Antihypertension Medication Usage Pattern and Predictors of Evidence-based Medication among Hypertension patients

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Abstract

Background: Despite substantial guidelines on the effective management of hypertension, many studies demonstrated an underutilization of evidence-based medicine (EBM) for the treatment of hypertension patients. This study aimed to evaluate the antihypertension therapy and the impact of patients' specific predictors on the utilization of EBM among hypertension patients. **Materials and Methods:** A retrospective observational study designed to investigate the prescribing trends and patient's factors (predictors) affecting the utilization of antihypertensive medications. Patients' factors included age, gender, ethnicity, smoking status, and concurrent medical conditions. The study was conducted using a purpose-developed data collection form to assemble the patient's information. **Results:** A total of 170 hypertensive patients, comprising 83 males (48.82%) and 87 females (51.18%) were selected as subjects for this study. The findings suggested that the mean age of our study population was 59.32 years and 70% of them had two to three comorbidities. It was established that 98.8% of the patients had chronic kidney disease and 35.3% of them were in Stage V. Diuretics were the most commonly prescribed antihypertensive class under monotherapy. **Conclusion:** This study evaluated antihypertension medications usage pattern and patients' predictors affecting utilization of antihypertension medications among hypertension patients.

Key words: Antihypertensives, BBs, CCBs, EBM

INTRODUCTION

Hypertension has been recognized as one of the major global concerns. Many people with high blood pressure (BP) do not even know they have it. Often the signs and symptoms are misunderstood.[1] Globally, the World Health Organization (WHO) estimated that about 40% of adults aged 25 and over are having hypertension in 2008.[2] The prevalence of hypertension in Malaysia was 34.6% in 2006, 33.6% in 2011, and 35.3% in 2015. The awareness of hypertension in 2006, 2011, and 2015 was 35.6%, 40.7%, and 37.5%, respectively.[3] The chronic elevation in BP causes end-organ damage, consequently leading to increased morbidity and mortality.[4] The progression of the condition is strongly associated with structural and functional cardiac or vascular abnormalities that damage the heart, kidneys, brain, vasculature, and affects other organs as well.[5]

Moreover, the high and increasing prevalence of hypertension still contributes to considerable socioeconomic burden globally.[6-8] First-line medications used in the treatment of hypertension include diuretics, angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARBs), beta-blockers (BBs), and calcium channel blockers (CCBs). Some patients will require two or more antihypertensive medications to achieve their BP target.[9] In fact, the effectiveness of at least several classes of drugs in treating hypertension and preventing cardiovascular disease

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CVD events is well documented. These evidence-based medications (EBM) should be initiated immediately after the diagnosis of hypertension.[10]

There are several guidelines set to help physicians have better control in managing hypertension. Despite the existing guidelines for the treatment of hypertension in Malaysia, it remains inadequately managed in a large number of hypertensive individuals, therefore, causing major organ damages, mainly in patients with higher or uncontrolled BP. The main objectives of the study were to (1) review antihypertension therapy in a Malaysian hospital, and (2) study the impact of patients' specific predictors on the utilization of antihypertension EBM among hypertension patients.

MATERIALS AND METHODS

This cross-sectional study was conducted at a hospital in Selangor, Malaysia. This hospital is among the top cardiac centers in Selangor. The data were retrieved from the hospital's online medical records system among a cohort of hypertensive patients ($n = 170$) using a specially designed data collection form. A range of clinical data was extracted from patients' medical records including patient demographics, clinical characteristics, and prescribed medications.

Patient sampling and data collection

A total number of 250 hypertensive patients who were present in the studied cohort were initially identified from the medical record database. The selection criteria were carried based on hypertension as the primary diagnosis, with or without comorbidities as evaluated by the physicians of the hospital. From January 2017 to May 2017, a random sample of 170 medical records of those hypertensive patients who met the inclusion criteria was further assessed for review. The patients with incomplete medical profile and insufficient data on prescribed antihypertensive medications were excluded from the review. All aspects of the study protocol were approved by the Malaysian national medical research register (Ref: 846-21060) and from the clinical research center of the hospital.

Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 24, and all recorded data were coded into variables. For descriptive statistics, categorical data were presented as frequency (*n*) and percentage (%) while continuous data reported as means with standard deviation. To identify the factors that were predictive of the prescribing of various antihypertensive medications, multivariate analysis using forward stepwise logistic regression was performed and adjusted odds ratio (OR)

with 95% confidence interval (CI) was calculated. The following variables were inserted into the multivariate model: Patients' age, gender, and medical conditions such as hyperlipidemia, diabetes mellitus, respiratory or renal impairment, and concurrent prescribed medications. All aspects of the study protocol were approved by the concerned ethics committee and the clinical research center of the concerned hospital.

RESULTS

A total number of 250 hypertensive patients within the 3-month study period were initially identified from the medical records database, of which 170 patients were ultimately included in the present study. However, only 164 patients' data were used in the logistic regression analysis. Four patients from other ethnic backgrounds and two patients without chronic kidney disease (CKD) were excluded to ensure the precision and accuracy of the results.

Patient characteristics

The mean age of the study population was 59.32 years (range 22–83 years) with 55.9% of patients aged over 60 years. The proportion of male and female patients was almost similar, and most of them were Malay (56.7%) and non-smokers. Patients with ≥2 comorbidities accounted for 85% of the sample, whereas 15% had only one or no comorbidities. The findings showed that 98.8% of them were having CKD, 73.5% were diabetic, 30.0% were having other CVDs, 29.4% were obese, 21.8% had dyslipidemia, and 3.5% had lung diseases. Table 1 shows the demographics and clinical characteristics of the patients.

Antihypertension medications usage pattern

The most common antihypertensive medications prescribed as monotherapy were diuretics with 74.2% (126), followed by CCBs with 71.8% (122) and the least recorded were drugs acting on the renin-angiotensin system with 17.1% (29). Our findings [Table 2] revealed that among the patients who received diuretics, 60.6% (103) were prescribed with furosemide. Amlodipine 34.7% (59) and felodipine 34.7 (59) were the most frequently prescribed dihydropyridine (DHP) CCBs, while diltiazem 2.4% (4) was the top non-DHP CCBs. About 45.3% of patients prescribed with BBs, of which 17.6% (30) were taking metoprolol, followed by 13.5% (23) bisoprolol and 12.9% (22) atenolol. Around 62% of hypertensive patients who had concurrent CVDs were prescribed with BBs. The most frequently prescribed combination of three classes of antihypertensives used was CCBs, BBs, and diuretics; followed by the combination of two classes of antihypertensive drugs which were CCBs and diuretics.

Table 1: Patients' demographics and clinical characteristics

Variable	n (%)
Gender	
Male	83 (48.82)
Female	87 (51.18)
Age	
<40 years	82 (48.2)
40–60 years	83 (48.8)
>60 years	5 (2.9)
Ethnicity	
Malay	96 (56.5)
Chinese	45 (26.5)
Indian	25 (2.4)
Others	4 (2.4)
Smoking status	
Never	152 (89.4)
Active and ex-smokers	18 (10.6)
No. of comorbidities	
≤1	24 (14.1)
2–3	120 (70.6)
≥4	26 (15.3)
Comorbidities	
Chronic kidney disease	168 (98.8)
Diabetes mellitus	125 (73.5)
Cardiovascular diseases	51 (30.0)
Obesity	50 (29.4)
Dyslipidemia	37 (21.8)
Lung disease	6 (3.5)

SD: Standard deviation

Table 2: Proportion of hypertension patients receiving pharmacotherapy

Characteristics	n (%)
Diuretics	
Furosemide 40 mg	103 (60.6)
HCTZ 50 mg	12 (7.1)
HCTZ 25 mg	11 (6.5)
Calcium antagonists	
Amlodipine 10 mg	59 (34.7)
Felodipine 10 mg	59 (34.7)
Diltiazem	4 (2.4)
BBs	
Metoprolol 100 mg	30 (17.6)
Bisoprolol 2.5 mg	23 (13.5)
Atenolol 100 mg	22 (12.9)
ACEIs	
Perindopril 4 mg	24 (14.1)
Perindopril 8 mg	19 (11.2)
Enalapril 10 mg	3 (1.8)
ARBs	
Irbesartan 300 mg	7 (4.1)
Telmisartan 40 mg	7 (4.1)
Telmisartan 80 mg	6 (3.5)
Other classes	
Prazosin 1 mg	10 (5.9)
Prazosin 2 mg	10 (5.9)
Methyldopa	1 (0.6)

ACEI: Angiotensin-converting enzyme inhibitors, ARBs: Angiotensin receptor blockers, BB: Beta-blockers, CCB: Calcium channel blockers, BP: Blood pressure

Patients' factors affecting the utilization of EBM

All patients' factors such as age, gender, ethnicity, medical conditions, concurrent comorbidities, antihypertensives, and the concurrently prescribed medicines that ultimately led to the changes in the utilization of each EBM and the management of hypertension was analyzed using logistic regression. The factors affecting the utilization of EBM are listed in Table 3.

DISCUSSION

This study provides an insight into the current pharmacotherapeutic management of hypertension patients in Selangor, Malaysia. Data on prescribed medication and patients' factors affecting the utilization of the antihypertensive EBM can be used to improve patient care practices in Malaysia.[10-12]

Antihypertensive classes prescribed in this study included CCBs, diuretics, ACEIs, ARBs, BBs, and other groups (alpha-blockers, and alpha-adrenergic agonists).[13,14] Our results showed that the majority of the study population was on poly-therapy, where most of them got two to three antihypertensive medications while only 23.5% was on monotherapy. This might be to increase the adverse drug reactions caused by polytherapy, moreover, the use of polypharmacy leads to decrease in the adherence rate. Ayushi *et al.* reported that more patients were compliant on monotherapy (75.1%) as compared to polytherapy (69.2%).[15] In contrast to our results, Sang *et al.* stated that most patients were prescribed with monotherapy (66.7%) rather than combination therapy (33.3%).[16]

Among diuretics, furosemide was the most prescribed (60.6%). In contrast to this result, Tadesse *et al.* reported that hydrochlorothiazide was the most prescribed diuretics.[17] Felodipine and amlodipine were the most prescribed CCBs. Similarly, Noah *et al.* reported that amlodipine was the most prescribed CCBs.[18] Metoprolol was the most prescribed BBs. Perindopril was the most prescribed ACEI, in contrast

Table 3: Multivariate analysis of factors influencing utilization of EBM			
Variables	**Odds ratio**	**95% CI**	***P*-value**
Diuretics			
Patients age	1.036	1.003–1.071	0.033*
CKD Stage IV	0.312	0.120–0.810	0.017*
Lung disease	0.020	0.001–0.310	0.005*
Dyslipidemia	5.306	1.464–19.232	0.011*
Calcium antagonists			
Diuretics	0.411	0.175–0.963	0.041*
BBs			
CVDs	2.690	1.322–5.470	0.006*
Other antihypertensive class	6.400	2.010–20.382	0.002*
ACEIs			
CKD Stage V	2.784	1.147–6.756	0.024*
ARBs	0.214	0.059–0.783	0.020*
ARBs			
CKD stage III	8.668	1.315–57.123	0.025*
ACEIs	0.214	0.059–0.783	0.020*
Other classes			
BBs	8.858	2.665–29.441	0.001*

*Significant at <0.05; CI: Confidence interval. ACEI: Angiotensin-converting enzyme inhibitors, ARBs: Angiotensin receptor blockers, BB: Beta-blockers, CCB: Calcium channel blockers, BP: Blood pressure

to that Tadesse *et al*. reported that enalapril was the most prescribed ACEI.[17] Irbesartan and telmisartan 40 mg were the most prescribed ARBs and prazosin was the most prescribed among other classes.

Patients' factors were assessed using univariate analysis and the results showed patient's age, presence of CKD, dyslipidemia, and lung disease affected the utilization of diuretics. Binary logistic regression analysis showed that there was a positive association between the utilization of diuretic and the patient's age (OR = 1.038, 95% CI = 1.003–1.071, *P* = 0.033). Patients having CKD Stage IV (OR = 0.312, 95% CI = 0.120–0.810, *P* = 0.017) and lung disease (OR = 0.020, 95% CI = 0.001–0.310, *P* = 0.005) as comorbidities were less likely to be prescribed with diuretics. In addition, patients with dyslipidemia (OR = 5.306, 95% CI = 1.464–19.232, *P* = 0.011) were more likely to receive diuretics for the management of hypertension.

Multivariate analysis also determined that the utilization of calcium antagonists had a positive association with concurrent use of diuretics (OR = 0.411, 95% CI = 0.175–0.963, *P* = 0.041). Thereby patients who were prescribed with diuretics were less likely to be coprescribed with CCBs. Regression analysis further showed that there was an association between the utilization of BBs and the patients who were having CVDs as concurrent comorbidities (OR = 2.690, 95% CI = 1.322–5.470, *P* = 0.006); and also those who were prescribed with other classes of

antihypertensive agents, for example, alpha-blocker and centrally acting agent (OR = 6.400, 95% CI = 2.010–20.382, *P* = 0.002). It was noted that there was an association between utilization of ACEIs and the comorbid patients having CKD Stage V (OR = 2.784, 95% CI = 1.147–6.756, *P* = 0.024). The results also suggested that the antihypertensive patients with CKD Stage V were more likely to be prescribed with ACEIs in comparison to the patients prescribed with ARBs (OR = 0.214, 95% CI = 0.059–0.783, *P* = 0.020) who were less likely to be coprescribed with ACEIs.

Binary logistic regression analysis model found that patient's age, the presence of CKD, dyslipidemia and lung disease was the pure predictors of the utilization of diuretics. Moreover, patients who were prescribed with diuretics affected the utilization of CCBs; this result may be due to some ethnic variations among them. It was also found that there was an association between the utilization of BBs and the patients who were having CVDs as concurrent comorbidities and also those who were prescribed with other classes of antihypertensive agents such as alpha-blocker and centrally acting agent. The use of BBs with alpha-blockers and centrally acting agents increase the control of hypertension because BBs had a direct effect on the heart and alpha-blockers or centrally acting agent affect the vessels.[19] Similar to the present study several studies across the globe, that is, Malaysia,[12] South Africa,[20] Zimbabwe,[21] China,[14] India,[22] Cyprus,[23] and the US[13,24] suggested to minimize the wider gap between the actual clinical practices of the prescribers and the recommendations

of the guidelines to successfully treat hypertension and its comorbidities.[12-14]

This study was conducted in a single-based center and the hypertensive patients enrolled were representative of a single center. The available number of patients taken as sample was inadequate to produce more significant correlations and justifications. Hence, the results of the study cannot be generalized. Besides that, the patients without complete medical history and prescription records had to be excluded from this study.

CONCLUSION

Hypertension is a globally recognized public health issue. Several guidelines have established appropriate therapies based on numerous clinical trials to reduce the incidence of hypertension and its complications. This study aimed to evaluate the antihypertensive medications' EBM as well as patients' predictors affecting utilization of antihypertension medications among hypertension patients.

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