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INTRODUCTION Patients with hypertension often show evidence of insulin resistance, and up to 75% of adults with diabetes also have hypertension¹. Many factors can increase the risk of hypertension, one of which is diabetes mellitus (DM)². Peripheral artery resistance and body fluid volume increase in DM patients, both of these mechanisms can increase blood pressure³. Type 2 diabetes mellitus (T2DM) is associated with a high risk of mortality in hypertension patients⁴. Hypertension treatment aims to reduce mortality and morbidity, where drug selection is essential in therapy success⁵. Some references show that the potential for drug-related problems increases in patients with chronic diseases, including T2DM^{6,7}.

Our previous research has found that T2DM is a common comorbid disease in hypertension patients⁸. However, there is no research on drug-related problems in hypertension with comorbid T2DM patients at Primary Health Care Center at Batununggal District, Bandung. Therefore, researchers are interested in researching drug-related problems in hypertension with comorbid T2DM patients, which has never been done before.

This research aimed to find whether there are drug-related problems in hypertension with comorbid T2DM patients, providing information for other health professionals to improve patients' service and achieve treatment targets. MATERIALS AND METHODS Materials The tool for data collection was a laptop, and the materials used were a prescription sheet of hypertension with comorbid T2DM patients, references, i.e., research journals, and textbook (Pharmacotherapy: A Pathophysiology Approach)⁹. The data for the study was taken from a prescription sheet.

Data collected included patient name (initials), gender, age, diagnosis, drugs data (name, dosage strength, dosage form, quantity, and frequency of use). A prescription sheet of hypertension comorbid T2DM patients between January and December 2019 was obtained with a total of 303 samples. Methods The research conducted was an observational study with retrospective data collection and descriptive analysis. The aim was to identify any drug-related problems in hypertension with comorbid T2DM patients at Primary Health Care Center Batununggal District Bandung. The samples taken were adjusted to the inclusion and exclusion criteria that had been set.

Inclusion criteria: Patients aged 30-75 years, Patients diagnosed with hypertension with comorbid T2DM, and patients treated in January-December 2019. Exclusion criteria: Patients who were pregnant or breastfeeding and patients with an incomplete prescription. Data that met the inclusion criteria were taken and analyzed quantitatively (number of patients based on gender, age, and diagnosis; data of drug use; percentage of drug-related problems case) and qualitatively (analysis of drug-related problems).

This study has received ethical approval from The Health Research Ethics Committee of the Faculty of Medicine of Universitas Jenderal Achmad Yani with reference number 032/UM4.10/2020.

RESULTS AND DISCUSSION The research was conducted at Primary Health Care Center at Batununggal District Bandung. Data used in this research were from January to December 2019, with the number of samples obtained as many as 268 met inclusion criteria. The samples used were patients with a diagnose of hypertension with comorbid T2DM according to the inclusion criteria. Table I showed that from 268 patients, 69 patients (25.75%) were male, and 199 patients (74.25%) were female. These results were in line with the previous research conducted at the same Primary Health Care Center in 2019, in which the most treated patients were female patients.

Likewise, the result of Riset Kesehatan Dasar (Riskesdas) 201810, the percentage of hypertension prevalence in female patients was higher than in male patients. The incidence of hypertension is higher in women because in the menopause phase, there is a hormonal imbalance, which is a decrease in the ratio of estrogen and androgen, which causes an increase in the release of renin, which will lead to an increase in blood pressure¹¹. Apart from gender, age also affects the incidence of hypertension, the age range 55-90 years has a four times higher risk than those aged 18-54 years¹².

The patients taken were at least 30 years old because, from previous research⁸, patients admitted to Primary Health Care Center at Batununggal District Bandung were at least 30 years old. In this study, patients aged 60-75 years (61.20%) had the most hypertension due to increasing age, structural and functional changes that caused the arteries to lose their flexibility. When the flexibility decreases, the blood vessels become stiff; therefore, the blood with each heartbeat is forced through the narrow blood vessels, increasing blood pressure¹³.

Factors like gender, smoking, alcohol consumption, overweight, and obesity also were associated with hypertension, diabetes, and dyslipidemia¹⁴. The majority of hypertension with comorbid T2DM patients suffer from other comorbidities. Due to this multi-diagnosis condition, the patient takes a wide range of drugs and increases the risk of drug-related problems¹⁵. Another comorbidity with the highest percentage in hypertension with comorbid T2DM patients was hyperlipidemia (31.34%). Table I.

Characteristics of hypertension patients with comorbid T2DM at Primary Health Care Center at Batununggal District Bandung

Parameters	Number of Patients	Percentage (%)
Gender		
Male	69	25.75
Female	199	74.25
Total	268	100
Age (year)		
30-44	4	1.49
45-59	100	37.31
60-75	164	61.20
Total	268	100
Diagnose		
Hypertension + T2DM	86	32.09
Hypertension + T2DM + Other		

Comorbidities _182_67.91 __Total _268_100 __Other comorbidities __Hyperlipidemia _84_31.34 __Hyperuricemia _23_8.58 __Joint and Connective Tissues Diseases _51_19.03 __Gastrointestinal System Diseases _22_8.21 __Skin and Subcutaneous Tissue Diseases _13_4.85 __Respiratory System Diseases _10_3.73 __Infectious Diseases _6_2.24 __Gastrointestinal Diseases _5_1.87 __Circulatory System Diseases _4_1.49 __Eye Diseases _4_1.49 __Genitourinary System Diseases _2_0.75 __Psychiatric Diseases _1_0.37 __Others (Hemoptysis; Cough; Other chest pain; Fever, unspecified; Headache; Localized edema; Obesity; Superficial injury of shoulder and upper arm; Disorders of vestibular function) _20_7.46 __Total _268_100 __ Tables II and III showed data on antihypertension and antidiabetic use. All hypertension with comorbid T2DM patients uses antihypertension and antidiabetic drugs by the oral route of administration, either single or in combination.

In addition, hypertension with comorbid T2DM patients with other comorbidities also receives medication according to the patient's diagnosis. Table II. Data of antihypertension used in patients with comorbid T2DM at Primary Health Care Center at Batununggal District Bandung Drug Name _Routes of Drug Administration _Number of Patients _Percentage (%) __Amlodipine _Oral _264_98.51 __Amlodipine + Captopril _Oral _4_1.49 __Total _268_100 __ Table III.

Data of antidiabetic used in patients with comorbid T2DM at Primary Health Care Center at Batununggal District Bandung Drug Name _Routes of Drug Administration _Number of Patients _Percentage (%) __Metformin _Oral _240_89.55 __Glimepiride _Oral _1_0.37 __Metformin + Glimepiride _Oral _18_6.72 __Metformin + Glibenclamide _Oral _9_3.36 __Total _268_100 __ Table IV showed data of drug uses based on drug class. Besides antihypertension and antidiabetic drugs that were often used, from 268 patients, there was 170 use of vitamins: B1, B6, B12, or B complex.

Vitamin B complex, B12, and B1 were widely used as supporting vitamins in reducing blood pressure and cholesterol levels. Vitamin B12 is prescribed to reduce complaints of aches suffered by patients and meet vitamin intake to avoid vitamin B12 deficiency¹⁶. Vitamin B12 deficiency can increase homocysteine ??levels, where high homocysteine ??levels can increase the risk of increased blood pressure through decreased availability of nitric oxide, thereby interfering with vascular vasodilation. Hyperhomocysteinemia can also damage the endothelium and cause atherosclerosis; therefore, vitamin B12 needs to be added^{17,18}.

In hypertension with comorbid T2DM patients, pharmacists can also provide advice on non-pharmacological therapies such as lifestyle modification. Besides lowering blood pressure in patients with hypertension, lifestyle modification can also reduce blood

pressure progression to hypertension in patients with prehypertension blood pressure¹⁹. A vital lifestyle modification that appears to lower blood pressure is weight loss for obese or obese individuals; adopt the DASH (Dietary Approach to Stop Hypertension) diet rich in potassium and calcium; low sodium diet; physical activity; and consume only a little alcohol. In several patients with reasonable blood pressure control with single antihypertensive drug therapy, reducing salt and weight can relieve patients from using the drugs²⁰.

Lifestyle modification alone is an appropriate therapy for patients with prehypertension. Patients diagnosed with stage 1 or 2 hypertension should be placed on concurrent lifestyle modification and drug therapy²¹. Table IV. Data of drug used based on drug class in patients with comorbid T2DM at Primary Health Care Center at Batununggal District Bandung

Drug Class	Routes of Drug Administration	Number of Patients	Percentage (%)
Antidiabetic	Oral	295	27.16
Antihypertension	Oral	272	25.05
Vitamin	Oral	170	15.65
Antihyperlipidemia	Oral	79	7.27
Analgesics			
Antipyretic	Oral	68	6.26
NSAID	Oral	34	3.13
Antihistamine	Oral	30	2.76
Antihyperuricemia	Oral	24	2.21
Cough medicine	Oral	23	2.12
Calcium Lactate	Oral	23	2.12
Antacids	Oral	17	1.57
H2 Receptor Antagonist	Oral	7	0.64
Proton Pump Inhibitor	Oral	7	0.64
Antibiotics	Oral	5	0.46
Potent Diuretic	Oral	4	0.37
Antivertigo	Oral	4	0.37
Antidiarrheal	Oral	4	0.37
Antiemesis	Oral	3	0.28
Laksative	Oral	1	0.09
Antifungi	Topical	6	0.55
Corticosteroids	Topical	3	0.28
Antibiotics	Topical	3	0.28
Antibiotics	Ocular	4	0.37
Total Usage		1086	100

Figure 1 shows the percentage of drug-related problems cases in patients with comorbid T2DM at Primary Health Care Center at Batununggal District Bandung.

Problems related to the drugs analyzed were improper drug selection, overdose, subdose, and drug interactions. There are no cases of improper drug selection because patients received drugs according to therapy guidelines and drugs available at Primary Health Care Center at Batununggal District Bandung. There are also no cases of subdose. Based on the analysis results, it was found that 1 case (0.37%) out of 268 patients experienced problems related to drug overdose, in which the patient received amlodipine 15 mg/day. The maximum dose of amlodipine is 10 mg /day²². / Figure 1.

Percentage of drug-related problems cases in patients with comorbid T2DM at Primary Health Care Center at Batununggal District Bandung In addition to overdoses, a potential drug-related problem is drug interactions. Figure 1 showed that 34 cases (12.69%) out of 268 patients have potential drug interactions. Based on the analysis results in Table V, there was an interaction between amlodipine and non-steroidal anti-inflammatory drugs like diclofenac sodium and mefenamic acid. Non-steroidal

anti-inflammatory drugs can increase blood pressure and reduce the hypotensive effect of antihypertension^{23,24}.

These results can be considered so that the drug administration service to patients also provides suggestions for monitoring blood pressure. Home blood pressure monitoring (HBPM) is a self-monitoring tool recommended for patients with hypertension²⁵. Table V. Potential drug interactions in patients with comorbid T2DM at Primary Health Care Center at Batununggal District Bandung Drug Interactions _Effects of Drug Interactions²⁴ _Treatment of Drug Interactions _Number of Patients _Amlodipine + Sodium Diclofenac _NSAIDs can increase blood pressure and reduce the hypotensive effect of antihypertension _Blood pressure monitoring _16 _Amlodipine + Mefenamic Acid _NSAIDs can increase blood pressure and reduce the hypotensive effect of antihypertension _Blood pressure monitoring _18 _Total _34 _ The results in this study show a slight variation compared to other similar studies conducted in other locations.

Other research results showed that drug-related problems with the highest prevalence in clinical practice were caused by drug or dose selection²⁶. Another study in patients with hypertension showed that the most identified drug-related problem was drug interactions²⁷. At the same time, other research showed that the most common drug-related problems that occurred in T2DM with hypertension were insufficient awareness of health and diseases (26%), drug choice problems (23%), dosing problems (16%), and drug interactions (16%)²⁸. Differences in research locations are important factors related to the types of drug-related problems encountered, especially for hypertensive patients with comorbid T2DM.

CONCLUSION In the January-December 2019 period at Primary Health Care Center Batununggal District Bandung, drug-related problems on hypertension with comorbid T2DM patients were overdose and potential drug interactions. The pharmacist's role is needed in identifying drug-related problems and being able to communicate these problems with other health professionals. It is recommended to carry out further research at the same health center or other health centers in order to obtain a more comprehensive conclusion.

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