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Original Article

Prevalence and Predictors of Potentially Inappropriate Medications Among Elderly Patients Attending Government Primary Care Clinics in Negeri Sembilan, Malaysia

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Abstract

Introduction: PIM (Potentially Inappropriate Medication) has been defined as medication unsuitable for patients based on age, laboratory findings, and medical history, which may lead to further complications in health. The purpose of this study was to find out the prevalence and predictors of PIM in elderly patients attending government primary care clinics in the Seremban District. **Method:** Prescribed medications were analysed by using the Screening Tool of Older Persons' Potentially Inappropriate Prescription (STOPP) criteria and were identified as PIM if the medication was included in STOPP with a similar description. Simple logistic regression was applied to determine the crude odd ratio and variables with *p* 0.25 were entered into the multivariate logistic regression model to determine predictors for PIM. **Result:** 792 randomly selected elderly patients were recruited in this study. Elderly patients aged less than 70 were less likely to have PIM compared to patients above the age of 70 (AOR = 0.974, 95% CI 0.721 to 1.316). Patients who took five or fewer medications were less likely to have PIM (AOR = 0.850, 95% CI 0.628 to 1.152). PIM was less likely in patients with fewer than three illnesses (AOR = 0.494, 95% CI 0.301 to 0.811). Predictors of PIM based on this study were age (> 70 years), number of prescribed medications (> 5), number of illnesses (> 3), and endocrine disease, renal disease, and urogenital disease. **Conclusion**: The prevalence of PIM is found to be high, at 37% based on STOPP criteria. The findings of the study can be used as a baseline study on PIM among the elderly in Malaysia's primary care setting.

Keywords: *Elderly, PIM, primary care, STOPP*

Introduction

Sample Malaysia is reaching the status of an ageing country. By the year 2035, about 14% of the Malaysian population will be elderly, aged 60 years and above (Minhat & Amin, 2012). With a growing older population, use of prescription medication is projected to increase as chronic conditions such as diabetes, hypertension, mental illness, and many more require more intensive therapy. Many developed countries have accepted 65 as the age for the definition of elderly (World Health Organization, 2013) while in Malaysia it is taken as 60 years and older. These groups of elderly patients often suffer from age-related pharmacodynamic and pharmacokinetic issues with their medications.

PIM (Potentially Inappropriate Medication) has been defined as the use of medication with a risk greater than benefit, inappropriate dosing duration, prescriptions that lead to clinically significant drug–drug and drug–disease interactions, and the under-use of potentially beneficial medications

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(Al-Aqqad, Chen, Shafie, Hassali, & Tangiisuran, 2014). The study reported, elderly patients were prescribed more medications than younger patients. These high levels of medications may lead to an increased risk of inappropriate medications in their regime. PIM among elderly patients is associated with negative healthcare outcomes such as adverse drug events, drug-related morbidity, hospitalisation mortality, and unnecessary health care use (Lau et al., 2010). Inappropriate medication occurs frequently in nursing home residents due to the high prevalence of frailty, multiple comorbidities, and functional restrictions (Aparasu & Mort, 2000).

Primary care services in Malaysia include private general practices, government primary care clinics in the community, and government primary care clinics within teaching hospitals. Primary health care services are currently responding to the changes in patient demography, such as increasing numbers of young people and adults, and shifting the burden of disease from infectious to non-communicable and chronic diseases (Jaafar, Noh, Muttalib, Othman, & Healy, 2013). It is essential for Malaysia to develop a health policy on chronic diseases, especially for its ageing population. The changes in treating elderly patients, such as with updated guidelines on acute and chronic diseases and drug management based on age, will make vast improvements in the current and future ageing population. At primary care, patients will be regionalized and health care practitioners can provide regular check-ups and close monitoring of their health conditions. Patients tend to have follow-ups in both primary care clinics and specialists in hospitals, so PIM may be prevalent in primary care settings. Issues with double prescriptions from clinics and hospitals; a lack of communication among doctors in both facilities; patient understanding and adherence to medication regimens; a lack of drugs prescribed by specialists in primary care (Ismail, Jamsiah, Amin, Ali, & Munizam, 2019); and cost are all important factors that could contribute to PIM.

The prevalence of the PIM definition may differ between countries due to the differences in clinical practises and patient characteristics. Thus, there is a need for research on existing globally used screening tools and the development of screening tools to identify PIM in Malaysia by considering the clinical guidelines and population characteristics of Malaysia. Identifying the factors associated with PIM at primary care clinics is an essential step in our health care system to address the problem of PIM, especially among elderly patients. The study provides the prevalence and predictors of PIM. By identifying PIM and finding the outcome, frequent hospitalisation can be prevented, which will reduce the financial and manpower burden on the health care system. PIM among the elderly also leads to many health issues such as adverse drug events, which are one of the major challenges facing the healthcare system. By assessing PIM using a screening tool, elderly patients' quality of life will be improved as there will be extra caution taken when prescribing medication. The results can determine whether existing guidelines such as STOPP are adequate or the urge to develop a more extensive guideline which could cater to the ageing population in our country for better health. It also gives an opportunity for new guidelines and measures to be developed. Knowing the needs of the patients is vital for the planning of actions that aim to adequately meet their needs and provide the best level of comfort, which may contribute to a decrease in PIM.

Material and Method

The study was conducted at randomly selected health clinics in Seremban district, Negeri Sembilan, Malaysia. There were twelve health clinics under Seremban District.

Study Design

Cross-sectional study design was used in this study.

Study Population

Elderly patients aged 60 and above, attending health clinics in Seremban district, Negeri Sembilan.

Sampling Frame

Elderly patients were selected at the pharmacy counter by using systematic random sampling when collecting medication and attending six randomly selected health clinics (fish bowl method) in Seremban district.

A Sampling Unit

An elderly patient receiving treatment from one of the randomly selected health clinics who fulfilled the criteria.

Estimation of Sample Size

The sample size was calculated based on the formula by Lemeshow, Hosmer, Klar, & Lwanga (1990). This formula was used because the research will be testing hypotheses with respect to the differences between two groups, male and female, in terms of appropriate and inappropriate medication used. The sample sizes for other variables were calculated and compared through which gender was selected as it was the highest. Table 1 presents the potentially inappropriate medication (PIM) between the genders, male and female (Wahab, Nyfort-Hansen & Kowalski, 2012).

Table 1: Potentially Inappropriate Medication (PIM) between male and female

	PIM	**No PIM**	**Total**
P_1 (female)	33	16	49
P_2 (male)	27	24	51
Total	60	40	100

Where,
n =sample size
$Z_{1-\alpha/2}$ = standard errors associated with confidence intervals (95%) = 1.96
$Z_{1-\beta}$ = standard errors associated with power (80%) = 0.842
P_1 = estimated proportion (larger) = 0.673 (PIM detected among elderly females, Wahab et al., 2012)
P_2 = estimated proportion (smaller) = 0.529 (PIM detected among elderly males, Wahab et al., 2012)
$\dot{P} = (P_1 + P_2) / 2 = (0.673 + 0.529) / 2 = 0.601$

$$n = \frac{\{(1.96)\sqrt{2\,(0.601)\,(0.399)} + (0.842)\,\sqrt{(0.673)(0.327)+(0.529)(0.471)}\}^2}{(0.673-0.529)^2}$$

n = 180

Adjusting for 2 proportions (gender): This was done by multiplying by 2 again as the research will be testing hypotheses between two groups.

n = 180 x 2 = **360**

Adjusting for design effect: Design effect was estimated to be high, hence the result was multiplied by 2 (Aday, 1989).

n = 360 x 2 = **720**

By considering the possibility of non-responses, an additional of 10% is needed.

So, final sample size was calculated as below.

Sample size, n = 720 + (10% of 720)

n =**792**

So, total sample size was calculated as **792**.

Sampling Technique

Step 1:

i Six health clinics were chosen based on random sampling method using fish bowl method. Probability proportionate to size technique was used to determine number of samples needed from selected health clinics. The total number of elderly patients in selected health clinics were used to multiply with the overall sample size needed for the study.

Step 2:

i Samples were collected on several days within data collection period. Data collection days were based on patient appointment day which varies in each health clinic (Monday to Thursday).

ii Patients' prescriptions were selected at pharmacy screening counter when patients come to collect medication. Prescriptions were randomly selected based on Random Table, repetition of number three. Process of sampling was started with first eligible elderly patient presented at pharmacy to collect medication. First and second elderly patients were excluded from the sample and data collection was started with third elderly patient presented to pharmacy, followed by six and nine until calculated sample size was achieved. Similar sampling techniques were done on every data collection day at chosen health clinics.

Step 3:

i Elderly patients' sociodemographic characteristics, medical history, prescribed medication, and laboratory findings were obtained from patients' prescriptions and medical database as patients present at pharmacy to collect medication. Patient's history of fall were derived from medical history and hospitalisation records.

ii Prescribed medications and laboratory finding were analysed by using STOPP criteria and were identified as PIM if the medication were included in STOPP with similar description.

iii Prescriptions were processed, and medications were prepared by pharmacist in charged in the health clinic once the researcher has obtained complete data from patient's prescription and medical records based on STOPP criteria.

Dependent Variable

Potentially Inappropriate Medication (PIM) based on STOPP criteria is considered the dependent variable. PIM is considered when a medication in a patient's regime is inappropriate based on drug-drug interaction, drug-disease interaction, or polypharmacy. PIM can be identified using STOPP based on prescribed medication, lab findings, fall incidence, and medical history.

Independent Variables

Socio Demographic Characteristics

i Age

ii Gender

iii Ethnicity

Clinical Characteristics

i Number of illnesses

ii Number of prescribed medication

iii Type of illnesses (based on clinical diagnosis by medical officer done at the health clinic)

Inclusion Criteria

i Elderly patients, 60 years old and above attending selected health clinic during data

collection period

ii Malaysian citizen

iii Has prescription with three drugs and above

Exclusion Criteria

i Prescriptions from Emergency Department

ii Walk in patients from other health clinics (no follow up at health clinic in the study)

Data Collection

Patient's information

Sociodemographic data (age, gender, and ethnicity), number of illnesses, number of prescribed medications, and type of illnesses were recorded on patients' proforma.

Screening Tool of Older Persons' Prescriptions (STOPP)

Al-Aqqad and colleagues, 2014). STOPP generally integrates encountered instances of PIM among elderly patients, including drug–drug and drug–disease interactions; drugs which adversely affect elderly patients at risk of falls due to side effects of medication; and duplicate drug class prescriptions. Each criterion was accompanied by a brief justification of the reason for PIM of the prescription (O'Mahony et al., 2015). The STOPP tool used for this study was a revised version of STOPP version 2, which has 79 criteria. The tool was revised based on Seremban Health Clinic's drug formulary. The drugs which were not listed in this formulary were taken out of the STOPP tool (explanation on STOPP category and medication which are taken into consideration while identifying PIM).

STOPP criteria was divided into 13 sections.

- Section A: Indication of medication
- Section B: Cardiovascular system
- Section C: Antiplatelet/anticoagulant drugs
- Section D: Central nervous system and psychotropic drugs
- Section E: Renal system
- Section F: Gastrointestinal system
- Section G: Respiratory system
- Section H: Musculoskeletal system
- Section I: Urogenital system
- Section J: Endocrine system
- Section K: Drugs that predictably increase the risk of falls in older people
- Section L: Analgesic drugs
- Section M: Antimuscarinic /anticholinergic drug burden

Laboratory finding, fall incidence, type of medication taken and medical history were derived from the patient's prescriptions and electronic medical database to determine PIM.

Quality Control (Validity and Reliability)

Content Validity

The instrument contents were assessed by the members of the supervisory team and other experts in this field. The tool had gone through a validity check where panels of experts included family medicine specialists, epidemiologists, clinical psychologists, and pharmacists from Universiti Putra Malaysia. Items that were unsuitable were excluded from the criteria.

- Criteria removed from STOPP was the drugs which were not available in the study locations

Section H: Musculoskeletal System – Oral bisphosphonates in patients with a current or recent history of upper gastrointestinal disease i.e. dysphagia, oesophagitis, gastritis, duodenitis, peptic ulcer disease, or upper gastrointestinal bleeding.

Face Validity

The instrument had undergone face validity during pretesting to determine the suitability of the language and content of STOPP criteria for the study and to ensure that the researchers understood the terms properly.

STOPP Criteria Reliability

The reliability of the STOPP criteria was measured by using Cronbach Alpha and the score was identified as 0.71 based on the pilot study. The Cronbach alpha measures the quality of relations among individual components within a particular section of a questionnaire and the level of measuring all the same thing. Reliable questionnaires have a Cronbach alpha value of 0.7 or more (Dawson & Trapp, 2001).

Pretesting

A total sample of 80 elderly patients attending one health clinic in Seremban district was chosen based on inclusion criteria to participate in the study. Selected patients' medications were compared with STOPP criteria to identify PIM. The health clinic selected for pretesting was not included in the main study.

Data Analysis

The IBM Statistical Package for Social Sciences Software (SPSS) version 22 was used to analyse the data. Descriptive statistics of the patients were obtained as mean, frequency, and percentage. The Chi square method was used to determine the association among variables. The confidence interval was set at 95% and the level of significance as p 0.05. Simple logistic regression was applied to determine the crude odd ratio and variables with a p value of 0.25 were entered into the multivariate logistic regression model to determine significant predictors for PIM among elderly patients (Hosmer & Lemeshow, 2000). The results were interpreted based on the obtained adjusted odds ratio and p-value. A p value less than 0.05 was considered statistically significant.

Ethical Issues and Consent

Approvals were obtained from the Ethics Committee for Research Involving Human Subjects, Universiti Putra Malaysia and the National Medical Research Register (NMRR) prior to data collection, NMRR-17-1998-36445 (IIR). Approvals were also obtained from the Negeri Sembilan State Health Department Director, the Head of Pharmacist of Seremban District, and the Head of Pharmacist from all health clinics selected for the study. The STOPP criteria were published by Oxford University Press on behalf of the British Geriatrics Society as an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permitted non-commercial re-use, distribution, and reproduction in any medium, and the original work was cited properly (O'Mahony *et al*., 2015). A consent form was not needed from the patient as there was no communication involved between researcher and patient (only medical records involved).

Results

Sociodemographic Characteristics of Elderly Patients

The mean age of patients is 68.09±SD= 6.40. The majority of patients were from the age group of 60-64 (36.9%). Out of the 792 patients, the majority were female patients (54.4%) and were from Malay ethnicity (46.6%).

Clinical Characteristics of Elderly Patients

The mean number of illnesses was 2.22±SD = 0.9. The Majority of elderly patients had two types of illnesses (50.4%), followed by three types of illnesses (22.6%).

Table 2: Number of illnesses of elderly patients (n=792)

Number of Illnesses	Frequency	Percentage (%)
1	152	19.2
2	399	50.4
3	179	22.6
4	43	5.4
5	14	1.8
6	5	0.6
Total	792	100.0

The mean number of prescribed medications taken by a patient was 5.68± SD = 1.9. The majority of patients (24.1%) were taking five medications for their illnesses. The highest number of prescribed medications taken by a single elderly patient in this study was 12 medications (0.6%).

Patients with Cardiovascular Diseases had the highest rate (94.9%), followed by those with Endocrine Diseases (66.0%).The least common types of illnesses suffered by patients were related to fall incidences (1.6%) and ophthalmology diseases (1.4%).

PIM prevalence in elderly patients

Table 3 shows the percentage of PIM among elderly patients. There were 293 PIM incidences reported in this study, involving 37 percent.

Table 3 Percentage of PIM among elderly patients

Variables	Frequency	Percentage (%)
PIM		
Yes	293	37.0
No	499	63.0
Total	792	100

Patients between 60 to 64 years old were the highest in the study, while Table 4 shows the distribution of patients by number of illnesses, number of prescribed medication and type of illnesses.

Table 4 Distribution of patients by age, gender and ethnicity

Age	Frequency (n)	Percentage (%)
60-64	292	36.9
65-69	235	29.7
70-74	134	16.9
75-79	85	10.7
80-84	33	4.2
85-89	9	1.1
90-94	4	0.5
Gender		
Female	167	21.1
Male	126	15.9
Ethnicity		
Malay	131	44.7
Chinese	96	32.8
Indian	63	21.5
Others	3	1.0

Multivariate logistic regression analysis of Predictors of PIM

In the simple logistic regression for PIM, 11 factors (age, number of illnesses, number of prescribed medications, endocrine disease, renal disease, urogenital disease, cancer, immune disease, and dermatology disease) were selected for multivariate analysis based on *p* 0.25. All these factors were entered into the multivariate logistic regression models to identify the significant predictors.

Out of 11 factors, only six factors were selected using the stepwise selection method to identify the predictors of PIM. Predictors of PIM based on this study were age (>70), number of prescribed medications (>5), number of illnesses (>3), endocrine disease, renal disease, and urogenital disease with *p*> 0.05. Elderly patients aged above 70 were more likely to have PIM (AOR = 1.721, 95% CI 1.316–1.974) compared to patients younger than 70 years old. Patients who were taking more than five prescribed medications were more likely to have PIM (AOR = 1.628, 95% CI 1.152-1.850) compared to patients taking less than five prescribed medications. Patients with more than three illnesses were more likely to have PIM (AOR = 1.494, 95% CI 1.301-1.811) compared to patients with less than three illnesses.

Patients with endocrine disease were 1.728 times more likely to have PIM in their regime compared to patients without the disease. Patients with renal disease were 3.408 times more likely to have PIM compared to patients without renal disease. Patients with urogenital were more likely to have PIM (AOR = 4.194, 95% CI 1.484–11.853). The value of Nagelkerke R square was 0.148. This showed that the whole model explained 14.8 % of the variance in PIM. The Hosmer and Lemeshow tests indicated that this model was fit (*p = 0.05*). Based on the classification table, 66% of cases were classified correctly.

Discussion

Prevalence of Potentially Inappropriate Medication (PIM)

The prevalence of PIM in this study was 37% (n = 293). The highest number of PIM for a single prescription was five. One patient was reported to have five PIMs in the prescription. A study by Lang *et al.* (2010) which studied PIM in acutely ill hospitalised patients using STOPP reported a high prevalence of PIM of 77%. Similarly, a study by Oliveira et al. (2015) reported a high prevalence of PIM, 33.8% according to STOPP criteria. A total of 346 PIMs were prescribed for 284 patients in the study done by Ryan *et al*. (2009). Based on the study, 232 patients had one PIM and 52 patients had more than one PIM in their prescription.

STOPP as PIM Identifying Tool

STOPP is to provide an explicit, evidence-based tool to avoid PIM. By applying this guideline during prescribing, medication appropriateness can be improved, and ADR and DRP can be prevented (Ryan *et al*., 2009). According to the author, STOPP displayed higher detections of ADE, which caused hospitalization. The study also suggested that STOPP is more applicable and relevant to detecting PIM in primary care in Ireland. STOPP criteria are more sensitive in identifying PIM that leads to ADE; thus, STOPP is more clinically relevant (Hamilton *et al.,* 2011). There were 293 PIM reported in this study. The highest number of PIMs are detected from medication for endocrine diseases. Glibenclamide (36.6%) for treatment of T2DM, which contributes to the risk of prolonged hypoglycaemia. followed by PIM under Section Indication of Medication, (13.2%) involving duplicate drug class prescription. This criteria detects PIM if there is failure in optimization of monotherapy within a single drug class prior to adding a new drug class. PIM under the Antiplatelet or Anticoagulant section involves Aspirin. Patients with a history of peptic ulcer disease who did not have a concomitant proton pump inhibitor (PPI) were given aspirin (6.8%). This practise could increase the risk of recurrent peptic ulcers for the elderly.

Another medication which was considered as PIM under the Antiplatelet/Anticoagulant section was Ticlopidine. The prevalence of PIM for this category was 9.4%. STOPP criteria does not

recommend Ticlopidine usage in any circumstances for elderly patients. Clopidogrel and Prasugrel are suggested as they have similar efficacy, stronger evidence and fewer side-effects. First generation antihistamines were also detected as PIM using STOPP in this study (6.4%). PIM is associated with PPI use for uncomplicated peptic ulcer disease or erosive peptic oesophagitis at full therapeutic dosage for 8 weeks. Dose reduction or earlier discontinuation is indicated for the elderly on PPI.

In this study, (3%) elderly patients were prescribed with PPI for more than 8 weeks without risk of uncomplicated peptic ulcer disease or erosive peptic oesophagitis. Vasodilator drug usage with persistent postural hypotension was identified as PIM (3.8%). Drugs under the vasodilator category are Alpha 1 Receptor Blockers, Calcium Channel Blockers, Long Acting Nitrates, ACE Inhibitors, and Angiotensin I Receptor Blockers. The use of vasodilators in the elderly with persistent postural hypotension may increase the risk of syncope and falls. Patients with PIM in this category were identified to have an incidence of falls in their illness history. According to Oliveira *et al.* (2015), the difference in the proportion of the use of Glibenclamide as a PIM is due to an informational discrepancy between the screening criteria. Yayla *et al.* (2013) reported that the major disadvantage of the STOPP criteria is the citation as references, as they are mostly review articles and not clinical studies. Though STOPP criteria act as a tool to identify PIM in elderly patients, they cannot replace the clinical judgement of the physician and therefore recommend a regular update of the tool.

Factors Associated with PIM

Age

The mean age of patients is 68.09, with an SD of 6.404. The majority of patients are in the age group of 60–64 (36.9%). Patients aged 90-94 made up the smallest proportion of the population (0.5%). PIM was highly prevalent in the age groups 60-64 (n = 92), 65-69 (n = 96) and 75-79 (n = 45). Age above 70 years is found to be a predictor of PIM in this study, p 0.001, (AOR = 1.721, 95% CI 1.316-1.974). Similar to this study, Ryan *et al*. (2009) found a positive correlation between age and PIM using STOPP (p 0.01). Fiss et al. (2011) found no statistically significant associations between age and PIM (p = 0.9603), which contradicts the findings of the study. A study by Al-Shamri (2014) found that patients aged 70–74 were more susceptible to the use of PIMs than those aged 90 and over. It was generally noted that patients aged 90 and older had a lower number of PIMs compared with those under 90.

Gender

There were 792 participants included in the study. The male population was (45.6%) and females (54.4%) in the study. Female elderly patients received more PIM (54.42%) than males. However, based on the data analysis, the p value was found to be 0.264, which proves no association between gender and PIM. Few studies have reported the absence of gender association with PIM (O'Sullivan *et al*., 2013; Vishwas, Harugeri, Parthasarathi & Ramesh, 2012). Similarly, there was no association between gender and PIM irrespective of the tool used to detect them (Al-Shamri, 2014). According to Gallagher & O'Mahony (2008), multivariate regression analysis accounting for age, gender, and numbers of medications showed that females were more likely to be admitted with a PIM related ADE than males (STOPP criteria odds ratio 1.87,p = 0.014).

Ethnicity

This study involved four ethnicities: Malay, Chinese, Indian, and others, which comprised Iban and Kadazan. In the study, the Malays have the highest ratio (44.7%), followed by Chinese (32.8%), Indians (21.5%), and others (1%). The analysis yields p = 0.416, which proves ethnicity is not statistically associated with PIM. A study by Cahir et al. (2010) showed a negative association of gender with PIM. However, a study by Lim *et al*. (2017) done in Malaysia in 2017 reported that polypharmacy was more prevalent among Indian participants compared to the Malay and Chinese. The study also revealed 56.9% of the respondents in the study stated the

use of at least one dietary supplement in a group with polypharmacy. The Chinese ethnic background population was reported to be using the highest number of dietary supplements for oncology, musculoskeletal and GIT related diseases.

Association between Number of Illness and PIM

The number of illnesses shows a significant association with PIM in this study (p = 0.005) (AOR=1.494, 95% CI 1.301-1.811). Patients in these studies were reported to have a number of illnesses ranging from 1 to 6 (12.6%) of PIM identified among patients who were diagnosed with more than three illnesses. A study by Al-Shamri in 2014 reports that having multiple illnesses does not necessarily mean that PIM incidences are higher. In this study, there were no predictable or significant associations between the number of illnesses and PIM. In contrast to that study, Undela, Bansal, D'Cruz, Sachdev, & Tiwari (2014) claimed patients who had more than three illnesses were found to have PIM than those with fewer illnesses. A study done in India suggested multiple illnesses (4) and a higher number of medications were predictors of PIM (Vishwas *et al*., 2012).

Association between Type of Illness and PIM

The types of illness suffered by patients in this study were classified under the cardiovascular, endocrine, renal, haematology, gastrointestinal, urogenital, musculoskeletal, respiratory, infection, ophthalmology, cancer & immune, dermatology, and fall categories. Most patients in this study were found to have cardiovascular diseases (94.9%) and endocrine diseases (66%). However, it did not show any association with PIM(p = 0.789). Endocrine, renal, and urogenital diseases were found to be predictors in this study, where all the diseases were found to be statistically significant when compared with PIM (p <0.05).

Hospitalized patients revealed a higher prevalence of PIM than reported in patients prone to falls (14.2–15.2%) (Kovaevi *et al*., 2014). A study carried out in Malaysia reported that patients with cardiovascular, endocrine, or gastrointestinal diseases were associated with a significant increase in medication use compared to other disease conditions. An increase in medication use due to certain illnesses could be a risk factor for PIM. Urogenital and neurological diseases are not associated with the incidence of PIM (Al-Shamri, 2014).

Association between Number of Prescribed Medication and PIM

This study proves that there is a significant association between the number of medications taken by patients and the occurrence of PIM (p<0.01). In this study, patients were taking at least three medications and up to 12 medications. Patients in this study who took more than five medications were more likely to have PIM (AOR = 1.628, 95% CI 1.152-1.850). A study by Lang *et al*. (2010) revealed an independent predictor for PIM was an increased number of concomitant drugs. Gallagher & O'Mahony (2008) reported that patients prescribed five or fewer medications were less likely to present to a hospital with a PIM related adverse event than those prescribed six or more medications. Al-Shamri *et al*. (2014) reported that PIM was lower in the older age group.

This could be due to patients with advanced age taking fewer medications compared to younger people. The number of PIM therefore increases directly with the number of medications taken by patients. The prevalence of PIM use was found to be higher among patients who used four or more drugs (Oliveira *et al*., 2015). A study by Ryan et al. (2009) reported a significant correlation was found between the number of medicines prescribed and the occurrence of PIM when calculated using STOPP (p<0.01).

Type of Medication Identified As PIM

Medications used to treat cardiovascular disease identified the most PIM (41.2%), followed by drugs used to treat endocrine disease (37.3%). Aspirin, Clopidogrel, and Ticlopidine show the highest prevalence of PIM at 14.8%. Drugs identified as PIM are Aspirin, Clopidogrel, and Ticlopidine. Aspirin alone contributed to 8.7% of PIM in this study. A similar finding was found in a

study by Yayla *et al.* (2013) where PIM related to acetylsalicylic acid at a dose of 150mg/day was found to be 18.8%. study by Oliveira et al. (2015) showed the most prevalent PIMs according to the STOPP criteria were acetylsalicylic acid (32.9%). A study by Lang *et al.* (2010) was done among mentally ill patients.

Benzodiazepines and antipsychotics were clearly frequently prescribed as PIM based on STOPP. However, medications for cardiovascular, musculoskeletal, and urogenital conditions were also found to be inappropriately prescribed. The diuretic class of medications, which includes frusemide and hydrochlorothiazide, was found to contribute 11.7% of PIM in this study. Drugs under Endocrine Disease contributed to 37.4 % of PIM, where Glibenclamide (Sulphonylurea) was 36.6% and Metformin 0.8%. According to Malaysian Statistics on Medicines (2009 & 2010) (Ministry of Health Malaysia, 2014), the use of Sulphonylurea in 2009/2010 had increased by 16.2% as compared to 2007/2008. The overall use of Glibenclamide had been reduced, and chlorpropamide was not used in the public sector at all. According to Clinical Practice Guidelines for Diabetes Mellitus (Ministry of Health Malaysia, 2015), Gliclazide was still the main sulphonylurea being used in both the public and private sectors. This was consistent with the trend of second-generation sulphonylureas being used more widely due to lower hypoglycemia.

Glibenclamide has been shown to be associated with a significant risk of hypoglycaemia and the WHO recommends against its use in those over 60 years of age (World Health Organization, 2013). Many countries worldwide stopped using Glibenclamide. However, it was still used among the elderly in Malaysia till the Ministry of Health (MOH) announced changes in Drug Formulary No. 1/2018 in March 2018 where Glibenclamide was removed from the MOH formulary due to the risk of hypoglycaemia, especially among the elderly, and better alternative drugs were available. In this study (Ryan *et al.,* 2009), omeprazole and pantroprazole caused 3% PIM. The highest prevalence of PIM was in relation to the PPI. Similar to this study, a study done in Malaysia by Al-Aqqad et al. (2014) found the most commonly prescribed PIM were first generation antihistamines, prescriptions of duplicate drug classes, and Glibenclamide for type 2 diabetes mellitus. Huri & Ling (2013) concluded that the high number of medications and combination of multiple drug classes contributed to the high prevalence (17.5%) of potential drug-drug interactions or drug-disease interactions in the study. This result was consistent with a study by Van Roozendaal & Krass (2009) in which about 15% of potential drug interactions were encountered.

Conclusion

This chapter concludes and summarises the results and findings of the study. The chapter also presents some recommendations based on the findings. The prevalence of PIM in this study was found to be high, at 37% based on STOPP criteria. Predictors of PIM based on this study were the patient's age category above 70, the number of prescribed medications above five, the number of illnesses above three, the presence of endocrine disease, renal disease, and urogenital disease. STOPP criteria were applicable in this study, though a few amendments had to be made to remove medications that were not available in the studied facility. The STOPP criteria were easy to administer as they were divided based on physiological systems and narrowed down to drug-disease for each category.

Strength and Limitations

The strength of this study is the sample size, which was large, covering the main health clinics in Seremban district. The information gathered in this study was reliable and was cross-checked with the electronic database and patients' manual prescriptions. The limitations of the study would be time constraints as the data was collected during a specific time frame and subjected to dates agreed by the health clinics. The mode of data collection was adjusted according to the facility rules.

There are limitations in accessing information from medical practitioners, pharmacists, patients,

and prescriptions. Over the counter (OTC) drugs were not taken into consideration while assessing PIM. OTC drugs can be self-purchased by patients at pharmacies without a doctor's prescription. OTC drugs have a high tendency to contribute to PIM. A few more patient factors could be studied, such as medical officer prescribing pattern, medical personnel experience and workload. The patient's level of education, income level, activities of daily life and disabilities in performing daily chores may contribute to PIM. However, those variables could not be included due to the time limit.

Recommendations

The findings of the study can be used as a baseline study on PIM among the elderly in Malaysia's primary care setting. By identifying PIM, many health-related issues and medication errors among elderly patients can be reduced and resolved. Thus, this would eventually reduce ADE and DRP among elderly patients. A clinical audit at a health facility should be carried out regularly to monitor PIM. Balancing safety and quality of prescription with appropriate treatment of all illnesses is complex and challenging. Recording necessary data by doctors, especially geriatricians and pharmacists, for review on disease and therapeutic management may improve drug appropriateness among elderly patients. Primary care settings should have databases that are shared between health care professionals, such as doctors, pharmacists, and nurses.

By having a shared medical database, a patient's full medical record, counselling history, and many more details could be viewed by particular health care providers. Through accessible medical databases, for example, a doctor could review pharmacist counselling notes, adherence to medication scores and many more useful data. STOPP criteria can be used in a time-efficient manner by all disciplines involved in the care of elderly patients: primary, secondary, and tertiary care to ensure the appropriateness of drug treatment, with the intention of minimising the risk of medication error and adverse effects, which could lead to many other serious health issues and causes of deterioration of patients' health. However, STOPP criteria have to be reviewed from time to time as some of the drugs are not available in Malaysia and our guidelines are different from other countries. STOPP can be modified, adapted to Malaysian Health System practice, and used as a standardised guideline in prescribing for the elderly.

Drugs which were removed and listed as contraindicated for the elderly, such as Ticlopidine, Chlorpheniramine, and Diphenydramine, were still used in government primary care settings. In the future, Malaysia could invest more in clinical trials, update guidelines from time to time and look critically into cost management for fuelling subsidised health care services for a better quality of life for the nation.

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