

# Factors that affect adverse drug reaction reporting among hospital pharmacists in Western China

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**Abstract** *Background* Hospital pharmacists can make a considerable contribution to the spontaneous reporting system of adverse drug reactions. The factors that influence adverse drug reaction reporting among hospital pharmacists remain largely unknown in China. *Objective* This study aims to identify factors that affect hospital pharmacist-led adverse drug reaction reporting in Xi'an, and to obtain suggestions from pharmacists about how to improve the current adverse drug reaction reporting system. *Setting* Hospital settings throughout Xi'an, a region of Western China. *Method* A matched case–control study was conducted on a population of 2,814 hospital pharmacists in Xi'an during 2011. Cases included all pharmacists who had reported at least one adverse drug reaction between 2008 and 2010 and agreed to participate in the study (186/204; 91.2 %); controls (n = 372) were pharmacists who had not reported any adverse drug reaction during the same period. A self-administered questionnaire was distributed to the participants. Logistic regression was performed to evaluate the association between indicator variables and the outcome of having reported at least one adverse drug reaction. *Main outcome measure* Pharmacists'

knowledge, attitude and practice towards adverse drug reaction reporting and factors affecting reporting. *Results* Higher professional title (adjusted OR 1.44; 95 % CI 1.07–1.94;  $p = 0.018$ ), having received training about adverse drug reaction reporting (1.64; 1.04–2.57;  $p = 0.032$ ), better knowledge about reporting (1.53; 1.12–2.08;  $p = 0.007$ ), “lack of access to adverse drug reaction reporting form” (0.29; 0.12–0.72;  $p = 0.008$ ) was independently associated with adverse drug reaction reporting. Clinical pharmacists were more likely to report an adverse drug reaction than dispensary pharmacists (1/adjusted OR 5.26;  $p < 0.001$ ), pharmacy administrators (5.00;  $p = 0.003$ ), and other technicians (5.56;  $p = 0.001$ ). *Conclusions* Higher professional title, having received training, mastering knowledge about reporting, and being a clinical pharmacist were positive predictors of pharmacist-led adverse drug reaction reporting. Lack of access to reporting forms was a negative predictor. Continuous training and establishing incentive mechanisms are needed to promote adverse drug reaction reporting among hospital pharmacists.

**Keywords** Adverse drug reaction · Case–control study · China · Hospital pharmacists · Logistic regression

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## Impact of findings on practice

- There is a need to conduct regular training sessions that target hospital pharmacists to alter incorrect beliefs and communicating basic knowledge about ADR in Shaanxi Province, Western China.
- It's necessary to facilitate ADR reporting by making reporting forms easy to access.
- Regulatory authorities should establish incentive mechanisms to promote ADR reporting in Chinese hospitals.

## Introduction

Adverse drug reactions (ADRs) are an important cause of morbidity, mortality, and extra healthcare costs [1, 2], accounting for up to 6.5 % of all hospital admissions and occurring in 10.9 % of inpatients [1, 3]. Spontaneous reporting of ADRs forms the basis of pharmacovigilance systems in most countries [4, 5]. However, under-reporting can compromise the effectiveness of these systems; it is estimated that only about 6 % of all ADRs are reported [6]. As a consequence, many serious and fatal reactions are never brought to the attention of regulatory authorities.

In China, the National Center for ADR Monitoring was established in 1989. By the end of 2012, it had a network of 34 provincial centres and more than 230 municipal centres. All suspected adverse reactions of a drug should be reported within 5 years from the day of marketing approval or the first importation. After the 5-year period, only new and serious adverse reactions of a drug shall be reported. A serious adverse drug reaction refers to a drug reaction that leads to any of the following situations: (1) death; (2) life-threatening; (3) cancer, deformity and birth defect; (4) permanent or distinctive impairment and physical disabilities; (5) hospitalization or prolonged hospitalization; (6) permanent organ damages [7].

ADRs must be reported through the online ADR surveillance system or by mail to the ADR centres where reporting manufacturers, distributors, or healthcare institutions are located. There has been rapid growth in the number of ADR reports received, from 500 in 1998 [8] to more than 1,200,000 in 2012 (902 per million population) [9]. This rate of reporting is similar to rates in other developed countries [10, 11]. Approximately 20 % of these reports were new or serious; others were known or labelled. Hospitals remain the main source of ADR reporting, accounting for 74.8 % of reports, followed by drug manufacturers and distributors (24.4 %) and consumers (0.8 %).

There is increasing evidence showing that hospital pharmacists can make a considerable contribution to spontaneous reporting systems, both in terms of the quantity and quality of reports [12–14]. In China, hospital pharmacists worked in the area of dispensary, clinical pharmacy and administration, and reported ADRs as part of their professional responsibility. At present, the main pharmacist qualification system in Chinese hospitals is a specialized system, under which a pharmaceutical specialist is assigned a specific title, such as assistant pharmacist, pharmacist, pharmacist-in-charge, associate chief pharmacist, or chief pharmacist, according to their educational background, work experience, and professional skills. Hospital pharmacists have not traditionally been well educated to provide clinical pharmacy services [15,

16]; stocking and dispensing medications characterizes the image of the profession. However, hospital pharmacist roles have recently expanded to include rational drug use and a focus on patient care. This continued until 2002, at which time the government required hospitals to develop dedicated clinical pharmacy programmes [17]. Pharmacists have been invited to submit ADR reports since the ADR reporting systems were established in China; however, the contribution from pharmacists to the spontaneous reporting system is still considered low [18].

Many studies about the factors that influence ADR under-reporting have been conducted on physicians [19–27]. Of the few studies that have focused on under-reporting among pharmacists [28–32], only four studies [22, 24, 31, 32] adequately described their study design (all four were case-control studies). Only one study has focused on factors associated with ADR reporting among hospital pharmacists in China [33]; however, the authors did not specify the design.

## Aim of the study

This study aims to (1) identify factors that affect hospital pharmacist ADR reporting in the Xi'an region using the case-control method, and (2) obtain suggestions from pharmacists about how to improve the current ADR reporting system.

## Ethical approval

The study protocol was approved by the Health Science Center of Xi'an Jiaotong University, and ethical approval was obtained from the university's Research Ethics Committee. Permission to approach the pharmacists was obtained from the manager of the respective pharmacy department. Written informed consent was obtained from potential participants prior to enrolment.

## Method

### Study design and sample

A matched case-control method was used to explore differences in demographic factors, as well as knowledge, attitudes, and obstacles related to ADR reporting between the cases and controls. The study targeted 2,814 hospital pharmacists working in hospitals at the end of 2010 in Xi'an, the capital city of Shaanxi Province, Western China. The cases ( $n = 204$ ) were the totality of pharmacists who had reported at least one ADR to a regional ADR

monitoring platform between January 2008 and December 2010, and the controls ( $n = 372$ ) were randomly sampled from pharmacists who had not reported any ADR during the same period of time. For each case, two control pharmacists were randomly selected from the same hospital.

### Study setting

This study involved all the hospital settings in Xi'an, a region with direct jurisdiction over nine districts and four counties, and around 8.3 million residents.

### Survey instrument development and implementation

On the basis of the “Knowledge-Attitude-Practice Model” [34], and the items used in previous studies that involved medical practitioners and pharmacists [24, 26, 28, 29, 31], a questionnaire was developed to meet the objectives of the study. Some modifications were made to adapt the questions to the Chinese setting. The questionnaire was developed originally in Chinese. To ensure that an English equivalent would be produced, the questionnaire was translated by two translators (native English speakers), then back-translated by two independent English speakers fluent in Chinese. The questionnaire included six sections: (1) personal and professional data; (2) knowledge concerning reporting of ADRs; (3) attitudes concerning ADR reporting; (4) personal history of detecting and reporting ADRs; (5) obstacles that may discourage ADR reporting; and (6) suggestions for improving ADR reporting by pharmacists. Prior to the main data collection phase of the study, the questionnaire was tested in three hospital pharmacies. Minor modifications to the text were made based on comments received during the pilot study.

Most questions were closed-ended (respondents were allowed to choose from a pre-existing set of answers), while the suggestions for improvement section was open-ended. Agreement with the questions regarding attitudes linked to ADR reporting were measured using a 5-point Likert scale from 1 (totally disagree) to 5 (totally agree).

The level of knowledge concerning reporting of ADRs was measured using the sum of scores of four items: what, who, how, and where [35]. “What to report” and “who should report” used multiple-choice questions, where the respondents were asked to select the best answer from a list of choices (one point was assigned if the answer was right). “How to report” and “where to report” used multiple-choice questions that respondents were allowed to mark with more than one answer if necessary (0.25 points was assigned per answer). As a result, pharmacist knowledge was a discrete quantitative variable, with a value between 0 and 4. Data collection was conducted by two trained investigators (master's degree candidates) between June and

July 2011. The questionnaires were sent to pharmacists (who could retain the questionnaire for 1 week to give them time to consider the questions) and collected face-to-face by investigators. Respondents were told in a covering letter that the information they provided would be anonymous and would be gathered for the purposes of research. All forms were coded to facilitate anonymity. Control pharmacists who became unavailable were replaced by another randomly selected pharmacist from the same hospital.

The pharmacists managing ADR reporting (usually pharmacy directors) in all hospitals surveyed were interviewed to collect their suggestions for improving ADR reporting in the hospital setting. The pharmacists were visited at their respective offices to conduct the interview.

### Data analyses

Data were recorded in EpiData version 3.1 (EpiData Association, Odense, Denmark). Statistical analysis was performed with SAS statistical software version 9.1.3 (SAS Institute, Cary, NC, USA). Continuous variables were expressed as mean  $\pm$  SD; categorical variables were expressed as percentages. In the bivariate analysis, cases and controls were compared using the Mann–Whitney U test for continuous variables, and the Mantel–Haenszel Chi square test for categorical variables. In the multivariate analysis, conditional logistic regression was performed to evaluate the association between indicator variables and the outcome of having reported at least one ADR between 2008 and 2010. Variables in the conditional logistic regression model were selected according to results of the bivariate analysis with a  $p$  value  $<0.10$ . This  $p$  value is slightly above the conventional level of 0.05; the higher value was chosen to minimize type II errors during selection. Multicollinearity was assessed on all variables by examining tolerance. Finally, Spearman's correlation was tested to determine the association between pharmacists' knowledge concerning ADR reporting (expressed as a discrete quantitative variable) and the number of ADRs reported during the previous 3 years. For all such analyses, significance was evaluated at  $p < 0.05$ .

### Results

A total of 558 completed questionnaires were collected (186 from cases and 372 from controls). About 9 % of the case pharmacists could not be reached (owing to retirement, job transfers, or declining to participate in the research), resulting in a slightly lower response rate for cases (91.2 %) compared with controls (100.0 %). Of the 55 hospitals surveyed, 17 (30.9 %) were tertiary hospitals, and

the remainder were secondary (65.5 %) or primary (3.6 %) hospitals.

The distribution of personal and professional characteristics among case and control pharmacists is shown in Table 1. The bivariate analysis showed there were no significant differences in gender, mean age, or time since specialization between the cases and controls ( $p > 0.05$ ), while significant associations were found between ADR reporting and factors such as position type and professional title ( $p < 0.001$ ). Having received training about ADR reporting was significantly associated with ADR reporting ( $p = 0.003$ ).

### Knowledge and attitudes

Both groups of pharmacists have a relatively good awareness of the basic knowledge needed to report an ADR (who, what, how, and where). A comparison of sum scores of knowledge concerning ADR reporting showed that the cases scored higher than the controls (3.33 and 3.11, respectively;  $p = 0.005$ ). The result of Spearman's correlation indicated there was a significant positive correlation between the sum scores and ADRs reported ( $r = 0.157$ ;  $p = 0.033$ ). Most pharmacists were aware that suspected ADRs could be reported by submitting a paper reporting form (88.4 % of participants) or electronic reporting form (86.9 %). More than half of the pharmacists were not aware of the options to report ADRs by phone (54.1 % of participants) or e-mail (55.7 %). Significantly more pharmacists in the case group were aware that all suspected ADRs should be reported compared with the control group (94.1 and 82.3 %, respectively;  $p < 0.001$ ).

Table 2 shows pharmacists' grades in relation to their agreement with the six statements about ADR reporting (in terms of mean  $\pm$  SD), and their related influence on reporting (in terms of OR and 95 % CI). Only the statement "all serious ADRs are detected and documented by the time a drug is marketed" was found to be significantly associated with ADR reporting ( $p = 0.047$ ).

The majority of pharmacists from both groups agreed with the statements concerning the importance of the ADR reporting system (93.5 %) and their professional obligations regarding ADR reporting (91.0 %), which indicates a positive attitude towards ADR reporting. Moreover, most pharmacists (74.7 % of cases; 75.5 % of controls) reported a higher likelihood of reporting ADRs to drug surveillance units, if there was an easier method. A small number of pharmacists (8.1 % of cases; 9.6 % of controls) agreed with the statement "the one case an individual pharmacist might see can't contribute substantially to pharmaceutical knowledge".

### Detecting and reporting history

Most pharmacists had detected at least one ADR during their professional life (cases 100 %,  $n = 186$ ; controls 79.3 %,  $n = 295$ ). The two main mechanisms that pharmacists used to detect ADRs were outpatient reporting (70.1 % of cases; 79.5 % of controls) and spontaneous reporting by physicians or nurses (72.8 % of cases; 70.3 % of controls). A lower proportion of pharmacists had detected ADRs through questioning patients on ward rounds (34.2 % of cases; 18.4 % of controls), or by reviewing

**Table 1** Personal and professional characteristics of cases and matched controls

| Characteristics                             | Cases (n = 186)  | Controls (n = 372) | p value             |
|---|------------------|--------------------|---------------------|
| Gender [n (%)]                              |                  |                    |                     |
| Male  | 50 (26.9)        | 91 (24.5)          |                     |
| Female                                      | 136 (73.1)       | 281 (75.5)         | 0.533 <sup>a</sup>  |
| Mean age $\pm$ SD (years)                   | 37.66 $\pm$ 0.69 | 37.03 $\pm$ 0.54   | 0.392 <sup>b</sup>  |
| Position type [n (%)]                       |                  |                    |                     |
| Clinical pharmacist                         | 61 (32.8)        | 20 (5.4)           |                     |
| Dispensary pharmacist                       | 101 (54.3)       | 270 (72.6)         |                     |
| Pharmacy administrators                     | 14 (7.5)         | 42 (11.3)          |                     |
| Others (e.g. pharmacy stores administrator) | 10 (5.4)         | 40 (10.8)          | <0.001 <sup>a</sup> |
| Time since specialization                   |                  |                    |                     |
| Mean $\pm$ SD (years)                       | 14.76 $\pm$ 0.73 | 14.55 $\pm$ 0.56   | 0.698 <sup>b</sup>  |
| Professional title [n (%)]                  |                  |                    |                     |
| Assistant pharmacist                        | 20 (10.8)        | 104 (28.0)         |                     |
| Pharmacist                                  | 63 (33.9)        | 141 (37.9)         |                     |
| Pharmacist-in-charge                        | 68 (36.6)        | 101 (27.2)         |                     |
| Associate chief/Chief pharmacist            | 35 (18.8)        | 26 (7.0)           | <0.001 <sup>a</sup> |
| Received training on ADR reporting          |                  |                    |                     |
| In last 3 years [n (%)]                     | 110 (59.1)       | 172 (46.2)         | 0.003 <sup>a</sup>  |

<sup>a</sup> Mantel–Haenszel Chi square test

<sup>b</sup> Mann–Whitney U test

**Table 2** Attitudes and beliefs towards ADR reporting measured with a 5-Likert scale

| Statements   | Cases<br>(n = 186)<br>Mean $\pm$ SD | Controls<br>(n = 372)<br>Mean $\pm$ SD | OR (95 % CI)     | p value |
|--|-------------------------------------|--|------------------|---------|
| I would only report an ADR if I were sure that it was related to the use of a particular drug              | 3.30 $\pm$ 1.17                     | 3.33 $\pm$ 1.01                        | 0.96 (0.81–1.14) | 0.650   |
| All serious ADRs are detected and documented by the time a drug is marketed                                | 2.61 $\pm$ 1.22                     | 2.82 $\pm$ 1.21                        | 0.86 (0.74–1.00) | 0.047   |
| The one case an individual pharmacist might see can't contribute substantially to pharmaceutical knowledge | 2.03 $\pm$ 0.83                     | 2.13 $\pm$ 0.85                        | 0.84 (0.67–1.06) | 0.144   |
| I would be more likely to report ADRs to Drug-surveillance Unit if there was an easier method              | 3.82 $\pm$ 0.82                     | 3.78 $\pm$ 0.75                        | 1.06 (0.84–1.34) | 0.626   |
| Spontaneous reporting system make an important contribution to drugs' security knowledge                   | 4.34 $\pm$ 0.71                     | 4.23 $\pm$ 0.71                        | 1.26 (0.96–1.64) | 0.093   |
| Detecting and reporting ADRs is a professional obligation of hospital pharmacists                          | 4.26 $\pm$ 0.82                     | 4.16 $\pm$ 0.80                        | 1.19 (0.94–1.51) | 0.158   |

SD standard deviation, OR odds ratio, CI confidence interval

patients' clinical notes (20.1 % of cases; 8.9 % of controls).

All the cases (100 %) and 37 controls (9.9 %) had submitted an ADR report using a reporting form prior to 2008. Of these, 47.4 % of cases (n = 83) and 32.4 % of controls (n = 12) indicated it had been difficult to access the required information. However, 41.1 % of cases (n = 72) and 43.2 % of controls (n = 16) reported no difficulties using the reporting form.

#### Obstacles preventing the reporting of ADRs

Table 3 lists the top six obstacles that may have discouraged ADR reporting by respondents. Among them, only “lack of access to ADR reporting form” and “lack of time to fill in a report” were significantly associated with ADR reporting (p values 0.001 and 0.026, respectively).

#### Multivariate analysis

Table 4 shows the multivariate model, with all the explanatory variables of  $p < 0.10$  from the bivariate analysis. After adjusting for effects of the other variables (higher professional title, not having received ADR training, higher

scores on questions about basic ADR reporting knowledge), the obstacle “lack of access to ADR reporting form” remained an independent predictor of ADR reporting ( $p < 0.05$ ). In terms of position types, clinical pharmacists were more likely to report an ADR than dispensary pharmacists (1/adjusted OR 1/0.19 = 5.26; 95 % CI 2.50–11.11;  $p < 0.001$ ), pharmacy administrators (1/0.20 = 5.00; 1.75–14.29;  $p = 0.003$ ), and other technicians (1/0.18 = 5.56; 1.96–16.67;  $p = 0.001$ ). For the basic model, the tolerances of each potential predictor exceeded 0.80, which indicated there were no problems with multicollinearity.

#### Suggestions for improving reporting

A total of 55 pharmacy directors were interviewed. The most frequent suggestion offered to drug surveillance units was that they should promote the benefits and importance of ADR reporting (22/55, 40.0 %). The most common suggestions for hospital managers included conducting regular training sessions (34/55, 61.8 %) and establishing incentive mechanisms (29/55, 52.7 %) in relation to ADR reporting.

**Table 3** The obstacles that may discourage pharmacists from reporting ADRs

| Obstacles <sup>a</sup>                            | Cases (n = 186)<br>Agree % (n) | Controls (n = 372)<br>Agree % (n) | p value <sup>b</sup> | Overall (n = 558)<br>Agree % (n) |
|---|--------------------------------|-----------------------------------|----------------------|----------------------------------|
| Did not think it was a serious ADR                | 53.8 (100)                     | 55.9 (208)                        | 0.900                | 55.2 (308)                       |
| Did not think it was an unexpected ADR            | 41.9 (78)                      | 38.4 (143)                        | 0.347                | 39.6 (221)                       |
| ADR reporting is not mandatory                    | 30.6 (57)                      | 24.7 (92)                         | 0.289                | 26.7 (149)                       |
| Concern that a report will generate an extra work | 15.6 (29)                      | 12.9 (48)                         | 0.661                | 13.8 (77)                        |
| Lack of access to ADR reporting form              | 5.4 (10)                       | 17.2 (64)                         | 0.001                | 13.3 (74)                        |
| Lack of time to fill in a report                  | 16.1 (30)                      | 8.9 (33)                          | 0.026                | 11.3 (63)                        |

<sup>a</sup> Statement that agreed by over 10 % of overall respondents are listed

<sup>b</sup> Mantel–Haenszel Chi square test

**Table 4** Variables associated with the pharmacists' adverse drug reaction reporting

| Variables   | Crude analysis   |                | Adjusted analysis <sup>a</sup> |                |
|---|------------------|----------------|--------------------------------|----------------|
|   | OR (95 % CI)     | <i>p</i> value | OR (95 % CI)                   | <i>p</i> value |
| Higher education status   | 1.98 (1.54–2.53) | <0.001         | 1.18 (0.86–1.62)               | 0.299          |
| Position types  |                  |                |                                |                |
| Clinical pharmacist   | (Reference)      |                | (Reference)                    |                |
| Dispensary pharmacist   | 0.14 (0.08–0.26) | <0.001         | 0.19 (0.09–0.40)               | <0.001         |
| Pharmacy administrator  | 0.18 (0.07–0.47) | 0.001          | 0.20 (0.07–0.57)               | 0.003          |
| Others  | 0.09 (0.04–0.22) | <0.001         | 0.18 (0.06–0.51)               | 0.001          |
| Higher professional title   | 1.81 (1.46–2.24) | <0.001         | 1.44 (1.07–1.94)               | 0.018          |
| Having received education or training on ADR reporting in last 3 years  | 1.77 (1.21–2.58) | 0.003          | 1.64 (1.04–2.57)               | 0.032          |
| Higher scores on questions about basic knowledge for ADRs reporting   | 1.54 (1.19–1.99) | 0.001          | 1.53 (1.12–2.08)               | 0.007          |
| Higher grade of agreement with: “All serious ADRs are detected and documented by the time a drug is marketed” | 0.86 (0.74–1.00) | 0.047          | 0.98 (0.81–1.18)               | 0.824          |
| Grade of agreement with: “ADRs reporting system made an important contribution to drugs security knowledge”   | 1.26 (0.96–1.64) | 0.093          | 1.22 (0.89–1.68)               | 0.216          |
| Lack of access to ADR reporting form  | 0.28 (0.14–0.57) | 0.001          | 0.29 (0.12–0.72)               | 0.008          |
| Lack of time to fill in a report  | 1.74 (1.01–3.00) | 0.046          | –                              | –              |

OR odds ratio, CI confidence interval

<sup>a</sup> Multivariate analysis adjusted for the effects of the other variables in this table

For respondents who had not received any ADR reporting education or training within the previous 3 years (cases: 40.9 %, *n* = 76; controls: 53.8 %, *n* = 199; refer to Table 1), almost all of them (94.7 % of cases and 95.8 % of controls) indicated they were interested in receiving this kind of training.

## Discussion

In this first study to investigate ADR reporting patterns of hospital pharmacists in China using a matched case–control design, the results indicate that clinical pharmacists are more likely to report an ADR than dispensary pharmacists, pharmacy administrators, and other technicians. Such position-related differences could be because clinical pharmacists are better informed regarding pharmacovigilance, have regular contact with physicians [36], can screen medical records, and question patients if an ADR is suspected [37]. Furthermore, clinical pharmacists are involved in more patient-facing activities, and therefore have more potential to detect suspected ADRs than other roles do.

Having received education or training was an independent risk factor for pharmacists' reporting behaviour. This finding confirms results from previous studies, in which those who received training were more likely to have reported an ADR [28, 29]. Findings from this study indicate that a higher knowledge score about ADR reporting is an

important factor for predicting reporting behaviour by pharmacists. These findings are similar to results from other related studies [19, 31].

Unlike other studies that have explored the attitudes and beliefs strongly associated with ADR reporting [32, 38], the only statement in our study that seemed to be associated with ADR reporting was “all serious ADRs are detected and documented by the time a drug is marketed”. However, when adjusted for the effects of other variables, this statement did not remain an independent predictor for reporting behaviour; this is probably because cases and controls held similar attitudes towards ADR reporting. In addition, use of a 5-point Likert scale to assess attitudes, instead of a visual analogue scale, could be the reason why subtle differences in the pharmacists' attitudes were not detected. In general, hospital pharmacists working in Xi'an have a positive attitude towards ADR reporting. This finding is consistent with that of earlier studies [30, 39].

A major obstacle that discouraged pharmacist-led ADR reporting was the perception that it was not a serious or unexpected ADR, which corroborates the results of previous research [20, 25, 31]. In addition, “reporting is not mandatory” and “concern that a report will generate extra work” were identified as minor deterrents, both of which were reported in a similar study among community pharmacists in Turkey [40]. “Lack of access to ADR reporting form” was negatively associated with ADR reporting, which may indicate that pharmacists who cannot access



reporting forms are less likely to report an ADR than pharmacists who can.

The survey results suggest that the current level of education may not be satisfactory. Almost all respondents who had not received any training about ADR reporting indicated they were interested in receiving this kind of training. Establishing incentive mechanisms was another option suggested by the pharmacists to improve the spontaneous reporting system. This suggestion has been proposed in previous studies as well [28, 29, 41, 42]. This may include encouragement from managers and departments by issuing certificates or recognition awards, and additional remuneration for every reported case.

This study has several limitations. The first limitation was the possibility of selection bias. For each case, two control pharmacists were selected from the same hospital—i.e. controls were matched by hospital. As a result, we eliminated our ability to estimate the effect of certain environmental factors on ADR reporting (e.g. the hospital's local ADR scheme's effect) [43]. Furthermore, matching may have indirectly manipulated our exposure assessment, so that the control group did not reflect exposure in the population who had not reported an ADR. This could be a possible reason for the null findings observed in some factors studied. Second, there was a possibility of information bias. The questionnaire's reliability and validity had not been previously established; however, the questionnaire was drafted based on questions that were tested and validated in previous studies. In addition, a pilot study was carried out and appropriate modifications were made based on participant feedback. Third, the use of a face-to-face survey enabled achievement of a high response rate because an interviewer was physically present to collect the data. However, this advantage comes with additional potential sources of response bias. To reduce this type of bias, investigators were trained to explain to respondents the purposes of collecting information accurately and precisely, and to avoid bias that may result from suggesting responses to pharmacists.

## Conclusions

Positive predictors of pharmacist-led ADR reporting included being a clinical pharmacist, having a higher professional title, having received training about reporting ADRs, and mastering knowledge about reporting. Lack of access to an ADR reporting form was a negative predictor. Education that focuses on altering incorrect beliefs and communicating basic knowledge about ADR reporting should be incorporated into vocational pharmacy training. Establishing incentive mechanisms may increase ADR reporting in hospitals.

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