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Emergency department visits caused by adverse drug reactions: results of a Turkish university hospital

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Background/aim: We aimed to evaluate adverse drug reaction (ADR)-related emergency department (ED) visits in the ED of the Dokuz Eylül University Hospital prospectively.

Materials and methods: Patients who were admitted to the ED during 1-week periods of four different seasons between July 2010 and April 2011 were enrolled. Demographics of patients, previous ADR history, clinical progress, and outcomes were recorded. Causality assessment was done according to World Health Organization Uppsala Monitoring Centre categories. ADRs were categorized as certain, probable, or possible.

Results: Patients who were on medications (26.5%, n = 1838) were evaluated for ADR-related ED admissions. ADRs accounted for 5.9% of cases (n = 108). The most frequently affected systems were the gastrointestinal (35.2%, n = 38), dermatological (23.1%, n = 25), and hematological (10.2%, n = 11) systems (7.4%, n = 8). The most common causes of ADRs were antiinfectives (31.6%, n = 33). Amoxicillin, Coumadin, and paracetamol were the most common medications that caused ADRs.

Conclusion: Nearly 6% of the admissions were ADR-related. ADRs should always be considered when patients who are on medication are admitted to the ED. Multicenter epidemiologic studies are required to know the real rates of ADR cases in EDs in Turkey.

Key words: Adverse drug reactions, emergency department, World Health Organization Uppsala Monitoring Centre

1. Introduction

Adverse drug reactions (ADRs) are noxious and unintended reactions that occur at therapeutic, diagnostic, or prophylactic doses used in humans. They are one of the known causes of mortality and morbidity throughout the world (1–3) and one of the causes of hospital or emergency service admissions (4). Nearly 2% of the patients who are hospitalized suffer from ADRs that increase the hospitalization length and costs (5). Elderly patients and patients on a large number of medications have a greater risk of ADRs, resulting in increased mortality and morbidity rates, lengthened hospital stay, and significant economic burdens (2,3,6). Most ADRs are preventable and may be reversible by withdrawal of the drug (2,7).

ADR, which have many causes such as inappropriate medication or dosing, drug–drug interactions (D-DIs), and patient incompliance (8), are one of the causes of emergency department (ED) admissions. Because many ADRs are preventable, to detect ADRs in time and to determine the seriousness or frequency of ADRs is very important (9). Studies related to the frequency and properties of ADRs are generally from developed countries. There are no data about ADR-related ED admissions in Turkey. Therefore, we aimed to evaluate the frequency and characteristics of ADR-related ED visits at the ED of Dokuz Eylül University Hospital (EMDEU). We also identified the most common type of ADRs, the medications most frequently involved, and D-DI rates.

2. Materials and methods

2.1. Design

This descriptive observational study was conducted at EMDEU, a tertiary reference hospital with an annual census of about 89,600 patients, with approval by the Institutional

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Ethics Committee of the Dokuz Eylül University School of Medicine (28.07.2010 no: 08 – 18 / 2010). Because of some seasonal features of diseases, patients admitted to the ED over four seasons with 1-week periods (24 h / 7 days), the first in July 2010, second in October 2010, third in January 2011, and fourth in April 2011, were enrolled. Before the study began, all of the ED physicians and residents were given a half-day training on pharmacovigilance and definitions of ADRs by Department of Medical Pharmacology faculty physicians. Additionally, they were trained on the study and the details of the standardized data registration form that was prepared by the study team. A 1-day preliminary work was performed to test the ED physicians" adequacy in filling out the standardized data registration form.

The trained ED physicians filled out the standardized data registration forms for all the patients who had a medication history in the last 15 days prior to the study period. Sociodemographic data were also collected. All types of medications including herbal drugs, vitamins and over-the-counter drugs and the route and duration of the medication, previous ADR history, clinical progress, and outcomes of the patients were recorded. All admitted patients were followed until hospital discharge. Drugs were classified according to the Anatomical Therapeutic Chemical (ATC) classification system (10).

All of the data registration forms of the study were evaluated by the project team on the day following the patients' admission and a causality assessment was done according to the World Health Organization Uppsala Monitoring Centre (WHO-UMC) causality assessment criteria as certain, probable/likely, possible, unlikely, conditional/unclassified, and unassessable/unclassifiable (1). For the evaluation, the Micromedex Healthcare Series and Rx Media Pharma were used (11). D-DIs were also examined.

2.2. Patients

Patients who presented to the EMDEU with a medication history were enrolled in the study. Patients who were younger than 17 years, who did not have any medication history in the last 15 days, who were admitted to the ED for a drug overdose or alcohol poisoning, and who had a drug abuse history or trauma were excluded. Patients who presented to the EMDEU for a gynecologic illness were also excluded.

2.3. Statistical analysis

SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA) was used. Statistical analysis was performed by using the chi-square test. Results were considered statistically significant at $P < 0.05$.

3. Results

In the four study periods, a total of 6928 patients were admitted to the EMDEU. Patients who did not have any medication history in the last 15 days or who had any other exclusion criteria were excluded from the study (n = 5090, 73.5%; Figure).

ADR-related ED admissions were identified in 5.9% (n = 108) of the patients that were enrolled in the study (n = 1838). The mean age of the patients was 51.5 ± 1.9 years (48.2 ± 2.6 in women vs. 54.8 ± 2.8 in men). Most of the patients were younger than 65 years (67.6%, n = 73). While the female/male ratio was 1.2, there was no relationship between the sexes for ADR-related ED admissions (χ^2 = 0.2497, P = 0.6173). While the rates of certain, probable, and possible ADR-related ED admissions were 4.6% (n = 5), 44.5% (n = 48), and 50.9% (n = 55), respectively, the rate of conditional/unclassified and unassessable/unclassifiable cases was found to be 2.9% (n = 54). Duration of medication use was shorter than 15 days in 75.0% (n = 81) of the patients. While one-third of the patients 35.2% (n = 38) were on a single medication, 33.3% (n = 36) of them were on two drugs and the remaining patients (31.5%, n = 34) were on more than two drugs (Table 1).

Oral ingestion (n = 95, 88.0%) was the most common exposure route of the medications. Intramuscular and intravenous exposure rates were 10.2% (n = 11) and 1.8% (n = 2), respectively. Most of the patients (87.0%) were taking their medications in compliance with their physicians' prescriptions.

The most common medications identified according to ATC classification were antiinfectives (31.6%, n = 33), medications related to the alimentary tract and metabolism (12.9%, n = 14), and medications related to blood and blood-forming organs (12.9%, n = 14) (Table 2). Amoxicillin (n = 9, 8.3%), Coumadin (n = 8, 7.4%), and paracetamol (n = 7, 6.5%) were the most common medications that caused ADRs.

The systems most frequently affected by ADRs were the gastrointestinal (35.2%, n = 38), dermatological (23.1%, n = 25), hematological (10.2%, n = 11), and cardiovascular (7.4%, n = 8) systems (Table 3).

The number of patients who had previous ADR history was significantly (χ^2 = 10.273, P = 0.0014, Table 4) higher than that of the patients without any previous ADR history. Of 11 patients who had previous ADR history, 5 of them presented to the ED with the same ADR (Table 5).

D-DIs were reported in four cases (0.03%). Bradycardia was determined in a patient who was on metoprolol and amlodipine, gastrointestinal hemorrhage was determined in a patient who was on Coumadin and acetylsalicylic acid, hypertension was determined in a patient who was on metoprolol and etodolac, and acute renal failure was determined in a patient who was on valsartan-

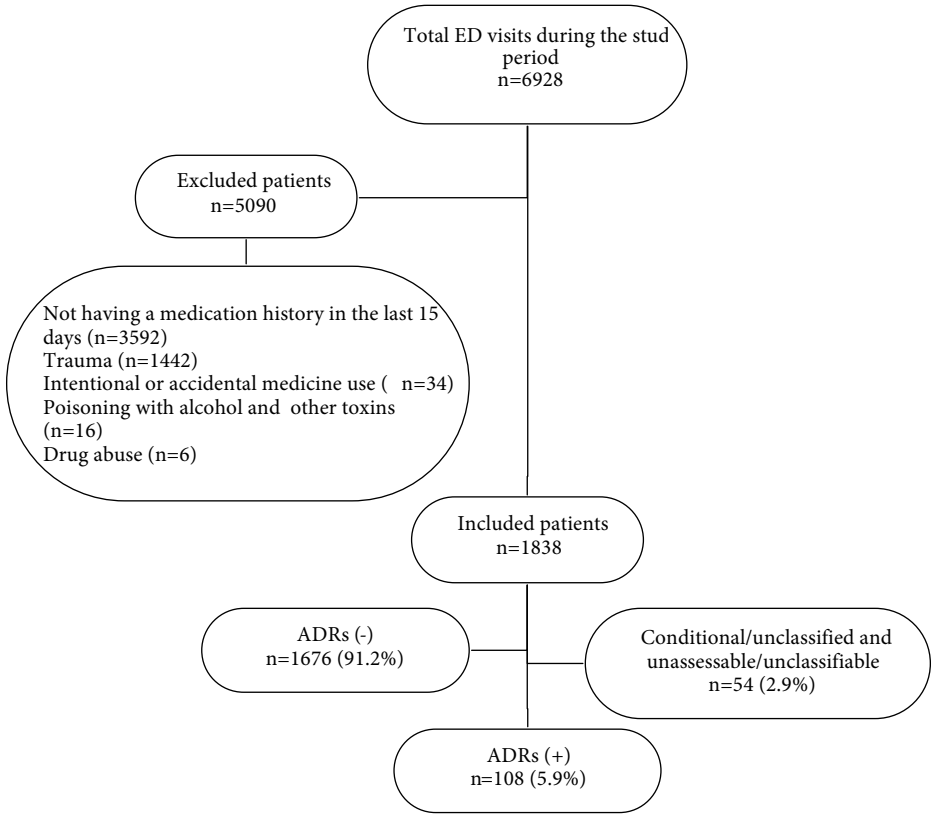

Figure. Flow diagram of patients through the study. ADRs: Adverse drug reactions.

Table 1. Demographics of the patients with adverse drug reactions (ADRs).

Patients characteristics	Patients with ADRs (n=108) No. (%)
Age (years)	
>65 years	35 (32.4)
<65 years	73 (67.6)
Sex	
Male	49 (45.3)
Female	59 (54.7)
Number of medications taken	
One drug	38 (35.2)
More than one drug	70 (64.8)
Classification of ADRs	
Certain	5 (4.6)
Probable	48 (44.5)
Possible	55 (50.9)
Duration of medication exposure	
<15 days	81 (75.0)
>15 days	27 (25.0)

Table 2. ATC classification of the medications that caused ADRs.

ATC		n	%
J	Antiinfectives for systemic use	33	30.6
A	Alimentary tract and metabolism	14	12.9
B	Blood and blood-forming organs	14	12.9
M	Musculoskeletal system	12	11.1
N	Nervous system	12	11.1
C	Cardiovascular system	7	6.5
R	Respiratory system	5	4.7
V	Various	4	3.7
	Herbal products	3	2.8
H	Systemic hormonal preparations, excluding sex hormones and insulins	2	1.9
D	Dermatologicals	1	0.9
G	Genitourinary system and sex hormones	1	0.9
Total		108	100.0

Table 3. Distribution of medications that caused ADRs.

System	n	%
Gastrointestinal system reactions		
Dyspepsia (n = 23), gastroenteritis (n = 13), gastrointestinal hemorrhage (n = 2)	38	35.2
Skin reaction		
Urticaria (n = 25)	25	23.1
Hematological system		
Hemorrhage (n = 9), epistaxis (n = 2)	11	10.2
Cardiovascular system reactions		
Palpitation (n = 4), hypertension (n = 2), bradycardia (n = 1), hypotension (n = 1)	8	7.4
Renal diseases		
Acute renal failure (n = 6)	6	5.6
Central nervous system reaction		
Loss of consciousness (n = 1), suicide idea (n = 1), headache (n = 1), dystonic reaction (n = 1), vertigo (n = 1)	5	4.6
Endocrine		
Hypoglycemia (n = 5)	5	4.6
Digestive system diseases		
Constipation (n = 1)	1	0.9
Other		
Angioedema (n = 7), upper respiratory tract infection (n = 1), fatigue (n = 1)	9	8.3

Table 4. ADRs and previous ADRs in all patients admitted to the EMDEU.

	ADRs (+)		ADRs (–)		Total	
	n	%	n	%	n	%
Previous ADRs (+)	11	10.2	61	3.5	72	3.9
Previous ADRs (–)	97	89.8	1669	66.5	1766	66.1
	108	100	1730	100	1838	100

Table 5. Medications that caused ADRs in cases with previous ADR history.

Medications that caused the previous ADRs	ADRs that caused the ED admission
Unknown drug	Ciprofloxacin
Unknown drug	Ciprofloxacin
Unknown drug	Paracetamol
Penicillin	Oxolamine citrate
Penicillin	Penicillin
Metoprolol	Metoprolol
Metoprolol	Etodolac
Clarithromycin	Clarithromycin
Insulin	Insulin
Fentanyl	Fentanyl
Unknown antibiotic	Gentamicin

hydrochlorothiazide and diclofenac. All of the patients that had a D-DI were older than 65 years (between 68 and 83 years).

Most of the patients were discharged without any sequelae (n = 96, 88.9%). Only 1.9% (n = 2) of them were referred to the intensive care unit. We did not observe any ADR-related deaths in our study (Table 6).

4. Discussion

The WHO defines ADRs as "a response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for modification of physiological function" (1). ADRs are one of the reasons for hospital or ED admissions. In this study, we investigated the ADR-related ED visits at our

Table 6. Outcomes of the patients admitted to the EMDEU.

	ADRs (+)		ADRs (–)		Total	
	n	%	n	%	n	%
Discharged	96	88.9	1467	84.8	1563	85.0
Clinic treatment	6	5.5	128	7.4	134	7.3
Intensive care treatment	2	1.9	26	1.5	28	1.5
Death	0	0	5	0.3	5	0.3
Dispatched	0	0	4	0.2	4	0.2
Discharged at their request	4	3.7	100	5.8	104	5.7
Total	108	100	1730	100	1838	100

hospital. This is the first descriptive study that estimates ADR-related ED visits in Turkey.

In our study period, 6928 patients were admitted to the EMDEU and 26.5% (n = 1838) of them were included in the study. ADRs were determined in 5.9% of the included patients. In various studies, the rate of ADR-related ED admissions are in a wide range between 0.8% and 29% (7,12–17). Although in a study by Andrezza et al. in southern Brazil a very high ED admission rate (28.5%) due to ADRs was reported, their study population included patients older than 12 years old and the study period was limited to only 1 month (15). Quenau et al. reported another high ED admission rate (21.0%) (7). In a study by Ma et al., the rate of ED admissions was found to be 7.4% in the elderly in China (12). In a retrospective study by Hafner et al. the rate of ADRs was 2.5% in the patients admitted to the ED in Peoria, Illinois (16). Another study by Chen et al. reported a very low ADR rate (0.8%) in nontraumatic patients older than 18 years (14). In the studies described above the range of the rate of ADR-related ED admissions is wider. The different rates of ADR-related admissions can be explained by different inclusion criteria of the patient populations and different methodologies that were used in the studies from various countries. However, our ADR-related ED admission rate was compatible with the previous reports.

While a slight predominance was determined in females among patients with ADRs in our study population (54.7% in woman vs. 45.3% in men), ADRs were not significantly more common in women than men, contrary to many reports of previous studies (6,15,16).

In the elderly population, use of medications and polypharmacy to treat chronic diseases, to alleviate pain, or to improve the quality of life increases the frequency of ADRs (18,19). In our study, while most of the patients who had ADRs were younger than 65 years, almost one-third of them were older than 65 years.

There are some scales establishing the causal assessment between medication use and ADRs. The World Health Organization Collaborating Centre for International Drug Monitoring Scale, the WHO-UMC Scale, and the Naranjo Probability Scales are the most widely used methods to evaluate causality assessment (20). These scales are very practical to evaluate the causality assessment for ADRs (3,21). In our preliminary study, we used both the Naranjo scales and WHO-UMC causality assessment criteria while evaluating the causality. As the WHO-UMC causality assessment scale was found to be more practical by the project team, we decided to use WHO-UMC causality assessment criteria in our study.

Antiinfectives were the primary cause of the ADRs according to our results. Additionally, medications related to the alimentary tract and metabolism and to blood and blood-forming organs were other frequent causes of ADRs. Similar to our results, in a study by Capuano et al., antiinfective-related ADRs were also more frequently encountered (4). In another study from Italy, nonsteroidal antiinflammatory drugs (NSAIDs) were the most common medications causing ADRs (22). Hafner et al. reported that antiinfectives were in the second rank (16). Tranquillizers and/or hypnotics, antidepressants, or antipsychotics most frequently caused ADRs in the study by Quenau et al. (7). Anticoagulants, antiinfectives, NSAIDs, hypoglycemics, and angiotensin-converting enzyme inhibitors were the main causes of ADR-related ED visits respectively in a study by Zanocchi et al. (17). In another study, the most common ADR-related medications were anticonvulsants, antiinfectives, and respiratory system drugs (23). In a study by Chen et al., analgesics, anticoagulants, and antiinfectives were found to be the most common reason of ADRs (14). While antihypertensive medication-related ADRs are more common in the elderly in some studies (12), antiinfective and NSAID-related ADRs are more common in others (4,22). The higher frequency of antiinfective medication-related ADRs may be explained by the ability to obtain these medications without a prescription from pharmacies easily in Turkey. Amoxicillin, ciprofloxacin, and cephalosporins were the major medications that caused ADRs among the antiinfective medications in our study. It was reported that amoxicillin and cefuroxime were the most frequently prescribed antiinfectives, followed by ciprofloxacin, in ten provinces across Turkey (24).

In our study, the systems most frequently affected by ADRs were the gastrointestinal system and the skin. Chen et al. reported that skin reactions followed by dizziness, coagulopathy, and mental disorders were the most pronounced signs and symptoms of ADRs (14). Although in a study by Capuano et al., skin reactions due to ADRs ranked first, the ranking differs in different studies (22). Quenau et al. reported that gastrointestinal symptoms were the most commonly encountered symptoms due to ADRs, similar to our findings (7).

We found that ADRs were more common in patients who had previous ADR history. Nearly half of the patients who presented to the ED had the same ADRs caused by the same medication. It is possible that subsequent exposures to the same medication could cause the same ADRs. Smith et al. suggested that medications with similar pharmacological mechanisms of action could cause ADRs with similar severity (25). Five patients with previous ADR history from penicillin, metoprolol, clarithromycin, insulin, and fentanyl were admitted to the EMDEU with the same ADRs by the same drug and their ADR was accepted as certain.

While in the current study, nearly two-thirds of the patients were using more than one medication, we determined D-DIs in only four patients (0.03%). In a study by Becker et al. the rate of ADRs due to D-DIs was found to be higher than that of ours (0.05%) (26). Polypharmacy is

suggested as one of the common causes of D-DI, especially in the elderly (27). It was also reported that D-DI-related ADRs are preventable and they are one of the main causes of hospital and ED admissions (26). Our finding of D-DIs in patients older than 65 years is compatible with this.

ADR-related deaths were also reported. The rate of ADR-related death was nearly 1.0% in a study by Shepherd et al. in an 8-year period (28). In another study, in a 1-year period, the rate of death was 0.5% in Brazil (29). In our study, 7.4% of the patients who had ADRs were followed in a clinic or intensive care unit and all of them were discharged from the ED without any sequelae or death.

Basic limitations of our study were the low number of patients and the study being conducted at a single center. We completed the study in four different seasons in 1-week periods. Another limitation is that the study could not be done in longer durations in these seasons.

In this first descriptive study investigating ADR-related ED admissions in Turkey, we found that nearly 6% of ED admissions were ADR-related, compatible with previous reports. While antiinfective medication-related ADRs were more common, gastrointestinal signs and symptoms were the most encountered findings due to ADRs. We did not observe any deaths due to ADRs. As our results are limited to data from only one ED's admissions, multicenter epidemiologic studies are required to know the real rates of ADRs in EDs. Training on diagnosing and managing ADR-related admissions might be planned for emergency medicine physicians.

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References

1. Edwards IR, Aronson JK. Adverse drug reactions: definitions, diagnosis, and management. Lancet 2000; 356: 1255-1259.
2. Wu TY, Jen MH, Bottle A, Molokhia M, Aylin P, Bell D, Majeed A. Ten-year trends in hospital admissions for adverse drug reactions in England 1999-2009. J R Soc Med 2010; 103: 239-250.
3. Rehan HS, Chopra D, Kakkar AK. Physician's guide to pharmacovigilance: terminology and causality assessment. Eur J Intern Med 2009; 20: 3-8.
4. Capuano A, Irpino A, Gallo M, Ferrante L, Illiano ML, Rinaldi B, Filippelli A, Rossi F. Regional surveillance of emergency-department visits for outpatient adverse drug events. Eur J Clin Pharmacol 2009; 65: 721-728.
5. Patel KJ, Kedia MS, Bajpai D, Mehta SS, Kshirsagar NA, Gogtay NJ. Evaluation of the prevalence and economic burden of adverse drug reactions presenting to the medical emergency department of a tertiary referral centre: a prospective study. BMC Clin Pharmacol 2007; 7: 8.
6. De Paepe P, Petrovic M, Outtier L, Van Maele G, Buylaert W. Drug interactions and adverse drug reactions in the older patients admitted to the emergency department. Acta Clin Belg 2013; 68: 15-21.
7. Queneau P, Bannwarth B, Carpentier F, Guliana JM, Bouget J, Trombert B, Leverve X, Lapostolle F, Borron SW, Adnet F et al. Emergency department visits caused by adverse drug events: results of a French survey. Drug Saf 2007; 30: 81-88.
8. Wilbur K, Hazi H, El-Bedawi A. Drug-related hospital visits and admissions associated with laboratory or physiologic abnormalities-a systematic-review. PLoS One 2013; 27; 8: e66803.
9. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. JAMA 1998; 279: 1200-1205.
10. Üstünes L, editor. RxMediaPharma İnteraktif İlaç Bilgi Kaynağı. İzmir, Turkey: GEMAŞ; 2011.
11. Klasco RK, editor. DRUGDEX® System. Greenwood Village, CO, USA: Thomson Micromedex (Vol. 149 expires 09/2011).
12. Ma J, Wang Y, Gao M, Meng Q, Liu J. Adverse drug reactions as the cause of emergency department admission of patients aged 80 years and older. Eur J Intern Med 2012; 23: e162-163.
13. Roulet L, Asseray N, Dary M, Chiffoleau A, Potel G, Ballereau F. Implementing a clinical pharmacy survey of adverse drug events in a French emergency department. Int J Clin Pharm 2012; 34: 902-910.
14. Chen YC, Fan JS, Hsu TF, Chen MH, Huang HH, Cheng KW, Yen DH, Huang MS, Lee CH, Chen LK et al. Detection of patients presenting with adverse drug events in the emergency department. Intern Med J 2012; 42: 651-657.
15. Andreazza RS, Silveira De Castro M, Sippel Köche P, Heineck I. Causes of drug-related problems in the emergency room of a hospital in southern Brazil. Gac Sanit 2011; 25: 501-506.
16. Hafner JW Jr, Belknap SM, Squillante MD, Bucheit KA. Adverse drug events in emergency department patients. Ann Emerg Med 2002; 39: 258-267.
17. Zanocchi M, Tibaldi V, Amati D, Francisetti F, Martinelli E, Gonella M, Cerrato F, Ponte E, Luppino A, Bardelli B et al. Adverse drug reactions as cause of visit to the emergency department: incidence, features and outcomes. Recenti Prog Med 2006; 97: 381-388 (in Italian with English abstract).
18. Okezie EO, Olufunmilayo F. Adverse drug reactions reporting by physicians in Ibadan, Nigeria. Pharmacoepidemiol Drug Saf 2008; 17: 517-522.
19. Brahma DK, Wahlang JB, Marak MD, Sangma MC. Adverse drug reactions in the elderly. J Pharmacol Pharmacother 2013; 4: 91-94.

20. Zaki SA. Adverse drug reaction and causality assessment scales. Lung India 2011; 28: 152-153.

21. Juntti-Patinen L, Kuitunen T, Pere P, Neuvonen PJ. Drug-related visits to a district hospital emergency room. Basic Clin Pharmacol Toxicol 2006; 98: 212-217.

22. Capuano A, Motola G, Russo F, Avolio A, Filippelli A, Rossi F, Mazzeo F. Adverse drug events in two emergency departments in Naples, Italy: an observational study. Pharmacol Res 2004; 50: 631-636.

23. Prince BS, Goetz CM, Rihn TL, Olsky M. Drug-related emergency department visits and hospital admissions. Am J Hosp Pharm 1992; 49: 1696-1700.

24. Mollahaliloglu S, Alkan A, Donertas B, Ozgulcu S, Akici A. Assessment of antibiotic prescribing at different hospitals and primary health care facilities. Saudi Pharm J 2013; 21: 281-291.

25. Smith W. Adverse drug reactions - allergy? side-effect? intolerance? Aust Fam Physician 2013; 42: 12-16.

26. Becker ML, Kallewaard M, Caspers PW, Visser LE, Leufkens HG, Stricker BH. Hospitalisations and emergency department visits due to drug-drug interactions: a literature review. Pharmacoepidemiol Drug Saf 2007; 16: 641-651.

27. Alomar MJ. Factors affecting the development of adverse drug reactions (Review article). Saudi Pharm J 2014; 22: 83-94.

28. Shepherd G, Mohorn P, Yacoub K, May DW. Adverse drug reaction deaths reported in United States vital statistics, 1999-2006. Ann Pharmacother 2012; 46: 169-175.

29. Noblat AC, Noblat LA, Toledo LA, Santos Pde M, Oliveira MG, Tanajura GM, Spinola SU, Almeida JR. Prevalence of hospital admission due to adverse drug reaction in Salvador, Bahia. Rev Assoc Med Bras 2011; 57: 42-45 (in Portuguese with English abstract).