Advances in Pharmacoepidemiology & Drug Safety

Obara et al., Adv Pharmacoepidemiol Drug Saf 2015, 4:5
DOI: 10.4172/2167-1052.1000191

Research Article Open Access

Prevalence, Determinants, and Reasons for the Non-Reporting of Adverse Drug Reactions by Pharmacists in the Miyagi and Hokkaido Regions of Japan

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Abstract

Little is known about the potential of adverse drug reaction (ADR) non-reporting by Japanese pharmacists. The aim of the present study was to clarify the prevalence, determinants, and reasons for ADR non-reporting by pharmacists in the Miyagi and Hokkaido regions of Japan. In this cross-sectional, self-administered questionnaire-based study, we contacted 3,164 pharmacists who belonged to the Miyagi Prefecture Hospital Pharmacists Association or the Hokkaido Society of Hospital Pharmacists during the 3-month period between January to March 2013. Of the 1,795 respondents 22.4% were <30 years of age, 25.6% were ≥ 50 years of age, and 42.1% were female. A total of 77.6% of the respondents did not have a personal history of ADR reporting. The multivariate logistic regression analysis showed that female sex (odds ratio, 1.52; 95% confidence interval, 1.17-1.97), having <10 years of practical experience (2.59, 1.39-4.82 for 5-9 years; 7.03, 2.94-16.83 for <5 years), working at a community pharmacy or drugstore (1.90, 1.16-3.12), having <5 pharmacists in the workplace (2.01, 1.48-2.75), and not understanding the ADR reporting system (5.93, 4.23-8.33) were significantly and independently associated with not having a personal history of ADR reporting. The most common reason for ADR non-reporting was "It was a well-known adverse drug reaction" (43.0%) followed by "Association between the drug and adverse reaction was not clear" (38.0%), "It was a minor adverse drug reaction" (29.0%), "Did not know how to make a report" (17.4%), and "Never been consulted about ADRs" (17.2%). As an understanding the ADR reporting system was strongly associated with ADR reporting, a more aggressive promotion of the ADR reporting system among pharmacists is warranted.

Keywords: Adverse drug reaction; Pharmacist; Questionnaire

Abbreviations

ADR: Adverse Drug Reaction; JADER: The Japanese Adverse Drug Event Report Database; PMDA: The Pharmaceutical and Medical Devices Agency

Introduction

A spontaneous adverse drug reaction (ADR) reporting system is traditionally used for postmarketing drug safety surveillance in many countries. There are several reports from various countries that have demonstrated both knowledge and attitudes of health professionals are associated with spontaneous ADR reporting [1,2]. However, ADR reporting systems can differ depending upon the particular region, with the guidelines for determining relevant cases and reporting methods found to vary from country to country. Japan first began collecting information on adverse reactions to drugs after the enactment of a law in 1961. Since then, there has been an accumulation of information on serious adverse events from individual case and study reports from industries, direct voluntary reports from medical institutions, and study results from treatment outcome studies (all-case surveillance), as well as postmarketing clinical trials.

As a result, information from approximately 350,000 adverse event cases has been reported. Events that occurred after 2004 have been compiled in the Japanese Adverse Drug Event Report database (JADER), with this information becoming available for download through the Pharmaceutical and Medical Devices Agency (PMDA) website starting in 2012 (http://www.pmda.go.jp/safety/reports/hcp/0001.html). Within the clinical setting, pharmacists have the professional responsibility for pharmacovigilance. However, little is known regarding the potential non-reporting of ADRs by Japanese pharmacists. Therefore, the aim of the present study was to clarify the prevalence, determinants, and reasons for ADR non-reporting by pharmacists in the Miyagi and Hokkaido regions of Japan.

Methods

This study was a cross-sectional, self-administered questionnaire-based study involving pharmacists who belonged to the Miyagi Prefecture Hospital Pharmacists Association or the Hokkaido Society of Hospital Pharmacists. The questionnaire was developed based on previous studies [1,3,4] and was pre-tested on a sample group that consisted of ten pharmacists and five pharmacovigilance professionals to whom the purpose of the study was explained. Based on the comments received during the pilot testing, slight modifications to the wording of the questionnaire were made prior to its use in this study. Data from the pilot study were not included in the final analysis.

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Received August 08, 2015; **Accepted** September 08, 2015; **Published** September 10, 2015

Citation: Obara T, Yamaguchi H, Satoh M, Iida Y, Sakai T, et al. (2015) Prevalence, Determinants, and Reasons for the Non-Reporting of Adverse Drug Reactions by Pharmacists in the Miyagi and Hokkaido Regions of Japan. Adv Pharmacoepidemiol Drug Saf 4: 191. doi:10.4172/2167-1052.1000191

The final questionnaire consisted of five sections: (a) Characteristics of the pharmacists (age, sex, workplace, experience as a pharmacist, postgraduate degree, and the number of pharmacists in the workplace); (b) Knowledge of the ADR reporting system; (c) Personal history of ADR reporting; (d) Reasons for not having reported an ADR; (e) Personal opinion on pharmacovigilance (preference for receiving information on pharmacovigilance, and who was responsible for pharmacovigilance within the clinical practice); and (f) Knowledge of recent developments in pharmacovigilance in Japan and terminology related to pharmacovigilance (payment system for medical services, database for pharmacovigilance, 'pharmacovigilance per se', and 'regulatory science'). The questionnaire was distributed and collected by mail, with the study conducted over the 3-month period between January to March 2013. Parts of the responses to the questionnaire were used for this paper.

Pharmacists who did not know about the ADR reporting system or who knew about it but did not understand how the ADR reporting system worked were defined as the 'not understanding the ADR reporting system' group. After classifying the participants, a chi-square test was used to compare the prevalence of pharmacists who did not understand the ADR reporting system and who did not have a personal history of ADR reporting (ADR non-reporting) in each category (age, sex, level of education, years of practical experience, workplace, number of pharmacists within the workplace, and region).

Determinants of 'not understanding the ADR reporting system' and 'ADR non-reporting' were identified through the use of multilevel and multivariate logistic regression analyses to estimate odds ratios (ORs) with 95% confidence intervals (CIs) for not understanding the ADR reporting system and ADR non-reporting. Multivariate logistic regression analysis was adjusted for variables that were significantly related to not understanding the ADR reporting system and ADR non-reporting on univariate analyses. Data are shown as means ± standard deviation (SD). A p-value less than 0.05 were defined as significant. All statistical analyses were conducted with SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Of the 3,164 pharmacists who were sent questionnaires, 1,877 (59.3%) responded. The analysis excluded those pharmacists who did not completely answer the questions about age, sex, knowledge of the ADR reporting system, and personal history of ADR reporting. Characteristics of the 1,795 pharmacists who were eligible for the analysis was shown in Table 1. 22.4% were <30 years of age, 25.6% were ≥ 50 years of age, and 42.1% were women. The analysis showed that 3.0% of the pharmacists had a doctorate, 35.2% had ≥ 20 years of experience as a pharmacist, ≥88.1% worked in a hospital, and 43.3% worked at a place where there were ≥ 10 pharmacists. The prevalence of pharmacists who did not understand the ADR reporting system and who did not have a personal history of ADR reporting was shown in Figure 1. The percentages of pharmacists who did not understand the ADR reporting system and who did not have a personal history of ADR reporting were 38.7% and 77.6%, respectively. The analysis revealed that not understanding the ADR reporting system and ADR non-reporting were significantly associated with being female, younger, not having a postdoctoral degree, having a shorter period of experience, working in a community pharmacy, and having fewer pharmacists in their workplace.

Results of the multivariate logistic regression analyses for not understanding the ADR reporting system and not having a personal history of ADR reporting were shown in Table 2. The multivariate logistic regression analysis showed that having a master's degree (OR, 2.80; 95% CI, 1.19-6.63), bachelor's degree (3.02, 1.30-7.01), <20 years of practical experience (1.63, 1.12-2.35 for 10-19 years; 3.13, 1.96-4.97 for 5-9 years; 2.60, 1.50-4.48 for <5 years), and having 5-9 other pharmacists in the workplace (1.41, 1.10-1.81) were significantly associated with not understanding the ADR reporting system. The multivariate logistic regression analysis also showed that the female sex (1.52, 1.17-1.97), having <10 years of practical experience (2.59, 1.39-4.82 for 5-9 years; 7.03, 2.94-16.83 for <5 years), working at a community pharmacy or drugstore (1.90, 1.16-3.12), having <5 pharmacists in the workplace (2.01, 1.48-2.75), and not understanding the ADR reporting system (5.93, 4.23-8.33) were significantly and independently associated with not having a personal history of ADR reporting.

Reasons for ADR non-reporting among pharmacists who did not have a personal history of ADR reporting are shown in Table 3. Overall, the most common reason for ADR non-reporting was "It was a well-known ADR" (43.0%) followed by "Association between the drug and adverse reaction was not clear" (38.0%), "It was an insignificant ADR" (29.0%), "Did not know how to make a report" (17.4%), and "Never been consulted about ADRs" (17.2%). Among pharmacists who selected 'Other' as the reason for ADR non-reporting, the most common response was "Report was sent to the pharmaceutical company". A significantly greater proportion of pharmacists who did not understand the ADR reporting system selected "Did not know how to make a report," "Did not have time to make a report," "Believe reporting is the responsibility of the physician," and "Did not understand the significance of reporting" as the reasons for ADR non-reporting compared to the pharmacists who did understand the ADR reporting system.

Discussion

The present study found that 1) 77.6% of pharmacists did not have a personal history of ADR reporting; 2) the determinants of ADR non-reporting included being female, having <10 years of practical experience, working at a community pharmacy or drugstore, and having <5 pharmacists in the workplace; and 3) the most common reason for ADR non-reporting was "It was a well-known ADR."

This is the first report to examine the awareness and practice of Japanese pharmacists with respect to the ADR reporting system. The voluntary ADR reporting system is a method of collecting information on adverse events that has already been implemented in many countries globally. In order to obtain information on adverse events and achieve proper usage of pharmaceutical products, it is essential to assess the awareness of the ADR reporting system among healthcare providers including pharmacists.

Prevalence

Although there were some variations with regard to the age, sex, level of education, years of practical experience, workplace, and number of pharmacists in the workplace, the present study demonstrated that 38.7% of the pharmacists did not understand the ADR reporting system and that 77.6% did not have a personal history of ADR reporting. In particular, the percentage of pharmacists who did not understand the ADR reporting system or did not have experience with reporting was highest among pharmacists who were women, were younger, did not have a doctorate degree, had less experience as a pharmacist, worked at

Sex	
Female, %	42.1
Male, %	57.9
Age	
<30 years, %	22.4
30-39 years, %	30.4
40-49 years, %	21.6
≥ 50 years, %	25.6
Highest level of education	
Bachelors, %	65.4
Masters, %	17.0
Doctorate, %	3.0
No answer, %	14.6
Years of practical experience as a pharmacist	
<5 years, %	16.0
5-9 years, %	22.0
10-19 years, %	25.0
≥ 20 years, %	35.2
No answer, %	1.8
Workplace	
Hospital, doctor's office, or clinic, %	88.1
Community pharmacy or drugstore, %	9.8
Other, %	2.0
No answer, %	0.2
Number of pharmacists in the work place	
<5, %	31.8
5-9, %	24.7
≥ 10, %	43.3
No answer, %	0.1
Region	
Miyagi, %	25.4
Hokkaido, %	74.7
Understanding the ADR reporting system	
I understand what it is, %	61.3
I have heard of it, but do not understand what it is, %	35.2
I do not know what it is, %	3.5
Personal history of ADR reporting	
No, %	77.6
Yes, %	22.4
Understanding the ADR reporting system for patients and their family	
I understand what it is, %	34.5
I have heard of it, but do not understand what it is, %	28.4
I do not know what it is, %	36.8
No answer, %	0.2

ADR: Adverse Drug Reaction

Table 1: Characteristics of participants (n=1,795).

a community pharmacy, and had fewer pharmacists in their workplace. Previously published studies have shown that the percentage of pharmacists without experience in making reports ranged between 75.0% and 85.4% [1,3-5], which indicates that the understanding and the specific measures pursued with regard to ADR reporting among pharmacists may be similar between Japan and other countries. Since the role of pharmacists and the ADR reporting systems is known to differ slightly between countries, it may not be appropriate to directly compare the present results with the findings from these previous studies. However, at a fundamental level, the role of pharmacists in drug safety evaluations is most likely quite similar countries of the developed world.

Factors related to not understanding the reporting system and non-reporting

The present study found that the determinants of not understanding the reporting system were: having a master's or bachelor's degree as the highest level of education (vs. doctorate degree), <20 years of practical experience, and 5-9 pharmacists in the workplace. Furthermore, the determinants for the non-reporting included: female sex, <10 years of practical experience, working at a community pharmacy or drugstore, and <5 pharmacists in the workplace. Factors that reflected an inadequate education or information presentation were extracted as the determinants for not understanding the system. It has been previously reported that enrichment of the pharmacy education and a continuing

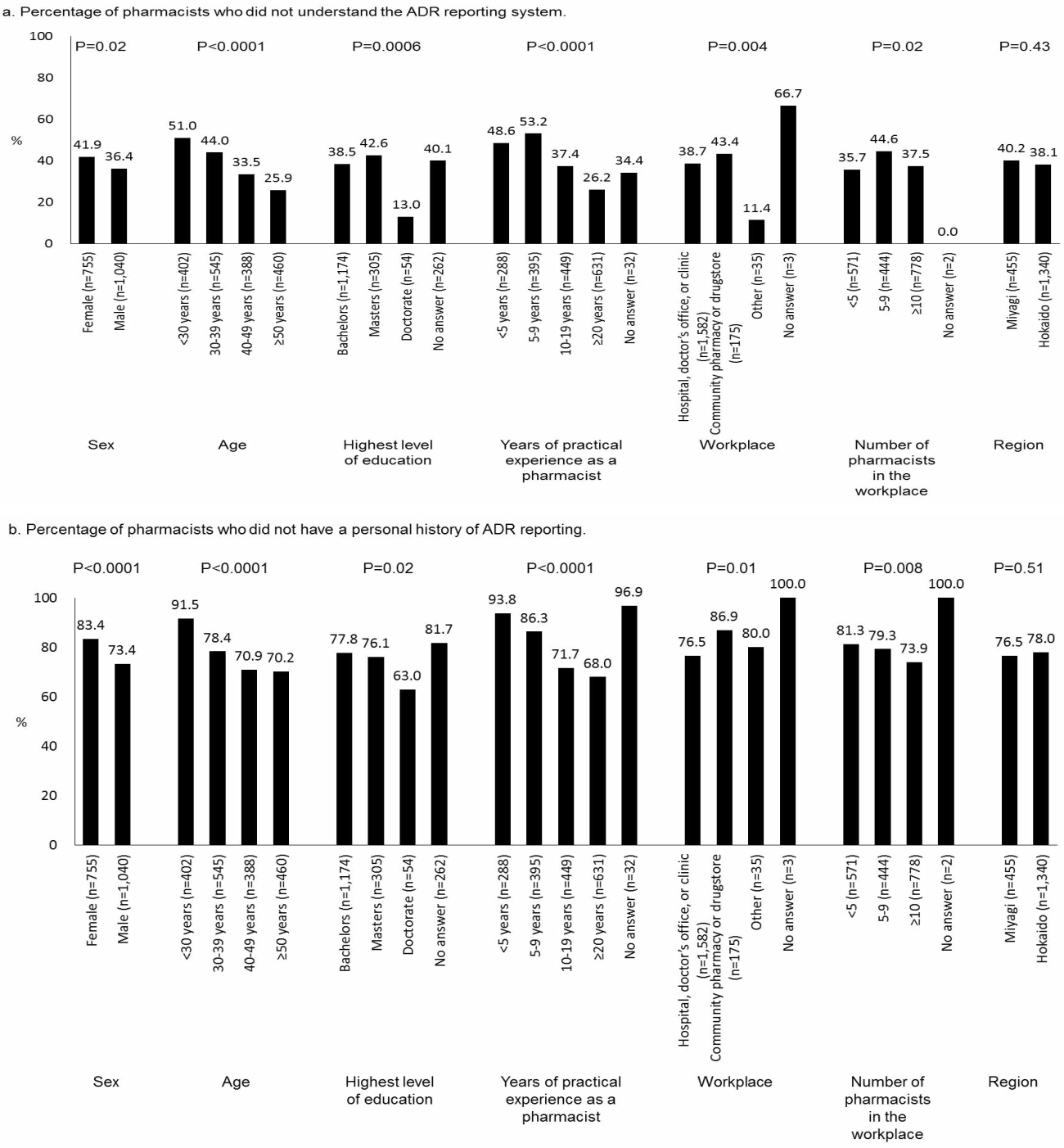

Figure 1: The prevalence of pharmacists who did not understand the ADR reporting system and who did not have a personal history of ADR reporting.

	Not understanding the ADR reporting system				Not having a personal history of ADR reporting			
Variables	OR	95%CI			OR	95%CI		
Sex								
Female	1.12	0.92	-	1.38	1.52	1.17	-	1.97
Male	1				1			
Age								
<30 years	1.25	0.73	-	2.14	12.0	0.55	-	2.62

30-39 years	1.18	0.76	-	1.83	1.09	0.64	-	1.86
40-49 years	1.27	0.92	-	1.75	1.05	0.74	-	1.49
≥ 50 years	1				1			
Highest level of education								
Bachelors	3.02	1.30	-	7.01	1.42	0.73	-	2.80
Masters	2.80	1.19	-	6.63	0.96	0.47	-	1.95
Doctorate	1				1			
Years of practical experience as a pharmacist								
<5 years	2.60	1.50	-	4.48	7.03	2.94	-	16.83
5-9 years	3.13	1.96	-	4.97	2.59	1.39	-	4.82
10-19 years	1.63	1.12	-	2.35	1.16	0.75	-	1.80
≥ 20 years	1				1			
Workplace								
Hospital, doctor's office, or clinic	1				1			
Community pharmacy or drugstore	1.37	0.98	-	1.93	1.90	1.16	-	3.12
Other	0.36	0.12	-	1.06	2.10	0.84	-	5.23
Number of pharmacists in the workplace								
<5	1.19	0.92	-	1.54	2.01	1.48	-	2.75
9-May	1.41	1.10	-	1.81	1.36	0.99	-	1.87
≥ 10	1				1			
Understanding the ADR reporting system								
Not understanding	-	-	-	-	5.93	4.23	-	8.33
Understanding	-	-	-	-	1		-	

ORs for 'no answer' to each question are not shown. ADR: Adverse Drug Reaction; OR: Odds Ratio; CI: Confidence Interval

Table 2: The multivariate logistic regression analyses for not understanding the ADR reporting system and not having a personal history of ADR reporting.

	Total	Understanding the ADR reporting system		
		No	Yes	
	n=1,393	n=649	n=744	P
It was a well-known ADR	43.0	41.6	44.2	0.32
Association between the drug and adverse reaction was not clear	38.0	36.2	39.5	0.2
It was an insignificant ADR	29.0	25.6	32.0	0.009
Did not know how to make a report	17.4	29.6	6.9	<.0001
Never been consulted about ADRs	17.2	15.1	19.0	0.06
Sufficient information could not be obtained from patients	8.3	8.6	8.1	0.7
ADR reporting system is very complicated	6.8	6.8	6.9	0.96
Did not have time to make a report	6.3	7.9	4.8	0.02
Believe reporting is the responsibility of the physician	4.2	5.4	3.2	0.045
Did not understand the significance of reporting	0.7	1.4	0.1	0.008
There was a concern of possibly being legally responsible	0.1	0	0.3	0.5
Other	8.1	5.7	10.2	0.002

ADR: Adverse Drug Reaction

Table 3: Reasons for ADR non-reporting among the 1,392 pharmacists who did not have a personal history of ADR reporting.

postgraduate education dealing with general adverse event reporting enhanced the understanding the ADR reporting system [5-9]. Although pharmacists have the legal and social responsibilities in ADR reporting, the opportunity of systematic learning ADR reporting system has been limited only at the pharmacy school curriculum in Japan. Therefore, we ought to provide for Japanese pharmacists the opportunity to receive education and hands on training in ADR reporting. Factors that reflect less experience and were extracted as determinants of non-reporting included, medical work environments with difficulties in obtaining detailed patient information, fewer opportunities to see patients with serious illnesses, or fewer patients likely to have ADRs. This study showed that being a pharmacist with both <10 years of practical experience and having contact with <10 pharmacists in the workplace were common factors for not understanding and for non-reporting the ADR. Thus, in the future it will be necessary to proactively provide information regarding the ADR reporting system to these individuals who have had less experience and limited access to other pharmacists. Female sex was one of the determinants for the ADR non-reporting. Sex difference might reflect the difference of factors that we could not evaluate in this study such as employment status.

Reasons for ADR non-reporting

Pharmacists who understand the ADR reporting system but have had no experience in ADR reporting responded that the reasons

for ADR non-reporting were "It was a well-known ADR" (43%), "Association between the drug and adverse reaction was not clear" (38%), and "It was an insignificant ADR" (29%). These responses were similar to those reported in other previous studies [4,6,7,10,11]. In Japan, the information (or cases) that the government views as being appropriate to report includes "the onset of adverse reaction, infection, or malfunction through the usage of pharmaceutical products, medical devices, or regenerative medicine products, that is determined to require a report from the perspective of preventing the onset or spreading of health and hygiene hazards." However, since the definition of what the government requires is somewhat complicated and open to different interpretations, the results from our current study may more closely reflect the actual situation, with the decision on whether or not to report ADR information made at the discretion of the healthcare worker. By clarifying the definition of what cases are appropriate for reporting, it is anticipated that this should lead to a further accumulation of adverse event information, as well as improvements in the usability of this database system in the future.

Limitations

Limitations of current study may include making generalizations from the present study results that are based on information from pharmacists from only two regions of forty-seven prefectures in Japan. We need to examine whether or not there are big differences in the pharmacovigilance among different states of Japan. In addition, pharmacists who have an interest in this study subject have been the ones who are proactively providing responses. Thus, the proportion of pharmacists who understand the ADR reporting system or have experience in ADR reporting may be even lower in the actual overall pharmacist population. Nonetheless, since the response rate of this study survey was approximately 60%, this presumably indicates that these results do largely reflect the pharmacists' viewpoint within the overall study region.

Perspectives

In 2012, the ADR database containing the reports collected since 2004 became available on the PMDA website. This has helped facilitate the effective usage of the adverse event information collected by pharmacists in clinical settings. With continued education and training, in the future, both researchers and pharmacists working in a clinical setting will be able to compile and analyze the information contained in this database. Furthermore, over time it is also anticipated that pharmacists will be able to better contribute to the appropriate usage of pharmaceutical products in Japan.

Conclusion

This study examined the prevalence of pharmacists who had a personal history of ADR reporting and clarified the determinants and reasons for ADR non-reporting. As a better understanding the ADR reporting system was strongly associated with the ADR reporting, this indicates that a more aggressive promotion of understanding the ADR reporting system among pharmacists is warranted.

Acknowledgement

The authors would like to thank the Miyagi Prefecture Hospital Pharmacists Association and the Hokkaido Society of Hospital Pharmacists and pharmacists and pharmacovigilance professionals who helped to develop the questionnaire. This research was partially supported by the Research on Regulatory Harmonization and Evaluation of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics from Japan Agency for Medical Research and Development, AMED.

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