years. Most participants have never attended any pharmacovigilance course, which is similar to the study in Central Referral Hospital attached to Sikkim Manipal Institute of Medical Sciences, Sikkim, India.[19] Pharmacovigilance topics are included in medical and pharmacy curriculum but not included in the nursing course. This might be a reason that most of the participants were unaware of national pharmacovigilance center and RPC. However, the participants had a positive opinion that ADR monitoring center should be established in the hospital. Similar to our study, another study by Rashmi et al. (2019) in a tertiary care hospital in Kathmandu, Province No. 3 found a similar result, where attitude of doctors and nurses towards pharmacovigilance was positive.[14]

Majority of HCPs were in the age group of 20 to 29 years and with regard to work experience, the HCPs working in the hospital were less experienced.

The findings of our study showed that the knowledge and awareness of pharmacovigilance and ADR reporting were better among pharmacists and medical doctors than among nurses. This study showed a result similar to studies done in Nepal,[42] Ethiopia,[36] and Jordan.[37] In contradiction, a study conducted in Pakistan found that doctors have adequate knowledge regarding ADR.[44] Our study also found that pharmacists had better knowledge regarding pharmacovigilance than medical doctors and nurses. However, regarding definitions and types of ADR, medical doctors were more aware than pharmacists. This might be due to the lack of pharmacists' participation in clinical settings. In the curricula of undergraduate MBBS, BSc Nursing, and BPharm in Nepal, the content of pharmacovigilance, ADR and ADR reporting is not sufficiently covered. However, as a part of the MBBS course in some institutions students are trained in ADR reporting and causality assessments.[45] Knowledge regarding ADR and pharmacovigilance is very important for HCPs to report ADR to RPC and have a positive attitude toward reporting.

The majority of the HCPs responded "To identify safe drugs and improve patient safety" as an important reason for reporting ADR. The findings of this study showed that there is a positive perception among HCPs regarding ADR reporting and pharmacovigilance. This is found to be similar to the study done in Jordan.[37]

Underreporting has been a worldwide problem[7,46-48] even in developed nations such as the United Kingdom with more organized pharmacovigilance systems.[49] This study showed that the major reason behind the underreporting of ADR was a lack of promotion by relevant authorities as DDA, RPC, and also the HCPs did not know where and how to report ADR. The findings of this study are similar to a previous study.[36] In contrast to this, a study conducted in Iran found the main reason for not reporting ADR was an uncertain association between the medicine and the ADR according to the health professionals.[50] While in South India it was found that lack of remuneration was the main reason for not reporting ADR.[51] The study conducted in Manipal Teaching Hospital by Palaian et al[42] found that the HCPs had not come across ADR and they were unaware of the presence of RPC, while the study done in India by Desai et al.[52] found ignorance of the reporting system among participants.

Implications for Practice

There are 12 pharmacovigilance centers in 7 provinces of Nepal. However, there are no RPCs in Province No. 5 of Nepal. RPC should be established in the near future, and training must be provided to all HCPs regarding pharmacovigilance and ADR reporting. Also, the national pharmacovigilance center should encourage all concerned individuals and organizations to report ADR. To improve ADR reporting, continuing professional education and pharmacovigilance training should be provided.

This study also suggests that future interventional studies should focus on educating HCPs about ADR and how to report ADR, and further improve the perception of health professionals toward ADR and pharmacovigilance.

Limitation

There are some limitations to our study. The findings could not be generalized to the whole country since this study was

done among the HCPs in a teaching hospital in Bhairahawa in the southern Terai region during a limited period of time. Thus, it is recommended that more studies be conducted to assess the knowledge, attitude, and practices of HCPs regarding pharmacovigilance, drug safety, and ADR reporting, to have a thorough understanding of the condition in Province 5 and other regions of Nepal.

Conclusions

This study highlights that the HCPs working at a teaching hospital in Nepal have low knowledge about ADR and pharmacovigilance. This study also provided positive perceptions regarding the importance of ADR reporting and establishment of pharmacovigilance in a hospital, though RPC was lacking at this hospital.

This study also highlights a need for RPC and future intervention studies should focus on educating HCPs about ADR and how to report ADR, and the perception of health professionals in the hospital toward ADR and pharmacovigilance.

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Author Contributions

K.D. conceptualized the idea of this study, did a literature review, study design, data collection and wrote the initial version of the manuscript. S.S. added his ideas and content to the initial version, did a literature review, study design, data analysis and helped substantially in improving manuscript through all stages of the manuscript writing. S.A. added his ideas to the content of the initial version, did a literature review, added the content of the manuscript, and revised it substantially. P.R.S. added his ideas and content to the initial version and helped substantially in improving manuscript through all stages of the writing process.
All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

The study was approved by the Institutional Review Committee (IRC) of Universal College of Medical Sciences. The IRC approval registration number is UCMS/IRC/85/18. Written informed consent was obtained from the participants prior to the data collection. Participation of HCPs was voluntary and their responses were dealt with a high level of confidentiality and anonymity. Participants were informed about the objectives and the significance of this research prior to data collection.

Declaration of Conflicting Interests

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