### An Educational Intervention to Improve Adverse Drug Reaction Reporting: An Observational Study in a Tertiary Hospital in Vietnam

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### Abstract

Context: Under-reporting of adverse drug reactions (ADRs) are common. Aims: The study aimed to describe ADR reports after an educational intervention for physicians and nurses by clinical pharmacists. Methods and Material: Pharmacists conducted two separate training sessions for physicians and nurses in January and February 2019 in a tertiary hospital. The hospital collected all ADR reports from January to December 2019. Results: In 2019, the hospital reported 147 ADR cases, increasing 12.25 times compared to 2018. All ADR reports had complete information fields. The majority of ADR reports were collected by physicians (64.6%) and pharmacists (24.5%). The departments reporting the most ADRs were internal respiratory medicine (21.8%) and obstetrics (14.3%). Most ADRs were not serious (90.5%). The most-reported clinical signs were pruritus (64.0%) and erythema/redness (61.9%). All cases recovered without any complication after treatment. ADR reports were mainly related to the parenteral route (79.6%), and antibiotics (66.0%), analgesics (18.3%). Conclusions: Training of physicians and nurses by pharmacists on ADR significantly increased the quantity and quality of ADR reporting. More intensive and specific training and other measures are needed to improve the under-reporting of ADRs.

Keywords: hospital, reporting, ADR, pharmacovigilance, education

### INTRODUCTION

The under-reporting of adverse drug reactions (ADR) is a challenge of pharmacovigilance in the world [1-3]. The median under-reporting rate across the 37 studies from 12 countries was 94% (interquartile range 82-98%) [2]. The major factors found to be responsible for underreporting of ADR include lack of knowledge and awareness of pharmacovigilance program [4], inadequate risk perception about newly marketed drugs, fear factor, lack of training programs for health care providers on pharmacovigilance, work overload [5].

Many initiatives to improve reporting include using information systems <sup>[6, 7]</sup>, a hospital written policy <sup>[8]</sup>, health care provider (HCP) reporting and direct patient reporting <sup>[9]</sup> as well as improved education and training of healthcare professionals <sup>[8, 10, 11]</sup>. Pharmacists have shown to play an important role in improving patient safety, including increasing the quantity and quality of ADR reporting in hospitals <sup>[12-14]</sup>.

Vietnam launched its National Drug Information and Adverse Drug Reaction Monitoring Centre in 2009, a significant step towards catching up with international trends. The number of reports has increased rapidly, with some important signals generated from the national database leading to regulatory actions at a national level. Many opportunities remain to enhance the system, particularly in the evaluation of the impact of the intervention to improve ADR reporting [15].

Nguyen Tri Phuong Hospital (NTPH) has stepped up cooperation with Pham Ngoc Thach University of Medicine (UPNT) in Ho Chi Minh in deploying clinical pharmacy since the beginning of 2019. One of the first missions of the clinical pharmacy unit at the hospital was to improve the quantity and quality of ADR reporting. This study aimed to describe the

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quantity and quality of ADR reporting in the hospital after an education intervention for physicians and nurses.

## SUBJECTS AND METHODS: Study design and setting

An observational study was carried over a period of 12 months from January to December 2019 in a tertiary teaching hospital (Nguyen Tri Phuong hospital - NTPH) at Ho Chi Minh, Vietnam. NTPH, the 800-bedded public teaching hospital offers both medical and surgical care. The average daily out-patient consultancy is 1500-2000 and inpatient is 100–200. To improve clinical pharmacy practice in NTPH, four lecturers on clinical pharmacy from the Pham Ngoc Thach University of Medicine have worked as part-time clinical pharmacists with four hospital clinical pharmacists in the Clinical Pharmacy Unit (CPU) in NTPH since January 2019.

#### Educational interventions

The Clinical Pharmacy Unit conducted 2 training sessions: one two-hour session was "Reporting of ADRs" on January 22, 2019, for nurses with the following main contents: (1) Introduction of common clinical manifestations of ADR in different organ systems, (2) List of patients at high risk of ADR to be monitored, (3) List of Drugs/drug groups with a high risk of ADR, (3) Benefits of ADR reporting in hospitals, and (4) ADR reporting process. The second one-hour session was "Diagnosis, Treatment, and Reporting of ADR" on February 27, 2019, for physicians focusing on the following topics: (1) Introduction of ADR clinical manifestations in organ systems, (2) high-risk factors for ADR, (3) Benefits of ADR reporting in hospitals, (4) ADR diagnosis and management, (5) ADR reporting procedures.

### The functioning of the ADR reporting system

On daily basis, whenever HCPs suspected any symptoms/signs observed through the clinical review process of inpatients as a reaction to a drug(s), they reported in a national ADR notification form in paper [16] and sent it to clinical pharmacists. Pharmacists analyzed them for their completeness, credibility, and correctness. Data were carefully evaluated for quality, based on the following essential elements: patient initials, age, gender, date of reaction (onset), description of the reaction or problem, suspected medication(s), indications for use, concomitant medical products, severity, causality, de-challenge, rechallenge, management, and outcomes.

If additional details were required to collect by pharmacists or HCPs demanded pharmacists to visit clinical wards and manage clinical cases together, pharmacists would interview directly with the reporter and patients, and HCPs, and/or evaluation of patient medical records. Pharmacists collected information concerning previous allergies, concomitant medications, co-morbidities, and discussed with HCPs on ADR management. Suspected ADRs that met ADR reporting criteria were then sent via email to the national ADR center

in Hanoi. Pharmacists wrote an ADR summary every 6 months and one year and sent them to HCPs in the hospital, and the hospital awarded one clinical department, which had the highest number of ADR reports at the end of the year.

#### Data collection

The reactions were categorized based on (1) reporter status (reporter, time, clinical department), (2) ADR characteristics (patient demographics (age and gender), organ system affected, severity, causality, outcome, and management), (3) drug characteristics (route of administration, drug groups, and drug name), and All data were collected by a national ADR reporting form [16]. We have assessed the causality to establish the relationship between the drug and the reaction by using the Naranjo scale [17]. All drugs were categorized according to the Anatomical Therapeutic Chemical (ATC) classification system and differentiated to the second level of the ATC code. The seriousness of the ADRs was assessed into 6 categories: death. life-threatening, hospitalization/prolongation of hospitalization, permanent or significant disability, fetal anomalies, and no severity [16]; ADR outcomes were classified as: fatal due to ADR, fatal not related to the drug, not recovered, recovering, recovered with complications, recovered without complications, and unknown. A method for estimating the causality of ADRs was Naranjo scale [17]: doubtful, possible, probable, definite, not yet classified, and unable to classify.

### Ethical considerations:

The study was approved by the local antibiotic stewardship program board. The study was conducted in a spirit of respecting the private information related to patients and health care providers. Information, which was collected from routine data of drug charts was anonymized.

### Statistical Analysis

All data were analyzed by using SPSS software version 20.0. Data were expressed in frequency, percentage, and mean  $\pm$  SD.

### RESULTS

### Quantity and quality of ADR reporting and characteristics of reporters

From January 1 to December 31, 2019, a total of 147 ADR reports were collected and reported to the National ADR Center, compared to 12 reports in the previous year (increased by 12.25 times). In particular, the report increased sharply from February when the two training sessions by pharmacist ended (**Figure 1**). The hospital reports an average of 12.25 ADR cases per month. All ADR reports were then reviewed by the clinical pharmacist before sending it to the national ADR center, thus ensuring 100% of ADR reports fill in the necessary information fields.

The majority of ADR reports were collected by physicians (accounting for 64.6%) and pharmacists (24.5%). All ADR reports were then reviewed by the clinical pharmacists to ask

the reporter to supplement the missing information field and assess the causal relationship between the drug and reactions. The department reporting the most ADR was the department of internal respiratory medicine (21.8%) and obstetrics (14.3%) (**Table 1**).

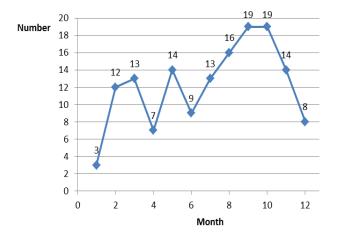


Figure 1. Number of ADR reports by the month of 2019

Table 1. Characteristics of reporters of ADRs Percentage N **Parameter** (%) Reporters Reporter professional status Physician 95 64.6 Pharmacist 36 24,5 Nurse 13 8,8 Medical assistant 03 2,1 Clinical department Department of Respiratory Medicine 32 21,8 Department of Obstetrics 21 14,3 Neurology Surgery 16 10,9 Emergency department 10 6,8 Department of Cardiology internal medicine 08 5,4 Department of anesthesiology and resuscitation 08 5,4 52 Others 35,4

### Characteristics of ADRs

The majority of patients with ADR reported were 18-60 years old (64.0%) and female (64.0%). The most-reported manifestations were not serious (90.5%), which were pruritus (64.0%), erythema/redness (61.9%). Most cases recovered without complications (66.0%). The majority of ADRs were categorized as probable (49.7%) followed by possible (45.6%) in nature. The withdrawal of the offending drug and/or addition of other drugs to treat ADRs were common to manage ADRs (59.2%) and 53.1%, respectively) (**Table 2**).

Table 2. Characteristics of ADR reporting (n=147)

Parameter	N	Percentage (%)
Patient profile		
Age group		
< 18 years	1	0.7
18 - 60 years	94	64.0
> 60 years	52	35.3
Sex		
Male	53	36.0
Female	94	64.0
Characteristics of ADRs		
Severity		
No	133	90.5
Hospitalization initial/prolonged	4	2,7
Life-threatening	10	6,8
Death	0	0
Organ system involved		
Pruritus	94	64,0
Rash erythematous/Rash/Urticaria	91	61,9
Eye swelling/Eyelid edema/Eye edema	17	11,6
Dyspnea	15	10,2
Shiver/Chills	12	8,2
Fever	5	3,4
Hypotension	5	3,4
Weak or absent pulse	5	3,4
Others (purple lips, sweat, chest pain, facial	9	6,1
numbness)		0,1
Causality		
Doubtful	4	2.7
Possible	67	45.6
Probable	73	49.7
Definite	3	2.0
ADR management		
Addition of another drug to treat ADR	87	59.2
symptoms	0,	37.2
Stop suspected drug(s)	78	53.1
Change to another drug	53	36.1
No change	2	1.4
Dose or drug infusion reduced	5	3.4
No information	25	17.0
ADR outcomes		
Recovering	50	34.0
Recovered without complications	97	66.0

### Characteristics of suspected drugs

All reported ADRs were related to intravenous injection (16/79,6%), oral (16/10.9%), rectal (9/6.1%), subcutaneous (3/2.0%), and hemodialysis (2/1.4%). A higher number of

ADRs were reported for antibiotics 97 (66.0%) followed by analgesics and antipyretics, 27 (18.3%). A detailed list of offending drugs is shown in **Table 3**.

Table 3. Suspected drug groups and drugs of ADRs

Drug group   Name   N   N   %	rable 3. Su	spected drug groups	and d	rugs of	ADRS
Ceftriaxon	Drug group	Name	N	N	%
Vancomycin   14   Clindamycin   5   Imipenem + cilastatin   4   Ampicillin + Sulbactam   3   Moxifloxacin   3   Ciprofloxacin   3   Cefmetazol   2   Amoxicillin + Acid   Clavulanic   Piperacillin + Tazobactam   1   Sparfloxacin   1   Ertapenem   1   Cefopime   1   Linezolid   1   Analgesics & Antipyretics   Diclofenac   10   Celecoxib   3   Contrast agents   Iohexol   3   6   4.1   Anino acid   1   23   15.6   Sodium chloride   1   Human albumin   1   Sitagliptin   2   Metoclopramide   1   Tranexamic acid   2   Immune globulin   1   Amino acids + peptides   1   Dialysis solution   1   Dobutamin   1   Lidocain   2   Hydrocortison   1   Acetyl leucine   1   Affuzosin   1   Omeprazole   1   N-acetylcysteine   2   Colchicine   Colchicine	Antibiotics	Levofloxacin	35	97	66.0
Clindamycin   5   Imipenem + cilastatin   4   Ampicillin + Sulbactam   3   Moxifloxacin   3   Ciprofloxacin   3   Ciprofloxacin   3   Cefmetazol   2   Amoxicillin + Acid   Clavulanic   2   Clavulanic   2   Cefotaxim   1   Sparfloxacin   1   Ertapenem   1   Cefepime   1   Linezolid   1   Analgesics & Paracetamol   14   27   18.3   27   18.3   27   28   3   3   4   4   4   4   4   4   4   4		Ceftriaxon	19		
Imipenem + cilastatin 4 Ampicillin + Sulbactam 3 Moxifloxacin 3 Ciprofloxacin 3 Cefmetazol 2 Amoxicillin + Acid Clavulanic Piperacillin + Tazobactam 2 Cefotaxim 1 Sparfloxacin 1 Ertapenem 1 Cefepime 1 Linezolid 1 Analgesics & Paracetamol 14 27 18.3  Contrast agents Iohexol 3 6 4.1 Iobitridol 2 Iodixanol 1 Other Amino acid 1 23 15.6 Sodium chloride 1 Human albumin 1 Sitagliptin 2 Metoclopramide 1 Tranexamic acid 2 Immune globulin 1 Amino acids + peptides 1 Dialysis solution 1 Dobutamin 1 Lidocain 2 Hydrocortison 1 Acetyl leucine 1 Alfuzosin 1 Omeprazole 1 N-acetylcysteine 2 Colchicine 2		Vancomycin	14		
Ampicillin + Sulbactam 3 Moxifloxacin 3 Ciprofloxacin 3 Cefmetazol 2 Amoxicillin + Acid 2 Clavulanic 2 Piperacillin + Tazobactam 2 Cefotaxim 1 Sparfloxacin 1 Ertapenem 1 Cefepime 1 Linezolid 1 Analgesics & Paracetamol 14 27 18.3  Contrast agents Iohexol 3 6 4.1 Iobitridol 2 Iodixanol 1 Other Amino acid 1 23 15.6 Sodium chloride 1 Human albumin 1 Sitagliptin 2 Metoclopramide 1 Tranexamic acid 2 Immune globulin 1 Amino acids + peptides 1 Dialysis solution 1 Dobutamin 1 Lidocain 2 Hydrocortison 1 Acetyl leucine 1 Alfuzosin 1 Omeprazole 1 N-acetylcysteine 2 Colchicine 2		Clindamycin	5		
Moxifloxacin   3   Ciprofloxacin   3   Cefmetazol   2		Imipenem + cilastatin	4		
Ciprofloxacin   3   Cefmetazol   2   Amoxicillin + Acid   Clavulanic   2   Cefotaxim   1   Sparfloxacin   1   Ertapenem   1   Cefepime   1   Linezolid   1   Analgesics & Antipyretics   Diclofenac   10   Celecoxib   3   6   4.1		Ampicillin + Sulbactam	3		
Cefmetazol   2		Moxifloxacin	3		
Amoxicillin + Acid Clavulanic  Piperacillin + Tazobactam 2  Cefotaxim 1  Sparfloxacin 1  Ertapenem 1  Cefepime 1  Linezolid 1  Analgesics & Paracetamol 14 27 18.3  Contrast agents Diclofenac 10  Celecoxib 3  Contrast agents Iohexol 3 6 4.1  Iobitridol 2  Iodixanol 1  Other Amino acid 1 23 15.6  Sodium chloride 1  Human albumin 1  Sitagliptin 2  Metoclopramide 1  Tranexamic acid 2  Immune globulin 1  Amino acids + peptides 1  Dialysis solution 1  Dobutamin 1  Lidocain 2  Hydrocortison 1  Acetyl leucine 1  Alfuzosin 1  Omeprazole 1  N-acetylcysteine 2  Colchicine 2		Ciprofloxacin	3		
Clavulanic		Cefmetazol	2		
Clavulanic		Amoxicillin + Acid	2		
Cefotaxim   1   Sparfloxacin   1   Ertapenem   1   Cefepime   1   Linezolid   1		Clavulanic	2		
Sparfloxacin 1 Ertapenem 1 Cefepime 1 Linezolid 1  Analgesics & Paracetamol 14 27 18.3  Paracetamol 10 Celecoxib 3 Contrast agents Iohexol 3 6 4.1 Iobitridol 2 Iodixanol 1 Other Amino acid 1 23 15.6 Sodium chloride 1 Human albumin 1 Sitagliptin 2 Metoclopramide 1 Tranexamic acid 2 Immune globulin 1 Amino acids + peptides 1 Dialysis solution 1 Dobutamin 1 Lidocain 2 Hydrocortison 1 Acetyl leucine 1 Alfuzosin 1 Omeprazole 1 N-acetylcysteine 2 Colchicine 2		Piperacillin + Tazobactam	2		
Ertapenem 1 Cefepime 1 Linezolid 1  Analgesics & Paracetamol 14 27 18.3  Antipyretics Diclofenac 10 Celecoxib 3  Contrast agents Iohexol 3 6 4.1  Iobitridol 2 Iodixanol 1 Other Amino acid 1 23 15.6  Sodium chloride 1 Human albumin 1 Sitagliptin 2 Metoclopramide 1 Tranexamic acid 2 Immune globulin 1  Amino acids + peptides 1 Dialysis solution 1 Dobutamin 1 Lidocain 2 Hydrocortison 1 Acetyl leucine 1 Alfuzosin 1 Omeprazole 1 N-acetylcysteine 2 Colchicine 2		Cefotaxim	1		
Cefepime		Sparfloxacin	1		
Analgesics & Antipyretics  Diclofenac Diclofenac Celecoxib 3 Contrast agents  Iohexol Johitridol Cother Amino acid Sodium chloride Human albumin Sitagliptin Sitagliptin Tranexamic acid Immune globulin Amino acids + peptides Dialysis solution Dobutamin Lidocain Acetyl leucine Alfuzosin Omeprazole N-acetylcysteine Colchicine  14 27 18.3 18.3 18.3 19.3 19.3 10.3 10.3 10.3 10.3 10.3 10.3 10.3 10		Ertapenem	1		
Analgesics & Paracetamol 14 27 18.3  Antipyretics Diclofenac 10 Celecoxib 3 Contrast agents Iohexol 3 6 4.1 Iobitridol 2 Iodixanol 1 Other Amino acid 1 23 15.6 Sodium chloride 1 Human albumin 1 Sitagliptin 2 Metoclopramide 1 Tranexamic acid 2 Immune globulin 1 Amino acids + peptides 1 Dialysis solution 1 Dobutamin 1 Lidocain 2 Hydrocortison 1 Acetyl leucine 1 Alfuzosin 1 Omeprazole 1 N-acetylcysteine 2 Colchicine 2		Cefepime	1		
Paracetamol   14   27   18.3		Linezolid	1		
Celecoxib   3		Paracetamol	14	27	18.3
Contrast agents         Iohexol         3         6         4.1           Iobitridol         2         2         1         1         2         1         1         2         1         1         2         15.6         1		Diclofenac	10		
Iobitridol   2		Celecoxib	3		
Todixanol   1	Contrast agents	Iohexol	3	6	4.1
Other         Amino acid         1         23         15.6           Sodium chloride         1         1         4         4         1         1         1         1         4         1         <		Iobitridol	2		
Sodium chloride 1 Human albumin 1 Sitagliptin 2 Metoclopramide 1 Tranexamic acid 2 Immune globulin 1 Amino acids + peptides 1 Dialysis solution 1 Dobutamin 1 Lidocain 2 Hydrocortison 1 Acetyl leucine 1 Alfuzosin 1 Omeprazole 1 N-acetylcysteine 2 Colchicine 2		Iodixanol	1		
Human albumin 1 Sitagliptin 2 Metoclopramide 1 Tranexamic acid 2 Immune globulin 1 Amino acids + peptides 1 Dialysis solution 1 Dobutamin 1 Lidocain 2 Hydrocortison 1 Acetyl leucine 1 Alfuzosin 1 Omeprazole 1 N-acetylcysteine 2 Colchicine 2	Other	Amino acid	1	23	15.6
Sitagliptin         2           Metoclopramide         1           Tranexamic acid         2           Immune globulin         1           Amino acids + peptides         1           Dialysis solution         1           Dobutamin         1           Lidocain         2           Hydrocortison         1           Acetyl leucine         1           Alfuzosin         1           Omeprazole         1           N-acetylcysteine         2           Colchicine         2		Sodium chloride	1		
Metoclopramide       1         Tranexamic acid       2         Immune globulin       1         Amino acids + peptides       1         Dialysis solution       1         Dobutamin       1         Lidocain       2         Hydrocortison       1         Acetyl leucine       1         Alfuzosin       1         Omeprazole       1         N-acetylcysteine       2         Colchicine       2		Human albumin	1		
Tranexamic acid 2 Immune globulin 1 Amino acids + peptides 1 Dialysis solution 1 Dobutamin 1 Lidocain 2 Hydrocortison 1 Acetyl leucine 1 Alfuzosin 1 Omeprazole 1 N-acetylcysteine 2 Colchicine 2		Sitagliptin	2		
Immune globulin 1 Amino acids + peptides 1 Dialysis solution 1 Dobutamin 1 Lidocain 2 Hydrocortison 1 Acetyl leucine 1 Alfuzosin 1 Omeprazole 1 N-acetylcysteine 2 Colchicine 2		Metoclopramide	1		
Amino acids + peptides 1 Dialysis solution 1 Dobutamin 1 Lidocain 2 Hydrocortison 1 Acetyl leucine 1 Alfuzosin 1 Omeprazole 1 N-acetylcysteine 2 Colchicine 2		Tranexamic acid	2		
Dialysis solution 1 Dobutamin 1 Lidocain 2 Hydrocortison 1 Acetyl leucine 1 Alfuzosin 1 Omeprazole 1 N-acetylcysteine 2 Colchicine 2		Immune globulin	1		
Dobutamin 1 Lidocain 2 Hydrocortison 1 Acetyl leucine 1 Alfuzosin 1 Omeprazole 1 N-acetylcysteine 2 Colchicine 2		Amino acids + peptides	1		
Lidocain 2 Hydrocortison 1 Acetyl leucine 1 Alfuzosin 1 Omeprazole 1 N-acetylcysteine 2 Colchicine 2		Dialysis solution	1		
Hydrocortison 1 Acetyl leucine 1 Alfuzosin 1 Omeprazole 1 N-acetylcysteine 2 Colchicine 2		Dobutamin	1		
Acetyl leucine 1  Alfuzosin 1  Omeprazole 1  N-acetylcysteine 2  Colchicine 2		Lidocain	2		
Alfuzosin 1 Omeprazole 1 N-acetylcysteine 2 Colchicine 2		Hydrocortison	1		
Omeprazole 1 N-acetylcysteine 2 Colchicine 2		Acetyl leucine	1		
N-acetylcysteine 2 Colchicine 2		Alfuzosin	1		
N-acetylcysteine 2 Colchicine 2		Omeprazole	1		
Colchicine 2			2		
Erythropoietin 1			2		
		Erythropoietin	1		

# DISCUSSIONS Quantity and quality of ADR reporting and characteristics of reporters

The knowledge and attitudes of physicians and nurses involved in ADR reporting are limited. A study of Lai QP<sup>[18]</sup> interviewed 683 Vietnamese doctors and nurses about perceptions, attitudes, and practice of pharmacovigilance in 2014 showed that 91.7% clinicians understood that reporting of ADRs was their responsibility but only 34.8% of staff knew the ADR reporting form, 82.1% of people encountered ADRs but only 40.3% ever reported ADRs. However, education on ADR reporting was provided by only 69 percent of pharmacy departments in the United Kingdom <sup>[13]</sup>. Our study confirmed that educational intervention tailored to physicians and nurses conducted by clinical pharmacists could increase significantly the number of ADR reporting rate.

The educational intervention helped to increase the number of ADR reported in 2019 by 12.25 times compared to 2018 (147 vs 12 reports). This was a very high increase compared to other interventions. A systematic review found that reports using information systems doubled the number of ADR reports <sup>[7]</sup>. The study of Herdeiro *et al.* stated that the workshop intervention increased the ADR reporting rate by an average of 4-fold while telephone interviews, in contrast, led to no significant difference (p = 0.052) <sup>[10]</sup>. One-hour educational outreach visits tailored to physicians also showed to increase in ADR reporting rates <sup>[19]</sup>.

It is necessary to operate and constant interventions, which encourage ADR reporting [20]. Whereas telephone interventions only increased spontaneous reporting in the first 4 months of follow-up, workshops significantly increased both the quantity and relevance of spontaneous ADR reporting for more than 1 year [10]. In our study, the number of ADR reports had an increasing trend in the first 8 months of follow-up (from March to October) and started to decrease in the last two months (November and December).

The majority of ADR reports were collected by physicians (64.6%), but reporting by nurses was still limited (8.8%). This showed the very important role of physicians in reporting ADRs, especially in detecting and diagnosing ADRs. That was the reason why the training sessions were organized separately for doctors and nurses. The training session for physicians focused primarily on the principles of ADR diagnostic principles while one session for nurses focused primarily on suspected clinical manifestations of ADRs. In reality, in many cases, both nurses and physicians contributed to the reporting of ADRs, but only physicians who had higher status than nurses signed in the ADR form. These phenomena could explain why the proportion of ADR reporting by nurses was not as high as that by physicians.

Pharmacists were the second most common HCPs reported ADRs (24.5%). This reflected a fact that in many situations

when an ADR was detected, a physician or nurse often called a clinical pharmacist to visit a clinical ward to assist them with ADR recording and discuss on how to manage the ADR, such as discontinuation of the drug, changing of drugs, the introduction of drugs to treat allergy symptoms, and changing of the rate of drug infusion. Thanks to these opportunities, physicians, and nurses change their perceptions on the role of clinical pharmacists in the promotion of safety and effectiveness of drug use [21, 22]. In the national report for the first 3 quarters of 2019, pharmacists accounted for 46.3% as reporter professional status [23], which showed Vietnamese pharmacists played a core role in pharmacovigilance activities.

### Characteristics of ADR reports

ADR reporting is an ongoing and continuous process. Studies from the individual hospital help to identify the problems related to ADR reporting to resolve.

ADR is an important clinical problem for children. A systematic review found that incidence rates for ADRs causing hospital admission ranged from 0.4% to 10.3% of all children and from 0.6% to 16.8% of all children exposed to a drug during hospital stay <sup>[24]</sup>. Our study reported only one ADR related to children, which implicated that further interventions should target to improve ADR reporting in the pediatric population.

The need for early detection and reporting of serious ADRs was important because they may increase costs due to increased hospitalization, prolongation of hospital stay, additional investigations, and drug therapy, and mortality rate in more serious cases [25, 26]. The proportion of serious ADRs in our study was 9.5% with life-threatening (6.8%) and hospitalization/prolongation of hospitalization (2.7%). This result was similar to other studies, in which serious ADRs accounted for 5.1-12.6% of the total number of ADRs [26, 27]. However, the incidence of serious and fatal ADRs in hospitals was found to be extremely high in literature. Serious ADRs accounted for 6.7% of all hospital admissions and occurred in 10-20% of hospitalized patients [25]. For five of the eight hospital-based studies, the median under-reporting rate for more serious or severe ADRs remained high (95%) [2]. Ramesh et al. stated that factors that discouraged ADR reporting were well-known reactions, mild reactions, and immediate management of ADRs [20].

The ADR manifestations collected in the hospital were mainly noticeable signs related to drug allergic reactions. The most common clinical presentation involved was skin and subcutaneous tissue disorders with pruritus (64,0%), rash erythematous/rash/urticaria (61,9%), followed by anaphylactic shock, fever, chills; which was similar to another study [28]. However, many other ADRs, such as hemodynamic changes, elevated liver enzymes, and renal failure, bleeding, etc. have not been reported. This indicated that pharmacists need to focus the next training for HCPs on how to recognize and report ADRs on specific organ systems.

### Drugs involved in ADRs

ADR reports were mainly related to the parenteral route, accounting for 79.6%, higher than 48.6%, the rate recorded from the national summary [23]. Antibiotics and analgesics and antipyretics comprised the major groups of drugs causing ADRs (66.0% and 18,3%, respectively). Among them, the drugs most suspected to cause ADR were levofloxacin (35 cases), ceftriaxone (19 cases), vancomycin (14 cases), and paracetamol (14 cases). The study of Venkatasubbaiah et al. found that a higher number of ADRs were reported for followed antibiotics, by antipsychotics, analgesics, and antipyretics [27]. The study of Pathak et al. revealed that antibiotics and anticancer drugs are the most common drugs implicated [29]. In summary, antibiotics were more commonly implicated in ADRs [28]. A total of 298 (20%) patients experienced at least 1 antibiotic-associated ADE. The study of Tamma et al. in 2017 found that 20% of hospitalized patients receiving at least 24 hours of antibiotic therapy developed an antibiotic-associated ADR [30]. Some activities of the CPU include patient ward rounds, writing local drug use protocol (such as therapeutic drug monitoring of vancomycin), medication review [31], educational interventions [32], drug information, and ADR management. Further educational interventions should focus on how to reduce and manage ADRs related to antibiotics, and specific drug groups.

### CONCLUSIONS

Training for physicians and nurses by pharmacists on diagnosis, reporting, and treatment of ADRs helped to increase the number of ADR reports by more than 12 times. More intensive and specific training and other measures are needed to solve under-reporting ADRs.

### **Abbreviations**

HCP: health care provider ADR: Adverse drug reaction

NTPH: Nguyen Tri Phuong Hospital

UPNT: Pham Ngoc Thach University of Medicine

CPU: Clinical Pharmacy Unit

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