Adverse drug reactions reporting by undergraduate medical students in a tertiary care teaching hospital of India: Content and quality analysis in comparison to physician reporting

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Abstract

Background: An important challenge to spontaneous reporting system is underreporting. The sensitization and involvement of undergraduate medical students can reduce underreporting in pharmacovigilance program.

Objective: To analyze the clinical characteristics and reporting quality of adverse drug reactions (ADRs) by undergraduate medical students in comparison with physicians' reporting.

Methods: We sensitized the second professional year undergraduate medical students about pharmacovigilance and asked them to submit reports of ADR observed during their clinical posting from January to December 2015. We compared students' reports with those sent by physicians (Department of Medicine and Allied Branches, Paediatric, Obstetrics and Gynaecology) of our institute during the same time period. We included ADRs of "certain," "probable," or "possible" categories as per the World Health Organization causality definitions in analysis of both groups. We excluded "unlikely," "unclassified," and "unclassifiable" causality ADRs from the analysis due to questionable association of reactions with suspected drugs. We collected data of demographics, pattern of ADRs, causative drugs, seriousness, other clinical characteristics, and quality of reporting.

Results: We analyzed a total number of 176 students' reports having 269 ADRs and 143 physicians' reports covering 180 ADRs. The students predominantly reported ADRs of single drug suspect (84.09% vs. 43.35%), "probable" causality (63.94% vs. 21.11), and augmented type reactions (67.29% vs. 55%) than physicians. Both groups did not differ in reporting of serious reactions (6.25% vs. 9.09%). Students most frequently suspected gastrointestinal disorders (35.68%), whereas physicians most frequently reported skin and appendages disorders (41.11%). Students and physicians more commonly suspected ADRs due to systemic anti-infective (33.64%) and nervous system (42.07%) class of drugs, respectively. The quality analysis suggested no substantial difference in most domains of ADR reporting among both groups.

Conclusion: Students' reported valuable and clinically relevant ADRs. Medical students should be exposed to ADR reporting during their clinical teaching posting and should be actively involved in pharmacovigilance program to improve detection rate.

Keywords: Adverse drug reactions, pharmacovigilance, physician, undergraduate medical students

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How to cite this article: Patel PB, Patel TK, Anturlikar S, Khatun S, Bhabhor P, Saurabh MK. Adverse drug reactions reporting by undergraduate medical students in a tertiary care teaching hospital of India: Content and quality analysis in comparison to physician reporting. Perspect Clin Res 2017;8:137-44.

INTRODUCTION

Adverse drug reactions (ADRs) are a major health issue in outpatient and inpatient clinical settings.[1] ADR reporting form is an essential part of the pharmacovigilance system. It is a tool to collect information of ADRs to establish the causal relationship between the suspected drug and the reaction. If relevant information about ADR is not adequately captured, it is of no use for the regulatory authority to draw any conclusion.[2] Central Drug Standard Control Organization (CDSCO) considers following information mandatory in its spontaneous reporting form for the analysis: Patient initials, age at onset of reaction, reaction term, date of onset of the reaction, suspected medication, and reporter's information. Pharmacovigilance plays an important role in the rational use of medicines.[3,4] Its knowledge is important for effective treatment.

India is a part of a World Health Organization (WHO) program to monitor the ADRs through spontaneous reporting. This reporting system remains one of the most effective methods to detect new, serious, and rare drug reactions.[1,5] It has resulted in the withdrawal of many marketed drugs due to serious ADRs worldwide.[6] In this system, physicians are encouraged to report all suspected ADRs in a voluntary basis. ADR reporting to national and international databases by the health-care professionals is the main source of information to generate new signals. [1] Hence, the success of it depends on the willingness of physicians to report ADRs. Physicians are the principal contributors of ADR reports to the spontaneous reporting system in India. Although physicians are aware of the ADRs and importance of their reporting, actual practice of ADR reporting is deficient.[7,8] One method to reduce underreporting could be to expose them to the ADR reporting during their undergraduate study period. The practical teaching of pharmacovigilance to the undergraduate students can cultivate ADR reporting habits and can enhance their participation as a physician in the future. At our institute, we use case-based ADR exercises to teach pharmacovigilance. In this study, we want to explore undergraduate students as a future health-care professional in the reporting scheme and to strengthen the national pharmacovigilance system. Hence, we conducted this study to analyze content and quality outcome of students' reporting with physicians in the same period, considering that they work in the same setting.

METHODS

This prospective, cross-sectional study was carried out in the Department of Pharmacology. The study was approved by the Institutional Human Ethics Committee (IHEC), GMERS Medical College, Gotri, Vadodara, Gujarat, India. The consent waiver was requested to IHEC for analyzing the ADR reports submitted by medical students and faculties.

Our institute is the recognized ADR monitoring center (AMC) under the "pharmacovigilance program of India." The AMC collects suspected ADR reports from physicians of our institute as well as nearby teaching institutes. We transmit reports to the "VigiFlow software" of the WHO for the global monitoring of ADRs provided by Indian Pharmacopoeia Commission, Ghaziabad, India.

Study procedure

In our department, we taught and sensitized the 2nd year MBBS students about pharmacovigilance through interactive theory and practical class teaching. The learning objectives of theory teaching were different terminologies related to ADRs, the difference between ADR and adverse drug events, types of ADRs, and their management. The practical class teaching included spontaneous reporting system in pharmacovigilance program of India and filling of suspected ADR reporting form. The students were also challenged with ADR exercises related to the clinical scenario (case-based exercise) in a small group (n = 8–12 for each group). The demonstrators acted as a facilitator to stimulate the students in active learning and ensured that each student is participating in it.

In our setup, 2nd-year students have postings for 3 h in the morning in various clinical departments of medicine, pediatrics, obstetrics and gynecology, dermatology, psychiatry, etc., Students are divided into groups of about thirty students for clinical postings on a rotation basis to different departments as per the academic schedules. During this time period, students attend the outpatient departments, wards, and operation theaters. This is the first time of MBBS course when they come across patients. The clinical teaching focuses on the history taking, differential diagnosis, provisional diagnosis, and management. We allotted each student specific inpatient ward or outpatient department and encouraged them to report two ADRs during their 4th and 5th semester clinical posting. Students were asked to vigilant about ADRs while patient interview, case and laboratory record review, and discussion with the clinicians for the differential and provisional diagnosis. We encouraged students to report all untoward/noxious consequences suspected after the drug administration. We also encouraged the students to discuss with the clinicians and pharmacologists in case of a query. We asked them to report suspected reactions

as early as possible, preferably within 1 week to the Department of Pharmacology. We included ADR forms in the pharmacology practical journal for the purpose of reporting. We used an ADR reporting form designed by the CDSCO, India. The ADR reporting form has elements such as patient-related information (initials, age, and gender), suspected ADRs (date of reaction, its recovery date, and description), suspected medications (name, manufacturing details, dose, route, frequency, therapy dates, and indications), dechallenge, rechallenge, concomitant medications, relevant laboratory test, other relevant history (allergy, pregnancy, hepatic and renal dysfunctions, etc.,), seriousness, outcome, and reporters' details.

Selection criteria

We included all suspected ADRs reported by 2nd-year undergraduate medical students of 4th and 5th semester batch (n = 116) during their clinical teaching posting at our tertiary care hospital for a period of January 2015 to December 2015. We included ADRs of "certain," "probable," and "possible" categories as per the WHO causality definitions.[9]

Adverse events are not always specific for the drug. To improve reporting quality, we excluded ADR reports showing "unlikely," "unclassified," or "unclassifiable" categories as per the WHO causality definitions. They suggest a questionable association of reactions with suspected drugs. In case of "unlikely" causality, either time relationship between drug intake and reactions that make a relationship improbable or underlying disease or other drugs provide plausible explanations for the ADRs. Unclassified and unclassifiable categories report lack the relevant data for the assessment.[9] We also excluded duplicate reports from the analysis.

The comparator group consisted of ADR reports received from physicians (Department of Medicine and Allied Branches, Paediatrics, Obstetrics and Gynaecology) of our institute through spontaneous reporting system during the same time periods. We applied same selection criteria to analyze physicians' reports.

Data collection

The ADR reports of undergraduate students and physicians were assessed for diagnosis of ADRs, types (augmented or bizarre), their organ system involvement as per the WHO – ADR adverse reaction terminology,[10] suspected medications, their WHO-anatomical therapeutic chemical (ATC) classification codes,[11] concomitant medications, causality assessment as per the WHO causality definitions,[9] seriousness as per the International

Conference on Harmonisation E2A guidelines,[12] and outcome of reactions.

We assessed the ADR reporting quality as described earlier by Gedde-Dahl *et al*.[13] Two investigators assessed the ADR reporting quality subjectively based on the completeness of the information. We resolved any discrepancy and difference of opinion through discussion and consensus. We considered 18 different domains of ADR reporting in quality assessment. It included patient-related information (age and gender), suspected ADR (onset date, duration, descriptions of the nature, and localization of the reactions), suspected drugs (dosage, route, indication for use, starting, and stoppage date), dechallenge, rechallenge, concomitant medications, relevant history, laboratory investigations, seriousness, outcome, and reporter's information. In case of reporting of more than one reaction, we analyzed them separately for nature and localizations. Similarly, we analyzed the dechallenge and rechallenge information for all suspected drugs.

Outcome analysis and statistical considerations

We extracted data into Microsoft Excel sheet, 2010. Two investigators cross-checked to ensure its accuracy. We used percentage to present data of gender, age groups, ADRs, organ systems, causative drugs, ATC drug system and groups, causality, seriousness, and outcome. We used percentage to present quality assessment data of each domain of ADR form. We used unpaired *t*-test to compare continuous data and Chi-square test/Fisher's exact test for categorical data. To compare the student and physicians group and to establish whether significant differences were present, we calculated odds ratio (OR) as well as the corresponding 95% confidence intervals. We used GraphPad Prism 6.0 demo version (GraphPad Software, Inc., La Jolla, CA 92037 USA) for statistical analysis and considered $P < 0.05$ as statistically significant difference.

RESULTS

Medical students submitted a total of 208 reports during study periods. We excluded 32 reports from the analysis, thirty due to "duplication" and two due to "unclassified" causality. Therefore, we analyzed 176 ADR reports having 269 ADRs of medical students. Physicians submitted the total of 166 reports during the same time period. We excluded 23 physicians' reports due to "unclassified" causality. We analyzed the 143 physicians" reports having 180 ADRs.

Characteristics of reports

The mean age of patients in the reports of medical students and physicians was 35.40 ± 16.30 and 37.31 ± 16.22 years,

respectively. The reports of students and physicians did not significantly differ in the age group percentage distribution of pediatrics - ≤12 years (3.45 vs. 4.20), adults (90.34 vs. 88.11), and elderly - ≥65 years (6.25 vs. 7.70) (*P* = 0.81, Chi-square test). Both groups did not differ in gender distribution (% of female patients: Students - 57.39, physicians - 55.94; *P* = 0.88, Chi-square test).

The medical students suspected significantly less number of drugs per reports as compared to physicians (1.25 ± 0.64 vs. 2.03 ± 1.19; *P* < 0.0001). As shown in Table 1, the students reported a higher percentage of single drug suspect as compared to physicians (84.09% vs. 43.35%, OR = 6.67 [95% confidence interval (CI): 3.97–11.18]). Medical students reported higher frequency of augmented type reactions (67.29% vs. 55%, OR = 1.68 [95% CI: 1.14–2.48]). They reported higher proportions of "probable" ADRs (63.94% vs. 21.11%, OR = 6.63 [95% CI = 4.28–10.23]) and lower proportions of "possible" ADRs (36.06% vs. 78.33%, OR = 0.16 [95% CI = 0.10–

0.24]) than physicians. Only one physician report was classified as "certain." Both groups did not show differences in the reporting of serious ADRs (6.25% vs. 9.09%; *P* = 0.59).

Characteristics of adverse drug reactions

Table 2 shows ADRs reported as per the WHO ART system-organ classification. Medical students reported more gastrointestinal disorders than physicians (35.68% vs. 16.11%, OR = 2.9, 95% CI = 1.8–4.6). However, they reported less ADRs related to skin and appendages disorders (31.59% vs. 41.11%, OR = 0.27 [95% CI = 0.09–0.77]) and metabolic and nutritional disorders (1.86% vs. 6.67%, OR = 0.66 [95% CI = 0.45–0.98]). We observed minor difference in neurological disorders, body as a whole-general disorder, immune disorders, and infections among both groups.

Table 3 shows the top ten most frequently reported ADRs sent by medical students and physicians. Medical students most frequently reported the rash, pruritus, and diarrhea.

Table 1: Characteristic of reports

Characteristics	Medical students, *n* (%)	Physicians, *n* (%)	*P*	OR (95% CI)
Number of suspected drugs				
1	148 (84.09)	62 (43.35)	<0.0001	6.67 (3.97-11.18)
2-4	28 (15.91)	74 (51.75)	<0.0001	0.18 (0.11-0.31)
≥5	0	7 (4.90)	0.003	0.05 (0.01-0.91)
Type of ADRs				
Augmented	181 (67.29)	99 (55)	0.01	1.68 (1.14-2.48)
Bizarre	88 (32.71)	81 (45)	-	-
Causality assessment				
Certain	0	1 (0.56)	0.40	0.22 (0.01-5.49)
Probable	172 (63.94)	38 (21.11)	<0.0001	6.63 (4.28-10.23)
Possible	97 (36.06)	141 (78.33)	<0.0001	0.16 (0.10-0.24)
Serious ADRs	12 (6.78)	13 (9.09)	0.59	0.73 (0.32-1.66)

ADRs=Adverse drug reactions, OR=Odds ratio, CI=Confidence interval

Table 2: Comparison of adverse drug reaction reporting as per the World Health Organization-adverse drug reaction terminology system organ classification between medical students and physicians

SOC	Medical students, *n* (%)	Physicians, *n* (%)	*P*	OR (95% CI)
GI disorders	96 (35.68)	29 (16.11)	<0.0001	2.9 (1.8-4.6)
Skin and appendages disorders	85 (31.59)	74 (41.11)	0.04	0.66 (0.45-0.98)
Neurological disorders	36 (13.38)	29 (16.11)	0.42	0.80 (0.47-1.4)
Psychiatric disorders	11 (4.09)	8 (4.44)	0.85	0.92 (0.36-2.3)
Body as a whole-general disorders	11 (4.09)	12 (6.67)	0.22	0.60 (0.26-1.4)
Vision disorders	5 (1.86)	1 (0.56)	0.24	3.4 (0.39-29)
Immune disorders and infections	6 (2.23)	6 (3.33)	0.48	0.66 (0.21-2.1)
Metabolic and nutritional disorders	5 (1.86)	12 (6.67)	0.01	0.27 (0.09-0.77)
Urinary tract disorders	4 (1.49)	0	0.15	6.1 (0.33-114)
Respiratory system disorders	2 (0.74)	2 (1.11)	1.00	0.67 (0.09-4.8)
Cardiovascular disorders	2 (0.74)	1 (0.56)	1.00	1.3 (0.12-15)
Hearing, vestibular and special senses disorders	2 (0.74)	0	0.52	3.4 (0.16-71)
Blood disorders	1 (0.37)	0	1.00	2.0 (0.08-50)
Liver and biliary disorders	1 (0.37)	0	1.00	2.0 (0.08-50)
Musculoskeletal disorders	1 (0.37)	2 (1.11)	0.57	0.33 (0.03-3.7)
Reproductive disorders	1 (0.37)	3 (1.67)	0.31	0.22 (0.02-2.1)
Endocrine disorders	0	1 (0.56)	0.40	0.22 (0.01-5.5)
Total	269 (100)	180 (100)	-	-

SOC=System organ classification, OR=Odds ratio, CI=Confidence interval, GI=Gastrointestinal

Physicians most frequently reported the extrapyramidal symptoms, rash, and urticaria.

Characteristics of suspected drugs

Medical students suspected higher frequency of drugs of blood and blood-forming organs (9.21% vs. 1.03%, OR = 9.7, [95% CI = 2.8–33]), musculoskeletal system (8.29% vs. 2.76%, OR = 3.2, [95% CI = 1.4–7.5]), and respiratory system (5.07% vs. 1.38%, OR = 3.8, 95% CI = 1.2–12) than physicians. They reported a lower frequency of ADRs due to nervous system class of drugs (21.65% vs. 42.07%, OR = 0.38 [95% CI = 0.26–0.57]) compared to physicians. Both groups reported similar frequency of ADRs due to general anti-infective system, alimentary tract and metabolism, parasitology, and cardiovascular system class of drugs [Table 4].

Table 5 shows the top ten drugs most frequently reported by medical students and physicians. Medical students most frequently reported ADRs due to diclofenac, Amoxicillin+clavulanic acid, and ferrous sulfate. Physicians most frequently reported drugs due to paracetamol, olanzapine, and rifampicin

Table 3: Top 10 most frequently reported adverse drug reactions reports by medical students and physicians

Medical students	n (%)	Physicians	n (%)
Rash	37 (13.75)	Extrapyramidal symptoms	22 (12.22)
Pruritus	24 (8.92)	Rash	19 (10.56)
Diarrhea	16 (5.95)	Urticaria	17 (9.44)
Headache	21 (7.81)	Pruritus	12 (6.67)
Vomiting	18 (6.69)	Weight gain	11 (6.11)
Constipation	17 (6.32)	Fixed drug eruptions	10 (5.56)
Dizziness	11 (4.09)	Erythema multiforme/SJS	9 (5.00)
Urticaria	9 (3.35)	Ankle edema	8 (4.44)
Gastritis	12 (4.46)	Gastritis	7 (3.89)
GI intolerance	7 (2.60)	Diarrhea	5 (2.78)

GI=Gastrointestinal, SJS=Stevens Johnson Syndrome

Quality of reports based on domains of adverse drug reaction forms

Table 6 shows the subjectively assessed completeness of information provided in the ADR reports. We observed no difference in reporting of patient information, onset date, detailed description, indications of suspected drugs, their routes, starting date, dechallange, and severity of the reaction. The medical students reported in high frequency about duration of ADRs, suspected drug dosage, their stoppage date, and rechallange as compared to physicians. They reported in low frequency about the use of concomitant drugs, relevant history, and outcome as compared to physicians.

DISCUSSION

In this study, we compared ADR reporting of undergraduate medical students and physicians for the pattern of ADRs, causative drugs, other clinical characteristics, and quality of reporting. To improve the data reporting quality, we excluded duplicate reporting and reactions with "unlikely," "unclassified," and "unclassifiable" causality. The main reason for exclusion of students' reports was duplicate reports. It could be due to batch size of the students. We observed the certain difference between the reporting pattern of reactions and suspected drugs between groups. Both groups showed a pattern similar to previous spontaneous reporting studies. We observed the acceptable level of reporting quality of undergraduate medical students. Use of problem-based exercise in classroom teaching and early clinical exposure of students to report ADRs seem important steps to inculcate ADR reporting habits among the future physicians.

The demographic data suggest a preponderance of female and adults in the reporting of students and physicians. No

Table 4: Comparison of reporting drug class system as per the World Health Organization-anatomical therapeutic chemical codes between students and physicians

ATC-drug system	Medical students, n (%)	Physicians n (%)	P	OR (95% CI)
General anti-infective systemic	73 (33.64)	104 (35.86)	0.60	0.91 (0.63-1.3)
Nervous system	47 (21.65)	122 (42.07)	<0.0001	0.38 (0.26-0.57)
Blood and blood forming organs	20 (9.21)	3 (1.03)	<0.0001	9.7 (2.8-33)
Musculoskeletal system	18 (8.29)	8 (2.76)	<0.01	3.2 (1.4-7.5)
Alimentary tract and metabolism	17 (7.83)	17 (5.86)	0.38	1.4 (0.68-2.7)
Parasitology	16 (7.37)	15 (5.17)	0.31	1.5 (0.70-3.0)
Respiratory system	11 (5.07)	4 (1.38)	0.02	3.8 (1.2-12)
Cardiovascular system	8 (3.69)	10 (3.45)	0.89	1.1 (0.42-2.8)
Dermatologicals	3 (1.38)	0	0.08	9.5 (0.49-185)
Genitourinary system and sex hormones	2 (0.92)	0	0.18	6.7 (0.32-141)
Systemic hormonal preparations	1 (0.46)	2 (0.69)	1.00	0.67 (0.06-7.4)
Sensory organs	1 (0.46)	0	0.43	4.0 (0.16-99)
Ophthalmologicals	1 (0.46)	0		
General Anti-infective systemic+parasitology	0	3 (1.03)	0.26	0.19 (0.01-3.7)
Hospital solutions	0	2 (0.69)	0.51	0.27 (0.01-5.6)
Total	217 (100)	290 (100)		

ATC=Anatomical therapeutic chemical, OR=Odds ratio, CI=Confidence interval

significant differences in demographic data suggest a lack of bias to select the patients by students to report ADRs. The students reported a high frequency of ADRs with the single drug suspect and probable causality. This could be due to their more emphasis to report ADRs with more degree of causal association. It also suggests their less confidence in the reporting of ADRs in a situation where other drugs and underlying disease condition could not be ruled out. Although both groups predominantly reported augmented type reactions, the ratio of augmented to bizarre reactions was higher among students' reporting. Students could have easily correlated the augmented type reactions with mechanisms and pharmacological actions of the drugs. On the other hand, physicians reported troublesome allergic reactions in clinical practice. We observed no difference in the frequency of reporting of serious reactions in both groups. One of the important aims of the spontaneous

reporting system is to detect serious reactions for regulatory decisions and patient safety.[14]

The students and physicians most frequently reported gastrointestinal and cutaneous reactions, respectively. Both are consistent with the data of earlier Indian spontaneous reporting studies. The literature shows both gastrointestinal[15,16] and cutaneous reactions[17-19] as a predominantly affected system. The Western literature shows cutaneous reactions,[1] musculoskeletal and connective tissue disorders,[20] and nervous system disorders[13] as most frequently suspected organ systems. Neurological disorders were third most frequently reported reactions in both groups of our study. However, musculoskeletal disorders were quite rarely reported in this study. This discrepancy could be due to cultural, historical, and organizational differences between different countries.[1] In our study, there was no much difference in the reporting pattern of organ systems in both study groups except high frequency of metabolic and nutritional disorders in physicians group. The top ten list of the most frequently reported ADRs suggests rash, pruritus, diarrhea, gastritis, and urticaria as common in both groups. The students and physicians most frequently identified the rash and extrapyramidal symptoms, respectively. The rash is most frequently reported ADR in earlier studies.[17-19]

The students and physicians both suspected systemic anti-infective agents in almost similar frequency. The anti-infective agents were most frequently reported offending drug class in earlier Indian spontaneous reporting studies.[16,17,19] Few Indian studies also reported

Table 5: Top 10 most frequent suspected drugs by medical students and physicians

Medical students	n (%)	Physicians	n (%)
Diclofenac	15 (6.91)	Paracetamol	14 (4.83)
Amoxicillin+clavulanic acid	14 (6.45)	Olanzapine	14 (4.83)
Ferrous sulfate	10 (4.61)	Rifampicin	12 (4.14)
Paracetamol	8 (3.69)	Isoniazid	11 (3.79)
Azithromycin	8 (3.69)	Risperidone	11 (3.79)
Chloroquine	8 (3.69)	Diclofenac	10 (3.45)
Ofloxacin	6 (2.76)	Ethambutol	10 (3.45)
Aspirin	6 (2.76)	Pyrazinamide	9 (3.10)
Pyrazinamide	5 (2.30)	Amlodipine	9 (3.10)
Amoxicillin	5 (2.30)	Metronidazole	9 (3.10)
-	-	Ciprofloxacin	9 (3.10)
-	-	Amoxicillin+clavulanic acid	9 (3.10)

Table 6: Comparison of quality assessment of adverse drug reaction reports between students and physicians based on completeness of domains of adverse drug reaction forms

Information included in ADR form	Students, n (%)	Physicians, n (%)	P	OR (95% CI)
Patient information				
Age	176 (100)	143 (100)	-	-
Gender	176 (100)	143 (100)	-	-
Suspected ADRs				
Onset date	174 (98.86)	140 (97.90)	0.66	1.86 (0.30-11.32)
Duration	128 (72.72)	30 (20.98)	<0.0001	10.04 (5.96-16.93)
Nature-description	111 (41.26)	80 (44.44)	0.56	0.88 (0.60-1.29)
Localization-description	125 (46.47)	91 (50.55)	0.45	0.85 (0.58-1.24)
Suspected drugs				
Dosage	187 (86.17)	206 (71.03)	<0.0001	2.54 (1.60-4.03)
Route of administration	213 (98.16)	269 (92.76)	0.07	2.37 (0.99-5.69)
Indication for use	209 (96.31)	286 (98.62)	0.14	0.36 (0.11-1.23)
Drug started	215 (99.07)	282 (97.24)	0.20	3.05 (0.64-14.51)
Drug stopped	208 (95.85)	252 (86.89)	0.001	3.49 (1.65-7.37)
Dechallenge	181 (83.41)	243 (83.79)	0.91	0.97 (0.61-1.56)
Rechallenge	175 (80.65)	205 (70.69)	0.01	1.73 (1.13-2.63)
Use of concomitant drugs	114 (66.48)	125 (87.41)	<0.001	0.26 (0.15-0.47)
Relevant history	143 (81.25)	132 (92.30)	0.007	0.36 (0.17-0.74)
Outcome	167 (94.88)	143 (100)	0.004	0.06 (0.01–1.07)
Severity of reactions	169 (96.02)	139 (97.20)	0.76	0.69 (0.20–2.42)

ADRs=Adverse drug reactions, OR=Odds ratio, CI=Confidence interval

antineoplastic agents[18] and cardiovascular drugs[15] as most frequent culprit drug class system. The Western literature most frequently showed the musculoskeletal system[13] and antineoplastic agents.[1] The physicians most frequently reported ADRs due to nervous system class drugs. This discrepancy could be due to high frequency of ADR reporting due to psycholeptic and psychoanaleptic medications by psychiatrists to our AMC. The students most frequently reported ADRs due to blood, musculoskeletal, and respiratory system than physicians. This could be due to their more familiarity with iron preparations, nonsteroidal anti-inflammatory drugs (NSAIDs), and antihistamines. They suspected iron preparations in gastrointestinal ADRs in a pregnant woman, NSAIDs in cutaneous reactions, and antihistamines in central nervous system adverse effects. The top ten list of the most frequently suspected causative drugs suggests diclofenac, Amoxicillin+clavulanic acid, paracetamol, and pyrazinamide as common in both groups. This is in line with commonly used drugs in our setup. Surprisingly, physicians reported chloroquine and aspirin-induced ADRs in less frequency despite its widespread use. Among the anti-infective agents, students reported more ADRs due to Amoxicillin+clavulanic acid and azithromycin than fluoroquinolones and antitubercular drugs compared to physicians. This could be due to the widespread use of Amoxicillin+clavulanic acid and azithromycin in outpatients. Physicians reported troublesome ADRs in their practice due to reserve group such as fluoroquinolones and first-line antitubercular drugs in the spontaneous reporting system. This suggests students' reporting pattern of causative drugs is in line with the drug utilization pattern of the institute.

Complete information sent to the spontaneous reporting system helps the assessors to investigate the association between a drug and ADRs. This is important to generate signals and strengthen the database.[21] The students satisfactorily documented demographics, onset date, duration, routes, indication to use suspected drugs, their starting and stoppage information, dechallenge, and rechallenge. They gave less importance to concomitant drugs and other relevant history. Both groups lack the detailed reaction description in almost half of the report. This seems an organizational problem that requires attention through sensitization program.

A recent systematic review of Indian patients suggested the significant burden of ADRs in the hospitalized patients. The median incidence of ADR that leads to hospitalization and ADRs occurred following hospitalizations were 2.85% (interquartile range [IQR]: 1.25%–3.93%) and 6.34% (IQR: 3.36%–16.37%), respectively.[22] However, this incidence is not reflected in the spontaneous reporting system. Although India is the second largest populous country in the world, its contribution to the WHO – Uppsala Monitoring Centre's global drug safety database (VigiBase) was 2% in the year 2013. This does not show the total ADR burden of India. Due to lack of an adequate database on ADRs, India has to depend on data of Western countries to take regulatory decisions of patient safety. The poor participation of health-care professionals in the ADR reporting is due to lack of sensitization, ignorance, apprehension, time constraints, and patients' overload.[23] Undergraduate students from their 2nd professional years onward are posted in the outpatient departments, wards, and intensive care units as a part of clinical posting. Their involvement and constant encouragement may cultivate habits of ADR reporting into future practitioners of all setup and specialties. Students can also assist the physicians to notify ADRs to pharmacovigilance program of India. This could be a possible way to reduce the underreporting rate of India to the global WHO VigiFlow database.

CONCLUSION

Our findings suggest students' reports were valuable and offered clinically relevant information. Their reporting pattern resembles with earlier Indian spontaneous reporting studies. ADR monitoring through spontaneous reporting system helps to ensure patient safety through detection of new, serious, and rare drug reactions. Its success depends on the active participation of the physicians. Undergraduate students as a future health-care professional should be exposed to ADR reporting during their clinical teaching posting. Moreover, students can be involved in pharmacovigilance program after proper teaching and sensitization. We suggest following the role of the students to improve the detection rate: They should remain vigilant about ADRs in patient interviews, case and laboratory record review as well as case discussion with the clinicians during clinical teaching posting. On suspicion, they should discuss the possibility of ADRs to the clinical teacher concerned or pharmacologist and should seek their guidance. Then, they should notify all suspected reactions to the AMC. It may inculcate reporting culture among the future physicians.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Conforti A, Opri S, D'Incau P, Sottosanti L, Moretti U, Ferrazin F, *et al*. Adverse drug reaction reporting by nurses: Analysis of Italian pharmacovigilance database. Pharmacoepidemiol Drug Saf 2012;21:597-602.
2. Bandekar MS, Anwikar SR, Kshirsagar NA. Quality check of spontaneous adverse drug reaction reporting forms of different countries. Pharmacoepidemiol Drug Saf 2010;19:1181-5.
3. Thawani V. Rational use of medicines: Achievements and challenges. Indian J Pharmacol 2010;42:63-4.
4. Shankar PR, Subish P, Mishra P, Dubey AK. Teaching pharmacovigilance to medical students and doctors. Indian J Pharmacol 2006;38:316-9.
5. Olsson S. The role of the WHO programme on International Drug Monitoring in coordinating worldwide drug safety efforts. Drug Saf 1998;19:1-10.
6. Mann RD, Andrews EB, editors. Introduction. In: Pharmacovigilance. England: John Wiley & Sons, Ltd.; 2007. p. 3-11.
7. Gupta SK, Nayak RP, Shivaranjani R, Vidyarthi SK. A questionnaire study on the knowledge, attitude, and the practice of pharmacovigilance among the healthcare professionals in a teaching hospital in South India. Perspect Clin Res 2015;6:45-52.
8. Desai CK, Iyer G, Panchal J, Shah S, Dikshit RK. An evaluation of knowledge, attitude, and practice of adverse drug reaction reporting among prescribers at a tertiary care hospital. Perspect Clin Res 2011;2:129-36.
9. World Health Organizations. Definitions – World Health Organizations. Available from: http://www.who.int/medicines/areas/quality_safety/safety_efficacy/trainingcourses/definitions.pdf. [Last cited on 2016 Apr 15].
10. The Uppsala Monitoring Centre, WHO Collaborating Centre for International Drug Monitoring. The WHO Adverse Reaction Terminology. Available from: http://www.umcproducts.com/graphics/3149.pdf. [Last cited on 2016 Mar 01].
11. World Health Organization (WHO) Collaborating Center for Drugs Statistics Methodology. ATC/DDD Index; 2014. Available from: http://www.whocc.no/atc_ddd_index/. [Last cited on 2016 Apr 15].
12. ICH E2A Guideline. Note for Guidance on Clinical Safety Data Management: Definitions and Standards for Expedited Reporting. Available from: http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E2A/Step4/E2A_Guideline.pdf. [Last cited on 2016 Mar 20].
13. Gedde-Dahl A, Harg P, Stenberg-Nilsen H, Buajordet M, Granas AG, Horn AM. Characteristics and quality of adverse drug reaction reports by pharmacists in Norway. Pharmacoepidemiol Drug Saf 2007;16:999-1005.
14. Suke SG, Kosta P, Negi H. Role of pharmacovigilance in India: An overview. Online J Public Health Inform 2015;7:e223.
15. Ramesh M, Pandit J, Parthasarathi G. Adverse drug reactions in a South Indian hospital – Their severity and cost involved. Pharmacoepidemiol Drug Saf 2003;12:687-92.
16. Rao PG, Archana B, Jose J. Implementation and results of an adverse drug reaction reporting programme at an Indian teaching hospital. Indian J Pharmacol 2006;38:293-4.
17. Arulmani R, Rajendran SD, Suresh B. Adverse drug reaction monitoring in a secondary care hospital in South India. Br J Clin Pharmacol 2008;65:210-6.
18. Jose J, Rao PG. Pattern of adverse drug reactions notified by spontaneous reporting in an Indian tertiary care teaching hospital. Pharmacol Res 2006;54:226-33.
19. Uppal R, Jhaj R, Malhotra S. Adverse drug reactions among inpatients in a north Indian referral hospital. Natl Med J India 2000;13:16-8.
20. van Hunsel F, Passier A, van Grootheest K. Comparing patients' and healthcare professionals' ADR reports after media attention: The broadcast of a Dutch television programme about the benefits and risks of statins as an example. Br J Clin Pharmacol 2009;67:558-64.
21. Alshammari TM, Al-Kathiri WH, Le Louet H, Aljadhey HS. Completeness of adverse drug reactions reports of the Saudi adverse event reporting system. Saudi Med J 2015;36:821-8.
22. Patel TK, Patel PB. Incidence of adverse drug reactions in Indian hospitals: A systematic review of prospective studies. Curr Drug Saf 2016;11:128-36.
23. Lihite RJ, Lahkar M. An update on the pharmacovigilance programme of India. Front Pharmacol 2015;6:194.