

## DRUG THERAPY PROBLEMS IN MANAGEMENT OF HYPERTENSIVE OUTPATIENTS ADMITTED TO FOUR INDONESIAN PRIMARY HEALTH CENTERS

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### ABSTRACT

**Objective:** This study aimed to evaluate the antihypertensive utilization and drug therapy problems (DTPs) in the treatment of patients with hypertension.

**Methods:** This prospective analytical study used a self-determined questionnaire to collect 2-month period data of hypertensive patients (n=107) admitted to four primary health centers in Medan (Medan Deli, Helvetia, Glugur Darat, and Teladan). Inclusion criteria were patients diagnosed with hypertension, age  $\geq 18$  years, and under treatment of antihypertensive drugs. Data collected include gender, age, education, the administered antihypertensive drugs, and DTPs. Characteristics of the patients were descriptively analyzed. DTPs were identified based on strand classification system and trustable literature. All analyzes were performed using Statistical Package for the Social Sciences (SPSS, version 19, Chicago, IL, USA) ( $p < 0.05$  was considered significant).

**Results:** Characteristics of the patients: Male, 25.2%; female, 74.8%; mean age,  $61.6 \pm 10.3$  (years). Education: Primary school, 25.2%; junior high school, 17.8%; senior high school, 43.9%; university, 13.1%. The most frequently provided antihypertensive drugs were amlodipine (47.7%) and captopril (22.4%). Overall, there were 66 DTPs experienced by 45.8% of the patients. Patients experienced: 1 DTP, 75.5%; 2 DTPs, 18.3%; 3 DTPs, 2.1%; 4 DTPs, 4.1%. There was no significant association between the patients' education and DTPs,  $p = 0.88$ . The most frequently occurred DTP (47%) was indication without drug therapy in which patients with hypertension Stage 2 only received single antihypertensive drugs mostly was captopril.

**Conclusion:** The most frequently provided antihypertensive drug was captopril. DTPs in the management of hypertensive patients are still high in primary health centers in Medan and need to be resolved.

**Keywords:** Hypertension, Drug therapy problems, Strand classification.

### INTRODUCTION

Hypertension remains a worldwide public health threat, especially in lower-middle income countries including South-East Asia. It is the silent contributor to stroke, cardiovascular diseases, and kidney disorders that ultimately cause inability and even death. Inadequate control and treatment of hypertension are strongly associated with risks for developing stroke and increasing mortality [1,2]. A study indicated that about 35% of adults in South-East Asia have blood pressure (BP) above normal and result in death as many as 1.5 million people per year. It has been proved that the prevalence of hypertension is high in almost all South-East Asian countries of which the highest one was located in Indonesia which reached 41.1% [3].

Treatments of hypertension without referring to established clinical practice guidelines can result in drug therapy problems (DTPs), failure to achieve targeted BP, various complications as previously mentioned, and high consumption of health care costs. DTPs are generally defined as events or circumstances involving drug therapy that actually or potentially interfere with desired health outcomes [4]. DTPs have been classified by different groups with different ways of classification in various countries; four of the most widely applied classifications are Strand (in the US), Apoteket (in Sweden), Granada-II (in Spain), and Pharmaceutical Care Network Europe (PCNE) (in Europe) classification systems. Nevertheless, these classification systems deal with drug choice, drug dosage, drug interaction, adverse drug reactions, and adherence problems.

Few studies on DTPs applying different classification methods have been undertaken and associated with patients' outcomes, as well as healthcare costs. A study performed in Jepara, Indonesia in 2007 indicated that 64 (77.11%) of 83 hypertensive patients with Type 2 diabetes mellitus

experienced DTPs of which unsafe drug choice contributed 49.19% of the overall incidence [5]. Subsequently, a pooled analysis proved that incorrect drug doses reached 20.4% of the overall DTPs occurrence [6]. Ernst and Grizzle [7] found that every US \$1 spent for medication required US \$1.77 to resolve DTPs. Up to now, there have been limited studies conducted locally to identify, analyze, and document DTPs in the management of patients with hypertension. Therefore, DTPs become critical issues and challenge to healthcare providers.

Kidney Disease Quality Outcomes Initiatives Clinical practice guidelines in Guidelines 2 and 13 state that strategies are emphasized on identification and prevention. These statements imply that risk factors for kidney disease, one of which is hypertension, should be identified and managed properly to prevent further progression of kidney damage. Thus, medication reviews, evaluation, and resolving DTPs in the management of hypertension are the main points required to be implemented to improve treatment outcomes and to reduce costs. Subsequently, recommendations to resolve the DTPs, based on the findings, should be informed by pharmacists to health care providers as well as patients to improve health services [8,9].

In relation to the above problems, the present study focused on antihypertensive utilization, identification, and analysis of DTPs in the management of hypertensive patients as well as the association between the patients' education and occurrence of DTPs in four primary health centers in Medan.

### METHODS

This study was initiated with a preliminary survey undertaken by the researchers to obtain the frequency of hypertensive patients' admission

to primary health centers located in Medan, North Sumatera. It was found that four of the health centers with the highest admission of hypertensive patients were Medan Deli, Helvetia, Glugur Darat, and Teladan. Therefore, these health centers were selected as locations of the study. The study was approved by the Department of Health North Sumatera and Health Research Ethical Committee of North Sumatera, School of Medicine, University of Sumatera Utara, Indonesia. Patients diagnosed with hypertension, age  $\geq 18$  years, and under treatment of antihypertensive drugs were included in this study. This prospective analytical study was undertaken by distribution a self-determined questionnaire to hypertensive patients (n=107) for a 2-month period in the four primary health centers. Data collected to obtain the characteristics of the patients were gender, age, and education of the patients. The administered antihypertensive drugs and DTPs were assessed. Characteristics of the patients were descriptively analyzed. DTPs, but limited only to antihypertensive drugs provided to the patients, were identified and analyzed based on Strand classification system (including medical condition without receiving drug therapy, receiving drug therapy without indication, too low doses, too high doses, ineffective provided drug, adverse drug reaction, non-compliance/non-adherence) [10] by referring to trustable literatures [11,12] and guidelines for the management of hypertension provided by The Seventh Report of the Joint National Committee (JNC 7) on prevention, detection, evaluation, and treatment of high BP [13]. All analyzes were performed using Statistical Package for the Social Sciences (SPSS, version 19, Chicago, IL, USA) ( $p < 0.05$  was considered significant).

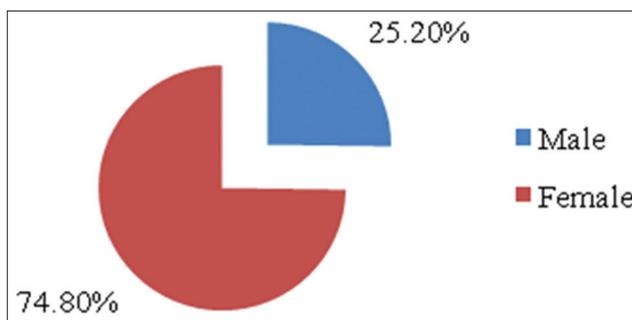
**RESULTS**

During the study period, 132 admissions of patients with hypertension were found of which 107 patients fulfilled the inclusion criteria. Characteristics of the patients by gender are shown in Fig. 1. It was obtained that female had higher admission (74.8%) compared to those of male (25.2%). Mean age of the hypertensive patients was  $61.6 \pm 10.3$  (years). 57 of the hypertensive patients were in Stage 1, and 50 patients were in Stage 2. According to education, characteristics of the patients are demonstrated in Fig. 2. As shown in Fig. 2, about a quarter of them (25.2%) graduated from primary schools. Less than one fifth of them (17.8%) have junior high school education. Most of the hypertensive patients (43.9%) graduated from senior high schools. Only 14 (13.1%) of them graduated from universities.

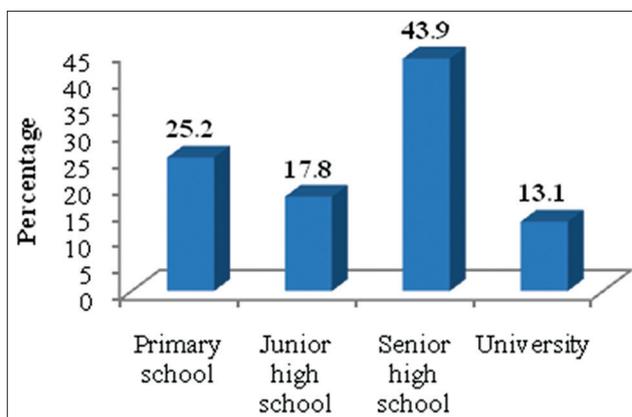
Listed in Table 1 are the antihypertensive drugs in decreasing order provided to the patients with hypertension. As shown in Table 1, the most frequently provided antihypertensive drug was amlodipine (47.7%) followed by captopril (22.4%), and their combination (16.8%). Combination therapy of hydrochlorothiazide and amlodipine was only provided to 5.6% of the hypertensive patients. As also listed in Table 1, combination therapy of HCT and amlodipine was only provided to 2.8% of the patients. Each of the rest antihypertensive combinations was only provided to one patient. The utilization pattern of the antihypertensive drugs in the treatment of the hypertensive patients is mostly affected by the disease severity as recommended by the National Formulary as well as JNC 7.

With regards to DTPs, overall, there were 66 DTPs experienced by 49 (45.8%) of the hypertensive patients as shown in Table 2. The 66 DTPs experienced by the 49 hypertensive patients vary from 1 to 4 occurrences. 37 (75.5%) of the 49 patients experienced one DTP. 9 (18.3%) of the 49 patients experienced 2 DTPs. 1 (2.1%) of the 49 patients experienced 3 DTPs. 2 (4.1%) of the 49 patients experienced 4 DTPs. There was no significant association between the patient's education and the number of DTPs occurrences,  $p = 0.88$ . In details, the categories of the DTPs in decreasing order experienced by the hypertensive patients are listed in Table 2.

Among the 66 DTPs identified, the most frequently occurred DTP (47%) felt into the first category (indication without drug therapy). In this case, each of these patients with hypertension Stage 2 only received single antihypertensive drugs mostly was captopril. Ineffective outcome (no



**Fig. 1: Characteristics of the hypertensive patients by gender (n=107)**



**Fig. 2: Characteristics of the hypertensive patients by education (n=107)**

**Table 1: Antihypertensive drugs provided to the hypertensive patients (n=107)**

Antihypertensive drugs	Utilization	
	Frequency	Percentage
Amlodipine	51	47.7
Captopril	24	22.4
Captopril+amlodipine	18	16.8
Nifedipine	6	5.6
HCT+amlodipine	3	2.8
Micardis (telmisartan)+lisinopril	1	0.9
Amlodipine+micardis	1	0.9
Amlodipine+furosemide	1	0.9
Amlodipine+bisoprolol	1	0.9
Nifedipine+captopril	1	0.9
Total	107	100.0

HCT: Hydrochlorothiazide

BP reduction) was observed in 21.2% of the overall DTPs, even though the patients were on Stage 2 and provided captopril and amlodipine combination. In addition, non-adherence of the hypertensive patients to the prescribed medications was also observed in 13.6% of the DTPs occurred. Subsequently, adverse drug reaction (cough) was noticed in 9.1% of the DTPs occurred. In addition, drug therapy without indication was detected in 7.6% of the DTPs experienced by the patients. Too low dose of captopril was only noticed in 1.5% of the DTPs. None of the hypertensive patients experienced problems with too high dose and drug interaction.

**DISCUSSIONS**

By gender, it was obtained that female had higher admission (74.8%) compared to those of male (25.2%). This finding supports previous

Table 2: Category of DTPs in decreasing order experienced by the hypertensive patients

DTP category	Frequency	Percentage	Description
Indication without drug therapy	31	47.0	Provision of single antihypertensive drugs (mostly captopril) to patients with Stage 2
Ineffective provided drug	14	21.2	Ineffective combination of captopril and amlodipine provided to patients with Stage 2
Non-adherence	9	13.6	Patients stop taking antihypertensive drugs
Adverse drug reaction	6	9.1	Cough
Drug therapy without indication	5	7.6	Provision of captopril and amlodipine combination to patients with Stage 1
Too low dose	1	1.5	too low dose of captopril (12.5 mg per 12 hrs)

DTP: Drug therapy problems

studies on hypertensive patients undertaken in Malaysia, USA, and Ghana [14-16]. The present study revealed that mean age of the hypertensive patients was 61.6±10.3 years. Mean age of hypertensive patients varies from one patient group to another. A retrospective study conducted on hypertensive patients but with the complication of Type 2 diabetes in a tertiary hospital revealed that the mean age of the patients was 62.3±12.7 years [17]. Other study proved that the mean age of hypertensive patients was 62.2±9.7 years [18]. Also, another study on hypertensive patients with coronary heart disease conducted at a tertiary care teaching hospital in Chidambaram, South India found that the mean age of the hypertensive patients was 58.78±12.53 years [19].

The utilization pattern of antihypertensive drugs varies of which amlodipine (47.7%), captopril (22.4%), and their combination (16.8%) were the most frequently provided antihypertensive drugs to the hypertensive patients. Few studies on utilization of antihypertensive drugs in patients with hypertension have been undertaken elsewhere. A prospective, randomized, controlled study undertaken in a private hospital located in Tamil Nadu found that the most widely provided antihypertensive drug to patients with hypertension was captopril (80.2%) [18]. A similar study conducted in a tertiary care teaching hospital Chidambaram, South India found that calcium channel blocker (amlodipine), beta blocker (atenolol or metoprolol or carvedilol), and angiotensin receptor blocker (telmisartan) were the most frequently prescribed drugs in hypertensive patients [19].

The present study proved that 49 (45.8%) of the hypertensive patients experienced 66 DTPs felt into seven categories of DTPs in which three of the most frequently occurred in decreasing order were indication without drug therapy, provision of ineffective antihypertensive drugs, and non-adherence of the hypertensive patients to the treatment. 47% of the overall DTPs were indication without drug therapy in which the patients were on Hypertension Stage 2, but they were only provided single antihypertensive drugs, mostly was captopril. According to clinical practice guidelines, these patients should be provided at least two antihypertensive combinations [13]. Failure to reduce BP was the second highest incidence (21.2%) of DTPs found in the present study, even though a combination of antihypertensive drugs (captopril and amlodipine) have been provided to the hypertensive patients with Stage 2. In this condition, other classes of antihypertensive drugs may be required to improve the patients' outcome [20]. However, due to resources limitation available in these health centers, these antihypertensive classes were not provided to these patients. In addition, non-adherence of the hypertensive patients to the prescribed medications contributed to 13.6% of the DTPs occurred. In this case, the patients stopped taking antihypertensive drugs because they either felt that they were cured or missed doses due to irregular visits to physicians. Few studies proved that provision of counseling to hypertensive patients improved their adherence to their medications [21-23]. Adverse drug reaction (cough) contributed to 9.1% of the overall DTPs occurred. This adverse drug reaction was noticed in patients provided captopril therapy. Other classes of antihypertensive drugs should be provided if the patients were not complied with the treatment. In addition, drug therapy without indication (drug overuse) was detected in 7.6% of the DTPs experienced by the patients. In this case, patients with Stage 1 received combination therapy. Risk for sudden hypotension may occur in a certain patient group such as older

persons. Thus, caution is required. Single antihypertensive drug should have been initially provided to these patients. When the provision of a single drug therapy is inadequate to lower BP, combination therapy should be provided instead. Too low dose of captopril was only noticed in 1.5% of the DTPs. Frequently BP monitoring should be practiced to consider if dose adjustment is required [13].

This study was limited by the relatively a short time horizon that may have impacts on the results of the study.

## CONCLUSIONS

Various classes of antihypertensive drugs were provided to the patients with hypertension. The three most frequently provided antihypertensive drugs were amlodipine (47.7%), captopril (22.4%), and their combination (16.8%). Nearly half of the patients experienced DTPs. The most frequently occurred DTP (47%) felt into the first category (indication without drug therapy) in which patients with hypertension Stage 2 only received single antihypertensive drugs. DTPs occurrence in the management of patients with hypertension in primary health centers in Medan was still high and need to be resolved.

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