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# Angiotensin-Converting Enzyme Gene Polymorphism in Obesity and Its Interaction with Blood Pressure in Academicians

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**Abstract:** Obesity is one of the risk factors for hypertension. Obesity in hypertensive patients determines the severity of hypertension. Angiotensin-converting enzyme (ACE) is an enzyme that triggers vasoconstriction. ACE gene insertion/deletion polymorphisms may be associated with hypertension. This study aims to determine an association between ACE gene polymorphisms and blood pressure in obese patients. This research used an analytic observational study with a cross-sectional design. The research sample consisted of 36 obese academicians. Blood samples were taken from the patients to examine the ACE gene polymorphism. The correlative hypothesis used the Kruskal-Wallis test. The results showed that the most common types of ACE gene polymorphisms were type II (55.6%), type ID (33.3%), and type DD (11.1%)—the mean value of systolic blood pressure type II 123.29mmHg, type ID 125.82mmHg, DD 134.5mmHg. The mean value of diastolic pressure in ACE gene polymorphism type II was 81.57mmHg, type ID was 79.73mmHg, and type DD was 82.5mmHg. The Kruskal-Wallis test showed a relationship between ACE polymorphism and systolic pressure at p=0.705 (p>0.05) and the relationship between ACE polymorphism and diastolic pressure at p=0.980 (p>0.05). It concluded that there is no relationship between the ACE gene polymorphism and blood pressure in obese academicians.

**Keywords:** Angiotensin-converting enzyme (ACE) gene, Blood Pressure, Obesity.

## INTRODUCTION

Obesity is one of the risk factors for hypertension.[1] The population aged more than 18 years is obese, as many as 650 million people. Overall, the number of obese rural residents can reach more than 13%. About 13% of the adult population in the world, namely 11% of men and 15% of women, are obese.[2] The prevalence of obesity worldwide in 2016 reached more than 1.9 billion adults, 18 years and over, with excess body weight.[3] In Indonesia, the prevalence of obesity continues to increase in adult men at 19.7%, while in women, it is 32.9%. Hypertensive disease with obesity is still common. The prevalence of hypertensive disease accompanied by obesity also continues to increase.[4,5]

According to several studies, obesity and hypertension have a significant relationship.[6-8] From Jullaman's research, it is explained that if a patient has an obese BMI, they will have a 1.64 times higher risk of suffering from hypertension compared to a normal BMI.[9] Based on the results of Riskesdas, the increasing incidence of hypertension in Indonesia is also followed by an increasing proportion of the Indonesian population who are overweight or obese.[10]

The presence of obesity in hypertensive patients will determine the severity of hypertension. The larger a person's body, the more blood is needed to supply nutrients and oxygen to other tissues and muscles. Obesity increases the length of blood vessels, which results in increased resistance to blood flow,

making it more difficult for blood to travel longer distances.[11] With increased resistance, blood pressure becomes higher. This situation can be caused by fat cells producing compounds that are detrimental to the heart and blood vessels.[12]

The renin-angiotensin system (RAS) is a hormonal regulator of fluid volume and blood pressure.[13] Angiotensin-converting enzyme (ACE) is a key enzyme in the RAS system that converts angiotensin I into angiotensin II, a molecule that triggers vasoconstrictors and is involved in cell proliferation, differentiation, apoptosis, and angiogenesis. ACE gene insertion/deletion polymorphisms may be associated with hypertension and fat accumulation.[14] This study aims to determine the association between ACE gene polymorphisms and blood pressure in obese patients.

**MATERIALS AND METHOD**

This research was an analytic observational study with a *cross-sectional* approach. The population in this study was Universitas Muhammadiyah Sumatera Utara (UMSU) academics who were obese. The research samples consisted of subjects selected from the population who met the inclusion criteria: a body mass index value of 25 or higher, aged between 20 and 59 years, and willing to participate in the study by signing *an informed consent* form. The exclusion criteria in this study were patients who consumed antihypertensive drugs. Sampling was conducted on the UMSU campus with a total sample of 36 people and examined for blood pressure. Subsequently, blood samples were taken from the patients to examine the ACE gene polymorphism. Blood examination for the ACE gene polymorphism was carried out in the Biochemistry laboratory of the Faculty of Medicine, Universitas Muhammadiyah Sumatra Utara.

The examination of ACE gene polymorphism levels was carried out by first isolating DNA using procedures and materials from the Wizard Genomic DNA Purification Kit. After the DNA sample was stored at 2-8°C, it was continued with the PCR (*Polymerase Chain Reaction*) method using primer 3 F 5' - GAT GTG GCC ATC ACA TTCGTC AGAT -3' and Primer 3 R 5' - CTG GAC ACC ACT CCC ATC CTT TCT -3' by producing products in the form of DNA bands at 490 bp and 190 bp. The PCR used a *thermal cycler* method, where the first sequence consists of 2 minutes at 98 °C, followed by 31 cycles at 98 °C for 15 seconds, 58 °C for 1 minute, and 75 °C for 30 seconds. After 31 cycles at 75°C for 5 minutes, the samples were stored at 4°C. PCR results were read using 2% *agarose gel electrophoresis* stained with Gel Red. The interpretation of the PCR results is polymorphism II if there is only one DNA band at 490 bp, DD polymorphism if there is only one DNA band at 190 bp, and ID polymorphism if there are 2 DNA bands found, namely at 490 bp and 190 bp. [15]

Univariate analysis was performed to describe each variable studied, both dependent and independent variables, to examine frequency distribution tables, and to determine the number and percentage of each variable. Data analysis included descriptive analysis and hypothesis testing. The normality test used the Shapiro-Wilk test. The correlative hypothesis used the *Kruskal-Wallis* test.

This study has received approval from the FK UMSU ethics commission for the implementation of research activities with letter number 1034/KEPK/FK UMSU/2023. This sampling was carried out from July to August 2023.

**RESULT**

Based on Table 1, from 36 samples collected, the most common gender is male, with 21 people (58.3%), while there are 15 samples with females (41.7%).

**Table 1.** Frequency Distribution Based on Gender

| Gender | Number (people) | Percentage (%) |
|---|---|---|
| Male | 21 | 58.3 |
| Female | 15 | 41.7 |
| **Total** | **36** | **100.00** |

Based on Table 2, from 36 samples, the most common types of polymorphisms were the II gene type, as many as 20 people (55.6%), then the ID gene, as many as 12 people (33.3%), and the least was the DD gene, which was four people (11.1%).

**Table 2.** Frequency Distribution of ACE Gene Polymorphisms in Obesity

| Polymorphism | Number (people) | Percentage (%) |
|---|---|---|
| II | 20 | 55.6 |
| ID | 12 | 33.3 |
| DD | 4 | 11.1 |
| **Total** | 36 | 100.00 |

Based on Table 3, the mean age value in obese patients with type II polymorphism is 29.67, type ID is 33.27, and type DD is 41.50, with a significant correlation of p = 0.011( < 0.05), which indicates that there is a significant age difference in each type of ACE polymorphism. The mean value of systolic blood pressure in type II polymorphism was 123.29 mmHg; in type ID polymorphism, it was 125.82 mmHg; and in type DD polymorphism, it was 134.5 mmHg. The mean value of diastolic pressure in type II polymorphism was 81.57 mmHg; in type ID polymorphism, it was 79.73 mmHg; and in type DD polymorphism, it was 82.5 mmHg.

**Table 3.** Sample characteristics based on ACE gene polymorphism

| Parameter | II (n=20) | ID (n=12) | DD (n=4) | P value |
|---|---|---|---|---|
| Age | 29.67±8.422 | 33.27±7.016 | 41.50±8.851 | 0.011 |
| Systole | 123.29±14.308 | 125.82±16.594 | 134.50±26.350 | 0.245 |
| Diastole | 81.57±8.824 | 79.73±5.798 | 82.50±12.583 | 0.906 |

Based on the statistical results of the Shapiro-Wilk normality test, the data were not normally distributed (p > 0.05); therefore, the data were analyzed using the nonparametric Kruskal-Wallis test. The hypothesis test of the relationship between ACE polymorphism and systolic pressure, the value of p = 0.705 (p > 0.05). The hypothesis test of the relationship between ACE polymorphism and diastolic pressure, the value of p = 0.980 (p > 0.05), indicating that there is no relationship between ACE gene polymorphism and blood pressure in obese patients.

**DISCUSSION**

The results of this study found that the most common types of ACE polymorphisms in obese patients were type II (insertion), which accounted for 55.6%, followed by type ID, which accounted for 33.3%, and the least common was type DD, which accounted for 11.1%. According to research conducted in Malaysia, the most common types of ACE gene genotypes in obesity were type II (insertion), at 54.5%, followed by type ID at 36.6%, and type DD at 8.9%. There was no significant difference in the type of allele or genotype of the ACE gene between obese individuals and those of normal weight. Research in Korea showed that the type of ACE gene genotype most prevalent in obese people was type ID (57.1%), followed by type II (30.8%), and the least common was type DD (12%).[17] Another study conducted in Brazil showed that the most genotypes found in obese patients are type ID and the least are type II. 18 In the three studies mentioned, there was no relationship between ACE gene polymorphism and obesity.[16-18]

This study found no association between ACE gene genotypes and systolic and diastolic blood pressure. Previous studies have also reported no association between ACE gene polymorphisms and blood pressure or obesity.[17,19] Previous studies have stated that there is an association between ACE gene polymorphisms and blood pressure.[20-23] Another study mentioned that the DD gene polymorphism tends to increase systolic and diastolic blood pressure compared to the ID and II gene polymorphisms.[24] According to the results of this study, which showed that the DD gene polymorphism had higher mean values of systole (134.50±26.350) and diastole (82.50±12.583) blood pressure compared to II and ID gene polymorphisms. Obesity is one factor that can contribute to an increase in blood pressure.[25,26] However, in this case, genetic variations, lifestyle, and environment can influence the relationship between ACE genes and blood pressure.[27]

## CONCLUSION

The angiotensin-converting enzyme (ACE) gene polymorphism in obese patients in the UMSU academic community was found to be predominantly type II, with the least common type being DD. The kind of ACE gene polymorphism in obese patients has no relationship with blood pressure values.

## CONFLICT OF INTEREST

The authors have no conflict of interest.

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