PREVALENCE OF POTENTIALLY INAPPROPRIATE MEDICATION (PIM) AND FACTORS ASSOCIATED WITH PIM IN ELDERLY OUTPATIENT PRESCRIPTIONS AT A DISTRICT HOSPITAL IN THE SOUTHERN REGION OF THAILAND

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ABSTRACT: The aims of study are to know the prevalence of, and to describe factors associated with prescribing PIM at a district hospital in the South of Thailand. A cross-sectional study conducting the retrospective data in a district hospital during October 1, 2011 to September 30, 2012, the study participants were a ≥ 65-year outpatient and had at least 1 prescribed medication from the hospital. Overall, 430 out of 5,265 participants were randomized and their 2,128 prescriptions were examined. The 2012 Beers criteria was applied to detect PIM. Prevalence of PIM were calculated by their total prescriptions. Prescription, patient, and prescriber characteristics associated with PIM were analyzed by logistic regression. Results showed that 39.1% of all participants were female and 53.7% aged 65-74 years; 28.1% of total prescriptions had at least 1 PIM. The highest prevalence of PIM prescription was observed in mental and behavioural disorders, while, Lorazepam was mostly frequent prescribed. Results showed the statistically significantly positive association between the presence of PIM and the number of medications. There was the more likelihood of a patient receiving PIM at outpatient department increased significantly when that patient was prescribed more medications ($p<0.01$). In addition, the positively associated factors to the presence of PIM were age of participant (OR=1.018, p= 0.040) and age of prescriber (OR=1.105, p=0.046). In contrast, the result showed a likelihood of an elderly outpatient who had more frequent outpatient visits had less PIM prescription as compared to the reference (outpatient visits: 4-6 vs. ≥7: OR = 0.578, p=0.002 vs. OR=0.674, p=0.011, respectively). However, no statistically significant associations between the presence of PIM and participant's gender, number of diagnoses, health insurance schemes, hospitalizations, prescriber's gender, types of prescriber and length of prescriber's years work were observed. In conclusion, similar to other international studies, the prevalence of PIM prescription among elderly outpatients in this study hospital was 28.1%. The significant factors associated with PIM prescriptions were number of medications, participant's age, prescriber's age, and outpatient visits.

Keywords: Potentially Inappropriate Medication (PIM), Elderly, Beers criteria, Outpatient, Thailand

INTRODUCTION

Elderly population tends to rise rapidly around the world. An estimated 524 million people, who were over 65 years or 8 per cent of the global populations, are projected to 1.5 billion or to nearly 3folds, representing 16 per cent of world's population by 2050 [1]. Because most elderly populations have aged-related physiological changes, the presence of Non-communicable disease (NCD), and consume types and numbers of prescribed and non-prescribed medicines, they are all at risk for

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medication-related problems (MRP) [2].

To prevent those MRP among elderly, potentially inappropriate medication (PIM) should be assessed by process or outcomes measures. These measures are screening tools, which are mainly divided into 2 categories; explicit or criterion-based measures and implicit or judgment-based measures that this study focuses only on explicit criteria, namely, Beers criteria.

The Beers criteria were initiated by Beers and colleagues in 1990. The criteria were revised in 1997 and 2003 and the latest revision of Beers' list of medications was published in 2012 [3].

Beers criteria was selected to be a screening tool of PIM to determine inappropriate prescription that firstly used in nursing home in United States and later expand to use properly in all healthcare settings. The Beers criteria 2012 comprise of list of high-risk drugs, which should not be taken or taken with cautions in older patients. The list of drugs in Beers list is evidently associated with adverse events; the numerous research studies have employed the Beers criteria to evaluate PIM prescribing and ADE in out- and in-patient setting [4].

In this study, the unconditional list of 2012 Beers criteria are used purposively to determine PIM prescribing in elderly outpatients because of their easy applicability to computerized administrative databases in outpatient compared to other explicit tools. The feasibility of Beers criteria in detecting PIM were clearly found by many international researches that used Beers as a screening tool of PIM [4].

Most studies indicated that the prevalence of PIM among elderly is ranged from 11.5 per cent to 62.5 per cent. The use of PIM is high among community-dwelling elderly and associated with significant factors, such as, female sex, advanced age, and the number of drugs prescribed [2]. Comorbidity additionally exposes to a large number of medications, which were prescribed from many general practitioners and specialists [4].

In outpatient study, Chen et al. [5] studied the prevalence, predictors, and outcomes of PIM prescribed at emergency department in Taiwan with the application of 2003 Beers criteria. The results were found that older females were prescribed more PIM than males. People aged 65-69 years had the highest percentage of PIM use, followed by those in age ranges 70-74, 75-79, and those aged over 80 years. Furthermore, female and older physicians prescribed more PIM than male and young doctors. Interestingly, PIM was used more at emergency department of Taiwanese local community hospitals than in metropolitan hospitals and academic medical centers. Likewise most other studies, the percentages of PIM correlated with the number of medications prescribed at emergency department.

Another Taiwanese study, which focused on ambulatory care visits among elderly patients covered by the Taiwanese National Health Insurance, revealed that patients who received PIM also had significantly more emergency department visits ($p<0.01$) and hospital admissions ($p<0.01$) than those without PIM. The elderly Taiwanese patients who were prescribed with PIM had also significantly higher mean number of hospitalizations per patient than the nonuser ($p<0.001$) [6].

In Thailand, only one cross sectional descriptive study was found that has used the Winit-Watjana criteria in older patients. This was a community based study in Central Thailand. The prevalence of high-risk medication use in the community was 18.7%, which most of those were level 3 according to Winit-Watjana [7, 8]. However, this study was conducted only in a Thai community. Likewise international experiences, a study of PIM use in Thai older outpatients in district hospital is essential as a result of the statistically increasing number of elderly outpatient visits that those elderly outpatients are highly prescribed with PIM. Therefore, the study of prevalence and factors associated with PIM use among elderly Thai outpatients is required.

MATERIALS AND METHODS

Study design

This study is a cross-sectional study conducting the retrospective database in the Thai fiscal year 2012 (October 1, 2011 through September 30, 2012).

Study population and sample

The total number of elderly outpatients in the study hospital was 5,948 in the fiscal year 2012. The inclusion criteria of study populations are outpatients who were 65 years old or older at the fiscal year 2012 and had at least 1 prescribed medication from outpatient department in fiscal year 2012, which were 5,265 (N). A computerized systematic random sampling was used to randomize any study units by Hospital Patient Number (HN) from the retrieved dataset of outpatient in the district hospital at the fiscal year 2012. Overall, the number of outpatients was 430 participants with 2,128 outpatient prescriptions.

Table 1 Prescription's characteristics between outpatient PIM prescription versus non-PIM prescription.

Characteristics	Prescriptions with at least 1 PIM (%)(n=598)	Prescriptions without PIM (%)(n=1530)	Total number of prescriptions (%) (n=2,128)
Number of medications			
1-4	134(22.4)	783(51.2)	917(43.1)
5-7	205(34.3)	469(30.7)	674(31.7)
8-10	177(29.6)	207(13.5)	384(18.1)
11-14	73(12.2)	69(4.5)	142(6.7)
≥15	9(1.5)	2(0.1)	11(0.5)
Patient' s gender			
Female	350(58.5)	858(56.1)	1208(56.8)
Male	248(41.5)	672(43.9)	920(43.2)
Patient's age			
65-69 years	100(16.7)	37(2.4)	477(22.4)
70-74 years	166(27.8)	430(28.1)	596(28.0)
75-79 years	197(32.9)	375(24.5)	572(26.9)
>=80 years	135(22.6)	348(22.7)	483(22.7)
Number of diagnoses (ICD-10)			
1-2	362(60.5)	1141(74.6)	1,503(70.6)
3-4	208(34.8)	348(22.7)	556(26.1)
>=5	28(4.7)	41(2.7)	69(3.2)
Health insurance schemes			
UHC	456(76.3)	1,124(73.5)	1,580(74.2)
Non-UHC	142(23.7)	406(26.5)	548(25.8)
Prescriber's gender			
Female	361(60.4)	945(61.8)	1,306(61.4)
Male	237(39.6)	585(38.2)	822(38.6)
Prescriber's age			
20 - 28	314(52.5)	864(56.5)	1,178(55.4)
29 - 37	79(13.2)	196(12.8)	275(12.9)
38 - 46	127(21.2)	279(18.2)	406(19.1)
47 - 55	78(13.0)	191(12.5)	269(12.6)
Types of prescriber			
GP	418(69.9)	1,011(66.1)	1,429(67.2)
SP	75(12.5)	149(9.7)	224(10.5)
Nurses	100(16.7)	316(20.7)	416(19.5)
Others (dentist, traditional medicine, rehabilitator)	5(0.8)	54(3.5)	59(2.8)
Lengths of years working			
≤3	311(52.0)	864(56.5)	1,175(55.2)
4-10	83(13.9)	180(11.8)	263(12.4)
11-20	119(19.9)	225(14.7)	344(16.2)
≥21	85(14.2)	261(17.1)	346(16.3)

Measurement tool

Outpatient database in HOSxp software and administrative hospital database were used for collecting individual characteristics of outpatient and prescriber information. The 2012 Beers criteria were applied as a screening tool for detecting any PIM in prescription. Unconditionally inappropriate list in 2012 Beers criteria that those medications are generally considered inappropriate under all circumstances, with inappropriateness not dependent on the presence of particular diseases or receipt of specific dosage for older adults were used in this study.

Data collection

The secondary data of patient and prescriber‘s characteristics were retrieved from HOSxp and administrative hospital database during the fiscal year 2012. HOSxp is hospital software used widely in public hospitals in Thailand. It collects the data of prescription with patient’s profile. This program allows users to access remotely in “Electronic Medication Record or EMR”. In this study, the following outpatient’s data were retrieved-Hospital No. (HN), age, gender (Male/Female), prescriber’s diagnosis by ICD-10-TM codes, generic name of medication, date of prescription, prescriber’s

Table 2 Outpatient visits and Hospitalizations between PIM user and nonuser

Characteristics	Participants with at least 1 PIM (%)(n=214)	Participant without PIM (%)(n=216)	Total number of participants (%) (n=430)
OPD visits			
1-3	82(38.3)	144(66.7)	226(52.6)
4-6	36(16.8)	41(19.0)	77(17.9)
≥7	96(44.9)	31(14.4)	127(29.5)
Hospitalizations			
0	176(82.2)	191(88.4)	367 (85.3)
≥1	38(17.8)	25(11.6)	63(14.7)

identity code number of outpatient visits, number of hospitalizations, and health insurance schemes.

The administrative hospital database is the source for collecting the administrative data. In the study, human resource database is required in order to collect the prescribers' profile as listed--prescriber's identity codes, types of prescribers, age, gender, length of years working in career.

Data analysis

Collected data were entered into the worksheets in the licensed MS Excel 2007. All retrieved data was verified by 3 licensed pharmacists, including the researcher. Any interested variables were coded properly. The descriptive data were collected and managed by licensed software MS Excel and MS Access, and then analyzed by the licensed SPSS software version 17. Patient and prescriber's characteristics were described. Descriptive statistic was used for continuous data, such as, numbers, percentages described characteristics of associated factors. Analytical statistic is used for measuring the differences between PIM user and nonuser independent sample t-test for continuous and Chi-square test for categorical data.

Binary logistic regression was used for determining the statistical association of independent variables and PIM use. The results were reported as individual odds ratio (OR) with 95% confidence interval (CI). A p-value < 0.05 was considered to be statistically significant.

Ethical consideration

The Ethics Review Committee for Research involving Human Research Subjects, Health science group, Chulalongkorn University approved this study (Research Number 189.1/55) on February 20, 2013. Necessary changes and revision were carried out as per the feedback from the committee board before collecting data.

RESULTS

Overall 2,128 prescriptions, 56.8% of them were given to female patients. The ranges of number of medications per prescription was between 1 and 15 or more items. Table 1 showed the prevalence of PIM that 28 % of their prescriptions during the fiscal year 2012 received one or more PIM defined by the 2012 Beers criteria. In Table 2, the number of outpatient visits and hospitalizations was presented. PIM user were more observed among elderly outpatients who visited frequently at outpatient department; it raised from 38.3 % with 1-3 visits to 44.9% with 7 or more visits. In contrast, there were a similar number of hospitalizations between PIM user and non-PIM.

According to the prescribing of PIM classified by pharmacologic category, Central nervous system category was mostly common observed among PIM prescriptions (45% [321/716]). Following that 27% (193/716) of those PIM were pain medications and 19% (137/716) of them were cardiovascular drugs Lorazepam and Diclofenac, which comprised of 34% out of all PIM observations, were more frequently prescribed than other PIMs, (Table 3).

Regarding the result of logistic regression, Table 4 presents the positive association between age of elderly outpatient (OR=1.018, p= 0.040, CI=1.001-1.035), age of prescriber (OR=1.105, p=0.046, CI=1.002-1.218) and the presence of PIM prescription, as well as, the significantly negative association between the number of outpatient visits and the presence of PIM prescription. Compared to the reference group, such as, an elderly patient who was prescribed more than 15 medications had 25-folds in receiving at least 1 PIM prescription (p<0.01). Moreover, prescriptions of elderly outpatient, who had more frequent outpatient visits, were prescribed less PIM (Outpatient visits: 4-6 vs. ≥7: OR = 0.581 [95%CI=0.408-0.828], p=0.003 vs. OR=0.704 [95%CI=0.526-0.493], p=0.019, respectively). However, no significant association between the presence of PIM and participant's gender, number of diagnoses, health insurance

Table 3 Frequency of prescribing PIM classified by pharmacologic and therapeutic or system categories

PIM	Pharmacologic category	Therapeutic /System Category	Frequency of prescribing PIM (n=716)	Percent	Percent Cumulative
Lorazepam	Benzodiazepine (short- and intermediate-acting)	Central nervous system	125	17.5	17.5
Diclofenac	Non-Cox-selective NSAIDs	Pain medication	123	17.2	34.6
Doxazosin	Alpha-1-blockers	Cardiovascular	109	15.2	49.9
Ibuprofen	Non-Cox-selective NSAIDs	Pain medication	67	9.4	59.2
Alprazolam	Benzodiazepine (short- and intermediate-acting)	Central nervous system	57	8.0	67.2
Amitryptyline	Tertiary Tricyclic Antidepressants (TCAs)	Central nervous system	55	7.7	74.9
Dipotassium chlorazepate	Benzodiazepine (long-acting)	Central nervous system	48	6.7	81.6
Chlorpheniramine	First-generation antihistamine	Anticholinergics (excluded TCAs)	26	3.6	85.2
Digoxin	Antiarrythmic drugs	Cardiovascular	26	3.6	88.8
Hydroxyzine	First-generation antihistamine	Anticholinergics (excluded TCAs)	22	2.9	91.9
Diazepam	Benzodiazepine (long-acting)	Central nervous system	18	2.5	94.4
Metoclopramide	Others	Gastrointestinal	17	2.4	96.8
Clonazepam	Benzodiazepine (long-acting)	Central nervous system	10	14	98.2
Imipramine	Tertiary TCAs	Central nervous system	4	0.6	98.7
Mefenamic acid	Non-Cox-selective NSAIDs	Pain medication	3	0.4	99.2
Spironolactone	Antiarrythmic drugs	Cardiovascular	2	0.3	99.4
Methyldopa	Alpha blockers central	Central nervous system	2	0.3	99.7
Trihexy phenidyl	Antiparkinson agents	Anticholinergics (excluded TCAs)	1	0.1	99.9
Thioridazine	Antipsychotic, first-generation agents	Central nervous system	1	0.1	100.0

schemes, hospitalizations, prescriber's gender, types of prescriber and length of prescriber's years work was observed in this study.

DISCUSSION

This study is to find the prevalence of and factors associated with PIM prescriptions measured by Beers criteria 2012 among the elderly outpatients at a district hospital in the South of Thailand. The overall prevalence of PIM found in this study was 28.1% of all study outpatient prescriptions. During 2001-2004, a study among Taiwanese elderly patients in ambulatory care who were members of Taiwanese National Health Insurance program was conducted that the prevalence of PIM prescribing was 19.1% of 176,661,994 ambulatory care visits involving a prescription [5]. In the Thai study, the prevalence of PIM was less than that in Taiwanese study that the number of patients in Taiwanese study was larger than this study. Compared to a systematic review study by Guaraldo, et al [2], however, the prevalence of PIM used in elderly outpatients in this study hospital was still in the range from 11.5 to 62.5%.

More prescriptions among elderly outpatients is related to the high prevalence of PIM prescription. Likewise the Taiwanese study, the increasing number of outpatient services and prescriptions among the Thai elderly is observed bcause there is not copayment in public health services and pharmacy expenses for the elderly outpatients in public health insurance schemes [6]. Other implications are inadequate pharmacist counseling when a number of medications are given to elderly patients in hospitals, failure to

Table 4 The results of binary logistic regression for PIM with factors in the study outpatient prescriptions

Factors	Regression Coefficient(B)	Standard Error (S.E.)	Odds Ratio (OR)	95%CI	*p-value*
Patients					
Gender					
Male	-	-	1	-	-
Female	0.084	0.105	1.088	0.885-1.337	0.423
Age	0.018	0.009	1.018	1.001-1.035	0.040
Thai health insurance schemes					
Non-UHC	-	-	1	-	-
UHC	0.088	0.120	1.092	0.864-1.380	0.462
Number of outpatient visits					
1-3	-	-	1	-	-
4-6	-0.543	0.181	0.581	0.408-0.828	0.003
≥7	-0.351	0.149	0.704	0.526-0.943	0.019
Number of inpatient admissions					
0	-	-	1	-	-
≥1	-0.156	0.127	0.856	0.668-1.098	0.220
Prescribers					
Gender					
Male	-	-	1	-	-
Female	0.020	0.120	1.020	0.806-1.290	0.869
Ages	0.100	0.050	1.105	1.002-1.218	0.046
Types of prescriber					
GP	-	-	1	-	-
SP	0.001	0.165	1.001	0.725-1.383	0.993
Nurses	-0.133	0.285	0.874	0.500-1.526	0.636
Others(dentist, traditional medicine, rehabilitator)	-0.595	0.498	0.552	0.208-1.463	0.232
Lengths of years working	-0.088	0.051	0.916	0.829-1.012	0.084
Prescription					
Number of medications					
1-4	-	-	1	-	-
5-7	0.913	0.133	2.491	1.919-3.234	<0.001
8-10	1.636	0.158	5.133	3.763-7.001	<0.001
11-14	1.877	0.215	6.535	4.290-9.956	<0.001
≥15	3.227	0.808	25.198	5.168-122.867	<0.001
Number of disease groups (ICD-10)	0.018	0.051	1.018	0.920-1.125	0.732

provide comprehensive drug evaluation for older people, and the lack of awareness of the risks of prescribing PIM among primary care physicians and hospital outpatient departments [6].

The study also presented that 45% of all PIM classified in central nervous system, such as Lorazepam, were frequently given to among elderly outpatients in the study hospital. Compared to international studies in elderly outpatients, a cohort study of PIM prescribing in elderly Italian outpatients showed that non-steroidal anti-inflammatory drugs (NSAIDs) were the most frequently prescribed (35.7%), followed by Ticlopidine (17.6%), and Doxazosin (15.5%) [9]. In Taiwan, the study showed that antihistamines with anticholinergic effects were the most frequently occurring PIM (27.6% of PIM prescriptions). The most second and third rank of drug class in PIM list were muscle relaxants and antispasmodics (22.6% of PIM prescriptions) and long-acting Benzodiazepines (13.7% of PIM prescriptions) [5]. In this study, the result shows that Non-Cox-selective NSAIDs and Benzodiazepine (short-and intermediate-acting) are the most first and second frequently prescribed among the elderly PIM prescriptions in this district hospital. Having said that, the difference of available PIM medications in hospital drug list among these study sites are explained for the different results.

The association of factors to the presence of PIM was assessed by logistic regression. Patient's age and prescriber's age showed positively significantly association to the presence of PIM in the study. Likewise the Taiwanese studied by Lai et al, 2009, older prescriber was significantly

associated with the presence of PIM. A lack of continuous medical education programs addressing PIM use was the implication of Taiwanese study [6]. Therefore, the same implication may be applied to the result in this study. To be more specific, nevertheless, the reasons of prescribing PIM from those Thai prescribers are required to study further.

The number of medications was likely to have a positively significant association with the presence of PIM. Similarly, a cross-sectional study in 2 primary care settings at the outpatient department in United States showed that patients who were receiving polypharmacy (over 5 medications used in a day) have a likelihood of receiving PIM [10]. Additionally, the Taiwanese study resulted that a greater number of chronic conditions were factors associated with a number of Beers list drugs use [6]. Hence, this study is implied that people who become older have a number of chronic diseases that were also prescribed more medications, which highly exposed PIM.

The Taiwanese study reported that a number of primary care visits and increased age were associated with a risk for being prescribed PIM [10]. As opposed to the Taiwanese study, a number of outpatient visits in this study had a likelihood of negatively significant association with the presence of PIM. It was explained that most elderly outpatients with the chronic diseases usually visited their doctors by appointed schedule, whilst, received a number of medications regarding their chronic diseases that highly caused the prescribing of PIMs.

Several limitations should be emphasized. One of them is the application of Beers criteria, which was only to measures any medications prescribed from the doctor in this hospital, that calculated prevalence of PIM only from the hospital outpatient prescription; self-medication use outside the hospital were not measured in this study. Moreover, any medications were considered as PIM without the consideration of specific diseases or other health conditions and under or over use of medications among those participants. Besides that the quality of ICD-10 coded in outpatient database is the major concern in order to match a single diagnosis with PIM. In this study, the researcher could not contact directly with prescribers because of the anonymity between researcher and prescribers. Therefore, the validity and completeness of diagnosis codes were not inevitably re-assessed.

In addition, the unit of analysis in inferential statistic is outpatient prescriptions that there might be the issue of multiplicity bias, which is a multiple count of PIM in participants' prescriptions. This could affect the significance level and 95% confidence interval of result. This study could not examine the cause-effect relationship between associated factors use and PIM use because it is a cross-sectional study with retrospective data that cannot prove whether all participants adhere to use their prescribed medication. In addition, this study was conducted in a district hospital that the result cannot be generalized to other district hospitals or different type of hospital.

For future studies, adverse effects associated with PIM should be measured. Both explicit and implicit criteria in assessing PIM should be applied and comparative studies of each tool should be evaluated, including appropriateness, validity and specificity of those tools. A country-specific criterion in assessing PIM is required in order to properly measure PIM prescription. To assess PIM prescribing effectively, the accuracy, relevancy and completeness of ICD-10 in dataset is a major concern. Prior to order medication in computerized prescription, the complete blockade of indicating serious ICD codes should be obligated by prescriber. Ultimately, qualitative study is strongly recommended in order to acquire more in-depth information, especially the reason of prescribing PIM among the prescribers.

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