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The Role of ACE I/D Polymorphism In End-Stage Renal Disease: Genetic Insights And Clinical Implications

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KEYWORDS

End stage renal disease (ESRD); angiotensin converting enzyme; insertion/deletion polymorphism.

ABSTRACT:

Introduction: End stage renal disease (ESRD), a severe consequence of chronic kidney failure, presents a global healthcare challenge. The Angiotensin-Converting Enzyme (ACE) gene's role in the renin-angiotensin-aldosterone system (RAAS) makes it of particular interest. This study investigates the potential links between genetic polymorphism in ACE gene, specifically the Insertion/Deletion (I/D) variant, and the risk of developing End Stage Renal Disease (ESRD). The goal is to shed light on the molecular basis of ESRD, potentially offering insights into personalized therapeutic strategies for this debilitating condition.

Material and methods: The study involved 180 ESRD patients and an equal number of matched healthy controls, with genetic and biochemical analyses performed. The genetic analysis of ACE I/D polymorphism in ESRD patients and controls revealed significant associations with disease susceptibility.

Results and conclusion: The DD genotype of ACE I/D was markedly more prevalent in ESRD patients than in controls, as were the D allele frequencies. Logistic regression analysis indicated no significant association between biochemical parameters and the ACE I/D polymorphism. Additionally, comparisons based on the presence or absence of this polymorphism revealed significant differences in various biochemical parameters, providing valuable insights into its potential role in ESRD pathogenesis. These findings underscore the importance of ACE genetic variations in ESRD susceptibility, opening avenues for further research and personalized therapeutic strategies.

1. Introduction

End Stage Renal Disease (ESRD) represents the culmination of chronic kidney failure, characterized by the presence of irreversible renal dysfunction. The etiology of this condition encompasses a range of contributing factors, including but not limited to hypertension, diabetes, and kidney diseases. ESRD is a pathological condition that arises from intricate molecular mechanisms encompassing inflammation, oxidative stress, and fibrosis. These processes collectively contribute to the progressive deterioration of kidney function. The clinical presentation of this condition comprises a range of manifestations, including uremia, electrolyte imbalances, and anemia. [1]

In the past few decades, there has been a significant advancement in our knowledge of disease etiology due to the increasing understanding of intricate genetic variations and their potential implications in disease susceptibilities. [2] The comprehensive elucidation of the intricate molecular mechanisms that establish a connection between genetic variations and their subsequent impact on clinical outcomes is the need of today's research. The intricate interplay between genetic polymorphisms and the development of ESRD has been extensively studied and documented in scientific literature. [3]

The Angiotensin-Converting Enzyme (ACE), which plays a crucial role in the RAAS cascade, has garnered

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significant attention in scientific research due to its genetic polymorphism referred to as the Insertion/Deletion (I/D) polymorphism. [4] The ACE gene, which is situated on the long arm of chromosome 17 at position 23 (17q23), encompasses an intron 16 region that contains a 287-base pair Alu repeat sequence. [5] This particular polymorphism pertains to the existence (insertion, I allele) or nonexistence (deletion, D allele) of the Alu repeat sequence, thereby leading to the formation of distinct ACE genotypes - II, ID, and DD. The ACE I/D polymorphism has been associated with variations in ACE levels and activity, leading to changes in the equilibrium between angiotensin II and angiotensin, which are essential regulators of blood pressure and vascular homeostasis. [6]

The expression of ACE plays a pivotal role in the RAAS. Variations in ACE expression have the potential to exert significant effects on the regulation of blood pressure, maintenance of sodium balance, and renal function. Consequently, these variations may have implications for the development of ESRD. [7]

2. Objectives

The purpose of this study was to investigate any potential links between the ACE I/D polymorphism and the risk of developing ESRD. Through a comprehensive investigation encompassing genetic, biochemical, and clinical aspects, we endeavour to elucidate whether these polymorphisms confer susceptibility to ESRD. By unravelling the molecular intricacies underlying these genetic variations, we seek to contribute to the broader understanding of ESRD pathogenesis, ultimately paving the way for more targeted therapeutic strategies and personalized interventions.

3. Methods

The current case-control study was carried out at the Government Medical College, Miraj, in the Department of Biochemistry. Institutional Ethics Committee approved the study protocol, (Ref No. EC/4/2014) Government Medical College, Miraj. From the Department of Medicine at Government Medical College, Miraj, 180 patients with ESRD who had received a clinical diagnosis were chosen. Eighty healthy individuals who matched in terms of age and gender were chosen as controls; these individuals had no indication of end-stage renal disease (ESRD), diabetes mellitus (DM), chronic kidney disease (CKD), or chronic liver disease. Following the acquisition of informed consent from each study participant, patients were instructed to fast for 12–14 hours overnight. Antecubital venous blood samples were obtained while adhering to aseptic procedures. Clear and unhemolyzed sera were collected in polythene tubes after the samples were centrifuged at 3000 rpm for 15 minutes after they were collected in plain vacuum-sealed containers. The tubes were labelled, corked, and kept between 0 and 4°C until they were analysed to estimate the biochemical parameters. DNA was isolated from the EDTA blood samples in order to perform a polymorphism analysis. Chemiluminescent immunoassay (CLIA) was used to measure the amount of renin [8]. Homocysteine was measured by an enzymatic technique [10] and the level of ACE by the FAPGG substrate method [9]. For routine biochemical parameter estimation, Erba Diagnostics Mannheim GmbH, Germany's commercially available kits were utilized.

Genetic Analysis of ACE I/D: [11]

Polymerase Chain Reaction (PCR) was used to determine whether polymorphism I/D of ACE was present in the whole blood samples obtained from each participant using the salting out method. The forward primer 5'-CTGGAGACCACTCCCATCCTTTCT-3' and the reverse primer 5'-GATGTGGCCATCACATTCGTCAGAT-3' were utilized to test the ACE gene for I/D polymorphism. (S Korea, Macrogen)

The PCR was carried out with a 25µl total volume. Following a brief vertex, 12.5 µl of PCR Master Mix (Qiagen) containing 2.5 units of TaqDNA Polymerase, 2x QIAGEN PCR Buffer, 3 mM MgCl2, and 400 µM of each dNTP was dispensed into each PCR tube. Subsequently, 0.5 µl of each primer and 1 µl of DNA template were added, and the final volume was adjusted to 25 µl using sterile distilled water. Initial denaturation at 94°C was carried out for 5 minutes in the PCR. This was followed by 35 cycle reactions of denaturation at 94°C for 30 seconds, annealing at 64°C for 30 seconds, elongation at 72°C for 45 seconds, and a final extension at 72°C for 7 minutes. An oligonucleotide ladder and all of the PCR products were run through a standard 2% agarose gel electrophoresis. To identify the I/D

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polymorphisms, the size of each band was compared to the reference DNA bands.

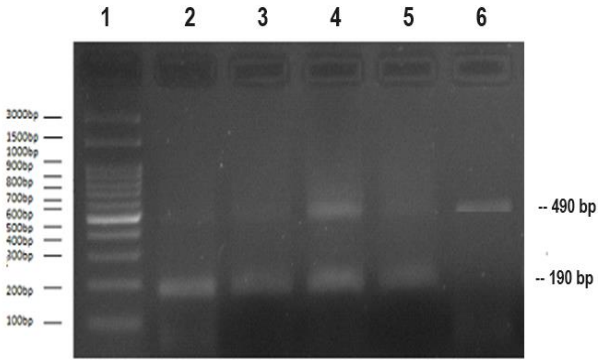

Figure*: ACE I/D genotypes by PCR

Lane 1: 100 bp ladder

Lane 2, 3 & 5: Homozygous for D allele

Lane 4: Heterozygous for ID alleles

Lane 6: Homozygous for I allele

Statistical Analysis:

ESRD patients and controls had their genotype and allele frequencies for both polymorphisms computed, and they were compared statistically using the Chi-square test. With respect to the respective 95% Confidence Interval (CI), the odds ratio was computed. The relationship between the ACE I/D polymorphism and biochemical markers was investigated using logistic regression analysis. The study employed the students unpaired 't' test to compare the impact of I/D polymorphism on demographic and biochemical variables within subgroups (II vs. ID+DD) of the ACE gene. The quantitative parameters were calculated as Mean ± Standard Error (SE). The results were considered significant when $p<0.05$. SNPStat online software and SPSS for Windows, version 26, were used for statistical analysis.

4. Results

In order to determine any associations with the disease, the genotype and allele frequencies of ESRD patients and controls were compared. In terms of ACE, I/D genotype frequencies, it was found that ESRD patients (40.56%) had the DD genotype more frequently than controls (20%) ($p = 0.0001$). In ESRD patients, the ID genotype frequencies were 36.67%, whereas in controls, they were 46.67%. In ESRD patients, the II genotype frequencies were 22.78%, while in controls, they were 33.33%. Allele frequencies showed that ESRD patients had higher frequencies of the D allele (0.59) than of the I allele (0.43) ($p = 0.0339$), while the frequencies of the I allele were 0.41 in ESRD patients and 0.57 in controls. (Table 1).

Table 1: Comparison of genotype and allele frequencies of ACE I/D polymorphisms among ESRD patients and controls

	Total (n=360)	ESRD (n=180)	Controls (n=180)	p value
ACE I/D Genotype frequencies: expressed as 'n (%)'				
II	101 (28.1)	41 (22.78)	60 (33.33)	0.0001*
ID	150 (41.7)	66 (36.67)	84 (46.67)	
DD	109 (30.3)	73 (40.56)	36 (20)	
Allele frequencies				
I	0.49	0.41	0.57	0.0339*
D	0.51	0.59	0.43	
Odds ratio (95% Confidence Interval): 1.70 (1.0635 to 2.702)				
*Statistically significant				

The relationship between the ACE I/D polymorphism and different biochemical and demographic parameters was investigated using logistic regression analysis. The ACE I/D polymorphism was not significantly correlated with any biochemical parameters, according to the findings. (Table 2)

Table 2: Association of ACE I/D polymorphism with demographic and biochemical parameters

Variable	ACE I/D		
	Coefficient	Std. Error	p value
BMI	0.0435	0.0568	0.4439
Systolic blood pressure	-0.0101	0.0166	0.5453
Diastolic blood pressure	-0.0220	0.0122	0.0706
Urea	-0.0367	0.1449	0.8000
Blood urea nitrogen	0.1050	0.3131	0.7374
Creatinine	-0.1060	0.1433	0.4593
Sodium (Na+)	-0.0401	0.0552	0.4680
Potassium (K+)	-0.5157	0.7015	0.4622
Total cholesterol	-0.0128	0.0085	0.1329
Triglycerides	0.0117	0.0101	0.2465
HDL Cholesterol	-0.0160	0.0112	0.1551
LDL Cholesterol	0.0055	0.0152	0.7181
ACE level	-0.0091	0.0092	0.3220
Renin level	-0.0016	0.0190	0.9323
Homocysteine	0.0147	0.0200	0.4625
BMI: Body mass index, ACE: Angiotensin converting enzyme			

A comparison of demographic and biochemical parameters based on the presence or absence of insertion/deletion polymorphism (II vs. DD+ID) was performed. The results revealed that significant

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differences were observed in BUN (p = 0.0230), Creatinine (p = 0.0374), HDL cholesterol (p = 0.0051), Homocysteine (p = 0.0282), LDL cholesterol (p = 0.0219), Na+ (p = 0.0080), SBP (p = 0.0350), TG (p = 0.0180), and Urea (p = 0.0235) between the groups. However, there were no significant differences in ACE level (p = 0.1186), BMI (p = 0.0562), DBP (p = 0.0651), K+ (p = 0.0538), Renin level (p = 0.0927) and TC (p = 0.0888) between the two groups. (Table 3)

Table 3: Comparison of demographic and biochemical parameters on the basis of status of insertion/deletion polymorphism

Variable	II (n=101)		DD+ID (n=259)		p value
	Mean	SD	Mean	SD	
BMI	24.73	2.90	25.38	2.89	0.0562
Systolic blood pressure	137.99	19.22	143.02	20.65	0.0350*
Diastolic blood pressure	77.62	8.14	74.54	15.93	0.0651
Urea	91.43	77.46	112.82	81.19	0.0235*
Blood urea nitrogen	42.82	36.39	52.90	38.12	0.0230*
Creatinine	4.90	5.12	6.16	5.15	0.0374*
Sodium (Na+)	136.36	4.69	135.06	3.93	0.0080*
Potassium (K+)	4.41	0.72	4.58	0.76	0.0538
Total cholesterol	215.87	52.02	226.89	56.19	0.0888
Triglycerides	179.65	50.99	194.28	53.07	0.0180*
HDL Cholesterol	49.09	19.12	43.51	15.90	0.0051*
LDL Cholesterol	121.14	48.93	134.30	48.66	0.0219*
ACE level	64.68	29.11	69.74	26.95	0.1186
Renin level	33.83	16.11	37.26	17.80	0.0927
Homocysteine	16.64	9.91	19.59	11.94	0.0282*

BMI: Body mass index, ACE: Angiotensin converting enzyme

*Statistically significant

5. Discussion

ESRD is characterized by a complex interplay of genetic and environmental factors that work together to impair renal function and homeostasis. [1] Once ESRD manifests, there is a substantial escalation in both the clinical and economic burden associated with the disease. Globally, it is estimated that approximately 2 million individuals are presently in need of renal replacement therapy (RRT) to manage ESRD. In the context of healthcare expenditure, it is observed that developed countries allocate a notable portion, specifically 2-3%, of their overall national health-care budget towards the provision of treatment for ESRD. It has been observed that a number of developing nations face significant challenges in allocating sufficient resources to establish and maintain comprehensive RRT within their medical systems. As a result, it is estimated that approximately one million individuals succumb to untreated ESRD annually. [12-14]

The management of ESRD presents considerable healthcare challenges, particularly in the context of dialysis or transplantation. [15] The exploration of the molecular underpinnings of ESRD holds the potential to unveil novel therapeutic approaches aimed at slowing down disease advancement and improving the overall quality of life for affected individuals.

The renin-angiotensin-aldosterone system (RAAS) is a crucial regulatory network that plays a significant role in controlling blood pressure, maintaining fluid-electrolyte balance, and regulating vascular tone. Researchers have shown great interest in genetic variations found within the genes responsible for encoding the components of the RAAS. This interest stems from the potential implications these genetic variants may have in the development and progression of ESRD. [16]

The etiology of ESRD is a complex phenomenon that arises from the intricate interplay of several factors, including genetic predisposition, environmental influences, and lifestyle choices. [17]

Although it is widely acknowledged that genetics play a significant role in disease susceptibility, further research is necessary due to the complexity of genetic associations. The ACE I/D polymorphism have attracted significant attention due to its potential involvement in the complex RAAS network and potential effects on renal function and hypertension. [18,19]

Genetic markers, particularly polymorphisms in the Angiotensin-Converting Enzyme (ACE), have been identified as important risk factors for ESRD. [20] ACE is a key component of the renin-angiotensin-aldosterone system (RAAS). [21] It establishes Angiotensin-II, a vasoactive peptide. Most chronic nephropathies slowdown in their progression when it is inhibited. [22] The balance between the vasoconstrictor and vasodilator components of the RAAS may change as a result of genetic variations within the ACE gene, such as the I/D polymorphism, which can affect ACE activity. [23]

In order to better understand how these polymorphisms, affect ESRD susceptibility, the current study investigated any possible associations between ACE I/D polymorphism and ESRD. The findings showed notable genotype and allele frequency differences between ESRD patients and controls, illuminating the possibility of genetic influences on the emergence of ESRD.

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Biochemical parameters are deranged in ESRD patients. Demographic and biochemical parameters are significantly altered in ESRD patients as compared to controls. [24]

In this study, ACE I/D polymorphism in ESRD patients had a significantly higher prevalence of the DD genotype than did controls. This result is similar with earlier research linking the D allele to cardiovascular conditions and hypertension because of its link to higher ACE activity, which in turn raises angiotensin II levels. [25-28]

Despite the fact that the majority of recent studies have indicated a high prevalence of the D allele among people with hypertension, there are still conflicting reports available. [28, 29] The genotype frequencies of CKD with hypertensive patients and controls did not significantly differ, according to Shanmuganathan R [28] et al. Beige J [29] et al concluded, insertion/deletion polymorphism of the ACE in the recipient or donor does not appear to be a significant predictor of transplant survival in Caucasian renal transplant patients.

Our results showed that the ACE I/D polymorphism has a significant impact on a number of parameters, including renal function markers (Urea, BUN, Creatinine), HDL cholesterol, LDL cholesterol, TG, homocysteine, Sodium (Na+). The presence or absence of ACE I/D polymorphism did not correlate with BMI, DBP, ACE, Renin, total cholesterol, and K+ levels.

According to our research, there is a substantial relationship between having an elevated homocysteine level and having the ACE I/D polymorphism. Numerous mechanisms, including the induction of inflammation and cell death, disruption of nitric oxide (NO) production, accumulation of reactive oxygen species (ROS) and oxidative stress, cellular hypomethylation, protein homocysteinylation, and aberrant lipid metabolism, have been linked to the endothelium's damage by hyperhomocysteinemia. (30) These results raise the possibility that the ACE I/D polymorphism affects metabolic and renal factors, perhaps by altering the RAAS pathway and resulting vascular regulation.

In the present study, presence of D allele showed positive correlation with number of biochemical parameters, in contrast to Abouleka Y [31] et al's report that there was no association between clinical or biochemical parameters and the presence of the D allele. According to Tripathi G. [26] et al, no correlation was found between the DD and non-DD genotypes for various biochemical parameters of the lipid profile and renal function,

In conclusion, this study provides strong support for the hypothesis that the ACE I/D polymorphism is related to ESRD susceptibility. The observed differences in genotype and allele frequencies, as well as the relationship between this polymorphism and different clinical indicators, imply that I/D genetic variation in the ACE gene may play a role in the emergence of ESRD. The findings highlight the importance of the RAAS system in controlling renal function and call for additional research into the molecular pathways that connect this polymorphism to the pathogenesis of ESRD. In managing this complex renal disorder, knowing the genetic causes of ESRD may open the door to targeted interventions and individualized treatment plans.

References

1. Gusev E, Solomatina L, Zhuravleva Y, Sarapultsev A. The Pathogenesis of End-Stage Renal Disease from the Standpoint of the Theory of General Pathological Processes of Inflammation. Int J Mol Sci. 2021; 22(21):11453.
2. Marian AJ. Clinical Interpretation and Management of Genetic Variants. JACC Basic Transl Sci. 2020; 5(10):1029-1042.
3. Saw KME, Ng RGR, Chan SP, Ang YH, Ti LK, Chew THS. Association of genetic polymorphisms with acute kidney injury after cardiac surgery in a Southeast Asian population. PLoS One. 2019; 14(4): e0213997.
4. Gintoni I, Adamopoulou M, Yapijakis C. The Angiotensin-converting Enzyme Insertion/Deletion Polymorphism as a Common Risk Factor for Major Pregnancy Complications. In Vivo. 2021; 35(1):95-103.
5. Martínez-Ríos MA, Peña-Duque MA, Fragoso JM, Delgadillo-Rodríguez H, Pérez-Hernández N, Miranda-Malpica E et al. No association found between the insertion/deletion of a 287-bp alu repeat sequence within intron 16 of the angiotensin-I-converting enzyme (ACE) gene in Mexican patients and binary restenosis after coronary stenting. Clin Chim Acta. 2008; 397(1-2):65-7.

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www.jchr.org

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6. Benenemissi IH, Sifi K, Sahli LK, Semmam O, Abadi N, Satta D. Angiotensin-converting enzyme insertion/deletion gene polymorphisms and the risk of glioma in an Algerian population. Pan Afr Med J. 2019; 32:197.
7. Bernstein KE, Giani JF, Shen XZ, Gonzalez-Villalobos RA. Renal angiotensin-converting enzyme and blood pressure control. Curr Opin Nephrol Hypertens. 2014; 23(2):106-12.
8. Frank Holger Perschel, Rudolf Schemer, Lysann Seiler, Martin Reincke, Jaap Deinum, Christiane Maser-Gluth et al. Rapid Screening Test for Primary Hyperaldosteronism: Ratio of Plasma Aldosterone to Renin Concentration Determined by Fully Automated Chemiluminescence Immunoassays. Clin Chem.2004; 50(9): 1650–1655.
9. J E Buttery, S Stuart. Assessment and optimization of kinetic methods for angiotensin-converting enzyme in plasma. Clin Chem. 1993 Feb;39(2):312-6.
10. Ueland PM, Refsum H, Stabler SP, Malinow MR, Andersson A, Allen RH. Total homocysteine in plasma and serum: methods and clinical applications. Clin Chem 1993;39(9):1764-79.
11. Sabir JSM, Omri AE, Ali Khan I, Banaganapalli B, Hajrah NH, Zrelli H et al. ACE insertion/deletion genetic polymorphism, serum ACE levels and high dietary salt intake influence the risk of obesity development among the Saudi adult population. J Renin Angiotensin Aldosterone Syst. 2019; 20(3):1470320319870945.
12. Eggers PW. Has the incidence of end-stage renal disease in the USA and other countries stabilized? Curr Opin Nephrol Hypertens. 2011; 20:241–245.
13. Levey AS, Atkins R, Coresh J, Cohen EP, Collins AJ, Eckardt KU et al. Chronic kidney disease as a global public health problem: approaches and initiatives—a position statement from Kidney Disease Improving Global Outcomes. Kidney Int. 2007; 72:247–259.
14. El Nahas M. The global challenge of chronic kidney disease. Kidney Int. 2005; 68:2918–2929.
15. Junaid Nazar CM, Kindratt TB, Ahmad SM, Ahmed M, Anderson J. Barriers to the successful practice of chronic kidney diseases at the primary health care level; a systematic review. J Renal Inj Prev. 2014; 3(3):61-7.
16. Muñoz-Durango N, Fuentes CA, Castillo AE, González-Gómez LM, Vecchiola A, Fardella CE et al. Role of the Renin-Angiotensin-Aldosterone System beyond Blood Pressure Regulation: Molecular and Cellular Mechanisms Involved in End-Organ Damage during Arterial Hypertension. Int J Mol Sci. 2016; 17(7):797.
17. Obrador GT, Schultheiss UT, Kretzler M, Langham RG, Nangaku M, Pecoits-Filho R et al. Genetic and environmental risk factors for chronic kidney disease. Kidney Int Suppl (2011). 2017; 7(2):88-106.
18. Alvi FM, Hasnain S. ACE I/D and G2350A polymorphisms in Pakistani hypertensive population of Punjab. Clin Exp Hypertens. 2009; 31(5):471-80.
19. Imran I, Syahrul S, Sofia S, Farida F, Musadir N, Fajar JK. Association of angiotensin-converting enzyme G2350A gene polymorphisms with hypertension among patients with intracerebral haemorrhage. J Taibah Univ Med Sci. 2019; 14(3):300-305.
20. El-Sayed Marei Y, Abdallah Bayoumy A, Mohamed Abulazm Nassar H, Mansour B, Bakeir Hamady A. The Relation between ACE Gene Polymorphism and the Severity of COVID-19 Infection. Int J Microbiol. 2023; 2023:4540287.
21. Fountain JH, Kaur J, Lappin SL. Physiology, Renin Angiotensin System. [Updated 2023 Mar 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470410/
22. Ruggenenti P, Perna A, Gherardi G. Renoprotective properties of ACE inhibition in non-diabetic nephropathies with non-nephrotic proteinuria. Lancet. 1999; 354:359–364.
23. Montes-de-Oca-García A, Perez-Bey A, Velázquez-Díaz D, Corral-Pérez J, Opazo-Díaz E, Rebollo-Ramos M et al. Influence of ACE Gene I/D Polymorphism on Cardiometabolic Risk, Maximal Fat Oxidation, Cardiorespiratory Fitness, Diet and Physical Activity in Young Adults. Int J Environ Res Public Health. 2021; 18(7):3443.
24. Asmita B Patil, Jayashree V Ganu. Exploring the Interplay of Homocysteine and Lipid Profile in End-Stage Renal Disease: Implications for Pathogenesis. RJPBCS. 2023 Sept.- Oct; 14(5): 113-118.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(5), 1252-1258 | ISSN:2251-6727

25. Su SL, Yang HY, Wu CC, Lee HS, Lin YF, Hsu CA et al. Gene-gene interactions in renin-angiotensin-aldosterone system contributes to end-stage renal disease susceptibility in a Han Chinese population. ScientificWorldJournal. 2014; 2014:169798.
26. Tripathi G, Dharmani P, Khan F, Sharma RK, Pandirikkal V, Agrawal S. High prevalence of ACE DD genotype among north Indian end stage renal disease patients. BMC Nephrol. 2006; 7:15.
27. Zhou TB, Yin SS, Qin YH. Association between angiotensin-converting enzyme insertion/deletion gene polymorphism and end-stage renal disease susceptibility. J Renin Angiotensin Aldosterone Syst. 2014; 15(1):22-31.
28. Shanmuganathan R, Kumaresan R, Giri P. Prevalence of angiotensin converting enzyme (ACE) gene insertion/deletion polymorphism in South Indian population with hypertension and chronic kidney disease. J Postgrad Med. 2015; 61(4):230-4.
29. Beige J, Schere S, weber A, Engeli S, offerman G, Opelz G et al. Angiotensin converting enzyme genotype and renal allograft survival. J Am Soc Nephrol. 1997; 8:1319–1323.
30. Esse R, Barroso M, Tavares DA I, Castro R. The contribution of homocysteine metabolism disruption to endothelial dysfunction: state-of-the-art. Int J Mol Sci. (2019) 20:867.
31. Abouleka Y, Mohammedi K, Carpentier C, Dubois S, Gourdy P, Gautier JF et al. ACE I/D Polymorphism, Plasma ACE Levels, and Long-term Kidney Outcomes or All-Cause Death in Patients With Type 1 Diabetes. Diabetes Care. 2021; 44(6):1377-1384.