

ORIGINAL ARTICLE

Gender disparity in the prescription of secondary prevention medications in a Malaysian primary care clinic

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Abstract

Introduction: Cardiovascular disease is the leading cause of death worldwide. Despite the proven benefit of secondary prevention medications (SPMs), their utilisation remains suboptimal in many countries. This study aimed to assess the use of SPMs in a Malaysian primary care clinic and factors associated with it.

Methods: A retrospective review of electronic medical records was conducted to assess the prescription of SPMs among patients with coronary artery disease who attended the clinic between 1st January 2018 and 31st December 2018. Prescriptions of SPMs were documented in numbers and percentages. Multiple logistic regressions were used to analyse factors associated with the prescription of SPMs.

Results: Of the 662 patients included in the study, 99.1% were prescribed statins, 97% antiplatelets, 81.7% angiotensin-converting enzyme (ACE)-inhibitors or angiotensin II receptor blockers (ARBs), and 78.7% beta-blockers. Male patients were more likely to be prescribed statins (OR = 8.584, 95% CI: 1.431 – 51.510) and antiplatelets (OR = 6.818, 95% CI: 2.294 – 20.257). Another significant factor for antiplatelets prescription was having diabetes (OR = 3.318, 95% CI: 1.148 – 9.590). Having hypertension was associated with ACE-inhibitors or ARBs prescription (OR = 4.008, 95% CI: 2.522 – 6.370).

Conclusion: Although the majority of patients received SPMs, there were significant disparities for some SPMs prescriptions among female patients. As these medications are widely available in the Malaysian primary care setting, steps should be taken to ensure that these medications are prescribed equally for all eligible patients.

Introduction

Cardiovascular disease (CVD) is the world's leading cause of death.¹ Approximately 17.9 million people die from CVD each year—approximately 31% of all deaths worldwide.¹ Furthermore, more than 75% of CVD deaths occur in low and medium-income countries, and 85% of all CVD deaths are due to heart attacks and stroke.¹

In Malaysia, ischaemic heart disease (IHD) remains the leading cause of death at 13.9%.² Death secondary to IHD among males has been increasing recently, from 15.3% in 2016 to 16% in 2017, and this pattern has also been observed among females.²

Nearly half of Malaysian adults have a clustering of CVD risk factors such as

smoking, obesity, hypercholesterolemia, hypertension and diabetes, with 43.2% of adults having at least two of these risk factors.^{3,4} According to the INTERHEART study, these risk factors, together with abdominal obesity, psychological stressors, poor dietary habits and lack of exercise, have contributed to more than 90% of initial myocardial infarctions.⁵

The reduction of CVD risk factors and subsequent CVD mortality can be achieved through improved treatment strategies, including non-pharmacotherapy management, pharmacotherapy management and intensive control of individual risk factors.³ Among these strategies, overwhelming evidence has demonstrated the effectiveness of secondary prevention medications (SPMs) for reducing CVD events and mortality.^{6,7} Despite this,

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the utilisation of these medications remains suboptimal worldwide, especially in low-income countries.⁸

Various factors contribute to low utilisation of SPMs, such as socioeconomic status, access to healthcare and patient-level barriers like medication adherence.⁹ Several studies have found that patients' demographic characteristics, such as gender and age, are significant determinants for prescription of SPMs.¹⁰⁻¹³

In Malaysia, Kassab et al. discovered that although utilisation of SPMs was generally good among patients discharged from hospital following acute coronary syndrome, older patients are less likely to be prescribed SPMs.¹⁴ Furthermore, the extent to which SPMs is prescribed among patients in a primary care setting remains unknown. This study therefore aimed to ascertain whether prescriptions of SPMs in the primary care clinic are in line with the Malaysian Primary and Secondary Prevention of Cardiovascular Disease and Stable Coronary Artery Disease guidelines.^{3,15} This study also aimed to assess the factors associated with prescription of SPMs among these patients.

Materials and Methods**Study design and population**

This study was conducted at a university primary care clinic in Selangor, Malaysia. A retrospective review of electronic medical records (EMR) was performed for patients with coronary artery disease (CAD) who attended the clinic between 1st January 2018 and 31st December 2018. A list of patients who attended the clinic during the study period was obtained from the clinic's information technology (IT) unit, and those patients were screened for eligibility. Patients with CAD who were older than 18 years of age and attended the clinic at least once for their CAD follow up were included in the study. The exclusion criteria were patients who were pregnant or who followed up at other clinics after attending our clinic for acute care or prescriptions only. CAD was defined as previous acute coronary syndrome (unstable angina, myocardial infarction) that required referral or admission to hospital, or established CAD confirmed through diagnostic cardiac procedures, such as coronary angiography, cardiac computed tomography scan, cardiac magnetic resonance imaging, echocardiography or an exercise stress test.

Sample size determination

A study conducted by Kassab et al. found that 95.7% of patients were prescribed antiplatelets, 80.3% beta-blockers, 95% statins and 69.7% angiotensin-converting enzyme (ACE)-inhibitors or angiotensin II receptor blockers (ARBs).¹⁴ Based on this, using a single proportion formula and taking the α value of 0.05 with an absolute precision of 5%, the minimum calculated sample sizes were 64, 244, 73 and 325, respectively. To ensure adequate sample size for logistic regression, Bujang et al. recommended a minimum sample size of 500 or the formula $n = 100 + 50i$, where i is the number of independent variables in the final model.¹⁶ This study proposed to include seven independent variables, therefore using this formula, the total minimum sample size required was 500. Overall, based on these calculation methods, this study aimed to sample a minimum of 500 patients.

Study procedure

The institution's permission to access the EMR was obtained prior to conducting the study. The list of patients who attended the clinic during the study period was gathered from the clinic's IT unit. The data were extracted in two stages. First, the data were extracted by visits and later they were sorted by patients' medical reference numbers to prevent duplicates. Based on the list, the patients were screened for eligibility. The clinic does not have a CAD registry, so systematic random sampling could not be performed. To minimise sampling bias, a consecutive sampling method was used until the target sample size was achieved.

The demographic and clinical details of the eligible patients were extracted from the EMR by the investigators, who were trained prior to data collection to ensure standardisation. The data were documented on a standardised data collection sheet that included demographic characteristics such as age, gender and ethnicity, as well as clinical data such as smoking status, Type 1 or 2 diabetes mellitus (DM), hypertension and dyslipidaemia history. The outcomes of this study were the prescriptions of four SPMs (statins, antiplatelets, ACE-inhibitors or ARBs, and beta-blockers). The four SPMs were chosen based on the Malaysian Clinical Practice Guidelines of Stable Coronary Artery Disease, which recommended these medications for patients with stable CAD, if appropriate.¹⁵ DM, hypertension and dyslipidaemia

were defined as a clinician's diagnosis of DM, hypertension or dyslipidaemia, and/or if the patient was taking at least one oral hypoglycaemic agent, antihypertensive agent or lipid-lowering agent. Smoking status was defined as current smoking status at the time of the study, as documented in the EMR. Other information collected included main treating physician (family medicine specialist, cardiologist or medical officer) and clinical history precluding patients from being prescribed SPMs, such as clinician's diagnosis of asthma, chronic obstructive pulmonary disease (COPD), dyspepsia, gastritis or peptic (gastric and/or duodenal) ulcer diseases.

Statistical Analysis

Data entry and statistical analysis were performed using IBM SPSS Statistics for Windows, Version 26.¹⁷ The descriptive analyses were expressed as mean with standard deviation (SD) or median with interquartile range (IQR) for normally distributed and non-normally distributed data, respectively. Categorical variables were described in numbers and percentages. Multivariate analysis using logistic regression with enter method was performed to assess the factors associated with prescription of SPMs. The demographic factors (age, race, gender) and clinical factors (treating doctor, diabetes, hypertension, dyslipidaemia) were the independent variables. For smoking status, 47.7% of the data was missing, so it was omitted as an independent variable in the logistic regression analysis. The dependent variables were prescriptions of the four SPMs: antiplatelets, statins, ACE-inhibitors or ARBs, and beta-blockers.

Four separate logistic regression analyses were conducted for factors associated with prescription of antiplatelets, statins, ACE-inhibitors or ARBs, and beta-blockers. The overall model fitness was assessed using the Hosmer–Lemeshow goodness-of-fit test and the receiver operating characteristic (ROC) curve. The Hosmer–Lemeshow goodness-of-fit tests for all four models were insignificant (p-values 0.302 – 0.888), indicating the models fit the data well.

All four models explained 3.6 – 22.9% (Nagelkerke R Square) of the variance in the prescription of SPMs, and were able to discriminate 60.5% (ROC = 60.5%, 95% CI: 0.554 – 0.656, $p < 0.05$) to 89.0%

(ROC=89.0%, 95% CI: 0.796 – 0.983, $p < 0.05$) of patients being prescribed or not being prescribed SPMs.

Results are presented as odds ratios (OR) with 95% confidence intervals (CI), and a p-value < 0.05 was considered statistically significant.

Results

Patient characteristics

A total of 662 eligible patients were identified from the EMR; their demographic and clinical characteristics are presented in **Table 1**. The mean (\pm SD) age of patients was 63 years (\pm 9.8). The patients were predominantly male (81.4%) and of Malay ethnicity (66.2%). The majority of patients had cardiovascular risk factors such as DM (55.4%), hypertension (80.5%) and dyslipidaemia (66.3%). As the data were retrieved from the EMR, some information was not available, such as smoking status and duration since quitting smoking for ex-smokers.

Prescription of secondary prevention medications

The proportions of patients being prescribed SPMs are illustrated in **Table 2**. Patients who were diagnosed with dyspepsia/gastritis/peptic ulcers and/or asthma/COPD were excluded from analyses for antiplatelet and beta-blocker prescriptions, respectively. Among the SPMs, the most commonly prescribed were statins (99.1%), followed by antiplatelets (97%), ACE-inhibitors/ARBs (81.7%) and beta-blockers (78.7%).

Factors associated with prescription of secondary prevention medications

The factors associated with prescription of SPMs among patients with CAD are shown in **Table 3**. Male patients were nearly seven times more likely to be prescribed antiplatelets (OR = 6.818, 95% CI: 2.294 – 20.257) and eight times more likely to be prescribed statins (OR = 8.584, 95% CI: 1.431 – 51.510) when compared to females. In addition, patients with diabetes were also more likely to be prescribed antiplatelets (OR = 3.318, 95% CI: 1.148 – 9.590). As expected, hypertensive patients were four times more likely to be prescribed ACE-inhibitors or ARBs (OR = 4.008, 95% CI: 2.522 – 6.370) than were patients without hypertension.

Table 1. Demographic and clinical characteristics of patients with coronary artery disease, n = 662

Variables	Frequency, n (%)	Mean (± SD)
All patients	662 (100)	
Age (years)		63 (9.8)
Age (years)		
< 30 years old	1 (0.2)	
30 – 39 years old	4 (0.6)	
40 – 49 years old	53 (8.0)	
50 – 59 years old	179 (27.0)	
≥ 60 years old	425 (64.2)	
Gender		
Female	123 (18.6)	
Male	539 (81.4)	
Race		
Malay	438 (66.2)	
Chinese	162 (24.5)	
Indian	60 (9.1)	
Others	2 (0.3)	
Smoking Status		
Smoker	242 (36.6)	
Non-smoker/ex-smoker	104 (15.7)	
Unknown	316 (47.7)	
Comorbidities		
Type 1 or 2 diabetes mellitus	367 (55.4)	
Hypertension	533 (80.5)	
Dyslipidaemia	439 (66.3)	
Asthma or chronic obstructive pulmonary disease	39 (5.9)	
Dyspepsia/gastritis/peptic ulcers	93 (14)	
Treating doctor		
Specialist (cardiologist or family medicine specialist)	241 (36.4)	
Medical officer	421 (63.6)	

Table 2. Prescription of secondary prevention medications to patients with coronary artery disease

	Antiplatelets*, n (%)	Statins+, n (%)	ACE-inhibitors or ARBs+, n (%)	Beta-blockers^, n (%)
Prescribed	552 (97)	656 (99.1)	541 (81.7)	490 (78.7)
Not prescribed	17 (3)	6 (0.9)	121 (18.3)	133 (21.3)

Notes

* excluded patients with dyspepsia/gastritis/peptic ulcers, n = 569

+ included all patients, n = 662

^ excluded patients with asthma or COPD, n = 623

ACE = angiotensin-converting enzyme

ARBs = angiotensin II receptor blockers

Table 3. Factors associated with prescription of secondary prevention medications to patients with coronary artery disease

Variables	Antiplatelets*		Statins+		ACE-inhibitors or ARBs+		Beta-blockers [^]	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Age								
<60 years old	1	Ref	1	Ref	1	Ref	1	Ref
≥60 years old	1.533 (0.511-4.593)	0.446	1.310 (0.204-8.417)	0.776	0.868 (0.559-1.347)	0.527	0.715 (0.469-1.091)	0.120
Gender								
Female	1	Ref	1	Ref	1	Ref	1	Ref
Male	6.818 (2.294-20.257)	0.001	8.584 (1.431-51.510)	0.019	0.996 (0.568-1.748)	0.990	1.321 (0.810-2.153)	0.264
Race								
Non-Malay	1	Ref	1	Ref	1	Ref	1	Ref
Malay	1.854 (0.677-5.071)	0.229	8.197 (0.931-72.192)	0.058	0.953 (0.615-1.476)	0.830	0.968 (0.641-1.462)	0.877
Treating doctor								
Medical officer	1	Ref	1	Ref	1	Ref	1	Ref
Specialist (cardiologist or family medicine specialist)	0.999 (0.350-2.854)	0.999	0.328 (0.057-1.884)	0.221	1.111 (0.718-1.718)	0.637	1.516 (0.996-2.309)	0.052
Dyslipidaemia								
No	1	Ref	1	Ref	1	Ref	1	Ref
Yes	0.413 (0.110-1.550)	0.190	2.226 (0.376-13.174)	0.378	0.926 (0.597-1.437)	0.732	0.616 (0.396-0.957)	0.031
Diabetes								
No	1	Ref	1	Ref	1	Ref	1	Ref
Yes	3.318 (1.148-9.590)	0.027	0.797 (0.124-5.111)	0.811	1.407 (0.924-2.142)	0.111	1.128 (0.758-1.677)	0.553
Hypertension								
No	1	Ref	1	Ref	1	Ref	1	Ref
Yes	0.762 (0.153-3.809)	0.741	0.943 (0.078-11.370)	0.963	4.008 (2.522-6.370)	<0.005	1.566 (0.957-2.562)	0.074

Notes

* excluded patients with dyspepsia/gastritis/peptic ulcers, n = 569

+ included all patients, n = 662

[^] excluded patients with asthma or COPD, n = 623

No multicollinearity

Factors analysed: age, race, gender, treating doctor, diabetes, hypertension and dyslipidaemia

ACE = angiotensin-converting enzyme

ARBs = angiotensin II receptor blockers

Discussion

This study demonstrated good pharmacotherapy management for patients with CAD in this primary care clinic. The majority of patients from this study received SPMs, ranging from 78.7% receiving beta-blockers to 99.1% receiving statins. Our findings were encouraging and comparable to a Malaysian study conducted in secondary care where 80.3% of patients received beta-blockers and 98.2% received statins upon discharge.¹⁴ The level of adherence among patients was lower at the two-year follow up, however.¹⁸ In contrast, Yusuf et al. reported much lower utilisation of SPMs in some communities in Malaysia. Among 289 patients with self-reported CAD, less than 20% received SPMs.⁸

International studies looking at the prescription of SPMs at the community level have yielded varying results. An audit conducted at a primary care setting in the United Kingdom showed that 98.4% of patients with CAD were prescribed antiplatelet therapy in the community, which is comparable to our findings.¹⁹ A study from Spain demonstrated that 37.7 – 85%

of their patients received SPMs.¹⁰ Larger community-based studies have demonstrated a smaller proportion of SPMs use in study populations.^{8,20} Among patients with CAD, 20.4 – 73.6% of patients in Europe and North America received SPMs, with smaller percentages in the Middle East, South America and Asia.⁸ Chen et al. reported much lower utilisation of SPMs in China, ranging from 1.4% to 12.3%.²⁰

Concerning factors associated with the prescription of SPMs, this study found that male gender was a significant factor, specifically for antiplatelets and statins therapy. Many studies have discovered similar outcomes.^{11,12,21,22} Recent literature has debated whether this is due to gender disparity for treatment initiation, or adherence issues among women. Smolina et al. found the former to be the factor contributing to suboptimal SPMs therapy among women, especially those younger than 55 years of age.¹² Magee et al., however, concluded that apart from antiplatelet therapy, women were being treated as aggressively as men.²³ Despite this, blood pressure and lipid control

among these women remained suboptimal. Biological factors and treatment adherence were among the reasons proposed to contribute to this.²³ In addition, women were more likely to discontinue statin therapy due to side effects such as muscle pain, as well as feeling dissatisfied with the consultation with their clinicians regarding statin therapy.²⁴ Despite having a lower prevalence of obstructive CAD from angiography, one study found that more women than men died from CAD and women were more likely to die from cardiac arrest prior to arriving at the hospital, in comparison to men.²⁵ Furthermore, women also experienced poorer quality of life and more adverse outcomes related to CAD.²⁵ Current evidence indicates that SPMs therapy, particularly statins, is as efficacious among men as it is among women for prevention of major vascular events.²⁶ Thus, treatment with SPMs should be appropriately and fairly prescribed for all women with CAD.²⁶ Patient factors such as medication adherence require intensive, multifaceted strategies for improvement, and are difficult to achieve.²⁷ Under-prescription by doctors should therefore be avoided to ensure optimal evidence-based care for patients in primary care, especially when SPMs is widely available.

Strengths, limitations and implications for future research and clinical practice

To the best of our knowledge, this is the first study assessing the factors associated with SPMs prescription in the Malaysian primary care setting. The findings address the gap in the literature and provide useful insight for primary care providers. This study does, however, have some limitations. Firstly, this is a single-centre study where the medical officers were pursuing postgraduate qualification in primary care medicine. Their medical knowledge and skills might be better compared to medical officers who are not pursuing postgraduate training in primary care. Hence, this study may not be representative of all medical officers serving primary care in Malaysia. Secondly, the majority of the patients in this study were Malays, so other ethnic groups in Malaysia, such as Chinese and Indians, were underrepresented. For this reason, the results may not be generalisable to other primary care clinics in Malaysia. Future research should include a larger, multi-centre study to improve the generalisability of the results. Finally, some factors that may affect the usage of SPMs, such as patients' attitudes and beliefs towards SPMs use, as well as the

socioeconomic status of the patients, were not available in the EMR and so were not explored in this study. The results from the multiple logistic regressions must therefore be interpreted with care. Future studies should include other factors that may affect the prescription of SPMs, as well as assessing adherence to SPMs among patients with CAD in primary care. In terms of clinical implications, the findings of this study will provide useful insights with which medical doctors can examine their own prescription practice to ensure that female patients are being prescribed SPMs fairly, as indicated. As for strategies for improvement, the findings of this study may be used to develop teaching materials for doctors' continuing professional development, which could help address potential gaps in knowledge, improving prescribing practice and, ultimately, patient care.

Conclusion

In conclusion, the majority of patients with CAD in this study received SPMs, but underutilisation of some of these medications was still observed among female patients. Given that SPMs is widely available in primary care, under-prescription of these medications by doctors should be avoided to ensure patients receive the best evidence-based treatment.

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Author's contributions

Baharudin N, Ahmad-Roslan AM, Zainal ANI, Sahar NH, Din NSS, Ibrahim IS, Rahim SNHA and Rosli NA designed the study and acquired the data. Baharudin N and Mohamed-Yassin MS analysed and interpreted the data. Baharudin N, Mohamed-Yassin MS and Ramli AS drafted and critically revised the manuscript. All authors reviewed and approved the final manuscript.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethics approval

This study was approved by the institutional Ethics Committee of Universiti Teknologi MARA (UiTM) [(600-IRMI(5/1/6) REC/349/19)].

How does this paper make a difference to general practice?

- This study provides useful insights for primary care doctors regarding the prescription of SPMs in a primary care clinic and factors associated with it.
- This study demonstrated gender disparities for antiplatelet and statin prescriptions among patients with CAD.
- The benefits of statins and antiplatelets are well-established for both genders. Primary care providers in Malaysia must therefore ensure that these medications are prescribed to both males and females appropriately, in the absence of contraindication.

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