

# Impact of Prescribers' Adherence to Clinical Practice Guidelines for Hypertension on Hypertension Control

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## Abstract

**Objective:** This study evaluates physicians' adherence to Malaysian Clinical Practice Guidelines for Hypertension 2013 (MCPGs-HPT-2013) and the factors influencing patients' adherence to antihypertensive medications. **Materials and Methods:** Among a cohort of randomly selected 170 hypertensive patients, the prescribing trends of physicians were compared with MCPGs-HPT 2013. Univariate and multivariate analyses (odds ratio [OR], 95% CI) were done to investigate the physician's adherence to MCPGs-HPT-2013. **Results:** Patients that had three concurrent clinical conditions and prescribed with angiotensin-converting enzyme inhibitors ( $P < 0.05$ , OR = 2.989) were affected the most with physicians' non-adherence with MCPGs-HPT-2013. **Conclusion:** Surprisingly, <50% of the total patients received guidelines compliant pharmacotherapy that emphasizes the need for strict adherence to MCPGs-HPT-2013 in Malaysia.

**Key words:** Adherence, CP guidelines, Hypertension, Malaysian clinical practice guidelines for hypertension 2013

## INTRODUCTION

The principal goal in ensuring an improved therapeutic regimen for hypertension (HPT) is to reduce morbidity, mortality and preventing cardiovascular, cerebrovascular, and renovascular diseases.<sup>[1,2]</sup> To control HPT, several management guidelines have been developed and disseminated worldwide. These guidelines consist of recommendations based on screening, diagnosis, and treatment of HPT. After a series of evidence-based clinical trials, HPT management guidelines have recommended various drug classes as preferred agents in the treatment of HPT with and without comorbidities. Therefore, they may be considered as the "gold standard" for assessing the quality of pharmacotherapy in daily medical practice. To improve HPT control, the Malaysian HPT Society is also developing, disseminating, and regularly updating HPT management guidelines since 1998.<sup>[3]</sup>

Several guidelines are currently in use for the effective management of HPT globally, such

as Eighth Joint National Committee, European Society of HPT/European Society of Cardiology Guidelines for the Management of Arterial HPT, 2011 Canadian Recommendations for the Management of HPT, and 2013 Malaysian Clinical Practice Guidelines (MCPGs) Management of HPT. Poor implementation of guidelines may be due to several factors such as lack of awareness, lack of agreement, and lack of expectation that a given behavior will lead to a particular consequence, the inertia of previous practice, and external barriers.<sup>[4]</sup> Some of the commonly cited predictors for nonadherence include the concurrent use of multiple medications, frequency of medication changes, socioeconomic status, cost, household composition, comorbidity, and accessibility to medical care.<sup>[5,6]</sup>

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Nonadherence may aggravate disease severity, leading to increased utilization of medical care services and inflating higher health care costs. According to some previous studies, patients who were nonadherent to antihypertensive therapy were significantly more likely to have higher rates of hospitalizations and emergency room visits due to cardiovascular-related hospitalizations as well as other causes.<sup>[7]</sup> The main objectives of the current study were to evaluate physicians' level of adherence to evidence-based therapies as recommended in MCPGs-HPT-2013 and to investigate different factors such as demographic, social, and medical socioeconomic influencing patients' nonadherence.

## MATERIALS AND METHODS

This retrospective and observational study was conducted from June 2014 to August 2014 at Hospital Serdang, which is a teaching hospital, located in Selangor, a major state in Malaysia. It provides primary, secondary, and tertiary services. This study gathered data for 6 months from Hospital Serdang online electronic medical records; eHIS live system ( $n = 170$ ) using a specially designed data collection form. The inclusion criteria were all hypertensive patients over 17 years old with or without comorbidities, prescribed with at least one antihypertensive medication by physicians in Hospital Serdang. Diagnosis of HPT and other comorbidities were based on documentation from patients' medical record. Patients with diabetes mellitus type 2 (DM), cardiovascular diseases, chronic kidney disease (CKD), lung disease, dyslipidemia, and obesity were reported individually. Patients having incomplete clinical information, missing medication history and pregnant women were excluded from this study.

### Instruments and tools

The data collection form was specifically designed to accumulate all information regarding the patients' demographic characteristics such as age, gender, ethnicity, and smoking status. The drug prescribing pattern for antihypertensive medications was also listed in the form and it included the following details: Medication prescribed for HPT, all concurrent comorbidities, medication prescribed for the comorbidities, the dosage of the prescribed medications, and contraindication to the antihypertensive medications.

### Adherence guidelines

The physician's compliance with CPGs was measured by comparing the prescribed antihypertensive medications according to MCPGs-HPT-2013, 4<sup>th</sup> Edition (as illustrated in the antihypertensive chart shown in Figure 1). Drugs prescribed to the antihypertensive patients were noted by their generic names. Antihypertensive medication with only one active ingredient was defined as monotherapy, while more than one active ingredient (either in combination or two

different single pills) was defined as polytherapy. A detailed review of the patients' medical records was conducted. Adverse drug reactions and contraindications to the prescribed medications were noted and compared with CPG 2013 to find acceptable rationales for the nonadherence to guidelines. The prescription was then classified as compliant or non-compliant according to the MCPGs-HPT-2013

### Antihypertensive chart

A score of one point was credited to each MCPGs-HPT-2013 compliant prescription, while zero (0) to each non-compliant prescription. The prescriptions were considered compliant to guidelines under the following scenario:

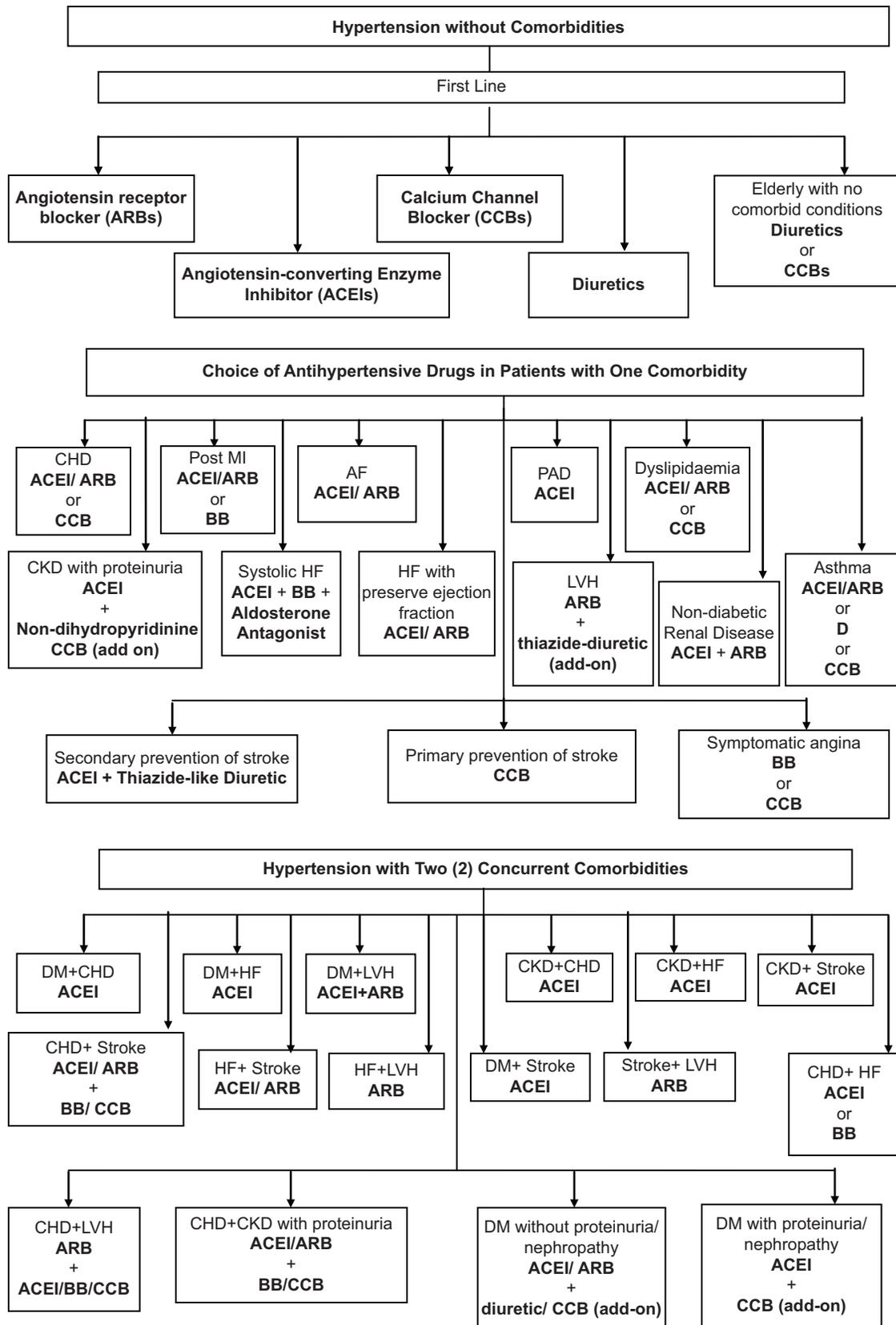
1. The first-line agent for the particular condition was prescribed according to MCPGs-HPT-2013
2. The first-line agents having no contraindication to its use were prescribed according to MCPGs-HPT-2013 to the patients with multiple comorbidities
3. The first-line agent for a particular condition was not prescribed according to MCPGs-HPT-2013 due to adverse drug reactions caused by the recommended drug or any contraindication to its use.

### Statistical analysis

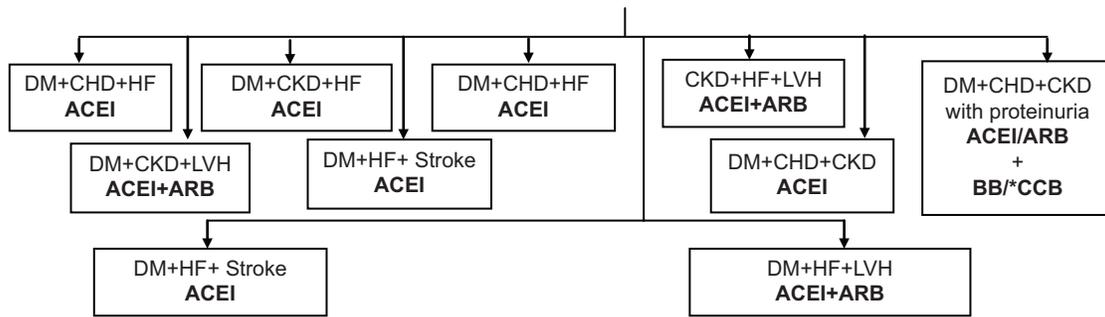
Data collected from e-HIS live system online database were analyzed using Statistical Package for the Social Sciences (SPSS) software version 20.0 for windows. Patients' sociodemographic characteristics such as age, gender, ethnicity, and smoking status were entered as categorical variables. Comorbidities and contraindications to antihypertensive medications were entered as dichotomous categorical data. The prescribing trends of antihypertensive medications, the number of antihypertensive medications prescribed, and the pattern of prescribing antihypertensive medications combination, contraindication to antihypertensive medications of the patients' and physicians' compliance to MCPGs-HPT-2013 were analyzed using descriptive statistics. Categorical data were presented as frequency and percentage while continuous data were reported as mean  $\pm$  standard deviation. Univariate analysis was used and the crude odds ratio (OR) with 95% confidence interval was calculated to investigate the patients' factors affecting the physicians' adherence to MCPGs-HPT-2013. To further assess the relationship between patients' factors and physicians' adherence to the guideline, adjusted OR (with 95% CI) was calculated using a multivariate test (multiple logistic regressions) only for variables with significant correlation from the univariate model.

### Ethics approval

The study commenced in June 2014 after the Clinical Research Centre and the National Medical Research Register for the Ministry of Health (MOH), National Institute of Health's approval (Research ID: 21060).



**Figure 1:** Criteria for measuring physician's compliance with medication recommendations of Malaysian Clinical Practice Guidelines for Hypertension 2013. ACEI: Angiotensin-converting enzyme inhibitors, AF: Atrial fibrillation, ARB: Angiotensin receptor blocker, BB: Beta-blocker, CCB: Calcium channel blocker, CHD: Coronary heart disease, CKD: Chronic kidney disease, DM: Diabetes mellitus, HF: Heart failure, LVH: Left ventricular hypertrophy, MI: Myocardial infarction, PAD: peripheral arterial disease, Proteinuria: >3 g day (*Contd...*)



**Figure 1:** (Continued) Criteria for measuring physician's compliance with medication recommendations of Malaysian Clinical Practice Guidelines for Hypertension 2013. ACEI: Angiotensin-converting enzyme inhibitors, AF: Atrial fibrillation, ARB: Angiotensin receptor blocker, BB: Beta-blocker, CCB: Calcium channel blocker, CHD: Coronary heart disease, CKD: Chronic kidney disease, DM: Diabetes mellitus, HF: Heart failure, LVH: Left ventricular hypertrophy, MI: Myocardial infarction, PAD: peripheral arterial disease, Proteinuria: >3 g day

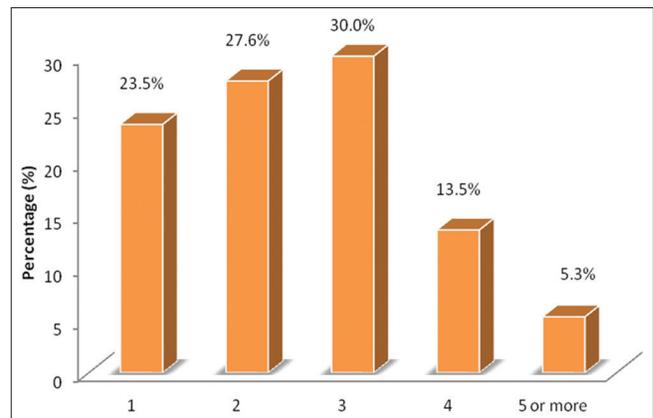
## RESULTS

The mean number of medications per prescription in this study was  $2.49 \pm 1.147$ . Only 40 (23.5%) of the patients were on monotherapy, while 47 (27.6%), 51 (30.0%), 23 (13.5%), and 9 (5.3%) were on 2, 3, 4, and more than 4 antihypertensive medications, respectively [Figure 2].

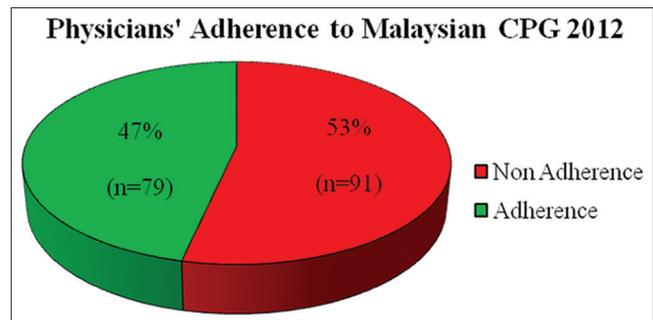
Demographics and clinical characteristics of the patients included in the final analysis are given in Table 1. Only about 79, that is, 47% of the patients received guidelines in accordance with compliant therapy [Figure 3]. On multivariate analysis, we found that CPG adherence had a significant association with the number of comorbidities and the utilization of angiotensin-converting enzyme inhibitors (ACEIs) and have been listed in Table 2.

### Patients' characteristics

Patients who were diagnosed with HPT from January 01, 2014, to May 31, 2014, were identified from the Hospital Serdang online database and were selected for review. A randomly selected cohort of 170 hypertensive patients who met the selection criteria was included in this study. The mean age of our study population was  $59.32 \pm 13.338$  years (range 22–83 years), with 55.9% of the patients aged over 60 years. There was a minor difference of 2.36% in the distribution of female and male hypertensive patients. Malay patients were the highest in number (56.5%), followed by Chinese (26.5%), Indian (14.7%), and others (2.4%). Our findings revealed that the majority of the patients were non-smokers, while only 2 patients were active smokers and 16 were ex-smokers. The mean number of comorbidities per patient in this study was  $2.56 \pm 1.026$ . Most of the patients had 2–3 comorbidities (70%), <15% had only one or no comorbidity, and approximately, another 15% of the patients had 4 or more concurrent clinical conditions as illustrated in Table 1.



**Figure 2:** Number of antihypertensive medications prescribed per patient



**Figure 3:** Percentage of physicians' compliance toward Malaysian clinical practice guidelines for hypertension 2013

## DISCUSSION

Antihypertensive drugs often divided into two main categories, (1) renin-angiotensin-aldosterone system blockers (directly or indirectly), i.e., ACEIs, ARBs, direct renin inhibitors, and  $\beta$ -blockers, and (2) sodium and water eliminators, i.e., diuretics and calcium channel blockers (CCBs).<sup>[8]</sup> ACEIs, which were originally discovered from the Brazilian pit viper's venom, are the first-line treatment or drug of choice in controlling HPT.<sup>[9]</sup> The second drug of choice is ARBs, especially in those patients where ACEIs are intolerant as they do not cause dry

**Table 1:** Patients' demographics and clinical characteristics

Variable	Mean±SD	n (%)
Gender		
Male		83 (48.82)
Female		87 (51.18)
Age	59.32±13.338	
<40		18 (10.6)
40–59		57 (33.5)
Over 60		95 (55.9)
Ethnicity		
Malay		96 (56.5)
Chinese		45 (26.5)
Indian		25 (14.7)
Others		4 (2.4)
Smoking status		
Never		152 (89.4)
Active and ex-smoker		18 (10.6)
No. of comorbidities		
≤ 1		24 (14.1)
2		61 (35.9)
≥ 3		85 (50.0)
Types of comorbidities		
Chronic kidney disease		168 (98.8)
Diabetes mellitus		125 (73.5)
Cardiovascular disease		51 (30.0)
Obesity		50 (29.4)
Dyslipidemia		37 (21.8)
Lung disease		6 (3.5)

**Table 2:** Multivariate analysis for physicians' adherence toward Malaysian clinical practice guidelines for hypertension 2013

Variable	Odds ratio	95% CI	P value
3 comorbidities	2.989	1.003–8.901	0.049
ACEIs	4.075	1.905–8.720	0.000

CI: Confidence interval, ACEIs: Angiotensin-converting enzyme inhibitors

cough like ACEIs.<sup>[9]</sup> CCBs are also considered the best choice for primary HPT, especially in older patients and in patients of African or Caribbean origin.<sup>[10]</sup>  $\beta$ -blockers are the last resort option to treat HPT unless there are other indications such as myocardial infarction or atrial fibrillation. Diuretics are often used as “add on” therapy, especially thiazide diuretics which are commonly prescribed in patients not responding to first and second-line antihypertensive therapies.<sup>[11]</sup>

The study findings showed that 53% of the prescriptions were not according to the recommendations in MCPGs-HPT-2013. This result was comparable to a retrospective cohort study done by Crocker *et al.*,<sup>[12]</sup> where the overall physicians' adherence toward guidelines was only about 57%. However, a different trend was shown in a previous study done at Penang, Malaysia, where an overall fair level of adherence to the MCPGs-HPT-2008 was observed and more than two-thirds (73.5 %) of the total prescriptions written were in compliance to the MCPGs-HPT-2008.<sup>[3,13]</sup>

Overall, diuretics were the most frequently prescribed antihypertensive class in this study. Regarding diuretics prescribing, these findings were aligned with the MCPGs-HPT-2013 that states that diuretics will enhance the efficacy of other classes when used in combination.<sup>[14,15]</sup> CCBs were the second most frequently prescribed class. MCPGs-HPT-2013 recommended ACEIs as the first-line antihypertensive therapy in the most conditions of HPT, with or without comorbidities.<sup>[16,17]</sup>

Despite the demonstrated efficacy and safety, and MCPGs-HPT-2013 recommendations of prescribing ACEIs in DM and renal disease,<sup>[18]</sup> they were underutilized in this study. Only 28.2% of the patients were prescribed with ACEIs. Besides that, thiazide-diuretics were widely used in patients with CKD stage IV and V.<sup>[19]</sup> This practice was not aligned with the MCPGs-HPT-2013 that states that thiazide-diuretics may not be effective in treating patients with GFR <30 ml/min/1.73 m<sup>2</sup>. Furthermore, both ACEI and thiazide-diuretics were prescribed in contraindicated patients with 23.2% and 3.0%, relatively.

Another practice that was not in conjunction with MCPGs-HPT-2013 was the utilization of methyldopa (alpha-adrenergic agonist). Even though methyldopa is only indicated for HPT in pregnancy, a few patients were still being prescribed with the medication.<sup>[20]</sup> Patients' factors that significantly affected the utilization of antihypertensive classes included age, type, and number of comorbidities and when used in combination with other antihypertensive classes.<sup>[21]</sup>

In total, the percentage of physicians who adhered to MCPGs-HPT-2013 was only 47% (as represented in Figure 3). Our results also revealed that physicians' adherence toward the MCPGs-HPT-2013 was affected by the number of comorbidities as well as when patients were prescribed with ACEIs ( $P < 0.05$ , OR = 2.989).

## CONCLUSION

Indeed, HPT is a global public health issue and reviews and guidelines establish the best therapies based on numerous clinical trials to reduce the incidence of HPT and its complications. To improve HPT control, various HPT management guidelines have been published, disseminated, and regularly updated throughout the entire world. These guidelines provide concise, evidence-based

recommendations to the prescribers to achieve optimal HPT control. Despite the positive impact of guidelines' implementation on HPT control, existing literature suggests that patients with HPT are not being treated according to the stipulated guidelines. Observational studies have shown that the health-care providers' attitudes, behavior toward HPT management, and deviation from the CPGs account for more than 66% of the poor control of HPT. The study findings indicate that physicians' adherence to MCPGs-HPT-2013 accounted for 47% and the remaining 53% were nonadherent to the suggestive guidelines by the MOH Malaysia for their hypertensive patients, whereas the prevalence and poor control of HPT are alarmingly high in Malaysia.

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