



RESEARCH ARTICLE

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Knowledge, attitude, and practice of pharmacovigilance among Nepalese health professionals

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ARTICLE INFO ABSTRACT



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Introduction: Although Nepal joined the WHO program for International Drug Monitoring in 2006, published data about Nepalese health professionals' understanding of pharmacovigilance and spontaneous reporting of adverse drug reactions (ADRs) is limited.

Objectives: The purposes of this study were to: (1) investigate awareness, knowledge, attitude, and practice (KAP) of pharmacovigilance among health professionals and (2) gain insight into the ADRs reported for statins in Nepal.

Methods: 125 health professionals (doctors, pharmacists/assistant pharmacists, and nurses) were recruited from health care institutions (hospitals, clinics, pharmacies) in Kathmandu, Nepal. Electronic and paper survey data were collected with the use of a validated questionnaire between April and December 2018. The multiple-choice questionnaire was structured to assess the KAP of pharmacovigilance, and ADRs associated with statins, and consisted of two open-ended questions for health professionals to give suggestions for the improvement of the pharmacovigilance system. Statistical Package for the Social Sciences (SPSS, version 25) was used to analyze the demographic and pharmacovigilance data. The main outcome measures were KAP of pharmacovigilance and ADRs reported for statins.

Results: 100 (80%) participants (44 doctors, 32 pharmacists / assistant pharmacists, 24 nurses) completed the self-administered questionnaire. Pharmacovigilance knowledge, attitude, and practice scores were 71%, 81%, and 53%, respectively. There was a significant difference between the number of knowledgeable health professionals (71 vs. 29%, $p < 0.05$) and had a favorable attitude (81 vs. 19%, $p < 0.05$) toward pharmacovigilance and ADR reporting compared with those who did not. The number of participants who did not report ADR was higher than those who did (90 vs. 10%, $p < 0.05$). The adverse reactions associated with statins were muscle symptoms (62%), elevated activity of liver enzymes (24%), and gastrointestinal symptoms (9%).

Conclusion: Despite the knowledge and willingness of health professionals to report ADRs, the practice of pharmacovigilance remains low in Nepal. There is a need for clear and enforceable regulations for monitoring and reporting ADRs, and effective educational interventions to promote pharmacovigilance practices.

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Introduction

Pharmaceutical drugs discovered and developed over the years have benefitted patients remarkably (Hasford *et al.*, 2002). Most of these drugs undergo a series of rigorous and extensive testing for safety and efficacy before getting regulatory approval (Junge, 2016). However, there is evidence that falsified and poor-quality generic drugs are readily accessible and widely used in countries with a poor legal framework for the production, licensing, and distribution of pharmaceuticals (Seiter, 2009). Regardless, adverse drug reactions (ADRs) are a major cause of morbidity and mortality worldwide (Beijer *et al.*, 2002; Pirmohamed *et al.*, 2004; Wester *et al.*, 2007).

Angamo and group reported median prevalence percentages of 6.3 and 5.5 of ADR-related hospitalization, 71.7 and 51.9 preventable, and 1.7 and 1.8 fatal ADRs in developed and developing countries, respectively (Angamo *et al.*, 2016). Bouvy and colleagues noted, that in Europe, about 3.6 % of all hospital admissions were due to ADRs, and up to 10 % of in-patients experience ADRs while in hospital (Bouvy *et al.*, 2015). Adverse drug reaction (ADR) related hospitalizations of 8.4 % in South Africa (Mouton *et al.*, 2016), 2.9 -5.6 % in Iran (Baniasadi *et al.*, 2008), 4.8 % in Germany, 5.6 % in the US (Stausberg *et al.*, 2014) and 6.5 % in the UK (Pirmohamed *et al.*, 2004) have been reported. In Nepal, the prevalence of ADRs was reported to be 0.86 % (Jha *et al.*, 2007) and drug-related complications led to 0.4 % of hospitalizations (Shrestha *et al.*, 2006). These low figures indicate a problem with the ADR reporting mechanism in the country.

Risk/predisposing factors for ADRs include polypharmacy, age, genetic background, nutritional status, social behavior, disease conditions, and gender (Alomar 2014; Aronson, 2007; Davies and Mahony, 2015). Mean prevalence of ADRs of 11.0 %, ADRs occurring during hospitalization of 11.5 % and median ADRs of 10.0 % leading to hospitalization have been reported in the elderly (Alhawassi *et al.*, 2014). Similarly, ADR incidence rates of 7.7 and 2.9 have been documented in children (Star *et al.*, 2011; Smyth *et al.*, 2012). Women compared to men have 1.5 to 1.7 times higher ADRs (Mouton *et al.*, 2016; Martin *et al.*, 1998).

The use of modern medicines has increased considerably in Nepal in the last four decades. In 2012/2013, the total revenue of pharmaceutical products was worth approximately £52.7 million (Khanal 2017) and about 41 % of the demand is supplied by Nepalese pharmaceutical companies (Rimal 2019). Most of the medications available in Nepal are generic drugs manufactured in developing countries (Ansari *et al.*, 2017; Poudel and Ishii, 2017; Rai, 2004). There is evidence some of these generic drugs are not well tested or falsified (Rai, 2004; Shrestha *et al.*, 2018; Wertheimer and Santella, 2005). In addition, Nepal faces problems with the use of medicines: polypharmacy, irrational combinations, and lack of drug information

services and package inserts (Alam *et al.*, 2009; Thapa *et al.*, 2017). Hence, there is a need for pharmacovigilance and post-marketing surveillance to monitor the effects of medicines, together with a gathering of drug safety data.

In 2004, the Department of Drug Administration (DDA) was nominated as the National Pharmacovigilance Centre (NPC) in Nepal to liaise with the Uppsala Monitoring Centre (UMC) in Sweden. Nepal gained full membership in the international pharmacovigilance program in 2006. The NPC and twelve out of fifteen Regional Pharmacovigilance Centres (RPCs) are located in the capital, Kathmandu. ADRs are collected by the health professionals who forward them to the RPC and then to the NPC. The NPC then sends the reports online via Vigiflow to the UMC (Department of Drug Administration, 2021).

The World Health Organization (WHO) global database contains over 30 million reports of suspected adverse effects of medicines (Uppsala Monitoring Centre, 2021). Nepal is one of the least developed nations and has a population of approximately 29 million (Pambos *et al.*, 2012; World Health Organization, 2019). The expected ADR reports per million population per year are 200 or more (Nwokike *et al.*, 2013). The total number of ADRs in Vigibase reported by Nepal since the country joined the International Drug Monitoring was 967 (Department of Drug Administration, 2021). The reasons for low reporting of ADRs (Nwokike *et al.*, 2013) are unclear but could be due to factors related to drug policy, stakeholders, health professionals, regulatory issues, or reporting procedures. There is a strong correlation between health KAP of pharmacovigilance and reporting of ADRs (Alsaleh *et al.*, 2017; Bhagavathula *et al.*, 2016; Gavaza *et al.*, 2011).

Very few studies have explored health professionals' perspectives on pharmacovigilance in Nepal (Palaian *et al.*, 2011; KC *et al.*, 2013; Shakya-Gurung *et al.*, 2019; Singh *et al.*, 2021). These studies were limited to the health professionals working in hospitals designated as RPCs. It is important to know whether the knowledge of pharmacovigilance has improved and whether positive attitudes have translated to pharmacovigilance practices in the past decades.

Aims of the study

The aims were to gain an insight into (1) the status of ADR reporting and its limitations, and (2) the occurrence of adverse effects due to the use of statins in Nepal. Statins were chosen since they were not among the top twenty medications whose adverse reactions have been reported to the UMC in Sweden by Nepal despite being widely prescribed in the management of hypercholesterolemia. The study investigated the knowledge, attitude, and practice of health professionals towards ADR reporting and pharmacovigilance in Kathmandu, Nepal.

Ethics approval

Ethical approval from London Metropolitan University and the Nepal Health Research Council was obtained. The study was conducted following the principles of the Declarations of Helsinki ([World Medical Association, 2013](#)).

Method

Subjects

125 health professionals (doctors, nurses, and pharmacists/assistant pharmacists) were recruited from health care institutions (hospitals, clinics, pharmacies) in Kathmandu, Nepal. The inclusion criteria were – aged 18 years and over, English and/or Nepalese language proficiency, computer and internet access, and employed by government accredited health care institutions. The exclusion criteria were – responsibility for pharmacovigilance or being aged under 18 years. Informed consent from the volunteers was obtained.

Sample size calculation ([Pourhoseingholi et al., 2013](#)) indicated a minimum of 96 participants would be required for the survey. The sample size was increased to 125 to take into consideration the anticipated non-response rate of 30%.

Data collection/survey method

Demographic and pharmacovigilance data were collected with the use of a validated questionnaire between April and December 2018. A professional translator fluent in both languages translated the questionnaire developed in English into Nepalese. The quality of the questionnaire was assessed through online and paper surveys for readability, ease of understanding, and filling in the answers. The paper (n=6) and online (n=4) questionnaires were pilot tested among 10 health professionals (3 doctors, 2 nurses, 3 pharmacists, and 2 assistant pharmacists). Internal consistency of the set of questions was evaluated (Cronbach alpha coefficient = 0.7). The multiple-choice questionnaire was structured to assess knowledge (5 questions), attitude (6 questions), practice (7 questions) of pharmacovigilance, ADRs with statins (1 question) and consisted of two open-ended questions for participants to give specific suggestions for improvement of spontaneous reporting of ADRs.

Data management and analysis

The data was systematically verified and checked for completeness and presented as mean $\pm$ standard deviation or percentage. Quantitative data were analyzed by a one-

way analysis of variance followed by Fisher's least significant difference test when significance was indicated. Chi-square (χ^2) was used to analyze qualitative data. The Pearson correlation test was used to assess the relationship between training and reporting of ADRs among health professionals. Differences were considered significant if the p-value was < 0.05 . Statistical Package for the Social Sciences (SPSS, version 25) was used to analyze the data.

Results

One hundred (80%) participants (44 doctors, 32 pharmacists/assistant pharmacists, and 24 nurses) completed the self-administered questionnaire (35 male; 56 female). The demographic characteristics of the participants are presented in **Table 1**. Respondents had a mean age of 32 ± 10 (36 ± 13 male; 30 ± 7 female) and a duration of service of 8 ± 10 (13 ± 14 male; 5 ± 4 female) years. The educational qualifications of the respondents were: 12 % Higher Certificate, 32 % Bachelor of Science (BSc), 23 % Doctor of Medicine (MD)/ Doctorate of Medicine (DM), 21 % Bachelor of Medicine and Surgery (MBBS), and 12 % Master of Science (MSc)/ Doctorate of Philosophy (Ph.D.).

There was no difference in mean age between the doctors and nurses, and between nurses and pharmacists/assistant pharmacists ($p > 0.05$). The doctors were older than the pharmacists/ assistant pharmacists ($p < 0.05$). There was no difference in professional experience between the three groups ($p > 0.05$). **Electronic and paper survey**

The response rates for the paper questionnaire were higher than for electronic questionnaires (65 vs. 35%, $p < 0.05$). There was no difference between the three professions in response rates to two modalities of data collection ($p > 0.05$).

Knowledge of ADRs and pharmacovigilance

Figure 1 illustrates the participants' knowledge of ADRs, pharmacovigilance and its objective, and NPC. The majority of the health professionals had an in-depth understanding of ADRs (82 correct vs. 18% incorrect answers, $p < 0.05$). In contrast, there were no differences between the numbers of respondents who were aware of the definition of pharmacovigilance (54 vs. 46%, $p > 0.05$) and of the ADR reporting forms (47 vs. 51%, $p > 0.05$) compared to those who were not. A higher number of the participants were aware that DDA is the NPC (85 vs. 15%, $p < 0.05$) and of the objective of pharmacovigilance (82 vs. 18%, $p < 0.05$).

Table 1: Demographic characteristics

	Doctors (n=44)	Nurses (n=24)	Pharmacists/ Assistant Pharmacists (n=32)
Gender * (M/F)	26/12	0/24	9/20
Average age	36 ± 13	31 ± 8	28 ± 7
Work Experience (Years)	11 ± 13	5 ± 2	7 ± 9
Higher qualifications			
MSc/PhD			
MD/DM	-	1	9
MBBS	19	-	-
BSc	18	-	-
Higher certificate	-	13	14
	-	4	6

DM, Doctorate of Medicine; Ph.D., Doctorate of Philosophy; MD, Doctor of Medicine; MSc, Master of Science; MBBS, Bachelor of Medicine and Surgery; BSc, Bachelor of Science

* Not all respondents indicated their gender.

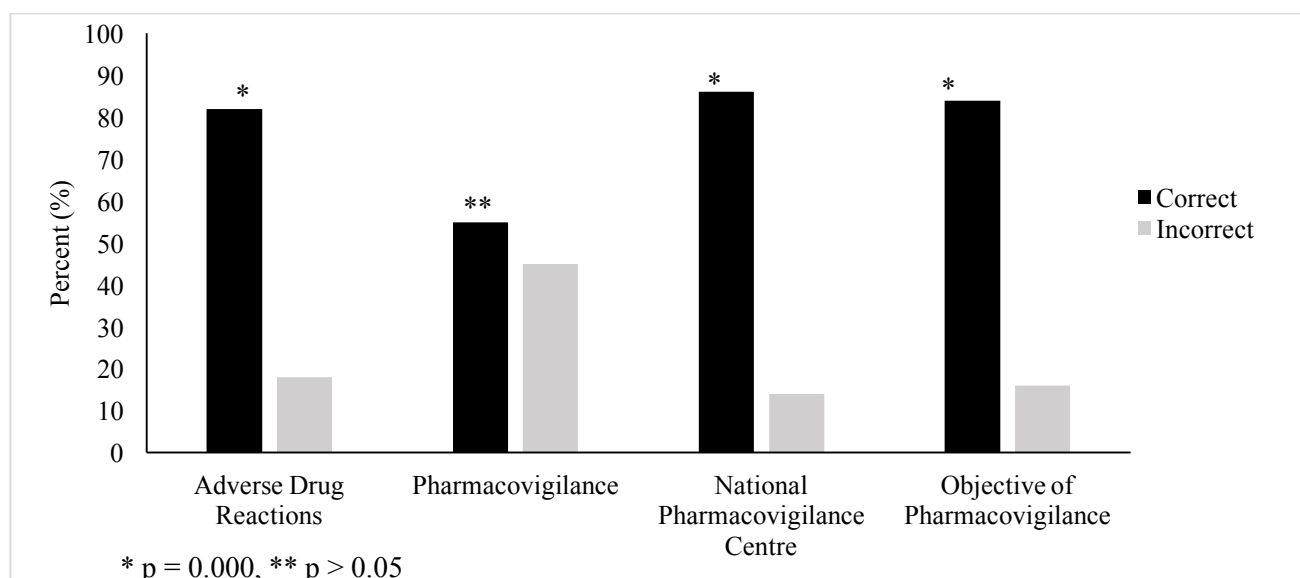


Figure 1: Knowledge of adverse drug reactions and pharmacovigilance

Attitude toward ADRs reporting and pharmacovigilance

Most of the participants stated pharmacovigilance awareness training programs (94 vs. 6%, $p < 0.05$) and ADR reporting (79 vs. 21%, $p < 0.05$) should be mandatory in every hospital. In addition, the majority of the

respondents felt reporting forms must be made available in local languages (93 vs. 7%, $p < 0.05$) and there should be a provision for patients to report ADRs (88 vs. 12%, $p < 0.05$). The reasons for underreporting ADRs stated by the surveyed health professionals are presented in **Table 2**.

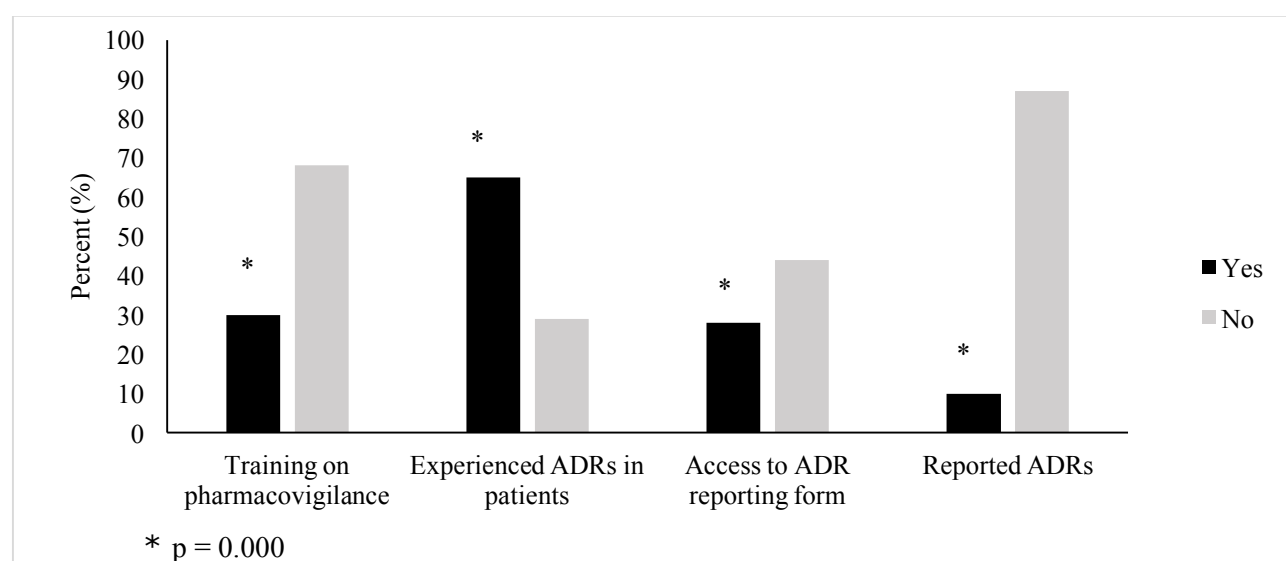
Table 2 Reasons for underreporting ADRs stated by the health professionals

Deterrents to reporting ADRs	Percentage of health professionals
Lack of knowledge about pharmacovigilance program	45
Lack of knowledge of the mechanism of reporting	35
Lack of access to ADR form	8
Lack of appreciation of the importance of a single ADR report to the database	6
Time constraints	4
Patient confidentiality issues	2

ADR training and reporting practice

A minority of the participants had training on ADR reporting (29 vs 71%, $p < 0.05$) and reported their patients' ADRs (10 vs 90%, $p < 0.05$). The number of respondents who stated that their patients had an ADR was higher than those who did not (64 vs. 26%, $p < 0.05$) (**Figure 2**). A

majority of respondents were willing to practice ADR reporting (95 vs 5%, $p < 0.05$). There was a positive relationship between the training of pharmacovigilance and reporting ADRs by the health professionals ($r = 0.331$, $n = 98$, $p < 0.001$).

**Figure 2:** Practice of adverse drug reactions reporting and pharmacovigilance**Method of ADR Reporting**

The health professionals preferred to report ADRs by filling in the ADR form (71%), direct contact with senior staff (17%), email (8%), and written correspondence (4%). A lower number of participants had access to the ADR reporting form (27 vs. 73%, $p < 0.05$) (**Figure 2**). One-fifth of the respondents had never seen an ADR reporting form whereas 8% did not know where they could be obtained. The number of respondents who considered that ADR reporting is a collective responsibility of all health

professionals was higher (67 vs 33%, $p < 0.05$) than those who thought otherwise.

Adverse reactions reported for statins

The adverse reactions associated with statins most commonly observed by the participants in their patients were muscle symptoms (62%), elevated activity of liver enzymes (25%), gastrointestinal symptoms (9%), and elevated glucose levels (4%).

Suggestions for improvement of pharmacovigilance

The participants identified the deficiencies of the current pharmacovigilance system, as is evident from the low number of ADRs reported annually. **Figure 3** illustrates the suggestions put forward by the respondents (29%) to strengthen the pharmacovigilance system in Nepal. The suggestions were: educational intervention and training

(46%), wider availability of simple and effective ADR reporting forms (29%), robust reporting system and policies (14%), and involvement of all stakeholders (11%).

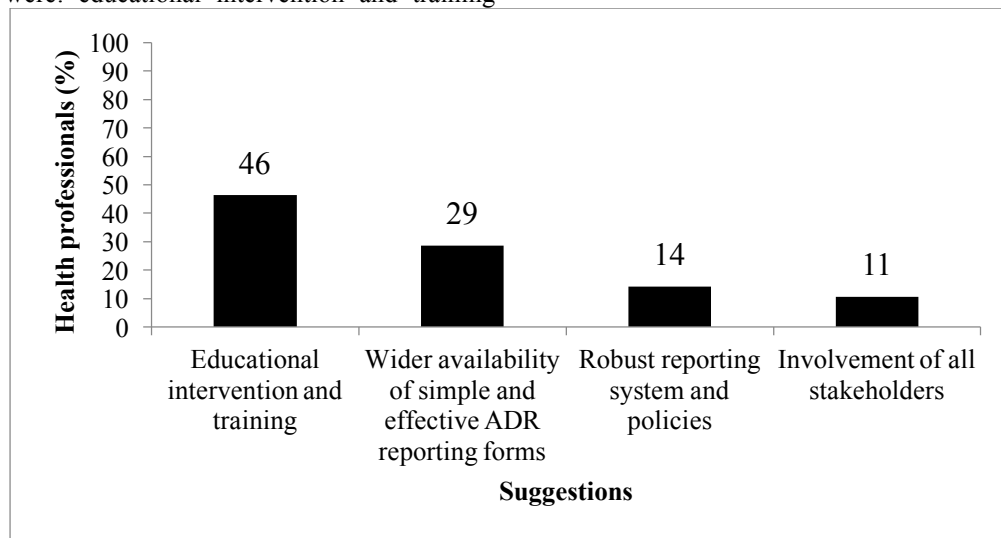


Figure 3: Suggestions to strengthen pharmacovigilance

Discussion

In the current study, the majority of the doctors were male, and nurses and pharmacists/assistant pharmacists were mostly female. This reflects the gender distribution and imbalance between health professionals in the country. In Nepal, nursing is a female ([Panthee et al., 2017](#); [Prakash et al., 2018](#)) and medicine is a male ([Hayes and Shakya, 2013](#)) dominated profession. The age and duration of service indicate that most of the professionals were in the early stages of their careers.

The response rate to the online survey was lower compared to the paper survey. This might be due to a lack of internet facilities and unfamiliarity with online surveys. Nepal is an under-developed country, access to private internet is not widespread and is expensive with income ([Regmi and Chautari, 2017](#)).

The majority of health professionals knew ADRs and the objective of pharmacovigilance. However, only half of them had an in-depth understanding of the broad concept of pharmacovigilance, similar to 47.3 % of the participants in a survey conducted by Shakya-Gurung et al., 2019 ([Shakya-Gurung et al., 2019](#)). Slightly more than one-third of the participants felt that it is limited to the detection of ADRs of marketed drugs only. As succinctly explained by WHO, pharmacovigilance encompasses the detection, assessment, understanding, and prevention of ADRs or any other drug-related problems ([World Health Organization, 2021](#)). There is a need to address the gap in the knowledge of health professionals. In this study, a greater number of participants knew that DDA is the NPC (85%) compared to

those in the studies of Palaian et al., 46.1% ([Palaian et al., 2011](#)) and KC et al., 53% ([KC et al., 2013](#)). This increase in knowledge is most likely due to the introduction of pharmacovigilance in the educational curriculum for MBBS and pharmacy students ([Palaian et al., 2009](#)), and to knowledge generation programs by DDA in Nepal. A survey found that a quarter of health facilities and pharmacies received drug safety bulletins from DDA ([Nwokike et al., 2013](#)). The knowledge is higher than in developing countries such as China ([Li et al., 2004](#)), India ([Rehan et al., 2012](#)), and Malaysia ([Ting et al., 2010](#)).

The main barriers to reporting ADRs are the lack of knowledge of pharmacovigilance, access to reporting forms, and time constraints. These findings are consistent with a previous study conducted by Saleh and colleagues ([Saleh et al., 2016](#)). Other challenges faced by developing countries include excessive workload, lack of expertise and funding, weak regulations, low literacy levels, use of counterfeit drugs, and self-medication ([Alshammari and Alshakka, 2014](#); [Shrestha and Bhandari, 2013](#)). The majority of respondents considered consumer pharmacovigilance necessary and this concurs with the responses of a survey conducted among consumers in Lalitpur, Nepal ([Jha et al., 2017](#)). Professionals from WHO, UMC and pharmacovigilance centers in the Netherlands and the UK considered patient reporting to be the future of pharmacovigilance ([Inácio et al., 2018](#)). Indeed, according to a survey conducted in fifty countries by Margraff and Bertram (2014) patient reporting- direct reporting, use of patient-specific reporting forms, and use of online forms were practiced in 44, 27, and 31 countries, respectively. The

necessity of educational interventions and training programs was highlighted by the respondents and this has proven to be highly effective in enhancing the level of KAP of pharmacovigilance (Jha *et al.*, 2017; Opadeyi *et al.*, 2019; Ribeiro-Vaz *et al.*, 2016; Shrestha *et al.*, 2020). The favorable attitude toward pharmacovigilance is consistent with the findings of similar studies in Nepal (KC *et al.*, 2013), Pakistan (Nisa *et al.*, 2018), Ghana (Amedome and Dadson, 2017), and the US (Gavaza *et al.*, 2011).

The gap between the observed and reported ADRs (64 vs 10 %) was wider compared to earlier studies in the country: (70.1 vs 33.7 %) in 2011 (Palaian *et al.*, 2011) and (49.1 vs 4.9 %) in 2019 (Shakya-Gurung *et al.*, 2019). These surveys were conducted in RPCs and this may explain the observed discrepancy. However, the gap is similar to the findings of a survey conducted by KC *et al.*, 2013 (74.8 vs 20.1 %) (KC *et al.*, 2013). Our finding is consistent with the worldwide ADR reporting rate, approximately 10 % (World Health Organization, 2018).

The contrast between adequate knowledge, positive perception, willingness to report, and low practice of pharmacovigilance could be due to barriers cited in **Table 2** and the absence of monitoring mechanisms by the healthcare institutions and regulatory bodies. This was highlighted by (Nwokike *et al.*, 2013) who reported a lack of an evaluation system to monitor the extent of implementation of pharmacovigilance in Nepal. A worldwide meta-analysis revealed ADR under-reporting rates to range from 59-100 % (Hazell and Shakir, 2006). The reporting rate could be increased by making it mandatory as in the case of some of the European countries and the US (Ekman and Backstrom, 2009; Hans and Gupta, 2018). Indeed, the participants believed that ADR reporting is a professional obligation and collective responsibility of all health professionals. A survey of fifty countries revealed that 91 % of the ADRs were reported by health professionals (Inacio *et al.*, 2018).

Although statins are widely used in Nepal, there are no published reports of adverse reactions. There is evidence that the under-reporting of ADRs associated with statins is a common phenomenon (Bamji, 2014; Johnson, 2015). In this study, the commonly observed adverse reactions reported for statins are similar to those reported worldwide (Hovingh *et al.*, 2016; Rosensen *et al.*, 2017) and further highlight low reporting.

The three study domains: knowledge, attitude, and practice of pharmacovigilance, which ultimately affects ADR reporting, are interrelated. Attitude and knowledge have been consistently found to be strong predictors of intention to report ADRs (Alsaleh *et al.*, 2017; Gavaza *et al.*, 2011; Guner and Ekmekci, 2019; Alshakka *et al.*, 2016; Bhagavathula *et al.*, 2016; Oshikoya and Awobusuyo, 2009; Li *et al.*, 2018). In the current study, the higher knowledge and positive attitude of the health professionals did not translate into practice. Hence, there is a need for

educational intervention and training, a simple and effective reporting system, and policies to monitor the implementation of pharmacovigilance and the contribution of all stakeholders. The frequency and intensity of public awareness, educational intervention, and periodic training programs to reinforce the role of pharmacovigilance in ensuring patient safety needs to be increased. The core curriculum put forward by WHO to teach pharmacovigilance to health professionals (Eekeren *et al.*, 2018) could be adopted. This will develop their competency in assessing the probability (Naranjo *et al.*, 1981), severity, and preventability (Hatwig *et al.*, 1992) of ADRs and further support the assessment of ADRs by the pharmacovigilance centers. Continuing Medical Education (CME) programs, seminars, print, media, and the internet can be effective ways to build the capacity of health professionals for ADR reporting. A standardized ADR reporting form should be made simpler and available in local languages and English in out-patients/ in-patients departments, clinics, and other health institutions. The national pharmacovigilance program should be enhanced with more ADR monitoring centers and timely dissemination of information on ADRs, and national and international drug safety information. ADR reporting should be made mandatory for all the stakeholders of pharmacovigilance. Two-way communication between the stakeholders of pharmacovigilance and NPC is vital to promoting pharmacovigilance practices. A well-defined reporting procedure and channel will contribute to making the system more efficient. This requires very close collaboration between all health professionals, pharmaceutical companies, and patients. Comprehensive understanding, management, and prevention of ADRs will ultimately enhance patient safety.

Strengths and limitations of the study

Previous studies have investigated the KAP of pharmacovigilance among health professionals in Nepal (Palain *et al.*, 2011; KC *et al.*, 2013; Shakya-Gurung *et al.*, 2019). The focus of these studies was participants who work in RPCs. In contrast, the professionals in this study were recruited mostly from non-reporting centers. The second strength is that it obtained data from key health professionals who continuously interact with patients. The results should be interpreted in light of the limitations of the study. The limitations are a small size and the survey was limited to the capital, Kathmandu and it did not survey patients and pharmaceutical companies.

Conclusion

The majority of health professionals were knowledgeable with a positive attitude to ADR reporting. However, positive knowledge and attitude were not reflected in practice. This mismatch between knowledge and practice is evident in the low ADR reports gathered by NPC. This is a very significant finding because it highlights a deficiency in the implementation and monitoring mechanism. It is

important to obtain adverse drug reaction data from diverse population groups because genetic makeup is a factor in the way patients respond to medications. The health professionals, regulatory bodies, patients, and other stakeholders of pharmacovigilance should work closely as a team to improve the current system of pharmacovigilance and make it fully functional in the country.

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Conflicts of Interest The authors report no conflicts of interest in this work.

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