INTRODUCTION

Adverse drug reactions (ADR) increase patient-related morbidity and mortality. Additionally, it is an important public health problem associated with prolonged hospital stay and increasing economic burden. Pharmacovigilance is central to reducing ADRs, so the development and growth of this science is critical to effective and safe clinical practice. The World Health Organization defines pharmacovigilance as “science and activities related to the detection, evaluation, understanding, and prevention of side effects or other possible drug-related problems”.¹²

Healthcare professionals are central to providing a robust pharmacovigilance system. Consumers are more likely to report ADRs to their physicians or pharmacists than to the pharmaceutical industry.⁴⁵ All health system sectors should be included in the reporting process.⁶ Pharmaceutical care involves assessing these risks on a patient-by-patient basis by “identifying and solving (or preventing)” drug therapy problems.

ABSTRACT

Objectives: Adverse drug reactions (ADRs) increase patient-related morbidity and mortality. Additionally, it is an important public health problem associated with prolonged hospital stay and increasing economic burden. Pharmacovigilance is central to reducing ADRs, so the development and growth of this science is critical to effective and safe clinical practice. The aim of the study was to evaluate the knowledge and behaviors of pharmacists toward pharmacovigilance and spontaneous ADR notifications in Türkiye.

Materials and Methods: The online questionnaire method was used with the pharmacists, whose prior consent was obtained to participate in the study. The survey was uploaded onto Google form. The survey link was distributed electronically to the eligible participants via social media channels. The knowledge of pharmacovigilance practice, ADR reporting compliance rates, reasons for not reporting ADR, and perceptions of the Turkish pharmacists on pharmacovigilance practice were evaluated.

Results: Four hundred six pharmacists (45%) agreed to participate in the study, 81.8% of whose correctly defined correctly defined the term pharmacovigilance. 91.6% knew the name of the Turkish Pharmacovigilance Center. Clinical and hospital pharmacists were found to have a more adequate knowledge than community pharmacists (p<0.05). 18.7% of pharmacists stated that they had previously reported ADRs. Most of the pharmacists stated that the most important reason for not reporting ADRs was not knowing how and where spontaneous reporting should be done, a single spontaneous reporting would not make a difference and the report would generate extra work.

Conclusion: These results showed that Turkish pharmacists had adequate knowledge about the concept of pharmacovigilance and the spontaneous ADR reporting system. However, they had little experience in reporting. Training programs should continue to increase the knowledge and reporting experience of pharmacists about the reporting process and requirements.

Key words: Adverse drug reaction reporting system, pharmacists, pharmacovigilance, knowledge, behavior
Therefore, pharmacists play an important role in safe drug use and should be aware of this. Unfortunately, the rate of self-reporting of ADRs by healthcare professionals around the world is extremely low, as it is not a mandatory requirement in most countries. After the thalidomide disaster in the 1960s, many countries developed their national pharmacovigilance centers. “Türkiye Adverse Drug Effects Monitoring and Evaluation Center” is Türkiye’s first national pharmacovigilance center, which was established in 1985. In 2005, its name was changed to “Turkish Pharmacovigilance Center” (TUFAM). According to the regulations, all healthcare professionals have to report a serious and unexpected ADR to TUFAM within 15 days, either directly by post, fax, or e-mail, or through the pharmacovigilance contact point in the healthcare institutions where they work. Many studies from other countries show the role and attitudes of pharmacists in ADR reporting. There is a limited number of studies evaluating the knowledge and behavior of pharmacists regarding pharmacovigilance and spontaneous ADR reporting in Türkiye. This study evaluates the knowledge and behaviors of pharmacists regarding pharmacovigilance systems and spontaneous ADR reporting in Türkiye.

MATERIALS AND METHODS

Study design and settings

This cross-sectional study was conducted between April 10th, and May 10th, 2021. The online questionnaire method was used with the pharmacists, whose prior consent was obtained to participate in the study. The survey was uploaded onto Google form. The first page of the survey contains information about the research subject. There was an option to either consent to or refuse participation in the survey at the end of this page. The individuals, who chose to participate, were allowed to complete the survey. The survey link was distributed electronically to the eligible participants via social media channels (Instagram, WhatsApp, and Facebook). Ethical approval for this study was obtained from the Gazi University Ethics Committee (approval number and date 2021-445/06.04.2021).

Sampling technique and sample size

An online questionnaire was applied to randomly selected community pharmacists, hospital pharmacists, and clinical pharmacists in Türkiye. Academic pharmacists working at the university and non-active pharmacists were excluded from the study. According to the data of the Turkish Pharmacists Association, there are 37,442 pharmacists in Türkiye. The online R-aosoft sample size calculator (http://www.raosoft.com/samplesize.html) estimated the sample size of a minimum of 381 pharmacists to provide a 95% confidence level with a 5% margin of error, assuming 50% of pharmacists express good knowledge.

Data collection

The questionnaire items and question selection were based on previous research and interviews with senior pharmacists on this subject. A draft questionnaire was designed to be subjected to tests and examinations by community pharmacists (n: 10) and hospital pharmacists (n: 10). The survey questions were then adjusted according to the qualitative feedback provided by the respondents and the results of the internal validity measurement. Cronbach alpha score was 0.6. There were 19 questions in the study. The first 5 questions were based on the demographic information of the participants, while 6-11 questions were about knowledge and 12-18 of the questions were about behavior.

Statistical analysis

Statistical analyses of the main survey data were performed using IBM SPSS (version 24.0) with significance levels set at ps0.05. Demographic variables and responses given to knowledge and behavior questions were analyzed using descriptive statistics. Descriptive analyses were used to represent the results as percentages and frequencies. For knowledge questions, correct answers were scored as 1, and wrong answers were scored as 0. Six questions were calculated as 6 points and corresponded to 100%. A score of more than 80% was accepted as adequate knowledge, while a total score ≤80% was classified as inadequate knowledge. Scoring was not done for behavior questions. Association between patients’ socio-demographic characteristics and ADR knowledge was also assessed using the Pearson chi-square test.

RESULTS

The questionnaires were sent to 900 pharmacists, whereas 406 pharmacists (45%) agreed to participate. 73.4% of the respondents were women and 51.3% of the respondents were between the ages 22-29. Community pharmacists constituted 65% of the respondents, while 21.4% were hospital pharmacists and 13.5% were clinical pharmacists. The respondents rated at 54.2% had a working period as a pharmacist in less than 5 years and 17.2% of them had a postgraduate degree. Socio-demographic characteristics of pharmacists are summarized in Table 1.

| Variables                  | n (%)       |
|----------------------------|-------------|
| Gender                     |             |
| Female                     | 298 (73.4)  |
| Male                       | 108 (26.6)  |
| Age, ranges                |             |
| 22-29                      | 210 (51.7)  |
| 30-44                      | 82 (20.2)   |
| 45-59                      | 90 (22.2)   |
| >60                        | 24 (5.9)    |
| Work place                 |             |
| Community pharmacist       | 264 (65)    |
| Hospital pharmacist        | 87 (21.4)   |
| Clinical pharmacist        | 55 (13.5)   |
| Experience as a pharmacist |             |
| <5 years                   | 220 (54.2)  |
| ≥5 years                   | 186 (45.8)  |
| Postgraduate degree (MSc, PhD) |         |
| Yes                        | 70 (17.2)   |
| No                         | 336 (82.8)  |
Knowledge
Table 2 demonstrates the responses to questions related to knowledge. The respondents rated at 81.8% defined the term pharmacovigilance correctly, whereas 46.3% of the respondents correctly answered the location of the world pharmacovigilance center. 91.6% knew the name of Türkiye’s National Pharmacovigilance Center. 79.8% of the respondents answered correctly, who could report ADRs and 83.3% knew which ADRs could be reported correctly. 70.4% of the respondents knew how to report an ADR. Table 3 shows the association with socio-demographic characteristics of patients and pharmacovigilance awareness as well as ADR knowledge and reporting of previously experienced ADRs. 57.6% of the respondents had sufficient knowledge of ADRs. The relationship of ADR information with age, gender, duration of the study, and postgraduate degree was not found to be statistically significant (p>0.05). The relationship between the pharmacist’s work area (clinical pharmacist or hospital pharmacist or community pharmacist) and the previous reporting of ADRs was significant (p<0.05). Clinical and hospital pharmacists were found to have better knowledge levels than community pharmacists.

Table 2. Knowledge of the pharmacists concerning pharmacovigilance and reporting ADRs

| Questions                                                                 | n (%)       |
|---------------------------------------------------------------------------|-------------|
| What is pharmacovigilance?                                               | 52 (12.8)   |
| Adverse drug reaction reporting                                          | 332 (81.8)  |
| Detection, recognition, evaluation, and prevention of adverse drug reactions* | 16 (3.9)    |
| The science of evaluating the benefit/risk profile of a medicinal product | 188 (46.3)  |
| Do not know                                                              | 6 (1.5)     |
| Where is the World Pharmacovigilance Center located?                     |             |
| United States of America                                                 | 174 (42.9)  |
| France                                                                   | 30 (7.4)    |
| United Kingdom                                                           | 14 (3.4)    |
| Sweden*                                                                  |             |
| Which institution is responsible for adverse reaction reporting and monitoring in Türkiye? |             |
| TUFAM*                                                                   | 372 (91.6)  |
| The Regional Board of Pharmacists                                        | -           |
| Turkish Pharmacists Association                                          | 20 (4.9)    |
| Do not know                                                              | 14 (3.4)    |
| Who can spontaneously report adverse drug reactions?                     |             |
| Doctor                                                                    | 12 (3)      |
| Pharmacist                                                                | 70 (17.2)   |
| Dentist                                                                   | -           |
| Nurse                                                                     | -           |
| All of above*                                                            | 324 (79.8)  |
| What types of adverse drug reactions are expected to be reported?        |             |
| Serious and unexpected                                                   | 58 (14.3)   |
| Not serious                                                               | -           |
| Expected adverse reactions                                               | 2 (0.5)     |
| All adverse reactions regardless of seriousness and expectedness*        | 338 (83.3)  |
| Do not know                                                              | 8 (2)       |
| Do you know how to report adverse drug reactions?                        |             |
| Yes*                                                                     | 286 (70.4)  |
| No                                                                       | 120 (29.6)  |

*True answer, ADRs: Adverse drug reactions, TUFAM: Turkish Pharmacovigilance Center
Behaviors
Table 4 shows that pharmacists’ behavior toward reporting ADRs. 40.4% of pharmacists stated that they did not experience ADRs in their patients at all, 39.9% experienced them once a year, 15.8% once a month, and 3.9% once a week. Previously, 76 pharmacists (18.7%) were found in the ADR notification. 55.2% were serious, 31.5% were unexpected, and 5% were rare type ADRs. The relationship between the pharmacist’s work area (clinical pharmacist, hospital pharmacist or community pharmacist) and the previous reporting of ADRs was significant ($p<0.05$). 35.6% of hospital pharmacists, 23.6% of clinical pharmacists, and 12.1% of community pharmacists, who participated in our study, declared that they had previously reported ADRs.

Some of the respondents (36.9%) stated that the most important reason for not reporting ADRs was that they did not know how and to where spontaneous reporting should be done. 19.2% of them stated that a single spontaneous reporting would not make a difference and 18.7% stated that the report would generate extra work (Table 5). Among the factors that encourage reporting ADRs are; the reaction was serious (31.5%), the reaction was unexpected (22.7%), the training of healthcare professionals (19.2%), and the reporting process was practical and easy (17.7%) (Table 6).

**DISCUSSION**

The results of our study revealed that although Turkish pharmacists had sufficient pharmacovigilance and theoretical knowledge about ADRs, they showed a low rate of ADR reporting. 81.8% of the respondents correctly defined the term pharmacovigilance. This was a fairly high rate. In the study by Kopciuch et al, 73% of the respondents, 69.5% of the respondents in the study by Su et al, and 81.9% of the respondents in the study by Li et al defined the term pharmacovigilance correctly. In the study by Suyagh et al, 25.5% of the participants correctly defined the term pharmacovigilance. In our study, 91.6% of respondents correctly knew the institution reporting national ADRs in Türkiye, while nearly half of the respondents in the study by Kopciuch et al knew this correctly in the study by Suyagh et al. 76% of the respondents declared that they did not know where to find the necessary forms for ADR reporting and 60% of the respondents did not know the national pharmacovigilance center in the study by Vigneshwaran et al. Toklu and Uysal evaluated the knowledge and attitudes of pharmacy pharmacists in Türkiye regarding ADRs in 2008.

Table 3. Association of pharmacists’ demographic characteristics with pharmacovigilance awareness, knowledge of adverse drug reaction reporting

| Variables                  | ADR knowledge                                      |
|----------------------------|----------------------------------------------------|
|                            | Adequate (score >80%)                              |
|                            | Inadequate (score <80%)                            |
| Gender                     | $p>0.05$                                           |
| Female                     | 176 (75.2)                                         |
|                            | 122 (70.9)                                         |
| Male                       | 58 (24.8)                                          |
|                            | 50 (29.1)                                          |
| Age (years)                | $p>0.05$                                           |
| 22-29                      | 132 (56.4)                                         |
|                            | 78 (45.3)                                          |
| 30-44                      | 52 (22.2)                                          |
|                            | 30 (17.4)                                          |
| 45-59                      | 38 (16.2)                                          |
|                            | 52 (30.2)                                          |
| >60                        | 12 (5.1)                                           |
|                            | 12 (7)                                             |
| Work place                 | $p=0.01$                                           |
| Community pharmacist       | 128 (54.7)                                         |
|                            | 136 (79.1)                                         |
| Hospital pharmacist        | 63 (26.9)                                          |
|                            | 24 (14)                                            |
| Clinical pharmacist        | 43 (18.4)                                          |
|                            | 12 (7)                                             |
| Experience as a pharmacist | $p>0.05$                                           |
| <5 years                   | 136 (58.1)                                         |
|                            | 84 (48.8)                                          |
| ≥5 years                   | 98 (41.9)                                          |
|                            | 88 (51.2)                                          |
| Postgraduate degree (MSc, PhD) | $p>0.05$                                   |
| Yes                        | 44 (18.8)                                          |
|                            | 26 (15.1)                                          |
| No                         | 190 (81.2)                                         |
|                            | 146 (84.9)                                         |

ADR: Adverse drug reaction
Table 4. Pharmacists behaviors towards reporting ADRs

| Question                                                                 | n (%)   |
|-------------------------------------------------------------------------|---------|
| **How often do you see ADRs in patient?**                               |         |
| Once a week                                                             | 16 (3.9)|
| Once a month                                                            | 64 (15.8)|
| Once a year                                                             | 162 (39.9)|
| Never                                                                   | 164 (40.4)|
| **Have you ever previously reported adverse drug reactions?**           |         |
| Yes                                                                     | 76 (18.7)|
| No                                                                      | 330 (81.3)|
| **If you have reported, what type of adverse drug reaction was the most common?** |   |
| Serious                                                                 | 42 (55.2)|
| Rare                                                                    | 10 (13.1)|
| Unexpected                                                              | 24 (31.5)|
| **Do you think adverse reaction reporting is important and necessary?** |         |
| Yes                                                                     | 404 (99.5)|
| No                                                                      | 2 (0.5)|
| **If your answer is yes, what is the most important reason?**          |         |
| To increase patient safety                                             | -       |
| To indicate relatively safe drugs                                       | 190 (47)|
| To determine the incidence of adverse reactions                        | 74 (18.3)|
| To identify new adverse reactions                                       | 140 (34.6)|

* n=76, n=404

Table 5. The most important factor that may discourage pharmacists from reporting adverse drug reactions

| Factor                                                                 | n (%)   |
|-----------------------------------------------------------------------|---------|
| Lack of time to complete reports                                      | 48 (11.8)|
| Concern that the report will generate extra work                      | 76 (18.7)|
| Not paying a fee for notification                                     | 2 (0.5)|
| Concern about submitting an inappropriate report                      | 18 (4.4)|
| Not knowing how and where spontaneous reporting should be done        | 150 (36.9)|
| Incomplete medical history of the patient                             | 34 (8.4)|
| The idea that a single spontaneous reporting cannot make a difference | 78 (19.2)|

Table 6. The most important factor that encourages pharmacists to report adverse drug reactions

| Factor                                                                 | n (%)   |
|-----------------------------------------------------------------------|---------|
| Reaction to a new drug                                                | 16 (3.9)|
| Unexpected reaction                                                   | 92 (22.7)|
| Serious reaction                                                      | 128 (31.5)|
| Payment asset for instant reporting                                   | 8 (2)|
| Requiring spontaneous notification                                    | 12 (3)|
| Practical and easy spontaneous reporting process                      | 72 (17.7)|
| Training of healthcare professionals                                  | 78 (19.2)|
In the study, 17% of pharmacists correctly defined what pharmacovigilance was. This low rate may have resulted from the question being an open-ended question and it was only 3 years ago that the regulation on the pharmacovigilance system (Regulation on Monitoring and Evaluation of the Safety of Medicinal Products for Human Use) came into force. 87% of pharmacists did not know where to get ADRs reporting forms. The results of our study showed that the level of knowledge on pharmacovigilance and ADRs reporting increased significantly in Türkiye. This was because pharmacovigilance courses are given in more places during the bachelor’s degree. In our study, 40.4% of pharmacists stated that they had never seen ADRs in their patients, which was a high rate. In the study by Suyagh et al., 8% of the patients never reported to their pharmacist, when ADRs developed. This might be because patients in Türkiye did not consult pharmacists, when ADRs developed. In the patient information leaflet of some medicines in Türkiye, there is the phrase “consult your doctor when you have an unexpected side effect”. This statement may have prevented patients who experienced ADR the pharmacist from consulting, when ADRs develop. Pharmacists should also be added to this statement in the patient information leaflet. Although 99.5% of the pharmacists thought that ADR reporting was important, 18.7% of pharmacists previously reported ADRs. This ratio was also supported by other scientific reports that concluded that the rates of ADRs reported by pharmacists in various countries ranged from 14.6% to 38%. But this ratio was 7% in the study by Toklu and Uysal. This situation demonstrated that the ADR reporting rate has increased in Türkiye.

CONCLUSION

These results showed that Turkish pharmacists had sufficient knowledge about the concept of pharmacovigilance and the spontaneous ADR reporting system. However, they had little experience in ADRs reporting. Training programs should be ongoing to enhance the role of pharmacists, their knowledge of the reporting process, and requirements and the reporting experience.

Ethics

Ethics Committee Approval: Ethical approval for this study was obtained from the Gazi University Ethics Committee (approval number and date 2021-445/06.04.2021). Informed Consent: Informed consent was obtained. Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.A., Design: A.A., B.K., Data Collection or Processing: A.A., B.K., Analysis or Interpretation: A.A., B.K., Literature Search: A.A., Writing: A.A., B.K.

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