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Healthcare professionals knowledge, attitude and practice of reporting adverse drug reactions in Ethiopia

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Abstract

Objective: The aim of this study was to assess the knowledge, attitude, and practice of adverse drug reactions (ADRs) reporting and identify factors associated with reporting ADRs among healthcare professionals (HCPs) working in Tigray region, Ethiopia.

Materials and Methods: A cross-sectional study was conducted between January and March of 2019 in a tertiary care hospital in Tigray region, Ethiopia. A self-administered, pretested questionnaire was administered to HCPs. Data were analyzed using STATA version 14.1 (STATA Corp, TX, USA). Logistic regression analysis was used to identify factors associated with poor ADRs reporting practice.

Results: In total, 362 questionnaires were distributed, and the response rate was 84.8% (n = 307). Of all respondents, 190 (61.9%) were nurses, 63 (20.5%) were pharmacist, and 54 (17.6%) were physicians. About 58.3% of HCPs had poor knowledge of ADRs reporting. The majority of the respondents had a positive attitude (59.9%), and only a few (32.1%) respondents have good ADRs reporting practice. Poor knowledge (Adjusted odds ratio (AOR)= 2.63, 95% confidence interval (CI): 1.26- 5.45), lack of training on ADRs reporting (AOR= 7.31, 95% CI:

3.42- 15.62) and work experience (≥10 years) (AOR= 0.36, 95% CI: 0.13- 0.97) were the predictors of poor ADRs reporting practice.

Conclusions: The majority of healthcare professionals had poor knowledge and practice, but a positive attitude toward reporting ADRs. Poor knowledge, less work experience and lack of training were predictors of poor ADRs reporting practice. Hence, strategies to improve the knowledge and practice of reporting ADRs should be implemented, particularly for untrained and less experienced HCPs.

Keywords: Adverse drug reaction, healthcare professionals, knowledge, practice

Strengths and limitations of this study

The article provides interesting information related to pharmacovigilance in Ethiopia and will help policymakers understand the factors for underreporting of ADRs in Ethiopia.

The cross-sectional design of this study may not establish a causal relationship between ADRs reporting and explanatory variables

Our study was conducted in a single centre.

Introduction

Adverse drug reactions (ADRs) are a major cause of morbidity and mortality and contribute to the occurrence of adverse events, leading to increased healthcare costs [1]. ADRs account for up to 6.5% of all hospitalizations [2]. Information on ADRs can be obtained from preclinical studies and clinical studies, but rare adverse reactions that occur only in a few cases after prolonged use of drugs or after interactions with other established drugs may not be detected during this period [3]. Therefore, a thorough study of post-marketing adverse drug reactions is essential to patient safety

[4]. Once a drug is registered and marketed, adverse reaction studies can be conducted using a variety of methods, such as observational studies, monitoring of prescription events, spontaneous reports and so on [5]. However, the health care system relies heavily on the spontaneous reporting of ADRs to monitor drug safety throughout the population during actual use [6].

Although different studies have documented that new adverse reactions are effectively discovered through spontaneous reporting compared to other methods, poor reporting practice is a major limitation of spontaneous reporting systems [7]. Low rates of adverse reaction reporting are a major health concern and may delay regulatory actions to remove drugs with an unacceptable safety profile from the marketplace [8]. Healthcare professionals are responsible for identifying, documenting and reporting ADRs. Their contribution to the early detection and reporting of ADR is essential [9]. However, ADR reporting is affected by many factors, including lack of awareness, ambiguity about who should report, difficulties with reporting procedures, lack of feedback on submitted reports, rapid resolution of adverse events, and so on [10, 11]. The knowledge and attitudes of health professionals are strongly related to ADRs reporting [12, 13]. Therefore, it is very important to understand the knowledge and practice of health care providers related to ADR reporting to improve reporting practices [14].

Although local regulatory authorities can make drug safety decisions using ADR data from other countries, it is essential to take into account a number of factors, such as local population traditions, genetics, diet, environmental factors, etc [15]. Therefore, it is very important to establish a local functional ADR monitoring center. Ethiopia established its own pharmacovigilance system under the Food and Drug Administration and control authority in 2002. Since the introduction of the

pharmacovigilance system, the number of adverse reactions reported to the center is limited [16]. In addition, studies on identifying factors and reasons for poor reporting practices are limited in our context. The aim of this study was therefore to determine the knowledge, attitudes and practices of reporting ADRs and to identify predictive factors for poor ADR reporting practices among health professionals in a tertiary hospital in the Tigray region, Ethiopia.

Materials and Methods

Study setting and period

The study was conducted at Ayder comprehensive specialized hospital (ACSH), Tigray region, Northern Ethiopia. ACSH is a teaching and referral hospital with 500 beds. The hospital serves for more than 9 million people in the catchment area. ACSH provides all the specialized and non-specialized hospital services including emergency services, outpatient services and inpatient services. Healthcare professionals working in all of these areas were included in this study between January and March of 2019.

Study design and population

An institutional based cross-sectional study was conducted. The target populations for this study were nurses, physicians and pharmacists working in ACSH during the study periods. Healthcare professionals who were refused or did not wish to participate in the study were excluded.

Sample Size Determination and sampling technique

The sample size was calculated using a single proportion sample size estimating formula

$$n = \frac{\left(z_{1-\alpha/2}\right)^2 P(1-P)}{d^2} = \frac{(1.96)^2 0.66(1-0.66)}{0.05^2} = 344.8 \approx 345$$

Where, n = sample size, Z = confidence interval (1.96) p = The proportion of health care professionals with poor knowledge of ADR reporting (65.8, p= 0.66), obtained from a study conducted in Amhara region of Ethiopia [17], and d = Margin of error to be tolerated (0.05). By adding 5% (345x0.05 = 17) of the sample size to compensate non-respondents, the total sample size required was 362. Subjects were recruited using stratified random sampling technique according to their profession.

Outcome measures

In this survey, knowledge of ADRs reporting was assessed using nine questions containing general knowledge about ADR and ADR reporting. Each correct answer had a score of 1 and each wrong answer had a score of 0. Thus, the total score ranged from 0 to 9 points. The overall level of knowledge was categorized using the mean score. Participants with above mean scores were classified as having good knowledge and below mean scores were classified as poor knowledge. Participants' attitudes were assessed using ten items rated as agreeing, neutral, and disagreeing on a three-point Likert scale. The "agree" responses received a score of 3, "neutral" a score of 2, and "disagree" a score of 1. An inverted score was made for the negative-worded questions. Therefore, the maximum possible attitude score was 30. The mean attitude score was calculated for each respondent on the basis of which their attitude was categorized as positive and negative. The level of practice of health professionals was assessed by determining whether they had encountered, documented and reported ADRs or not. Participants were classified as having good practice if they had reported one or more ADRs and poor practices, if they had never reported ADR, despite encountering ADRs.

Data collection

The Data Collection Tool is a questionnaire that was adopted from similar previous studies on the knowledge, attitudes, and practices of health care professionals on ADR reporting [18-20]. A pre-test was performed to validate the questionnaire and minor modifications were made accordingly The prepared self-administered questionnaire contained four different sections. The first section contained demographic information. The second section consists of nine questions used to measure the knowledge of HCPs related to ADR reporting. The third section consisted of ten questions, which assessed participants' attitudes toward ADR reporting. The fourth section is about the practice of ADR reporting..

Statistical methods

The data were coded, double-entered into Epi data management (version 4.2.0) and statistical analysis was performed using STATA version 14.1 (STATA Corp, TX, USA). Descriptive analysis was computed using mean (SD) for quantitative variables and frequency for categorical variables. To determine the factors associated with ADR reporting, univariate and multivariate logistic regression tests were used. The dependent variable was ADR reporting, while demographics, knowledge and attitude were included as the independent variables. Values were considered as significant at p-value of <0.05 ($\alpha=0.05$).

Ethical considerations

The ethical approval and clearance were obtained from Ethics Review Committee of the School of Pharmacy, College of Health Sciences, Mekelle University (reference number: CHS/161/pharm-11). In addition, a brief description of the objective of the study was provided for all the participants to avoid ambiguity and misunderstanding. The data collection process was initiated after the willingness of the health professionals was requested and formal written consent was obtained.

Patient and Public Involvement

No patient involved

Results

Demographic characteristics

In the current study, 362 questionnaires were distributed. Of these, 307 were duly completed and returned, giving a response rate of 84.8%. Of all respondents, 190 (61.9%) were nurses, 63 (20.5%) were pharmacist, and 54 (17.6%) were physicians. About 50% of respondents have less than five years of experience and more than half of the participants had not received any training on adverse drug reactions (table 1).

Table1: Socio-demographic characteristics of respondents at ACSH, Tigray Region, Northern Ethiopia, from January 2019 to March 2019 (n=307)

Variable	Frequency (%)
Sex	
Male	156 (50.8)
Female	151 (49.2)
Age	
<25	63(20.5)
25-34	199(64.8)
≥35	45(14.7)
Profession	
Physician	54 (17.6)
Pharmacy	63 (20.5)
Nurse	190 (61.9)
Work experience (years)	
< 5	156 (50.9)

5-9	121 (40)
≥10	28 (9.1)
Trained on ADR reporting	
Yes	138(44.95)
No	169(55.05)

Knowledge of adverse drug reaction reporting

There were nine questions assessing knowledge of adverse drug reactions. Only 29.3% of respondents knew the exact definition of adverse reactions and 36.8% of respondents knew what to report. A small proportion of respondents (19.5%) were aware of the classification of adverse drug reactions. Of the respondents, 39.4% of the respondents felt they were aware of the availability of the National Reporting Center in Ethiopia and a small proportion of the respondents (31.9%) knew where to report. The mean score ± SD of the level of knowledge of ADRs among health professionals was 4.17 ± 2.07 out of a maximum of 9 points. Overall, the majority (58.3%) of health professionals had poor knowledge of ADR reporting (table 2).

Table 2: knowledge of healthcare professionals toward ADR reporting in ACSH, Tigray Region, Northern Ethiopia, from January 2019 to March 2019 (n=307)

Variables	Frequency (%)
Which of the following defines ADR correctly?	
Any noxious or undesired effect of drug occurring at normal dose, during normal use*	90 (29.3)
Adverse health outcomes associated with inappropriate drug use	51 (16.6)
Harm resulting from the use of substandard/counterfeit drugs	26 (8.5)
Harm caused by drug overdose	67 (21.8)
All can define ADR	73 (23.8)
Which ADR should be reported?	
All series ADRs	113 (36.8)
ADRs to herbal and non-allopathic drugs	15 (4.9)
ADRs to new drugs	49 (16.0)
ADRs to vaccines drugs	8 (2.6)
Unknown ADRs to old drugs	9 (2.9)

All of the above*	113 (36.8)
The correct classification of the type of ADR	
Type A,B,C,D,E,and F*	60 (19.5)
Type 1,2,3,4,5,6 and 7	62 (20.2)
Known, unknown and common, uncommon	89 (29.0)
Reversible and irreversible	64 (20.8)
Do not know	31 (10.1)
Is there any center /ADR reporting system in Ethiopia	
Yes	121 (39.4)
No	141 (45.9)
Don't know	45 (14.7)
All ADRs are known before a medicine is marketed	
Yes	99 (32.2)
No*	168 (54.7)
Don't know	40 (13.0)
Are you aware of any drug that banned due to ADR	
Yes*	98 (31.9)
No	176 (57.3)
Don't know	33 (10.7)
Where it reported in Ethiopia	
Manufacturers	17 (5.5)
Ministry of health of Ethiopia	68 (22.1)
Ethiopian pharmaceutical association	47 (15.3)
DTC of respective health facility	49 (16.0)
FMHACA*	98 (31.9)
Pharmacy dept	28 (9.1)
Do you think that ADR is the same with side effect?	
Yes	127(41.4)
No*	180(58.6)
Which of the following is the major risk factor for the occurrence of maximum adverse drug reactions	
Arthritis	30 (9.8)
Renal failure*	147 (47.9)
Visual impairment	24 (7.8)
All of these	106 (34.5)
Overall knowledge score	
Good	128 (41.7)
Poor	179 (58.3)

ADR: adverse drug reaction, DTC: drug and therapeutic committee STG: standard treatment guideline DACA: Drug Administration and Control Authority, FMHACA: Food, Medicine and Healthcare Administration and Control Authority, *correct answers

Attitude of health professionals toward ADR reporting

Regarding healthcare professionals' attitudes to reporting adverse drug reactions, the majority (67.4%) of respondents agreed that it is necessary to report, while 37.8% agreed that reporting adverse drug reactions should be mandatory. Most respondents (51.1%) disagreed with the idea that only prescribed medication should be reported. Overall, about 60% of respondents showed a positive attitude towards reporting ADRs (table 3).

Table 3: Attitude of healthcare professionals toward ADR reporting in ACSH, Tigray Region, Northern Ethiopia, from January 2019 to March 2019 (n=307)

Items	Responses		
	Agree, n (%)	Neutral n (%)	Disagree n (%)
ADR reporting is necessary	207 (67.4)	23 (7.5)	77 (25.1)
Reporting ADR should be mandatory for all HCPs	116 (37.8)	62 (20.2)	129 (42.0)
ADR reporting increase patient's safety	148 (48.2)	66 (21.5)	93 (30.3)
Reporting ADR is important for health care system	135 (44.0)	73 (23.8)	99 (32.2)
There is a need to be sure that ADRs are related to the drug before reporting	194 (63.2)	35 (11.4)	78 (25.4)
Only ADR of prescription drug needs to be reported	82 (26.7)	68 (22.1)	157 (51.1)
One report of ADR makes no differences	103 (33.6)	78 (25.4)	126 (41.0)
The yellow card is difficult to fill up	177 (57.7)	88 (28.7)	42 (13.7)
Reporting creates additional workload and it is time consuming	199 (64.8)	78 (25.4)	30 (9.8)
Establishing ADR reporting center in every hospital is important	189 (61.6)	44 (14.3)	74 (24.1)
Overall level of attitude			
Positive	184 (59.9%)		
Negative	123 (40.1%)		

Practices of health professionals about ADR reporting

Of the 307 health professionals, 74.9% encountered ADR in last 12 month of their clinical practice, and 29.1% of them recorded in patient card. Although most health care professionals experienced ADR, only 32.1% reported it (table 4).

Table 4: Practice of healthcare professionals toward ADR reporting in ACSH, Tigray Region, Northern Ethiopia, from January 2019 to March 2019 (n=307)

Items	Category	Frequency (%)
Have you ever encountered patient with ADR in your clinical practice in the last 12 months	Yes	230(74.9)
	No	77 (25.1)
How many patients with ADR have you encountered during the last 12 months?	None	77 (25.1)
	One	13 (4.2)
	Two	58 (18.9)
	Three	61 (19.9)
	Four	52 (16.9)
	More than four	46 (15.0)
Have you noted the ADR you encountered on the patient clinical record (n=230)	Yes	67 (29.1)
	No	163 (70.9)
How often do you give advice to your patients on possible ADRs you prescribed, dispensed or administered	Usually	118 (38.4)
	Never	89 (29.0)
	Sometimes	69 (22.5)
	Always	31 (10.1)
If you encountered ADR, have you ever reported the ADR? (n=230)	Yes (good practice)	74 (32.1)
	No (poor practice)	156 (67.9)

Factors associated with poor ADR reporting practice

A univariable logistic regression analysis was performed to determine the association of each variable with the practice of ADR reporting. In the univariable analysis work experience of the HCPs (≥10 years) (crude odds ratio (COR)= 0.31, 95% CI: 0.15- 0.64), negative attitude (COR= 2.08, 95% CI: 1.17-3.72), poor knowledge (COR= 3.49, 95% CI: 1.95- 6.23), lack of training on

ADR reporting (COR= 7.67, 95% CI: 4.07- 14.46), and nursing profession (COR= 2.11, 95% CI: 1.06- 4.20), were associated with poor ADR reporting practice. Subsequent multivariable logistic regression model was conducted to identify the independent predictors. The full model containing all predictors was statistically significant ($X^2 = 69.78$, df = 10, P-value < 0.001). The results of the multivariate logistic regression indicated that only work experience of the HCPs (≥10 years) (AOR= 0.36, 95% CI: 0.13- 0.97), poor knowledge (AOR= 2.63, 95% CI: 1.26- 5.45), and lack of training on ADR reporting (AOR= 7.31, 95% CI: 3.42- 15.62) were the predictors of poor ADR reporting practice (table 5).

Table 5: Univariable and multivariable logistic regression analysis of associated factors of poor ADR reporting practice in Tigray Region, Ethiopia from January 2019 to March 2019 (n=230)

Variable	ADR reporting practice		P value	COR (95% CI)	AOR (95% CI)	P value
	Yes, n (%)	No, n (%)				
Gender						
Male	44 (59.5)	73 (46.8)		1	1	
Female	30 (40.5)	83 (53.2)	0.07	1.67(0.95, 2.92)	1.51(0.77, 2.94)	0.23
Age (years)						
<25	15(20.3)	29(18.6)		1		
25-34	48(64.9)	100(64.1)	0.84	1.09(0.53, 2.19)	1.22(0.46, 3.23)	0.68
≥35	11(14.9)	27(17.3)	0.62	1.27(0.49, 3.24)	3.40(0.93, 12.48)	0.07
Experience (years)						
< 5	27(36.5)	84(53.8)		1	1	
5-9	24(32.4)	50(32.1)	0.23	0.67(0.35, 1.28)	1.42(0.57, 3.52)	0.45
≥10	23(31.1)	22(14.1)	0.001	0.31(0.15, 0.64)	0.36(0.13, 0.97)	0.04
Profession						
Pharmacist	20(27.0)	26(16.7)		1	1	
Physician	16(21.6)	26(16.7)	0.61	1.25(0.53, 2.93)	2.15(0.70, 6.56)	0.18
Nurse	38(51.4)	104(66.7)	0.04	2.11(1.06, 4.20)	1.36(0.57, 3.26)	0.49

Attitude						
Positive	50(67.6)	78(50)		1	1	
Negative	24(32.4)	78(50)	0.01	2.08 (1.17, 3.72)	1.24(0.59, 2.59)	0.57
Knowledge						
Good	48(64.9)	54(34.6)		1	1	
Poor	26(35.1)	102 (65.4)	<0.001	3.49(1.95, 6.23)	2.63(1.26, 5.45)	0.01
Training provided						
Yes	56(75.7)	45(28.8)		1	1	
No	18(24.3)	111(71.2)	<001	7.67(4.07, 14.46)	7.31(3.42, 15.62)	<0.001

ADR: adverse drug reaction, AOR: adjusted odds ratio, COR: crude odds ratio

Discussion

One of the main goals of this study was to investigate the knowledge of HCPs towards ADRs and its reporting. This issue is critical for research to identify the necessary interventions, as HCPS cannot effectively participate in the reporting without sufficient knowledge of the ADR and its reporting process. We found that only 41.7 % of HCPs had good knowledge about ADR reporting, similar to the reports seen in Amhara region of Ethiopia (47%) [21], West Ethiopia (48 %) [22], Saudi Arabia (39.6%) [23], and Nepal (39.4%) [24]. These findings suggest that the knowledge of HCPs on ADRs reporting is insufficient. However, this result was lower compared to previous findings reported in Philippines (77%) [25] and in Kuwait (61.5%) [26]. This discrepancy may be due to differences in government involvement in national pharmacovigilance programs, study participants, and training level. The current study was conducted in a system where national ADR reporting methods were in its infancy and most HCPs (55%) did not receive any ADR reporting training.

Our study showed that 39.4% of HCPs were aware of the existence of an ADR system in Ethiopia. This meant that most of the participants did not have information about the authority responsible for monitoring ADR in Ethiopia. This is similar to the study conducted in Addis Ababa, Saudi Arabia, and Jordan, which reported lack of knowledge about the national ADR reporting system [27-29]. This is a critical observation, which is undoubtedly related to the current underreporting of ADRs. In addition, only 31.9 % of the HCPs know where to report ADR. This could be as a result of limited awareness and support for ADR monitoring.

Regarding the level of attitude, we found that about 60 % of HCPs had a positive attitude on ADR and its reporting. Although majority of the respondents have positive attitude, the result is lower compared to previous findings in Amhara region of Ethiopia (86%) [21] and India (90%) [29]. Most respondents (67.4%) felt that reporting adverse reactions is necessary, which is consistent with previous studies [20, 21]. However, 64.8% of the respondents agreed that reporting creates an additional workload, which is higher than the results obtained in the Amhara region (32.4%) [21]. Although it may take some time to complete the report forms, the high proportion of respondents with such perception found in our study may affect the motivation to report adverse reactions.

Another important finding was that ADRs reporting practices among HCPs were very poor. Although more than 75% of respondents encountered one or more ADRs in their daily practice, only 32.1% of respondents reported ADRs. This is consistent with a study conducted in Amhara Region of Ethiopia and south India [30, 31]. The study also identified predictors of poor ADR reporting practice. Less experienced HCPs were more likely to have poor ADR reporting practices. This finding is consistent with a study conducted in Uganda, where more experienced HCPs were four times more likely to have ever reported than less experienced professionals [31]. Health

professionals with poor knowledge were more likely to have a poor practice of reporting ADRs. The association of poor knowledge levels of health professionals with poor ADR reporting practice has been observed in many similar previous studies [31-35]. Moreover, health professionals who had not received ADRs reporting training were more likely to have poor practice. This is also supported by a study carried out in Spain [36]. However, only 44.95% of the respondents were trained in our study. Similarly, HCPs have shown limited training in areas of ADR and their reporting in studies conducted in Sudan [33] and Uganda [31]. Thus, more training regarding the identification of ADR, the purpose of the ADR reporting, and the availability of resources for ADR reporting is required.

These findings have important implications. The low level of knowledge of the adverse drug reaction and its reporting among HCPs should be enhanced by designing different strategies. Different studies have shown improved knowledge and attitude scores after educational interventions related to pharmacovigilance and ADR reporting's [37-40]. Therefore, empowering HCPs in detecting and reporting suspected drug reactions is essential to strengthening pharmacovigilance systems in Ethiopia. This is especially important for less experienced health professionals and for those who had never received training on ADR reporting. However, additional research needs to be done to investigate the impact of this intervention on the knowledge and practice of ADR reporting in our setting.

Finally, there are several limitations to this study. We used a self-report as the main method of inquiry, which may have introduced recall bias. The HCPs may have made explicit responses to the fear that they would be embarrassed if they did not report ADRs. However, because we used self-administered questionnaires without respondents' names, the potential for this bias was

reduced. The cross-sectional design we used may not establish a causal relationship between ADR reporting and explanatory variables. Finally, the study was conducted in a tertiary referral hospital and may not be generalized for all HCPs in different health care level in the country. Despite these limitations, our study has generated important insights on knowledge, attitude, and practice of ADR reporting and predictors of poor ADRs reporting practice.

Conclusion

The majority of health professionals had poor knowledge and practice, but a positive attitude toward reporting ADRs. Poor knowledge, less work experience and lack of training were predictors of poor ADR reporting practice. Therefore, strategies to improve knowledge and practices regarding ADR reporting should be implemented. Training should be provided to all HCPs, especially those who have never received training and less experienced professionals.

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Contributors: KG and MS conceived the study and drafted the manuscript and contributed to data entry, data analysis, draft manuscript and final proof reading. BYH, SWA and YLN participated in study design, data analysis and in the process of manuscript writing. All authors approved the final manuscript.

Data Availability

The dataset of this study is available from the corresponding author upon request.

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Conflicts of Interest

The authors have declared that there is no conflict of interests with respect to the authorship and/or publication of this study.

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	*5*
Study size	10	Explain how the study size was arrived at	4 and 5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	--
		(*c*) Explain how missing data were addressed	--
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	--
		(*e*) Describe any sensitivity analyses	--
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	---
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	--
Outcome data	15*	Report numbers of outcome events or summary measures	7-10
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11
		(*b*) Report category boundaries when continuous variables were categorized	12
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	---
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	---
Discussion			
Key results	18	Summarise key results with reference to study objectives	13 and 14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Healthcare professionals knowledge, attitude and practice of adverse drug reactions reporting in Ethiopia: a cross-sectional study

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Abstract

Objective: This study aimed to assess the knowledge, attitude, and practice of adverse drug reactions (ADRs) reporting and identify factors associated with ADRs reporting among healthcare professionals (HCPs) working in Tigray region, Ethiopia.

Materials and Methods: A cross-sectional study was conducted between January and March of 2019 in a tertiary care hospital in Tigray region, Ethiopia. A self-administered, pretested questionnaire was administered to HCPs. Data were summarized using descriptive statistics. Logistic regression analysis was used to identify factors associated with poor ADRs reporting practices.

Results: In total, 362 questionnaires were distributed, and the response rate was 84.8% (n = 307). Of all respondents, 190 (61.9%) were nurses, 63 (20.5%) were pharmacist, and 54 (17.6%) were physicians. About 58.3% of HCPs had poor knowledge of ADRs reporting. The majority of the respondents had a positive attitude (59.9%), and only a few (32.1%) respondents have good ADRs reporting practices. Poor knowledge (Adjusted odds ratio (AOR)= 2.63, 95% confidence interval (CI): 1.26- 5.45), and lack of training on ADRs reporting (AOR= 7.31, 95%

CI: 3.42- 15.62) were both negatively associated with ADRs reporting practice, whereas higher work experience (≥10 years) (AOR= 0.36, 95% CI: 0.13- 0.97) were positively associated with ADRs reporting practice.

Conclusions: The majority of healthcare professionals had poor knowledge and practice, but a positive attitude toward ADRs reporting. Poor knowledge, less work experience and lack of training were associated with poor ADRs reporting practice. Hence, strategies to improve the knowledge and practice of ADRs reporting should be implemented, particularly for untrained and less experienced HCPs.

Keywords: Adverse drug reaction, healthcare professionals, knowledge, practice

Strengths and limitations of this study

The article provides interesting information related to pharmacovigilance in Ethiopia and will help policymakers understand the factors for ADRs underreporting in Ethiopia.

The cross-sectional design of this study may not establish a causal relationship between ADRs reporting and explanatory variables

Our study was conducted in a single centre.

Introduction

Adverse drug reactions (ADRs) are a major cause of morbidity and mortality and contribute to the occurrence of adverse events, leading to increased healthcare costs [1]. ADRs have become a major public health problem in developing countries [2]. The median prevalence (with interquartile range [IQR]) of ADR-related hospitalization in developing countries was 5.5% (1.1-16.9) [3]. The information collected during the pre-marketing phase of drug development is inevitably

incomplete concerning possible ADRs. This is due to the participation of a limited and selected number of patients who are studied before marketing, the conditions of drug use in clinical trials are different from those of clinical practice, the duration of the clinical trials is short, and high-risk patients (such as elderly patients) are often excluded [4]. Therefore, post-marketing surveillance is important to allow detection of less common, but sometimes very serious ADRs. Once a drug is registered and marketed, adverse reaction studies can be conducted using a variety of methods, such as observational studies, monitoring of prescription events, spontaneous reports and so on [5]. However, the health care system relies heavily on spontaneous ADRs reporting to monitor drug safety throughout the population during actual use [6].

A spontaneous reporting system of ADRs is fundamental to effectively discover new adverse reactions but under-reporting is its major limitations [7, 8]. A systematic review of studies conducted in the European Union showed a significant and widespread healthcare professionals under-reporting of ADRs with a median rate of under-reporting of 94% [7]. The low rates of ADRs reporting may delay regulatory actions to remove drugs with an unacceptable safety profile from the marketplace. A worldwide systematic review of 462 medicines removed from the market for safety reasons showed that the median interval between the first reported adverse reaction and the year of first withdrawal was 6 years (IQR, 1-15) and the interval did not consistently shorten over time [9].

Healthcare professionals (HCPs) are responsible for identifying, documenting and ADRs reporting. Their contribution to the early detection and reporting of ADR is essential [10]. However, ADR reporting is affected by many factors, including lack of awareness, ambiguity about who should report, difficulties with reporting procedures, lack of feedback on submitted

reports, rapid resolution of adverse events, and so on [11, 12]. The knowledge and attitudes of health professionals are strongly related to ADRs reporting [8, 13]. Therefore, it is very important to understand the knowledge and practice of health care providers related to ADR reporting to improve reporting practices [14].

Although local regulatory authorities can make drug safety decisions using ADR data from other countries, it is essential to take into account a number of factors, such as local population traditions, genetics, diet, environmental factors, etc [15]. Therefore, it is very important to establish a local functional ADR monitoring center. Ethiopia established its own pharmacovigilance system under the Food and Drug Administration and control authority in 2002. Since the introduction of the pharmacovigilance system, only a small number of ADRs have been reported to the center [16]. Besides, studies on identifying factors and reasons for poor reporting practices are limited in our context. The aim of this study was therefore to determine the knowledge, attitudes, and practices of ADRs reporting and to identify predictive factors for poor ADR reporting practices among health professionals in a tertiary hospital in the Tigray region, Ethiopia.

Materials and Methods

Study setting and period

The study was conducted at Ayder comprehensive specialized hospital (ACSH), Tigray region, Northern Ethiopia. ACSH is a teaching and referral hospital with 500 beds. The hospital serves more than 9 million people in the catchment area. ACSH provides all the specialized and non-specialized hospital services including emergency services, outpatient services, and inpatient

services. Healthcare professionals working in all of these areas were included in this study between January and March of 2019.

Study design and population

An institutional-based cross-sectional study was conducted. The target populations for this study were nurses, physicians, and pharmacists working in ACSH during the study periods. Healthcare professionals who were refused or did not wish to participate in the study were excluded.

Sample Size Determination and sampling technique

The sample size was calculated using a single proportion sample size estimating formula

$$n = \frac{\left(z_{1-\alpha/2}\right)^2 P(1-P)}{d^2} = \frac{(1.96)^2 0.66(1-0.66)}{0.05^2} = 344.8 \approx 345$$

Where, n = sample size, Z = confidence interval (1.96) p = The proportion of health care professionals with poor knowledge of ADR reporting (65.8, p= 0.66), obtained from a study conducted in Amhara region of Ethiopia [17], and d = Margin of error to be tolerated (0.05). By adding 5% (345x0.05 = 17) of the sample size to compensate non-respondents, the total sample size required was 362. Subjects were recruited using stratified random sampling technique. A list of HCPs (pharmacists, physicians, and nurses) working at the hospital was obtained from the hospital's human resources department. All HCPs were first stratified according to the type of profession and this list was used as a sampling frame. Depending on the size of the profession in each category of HCPs, participants were randomly selected. We used a lottery method to randomly select a set of healthcare professionals as respondents from each category. We used this lottery method from the complete list of each category assuming that all the HCPs working in a similar profession (for example, all physicians) in different

departments and/or units were homogeneous with respect to knowledge, attitude, and practice of ADRs reporting.

Outcome measures

In this survey, knowledge of ADR reporting was assessed using nine questions containing general knowledge about ADR and ADR reporting. Each correct answer had a score of 1 and each wrong answer had a score of 0. Thus, the total score ranged from 0 to 9 points. The overall level of knowledge was categorized using the median score. Participants with above median scores were classified as having good knowledge and below the median scores were classified as having poor knowledge. Participants' attitudes were assessed using ten items rated as agreeing, neutral, and disagreeing on a three-point Likert scale. The "agree" responses received a score of 3, "neutral" a score of 2, and "disagree" a score of 1. An inverted score was made for the negative-worded questions. Therefore, the maximum possible attitude score was 30. The median attitude score was calculated for each respondent, on the basis of which their attitude was categorized as positive and negative. The level of practice of health professionals was assessed by determining whether they had encountered, documented and reported ADRs or not. Participants were classified as having good practice if they had reported one or more ADRs and poor practices, if they had never reported ADR, despite encountering ADRs.

Data collection

The Data Collection Tool is a questionnaire that was adopted from similar previous studies on the knowledge, attitudes, and practices of health care professionals on ADR reporting [18-20].

The questionnaire was reviewed for its content validity by consensus of a panel of three experts in the field derived from academia (one expert from pharmacoepidemiology and two experts from clinical pharmacy departments). The Index of consistency of the questionnaires was 0.86,

suggesting that the questions strictly adhered to the objectives of the study. A pre-test was performed on 5% of the sample (19 HCPS) in a different hospital and face validity of the questionnaire was tested. Minor modifications have been made accordingly to avoid ambiguities and improve clarity**.** These participants were not included in the final study.

The prepared self-administered questionnaire contained four different sections. The first section contained demographic information. The second section consists of nine questions used to measure the knowledge of HCPs related to ADR reporting. The third section consisted of ten questions, which assessed participants' attitudes toward ADR reporting. The fourth section is about the practice of ADR reporting. The questionnaires were distributed by two pharmacists in person. The completed questionnaires were then collected by the pharmacists in person at the end of the first, second, third, and fourth weeks. A remainder was provided to non-respondents twice (i.e. at the end of the second week and the end of the third week). If the questionnaires did not return by the end of the fourth week, the participant was considered non-respondent.

Statistical methods

The data were coded, double-entered into Epi data management (version 4.2.0) and statistical analysis was performed using STATA version 14.1 (STATA Corp, TX, USA). Descriptive analysis was computed using mean (SD) and median (IQR) for quantitative variables and frequency for categorical variables. To determine the factors associated with ADR reporting, univariate and multivariate logistic regression tests were used. The dependent variable was ADR reporting, while demographics, knowledge, and attitude were included as the independent variables. Values were considered significant at a p-value of <0.05 ($\alpha=0.05$).

Ethical considerations

The ethical approval and clearance were obtained from the Ethics Review Committee of the School of Pharmacy, College of Health Sciences, Mekelle University (reference number: CHS/161/pharm-11). In addition, a brief description of the objective of the study was provided for all the participants to avoid ambiguity and misunderstanding. The data collection process was initiated after the willingness of the health professionals was requested and formal written consent was obtained.

Patient and Public Involvement

No patient involved

Results

Demographic characteristics

In the current study, 362 questionnaires were distributed. Of these, 307 were duly completed and returned, giving a response rate of 84.8%. Of all respondents, 190 (61.9%) were nurses, 63 (20.5%) were pharmacist, and 54 (17.6%) were physicians. About 50% of respondents have less than five years of experience and more than half of the participants had not received any training on ADRs (table 1).

Table1: Socio-demographic characteristics of respondents at ACSH, Tigray Region, Northern Ethiopia, from January 2019 to March 2019 (n=307)

Variable	Frequency (%)
Sex	
Male	156 (50.8)
Female	151 (49.2)
Age	

<25	63(20.5)
25-34	199(64.8)
≥35	45(14.7)
Mean ± SD	29.1 ± 4.3
Median (range)	28 (23-51)
Profession	
Physician	54 (17.6)
Pharmacy	63 (20.5)
Nurse	190 (61.9)
Work experience (years)	
< 5	156 (50.9)
5-9	121 (40)
≥10	28 (9.1)
Trained on ADR reporting	
Yes	138(44.95)
No	169(55.05)

Knowledge of ADR reporting

There were nine questions assessing knowledge of ADRs. Only 29.3% of respondents knew the exact definition of adverse reactions and 36.8% of respondents knew what to report. A small proportion of respondents (19.5%) were aware of the classification of ADRs. Of the respondents, 39.4% of the respondents felt they were aware of the availability of the National Reporting Center in Ethiopia and a small proportion of the respondents (31.9%) knew where to report. The median with inter-quartile range (IQR) of the level of knowledge of ADRs reporting among HCPs was 4 (3–6). Overall, the majority (58.3%) of health professionals had poor knowledge of ADR reporting (table 2).

Table 2: knowledge of healthcare professionals toward ADR reporting in ACSH, Tigray Region, Northern Ethiopia, from January 2019 to March 2019 (n=307)

Variables	Frequency (%)
Which of the following defines ADR correctly?	
Any noxious or undesired effect of drug occurring at normal dose, during normal use*	90 (29.3)
Adverse health outcomes associated with inappropriate drug use	51 (16.6)
Harm resulting from the use of substandard/counterfeit drugs	26 (8.5)
Harm caused by drug overdose	67 (21.8)
All can define ADR	73 (23.8)
Which ADR should be reported?	
All series ADRs	113 (36.8)
ADRs to herbal and non-allopathic drugs	15 (4.9)
ADRs to new drugs	49 (16.0)
ADRs to vaccines drugs	8 (2.6)
Unknown ADRs to old drugs	9 (2.9)
All of the above*	113 (36.8)
The correct classification of the type of ADR	
Type A,B,C,D,E,and F*	60 (19.5)
Type 1,2,3,4,5,6 and 7	62 (20.2)
Known, unknown and common, uncommon	89 (29.0)
Reversible and irreversible	64 (20.8)
Do not know	31 (10.1)
Is there any center /ADR reporting system in Ethiopia	
Yes	121 (39.4)
No	141 (45.9)
Don't know	45 (14.7)
All ADRs are known before a medicine is marketed.	
Yes	99 (32.2)
No*	168 (54.7)
Don't know	40 (13.0)
Are you aware of any drug that banned due to ADR?	
Yes*	98 (31.9)
No	176 (57.3)
Don't know	33 (10.7)
Where are ADRs reported in Ethiopia?	
Manufacturers	17 (5.5)
Ministry of Health of Ethiopia	68 (22.1)
Ethiopian pharmaceutical association	47 (15.3)

DTC of respective health facility	49 (16.0)
FMHACA*	98 (31.9)
Pharmacy dept	28 (9.1)
Do you think that ADR is the same with side effects?	
Yes	127(41.4)
No*	180(58.6)
Which of the following is the major risk factor for the occurrence of maximum ADRs	
Arthritis	30 (9.8)
Renal failure*	147 (47.9)
Visual impairment	24 (7.8)
All of these	106 (34.5)
Overall knowledge score	
Good	128 (41.7)
Poor	179 (58.3)

ADR: Adverse drug reaction, DTC: drug and therapeutic committee STG: standard treatment guideline DACA: Drug Administration and Control Authority, FMHACA: Food, Medicine and Healthcare Administration and Control Authority, *correct answers

Attitude of health professionals toward ADR reporting

Regarding healthcare professionals' attitudes to ADRs reporting, the majority (67.4%) of respondents agreed that it is necessary to report, while 37.8% agreed that ADRs reporting should be mandatory. Most respondents (51.1%) disagreed with the idea that only prescribed medication should be reported. The median (IQR) of the attitude score of ADRs reporting among HCPs was 20 (17–22). Overall, about 60% of respondents showed a positive attitude towards ADRs reporting (table 3).

Table 3: Attitude of healthcare professionals toward ADR reporting in ACSH, Tigray Region, Northern Ethiopia, from January 2019 to March 2019 (n=307)

Items	Responses		
	Agree, n (%)	Neutral n (%)	Disagree n (%)
ADR reporting is necessary	207 (67.4)	23 (7.5)	77 (25.1)

ADR reporting should be mandatory for all HCPs	116 (37.8)	62 (20.2)	129 (42.0)
ADR reporting increase patient's safety	148 (48.2)	66 (21.5)	93 (30.3)
ADR reporting is important for health care system	135 (44.0)	73 (23.8)	99 (32.2)
There is a need to be sure that ADRs are related to the drug before reporting	194 (63.2)	35 (11.4)	78 (25.4)
Only ADR of prescription drug needs to be reported	82 (26.7)	68 (22.1)	157 (51.1)
One report of ADR makes no differences	103 (33.6)	78 (25.4)	126 (41.0)
The yellow card is difficult to fill up	177 (57.7)	88 (28.7)	42 (13.7)
ADR reporting creates additional workload and it is time consuming	199 (64.8)	78 (25.4)	30 (9.8)
Establishing ADR reporting center in every hospital is important	189 (61.6)	44 (14.3)	74 (24.1)
Overall level of attitude			
Positive	184 (59.9%)		
Negative	123 (40.1%)		

Practices of health professionals about ADR reporting

Of the 307 health professionals, 74.9% encountered ADR in the last 12 months of their clinical practice, and 29.1% of them recorded in patient cards. Although most health care professionals experienced ADR, only 32.1% reported it (table 4).

Table 4: Practice of healthcare professionals toward ADR reporting in ACSH, Tigray Region, Northern Ethiopia, from January 2019 to March 2019 (n=307)

Items	Category	Frequency (%)
Have you ever encountered patient with ADR in your clinical practice in the last 12 months	Yes	230(74.9)
	No	77 (25.1)
How many patients with ADR have you encountered during the last 12 months?	None	77 (25.1)
	One	13 (4.2)
	Two	58 (18.9)
	Three	61 (19.9)

	Four	52 (16.9)
	More than four	46 (15.0)
Have you noted the ADR you encountered on the patient clinical record (n=230)	Yes	67 (29.1)
	No	163 (70.9)
How often do you give advice to your patients on possible ADRs you prescribed, dispensed or administered	Usually	118 (38.4)
	Never	89 (29.0)
	Sometimes	69 (22.5)
	Always	31 (10.1)
If you encountered ADR, have you ever reported the ADR? (n=230)	Yes (good practice)	74 (32.1)
	No (poor practice)	156 (67.9)

Factors associated with poor ADR reporting practice

A univariable logistic regression analysis was performed to determine the association of each variable with the practice of ADR reporting. In the univariable analysis work experience of the HCPs (≥10 years) (unadjusted odds ratios (OR) = 0.31, 95% CI: 0.15- 0.64), negative attitude (unadjusted OR = 2.08, 95% CI: 1.17-3.72), poor knowledge (unadjusted OR= 3.49, 95% CI: 1.95-6.23), lack of training on ADR reporting (unadjusted OR= 7.67, 95% CI: 4.07- 14.46), and nursing profession (unadjusted OR= 2.11, 95% CI: 1.06- 4.20), were associated with poor ADR reporting practice. A subsequent multivariable logistic regression model was conducted to identify the independent predictors. The full model containing all predictors was statistically significant (X^2 = 69.78, df = 10, P-value < 0.001). The results of the multivariate logistic regression indicated that only work experience of the HCPs (≥10 years) (adjusted odds ratios (AOR)= 0.36, 95% CI: 0.13-0.97), poor knowledge (AOR= 2.63, 95% CI: 1.26- 5.45), and lack of training on ADR reporting (AOR= 7.31, 95% CI: 3.42- 15.62) were the predictors of poor ADR reporting practice (table 5).

Table 5: Univariable and multivariable logistic regression analysis of associated factors of poor ADR reporting practice in Tigray Region, Ethiopia from January 2019 to March 2019 (n=230)

Variable	ADR reporting practice		P value	COR (95% CI)	AOR (95% CI)	P value
	Yes, n (%)	No, n (%)				
Gender						
Male	44 (59.5)	73 (46.8)		1	1	
Female	30 (40.5)	83 (53.2)	0.07	1.67(0.95, 2.92)	1.51(0.77, 2.94)	0.23
Age (years)						
<25	15(20.3)	29(18.6)		1		
25-34	48(64.9)	100(64.1)	0.84	1.09(0.53, 2.19)	1.22(0.46, 3.23)	0.68
≥35	11(14.9)	27(17.3)	0.12	1.27(0.49, 3.24)	3.40(0.93, 12.48)	0.07
Experience (years)						
< 5	27(36.5)	84(53.8)		1	1	
5-9	24(32.4)	50(32.1)	0.23	0.67(0.35, 1.28)	1.42(0.57, 3.52)	0.45
≥10	23(31.1)	22(14.1)	0.001	0.31(0.15, 0.64)	0.36(0.13, 0.97)	0.04
Profession						
Pharmacist	20(27.0)	26(16.7)		1	1	
Physician	16(21.6)	26(16.7)	0.61	1.25(0.53, 2.93)	2.15(0.70, 6.56)	0.18
Nurse	38(51.4)	104(66.7)	0.04	2.11(1.06, 4.20)	1.36(0.57, 3.26)	0.49
Attitude						
Positive	50(67.6)	78(50)		1	1	
Negative	24(32.4)	78(50)	0.01	2.08 (1.17, 3.72)	1.24(0.59, 2.59)	0.57
Knowledge						
Good	48(64.9)	54(34.6)		1	1	
Poor	26(35.1)	102 (65.4)	<0.001	3.49(1.95, 6.23)	2.63(1.26, 5.45)	0.01
Training provided						
Yes	56(75.7)	45(28.8)		1	1	
No	18(24.3)	111(71.2)	<0.001	7.67(4.07, 14.46)	7.31(3.42, 15.62)	<0.001

ADR: adverse drug reaction, AOR: adjusted odds ratio, COR: crude odds ratio

Discussion

One of the main goals of this study was to investigate the knowledge of HCPs towards ADRs reporting. This issue is critical for research to identify the necessary interventions, as HCPs cannot effectively participate in the reporting without sufficient knowledge of the ADR and its reporting process. We found that only 41.7 % of HCPs had good knowledge about ADR reporting, similar to the reports seen in Amhara region of Ethiopia (47%) [21] and West Ethiopia (48 %) [22]. The reason for insufficient knowledge of ADRs reporting in these studies may be due to the poor access to information about ADR reporting and the lack of adequate training in this area, which allows them to acquire and integrate their knowledge of ADR reporting throughout the course of their clinical service [21, 23]. In addition, the low level of knowledge could be the result of insufficient provision of undergraduate training in pharmacovigilance, which may help prepare HCPs for the task of ADRs monitoring and reporting in their future careers. The lack of continuous medical education in this area could also contribute to poor knowledge of ADRs reporting.

The level of knowledge of ADRs reporting in our study was also lower compared to previous findings reported in the Philippines (77%) [24] and Kuwait (61.5%) [25]. This discrepancy may be due to differences in government involvement in national pharmacovigilance programs, study participants, and training level. The current study was conducted in a system where national ADR reporting methods were in its infancy and most HCPs (55%) did not receive any ADR reporting training.

Our study showed that 39.4% of HCPs were aware of the existence of an ADR system in Ethiopia. This meant that most of the participants did not have information about the authority responsible for monitoring ADR in Ethiopia. This is similar to the study conducted in Addis Ababa, Saudi Arabia, and Jordan, which reported lack of knowledge about the national ADR reporting system

[26-28]. This is a critical observation, which is undoubtedly related to the current underreporting of ADRs. In addition, only 31.9 % of the HCPs know where to report ADR. This could be as a result of limited awareness and support for ADR monitoring. Awareness-raising programs through advertising would appear necessary to improve ADRs reporting in our setting.

Regarding the level of attitude, we found that about 60 % of HCPs had a positive attitude on ADR and its reporting. Although the majority of the respondents had positive attitude, the result is lower compared to previous findings in Amhara region of Ethiopia (86%) [21]. This shows though there is some positivity in the attitude of HCPs towards ADRs reporting, the attitude level still could be enhanced. Most respondents (67.4%) felt that adverse reactions reporting is necessary, which is consistent with previous studies [20, 21]. However, 64.8% of the respondents agreed that reporting creates an additional workload, which is higher than the results obtained in the Amhara region (32.4%) [21]. Although it may take some time to complete the report forms, the high proportion of respondents with such perception found in our study may affect the motivation to report adverse reactions. Healthcare professionals should consider ADRs reporting as an obligation and should be aware of the existing pharmacovigilance systems.

Another important finding was that ADRs reporting practices among HCPs were very poor. Although more than 75% of respondents encountered one or more ADRs in their daily practice, only 32.1% of respondents reported ADRs. This is consistent with a study conducted in Amhara Region of Ethiopia and south India [29, 30]. Insufficient promotion of ADR reporting, poor distribution of ADR reporting forms, lack of knowledge, and lack of training were mentioned as factors for major cause of underreporting [12, 21].

The study also identified the predictors of poor ADR reporting practices. Less experienced HCPs were more likely to have poor ADR reporting practices. This finding is consistent with a study

conducted in Uganda, where more experienced HCPs were four times more likely to have ever reported than less experienced professionals [30]. Health professionals with poor knowledge were more likely to have a poor practice of ADRs reporting. The association of poor knowledge levels of health professionals with poor ADR reporting practice has been observed in many similar previous studies [30-34]. Moreover, health professionals who had not received ADRs reporting training were more likely to have poor practice. This is also supported by a study carried out in Spain [35]. However, only 44.95% of the respondents were trained in our study. Similarly, HCPs have shown limited training in areas of ADR and their reporting in studies conducted in Sudan [32] and Uganda [30]. Thus, more training regarding the identification of ADR, the purpose of the ADR reporting, and the availability of resources for ADR reporting is required.

These findings have important implications. The low level of knowledge of the ADR and its reporting among HCPs should be enhanced by designing different strategies. A systematic review of strategies to improve ADRs reporting has shown that multiple interventions appear to have had more impact than single interventions [13]. Several studies have shown improved knowledge and attitude scores after educational interventions, including oral workshops, oral presentations, group discussions, designing ADR newsletters in hospitals, and ongoing training in pharmacovigilance and ADR reporting [36-40]. Other studies have shown that ADRs reporting has been improved by offering incentives to health professionals [41, 42]. A study conducted in Spanish that involves both economic incentives and educational activities, resulted in up to a six-fold increase in the average ADR reporting [43]. Increasing the availability of yellow cards on wards as well as encouragement to use web-based reporting had improved reporting rates [44]. Therefore, empowering HCPs in detecting and reporting suspected drug reactions and using strategies that

are evidence-based is essential to strengthening pharmacovigilance systems in Ethiopia. This is especially important for less experienced health professionals and for those who had never received training on ADR reporting. However, additional research needs to be done to investigate the impact of these interventions on the knowledge and practice of ADR reporting in our setting.

Finally, there are several limitations to this study. We used a self-report as the main method of inquiry, which may have introduced recall bias. The HCPs may have made explicit responses to the fear that they would be embarrassed if they did not report ADRs. However, because we used self-administered questionnaires without respondents' names, the potential for this bias was reduced. The cross-sectional design we used may not establish a causal relationship between ADR reporting and explanatory variables. Finally, the study was conducted in a tertiary referral hospital and may not be generalized for all HCPs in different health care levels in the country. Despite these limitations, our study has generated important insights on knowledge, attitude, and practice of ADR reporting and predictors of poor ADRs reporting practice.

Conclusion

The majority of health professionals had poor knowledge and practice, but a positive attitude toward ADRs reporting. Poor knowledge, less work experience and lack of training were predictors of poor ADR reporting practice. Therefore, strategies to improve knowledge and practices regarding ADR reporting should be implemented. Training should be provided to all HCPs, especially those who have never received training and less experienced professionals.

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Data Availability

The dataset of this study is available from the corresponding author upon request.

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Conflicts of Interest

The authors have declared that there is no conflict of interests with respect to the authorship and/or publication of this study.

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	*5*
Study size	10	Explain how the study size was arrived at	4 and 5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	--
		(*c*) Explain how missing data were addressed	--
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	--
		(*e*) Describe any sensitivity analyses	--
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	---
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	--
Outcome data	15*	Report numbers of outcome events or summary measures	7-10
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11
		(*b*) Report category boundaries when continuous variables were categorized	12
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	---
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	---
Discussion			
Key results	18	Summarise key results with reference to study objectives	13 and 14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Healthcare professionals knowledge, attitude and practice of adverse drug reactions reporting in Ethiopia: a cross-sectional study

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Healthcare professionals knowledge, attitude and practice of adverse drug reactions reporting in Ethiopia: a cross-sectional study

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Abstract

Objective: This study aimed to assess the knowledge, attitude, and practice of adverse drug reactions (ADRs) reporting and identify factors associated with ADRs reporting among healthcare professionals (HCPs) working in Tigray region, Ethiopia.

Materials and Methods: A cross-sectional study was conducted between January and March of 2019 in a tertiary care hospital in Tigray region, Ethiopia. A self-administered, pretested questionnaire was administered to HCPs. Data were summarized using descriptive statistics. Logistic regression analysis was used to identify factors associated with poor ADRs reporting practices.

Results: In total, 362 questionnaires were distributed, and the response rate was 84.8% (n = 307). Of all respondents, 190 (61.9%) were nurses, 63 (20.5%) were pharmacist, and 54 (17.6%) were physicians. About 58.3% of HCPs had poor knowledge of ADRs reporting. The majority of the respondents had a positive attitude (59.9%), and only a few (32.1%) respondents have good ADRs reporting practices. Poor knowledge (Adjusted odds ratio (AOR)= 2.63, 95% confidence interval (CI): 1.26- 5.45), and lack of training on ADRs reporting (AOR= 7.31, 95%

CI: 3.42- 15.62) were both negatively associated with ADRs reporting practice, whereas higher work experience (≥10 years) (AOR= 0.36, 95% CI: 0.13- 0.97) were positively associated with ADRs reporting practice.

Conclusions: The majority of healthcare professionals had poor knowledge and practice, but a positive attitude toward ADRs reporting. Poor knowledge, less work experience and lack of training were associated with poor ADRs reporting practice. Hence, strategies to improve the knowledge and practice of ADRs reporting should be implemented, particularly for untrained and less experienced HCPs.

Keywords: Adverse drug reaction, healthcare professionals, knowledge, practice

Strengths and limitations of this study

- As strengths, this study included a good number of HCPs and includes nurses and pharmacists as well as physicians.
- Data collection was conducted prospectively and adjustment for confounding factors was performed with logistic regression analysis.
- There is a possibility that HCPs may not report their actual ADRs reporting practices since the information was self-reported.
- The cross-sectional design of this study may not establish a causal relationship between ADRs reporting and explanatory variables.
- Our study was conducted in a single center and may not be generalizable to HCPs in other hospitals.

Introduction

Adverse drug reactions (ADRs) are a major cause of morbidity and mortality and contribute to the occurrence of adverse events, leading to increased healthcare costs [1]. ADRs have become a major public health problem in developing countries [2]. The median prevalence (with interquartile range [IQR]) of ADR-related hospitalization in developing countries was 5.5% (1.1-16.9) [3]. The information collected during the pre-marketing phase of drug development is inevitably incomplete concerning possible ADRs. This is due to the participation of a limited and selected number of patients who are studied before marketing, the conditions of drug use in clinical trials are different from those of clinical practice, the duration of the clinical trials is short, and high-risk patients (such as elderly patients) are often excluded [4]. Therefore, post-marketing surveillance is important to allow detection of less common, but sometimes very serious ADRs. Once a drug is registered and marketed, adverse reaction studies can be conducted using a variety of methods, such as observational studies, monitoring of prescription events, spontaneous reports and so on [5]. However, the health care system relies heavily on spontaneous ADRs reporting to monitor drug safety throughout the population during actual use [6].

A spontaneous reporting system of ADRs is fundamental to effectively discover new adverse reactions but under-reporting is its major limitations [7, 8]. A systematic review of studies conducted in the European Union showed a significant and widespread healthcare professionals under-reporting of ADRs with a median rate of under-reporting of 94% [7]. The low rates of ADRs reporting may delay regulatory actions to remove drugs with an unacceptable safety profile from the marketplace. A worldwide systematic review of 462 medicines removed from the market for safety reasons showed that the median interval between the first reported adverse reaction and the

year of first withdrawal was 6 years (IQR, 1-15) and the interval did not consistently shorten over time [9].

Healthcare professionals (HCPs) are responsible for identifying, documenting and ADRs reporting. Their contribution to the early detection and reporting of ADR is essential [10]. However, ADR reporting is affected by many factors, including lack of awareness, ambiguity about who should report, difficulties with reporting procedures, lack of feedback on submitted reports, rapid resolution of adverse events, and so on [11, 12]. The knowledge and attitudes of health professionals are strongly related to ADRs reporting [8, 13]. Therefore, it is very important to understand the knowledge and practice of health care providers related to ADR reporting to improve reporting practices [14].

Although local regulatory authorities can make drug safety decisions using ADR data from other countries, it is essential to take into account a number of factors, such as local population traditions, genetics, diet, environmental factors, etc [15]. Therefore, it is very important to establish a local functional ADR monitoring center. Ethiopia established its own pharmacovigilance system under the Food and Drug Administration and control authority in 2002. Since the introduction of the pharmacovigilance system, only a small number of ADRs have been reported to the center [16]. Besides, studies on identifying factors and reasons for poor reporting practices are limited in our context. The aim of this study was therefore to determine the knowledge, attitudes, and practices of ADRs reporting and to identify predictive factors for poor ADR reporting practices among health professionals in a tertiary hospital in the Tigray region, Ethiopia.

Materials and Methods

Study setting and period

The study was conducted at Ayder comprehensive specialized hospital (ACSH), Tigray region, Northern Ethiopia. ACSH is a teaching and referral hospital with 500 beds. The hospital serves more than 9 million people in the catchment area. ACSH provides all the specialized and non-specialized hospital services including emergency services, outpatient services, and inpatient services. Healthcare professionals working in all of these areas were included in this study between January and March of 2019.

Study design and population

An institutional-based cross-sectional study was conducted. The target populations for this study were nurses, physicians, and pharmacists working in ACSH during the study periods. Healthcare professionals who were refused or did not wish to participate in the study were excluded.

Sample Size Determination and sampling technique

The sample size was calculated using a single proportion sample size estimating formula

$$n = \frac{\left(z_{1-\alpha/2}\right)^2 P(1-P)}{d^2} = \frac{(1.96)^2 0.66(1-0.66)}{0.05^2} = 344.8 \approx 345$$

Where, n = sample size, Z = confidence interval (1.96) p = The proportion of health care professionals with poor knowledge of ADR reporting (65.8, p= 0.66), obtained from a study conducted in Amhara region of Ethiopia [17], and d = Margin of error to be tolerated (0.05). By adding 5% (345x0.05 = 17) of the sample size to compensate non-respondents, the total sample size required was 362. Subjects were recruited using stratified random sampling technique. A list of HCPs (pharmacists, physicians, and nurses) working at the hospital was obtained from the hospital's human resources department. All HCPs were first stratified according to the type of profession and this list was used as a sampling frame. Depending on

the size of the profession in each category of HCPs, participants were randomly selected. We used a lottery method to randomly select a set of healthcare professionals as respondents from each category. We used this lottery method from the complete list of each category assuming that all the HCPs working in a similar profession (for example, all physicians) in different departments and/or units were homogeneous with respect to knowledge, attitude, and practice of ADRs reporting.

Outcome measures

In this survey, knowledge of ADR reporting was assessed using nine questions containing general knowledge about ADR and ADR reporting. Each correct answer had a score of 1 and each wrong answer had a score of 0. Thus, the total score ranged from 0 to 9 points. The overall level of knowledge was categorized using the median score. Participants with above median scores were classified as having good knowledge and below the median scores were classified as having poor knowledge. Participants' attitudes were assessed using ten items rated as agreeing, neutral, and disagreeing on a three-point Likert scale. The "agree" responses received a score of 3, "neutral" a score of 2, and "disagree" a score of 1. An inverted score was made for the negative-worded questions. Therefore, the maximum possible attitude score was 30. The median attitude score was calculated for each respondent, on the basis of which their attitude was categorized as positive and negative. The level of practice of health professionals was assessed by determining whether they had encountered, documented and reported ADRs or not. Participants were classified as having good practice if they had reported one or more ADRs and poor practices, if they had never reported ADR, despite encountering ADRs.

Data collection

The Data Collection Tool is a questionnaire that was adopted from similar previous studies on the knowledge, attitudes, and practices of health care professionals on ADR reporting [18-20].

The questionnaire was reviewed for its content validity by consensus of a panel of three experts in the field derived from academia (one expert from pharmacoepidemiology and two experts from clinical pharmacy departments). The Index of consistency of the questionnaires was 0.86, suggesting that the questions strictly adhered to the objectives of the study. A pre-test was performed on 5% of the sample (19 HCPS) in a different hospital and face validity of the questionnaire was tested. Minor modifications have been made accordingly to avoid ambiguities and improve clarity**.** These participants were not included in the final study.

The prepared self-administered questionnaire contained four different sections. The first section contained demographic information. The second section consists of nine questions used to measure the knowledge of HCPs related to ADR reporting. The third section consisted of ten questions, which assessed participants' attitudes toward ADR reporting. The fourth section is about the practice of ADR reporting. The questionnaires were distributed by two pharmacists in person. The completed questionnaires were then collected by the pharmacists in person at the end of the first, second, third, and fourth weeks. A remainder was provided to non-respondents twice (i.e. at the end of the second week and the end of the third week). If the questionnaires did not return by the end of the fourth week, the participant was considered non-respondent.

Statistical methods

The data were coded, double-entered into Epi data management (version 4.2.0) and statistical analysis was performed using STATA version 14.1 (STATA Corp, TX, USA). Descriptive analysis was computed using mean (SD) and median (IQR) for quantitative variables and frequency for categorical variables. To determine the factors associated with ADR reporting,

univariate and multivariate logistic regression tests were used. The dependent variable was ADR reporting, while demographics, knowledge, and attitude were included as the independent variables. Values were considered significant at a p-value of <0.05 (α=0.05).

Ethical considerations

The ethical approval and clearance were obtained from the Ethics Review Committee of the School of Pharmacy, College of Health Sciences, Mekelle University (reference number: CHS/161/pharm-11). In addition, a brief description of the objective of the study was provided for all the participants to avoid ambiguity and misunderstanding. The data collection process was initiated after the willingness of the health professionals was requested and formal written consent was obtained.

Patient and Public Involvement

As the study focused on the knowledge, attitudes and practices of healthcare professionals, patients or members of the public were not directly involved in the design or planning of this research study.

Results

Demographic characteristics

In the current study, 362 questionnaires were distributed. Of these, 307 were duly completed and returned, giving a response rate of 84.8%. Of all respondents, 190 (61.9%) were nurses, 63 (20.5%) were pharmacist, and 54 (17.6%) were physicians. About 50% of respondents have less than five

years of experience and more than half of the participants had not received any training on ADRs (table 1).

Table1: Socio-demographic characteristics of respondents at ACSH, Tigray Region, Northern Ethiopia, from January 2019 to March 2019 (n=307)

Variable	Frequency (%)
Sex	
Male	156 (50.8)
Female	151 (49.2)
Age	
<25	63(20.5)
25-34	199(64.8)
≥35	45(14.7)
Mean ± SD	29.1 ± 4.3
Median (range)	28 (23-51)
Profession	
Physician	54 (17.6)
Pharmacy	63 (20.5)
Nurse	190 (61.9)
Work experience (years)	
< 5	156 (50.9)
5-9	121 (40)
≥10	28 (9.1)
Trained on ADR reporting	
Yes	138(44.95)
No	169(55.05)

Knowledge of ADR reporting

There were nine questions assessing knowledge of ADRs. Only 29.3% of respondents knew the exact definition of adverse reactions and 36.8% of respondents knew what to report. A small

proportion of respondents (19.5%) were aware of the classification of ADRs. Of the respondents, 39.4% of the respondents felt they were aware of the availability of the National Reporting Center in Ethiopia and a small proportion of the respondents (31.9%) knew where to report. The median with inter-quartile range (IQR) of the level of knowledge of ADRs reporting among HCPs was 4 (3–6). Overall, the majority (58.3%) of health professionals had poor knowledge of ADR reporting (table 2).

Table 2: knowledge of healthcare professionals toward ADR reporting in ACSH, Tigray Region, Northern Ethiopia, from January 2019 to March 2019 (n=307)

Variables	Frequency (%)
Which of the following defines ADR correctly?	
Any noxious or undesired effect of drug occurring at normal dose, during normal use*	90 (29.3)
Adverse health outcomes associated with inappropriate drug use	51 (16.6)
Harm resulting from the use of substandard/counterfeit drugs	26 (8.5)
Harm caused by drug overdose	67 (21.8)
All can define ADR	73 (23.8)
Which ADR should be reported?	
All series ADRs	113 (36.8)
ADRs to herbal and non-allopathic drugs	15 (4.9)
ADRs to new drugs	49 (16.0)
ADRs to vaccines drugs	8 (2.6)
Unknown ADRs to old drugs	9 (2.9)
All of the above*	113 (36.8)
The correct classification of the type of ADR	
Type A,B,C,D,E,and F*	60 (19.5)
Type 1,2,3,4,5,6 and 7	62 (20.2)
Known, unknown and common, uncommon	89 (29.0)
Reversible and irreversible	64 (20.8)
Do not know	31 (10.1)
Is there any center /ADR reporting system in Ethiopia	
Yes	121 (39.4)
No	141 (45.9)
Don't know	45 (14.7)
All ADRs are known before a medicine is marketed.	

Yes	99 (32.2)
No*	168 (54.7)
Don't know	40 (13.0)
Are you aware of any drug that banned due to ADR?	
Yes*	98 (31.9)
No	176 (57.3)
Don't know	33 (10.7)
Where are ADRs reported in Ethiopia?	
Manufacturers	17 (5.5)
Ministry of Health of Ethiopia	68 (22.1)
Ethiopian pharmaceutical association	47 (15.3)
DTC of respective health facility	49 (16.0)
FMHACA*	98 (31.9)
Pharmacy dept	28 (9.1)
Do you think that ADR is the same with side effects?	
Yes	127(41.4)
No*	180(58.6)
Which of the following is the major risk factor for the occurrence of maximum ADRs	
Arthritis	30 (9.8)
Renal failure*	147 (47.9)
Visual impairment	24 (7.8)
All of these	106 (34.5)
Overall knowledge score	
Good	128 (41.7)
Poor	179 (58.3)

ADR: Adverse drug reaction, DTC: drug and therapeutic committee STG: standard treatment guideline DACA: Drug Administration and Control Authority, FMHACA: Food, Medicine and Healthcare Administration and Control Authority, *correct answers

Attitude of health professionals toward ADR reporting

Regarding healthcare professionals' attitudes to ADRs reporting, the majority (67.4%) of respondents agreed that it is necessary to report, while 37.8% agreed that ADRs reporting should be mandatory. Most respondents (51.1%) disagreed with the idea that only prescribed medication should be reported. The median (IQR) of the attitude score of ADRs reporting among HCPs was

20 (17–22). Overall, about 60% of respondents showed a positive attitude towards ADRs reporting (table 3).

Table 3: Attitude of healthcare professionals toward ADR reporting in ACSH, Tigray Region, Northern Ethiopia, from January 2019 to March 2019 (n=307)

Items	Responses		
	Agree, n (%)	Neutral n (%)	Disagree n (%)
ADR reporting is necessary	207 (67.4)	23 (7.5)	77 (25.1)
ADR reporting should be mandatory for all HCPs	116 (37.8)	62 (20.2)	129 (42.0)
ADR reporting increase patient's safety	148 (48.2)	66 (21.5)	93 (30.3)
ADR reporting is important for health care system	135 (44.0)	73 (23.8)	99 (32.2)
There is a need to be sure that ADRs are related to the drug before reporting	194 (63.2)	35 (11.4)	78 (25.4)
Only ADR of prescription drug needs to be reported	82 (26.7)	68 (22.1)	157 (51.1)
One report of ADR makes no differences	103 (33.6)	78 (25.4)	126 (41.0)
The yellow card is difficult to fill up	177 (57.7)	88 (28.7)	42 (13.7)
ADR reporting creates additional workload and it is time consuming	199 (64.8)	78 (25.4)	30 (9.8)
Establishing ADR reporting center in every hospital is important	189 (61.6)	44 (14.3)	74 (24.1)
Overall level of attitude			
Positive	184 (59.9%)		
Negative	123 (40.1%)		

Practices of health professionals about ADR reporting

Of the 307 health professionals, 74.9% encountered ADR in the last 12 months of their clinical practice, and 29.1% of them recorded in patient cards. Although most health care professionals experienced ADR, only 32.1% reported it (table 4).

Table 4: Practice of healthcare professionals toward ADR reporting in ACSH, Tigray Region, Northern Ethiopia, from January 2019 to March 2019 (n=307)

Items	Category	Frequency (%)
Have you ever encountered patient with ADR in your clinical practice in the last 12 months	Yes	230(74.9)
	No	77 (25.1)
How many patients with ADR have you encountered during the last 12 months?	None	77 (25.1)
	One	13 (4.2)
	Two	58 (18.9)
	Three	61 (19.9)
	Four	52 (16.9)
	More than four	46 (15.0)
Have you noted the ADR you encountered on the patient clinical record (n=230)	Yes	67 (29.1)
	No	163 (70.9)
How often do you give advice to your patients on possible ADRs you prescribed, dispensed or administered	Usually	118 (38.4)
	Never	89 (29.0)
	Sometimes	69 (22.5)
	Always	31 (10.1)
If you encountered ADR, have you ever reported the ADR? (n=230)	Yes (good practice)	74 (32.1)
	No (poor practice)	156 (67.9)

Factors associated with poor ADR reporting practice

A univariable logistic regression analysis was performed to determine the association of each variable with the practice of ADR reporting. In the univariable analysis work experience of the HCPs (≥10 years) (unadjusted odds ratios (OR) = 0.31, 95% CI: 0.15- 0.64), negative attitude (unadjusted OR = 2.08, 95% CI: 1.17-3.72), poor knowledge (unadjusted OR= 3.49, 95% CI: 1.95-6.23), lack of training on ADR reporting (unadjusted OR= 7.67, 95% CI: 4.07- 14.46), and nursing profession (unadjusted OR= 2.11, 95% CI: 1.06- 4.20), were associated with poor ADR reporting

practice. A subsequent multivariable logistic regression model was conducted to identify the independent predictors. The full model containing all predictors was statistically significant (X^2 = 69.78, df = 10, P-value < 0.001). The results of the multivariate logistic regression indicated that only work experience of the HCPs (≥10 years) (adjusted odds ratios (AOR)= 0.36, 95% CI: 0.13-0.97), poor knowledge (AOR= 2.63, 95% CI: 1.26- 5.45), and lack of training on ADR reporting (AOR= 7.31, 95% CI: 3.42- 15.62) were the predictors of poor ADR reporting practice (table 5).

Table 5: Univariable and multivariable logistic regression analysis of associated factors of poor ADR reporting practice in Tigray Region, Ethiopia from January 2019 to March 2019 (n=230)

Variable	ADR reporting practice		P value	Unadjusted OR (95% CI)	AOR (95% CI)	P value
	good, n (%)	poor, n (%)				
Gender						
Male	44 (59.5)	73 (46.8)		1	1	
Female	30 (40.5)	83 (53.2)	0.07	1.67(0.95, 2.92)	1.51(0.77, 2.94)	0.23
Age (years)						
<25	15(20.3)	29(18.6)		1		
25-34	48(64.9)	100(64.1)	0.84	1.09(0.53, 2.19)	1.22(0.46, 3.23)	0.68
≥35	11(14.9)	27(17.3)	0.12	1.27(0.49, 3.24)	3.40(0.93, 12.48)	0.07
Experience (years)						
< 5	27(36.5)	84(53.8)		1	1	
5-9	24(32.4)	50(32.1)	0.23	0.67(0.35, 1.28)	1.42(0.57, 3.52)	0.45
≥10	23(31.1)	22(14.1)	0.001	0.31(0.15, 0.64)	0.36(0.13, 0.97)	0.04
Profession						
Pharmacist	20(27.0)	26(16.7)		1	1	
Physician	16(21.6)	26(16.7)	0.61	1.25(0.53, 2.93)	2.15(0.70, 6.56)	0.18
Nurse	38(51.4)	104(66.7)	0.04	2.11(1.06, 4.20)	1.36(0.57, 3.26)	0.49
Attitude						
Positive	50(67.6)	78(50)		1	1	

Negative	24(32.4)	78(50)	0.01	2.08 (1.17, 3.72)	1.24(0.59, 2.59)	0.57
Knowledge						
Good	48(64.9)	54(34.6)		1	1	
Poor	26(35.1)	102 (65.4)	<0.001	3.49(1.95, 6.23)	2.63(1.26, 5.45)	0.01
Training provided						
Yes	56(75.7)	45(28.8)		1	1	
No	18(24.3)	111(71.2)	<0.001	7.67(4.07, 14.46)	7.31(3.42, 15.62)	<0.001

ADR: adverse drug reaction, AOR: adjusted odds ratio, Unadjusted OR: unadjusted odds ratio

Discussion

One of the main goals of this study was to investigate the knowledge of HCPs towards ADRs reporting. This issue is critical for research to identify the necessary interventions, as HCPs cannot effectively participate in the reporting without sufficient knowledge of the ADR and its reporting process. We found that only 41.7 % of HCPs had good knowledge about ADR reporting, similar to the reports seen in Amhara region of Ethiopia (47%) [21]. Lack of training on ADRs reporting was significantly associated with insufficient knowledge of ADRs reporting in a study conducted in the Amhara region (p =0.037) [21]. Similarly, in our study, more than half of the participants were untrained, which can lead to insufficient knowledge of the ADRs reporting. This represents an important issue that needs to be addressed, the pharmacovigilance center in Ethiopia should provide training for health care professionals. Our study showed that 39.4% of HCPs were aware of the existence of an ADR system in Ethiopia. This meant that most of the participants did not have information about the authority responsible for monitoring ADRs in Ethiopia. Similarly, lack of knowledge about the national ADR reporting system were reported in different regions of Ethiopia, including a study in Nekemte town which reported that only 30.8% of the HCPs knew the responsible body for ADRs reporting and in Amhara region that reported 49% of the HCPs

knew the national ADR reporting system [21, 22]. This is a critical observation, which is undoubtedly related to the current underreporting of ADRs.

Regarding the level of attitude, we found that about 60 % of HCPs had a positive attitude on ADR and its reporting. Although the majority of the respondents had positive attitude, the result is lower compared to previous findings in Amhara region of Ethiopia (86%) by Seid et al [21]. This difference could be due to differences in the measure of attitude in the two studies. In the study by Seid et al., an arbitrary cut-off value greater than 75% was used to classify participants with a positive or negative attitude while using the median value in our study. Most respondents (67.4%) felt that adverse reactions reporting is necessary, which is consistent with previous studies [20, 21]. However, 64.8% of the respondents agreed that reporting creates an additional workload, which is higher than the results obtained in the Amhara region (32.4%) [21]. Although it may take some time to complete the report forms, the high proportion of respondents with such perception found in our study may affect the motivation to report adverse reactions. Healthcare professionals should consider ADRs reporting as an obligation and should be aware of the existing pharmacovigilance systems.

Another important finding was that ADRs reporting practices among HCPs were very poor. Although more than 75% of respondents encountered one or more ADRs in their daily practice, only 32.1% of respondents reported ADRs. This is consistent with a study conducted in west Ethiopia which found only 38.8 % of the participants reported ADRs [22]. Many factors were mentioned as a reasons for under reporting of ADRs. A study in eastern Ethiopia found that unavailability of reporting form (53.9%), uncertainty of how to report (51.9%), and lack of feedback from the responsibe body (41%) were the reasons for under reporting [20]. Similarly, lack of awareness and knowledge on what, when, and to whom to report ADRs (30.8%) and lack

of commitments from HCPs(25.5%) were the reason for under reporting of ADRs in a study in West Ethiopia [22].

The study also identified the predictors of poor ADR reporting practices. Less experienced HCPs were more likely to have poor ADR reporting practices. This finding is consistent with a study conducted in Uganda, where more experienced HCPs were four times more likely to have ever reported than less experienced professionals [23]. Health professionals with poor knowledge were more likely to have a poor practice of ADRs reporting. The association of poor knowledge levels of health professionals with poor ADR reporting practice has been observed in many similar previous studies [23-27]. Moreover, health professionals who had not received ADRs reporting training were more likely to have poor practice. This is also supported by a study carried out in Spain [28]. However, only 44.95% of the respondents were trained in our study. Similarly, HCPs have shown limited training in areas of ADR and their reporting in studies conducted in Sudan [25] and Uganda [23]. Thus, more training regarding the identification of ADR, the purpose of the ADR reporting, and the availability of resources for ADR reporting is required.

These findings have important implications. The low level of knowledge of the ADR and its reporting among HCPs should be enhanced by designing different strategies. A systematic review of strategies to improve ADRs reporting has shown that multiple interventions appear to have had more impact than single interventions [13]. Several studies have shown improved knowledge and attitude scores after educational interventions, including oral workshops, oral presentations, group discussions, designing ADR newsletters in hospitals, and ongoing training in pharmacovigilance and ADR reporting [29-33]. Other studies have shown that ADRs reporting has been improved by offering incentives to health professionals [34, 35]. A study conducted in Spanish that involves

both economic incentives and educational activities, resulted in up to a six-fold increase in the average ADR reporting [36]. Increasing the availability of yellow cards on wards as well as encouragement to use web-based reporting had improved reporting rates [37]. Therefore, empowering HCPs in detecting and reporting suspected drug reactions and using strategies that are evidence-based is essential to strengthening pharmacovigilance systems in Ethiopia. This is especially important for less experienced health professionals and for those who had never received training on ADR reporting. However, additional research needs to be done to investigate the impact of these interventions on the knowledge and practice of ADR reporting in our setting.

Finally, there are several limitations to this study. We used a self-report as the main method of inquiry, which may have introduced recall bias. The HCPs may have made explicit responses to the fear that they would be embarrassed if they did not report ADRs. However, because we used self-administered questionnaires without respondents' names, the potential for this bias was reduced. The cross-sectional design we used may not establish a causal relationship between ADR reporting and explanatory variables. Finally, the study was conducted in a tertiary referral hospital and may not be generalized for all HCPs in different health care levels in the country. Despite these limitations, our study has generated important insights on knowledge, attitude, and practice of ADR reporting and predictors of poor ADRs reporting practice.

Conclusion

The majority of health professionals had poor knowledge and practice, but a positive attitude toward ADRs reporting. Poor knowledge, less work experience and lack of training were predictors of poor ADR reporting practice. Therefore, strategies to improve knowledge and

practices regarding ADR reporting should be implemented. Training should be provided to all HCPs, especially those who have never received training and less experienced professionals.

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Contributors: KG and MS conceived the study and drafted the manuscript and contributed to data entry, data analysis, draft manuscript and final proof reading. BYH, SWA and YLN participated in study design, data analysis and in the process of manuscript writing. All authors approved the final manuscript.

Data Availability

The dataset of this study is available from the corresponding author upon request.

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Competing interest

None declared

Patient consent for publication

Not required

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	*5*
Study size	10	Explain how the study size was arrived at	4 and 5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	--
		(*c*) Explain how missing data were addressed	--
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	--
		(*e*) Describe any sensitivity analyses	--
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	---
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	--
Outcome data	15*	Report numbers of outcome events or summary measures	7-10
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11
		(*b*) Report category boundaries when continuous variables were categorized	12
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	---
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	---
Discussion			
Key results	18	Summarise key results with reference to study objectives	13 and 14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.