Original Research

GENETIC ASSOCIATION OF ACE INSERTION/DELETION POLYMORPHISM WITH ESSENTIAL HYPERTENSION IN THE SOUTH INDIAN POPULATION

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ABSTRACT

Background: Hypertension is a major global health problem and an important risk factor for cardiovascular and renal diseases. Genetic factors, particularly angiotensin-converting enzyme (ACE) gene insertion/deletion (I/D) polymorphism, have been implicated in the pathogenesis of hypertension. The present study aimed to evaluate the association between ACE gene I/D polymorphism and hypertension among the South Indian population.

Methodology: A hospital-based case-control observational study was conducted in the Department of General Medicine at Sree Mookambika Institute of Medical Sciences from February 2025 to May 2026. Newly diagnosed hypertensive patients and age- and sex-matched normotensive controls were included after obtaining informed consent. Genomic DNA was extracted from peripheral blood samples and assessed using agarose gel electrophoresis and nanodrop spectrophotometry. ACE gene I/D polymorphism was analyzed using polymerase chain reaction (PCR) technique with specific primers. Genotype frequencies were compared between cases and controls using appropriate statistical analysis.

Results: The study demonstrated the presence of II, ID, and DD genotypes among participants. The deletion (D) allele and DD genotype were observed more frequently among hypertensive patients compared to controls, suggesting a positive association with hypertension. Statistical analysis revealed a significant relationship between ACE gene polymorphism and elevated blood pressure.

Conclusion: ACE gene I/D polymorphism appears to be associated with hypertension in the South Indian population. The D allele may serve as a potential genetic risk factor for the development of hypertension.

Keywords: Hypertension, Ace Gene Polymorphism, Insertion/Deletion Polymorphism, Polymerase Chain Reaction, South Indian Population, Genetic Susceptibility.

INTRODUCTION

Hypertension is one of the most common non-communicable diseases and a major global public health concern because of its increasing prevalence and associated complications.[1] It is a chronic medical condition characterized by persistently elevated arterial blood pressure and is a leading contributor to cardiovascular and renal morbidity and mortality worldwide.[2] If left untreated, hypertension can result in severe complications such as coronary artery disease, myocardial infarction, stroke, heart failure, peripheral vascular disease, and chronic kidney disease.[3]

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The prevalence of hypertension has increased rapidly in developing countries, particularly due to urbanization, sedentary lifestyle, unhealthy dietary habits, obesity, stress, smoking, and alcohol consumption.[4]

Hypertension is considered an independent risk factor for cardiovascular diseases including ischemic heart disease, angina pectoris, cerebrovascular accidents, and atherosclerosis.[5] It contributes significantly to endothelial dysfunction, vascular remodeling, and increased arterial stiffness, ultimately leading to target organ damage.[6] In addition, hypertension frequently coexists with metabolic disorders such as obesity, diabetes mellitus, dyslipidemia, insulin resistance, oxidative stress, and chronic inflammation, which further increase the risk of cardiovascular complications.[7] According to the World Health Organization (WHO), approximately 1.28 billion adults worldwide are affected by hypertension, and nearly 9.4 million deaths annually are attributed directly to complications arising from uncontrolled hypertension.[8]

The pathogenesis of hypertension is multifactorial and involves a complex interaction between environmental, physiological, and genetic factors.[9] Among the various genetic determinants, the renin-angiotensin-aldosterone system (RAAS) plays a central role in blood pressure regulation and cardiovascular homeostasis.[10] Angiotensin-converting enzyme (ACE) is a key component of this pathway and is responsible for the conversion of angiotensin I to the potent vasoconstrictor angiotensin II, which increases blood pressure through vasoconstriction, sodium retention, aldosterone secretion, and sympathetic nervous system activation.[11]

The ACE gene is located on chromosome 17q23 and exhibits an insertion/deletion (I/D) polymorphism characterized by the presence or absence of a 287-base pair Alu repeat sequence in intron 16.[12] This polymorphism has been extensively studied because of its influence on circulating and tissue ACE levels. Individuals carrying the deletion (D) allele generally exhibit higher ACE activity compared to those carrying the insertion (I) allele.[13] Increased ACE activity may contribute to enhanced vasoconstriction, vascular hypertrophy, endothelial dysfunction, and increased susceptibility to hypertension and cardiovascular disease.[14]

Several studies have investigated the association between ACE gene I/D polymorphism and hypertension; however, the results remain inconsistent across different ethnic and geographic populations.[15] Genetic heterogeneity, environmental influences, dietary factors, and variations in sample size may contribute to these conflicting findings.[16] In the Indian population, especially among South Indians, limited data are available regarding the relationship between ACE gene polymorphism and hypertension. Understanding the genetic predisposition to hypertension may help identify high-risk individuals and facilitate personalized therapeutic strategies.

The Joint National Committee VIII (JNC VIII) guidelines recommend angiotensin-converting enzyme inhibitors, diuretics, beta blockers, calcium channel blockers, and angiotensin receptor blockers as first-line therapies for hypertension management.[17] Since ACE inhibitors target the RAAS pathway directly, studying ACE gene polymorphism may also provide insight into therapeutic response and disease prognosis.Therefore, the present study was undertaken to evaluate the association between angiotensin-converting enzyme gene (I/D) polymorphism and hypertension among the South Indian population.

Aim

To evaluate the association between angiotensin-converting enzyme (ACE) gene insertion/deletion (I/D) polymorphism and hypertension among the South Indian population.

Objectives

1. To determine the frequency distribution of ACE gene I/D polymorphism among hypertensive patients in the South Indian population.
2. To compare the prevalence of ACE genotypes (II, ID, and DD) between hypertensive patients and normotensive controls.

METHODOLOGY

This hospital-based case-control observational study was conducted in the Department of General Medicine at Sree Mookambika Institute of Medical Sciences during the period from February 2025 to May 2026. The study was undertaken to evaluate the association between angiotensin-converting enzyme (ACE) gene insertion/deletion (I/D) polymorphism and hypertension among the South Indian population. Newly diagnosed hypertensive patients attending the Department of General Medicine who fulfilled the inclusion criteria were enrolled in the study after obtaining written informed consent.

The study included newly diagnosed hypertensive patients aged above 18 years who were willing to participate in the study. Diagnosis of hypertension was established based on standard blood pressure measurement criteria. Age- and sex-matched normotensive individuals without a history of hypertension were included as controls. Patients who were smokers, alcoholics, pregnant or lactating women, individuals receiving steroid therapy, and patients with chronic infections such as tuberculosis or leprosy were excluded from the study. Patients with recent trauma, surgery, psychiatric illness, or co-morbid conditions involving hepatic, renal, or cardiac disease were also excluded. Individuals unwilling to provide informed consent or those with mental incapacity affecting study participation were not included in the study.

A detailed clinical history and physical examination were performed for all participants. Demographic details including age, gender, family history, body mass index (BMI), blood pressure measurements, and associated risk factors were recorded using a structured proforma. Blood samples were collected under aseptic precautions for biochemical and genetic analysis. Routine laboratory investigations including fasting blood sugar, lipid profile, renal function tests, and liver function tests were performed wherever necessary.

Genomic DNA was extracted from peripheral blood leukocytes using standard laboratory procedures. Detection of ACE gene I/D polymorphism was performed using polymerase chain reaction (PCR) technique. The amplified products were analyzed by agarose gel electrophoresis to identify the genotypes as insertion homozygous (II), deletion homozygous (DD), and heterozygous (ID). Genotype and allele

frequencies were compared between hypertensive patients and normotensive controls to determine the association between ACE gene polymorphism and hypertension.

Statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS) software version 25.0. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequency and percentage. Chi-square test was used to compare genotype and allele frequencies between cases and controls. Student's t-test was used for comparison of continuous variables between groups. Odds ratio (OR) with 95% confidence interval (CI) was calculated to assess the strength of association between ACE gene polymorphism and hypertension. A p-value of less than 0.05 was considered statistically significant.

RESULT

Table 1. Association of ACE Gene Variants (SNP 4343) With Hypertension Disease

Genotypes	Or (95% Ci)	P-Value
Dd Vs Ii	1.51 (0.68-2.97)	0.624
Id Vs Ii	0.45 (0.76- 0.98)	0.002*
Ii Vs Ii	0.50 (0.38-2.37)	0.357

p<0.05 indicates statistically significant

In table no-1 shown that patients suffering with hypertension have 0.45times more prone to attain ID variant of ACE gene. The p-value has found statistically significant (0.002).

Table 2. Genotypes of ACE Gene and Their Frequencies of Alleles in the Study Populations for Hypertension Cases.

S.N.	Genotype Of Ace	Frequency Of Alleles (Hypertension Patients)	P-Value	Adjusted Or Value	Ci (95%) Value
1.	Ii (37)	24.67%	0.058	Reference	Reference
2.	Id (47)	31.33%	0.050	1.42	1.35-2.67
3.	Dd (66)	40.00%	0.043	1.26	1.63-2.59

In this study, ACE gene polymorphisms related with hypertension was recorded the genotype and allele frequencies of the specific SNP (rs4343) in the study group. The genotype frequencies of the ACE gene in cases with hypertension were found in Hardy-Weinberg equilibrium. The rs 4343I/D gene polymorphism of the ACE gene was noticed statistically significant with hypertension, and the ID genotype was noted significantly higher in hypertension cases.

DISCUSSION

The present study evaluated the association between angiotensin-converting enzyme (ACE) gene insertion/deletion (I/D) polymorphism and hypertension among the South Indian population using molecular genetic analysis. Genomic DNA extraction and quality assessment were successfully performed using agarose gel electrophoresis and nanodrop spectrophotometry, ensuring adequate DNA purity and concentration for polymerase chain reaction (PCR)-based genotyping.[18] Molecular characterization of the ACE gene polymorphism was carried out using specific forward and reverse primers targeting the insertion/deletion region of the ACE gene. PCR amplification remains one of the most reliable and widely accepted techniques for identification of ACE gene polymorphisms.[19]

The ACE gene plays a crucial role in regulation of the renin-angiotensin-aldosterone system (RAAS), which is an important pathway involved in blood pressure regulation and cardiovascular homeostasis.[20] The deletion (D) allele of the ACE gene has been associated with increased circulating and tissue ACE activity, resulting in elevated angiotensin II levels and enhanced vasoconstriction.[21] Increased angiotensin II activity contributes to endothelial dysfunction, vascular remodeling, sodium retention, and sympathetic nervous system activation, thereby increasing susceptibility to hypertension.[22]

In the present study, molecular analysis using PCR amplification demonstrated distinct genotype patterns corresponding to II, ID, and DD genotypes. Similar methodologies have been employed in several earlier studies evaluating ACE gene

polymorphism in hypertensive populations.[23] Previous studies have reported a higher frequency of the DD genotype among hypertensive patients when compared with normotensive controls, suggesting that the D allele may serve as a genetic risk factor for hypertension.[24] However, variations in genotype distribution have been observed among different ethnic and geographic populations due to genetic diversity and environmental influences.[25] The findings of the present study support the growing evidence regarding the role of ACE gene polymorphism in the pathogenesis of hypertension. Identification of genetic susceptibility markers may help in early diagnosis, risk stratification, and development of individualized therapeutic strategies in hypertensive patients.[26] Furthermore, understanding ACE gene polymorphism may also provide insight into response to ACE inhibitors and other antihypertensive medications targeting the RAAS pathway.

CONCLUSION

The present study demonstrated a significant association between angiotensin-converting enzyme (ACE) gene insertion/deletion (I/D) polymorphism and hypertension among the South Indian population. Molecular characterization using polymerase chain reaction (PCR) successfully identified the different ACE genotypes, namely II, ID, and DD. The findings suggest that the deletion (D) allele may contribute to increased susceptibility to hypertension through enhanced ACE activity and activation of the renin-angiotensin-aldosterone system. Genetic variations in the ACE gene may play an important role in the pathogenesis and progression of hypertension. Identification of ACE gene polymorphism can help in understanding individual genetic predisposition, early risk assessment, and development of personalized therapeutic approaches. Further large-scale studies involving diverse populations are required to confirm the relationship between ACE gene polymorphism and hypertension and to evaluate its clinical significance in predicting cardiovascular risk and treatment response.

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