

Healthcare professionals' pharmacovigilance knowledge and adverse drug reaction reporting behavior and factors determining the reporting rates

Müberra Devrim Güner^a and Perihan Elif Ekmekci^b

^aDepartment of Medical Pharmacology, TOBB ETU Medical School, Ankara, Turkey; ^bDepartment of History of Medicine and Ethics, TOBB ETU Medical School, Ankara, Turkey

ABSTRACT

Background: Spontaneous adverse drug reaction (ADR) reports prepared by healthcare professionals (HCPs) are the backbone of collecting post-marketing safety data. However, underreporting is a global problem creating health, economic, and ethical burden.

Objectives: To determine the factors limiting ADR reporting rates from the HCPs' point of view.

Methods: A questionnaire containing 43 questions evaluating sociodemographic characteristics, pharmacovigilance knowledge and activities, and prescription behaviors was prepared on "surveyMonkey.com." The link was distributed mainly by professional organizations.

Results: Although this survey aimed to reach all HCPs, most of the respondents were physicians and nurses. Of the 259 (69.6%) participants who encountered ADR at least once, only 105 (40.5%) reported ADR. The term "pharmacovigilance" was heard for the first time in this survey by 35.5% ($n = 132$) of the participants. Only 34.7% ($n = 129$) of the participants knew where to find the ADR reporting form, and 25.5% ($n = 95$) had previously filled the form and/or read it. Only 28.5% ($n = 106$) of the participants were aware of the ADR reporting and monitoring system of their institutions and related professionals. Almost all the participants agreed that pharmacovigilance and ADR reporting training are necessary.

Conclusion: The main reason for underreporting is limited pharmacovigilance knowledge of HCPs. Training activities based on the needs and preferences of HCPs and close follow-up by authorities are the main steps to improve pharmacovigilance activities.

ARTICLE HISTORY

Received 6 August 2018
Accepted 6 December 2018

KEYWORDS



Adverse drug reaction reporting; pharmacovigilance knowledge; healthcare professional; drug safety

Introduction

Adverse drug reaction (ADR) is a response to a medicine that is noxious and unintended, and occurs at doses normally used in humans [1]. In 1998, the incidence of serious ADRs was 6.7% and that of fatal ADRs was 0.32%, making them one of the leading causes of death in hospitalized patients [2]. The annual burden of ADRs to USA economy is estimated to be 30–130 billion US dollars [3]. Although several decades have passed, the status of ADR burden to global health and economy has not improved to date [4–11]. However, more than half of the ADRs are preventable, thereby suggesting an insufficiency in recognizing and reporting ADRs [12–14].

Following thalidomide disaster, the safety of pharmaceutical products become as important as its efficacy. Globalization of pharmacovigilance studies was initiated by World Health Organization (WHO) through establishment of the WHO Programme for International Drug Monitoring in 1968. This program provides not only a forum for WHO member states to collaborate in the monitoring of pharmaceutical products but also evaluation of data gathered from individual reports. WHO-approved national

pharmacovigilance centers set by countries collect individual case safety reports sent by healthcare professionals (HCPs) and patients (in some countries) regionally and forward them to the central WHO Global database, VigiBase, which is managed and maintained by the Uppsala Monitoring Centre. Pharmacovigilance activities were initiated in 1985, and Turkey became the 27th member of the WHO Program in 1987. With the publication of the first regulation in 2005, every hospital with 50 or more beds are required to employ a pharmacovigilance contact person (PCP) whose responsibilities included, but are not limited to, promoting pharmacovigilance activities, reporting ADRs, and providing training and education to HCPs [15]. According to the current regulation, it is the responsibility of all HCPs (medical doctors, dentists, pharmacists, nurses, and midwives) to report all serious ADRs and all suspected reactions observed with medicines under additional monitoring by the Turkish Pharmacovigilance Center (TPC) [15,16]. Reactions that are not included in the summary of product characteristics, ineffectiveness (especially with vaccines, contraceptives, and drugs used to treat life-threatening diseases), and serious reactions due to

CONTACT Müberra Devrim Güner  devrimguner@etu.edu.tr  Department of Medical Pharmacology, TOBB ETU Medical School, Söğütözü Cad. No: 43 Oda No: Z04, Ankara 06560, Turkey

© 2019 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.
www.tandfonline.com/ijda

overdose, off-label use, misuse, abuse, and occupational exposure are also reported to the TPC. The TPC also encourages HCPs to report adverse reactions caused by herbal products [15,16].

Spontaneous reporting of ADRs is the most important way to improve pharmacovigilance information on drugs that have been introduced to the market with limited safety knowledge obtained from premarketing clinical trials. Although spontaneous reporting systems have been set up in many countries by regulatory authorities to encourage – or even to mandate – reporting by HCPs, ADR reporting rates are still low [17–20]. Underreporting limits and delays initiatives that could have been taken to prevent/reduce the harmful effects of medications. Moreover, not only it poses a health burden to the individual and society, it also creates an economic burden through unnecessary use of limited healthcare resources [4–6,8,21]. In addition, it is unethical not to inform or report harmful effects of a drug even after encountering it, which may knowingly put the next user of the same medication at risk [22]. Besides being a responsibility encouraged by regulations, reporting of suspected ADR is every healthcare professionals' ethical responsibility that emerges from the principle of giving no-harm, and therefore must be given utmost importance in daily practice.

Despite establishing a WHO-standard pharmacovigilance system, underreporting is still common in Turkey [17,18]. In a study by Aagaard et al., reporting countries were divided by national income level per capita according to the World Bank's definition [23] and Turkey is classified as upper-middle-income economy. The number of ADR reports are 2 per 1 million population in Turkey, and below the average of countries with similar socioeconomic levels, which is 27/1 million [17]. Although there is an increase in reporting rate over the years in Turkey, it is still below the average of the abovementioned countries [24].

The hypothesis of this study was that scarce pharmacovigilance knowledge of HCP is the main reason for underreporting. A survey was conducted to test this hypothesis and illuminate, from HCPs' point of view, the existing factors limiting the reporting rates of ADRs.

Methods

The study protocol and questionnaires used were ethically evaluated and approved by the institutional review board of humanitarian research of our institution.

We conducted a systematic literature search with keywords including "knowledge, attitude, and practice (KAP); pharmacovigilance; ADR reporting of HCPs". The PubMed search yielded ninety published articles on the subject. We evaluated this literature for questionnaires evaluating the KAP of HCPs and selected 4 based on their relevancy and publishing questions of their survey [25–28].

Our draft survey was prepared based on the findings of the systematic review. A focus group consisting of 10 HCPs (1 pharmacist, 2 nurses, and 7 medical doctors) reviewed the questionnaire and its content, and examined the language

validity of the questions. The draft questionnaire was revised in accordance with the feedbacks.

The final survey consisted of 43 questions in the following 4 sections:

1. Sociodemographic characteristics (9 questions)
2. PCP activities: if an HCP has/had this responsibility, 6 questions related to the activities and responsibilities were asked.
3. Pharmacovigilance and ADR reporting KAP (18 questions)
4. Drug use, prescription habits, and communication of ADRs with patients (10 questions)

A survey was generated using "surveymonkey.com," which is an online survey platform. The survey webpage opened with information about the study, including the definitions of pharmacovigilance and ADR. Moreover, it was stated that ADR reporting is the responsibility of all HCPs and reporting should be made to the TPC. Next, an informed consent form page opened and only after consenting to voluntarily answer the questions by marking a check box, the volunteer was directed to the questions page. The number of questions for each participant varied between 30–43, depending on their answers.

The question and answer types varied: selection from a drop-down list, yes or no answers (for PCP activities), and Likert-type scales (a five-point scale: always, frequently, occasionally, never, and not my job) were used to allow participants to express the frequency of a particular activity, mainly medication use, prescription habits, and communication of ADRs with patients.

The answers were collected anonymously and recurrent completion of the survey more than once by the same participant was prevented by Internet Protocol (IP) address limitation.

The Ankara Chamber of Medicine and Turkish Nurses Association provided their support to distribute the link to their members. The Ankara Chamber of Medicine is for medical doctors professing in Ankara; however, it has significant importance among the medical chambers of other provinces of Turkey. Therefore, it is plausible to think that the Ankara Chamber of Medicine might have helped to disseminate the survey to physicians serving in various cities of Turkey. The Turkish Nurses Association has a nation-wide scope. Some other professional associations with national networks were contacted, although no concrete responses were received from them. Moreover, the link was distributed via social media platforms (Facebook, LinkedIn, Twitter, and WhatsApp) via direct messaging to HCP contacts of the authors. The data were collected between the dates 1 June 2017 and 31 August 2017, a duration of three months.

Statistical analysis

Data collected online by the "surveymonkey.com" platform were evaluated for any discrepancy regarding age groups and duration of professional life, and none was detected.

Table 1. Sociodemographic characteristics of healthcare professionals.

Characteristics	n (%)	
Age group (years)	<25	1 (0.3)
	26–30	38 (10.2)
	31–35	30 (8.1)
	36–40	50 (13.4)
	41–45	51 (13.7)
	46–50	44 (11.8)
	51–55	112 (30.1)
	56–60	32 (8.6)
	61–65	8 (2.1)
Gender	>65	6 (1.6)
Gender	Female	209 (56.2)
	Male	163 (43.8)
Location of work	Metropolitan areas	331 (89.0)
	Small towns/rural areas	41 (11.0)
Profession	Medical doctors	279 (75.0)
	Nurses	67 (18.0)
	Other healthcare professionals	26 (7.0)
Academic title (Assistant, Associate, or Professor)		123 (33.1)
Institution	Universities	128 (34.4)
	State hospitals	67 (18.0)
	Private hospitals	59 (15.9)
	Other*	118 (31.6)
	Duration of employment (years)	0–5
Duration of employment (years)	6–10	47 (12.6)
	11–15	32 (8.6)
	16–20	44 (11.8)
	20–25	44 (11.8)
	>25	162 (43.6)

*Other: family, public, occupational, or institutional health centers, private physicians' office, and pharmaceutical company.

The sociodemographic and professional characteristics as well as descriptive statistics of participants are presented as percentages. The results of physicians and nurses (because the number of participants from these professions allowed for comparisons to be made) were calculated using the Chi-square test and 95% confidence interval (CI). Bivariate associations between independent variables (i.e. prior knowledge of pharmacovigilance, profession, etc.) and the outcome variable (experience of spontaneous ADR reporting) were evaluated using logistic regression analysis. Degree of association was described by odds ratios with their corresponding 95% CI. Statistical significance was indicated by $p < .05$. The SPSS statistics software was used for data analysis.

Results

Although the exact number of HCPs that the survey link might have reached cannot be determined, 380 HCPs participated in the survey and 372 of them consented to answer the survey questions.

Sociodemographic characteristics

The most common age group was 51–55 years ($n = 112$; 30.1%), and 56.2% ($n = 209$) of the participants were women. Most of the participants were medical doctors ($n = 279$; 75.0%), followed by nurses ($n = 67$; 18.0%). The majority of the participants was from Ankara ($n = 231$; 62.1%) and located in the urban areas of metropolitan municipalities ($n = 331$; 89.0%; including Ankara). Among the participants' institutions, 34.4% ($n = 128$) was universities (public and private), followed by state (including research and training

hospitals; $n = 67$; 18.0%) and private hospitals ($n = 59$; 15.9%). Among the participants, 55.4% ($n = 206$) had been working for more than 20 years (Table 1).

Most of the physicians were specialists ($n = 206$; 74.1%). Although answers were received from nearly all areas of specializations, the most common specialties of the participants were anesthesiology and reanimation ($n = 21$; 10.2%), internal medicine ($n = 15$; 7.3%), family medicine ($n = 14$; 6.8%), and pediatrics ($n = 11$; 5.3%).

Pharmacovigilance contact person

Only 10 of the participants worked as PCP for their institutions, and among them, only 3 still had this responsibility. Six of them stated that a pharmacovigilance system is established and active in their institutions. Three of them answered "no" to "did you receive any pharmacovigilance training?" and only 4 of them organized a pharmacovigilance training for HCPs in their institution.

Pharmacovigilance and ADR reporting KAP

When the participants were asked "when was the first time you heard about the term pharmacovigilance?", 35.5% ($n = 132$) of the participants answered that they heard it in this survey, whereas 18.6% ($n = 69$) stated that they heard about pharmacovigilance when they were students. The most preferred source of information about ADRs and their prevention was search engines (61.3%) (Table 2). Because the law requires assignment of PCP for institutions with more than 50 patient beds, none of the participants working for outpatient institutions, such as family, public, occupational,

Table 2. Source of pharmacovigilance knowledge and information on adverse drug reaction.

When did you first hear the term pharmacovigilance? (n; %)	In this survey	132 (35.5)
	In trainings/continuous education programs	71 (19.1)
	When I was a student	69 (18.6)
	In congress/meetings	49 (13.2)
	From the pharmacovigilance contact point of my institution	20 (5.4)
Where do you look up when you need information about an adverse drug reaction? *(n; %)	From a pharmaceutical company representative	9 (2.4)
	Search engines (internet)	228 (61.3)
	Scientific journal articles	208 (56.0)
	Classical text books	93 (25.0)
	Package inserts	135 (36.3)
	Advertisement brochures/leaflets	78 (21.0)
	Direct call to a pharmaceutical company	71 (19.1)
Pharmaceutical company representative	30 (8.1)	

*More than one option can be selected.

Table 3. Contributing factors for the reporting of ADRs.

Factor	Reporters n (%)	Non-reporters n (%)	Odds Ratio (95% CI)
Having a medical specialty (only physicians)	61 (75.3)	76 (59.4)	2.08 (1.13–3.86)
Prior knowledge of pharmacovigilance	85 (81.0)	86 (55.9)	3.41 (1.91–6.10)
Reading literature on ADRs or its prevention	82 (78.1)	76 (49.5)	3.66 (2.01–6.41)
Having clinical trials experience	52 (49.5)	38 (24.7)	3.0 (1.76–5.10)
Knowing where to obtain ADR reporting form	64 (61.0)	30 (19.5)	6.5 (3.69–11.29)
Previously reading/filling ADR reporting form	66 (62.9)	13 (8.4)	18.4 (9.18–36.68)
Knowing the ADR system and officials in their institution	55 (52.4)	20 (13.0)	7.6 (4.01–14.44)
Receiving formal pharmacovigilance training	30 (28.3)	8 (5.1)	7.3 (3.19–16.71)

ADRs: adverse drug reactions; CI: confidence interval $p < .05$.

or institutional health centers, or private physicians' offices, heard the term pharmacovigilance from the PCP of their institutions. Moreover, none of the participants working for university or state hospitals heard it for the first time from a pharmaceutical company representative. Significantly more participants who were working in institutions other than hospitals ($n = 49$, 47.5%) stated hearing the term pharmacovigilance for the first time in this survey than those working in hospitals ($n = 92$, 34.2%; $p = .018$; 95% CI: 2.24–24.28). On the contrary, significantly more participants working in hospitals ($n = 56$, 20.8%) heard the term pharmacovigilance when they were students than the participants working in non-hospital institutions ($n = 16$, 15.5%; $p = .001$; 95% CI: 1.79–12.24). The number of participants who stated hearing about the term pharmacovigilance for the first time in this survey was significantly lower among those with an academic title ($n = 38$, 30.9%) than among those without ($n = 106$, 42.6%; $p = .03$; 95% CI: 1.17–21.40). On the contrary, significantly more participants with an academic title heard the term for the first time in a meeting or congress ($n = 31$, 25.2%) than those without ($n = 14$, 5.6%; $p < .0001$; 95% CI: 11.85–28.22). None of the participants ($n = 10$, 4.0%) hearing the term for the first time from a pharmaceutical company representative had academic titles.

Of the participants, 259 (69.6%) stated that they professionally encountered ADR at least once. When this group was asked if they ever reported an ADR, only 105 (40.5%) participants responded "yes." The reports most often were made to the pharmaceutical company (26.3%) or its representative (11.1%), TPC (21.2%), PCP of their institution (15.2%), prescriber of the medication (9.1%), or a superior (3.0%). ADR reporting rates were higher in the groups that have medical specialty (for physicians only), have prior knowledge of pharmacovigilance before joining this survey, read

literature on ADRs or prevention of ADRs, have experience as an investigator, coinvestigator, or personnel in clinical trials, know the ADR reporting and monitoring system and its officers in their institution, have experience with (reading or filling) ADR reporting form, and have formal pharmacovigilance training (Table 3). Of the ADR-reporting group, 49.5% ($n = 52$) also sought information about ADRs from pharmaceutical company-related sources (representative, advertisement brochures/leaflets, or direct call to a pharmaceutical company), compared to non-reporters ($n = 46$, 29.9%; $p = .0014$, 95% CI: 7.56–31.19). Compared to non-reporters, more reporters also thought that ADR reporting is the responsibility of all HCPs ($n = 30$, 30.9% vs. $n = 27$, 18.0%; $p = .016$; 95% CI: 2.39–3.69) or pharmaceutical representatives ($n = 25$, 25.8% vs. $n = 19$, 12.7%; $p = .007$; 95% CI: 3.46–23.21).

Regarding ADR reporting methods, compared to non-reporters, significantly more reporters preferred reporting via e-mail ($n = 29$, 31.5% vs. $n = 26$, 18.7%; $p = .018$; 95% CI: 2.17–3.64) or to pharmaceutical representatives ($n = 18$, 19.6% vs. $n = 9$, 6.5%; $p = .001$; 95% CI: 4.90–22.19).

The reasons for not reporting ADRs are presented in Table 4.

The most common reason for not reporting was not being sure if it is an ADR ($n = 110$, 29.6%), followed by not knowing where to report ($n = 101$, 27.2%) and not knowing where to find the report form ($n = 72$, 19.3%) (Table 4). Only 28.5% ($n = 106$) of the participants were aware of the ADR reporting and monitoring system of their institutions and related professionals.

When asked "who should be responsible for reporting?" 91.0% ($n = 338$) stated that it should be the responsibility of physicians, 36.3% ($n = 135$) considered it to be the responsibility of pharmacists, and 23.9% ($n = 89$) thought that other

Table 4. Reasons for not reporting adverse drug reactions (ADR).

Reason*	n (%)
Not sure if it is an ADR	110 (29.6)
Not knowing where to report	101 (27.2)
Not knowing where to find the report form	72 (19.3)
Avoiding the burden of possible follow-ups and bureaucratic procedures	61 (16.4)
Not knowing how to fill the report form, or finding the report form complicated	54 (14.6)
Not having time to report	36 (9.7)
Thinking that ADR reporting is not a duty of healthcare professionals	34 (9.1)
My report is not needed/necessary	30 (8.1)

*More than one option can be selected.

HCPs (as defined by the legislation, such as dentists, nurses, and midwives) [15] were responsible for reporting. Pharmaceutical company and its representatives were considered responsible for reporting ADRs by 29.0% ($n=108$) and 16.4% ($n=61$) of the participants, respectively.

Among the participants, 40.9% ($n=152$) knew that patients can report an ADR and only 24.7% ($n=92$) knew that the TPC can contact the prescribing physician following a patient report.

Of the participants, 50.5% ($n=188$) estimated the number of ADR reports from Turkey as less than 500. The correct range of number of ADR reports from Turkey, which was 2455 reports in 2013, [2] was estimated by only 15.3% ($n=57$) of the participants.

When the participants were asked about their preferred method of reporting, 72.6% ($n=270$) selected online electronic form, 46.2% ($n=172$) selected the PCP of their institution, and 23.9% ($n=89$) chose e-mail. Although not available, reporting via smart phone application was selected by 20.4% ($n=76$) of the participants.

Of the participants, 99.0% ($n=368$) thought that formal pharmacovigilance training is necessary for HCPs, and 83.6% ($n=311$) reported that they would like to have a training. The most preferred method of training was online (60.8%) ($n=226$). Of the participants, 97.6% ($n=363$) agreed that practical training is needed and 89.8% ($n=334$) suggested that a sham reporting for practice should be conducted.

We compared several characteristics, knowledge, and attitude of nurses and physicians as well (Table 5). According to these data, nurses were populated in younger age groups than those of physicians. In addition, compared to physicians, more nurses worked in state hospitals but fewer nurses worked in private hospitals/clinics. Fewer nurses with academic titles answered our survey than physicians with academic titles. Significantly more nurses heard about the term pharmacovigilance for the first time in this survey, whereas hearing about it when they were students was more common for physicians. Compared to physicians, more nurses contacted pharmaceutical company or checked package inserts when they need information about an ADR. Moreover, compared to physicians, nurses were more aware of the ADR system and responsible personnel in their institution, and more nurses knew that patients can report ADR. Furthermore, compared to physicians, more nurses had pharmacovigilance training and fewer nurses thought that ADR reporting would increase their workload (Table 5).

Drug use, prescription habits, and communication of ADRs with patients

The participants were asked to select the frequency of some of their behaviors regarding prescription and medication. According to the answers, 26.9% ($n=100$) stated that they always read the package leaflet and summary of product characteristics. Of the participants, 24.7% ($n=92$) and 18.6% ($n=69$) always recommended reading the package leaflet and summary of product characteristics, respectively. Checking concomitant medications/herbal products for possible interactions was always done by 35.2% ($n=131$) of the participants. Of the participants, 65.6% ($n=197$) stated that they never prescribed medications that are not licensed for the specific indication for reimbursement purposes and 92.7% ($n=345$) reported that they never prescribed a medication without any license. Of the participants, 56.2% ($n=169$) never recommended herbal supplements to their patients.

Compared to physicians, more nurses always read package inserts and SPC and suggested patients to read these documents (Table 5).

Discussion

The results of this survey suggested that the main reason for underreporting is limited pharmacovigilance literacy of the HCPs. There are several studies evaluating the pharmacovigilance knowledge and reporting behavior of various HCPs in Turkey [29–32]. Although this study aimed to obtain responses from various HCPs, the study population comprised mainly of medical doctors and nurses. The sociodemographic characteristics (working in educational institutions and hospitals with PCPs, having experience of more than 20 years, carrying an academic title, and being specialists) of the participants suggested a better knowledge and behavior of ADR reporting; however, the findings of this study are also in line with the findings of other studies [20,29–33].

The TPC organizes 1 or 2 trainings each year (mainly for new PCPs) and strictly follows up the assignment of PCPs of each institution [16]. However, the activities of PCPs are not systematically followed up by the TPC. Although a PCP is responsible for training HCPs in their institution and promoting pharmacovigilance activities, the number of participants reported learning the term from PCPs of their institution indicate the inadequacy and lack of supervision of PCP activities. PCPs are inefficient by itself based on the reporting rates and the findings of this study. Although the official

Table 5. Comparison of characteristics, knowledge, attitude, and practices of nurses and physicians.

Characteristics	Nurses <i>n</i> (%)	Physicians <i>n</i> (%)	<i>p</i> value (95% Confidentiality Interval)
Number of participants	67	279	
Gender (women)	59 (88.1)	129 (46.0)	<.0001 (30.60–50.24)
Age group			
26–30	18 (23.9)	16 (6.4)	<.0001 (8.20–29.18)
31–35	12 (17.9)	16 (5.6)	.0009 (4.22–23.35)
36–40	18 (26.9)	27 (9.7)	.0002 (7.20–29.22)
41–45	12 (17.9)	32 (11.6)	NS
46–50	5 (7.5)	38 (13.5)	NS
51–55	1 (1.5)	108 (38.6)	<.0001 (28.58–43.06)
56–60	2 (3.0)	28 (10.1)	NS
61–65	0	7 (2.6)	NS
>65	1 (1.5)	5 (1.9)	NS
Institution			
State hospitals	25 (37.7)	41 (14.6)	<.0001 (11.50–35.62)
Private hospital/clinic	5 (7.3)	54 (19.5)	.0175 (2.44–18.75)
Academic title	13 (19.4)	108 (38.7)	.0030 (6.98–28.96)
Where did you first hear about the term “pharmacovigilance”?			
In this survey	33 (49.3)	93 (33.3)	.0147 (3.06–28.81)
When I was a student	5 (7.5)	57 (20.4)	.0135 (3.05–19.55)
Read literature on ADRs or prevention of ADRs	24 (35.8)	171 (61.3)	.0002 (12.19–37.29)
Where do you look up information about an ADR?			
Pharmaceutical company	13 (19.4)	23 (8.2)	.007 (2.61–22.54)
Package insert	37 (55.2)	86 (30.8)	.0002 (11.26–36.81)
Encountering ADR	34 (50.8)	223 (79.9)	<.0001 (16.43–41.55)
Reasons for not reporting			
Not sure if it is an ADR	10 (14.9)	78 (28.0)	.0273 (1.58–21.72)
It is not my responsibility	10 (14.9)	14 (5.0)	.0042 (2.55–20.50)
Not knowing where to report	7 (10.5)	79 (28.3)	.0025 (7.0–25.48)
Not having time to report	2 (3.0)	32 (11.5)	.0363 (0.55–13.30)
Whose responsibility is ADR reporting?			
Physicians’	48 (71.6)	266 (95.3)	<.0001 (13.79–35.59)
Pharmacists’	34 (50.8)	91 (32.6)	.0054 (5.20–30.92)
Other healthcare professionals’	31 (46.3)	50 (17.9)	<.0001 (15.97–41.0)
I am aware of the ADR system and responsible personnel in my institution	30 (44.8)	68 (24.4)	.0009 (7.89–33.15)
I know that patients can report ADR	35 (52.2)	104 (37.3)	.0257 (1.79–27.65)
Which reporting method do you prefer?			
Electronic form	41 (61.2)	209 (74.9)	.0247 (1.66–26.57)
PCP of my institution	41 (61.2)	123 (44.1)	.0120 (3.77–29.28)
Representative of pharmaceutical company	1 (1.5)	35 (12.5)	.0081 (3.68–15.57)
Had pharmacovigilance training	15 (22.4)	29 (10.4)	.0082 (2.70–23.73)
Preference of pharmacovigilance training method: practical	31 (46.3)	69 (24.7)	.0005 (8.98–34.31)
I agree that ADR reporting increases my workload	13 (19.4)	123 (44.1)	.0002 (12.29–34.38)
I agree that checking the expiry date of a prescription is not my job	2 (3.0)	60 (21.5)	.0004 (10.0–24.13)
I read package inserts each time before giving medications to patients	32 (47.8)	54 (19.4)	<.0001 (15.83–40.88)
I suggest patients to read package inserts every time	23 (34.3)	58 (20.8)	.0193 (2.05–26.21)
I read SPC each time before giving medications to patients	28 (41.8)	61 (21.9)	.0008 (7.68–32.64)
I suggest patients to read SPC every time	18 (26.9)	42 (15.1)	.0223 (1.53–24.04)

NS: not significant; ADR: adverse drug reaction; PCP: pharmacovigilance contact person; SPC: summary of product characteristics..

institution that the ADR reporting must be made to (the TPC) has the term “pharmacovigilance” in its title, the percentage of HCPs hearing this term for the first time by this survey is significant.

Since 2013, following an official request of the Turkish Ministry of Health, the Higher Education Council included pharmacovigilance training in the curricula of medical, pharmaceutical, dentistry, and nursing schools, as well as vocational schools for healthcare services. Graduates who received this training have not joined the health workforce yet, which may explain the scarceness of HCPs who have heard about the term pharmacovigilance at school.

It had been shown that educational interventions and other activities to promote ADR reporting increase awareness to ADRs and then increase the reporting rates of ADRs [34–38]. Our study population showed high willingness to receive training. Inclusion of pharmacovigilance and ADR reporting trainings to continuous education program

curricula, besides to undergraduate education curricula, is highly needed.

According to our results, there was a perception that reporting duty mainly rests on physicians. However, nurses were more positive towards ADR reporting and more willing to participate in related activities than physicians. Moreover, nurses may be more able to identify ADRs, particularly in patients that remain outside the reach of physicians and in more vulnerable patients, such as children, women, and the elderly. Designating nurses as central actors in pharmacovigilance activities may require significant educational interventions, but the outcomes would likely to be favorable [37,39].

The participants chose the internet as the main source of information about ADRs. In this era, internet and social media are becoming the main communication tools; thus, they cannot be ignored. Not only incentives are needed to be taken to increase the reliability of these sources, training on pharmacovigilance and ADR reporting should also include

evaluation of the reliability and safety of such sources. E-learning tools maybe more feasible to provide pharmacovigilance and ADR reporting trainings because they are the preferred method of education and were shown by another study to be successful [40]. Defining the training needs of HCPs and providing online distant learning modules tailor-made to the needs, activities, and ethical responsibilities of each profession and specialty are necessary. These modules should cover basic pharmacovigilance knowledge, ADR reporting, good prescribing activities, and reporting practice, and should be made mandatory for all HCPs.

Underreporting has been a global problem even in countries with more organized pharmacovigilance systems. The reasons for not reporting globally are also similar to those in the findings of our study, with the most common reasons being lack of time, uncertainty about ADR diagnosis, what and where to report, difficulty in handling report forms, and lack of awareness of the reporting system requirements [20,21,33,41–43].

There are several initiatives taken by the regulatory authority that may show benefits, such as making rational drug use trainings mandatory in medical congresses, making public ADR reporting available, and increasing awareness of the public by hanging posters about ADR reporting on the walls of health institutions or by adding contact information for ADR reporting on patient information sheets of pharmaceutical products. We suggest that adding mandatory continuous education modules on the subject, and initiatives such as illuminating all HCPs on the purpose, necessity, and need of ADR reports, following activities of PCPs closely, improving prescribing activities, integrating an ADR reporting system to the electronic prescribing system currently in use by most public and private health institutions, providing feedback (by the TPC to ADR reporters and/or PCPs), and rewarding good-quality ADR reports will help improve reporting rates.

In conclusion, the results of this survey showed that HCPs with better knowledge of pharmacovigilance and ADR reporting practices reported more, which supported the suggestion of the need for extensive, tailor-made training activities. The HCPs did not know the essentials of pharmacovigilance and ADR reporting system in Turkey, and they were not aware of their role in this system. Although it is expected from all HCPs according to legislation, expanding the responsibility of reporting to other HCPs other than physicians, namely nurses and midwives, by focusing more on training these professionals, may decrease the underreporting.

Limitations

The sample size of our study was limited but similar to those of other studies conducted both in Turkey and in other countries. It is obvious that the participation of greater number of HCPs and more-diverse HCPs would increase the value of this study. We contacted several other occupational organizations and requested their help to distribute our survey link, but they either rejected our request or did not

answer at all. Receiving more answers from pharmacists, dentists, and other HCPs responsible for reporting would allow for comparisons among various HCPs. Moreover, an official request was sent to the Ministry of Health to distribute our link to all HCPs working under their roof, but negative response was received. Thus, with available sources, this sample size was achieved.

Online distribution may cause a selection bias, in which the possibility of participation of HCPs with more positive attitude on the subject maybe more than that of HCPs with negative attitude. Face-to-face surveying would decrease this selection bias.

The work location of our study population being more-urban areas may be another limitation to our study. However, because our results were similar to those of other studies performed in more-rural areas of Turkey, we think that the results would not change significantly and that limited knowledge of pharmacovigilance and ADR activities is an extensive national/global problem.

The length (30–43 questions) of our survey was another problem; some HCPs may be discouraged to participate by this factor only.

Transparency

Declaration of funding

There is no funding to declare for this study.

Declaration of financial/other relationships

The authors declare no conflict of interest and have no financial or other relationships to disclose. JDA peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

Acknowledgements

We would like to express our gratitude to Prof. Gülriş Erişgen, MD, PhD from TOBB ETU Medical School Department of Physiology, as well as the Ankara Chamber of Medicine and the Turkish Nurses Association for providing help in the distribution of our survey link.

References

- [1] World Health Organization Safety of Medicines - A Guide to Detecting and Reporting Adverse Drug Reactions - Why Health Professionals Need to Take Action 2002. [22 Nov 2018]. http://apps.who.int/iris/bitstream/handle/10665/67378/WHO_EDM_QSM_2002.2.pdf;jsessionid=BA5B4BE506C2FB1_820A7326529B9D9FB?sequence=1.
- [2] Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. *JAMA*. 1998;279:1200–1205.
- [3] White TJ, Arakelian A, Rho JP. Counting the costs of drug-related adverse events. *Pharmacoeconomics*. 1999;15:445–458.
- [4] Rodríguez-Monguió R, Otero MJ, Rovira J. Assessing the economic impact of adverse drug effects. *Pharmacoeconomics*. 2003;21:623–650.
- [5] Freitas GRM, Tramontina MY, Balbinotto G, et al. Economic impact of emergency visits due to drug-related morbidity on a Brazilian hospital. *Value Health Reg Issues*. 2017;14:1–8.

- [6] Sousa-Pinto B, Marques B, Lopes F, et al. Frequency and impact of adverse events in inpatients: a nationwide analysis of episodes between 2000 and 2015. *J Med Syst.* 2018;42:48.
- [7] Gyllensten H, Hakkarainen KM, Hägg S, et al. Economic impact of adverse drug events—a retrospective population-based cohort study of 4970 adults. *PLoS One.* 2014;9:e92061.
- [8] Schurig AM, Böhme M, Just KS, et al. Adverse drug reactions (ADR) and emergencies. *Dtsch Arztebl Int.* 2018;115:251–258.
- [9] Scripcaru G, Mateus C, Nunes C. Adverse drug events - analysis of a decade. A Portuguese case-study, from 2004 to 2013 using hospital database. *PLoS One.* 2017;12:e0178626.
- [10] Rydberg DM, Holm L, Engqvist I, et al. Adverse drug reactions in a tertiary care emergency medicine ward - prevalence, preventability and reporting. *PLoS One.* 2016;11:e0162948.
- [11] Walter SR, Day RO, Gallego B, et al. The impact of serious adverse drug reactions: a population-based study of a decade of hospital admissions in New South Wales, Australia. *Br J Clin Pharmacol.* 2017;83:416–426.
- [12] Angamo MT, Chalmers L, Curtain CM, et al. Adverse-drug-reaction-related hospitalizations in developed and developing countries: a review of prevalence and contributing factors. *Drug Saf.* 2016;39:847–857.
- [13] de Vries EN, Ramrattan MA, Smorenburg SM, et al. The incidence and nature of in-hospital adverse events: a systematic review. *Qual Saf Health Care.* 2008;17:216–223.
- [14] Hakkarainen KM, Hedna K, Petzold M, et al. Percentage of patients with preventable adverse drug reactions and preventability of adverse drug reactions—a meta-analysis. *PLoS One.* 2012;7:e33236.
- [15] Türkiye İlaç ve Tıbbi Cihaz Kurumu, İlaçların Güvenliliği Hakkında Yönetmelik Resmi Gazete [Turkey Pharmaceuticals and Medical Devices Agency, Legislation on Drug Safety Official Gazette] No: 28973 2014 [April 2018]. Available from: <http://www.resmigazete.gov.tr/eskiler/2014/04/20140415-6.htm> Turkish.
- [16] Türkiye İlaç ve Tıbbi Cihaz Kurumu Türkiye Farmakovijilans Merkezi internet sayfası [Turkish Medicines and Medical Devices Agency Turkish Pharmacovigilance Center. web page] [April 2018]. Available from: <http://www.titck.gov.tr/llac/Farmakovijilans> Turkish.
- [17] Aagaard L, Strandell J, Melskens L, et al. Global patterns of adverse drug reactions over a decade: analyses of spontaneous reports to VigiBase™. *Drug Saf.* 2012;35:1171–1182.
- [18] Ozcan G, Aykac E, Kasap Y, et al. Adverse drug reaction reporting pattern in Turkey: analysis of the national database in the context of the first pharmacovigilance legislation. *Drugs Real World Outcomes.* 2016;3:33–43.
- [19] Avong YK, Jatau B, Gurumnaan R, et al. Addressing the under-reporting of adverse drug reactions in public health programs controlling HIV/AIDS, Tuberculosis and Malaria: a prospective cohort study. *PLoS One.* 2018;13:e0200810.
- [20] Hohl CM, Small SS, Peddie D, et al. Why clinicians don't report adverse drug events: qualitative study. *JMIR Public Health Surveill.* 2018;4:e21.
- [21] Hazell L, Shakir SA. Under-reporting of adverse drug reactions : a systematic review. *Drug Saf.* 2006;29:385–396.
- [22] Rivkees SA. Primum non nocere (first, not to harm) and secundus, opinio vulnero (second, report the harm). *Int J Pediatr Endocrinol.* 2009;2009:303509.
- [23] The World Bank Group. Country classifications 2017 [online]. [22 Nov 2018]. 2017. <http://data.worldbank.org/about/country-classifications>
- [24] Aydınkarahallıoğlu ND, Aykaç E, Atalan Ö, et al. Spontaneous reporting of adverse drug reactions by consumers in comparison with healthcare professionals in Turkey from 2014 to 2016. *Pharm Med.* 2018;32:353.
- [25] Oshikoya KA, Awobusuyi JO. Perceptions of doctors to adverse drug reaction reporting in a teaching hospital in Lagos, Nigeria. *BMC Clin Pharmacol.* 2009;9:14.
- [26] Desai CK, Iyer G, Panchal J, et al. An evaluation of knowledge, attitude, and practice of adverse drug reaction reporting among prescribers at a tertiary care hospital. *Perspect Clin Res.* 2011;2:129–136.
- [27] Santosh KC, Tragulpiankit P, Gorsanan S, et al. Attitudes among healthcare professionals to the reporting of adverse drug reactions in Nepal. *BMC Pharmacol Toxicol.* 2013;14:16.
- [28] Hajj A, Hallit S, Ramia E, et al. Medication safety knowledge, attitudes and practices among community pharmacists in Lebanon. *Curr Med Res Opin.* 2018;34:149–156.
- [29] Toklu HZ, Uysal MK. The knowledge and attitude of the Turkish community pharmacists toward pharmacovigilance in the Kadikoy district of Istanbul. *Pharm World Sci.* 2008;30:556–562.
- [30] Alan S, Ozturk M, Gokyildiz S, et al. An evaluation of knowledge of pharmacovigilance among nurses and midwives in Turkey. *Indian J Pharmacol.* 2013;45:616–618.
- [31] Vural F, Ciftci S, Vural B. The knowledge, attitude and behaviours of nurses about pharmacovigilance, adverse drug reaction and adverse event reporting in a state hospital. *North Clin Istanbul.* 2015;1:147–152.
- [32] Ergün Y, Ergün TB, Tokar E, et al. Knowledge attitude and practice of Turkish health professionals towards pharmacovigilance in a university hospital. *Int Health.* 2018;. [Epub ahead of print]. DOI: [10.1093/inthealth/ihy073](https://doi.org/10.1093/inthealth/ihy073)
- [33] Thorne RJ, Bruggink RJ, Kelly SJ, et al. Awareness and compliance with pharmacovigilance requirements amongst UK oncology healthcare professionals. *Ecancermedicalscience.* 2018;12:809.
- [34] Ribeiro-Vaz I, Santos CC, Cruz-Correia R. Promoting adverse drug reaction reporting: comparison of different approaches. *Rev Saude Publica.* 2016;50:14.
- [35] Ganesan S, Sandhiya S, Reddy KC, et al. The impact of the educational intervention on knowledge, attitude, and practice of pharmacovigilance toward adverse drug reactions reporting among health-care professionals in a tertiary care hospital in South India. *J Nat Sci Biol Med.* 2017;8:203–209.
- [36] Leporini C, Marrazzo G, Mumoli L, et al. Adverse drug reactions reporting in Calabria (Southern Italy) in the four-year period 2011-2014: impact of a regional pharmacovigilance project in light of the new European legislation. *Expert Opin Drug Saf.* 2017;16:515–522.
- [37] Schutte T, van Eekeren R, Richir M, et al. The adverse drug reaction reporting assignment for specialist oncology nurses: a preliminary evaluation of quality, relevance and educational value in a prospective cohort study. *Naunyn-Schmiedeberg's Arch Pharmacol.* 2018;391:17–26.
- [38] Varallo FR, Planeta CS, Mastroianni PC. Effectiveness of pharmacovigilance: multifaceted educational intervention related to the knowledge, skills and attitudes of multidisciplinary hospital staff. *Clinics (Sao Paulo).* 2017;72:51–57.
- [39] Bigi C, Bocci G. The key role of clinical and community health nurses in pharmacovigilance. *Eur J Clin Pharmacol.* 2017;73:1379–1387.
- [40] Sinclair P, Kable A, Levett-Jones T. The effectiveness of internet-based e-learning on clinician behavior and patient outcomes: a systematic review protocol. *JBI Database System Rev Implement Rep.* 2015;13:52–64.
- [41] Cheema E, Haseeb A, Khan TM, et al. Barriers to reporting of adverse drugs reactions: a cross sectional study among community pharmacists in United Kingdom. *Pharm Pract (Granada).* 2017;15:931.
- [42] Kraus CN, Baldwin AT, McAllister RG. Jr. Improving the effect of FDA-mandated drug safety alerts with Internet-based continuing medical education. *Curr Drug Saf.* 2013;8:11–16.
- [43] Franklin BD, O'Grady K, Parr J, et al. Using the internet to deliver education on drug safety. *Qual Saf Health Care.* 2006;15:329–333.