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Detection of adverse drug reaction (ADR)-related hospital admissions: A pilot study using administrative database for ADR monitoring in Thailand

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Abstract

This study aims to examine incidence, characteristics, and trend of ADR-related admissions at one tertiary care hospital in Thailand during a five-year period (2007-2011), using administrative database and spontaneous report. Data of all hospitalized patients during the year 2007 to 2011 were retrospectively obtained from routine administrative database. The 10th International Classification of Diseases (ICD-10) was used to identify patients with ADR. The number of admissions with the following diagnosis codes; "adverse drug reaction", "drug-induced", "due to drug", "due to medicament", "drug allergy" or "external causes code" (Y40-Y59) were obtained and analyzed. During the year 2007 to 2011, incidence of ADR-related hospital admissions detected through hospital database and spontaneous report was estimated at 2.74%, and 0.71%, respectively. Using the administrative database, incidence of ADR-related hospital admissions was increasing from 1.29% (2007) to 3.75% (2010) and then slightly decreasing to 3.47% in 2011. The most commonly involved drugs were hormones and their synthetic substitutes and antagonists (Y42; 23.8%), systemic antibiotics (Y40; 13.2%), agents primarily affecting blood constituents (Y44; 12.6%), and primarily systemic agent (Y43; 9.3%), respectively. Drug-induced neutropenia (46.35%), drug-induced hypoglycemia without coma (27.01%), and generalized skin eruption (11.06%) were the three most common ADRs identified from database. ADR-related hospital admission was an increasing important public health problem. Effort should be made to implement effective measure to reduce ADRs and to make greater use of administrative database to continuously monitor patient safety in national perspective.

Keyword: Adverse drug reaction, spontaneous report, database, pharmacovigilance, admission, monitoring

1. INTRODUCTION

According to the World Health Organization (WHO), ADR is "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]. ADR is a common public health problem leading to considerable morbidity, mortality, and extra costs[2-4]. Detection and reporting ADR is crucial for improving and monitoring drug safety[5]. According to a review of the 25 prospective studies, prevalence of ADRs among hospitalization patients was estimated at 5.3%[6]. Nevertheless, more recent reviews found that prevalence of ADR related hospitalization was approximately 17%[7] while ranging between 0.1% to 54%[8]. It should be noted that findings from the reviews[6-8] indicated high variation in prevalence of ADR across studies. This variation could possibly be explained by methodology used for ADR, methodology quality, settings, and population[6-8].

With respect to ADR identification methods, intensive methods for ADR detection such as medical chart review or intensive monitoring consistently found higher prevalence

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rates for ADRs than analysis of database and spontaneous reporting[6-9]. Nevertheless, medical chart review and intensive monitoring require high resource and technical intensive. In contrast, spontaneous reporting is a major method used globally to identify and to monitor ADRs. Although it is the easiest and cheapest method underreporting[10] and poor quality reports[11] are major concerns of this method.

Similar to spontaneous report, the use of administrative database required few resource and financial burden but resulted in higher rate of ADR detection. As the result, administrative database has substantial potential to be continuously used to monitor ADRs for national perspective as supplement to established methods such as spontaneous report. In fact, the use of hospital administrative data is proven to be a reliable and valid method for monitoring patient's safety in several developed countries[12-19]. To our knowledge, no study has been conducted to determine the prevalence of ADR among hospitalized patients in less developed country using administrative database before.

As compared to other countries, incidence of ADRs among hospitalized patients in Thailand was also high ranging between 1.7% to 22.6 % depending on methods, study settings and also study population[20]. It should be noted that all previous studies conducted in Thailand to examine prevalence of ADR among hospitalized patients[21-25] were short-term studies conducted using intensive ADR monitoring method in a few wards. Similar to many countries, spontaneous reporting system is a major method for ADR identification in Thailand. The aims of our study are to examine incidence and characteristics of ADR- related hospital admission using routine administrative database at one tertiary care hospital in Thailand, and to compare the incidence of ADR-related hospital admission identified using routine administrative database and spontaneous report.

2. MATERIALS AND METHODS

2.1 Study design

A retrospective study was conducted using hospital administrative database of one tertiary hospital in the northern region of Thailand during 2007 to 2011. The database is maintained by the hospital and is used for reimbursement purpose. The database contains information on patient identification, age, gender, admission date, discharge date, diagnosis relate group (DRG), and ICD-10th of all patients admitted to the hospital. This study was approved by the Mahidol University Institutional Review Board (MU-IRB), Thailand.

2.2 ADR identification

From 2007 to 2011, ADR-related hospital admissions were identified using the ICD-10th code which contained the following keywords: "adverse drug reaction, "drug-induced", "due to drug", "due to medicament"), as shown in Table 1. ICD-10th code Y40-Y59, which are the additional codes used to indicate an "external cause" relevant to drugs were also used to identified ADR related admission (Table 2). This excludes accidental or intentional poisoning due to drugs. Duplicated records were removed by matching date of birth, gender, date of admission, and date of discharge. Data on spontaneous ADR reporting during the study period were also obtained from the hospital to calculate the incidence of ADR- related hospital admissions.

Incidence of ADR-related hospital admissions and characteristics of ADR-related hospital admissions were analyzed using descriptive statistics (frequency, percentage, mean± standard deviation). Data were analyzed by Microsoft Access version 2013 and Microsoft Excel version 2013.

Table 1. ICD-10 for external cause mortality/morbidity

ICD-10	External cause mortality/ morbidity by:
Y40	**Systematic antibiotics:** Penicillins, cefalosporins and other beta-lactam antibiotics, macrolides, tetracyclines, aminoglycosides, rifamycin, antifungals, others
Y41	**Other systematic anti-infectives and antiparasitics:** Sulphonamides, other anti-mycobacterial, anti-malarials, anti-protozoal, anti-helminthics, anti-virals
Y42	**Hormones and substitutes:** Glucocorticoids, thyroid hormones, anti-thyroids, insulin, oral hypoglyceamics, oral contraceptives, oestrogen and progestogen, anti-gonadotrophins,anti-oestrogens, anti- progestogen, androgens
Y43	**Systemic agents:** anti-allergic and anti-emetic drugs, anti-neoplastic and immuno-suppressive drugs, acidifying/ alkalizing agents
Y44	**Agents affect blood constituents:** Iron preparations, anti-megaloblastic-anemia preparations, anticoagulants antagonists, antithrombotic drugs, thrombolytic drugs, blood products, plasma substitutes
Y45	**Analgesics, anti-pyretics and anti-inflammatory drugs:** Opioids and related analgesics, salicylates, propionic acid derivatives, nonsteroidal anti-inflammatory drugs, antirheumatics, 4-aminophenol derivatives
Y46	**Anti-epileptics and anti-parkinsonism drugs:** Succinimides, oxazolidinediones, hydatoin derivatives, deoxybarbiturates, iminostibenes, valproic acid, anti- parkinsonism drugs, anti-spasticity drugs
Y47	**Sedatives, hypnotics and anti-anxiety drugs:** Barbiturates, benzodiazepines, cloral derivatives, paraldehyde, bromine compounds, sedative, hypnotics and anti-anxiety drugs, unspecified
Y48	**Anaesthetics and therapeutic gases:** Inhaled/ parenteral anaesthetics, local anaesthetics, therapeutic gases
Y49	**Psychotropic drugs:** Tricyclic and tetracyclic antidepressants, monoamine-oxidase-inhibitor, phenothiazine antipsychotics and neuroleptics, butyrophenone and thioxanthene neuroleptics, other antidepressants, antipsychotics and neuroleptics
Y50	**Central nervous system stimulants**: Analeptics, opioid receptor antagonists, , methylxanthines, other central nervous system stimulants
Y51	**Drugs primarily affecting the autonomic nervous system:** Anticholinesterase agents, cholinergics, ganglionic blocking drugs, anti cholinergics, antimuscarinics, spasmolytics, alpha-adrenoreceptor agonists/ antagonists, beta-adrenoreceptor agonists/ antagonists, centrally acting and adrenergic-nervous-blocking agents
Y52	**Agents affecting the cardiovascular system:** Cardiac-stimulant glycosides, calcium-channel blockers, other anti-dysrhythmic drugs, other coronary vasodilators, angiotensin-converting-enzyme inhibitors, other anti-hypertensives, anti-hyperlipidaemic and anti-arteriosclerotic drugs, peripheral vasodilators, anti-varicose drugs

ICD-10	External cause mortality/ morbidity by:
Y53	**Agents affecting the gastrointestinal system:** Antacids, anti-gastric-secretion drugs, laxatives, anti-diarrhoeal, emetics
Y54	**Agents affecting water-balance and mineral and uric metabolism:** Mineralocorticoids, mineralocorticoids antagonists, carbonic-anhydrase inhibitors, benzothaidiazine derivatives, other diuretics, electrolytic, caloric and water-balance agents, agents affecting calcification, agents affecting uric acid metabolism
Y55	**Agents acting on smooth and skeletal muscles and the respiratory system:** Oxytocic drugs, skeletal muscles relaxants, anti-tussives, expectorants, anti-common-cold drugs, anti-asthmatics
Y56	**Topical agents primarily affecting skin and mucous membrane:** Local anti-fungal, anti-infective, anty-inframmatory drugs, anti-pruritics, local detergents, emollients, keratolytics, ophthalamological drugs,otrhinolaryngological drugs, dental drugs
Y57	**Other and unspecified drugs:** Appetite depressants, lipotropic drugs, antidotes and chelating agents, alcohol deterrents, X-ray contrast media, vitamin
Y58	**Bacterial vaccines**
Y59	**Other vaccines**: Viral/ rickettsial/ protozoal vaccines, immunoglobulin

Table 2. ICD-10 codes (primary diagnosis codes) for "adverse drug reaction", "drug-induced", "due to drug", "due to medicament" or "drug allergy" causing adverse effects in therapeutic use

ICD-10 chapter	ICD-10 codes	Primary cause mortality/ morbidity by:
D	D52.1	Drug-induced folate deficiency anaemia
	D59.0	Drug-induced autoimmune haemolytic anaemia
	D59.2	Drug-induced nonautoimmune haemolytic anaemia
	D61.1	Drug-induced aplastic anaemia
	D64.2	Secondary sideroblastic anaemia due to drugs and toxins
	D70	Agranulocytosis, Agranulocytic angina, Infantile genetic agranulocytosis Kostmann's disease, Neutropenia: drug-induced
E	E06.4	Drug-induced thyroiditis
	E15	Nondiabetic hypoglycaemic coma Drug-induced insulin coma in nondiabetic
	E16.0	Drug-induced hypoglycaemia without coma
	E23.1	Drug-induced hypopituitarism
	E24.2	Drug-induced Cushing's syndrome
	E03.2	Hypothyroidism due to medicaments and other exogenous substances
	E27.3	Drug-induced adrenocortical insufficiency
	E66.1	Drug-induced obesity

ICD-10 chapter	ICD-10 codes	Primary cause mortality/ morbidity by:
G	G24.0	Drug-induced dystonia
	G25.1	Drug-induced tremor
	G25.3	Drug-induced myoclonus
	G25.4	Drug-induced chorea
	G25.6	Drug-induced tics and other tics of organic origin
	G44.4	Drug-induced headache, not elsewhere classified
	G62.0	Drug-induced polyneuropathy
	G71.1	Myotonic disorders, Dystrophia myotonica [Steinert], Myotonia: drug-induced
	G72.0	Drug-induced myopathy
	G95.8	Other specified diseases of spinal cord, Cord bladder NOS, Myelopathy: drug-induced
H	H26.3	Drug-induced cataract
I	I42.7	Cardiomyopathy due to drugs and other external agents
	I95.2	Hypotension due to drugs
J	J70.2	Acute drug-induced interstitial lung disorders
	J70.3	Chronic drug-induced interstitial lung disorders
	J70.4	Drug-induced interstitial lung disorders, unspecified
K	K71	Toxic liver disease, Includes: drug-induced: idiosyncratic (unpredictable) liver disease, toxic (predictable) liver disease
	K71.1	Toxic liver disease with hepatic necrosis Hepatic failure (acute)(chronic) due to drugs
	K85.3	Drug-induced acute pancreatitis
L	L10.5	Drug-induced pemphigus
	L23.3	Allergic contact dermatitis due to drugs in contact with skin
	L24.4	Irritant contact dermatitis due to drugs in contact with skin
	L25.1	Unspecified contact dermatitis due to drugs in contact with skin
	L27.0	Generalized skin eruption due to drugs and medicaments
	L27.1	Localized skin eruption due to drugs and medicaments
	L64.0	Drug-induced androgenic alopecia
M	M10.2	Drug-induced gout
	M32.0	Drug-induced systemic lupus erythematosus
	M80.4	Drug-induced osteoporosis with pathological fracture
	M81.4	Drug-induced osteoporosis
	M83.5	Other drug-induced osteomalacia in adults
	M87.1	Osteonecrosis due to drugs
O	O68	Labour and delivery complicated by fetal stress [distress] Includes: fetal distress in labour or delivery due to drug administration
P	P58.4	Neonatal jaundice due to drugs or toxins transmitted from mother or given to newborn
	P93	Reactions and intoxications due to drugs administered to fetus and newborn Grey syndrome from chloramphenicol administration in newborn
R	R50.2	Drug-induced fever

3. RESULTS

3.1 Incidence and 5-year trend of ADR-related hospital admissions

Table 3 summarizes the annual number of total admissions, incidence and the number of ADR-related admissions identified from administrative and spontaneous report, as well as incidence and the total number of deaths among patients with ADR-related admissions. During the 5-year study period, there were 283,070 admissions and 7,756 admissions with diagnostic code indicative of ADRs (2.74%). Of these, 3,780 (1.34%) were "drug induced" codes and 3,976 (1.4%) were "external cause". As shown in Table 3, during the 5-year study period, incidence of ADRs was increasing from 1.29% in 2007 to 3.75% in 2010 and then slightly decreasing to 3.47% in 2011. Between 2007 and 2011, the total number of admissions increased by 17.08% while the total number of ADR-related admission identified from administrative database increased by 215.57%, resulting in 169% increase in the incidence of ADR-related admissions (from 1.29% in 2007 to 3.74% in 2011). On the other hand, incidence of ADR-related hospital admission identified from spontaneous report was 0.71%. Similarly, incidence and the total number of ADR-related admissions identified from spontaneous reports were also increased. With respect to the number of deaths among patients with ADR-related admissions, average case fatality between 2007 and 2011 was about 11%.

Table 3. Total number of ADR-related admissions from 2007 to 2011

Year	2007	2008	2009	2010	2011	total	% change 2007-2011
Total number of admissions	52,955	55,764	55,309	57,041	62,001	283,070	17.08
Administrative database							
Number of admissions with "Drug-induced" codes	479	507	882	1,003	909	3,780	89.77
Number of admissions with "external cause" codes	202	378	1,018	1,138	1,240	3,976	513.86
Total number of ADRs-related admissions	681	885	1,900	2,141	2,149	7,756	215.57
Incidence of ADRs-related admissions (%)	1.29	1.59	3.44	3.75	3.47	2.74	168.99
Total number of deaths among patients with ADRs-related admissions	68	66	226	273	214	847	214.71
Case fatality (%)	9.99	7.46	11.89	12.75	9.96	10.92	-0.3
Spontaneous repot							
Total number of ADRs-related admissions	263	363	496	418	463	2,003	76.05
Incidence of ADR-related admissions (%)	0.5	0.65	0.90	0.73	0.75	0.71	50.00

Table 4 describes the total number of ADRs with an "external cause" code during 2007 to 2011. As shown in the table, the most common classes of drug associated with ADRs were hormones and their synthetic substitutes and antagonists (Y42; 24%), systematic antibiotic (Y40; 13.2%), agents primarily affecting blood constitutes (Y44; 12.6%), systematic agents (Y43; 9.3%), other and unspecified drugs (Y57; 7.1%), and analgesic, antipyretic and anti-inflammatory drugs (Y45; 6.5%), respectively.

Table 4. Total number of admissions with an "external cause" code from 2007 to 2011

ICD-10	Description	2007 (%)	2008 (%)	2009 (%)	2010 (%)	2011 (%)	Total (%)
Y42	Hormones and their synthetic substitutes and antagonists	12(5.94)	11(2.91)	226(22.20)	324(28.47)	381(30.72)	954(23.99)
Y40	Systemic antibiotics	32(15.84)	61(16.14)	156(15.32)	147(12.92)	130(10.48)	526(13.23)
Y44	Agents primarily affecting blood Constituents	51(25.25)	100(26.46)	112(11.00)	112(9.84)	126(10.16)	501(12.60)
Y43	Primarily systemic agents	8(3.96)	11(2.91)	82(8.05)	125(10.98)	142(11.45)	368(9.26)
Y57	Other and unspecified drugs	32(15.84)	84(22.22)	51(5.01)	51(4.48)	63(5.08)	281(7.07)
Y45	Analgesic, antipyretics and anti-inflammatory drugs	11(5.45)	18(4.76)	76(7.47)	82(7.21)	70(5.65)	257(6.46)
Y52	Agents primarily affecting the cardiovascular system	18(8.91)	25(6.61)	72(7.07)	63(5.54)	60(4.84)	238(5.99)
Y41	Other systemic anti-infectives and antiparasitics	8(3.96)	11(2.91)	57(5.59)	66(5.80)	75(6.05)	217(5.46)
Y54	Agents primarily affecting water-balance and mineral and uric acid metabolism	4(1.98)	13(3.44)	58(5.70)	66(5.80)	76(6.13)	217(5.46)
Y46	Antiepileptic and anti-Parkinsonism drugs	11(5.45)	19(5.03)	37(3.64)	26(2.29)	39(3.15)	132(3.32)
Y51	Drugs primarily affecting the autonomic nervous system	2(0.99)	8(2.12)	36(3.54)	33(2.90)	36(2.90)	115(2.89)
Y49	Psychotropic drugs, not elsewhere Classified	2(0.99)	4(1.06)	15(1.47)	13(1.14)	15(1.21)	49(1.23)
Y47	Sedatives, hypnotics and anti-anxiety drugs	7(3.47)	4(1.06)	14(1.38)	8(0.70)	12(0.97)	45(1.13)
Y59	Other and unspecified vaccines and biological substance	1(0.50)	2(0.53)	3(0.30)	8(0.70)	3(0.24)	17(0.43)
Y55	Agents primarily act smooth and skeletal muscle and respiratory system	1(0.50)	1(0.27)	6(0.59)	3(0.26)	4(0.32)	15(0.38)
Y53	Agents primarily affecting the gastrointestinal system	1(0.49)	1(0.27)	5(0.49)	4(0.35)	3(0.24)	14(0.35)
Y56	Topical agent primarily affecting skin and mucous membranes	1(0.50)	2(0.53)	5(0.49)	3(0.26)	1(0.08)	12(0.30)
Y58	Bacterial vaccines	0(0)	2(0.53)	4(0.39)	4(0.35)	2(0.16)	12(0.30)
Y48	Anaesthetic and therapeutic gases	0(0)	0(0)	2(0.19)	0(0)	2(0.16)	4(0.10)
Y50	Central nervous system stimulants, not elsewhere classified	0(0)	1(0.27)	1(0.09)	0(0)	0(0)	2(0.05)
	Total	202	378	1,018	1,138	1,240	3,976

As shown in Table 5, diagnoses most frequently associated with ADRs were drug induced neutropenia (46.35%), drug induced hypoglycemia (22.99%), generalized skin eruption (11.06%), toxic liver disease with hepatic necrosis (5.58%), and hypotension (4.13%), respectively. When looking at the trend during the year 2007 to 2011, drug-induced hypoglycemia was the fastest growing ADRs.

In addition, we found that ADR-related admissions occurred slightly more frequent in female (54.6%). Approximately 46% and 44% of ADRs occurred among patients aged between 17-59, and 60 years or older, respectively. Average length of stay of patients with ADR-related admissions was estimated at 10.29 days.

Table 5. Total number of admissions with drug-induced codes from 2007-2011

ICD-10 codes	Description	2007	2008	2009	2010	2011	Total
D70	Drug-induced neutropenia	302(63.05)	321(63.31)	402(45.88)	389(38.78)	338(37.18)	1752(46.35)
E16.0	Drug-induced hypoglycaemia without coma	42(8.77)	53(10.45)	176(19.95)	316(31.51)	282(31.02)	869(22.99)
L27.0	Generalized skin eruption due to drugs and medicaments	71(14.82)	42(8.28)	112(12.70)	98(9.77)	95(10.45)	418(11.06)
K71.1	Toxic liver disease with hepatic necrosis	25(5.22)	39(7.69)	58(6.58)	42(4.19)	47(5.17)	211(5.58)
I95.2	Hypotension due to drugs	19(3.97)	18(3.55)	52(5.90)	37(3.69)	30(3.30)	156(4.13)
E15	Nondiabetic hypoglycaemic coma Drug-induced insulin coma in nondiabetic	3(0.63)	3(0.59)	21(2.38)	63(6.28)	62(6.82)	152(4.02)
G25.3	Drug-induced myoclonus	2(0.42)	10(1.97)	25(2.83)	12(1.20)	18(1.98)	67 (1.77)
G95.8	Drug-induced other specified diseases of spinal cord	3(0.63)	11(2.17)	10(1.13)	12(1.20)	6(0.66)	42(1.11)
E27.3	Drug-induced adrenocortical insufficiency	3 (0.63)	2(0.39)	7(0.79)	5(0.50)	1(0.11)	18(0.48)
D61.1	Drug-induced aplastic anaemia	1(0.21)	2(0.39)	2(0.23)	2(0.20)	8(0.88)	15(0.40)
L27.1	Localized skin eruption due to drugs and medicaments	1(0.21)	0	5(0.57)	5(0.50)	4(0.44)	15(0.40)
G72.0	Drug-induced myopathy	2(0.42)	2(0.39)	3(0.34)	2(0.2)	4(0.44)	13(0.34)
L25.1	Unspecified contact dermatitis due to drugs in contact with skin	0	1(0.20)	0	4(0.40)	6(0.66)	11(0.29)
R50.2	Drug-induced fever	0	0	0	8(0.8)	2(0.22)	10(0.26)
E03.2	Hypothyroidism due to medicaments and other exogenous substances	0	0	2(0.23)	2(0.20)	1(0.11)	5(0.13)
E24.2	Drug-induced Cushing's syndrome	0	0	3(0.34)	1(0.10)	0	4(0.11)
G24.0	Drug-induced dystonia	1(0.21)	0	0	1(0.10)	1(0.11)	3(0.08)
I42.7	Cardiomyopathy due to drugs and other external agents	0	0	0	1(0.1)	2(0.22)	3(0.08)
D59.0	Drug-induced autoimmune haemolytic anaemia	0	0	1(0.11)	1(0.10)	0	2(0.05)
G25.1	Drug-induced tremor	1(0.21)	0	0	1(0.10)	0	2(0.05)
G44.4	Drug-induced headache, not elsewhere classified	1(0.21)	1(0.20)	0	0	0	2(0.05)

ICD-10 codes	Description	2007	2008	2009	2010	2011	Total
G62.0	Drug-induced polyneuropathy	0	0	1(0.11)	0	1(0.11)	2(0.05)
M32.0	Drug-induced systemic lupus erythematosus	2(0.42)	0	0	0	0	2(0.05)
M87.1	Osteonecrosis due to drugs	0	0	0	1(0.1)	1(0.11)	2(0.05)
D64.2	Secondary sideroblastic anaemia due to drugs and toxins	0	1(0.2)	0	0	0	1(0.03)
K85.3	Secondary sideroblastic anaemia due to drugs and toxins	0	1(0.2)	0	0	0	1(0.03)
L23.3	Allergic contact dermatitis due to drugs in contact with skin	0	1(0.20)	0	0	0	1(0.03)
O68	Includes: fetal distress in labour or delivery due to drug administration	0	0	1(0.11)	0	0	1(0.03)
	Total	479	507	882	1,003	909	3,780

4. DISCUSSIONS

Incidence of ADR-related hospital admission, identified using administrative database was estimated at 2.74%. Our findings are in line with that of the previous review in which the rate of ADRs ranged from 0.16% to 15.7%[6]. Our findings are also in line with previous studies that use similar method to identify ADRs but slightly higher: Spain 1.69%[12], England 0.5% to 0.9%[15, 19], Portugal 1.26%[14]. However, it should be noted that previous studies were conducted nationwide while our study was conducted in one tertiary care hospital so the rate might be higher due to the use of more complex medications compared to other types of hospitals. Nevertheless, when compared our results with those of the previous studies in Thailand[21-25], which found that incidence of ADRs among hospitalized patients varied widely ranging from 0.07% to 38.64%, our detection rate was relatively low. It should be noted that method used in the previous studies were chart review while in this study administrative database was employed. Difference in method used to identify ADR may account for this difference. Nevertheless, we believed that the detection rate in our study may still under-estimated due to under-recognition and under-reporting of ADRs in routine hospital activity. However, when compared with the spontaneous report, our study confirmed that administrative database yields higher detection rate of ADRs than spontaneous report[9]. In this study, about 286 % increase in incidence of ADR-related hospital admission was detected when using administrative database (2.74 %), as compared to spontaneous report (0.71%).

When looking at trend of ADRs, similar to the previous studies[14-16, 19], we found that incidence of ADR-related hospital admission was increasing, which might be due to the introduction of new drugs, poly-pharmacotherapy, increasing aging population, and improvement of diagnostic and coding practice.

When looking at the major drugs groups most frequently associated with ADR, we found that hormones and their synthetic substitutes and antagonists e.g. insulin (Y42; 23.99%), systemic antibiotics (Y40; 13.23%), agents primarily affecting blood constituents e.g. anticoagulant (Y44; 12.60%), systematic agents e.g. anti-neoplastic and immunosuppressant (Y43; 9.26%), and analgesics, antipyretics and anti-inflammatory drugs (Y45; 6.46%) were the most involved drug groups. Our findings are broadly similar to the previous studies[12, 15, 19], which found that systematic agents particularly neoplastic drugs, analgesic drug, cardiovascular drug, antibiotics, anticoagulant were the most common drug classes associated with ADRs. The findings were also consistent to those previous studies in Thailand which found that

antibiotic were the most involved drug classes[20]. However, it should be noted that the total number of drug prescribed was not available so direct comparison of the total number of ADRs associated with the class of drugs may not be appropriate. In addition, the important limitation of the external cause code in terms of the lack of specification of drugs or the broad grouping of drugs used (e.g. anticoagulants, antithrombotic drug, blood products and plasma substitutes were all grouped in code Y45) should be noted.

When considered the most common ADRs identified by drug-induced codes, our study found that drug-induced neutropenia, drug-induced hypoglycemia, generalized skin eruption, toxic liver disease with hepatic necrosis, and hypotension were the most common ADRs identified from database. This is consistent with the major drugs groups most frequently associated with ADRs identified from external code as neutropenia was common side effect of anti-neoplastic drugs and systematic antibiotic while hypoglycemia was common side effect of insulin. In addition, our findings were similar to those of the previous study[14], which found that neutropenia, hypoglycemia were the common ADRs found from hospital database. According to our results, caution should be made to monitor safety among patients who were prescribed with those drugs.

In contrast with previous studies[4, 6, 15, 19], which found that incidence of ADR-related hospitalization was quite high among elderly, our study found that incidence of ADRs among elderly was similar to those of the adult population. Nevertheless, it should be noted that direct comparison of the total number of ADR in each age group may not be appropriate as the total number of elderly patients and adult patients were not taken into account in the analysis. When looking at gender, consistent with the previous studies[4, 15], we found that ADRs occurred slightly more frequent in female than male. It has suggested that pharmacological, immunological and hormonal differences and the fact that women take more medications may explain this gender difference [26].

It should be noted that our study was conducted in one tertiary care hospital in Thailand. Generalization of the findings to other settings should be made with caution. Another limitation is inherent to the use of administration database, which often contain inaccurate coding and incomplete information on ADR as they are used primarily for administrative purposes, they may be less concerned with accurate recording of ICD. In addition, as the database was used for reimbursement purpose code creeping (distorting DRG codes towards those with higher reimbursement) may also occur. Finally, further evidence on economic burden of ADR related hospitalization is clearly need to bring attention of hospital administrators and health care policy makers to improve patient safety as well as to save this unnecessary cost.

Our study was the first study in less developed country examining incidence of ADR-related hospitalization at one tertiary care hospital using hospital routinely administration database. We confirmed that administrative database is useful and easily accessible method to determine proportion of the adverse events caused by drugs in less developed countries. At present, the Thai national database aggregating data from all patients admitted to each hospital in Thailand, who were Universal health Coverage and Civil Servant Medical Benefit Scheme beneficiary, which accounted for 80% of total population is available. As it is mainly used for reimbursement purpose it contains useful information related to ADR monitoring such as: age, gender, admission date, discharge date, hospital, ICD-10th, Diagnosis Related Group (DRG). As the result, administrative database could be used to routinely monitor ADRs for national perspective as supplement to spontaneous reporting, which is currently used as a major surveillance mechanism to monitor ADRs in Thailand. As many less developed countries are moving towards Universal health care coverage, administrative database will be developed and made available for reimbursement purpose. Furthermore, future integration of computer systems within hospitals and the expansion of electronic prescribing and electronic health records in less developed countries will also make administrative database a more practical tool for pharmacovigilance at national level.

In conclusion, we found that ADR-related hospital admission was an increasing important public health problem accounted for 2.47% of total admissions. As detection and reporting ADR is crucial for improving and monitoring drug safety, we confirmed that administrative database is useful and feasible method to determine proportion of the adverse events caused by drugs in hospital in less developed countries. Nevertheless, improvement in the completeness, accuracy and standardization of coding should be promoted.

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