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Predictors of Blood Pressure Target Achievement in Tolaki and Muna Ethnic Groups Undergoing Candesartan Cilexetil Monotherapy: A Quasi-Experimental Study

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Abstract

Therapy adherence, sociodemographic factors, and lifestyle are factors that influence the achievement of blood pressure targets in hypertensive patients. This study aims to compare and examine the impact of therapy adherence, Sociodemographic, ethnicity, and lifestyle on the achievement of blood pressure targets in hypertensive patients of Muna and Tolaki ethnicities undergoing candesartan cilexetil monotherapy. This study employed a quasi-experimental design with a comparison group approach. A total of 147 patients were selected via consecutive sampling and categorized by ethnicity: Tolaki (n = 75) and Muna (n = 72). Both groups received a standardized dose of Candesartan Cilexetil (8 mg). The primary outcome was the change in blood pressure from baseline (pretest) to day 30 (posttest). Adherence, monitored via pill count, along with sociodemographic and lifestyle factors, was analyzed as a covariate to ensure a robust evaluation of the treatment's clinical impact across both ethnic groups. There was no significant difference in therapy adherence between participants of both ethnicities (p = 0.78). However, Tolaki participants experienced a greater reduction in 30-day systolic and diastolic blood pressure compared to Muna participants (p = 0.00). Furthermore, a greater percentage of Tolaki participants achieved blood pressure therapy targets (76%) compared to Muna participants (15.28%) (p < 0.001). Multivariate logistic regression analysis revealed that two variables that most significantly influence the attainment of blood pressure objectives are ethnicity (Tolaki ethnicity) (OR 21.44, 95% CI 6.69–53.40, and p=0.00) and a high level of therapy adherence (OR 10.89, 95% CI 2.96–40.07, and p=0.00). Ethnicity and therapy adherence are two important factors that need to be considered in efforts to achieve blood pressure therapy targets in the Tolaki and Muna tribes undergoing candesartan cilexetil monotherapy.

Keywords: Candesartan cilexetil; Ethnicity; Hypertension; Lifestyle; Sociodemographic; Therapy adherence

1. INTRODUCTION

It is essential to understand the clinically important factors related to blood pressure control in order to achieve the goals of hypertension therapy (Huguet et al., 2022). The main approach for successful hypertension therapy is controlling blood pressure using a

recommended lifestyle plus adherence to antihypertensive therapy (Bruno et al., 2018). Several studies indicate that lifestyle modifications, including reduced alcohol and sodium intake, smoking cessation, appropriate physical activity, and dietary adjustment, support the effectiveness of drug therapy and the achievement of target values (Blumenthal et al., 2021; Flack & Buhnerkempe, 2022).

Compliance with antihypertensive treatment is crucial for maintaining blood pressure regulation. Some reasons for poor compliance are not being able to start pharmacotherapy, taking antihypertensive drugs that do not follow the prescribed treatment plan, and not wanting to stick with long-term therapy (Alsofyani et al., 2022; Choudhry et al., 2022). Over 50% of individuals with hypertension discontinue their antihypertensive treatment within the first year after diagnosis, and only 25% adhere to the compliance standard of maintaining at least 80% of the prescribed antihypertensive regimen. This non-compliance results in around 75% of hypertension patients failing to attain adequate blood pressure management, hence preventing the achievement of therapeutic objectives (Pallangyo et al., 2022). The consequences of non-adherence to antihypertensive treatment in the long term are organ damage, decreased quality of life, death, increased hospitalization, and healthcare costs (Kulkarni & Graggaber, 2022).

Race and ethnicity are Sociodemographic factors that must be taken into account in clinical practice (Borrell, 2021). The JNC 8 hypertension treatment guidelines recommend different antihypertensive use in non-black populations and black populations with newly diagnosed hypertension, whether or not they have diabetes. Angiotensin Receptor Blockers/ARBs and Angiotensin-converting enzyme (ACE) inhibitors are not advised for use in hypertension monotherapy in Black individuals (Abel, 2015). The NICE Guidelines (2019) state that people with hypertension with or without diabetes of Black African or African-Caribbean ethnicity are advised to consider not using ARBs and ACE inhibitors as monotherapy. Results of an emulation analysis of the reference trial (Ontarget) in ethnic groups in the UK showed greater blood pressure reduction after initiation of treatment in white individuals compared with black and South Asian ethnic groups (Baptiste et al., 2024).

Genetic polymorphisms in metabolizing enzymes, transporters, or receptors at the site of drug action are a significant contributor to interethnic variability in drug pharmacokinetic profiles, even among individuals of the same ethnicity. Genetic variations significantly influence therapeutic effects and cause varying side effects or toxic effects in individuals with the same disease (Bernard et al., 2006). The CYP2C9 enzyme accounts for approximately 20% of the total cytochrome protein in liver microsomes and is responsible for the metabolism of approximately 25% of currently used drugs, including antihypertensives in the ARB class (Ingelman et al., 2007; Kim et al., 2017). The CYP2C9*2 and CYP2C9*3 alleles are clinically relevant variants associated with decreased enzyme activity and altered drug efficacy. Several studies have shown that the frequency of CYP2C9 alleles varies across populations (Bae et al., 2011; Lee et al., 2002).

In a previous study, candesartan was the only ARB among the three most frequently prescribed and routinely purchased antihypertensive drugs in 20 pharmacies across 10 sub-districts in Kendari City (Southeast Sulawesi) from January 2020 to March 2021 (Leorita et al.,

2024). The basis for selecting candesartan as the antihypertensive studied. Candesartan is metabolized by the enzyme CYP2C9, so its efficacy in each ethnic population may vary. Two studies involving Japanese patients with essential hypertension showed that candesartan was effective in lowering blood pressure. The use of candesartan cilexetil monotherapy for 4 to 8 weeks resulted in a reduction in systolic/diastolic blood pressure of more than 20/10 mmHg in 72% of patients. At the same time, another study found that candesartan 8 mg, administered as monotherapy for 12 weeks, was able to reduce blood pressure by 13.9/7.8 mmHg (Ogihara et al., 1999; Rakugi et al., 2013). Different results were obtained from a study involving African-American hypertensive patients at week 8; candesartan was only able to reduce systolic and diastolic blood pressure by an average of 6.4/5.1 mmHg (Association of Black Cardiologists (ABC) Candesartan Study Group, 2000).

Research on the effectiveness of antihypertensives and factors influencing the achievement of blood pressure targets in indigenous ethnic groups living in Eastern Indonesia is still limited, even though indigenous ethnic groups in this region are very diverse, both physically and in terms of lifestyle. Research conducted on the Tolaki and Muna ethnic groups reveals that the effectiveness of candesartan in lowering blood pressure varies significantly, with an average reduction in systolic and diastolic blood pressure of 33.76/14.67 mmHg in the Tolaki ethnic group, compared to 10.35/5.47 mmHg in the Muna ethnic group. The prevalence of Tolaki people achieving blood pressure therapy targets is higher than that of the Muna ethnic group. Hypertension sufferers in both ethnic groups show good tolerability of candesartan (Leorita *et al*., 2024). However, a previous study did not provide information on the differences in adherence levels, sociodemographics, and lifestyle of hypertensive patients between the two ethnic groups. Additionally, the impact of these factors on achieving blood pressure targets remains unclear. Therefore, research is needed that aims to understand the comparison and impact of medication adherence, sociodemographics, and lifestyle in achieving blood pressure therapy targets in hypertensive patients from the Tolaki and Muna ethnic groups receiving candesartan cilexetil monotherapy.

2. MATERIAL AND METHODS
2.1. Research design and population

This research design used a quasi-experimental design with a comparison group approach (**Figure 1**). Research conducted from August 2022 to July 2024, in seven health service units in Kendari city, Indonesia, consisting of six Posyandu Lansia (integrated community health centers for the elderly) and one general hospital (general poly). The population in this study consisted of all hypertension sufferers from the Tolaki and Muna tribes who were recorded in medical records or patient ledgers at the seven health service units where the study was conducted. Recruitment of participants used a consecutive sampling method, with inclusion criteria having to have primary hypertension or hypertension along with type 2 diabetes mellitus (DM type 2), uncontrolled blood pressure (>140/90 mmHg), irregular use of antihypertensives, have had hypertension for less than 3 years, not pregnant, native to the Tolaki or Muna tribe, and be at least 18 years old. The ethnic requirement is the original third generation of the Tolaki

or Muna ethnicity. One hundred forty-seven participants met the inclusion criteria. The study subjects were divided into two groups based on their ethnic background: the Muna ethnic group (n = 72) and the Tolaki ethnic group (n = 75). All subjects gave written informed consent to participate in this study. The local university's research ethics commission (Halu Oleo University) has approved the research procedure (Approval no.   075   /   UN29.17.1.3/ETIK/2021).
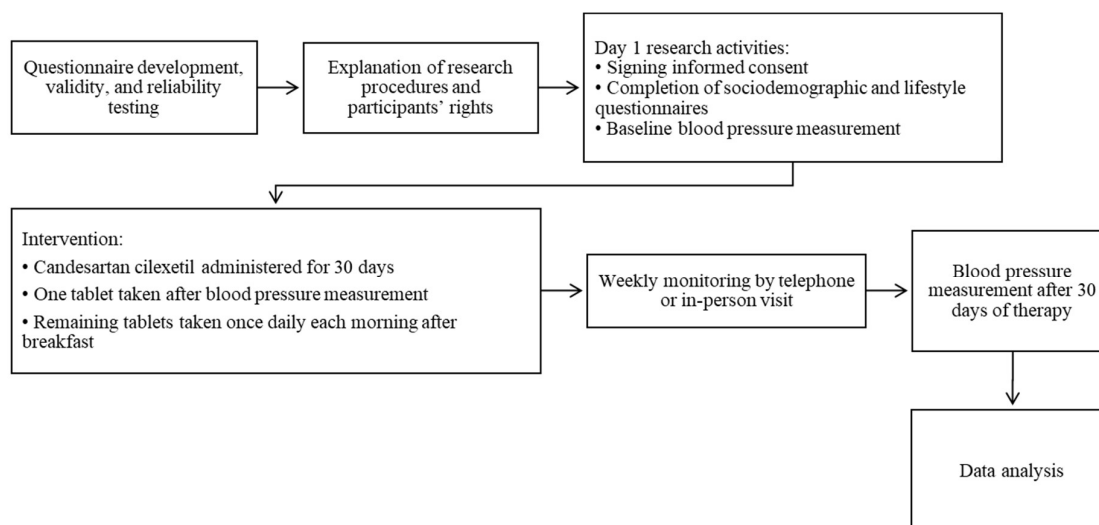

Figure 1. Study flowchart for blood pressure target achievement in Tolaki and Muna ethnic groups.

2.2. Preparation, validity, and reliability testing of questionnaires

The primary researcher developed the questionnaire based on theories regarding sociodemographic and lifestyle factors that influence blood pressure target achievement in patients with hypertension. After the questionnaire was completed, it was submitted to a team of experts for assessment of its feasibility and suitability in relation to the theory. The lifestyle questionnaire encompasses alcohol consumption habits, smoking behavior, physical activity, staple foods, traditional medicine use, and habits related to vegetable and fruit consumption, while the Sociodemographic questionnaire includes data on age, gender, occupation, education level, ethnicity, and type 2 diabetes comorbidities. Before the main study was conducted, the questionnaire was validated using a pilot test on 30 respondents who met the inclusion criteria. Validity testing was conducted using the Pearson Product-Moment correlation method. Question items were declared valid if the correlation coefficient (r count) was greater than the r table value at a significance level of 5%. Reliability was tested using Cronbach's alpha; if the alpha value was greater than 0.600, the instrument was considered reliable.

2.3. Data collections and outcomes

The study began with an explanation of the study's procedures, the subjects' rights, voluntary participation, and the subjects' right to stop at any time. Afterward, all subjects who agreed to participate signed an informed consent and completed two questionnaires: a

sociodemographics questionnaire and a lifestyle questionnaire. The research team provided counseling to all research subjects regarding the importance of adhering to the candesartan cilexetil therapy regimen, potential side effects, and advised them to contact the research team immediately if they experienced any adverse effects. The contact numbers of the researchers, doctors participating in the research, and nurses at the elderly health post are attached to the medicine box. The top was taken home.

Each research subject received 30 caplets of 8 mg candesartan cilexetil on the first day of the study. After the initial blood pressure measurement, all study subjects consumed one 8 mg candesartan cilexetil caplet, and 29 caplets were distributed to them to take home. Each day, after breakfast, the research subjects are required to consume one caplet of candesartan cilexetil. On Day 30, the final day of the therapy, the research subjects were asked to bring their medication box. The pill count form was used to record the quantity of candesartan cilexetil 8 mg caplets that were still present in the medication box. The caplet number of the compliance ratio method was used to measure compliance. Dividing the number of caplets taken by the number of caplets given at the start of the study, and then multiplying the result by 100. The consumption of ≥ 80% of the candesartan cilexetil caplets indicates a high level of compliance.

Blood pressure data was collected twice. On the first day, before the participants first took candesartan cilexetil, and on the 30th day after the completion of candesartan cilexetil therapy. The blood pressure was measured twice. Blood pressure measurements (systolic and diastolic) were taken on the upper arm of participants who had been sitting and resting for at least five minutes by a trained nurse. Participants were then given a one-minute rest period before the second blood pressure measurement. The HEM-8712 electronic blood pressure monitor (OMRON Corporation, Japan) was employed as a blood pressure measuring device. Blood pressure targets according to JNC 8: for participants aged <60 years, the blood pressure target is 140/90 mmHg, while for participants aged ≥60 years, it is 150/90 mmHg

Research subjects were measured in a standing position for height and weight. The Body Mass Index (BMI) is calculated by dividing body weight (kg) by the square of height (m). Regular exercise classified as <90 minutes per week (inactive) or ≥90 minutes per week (active). Research subjects who had a negative smoking history were classified as non-smokers. In contrast, those who had used cigarettes regularly within the past six months were classified as active smokers. Diagnose alcoholism by tracking the weekly consumption of alcoholic beverages. Participants who reported consuming vegetables or fruit at each meal were classified as "regularly consuming vegetables." In contrast, those who reported consuming veggies or fruit only occasionally or not at all were classified as "not regularly consuming vegetables." The consumption of staple foods is divided into two categories: the rice consumption group, and the rice consumption group plus sweet potatoes, sago, or maize. Traditional medicine is considered routine when consumed three times a week or more.

2.4. Data analysis

The data are presented as means and standard deviations (SD) for continuous variables or prevalence (%) for categorical variables. All data obtained from both ethnic groups were

compared using the chi-square test or Fisher's Exact test for variables with a categorical measurement scale, the independent samples t-test or Mann-Whitney test for variables with a continuous measurement scale. All tests were two-sided, with a p-value less than 0.05 indicating statistical significance.

Logistic regression multivariate analysis was used to identify variables influencing blood pressure target achievement. The multivariate statistical analysis consisted of two stages. The first stage selected all variables to be included in the logistic regression analysis. The requirement for inclusion was that all variables in the bivariate analysis (Chi-square) had a p-value <0.25. The second stage performed a backward logistic regression analysis. Odds ratios (OR) with 95% confidence intervals (CI) are reported. If the entire CI range (lower and upper limits) does not include 1, the result is considered statistically significant. (p < 0.05 for 95% CI).

3. RESULTS AND DISCUSSION

The participant recruitment and flow throughout the study are summarized in Figure 2. Initially, a total of 223 hypertensive patients from the Muna and Tolaki ethnic groups were identified through medical records and patient ledgers. Out of this initial pool, 67 individuals were excluded: 11 could not be reached, 15 declined to participate, and 41 did not meet the specific inclusion criteria for the study.

Consequently, 157 participants were enrolled in the study, comprising 81 individuals of the Muna ethnicity and 76 of the Tolaki ethnicity. By the conclusion of the study, 147 participants completed all research activities, including 72 Muna participants and 75 Tolaki participants. Ten participants (9 Muna and 1 Tolaki) discontinued their involvement or declined to complete the study before its conclusion.
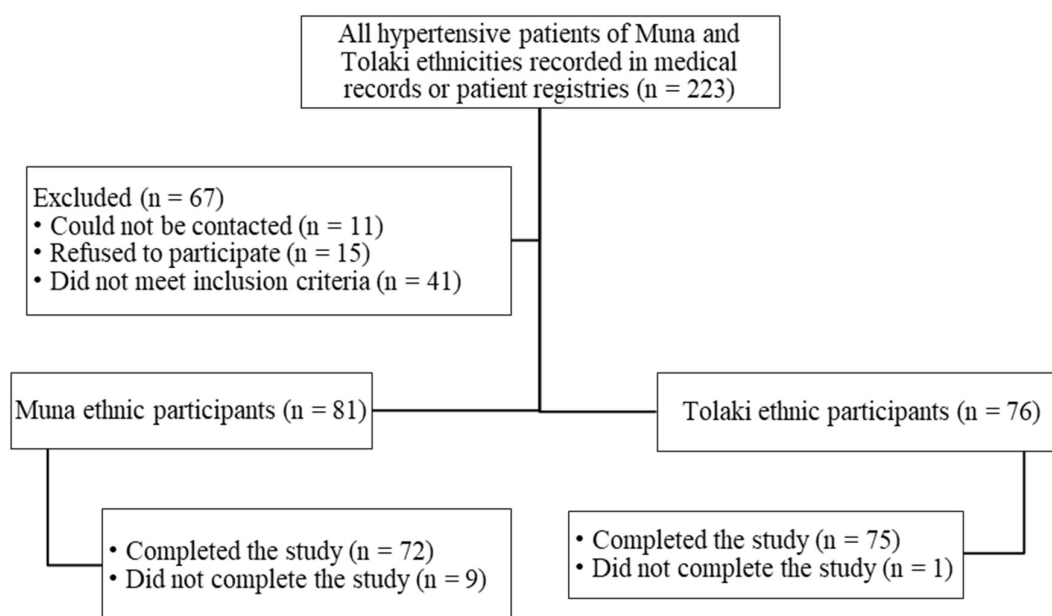

Figure 2. Flowchart of participant recruitment for the quasi-experimental study in Tolaki and Muna ethnic groups.

3.1. Results of validity and reliability tests

The results of the validity and reliability tests showed that the Sociodemographic and lifestyle questionnaire were suitable for use as research data collection instruments. The results of validity analysis of the Sociodemographic questionnaire showed that all questionnaire items were declared valid with a calculated r value greater than the r table value (r table = 0.361 at n = 30, α = 0.05). The calculated r value for all items ranged from 0.369 to 0.689. The results of the questionnaire reliability test showed a Cronbach's Alpha value of 0.628, indicating that the instrument is reliable.

The validity test of the lifestyle questionnaire was conducted on 6 questionnaire items that were piloted on 30 respondents. The validity test results showed that all questionnaire items were valid. The calculated r value for all items ranged from 0.414 to 0.668, which is greater than the table r value (r table = 0.361, α = 0.05). The reliability test results showed that the questionnaire had a Cronbach's Alpha value of 0.725, which means the instrument is reliable

3.2. Comparison of Sociodemographics of two ethnic groups

The Sociodemographic details of the research participants are shown in Table 1. The results of the comparative analysis showed that there were significant differences in the average age of the Tolaki ethnic research subjects, who were younger than the Muna ethnic when diagnosed with hypertension (p = 0.00). The Muna ethnic research subjects suffered more from type 2 DM (p = 0.05). However, there were no significant differences in BMI, gender, final education level, occupation, hypertension classification at the beginning of the study, and duration of hypertension in both ethnicities. The BMI of the Tolaki ethnicity was greater than that of the Muna ethnicity, although it was still in the normal category.

Several factors contribute to increased blood pressure in older adults. It is caused not only by macroscopic and microscopic changes in various organs but also by environmental and lifestyle factors. Based on the 2018 Basic Health Research (Riskesdas), in Indonesia, hypertension occurs in the age group 31-44 years (31.60%), 45-54 years (45.30%), and 55-64 years (55.20%) (Kementerian Kesehatan RI, 2019). In this study, it was found that Tolaki ethnic participants were more susceptible to hypertension at a younger age than Muna ethnic participants. The results of this study are similar to the results of previous studies using participants who were newly diagnosed with hypertension, where the Tolaki ethnic group was also diagnosed with hypertension at a younger age than the Muna ethnic group. In addition, the study's results also showed no significant differences in Sociodemographic and lifestyle risk factors for hypertension between the two ethnic groups. They are also living in the same neighborhood.

Genetic research related to the incidence of hypertension in the indigenous ethnic groups of Southeast Sulawesi is still minimal. There has only been one study ever conducted. This study involved 61 patients with primary hypertension from the Tolaki, Buton, and Muna ethnic groups. The results showed that there was a polymorphism in the AGT M235T gene, with a distribution of TT genotypes at 88.5%, MT at 11.5%, and no wild-type (MM) genotype at 0% (Raharjo et al., 2017). A weakness of this study was that it did not describe the distribution of

polymorphism frequencies within each ethnicity, making it impossible to determine whether the T allele has an influence on the incidence of hypertension in each ethnic group. The genetic variation of M268T (T allele) is associated with increased plasma angiotensinogen levels and the incidence of primary hypertension (Bis *et al.*, 2003; Kouhpayeh et al., 2021). Therefore, further research is needed into the influence of ethnicity (genetic factors) on the incidence of hypertension at a young age in the Tolaki ethnic group.

Table 1. Description of Sociodemographic characteristics. *Description*: Unpaired T independent test (*), Mann-Whitney test (**), and Chi-Square test (***).

Sociodemographic characteristics	Ethnic groups		p-value
	Tolaki	**Muna**	
Age * : (years)			0.00
Mean ± SD	53.81 ± 0.93	57.95 ± 0.98	
95% CI	51.97–55.66	56.00–59.89	
Gender *** : n (%)			0.70
Male	23 (30.67%)	20 (27.78%)	
Female	52 (69.33%)	52 (72.22%)	
Education ***: n (%)			0.08
Elementary School	6 (8.00%)	17 (23.61%)	
Junior High School	15 (20.00%)	11 (15.28%)	
Senior High School	35 (46.67%)	30 (41.67%)	
Diploma (D1-D3)	12 (16.00%)	6 (8.33%)	
Undergraduate-Postgraduate	7 (9.33%)	8 (11.11%)	
Employment***: n (%)			0.15
Housewife	30 (40.00%)	31 (43.06%)	
Traders and entrepreneurs	15 (20.00%)	17 (23.61%)	
Private employees, laborers, and farmers	12 (16.00%)	7 (9.72%)	
Retired civil servants, soldiers, and police	8 (10.67%)	14 (19.44%)	
Civil Servants and Teachers	10 (13.33%)	3 (4.17%)	
Body mass index (BMI) *			0.61
Mean ± SD	24.20 ± 0.43	22.965 ± 0.36	
95% CI	23.35–25.06	22.24–23.69	
Duration of hypertension ** (years)			0.76
Mean ± SD	2.07 ±0.19	1.982±0.20	
95% CI	1.70–2.44	1.59–2.37	
Min-Max	0.25–5.00	0.25–7.00	
Classification of hypertension (JNC 7) ***: n (%)			0.10
Grade 1 hypertension Systolic 140-159 or Diastolic 90-99 mmHg	15 (19.14%)	8 (11.11%)	
Grade 2 hypertension Systolic ≥ 160 or Diastolic ≥ 100 mmHg	60 (78.95%)	64 (88.89%)	
Comorbidities***: n (%)			0.05
Type 2 DM	4 (5.53%)	12 (16.67%)	
Does not suffer from type 2 DM	71 (94.67%)	60 (83.33%)	

Type 2 DM increases the risk of hypertension. People with hypertension who also have type 2 DM have a fourfold higher risk of developing cardiovascular disease (Alsaadon et al., 2022; Jia & Sowers, 2021; Sun et al., 2019). Hypertension and type 2 DM share similar risk factors. Individuals over 35 years of age with a poor lifestyle and a family history of diabetes

are more likely to develop type 2 DM (Basu, 2022; Chen et al., 2021; Liu et al., 2021). Based on the age at which hypertension was diagnosed, the Muna and Tolaki ethnic groups had similar odds of developing type 2 DM. However, when considering lifestyle risk factors such as a higher average BMI, irregular fruit and vegetable consumption, and lack of physical activity, the Tolaki ethnic group had a greater chance of developing type 2 DM. However, the analysis results showed that the Muna ethnic group suffered from type 2 diabetes more than the Tolaki ethnic group, with a p-value of 0.046. This confirms the results of previous studies, which also found that Muna people are more likely to suffer from type 2 diabetes than Tolaki people (Leorita et al., 2024). This shows ethnicity influences the incidence of type 2 DM in both ethnic groups involved in this study.

3.3. Comparison of the lifestyles of two ethnic groups

Based on lifestyle data in Table 2. Comparative statistical data indicate that there are no significant differences in lifestyle, including alcohol consumption habits, smoking habits, physical activity, and staple food types, between the two ethnicities. There are significant differences in the habit of eating vegetables and fruits at every meal, as well as the use of traditional medicine to treat hypertension and its associated symptoms.

Table 2. Description of the lifestyle of hypertensive patients of the Tolaki and Muna ethnicities. *Description*: Chi-Square test (*) and Fisher's Exact test (**).

Lifestyle	Ethnic Group		p-value
	Tolaki	**Muna**	
Habit of drinking alcohol ** : n (%)			0.11
Drink alcohol	1 (1.33%)	5 (6.94%)	
Do not drink alcohol	74 (98.67%)	67 (93.06%)	
Smoking habit * : n (%)			0.26
Smoke	13 (17.33%)	18 (25.00%)	
Do not smoke	62 (82.67%)	54 (75.00%)	
Physical activity **: n (%)			0.17
Active	7 (9.30%)	2 (2.8%)	
Not active	68 (9.33%)	70 (2.78%)	
Consume fruit or vegetables at meals *: n (%)			0.01
Routine	64 (85.33%)	70 (97.22%)	
Not routine	11 (14.67 %)	2 (2.78%)	
Using traditional medicine * : n (%)			0.03
Regular use	13 (17.33%)	24 (33.33%)	
Do not use	62 (83.67%)	48 (66.67%)	
Staple food *: n (%)			0.78
Rice	33 (44.00%)	30 (41.70%)	
Rice and additional (sweet potato, corn, or sago)	42(56.00%)	42 (58.30%)	

The Muna ethnic group has a long-standing tradition of using traditional medicine to treat illnesses or maintain physical stamina (Slamet et al., 2024). Twenty-four participants from the Muna tribe regularly ($\geq$ 3 times a week) use home herbal remedies as additional treatment to overcome hypertension symptoms such as dizziness or headaches. Traditional medicines used include homemade boiled water from meniran (Phyllanthus niruri L.), soursop leaves (Annona

muricata L.), or bay leaves (Syzygium polyanthum). This traditional medicine is not commonly used. There is no pharmacological evidence or clinical trial data on the blood pressure-lowering effect of this medicinal herb. Traditional medicines that some Tolaki ethnic participants routinely use are herbal medicines or jamu purchased at drug stores. Differences in the types and sources of traditional medicine between the two ethnic groups may reflect variations in cultural practices, accessibility, and health-seeking behavior. Further scientific research is needed to determine the efficacy and effectiveness of traditional medicines made by the Muna people. Furthermore, studies are needed on the use of traditional medicines in conjunction with generic antihypertensive medications to lower blood pressure and treat symptoms associated with high blood pressure.

3.4. Level of compliance and achievement of blood pressure therapy targets

At the end of the study, there was no significant difference in the number of candesartan caplets consumed for 30 days ($p = 0.83$) and the percentage of participants with a good level of therapy adherence (candesartan cilexetil 8 mg consumption $\geq 80\%$) ($p = 0.78$) in both ethnic groups (Table 3).

Therapy adherence plays a critical role in determining treatment success. Given the high prevalence of participants with good levels of therapy adherence in both ethnic groups and the absence of significant differences between them, the chances of achieving target blood pressure or blood pressure reduction should be nearly equal. However, the study results showed that despite both ethnic groups having high levels of therapy adherence and no significant differences, candesartan cilexetil 8 mg monotherapy was more effective in lowering systolic and diastolic blood pressure in the Tolaki ethnic group.

The findings are consistent with our previous studies, which also reported significant differences in blood pressure reduction between the two ethnic groups receiving candesartan monotherapy. Comparable patterns have been reported in other populations; a pooled analysis of NHANES 2013–2018 data demonstrated ower blood pressure control among non-Hispanic Black Americans had lower levels of blood pressure control (39%) than non-Hispanic White Americans (49%), even though both groups had similar levels of awareness and received hypertension treatment (Abrahamowicz et al., 2023). Similarly, study conducted in Egypt also reported greater difficulty in achieving blood pressure targets among Black patients compared with other other ethnic groups (Abuelsoud & Abdelraouf, 2025).

The effectiveness of candesartan cilexetil 8 mg monotherapy for 30 days in participants with uncontrolled hypertension was compared to the results of previous research that used patients newly diagnosed with hypertension, which found that the average reduction in systolic and diastolic blood pressure was greater in patients from Tolaki and Muna ethnicities who were newly diagnosed with hypertension (Leorita et al., 2024). These findings suggest that baseline blood pressure status may influence treatment response. Therefore, dose adjustment or early therapeutic optimization should be consideres when initiating candesartan cilexetil therapy in patients with uncontrolled hypertension, both in the Muna and Tolaki ethnic groups.

Table 3. Compliance level and blood pressure in hypertensive Tolaki and Muna participants. *Description*: Unpaired T independent test (*), Mann-Whitney test (**), and Chi-Square test (***).

	Ethnic Group		p-value
	Tolaki (n =75)	Munan=72	
The number of 8 mg candesartan caplets used during 30 days of therapy ** (caplet)			0.83
Mean ± SD	26.71 ± 0,36	26.61 ± 0.42	
Median (min-max)	28.00 (18–30)	28.00 (17–30)	
Percentage of 8 mg candesartan caplets used during 30 days of therapy ***: n (%)			0.78
< 80%	16 (21.33)	14 (19.44)	
≥ 80%	59 (78.67)	58 (80.56)	
Systolic before candesartan therapy **: (mmHg)			0.00
Mean ± SD	160.35 ± 1.20	167.22 ± 1.92	
Median (min-max)	158.00(140–197)	164.50 (141–215)	
Systolic after 30 days of candesartan therapy *: (mmHg)			0.00
Mean ± SD	135.04 ± 1.27	152.85 ± 2.03	
Systolic reduction value after 30 days of candesartan therapy**: (mmHg)			0.00
Mean ± SD	-25.41 ± 0.81	-14.35 ± 1.26	
Median (min-max)	24.00 (13–45)	12.00 (-4–52)	
Diastolic before candesartan therapy ** (mmHg)			0.30
Mean ± SD	90.89 ± 1.40	94.03 ± 1.328	
Median (min-max)	95.00 (63–1	94.50 (64–124)	
Diastolic after 30 days of candesartan therapy ** : (mmHg)			0.00
Mean ± SD	79.16 ± 1.31	86.19 ± 1.18	
Median (min-max)	80.00 (53–98)	86.00 (64–119)	
Diastolic reduction value after 30 days of candesartan therapy **: tmmHg			0.00
Mean ± SD	-11.11 ± 0.49	-7.96 ± 0.70	
Median (min-max)	-11.00 (-3– -22)	-8.00 (-9– -34)	
Achievement of therapeutic targets after 8 mg candesartan therapy for 30 days ***: (People) (%)			0.00
Achieved	57 (76.00)	11 (15.28)	
Not achieved	18 (24.00)	61 (84.72)	

The results of the multivariate logistic regression analysis, conducted using the backward method on nine variables that met the significance requirements for inclusion in the multivariate test, are presented in Table 5. This process was carried out in seven steps. The results of the regression analysis narrowed down to two variables that influenced the achievement of blood pressure targets, namely Tolaki ethnicity and good therapy adherence. Tolaki ethnic participants undergoing candesartan cilexetil 8 mg therapy had an OR 21.44 times greater for achieving blood pressure targets than Muna ethnic participants, 95% CI 6.69–53.40, did not exceed 1, and p = 0.00 indicated a significant effect. The variable of therapy adherence (consumption of ≥ 80% candesartan cilexetil caplets) also showed a statistically significant effect (95% CI 2.96–40.07, p = 0.00), having an OR of 10.89.

Table 4. The relationship between Sociodemographics, lifestyle, and therapy adherence in achieving candesartan cilexetil. *Description*: Chi-Square test (*) and Fisher's Exact test (**).

Variables	Target blood pressure achieved		The target blood pressure was not achieved		p
	n	%	n	%	
Age*					0.06
≤ 60 years old	52	51.50	49	48.50	
> 60 years old	16	34.80	30	65.20	
Gender*					0.78
Male	19	44.20	24	55.80	
Female	49	47.10	55	52.90	
BMI*					0.69
Ideal BMI	46	47.40	51	52.60	
Not ideal BMI	22	44.00	28	56.00	
Ethnicity*					0.00
Tolaki	57	76.00	18	24.00	
Muna	11	15.30	61	84.70	
Last level of education *					0.10
High School and College	50	51.00	48	49.00	
Elementary and Middle School	18	36.70	31	63.30	
Classification of hypertension (JNC 7)					0.01
Grade 1 hypertension	17	73.91	6	26.09	
Grade 2 hypertension	51	41,13	73	48.87	
Comorbidities *					0.07
Not suffering from type 2 DM Suffering	64	48.90	67	51.10	
from type 2 DM	4	25.00	12	75.00	
Level of therapy adherence*					0.00
Good	63	52.10	58	47.90	
Not optimal yet	5	19.20	21	80.80	
Consume vegetables or fruit regularly a	*				0.02
Routine	58	43.30	76	56.70	
Not routine	10	76.90	3	23.10	
Staple foods consumed*					0.54
Rice	31	49.20	32	50.80	
Rice plus sweet potatoes. Corn or sago	37	44.00	47	56.00	
Smoking behavior*					0.47
Do not smoke	55	47.80	60	52.20	
Smoke	13	40.60	19	59.40	
Alcohol drinking behavior**					0.22
Do not drink alcohol	67	47.50	74	52.50	
Drink alcohol	1	16.70	5	83.30	
Use of traditional medicine*					0.12
Routine	13	35.10	24	64.90	
Not routine	55	50.00	55	50.00	
Physical activity**					0.30
Active	6	66.70	3	33.30	
Not active	62	44.90	76	55.10	

    Therapy adherence, sociodemographic variables, and lifestyle all contribute to achieving blood pressure therapy targets in hypertensive patients (Adinkrah et al., 2020). Bivariate test results from this study showed that almost all sociodemographic factors (except ethnicity) and

lifestyle factors, such as staple food variety, smoking habits, physical activity, alcohol consumption habits, and the use of traditional medicine, did not affect blood pressure target achievement in the Muna and Tolaki ethnic groups using candesartan. These study findings differ from the results of several previously reported studies. A study conducted in one region of Russia found that age and comorbidities were contributing factors to uncontrolled blood pressure (Kiselev *et al*., 2017). A study in Japan found that BMI was a factor influencing the achievement of blood pressure targets (Yokokawa *et al*., 2022). Other studies state that education level, age, and type 2 diabetes are three factors that influence the achievement of blood pressure targets (Choi & Kim, 2023; Yang *et al*., 2024).

The uniqueness of this research lies in the fact that nearly all participants from the Tolaki and Muna tribes habitually consumed vegetables and fruit with every meal. Most of them stated that moringa leaves and young papaya fruit were the types of vegetables they consumed most often. Several studies have demonstrated that Moringa leaf extract exhibits antioxidant and anti-inflammatory properties. It can even lower systolic and diastolic blood pressure if consumed regularly (Chan et al., 2020; Menichetti et al., 2025). The habit of consuming Moringa leaves among the Muna and Tolaki tribes needs to be preserved and utilized as a nutraceutical for individuals with hypertension.

The results showed that ethnicity and adherence to therapy were the most important factors influencing the success of achieving blood pressure therapy targets in the Tolaki and Muna ethnicities using candesartan cilexetil 8 mg. The Tolaki and Muna ethnic groups, with excellent adherence, were 10 times more likely to achieve blood pressure therapy targets compared to those with poor adherence. Participants from both ethnic groups showed similar levels of therapy adherence; however, a higher percentage of the Tolaki ethnic group achieved therapy goals. The Tolaki ethnicity was 21 times more likely to achieve blood pressure therapy targets compared to the Muna ethnicity. Candesartan cilexetil 8 mg was more effective in lowering blood pressure in the Tolaki ethnicity.

Due to similar sociodemographic and lifestyle factors in both ethnic groups, there is a strong suspicion that genetic differences between the Tolaki and Muna ethnic groups contribute to the differences in candesartan efficacy. These genetic differences may be found in the candesartan-metabolizing enzyme gene (CYP2C9) or in the angiotensin 1 (AT1) receptor, which is the target of candesartan. Further research is needed to confirm this.

A limitation of this study was the absence of baseline and follow-up laboratory data, such as creatinine clearance (eGFR), blood urea nitrogen (BUN), and potassium levels. To mitigate this, side effects were rigorously monitored through weekly evaluations and active participant reporting via electronic messaging. While no participants used the telephone reporting line, six participants reported symptoms (dizziness and weakness) during weekly checks. Subsequent laboratory tests for those affected confirmed that their creatinine and potassium levels remained within normal limits. Despite these limitations, this study provides significant novelty as the first to explore the influence of sociodemographics, therapy adherence, and lifestyle on blood pressure control specifically within the Tolaki and Muna ethnic groups. Furthermore, it offers

essential baseline data on the effectiveness of ARB therapy (candesartan cilexetil) in these two indigenous populations of eastern Indonesia.

Table 5. Multivariate logistic regression results for predictors of blood pressure target achievement in Tolaki and Muna ethnic groups.

Variable	Coefficient	p	OR	CI 95% Min	CI 95% Max
Age ≤ 60 years	-0.14	0.79	0.87	0.32	2.41
Tolaki ethnicity	-3.14	0.00	21.44	6.69	53.40
High School and College	0.21	0.70	1.23	0.43	3.51
No type 2 diabetes mellitus	1.17	0.15	2.92	0.63	13.53
Therapy compliance (≥ 80% caplets)	2.29	0.00	10.89	2.96	40.07
Regularly consume vegetables and fruit	-1.16	0.22	0.32	0.05	1.99
Do not drink alcohol	1.71	0.37	5.55	0.17	182.62
Regularly consume traditional medicine	0.41	0.45	1.51	0.51	4.45
Hypertension classification	-1.41	0.01	0.80	0.05	0.17
Constant	6.09	0.00	0.00		

Given that ethnicity was identified as a significant factor influencing blood pressure target achievement, further research is warranted to explore the pharmacokinetics of candesartan cilexetil within the Tolaki and Muna populations. Such studies are essential to establish evidence-based dosage recommendations tailored to these specific ethnic groups. Furthermore, subsequent genetic investigations focusing on metabolizing gene polymorphisms (e.g., CYP2C9) and receptor gene polymorphisms (e.g., AGTR1) are recommended to understand better the underlying mechanisms of these inter-ethnic variations in drug response.

4. CONCLUSION

Out of 14 sociodemographic, lifestyle, and adherence variables, only ethnicity and therapy adherence significantly influenced blood pressure targets in hypertensive patients of Tolaki and Muna ethnicities. Candesartan cilexetil showed higher efficacy in the Tolaki group. Furthermore, patients with good adherence (≥80% consumption of an 8 mg dose) were significantly more likely to achieve therapy targets regardless of ethnicity.

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CONFLICT OF INTEREST

The authors declared no conflict of interest.

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