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Genetic Predictors of Chronic Kidney Disease in Children

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Abstract

Chronic kidney disease (CKD) in children is an important medical and social issue due to its potential for serious consequences, such as hypertension and kidney failure, as well as its impact on the quality of life of young patients. It is essential to comprehend the genetic foundation of CKD in order to create efficient diagnostic and treatment plans. In a cohort of children with CKD, this study sought to determine the impact of genetic variants in the ACE, AGTR1, and NOS3 genes on clinical markers of CKD, such as blood pressure, renal abnormalities, and proteinuria levels. In this study, which comprised 109 youngsters split into main and control groups, polymorphic loci in the renin-angiotensin system were thoroughly analyzed genetically. The results showed a substantial correlation between the ACE (DD) genotype and higher levels of proteinuria, indicating a more severe course of the disease and a higher risk of complications. This demonstrates how the ACE genotype may be used as a biomarker for pediatric CKD risk assessment and early diagnosis.

As opposed to the AA genotype, the AGTR1 (AC) genotype did not significantly correlate with the incidence of kidney abnormalities found by ultrasound. Similarly, compared to the bb genotype, the NOS3 (ab) genotype did not significantly raise blood pressure levels. These findings imply that whereas AGTR1 and NOS3 polymorphisms may have a less significant effect or be modified by other genetic or environmental variables, ACE polymorphisms are essential for the clinical presentation of CKD.

The work highlights the need for more research to examine other genetic markers and their interactions, as well as the intricacy of genetic relationships in the development of chronic kidney disease. A better comprehension of these genetic factors may result in the creation of more individualized and efficient treatment and diagnostic strategies. Because customized interventions based on individual genetic profiles are made possible by the integration of genetic testing into clinical practice, disease prognosis and management may be enhanced.

To sum up, this study emphasizes how crucial genetic analysis is to comprehending childhood CKD. Even while the ACE (DD) genotype is a notable predictor of disease severity, more research is needed to clarify the contributions of other genetic variables. These results lend credence to the idea of incorporating genetic testing into standard clinical practice in order to improve young patients' early diagnosis, risk evaluation, and tailored treatment of chronic kidney disease.

Keywords: Chronic Kidney Disease, Children, Genetic Predictors, Genotype

1. Introduction

Children with chronic kidney disease (CKD) face serious medical and social challenges that impair their quality of life and general health. renal failure and hypertension are two major consequences that can arise from this condition, which is defined by a progressive decrease of renal function [1]. Children with chronic kidney disease (CKD) face significant medical and social challenges because the disease can cause serious complications such renal failure as well as a significant decline in quality of life. The genetic foundation of chronic kidney disease (CKD) has drawn more attention from researchers in recent years since novel approaches to the illness's diagnosis, treatment, and prevention depend heavily on our ability to comprehend its genetic components [2].

Scientists have recently discovered a number of genetic markers that could have a role in children's development of CKD. Nephrotic syndrome in children has been linked to mutations in genes that encode proteins of the kidney filtration barrier, such as NPHS1 and NPHS2. These genes are essential for preserving the glomeruli's anatomical and functional integrity [3].

Genes linked to fibrotic and inflammatory processes in the kidneys are another example. Research indicates that specific gene variations, including TGFB1 and ACE, may raise the chance of getting chronic kidney disease (CKD). These genes have a role in controlling fibrosis and inflammatory reactions, which can eventually cause renal function to gradually decline [4].

Genetic variables are important in both the development of renal disease and childhood CKD [5]. Genetic variables also affect how well a patient responds to treatment. For instance, variations in the ACE gene, which controls the body's fluid balance and blood pressure, may have an impact on how well ACE inhibitors work, a frequent treatment for chronic kidney disease [6]. Physicians can select more tailored and successful treatment plans for each patient by having a better understanding of these genetic relationships [7].

Numerous factors influencing the development of chronic kidney disease (CKD) in children with congenital abnormalities of the kidney and urinary tract (CAKUT) are investigated in Saskia Isert's study. Prenatally diagnosed kidney or urinary tract malformations, as well as oligohydramnios or anhydramnios, have been linked to an increased risk of congenital kidney disease (CKD) in offspring. Additionally, it was discovered that premature birth increased the chance of chronic kidney disease (CKD) and its severe phases [8].

Iskenderova B.E. and Musabekova Zh.A.'s article states that single nucleotide polymorphisms in genes influencing the renin-angiotensin system are frequently seen in pediatric patients with different forms of nephropathy. Angiotensin II activity rises noticeably as a result of this. Angiotensinogen genetic polymorphisms in the forms Met-235-met and Thr-174-Thr are more commonly found in youngsters, which supports preliminary findings on its influence on the onset and course of chronic kidney disorders. The ACE gene polymorphism is especially concerning because it is primarily linked to the D allele. The majority of people with this polymorphism have chronic renal disease, usually in stages three through five. Furthermore, the ACE-D/D genotype is most frequently associated with elevated blood pressure [9].

As part of the Chronic Kidney Disease in Children (CKiD) initiative, an intriguing investigation on chronic kidney disease in children was carried out. This study looked at cases of focal segmental glomerulosclerosis (FSGS) in African American children with chronic kidney disease. To find correlations, more than 680,000 common single nucleotide polymorphisms (SNPs) were examined. Results for genetic variations in the FGFR4, ALMS1, and APOL1 genes were particularly noteworthy. In addition to new genes like GRB2 and ITGB1, which are crucial for the renal filtration barrier and kidney cell differentiation, these genes have already been connected to adult FSGS and chronic kidney disorders [10].

The main focus of Uwaezuoke's research is on the application of novel biomarkers to forecast the beginning and course of pediatric chronic kidney disease. The significance of identifying these biomarkers is emphasized in the article as a means of improving treatment outcomes, delaying the progression of the disease, and predicting late stages of CKD early. The authors provide a thorough study of the usefulness of CKD biomarkers in illness prediction, categorizing them into markers of renal function and markers of kidney damage [11]. Karin Luttropp's research examines the interplay between phenotypic and genotypic characteristics in relation to the risk of complications associated with chronic kidney disease (CKD). Researchers found risk variables for inflammation in individuals with chronic kidney disease (CKD) using the Relaxed Linear Separability (RLS) feature selection approach. In addition to examining 79 genetic polymorphisms and 57 anthropometric and biochemical measures, the study included 225 patients who were at stage 5 CKD at the start of dialysis. The findings indicated that hereditary factors significantly influenced inflammation, indicating that genotypic parameters should be considered in risk studies [12].

Renal dysgenesis has been linked to specific renin-angiotensin system genes, including AGT (angiotensinogen), ACE (angiotensin-converting enzyme), AGTR1 (angiotensin type 1 and 2 receptors), and AGTR2. Polymorphic genetic markers of the renin-angiotensin system have been found to be associated with features related to the onset and survival of chronic kidney disease in children. Further research in this area is necessary because these results do not definitively address the pathogenetic significance of particular single nucleotide mutations of the renin-angiotensin system genes in the progression of CKD in children [13].

It is important to remember that a thorough genetic panel assessment is necessary due to the genetic propensity to a multifactorial illness like chronic kidney disease (CKD). There has never before been a study done on the genetic indicators for CKD in the population of Kazakhstan [14].

In the context of developing novel techniques for diagnosis and treatment, research on the genetic components of childhood CKD is very pertinent. Treatment techniques for chronic kidney disease (CKD) can be drastically altered, and the prognosis for young patients can be greatly improved, if it is possible to forecast the course of the disease and choose the best course of action based on the patient's genetic profile [15]. According to Mrozikiewicz-Rakowska B.'s study, ischemic heart disease, hypertension, body mass, hip circumference, creatinine level, and diabetic retinopathy were among the risk factors for chronic kidney disease (CKD). Furthermore, in patients with type 2 diabetes and diabetic foot, the C allele of the rs3134069 polymorphism appears to have a protective effect against the development of chronic kidney disease (CKD) in the following allelic variants: [AA] vs. [AC] and [AA] vs. [AC + CC]. It was discovered that in patients with T2DM and diabetic foot, the C allele is less common than the A allele [16].

The foundation for using biomarkers in observational and interventional studies was presented by Provenzano M. Biomarkers can be categorized as predictive or prognostic.

While the latter type is used to assess whether a patient might benefit from a certain treatment, the former type is used to assess a patient's likelihood of reaching an endpoint regardless of treatment [17].

According to Varner's study "Genetic Testing for Steroid-Resistant-Nephrotic Syndrome in an Outbred Population," a major cause of chronic kidney disease (CKD) in children, steroid-resistant nephrotic syndrome (SRNS) is linked to particular genetic mutations. Important genes have been identified, including WT1, COL4A3, and INF2 [18].

Durand A. and Winkler C. state that genetic research has shown immunological system regulation's significance and functionally significant risk variables in primary FSGS in children, which has improved our knowledge of the disease's molecular pathophysiological mechanisms [19]. According to Faure A. and Bouty A., CNVs larger than 100 Kb are strongly linked to early-onset renal failure in kids with posterior urethral valves, suggesting a hereditary component to the decline in kidney function [20].

As to the paper titled "Genetic polymorphisms of the RAS-cytokine pathway and chronic kidney disease," variations in the cytokine pathway and renin-angiotensin system genes can influence the development of chronic kidney disease (CKD) and cardiovascular anomalies in children [21]. The association between particular genetic polymorphisms and the development of chronic kidney disease (CKD) in children has not been extensively examined, despite advances in our understanding of the genetic components of numerous diseases [22]. By bridging this information gap, our research may enhance childhood CKD prevention, diagnosis, and treatment.

This study aims to explore the connection between particular genetic markers and the clinical features of pediatric chronic kidney disease. Research on the polymorphisms of the ACE, AGTR1, and NOS3 genes and their possible significance in the onset and course of chronic kidney disease (CKD) is particularly focused on.

2. Methodology

A statistical study using correlation analysis, hypothesis testing, and descriptive statistics was carried out in order to meet the predetermined target. 109 children's medical records were examined in order to gather data; 63 children made up the main group and 46 made up the control group. Among other clinical characteristics, the investigation looked at the link between genetic markers and age, blood pressure, and proteinuria levels.

In the initial phase of the investigation, the "DNA-sorb-B" reagent kit for clinical material DNA extraction was used to extract genomic DNA from dried blood spots on DNA cards. The next step in the preparation of the DNA samples was to use a Nanodrop 2000 spectrophotometer (Thermo Scientific, USA) to measure the samples' concentration and purity.

The angiotensin-converting enzyme (ACE, (InsDel)) and the angiotensin type 1 receptor (AGTR1, rs5186 (1166A/C)) are the two polymorphic loci in the renin-angiotensin system that were the focus of the investigation. Table 1 presents the genotyping methods.

2.1. Statistical Analysis

Descriptive statistics are used to characterize the fundamental characteristics of the sample and to summarize the data.

2.2. Correlation Analysis

Used to investigate the connections between clinical indicators and genetic markers.

To ascertain the significance of observed relationships, hypothesis testing is used.
Implements and Machinery.

Thermo Scientific, USA's Nanodrop 2000 Spectrophotometer is used to evaluate the concentration and purity of DNA samples.

The "DNA-sorb-B" reagent kit is used to extract DNA from medical specimens.
Table 1 describes the unique genotyping methods and comprehensive approaches for the ACE and AGTR1 polymorphisms.

Gene	Polymorphic locus	Method of genotyping	Manufacturer
AGT	Thr174Met, rs4762	Real-time PCR in the presence of fluorescent probes	«Syntol» LLC
AGTR1	A1166C rs5186	Real-time PCR in the presence of fluorescent probes	«Syntol» LLC
AGTR2	G1675A rs1403543	Allele-specific real-time PCR with fluorescent dye	«Litech» LLC
AGTR2	A-1332G	Classical PCR followed by restriction enzyme digestion of amplification products and separation of the resulting fragments in a polyacrylamide gel	

Table 1: List of Loci and Methods of Genotyping

The distribution of genotypes for three NOS3 polymorphisms among the patient groups and the control group is shown in Figure 1.

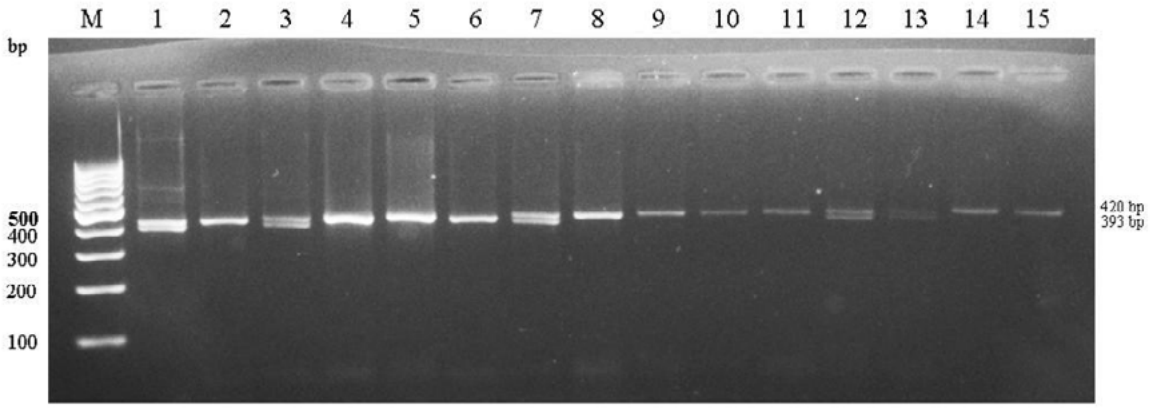

Figure 1: Electrophoresis of PCR Products

There were 27 females and 36 boys in the main group. In the major group, there was a 5 year minimum and a 16 year maximum age. With a standard deviation of roughly 3.58 years, the average age was roughly 11.65 years.

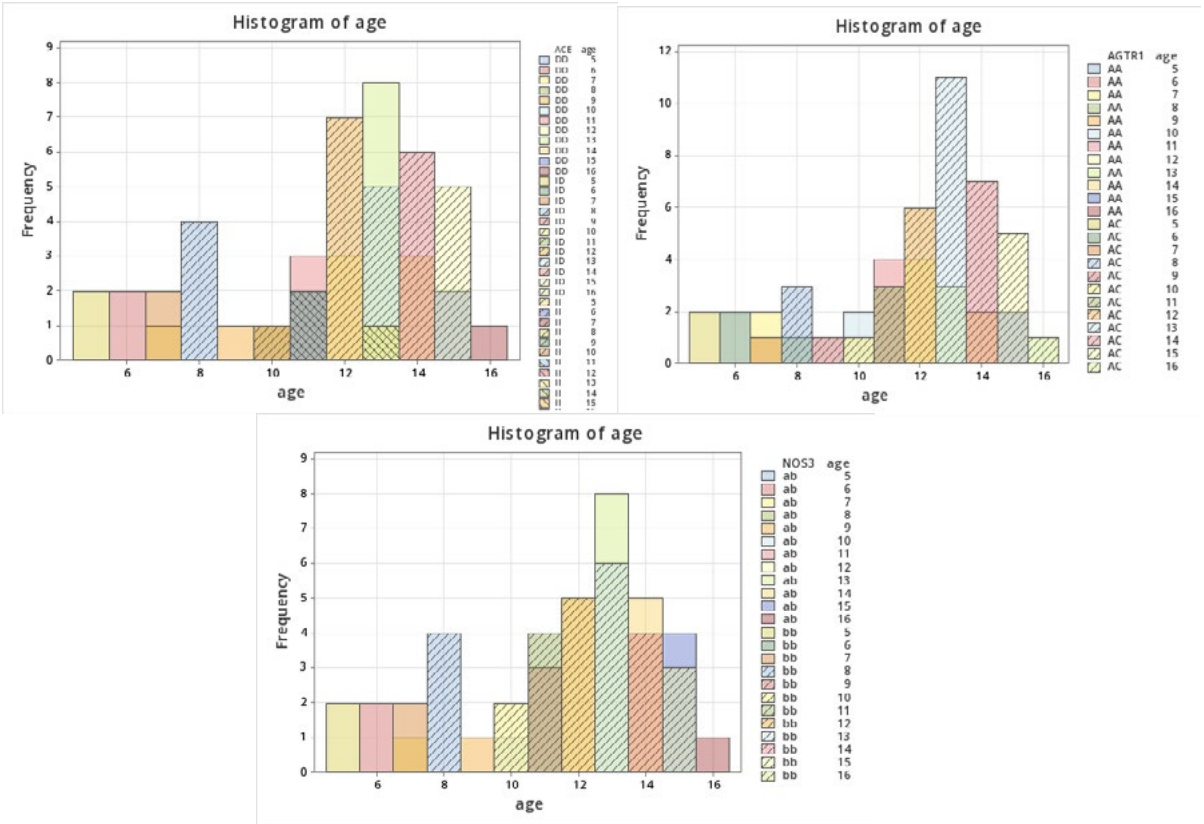

Figure 2: Frequency Distribution of ACE, AGTR1 and NOS3 Genotypes among Children with CKD by Age Group

The image illustrates the incidence of various genotypes among children with chronic kidney disease (CKD) by associating them with particular age ranges.

The genotypes bb (NOS3) and DD (ACE) are more prevalent in older children (12–14 years old), which may indicate a connection to a later onset and course of the illness.

Younger age groups have higher prevalence of the AA (AGTR1) and ab (NOS3) genotypes, which may indicate that these variants have an impact on the disease's early phases.

This distribution implies that the child's genetic predisposition may have an impact on the age at which the sickness manifests and how severe it is.

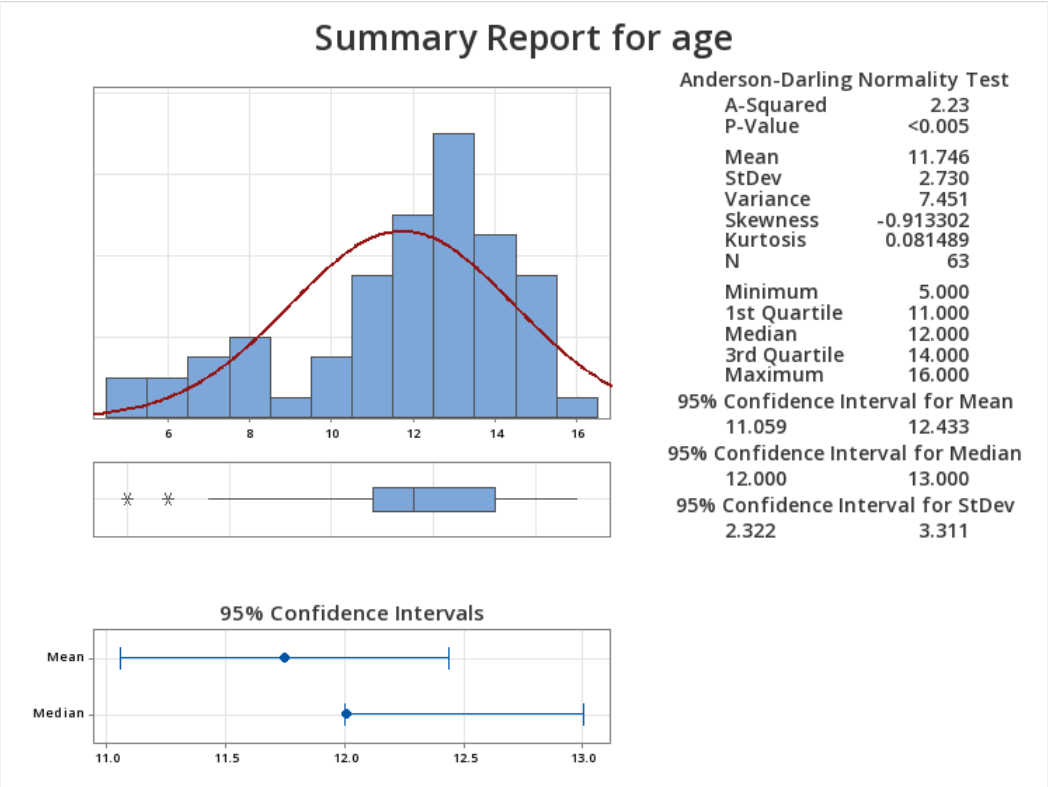

Figure 3: Summary Report of Age Distribution with Statistical Analysis for Children with CKD

The majority of youngsters, according to the histogram, are between the ages of 10 and 14, with a peak frequency occurring at 12. This implies that this is the time when the illness is most frequently diagnosed. The A-Squared value is 2.23 and the p-value is less than 0.005, indicating that the age distribution does not follow a normal distribution. This may indicate that there are anomalies in the sample or that specific age groups are more likely to be affected by the disease.

2.3. Parameters of Statistics

The sample's mean age of 11.746 years confirms the predominance of middle-aged children.

The peak displayed in the histogram also corresponds with the median age of 12 years.

Skewness: The skewness of the data is moderately negative (-0.913302), indicating that a greater percentage of children fall into the older age groups.

Kurtosis: A distribution shape that is roughly normal but has deviations is suggested by the value of 0.081489, which is quite close to zero.

Confidence Intervals: 11.059 to 12.433 is the 95% confidence interval for the mean.

The 95% confidence interval for the standard deviation is from 2.322 to 3.311, and the 95% confidence interval for the median is between 12 and 13.

It may be important to note that the majority of children fall within this age range while making a diagnosis and developing a treatment strategy.

Boxplot: The boxplot shows the age range, with five years as the minimum and sixteen years as the maximum. Two outliers in the lower range attest to the existence of younger children with CKD diagnoses.

Ultrasound scans of 46 of the 63 youngsters in the main group did not reveal any abnormal alterations in their kidneys. Ultrasonography revealed renal diseases in 17 of the remaining children, or 26.9%. This suggests that over 25% of the main group exhibits certain abnormalities that might call for extra observation or help.

Frequent disease relapses were seen in 26 children (41.2%), which could be a sign of a more serious disease course or inadequate current treatment. Concurrently, 37 kids (58.8%) experienced rare relapses, which might point to a milder version of the illness or the efficacy of the treatment being administered.

Thirty infants (47.6%) had edema, a clinical indication that is frequently linked to kidney disorders and may suggest compromised kidney function. 33 children (52.4%) did not have edema, which could be a sign of improved kidney function or a different stage of the illness.

39.7% of the individuals under investigation have the DD genotype. This genotype is connected to a higher risk of cardiovascular illnesses and some types of kidney dysfunction, and it is frequently associated with enhanced enzyme activity.

Among the group, the ID genotype is the most prevalent, accounting for 57.9% of participants. It is believed that the dangers connected to the DD and II genotypes are somewhat balanced by this heterozygous genotype. The rarest genotype, II, is seen in 2.4% of individuals. This genotype may be connected to a lower risk of cardiovascular illnesses as it is typically associated with lower enzyme activity.

AGTR1 Gene Polymorphism (Angiotensin II Type 1 Receptor): 68.3% of the participants have the AC genotype. An abnormal response to angiotensin II, which regulates blood pressure and blood volume, may be indicated by this genotype. Of the participants, 31.7% have the CC genotype. According to certain research, there may be a link between the CC genotype and a higher risk of cardiovascular illnesses.

Endothelial NO Synthase (NOS3 Gene Polymorphism): 49.2% of the subjects have the ab genotype. This genotype denotes heterozygosity and could affect blood circulation and vascular function in several ways. The bb genotype is also rather prevalent, present in 50.8% of the subjects. This genotype may be linked to different vascular responses depending on the situation.

To evaluate the effects of three hypotheses on clinical parameters in children with chronic kidney disease (CKD), each of which is connected to one of the genetic markers that have been examined (ACE, AGTR1, and NOS3).

2.4. Hypothesis 1

Compared to other genotypes (ID and II), children with CKD who have the ACE (DD) genotype have higher amounts of proteinuria.

2.5. Hypothesis 2

Compared to the AA genotype, the AGTR1 (AC) genotype is linked to a higher frequency of kidney abnormalities found by ultrasound.

2.6. Hypothesis 3

Compared to the bb genotype, children with CKD who have the NOS3 (ab) genotype have greater blood pressure.

In order to better understand the role that various genetic markers play in the pathophysiology of the disease and to aid in the development of patient-specific therapy and monitoring strategies, these hypotheses seek to investigate the impact of these markers on the clinical symptoms of childhood CKD.

Variable	ACE	N	N*	Mean	SE Mean	StDev	Minimum	Q1	Median	Q3	Maximum
proteinuria	DD	25	0	10.5296	3.27876	16.3938	1.47	3.64	4.5	6.53	62
	ID	34	0	2.66765	0.113864	0.663937	1.45	2.2	2.6	3.075	4.3
	II	4	0	1.9125	0.0590727	0.118145	1.75	1.7875	1.95	2	2

Table 2: Comparative Analysis of Proteinuria Levels among ACE Genotypes (DD, ID and II) in Children with Chronic Kidney Disease

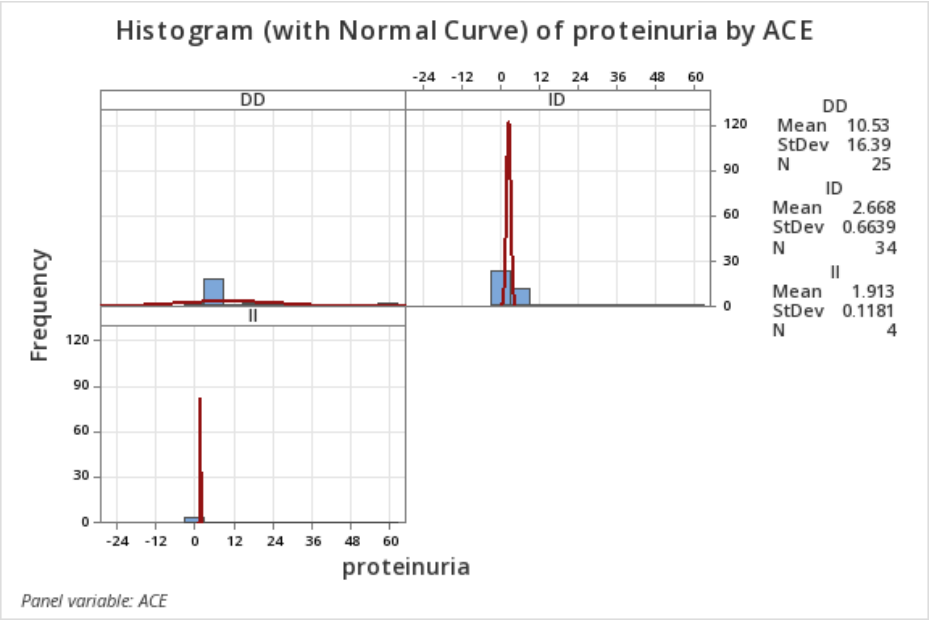

Figure 4: Distribution of Proteinuria Levels Depending on Ace Genotypes (DD, ID and II) in Children with Chronic Kidney Disease

Compared to the other genotypes, the DD genotype has a substantially higher mean proteinuria level of 10.5296 mg/ml. The mean proteinuria level for the ID genotype is 2.66765 mg/ml, which falls in the middle of the range for the DD and II genotypes. At 1.9125 mg/ml, the mean proteinuria level for the II genotype is the lowest. The idea that the DD genotype is linked to a more severe illness course is supported by these data, which show that children with this genotype had much greater levels of proteinuria. It demonstrates the wide range of proteinuria levels, including the highest values, in children with the DD genotype, suggesting their susceptibility to more severe illness symptoms.

Youngsters with the ID and II genotypes have more stable and reduced levels of proteinuria, as seen by their smaller ranges of values. These findings support Hypothesis 1, which states that children with the ACE (DD) genotype have a more severe course of chronic kidney disease than children with the ID and II genotypes. The ACE (DD) genotype is linked to greater levels of proteinuria.

AGTR1	Count	Percent	CumCnt	CumPct	Ultrasound	Count	Percent	CumCnt	CumPct
AA	20	31.75	20	31.75	With pathologies	17	26.98	17	26.98
AC	43	68.25	63	100.00	Without changes	46	73.02	63	100.00
N=	63				N=	63			

Table 3: Distribution of Renal Pathologies in Children with Chronic Kidney Disease based on AGTR1 Genotypes (AC and CC)

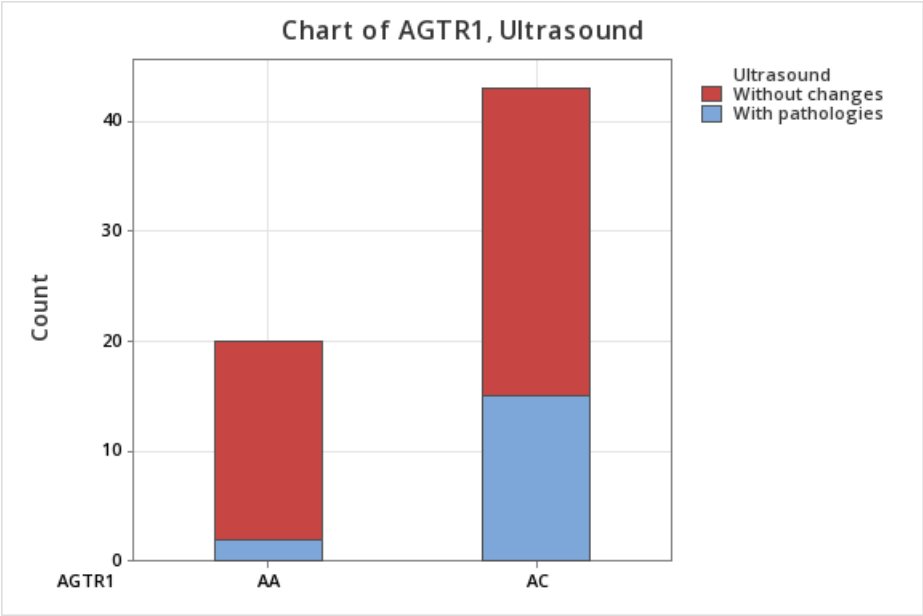

Figure 5: Distribution of the Frequency of Renal Pathologies Depending on the AGTR1 Genotypes (AC and AA) in Children with Chronic Kidney Disease

The distribution of renal abnormality frequency among children with chronic kidney disease based on the AGTR1 genotypes (AC and AA) is shown in Table 3.

AC Genotype: Found in 68.25% of children, of whom 26.98% had abnormalities and 73.02% had no abnormalities found by ultrasonography.

The AA genotype is present in 31.75% of kids. The prevalence of abnormalities in children with this genotype was found to be 26.98%, matching the frequency of abnormalities in children with the AC genotype.

Since the rates of abnormalities are the same for both genotypes, these results do not support the hypothesis that the AA genotype is associated with a higher frequency of abnormalities than the AC genotype.

NOS3	Count	Percent	CumCnt	CumPct	Blood pressure	Count	Percent	CumCnt	CumPct
ab	31	49.21	31	49.21	100/60	16	25.40	16	25.40
bb	32	50.79	63	100.00	100/65	3	4.76	19	30.16
N=	63				110/60	11	17.46	30	47.62
					120/80	2	3.17	32	50.79
					130/90	15	23.81	47	74.60
					140/90	9	14.29	56	88.89
					80/50	2	3.17	58	92.06
					80/60	3	4.76	61	96.83
					90/60	2	3.17	63	100.00
					N=	63			

Table 4: Comparative Analysis of Blood Pressure among NOS3 Genotypes (ab and bb) in Children with Chronic Kidney Disease

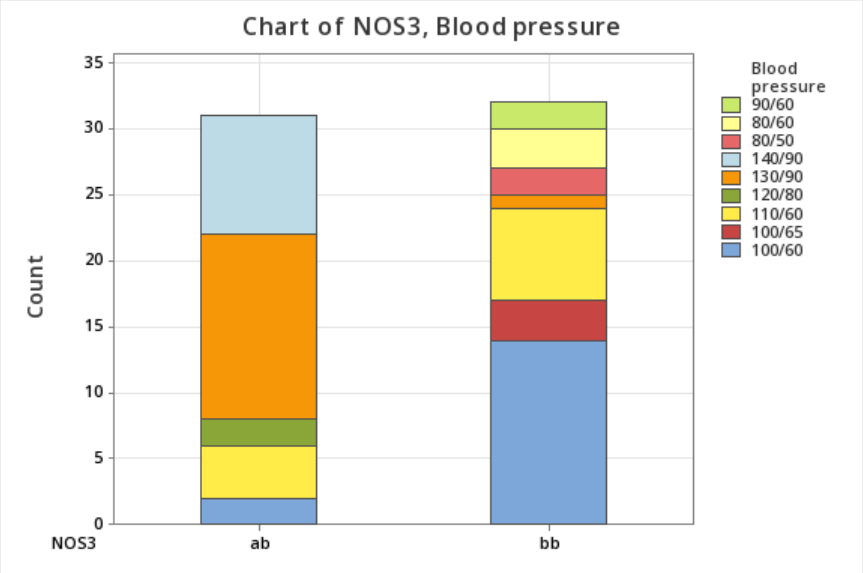

Figure 6: Distribution of Blood Pressure Levels Depending on NOS3 Genotypes (ab and bb) in Children with Chronic Kidney Disease

The distribution of blood pressure readings in children with various NOS3 genotypes is shown in Table 4.

ab Genotype: Identified in 49.21% of children; the two most prevalent blood pressure readings, which indicate high blood pressure, are 130/90 (23.81%) and 140/90 (14.29%).

The bb genotype is present in 50.79% of kids. Elevated blood pressure is also noted in this group, with 130/90 (23.81%) being the most common number. Nonetheless, the proportion of kids with a blood pressure reading of 140/90 is less (14.29%).

Despite the fact that there are no appreciable variations in the distribution between the two genotypes, these results show that both have high blood pressure values. As a result, Hypothesis 3 is unfounded. There are no appreciable changes in blood pressure based on genotype, as elevated blood pressure (130/90 and greater) is seen in a considerable proportion of children with both genotypes.

3. Discussion

The findings of this investigation underscore the importance of hereditary variables in the onset and advancement of pediatric chronic kidney disease (CKD). In particular, the effects of polymorphisms in the ACE, AGTR1, and NOS3 genes on clinical indicators like blood pressure, proteinuria levels, and the frequency of renal diseases were studied.

ACE Genotype and Proteinuria Levels: It was established that the ACE (DD) genotype is linked to greater levels of proteinuria than the ID and II genotypes. This hypothesis was validated. According to the results, children who carry the DD genotype have much greater amounts of proteinuria, which suggests that their CKD will progress more severely and that they will

experience more difficulties. This result is in line with earlier research that found a greater angiotensin-converting enzyme activity (ACEI) in the DD genotype, which may result in increased glomerular filtration and renal injury.

AGTR1 Genotype and Kidney Pathology Frequency: In contrast to the AA genotype, Hypothesis 2 proposed that the AGTR1 (AC) genotype is linked to a greater frequency of kidney diseases seen by ultrasonography. Since the frequency of anomalies was the same for both genotypes, the results did not support this theory. This could suggest that, contrary to earlier beliefs, the AGTR1 polymorphism has less of an effect on structural alterations in the kidneys. To fully comprehend the part this gene plays in the pathophysiology of chronic kidney disease (CKD), more investigation may be required. This investigation should include a wider spectrum of genetic markers and an examination of gene interactions.

Blood Pressure and the NOS3 Genotype: The third hypothesis, which stated that the NOS3 (ab) genotype is linked to higher blood pressure than the bb genotype, was likewise not supported by the data. The information showed that there are no appreciable variations between the two genotypes' high blood pressure levels. This implies that other, more important genetic or environmental factors may influence this parameter, or that the influence of NOS3 on blood pressure regulation may be less pronounced in the context of CKD.

Overall Findings: The study supported the utility of genetic testing, specifically with reference to the ACE genotype, in the prediction and diagnosis of childhood CKD. Nevertheless, it is still unknown how the NOS3 and AGTR1 genes contribute to the onset and course of CKD. To elucidate their influence on clinical indicators, additional investigation is required, encompassing a more extensive examination of genetic interactions and a bigger sample size.

These results highlight the necessity for tailored methods that consider the genetic profile of children when diagnosing and treating CKD. Patients' prognosis and quality of life will both benefit from this, and it will also aid in the development of more effective preventative and treatment plans that are customized to each child's unique genetic makeup.

4. Conclusion

The substantial influence of hereditary variables on the clinical course of childhood chronic kidney disease (CKD) has been shown by this study. It was discovered that children with the ACE gene polymorphism (DD genotype) have greater amounts of proteinuria, which suggests a more severe course of the condition. This result emphasizes how crucial genetic testing is for an early identification and prognosis of chronic kidney disease.

Simultaneously, the frequency of renal problems and blood pressure levels were not significantly affected by the polymorphisms of the AGTR1 or NOS3 genes. These results show the intricacy of interactions between numerous genetic factors in the development of CKD and the need for further study to investigate a larger spectrum of genetic markers and their interactions.

The results highlight the significance of creating customized strategies for the diagnosis and management of children with chronic kidney disease (CKD), considering their genetic makeup. Not only will this increase the efficacy of treatment, but it will also greatly improve the patients' quality of life. Future research should focus on expanding our knowledge of the role that hereditary variables play in the pathophysiology of chronic kidney disease (CKD) and creating novel preventative and therapeutic strategies that are customized to the unique needs of each patient.

To sum up, genetic research presents encouraging opportunities for developing tailored management plans for CKD patients, which may greatly enhance their long-term prognosis and lower their risk of problems.

Acknowledgement

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Statement of Ethics

This study protocol was reviewed and approved by The Ethics Committee of the RSE “SMU Semey”, approval number 3 from November 27, 2019. Written informed consent from parents/ legal guardians for ALL participants aged under 18.

Conflict of Interest Statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Author Contributions

I.B.Y.: analysis and interpretation of the data, drafting the work, and final approval of the version to be published; I.B.Y.:interpretation of the data, reviewing critically for important intellectual content, and final approval of the version to be published; and I.B.Y.:conception and design of the work, analysis and interpretation of the data, reviewing critically for important intellectual content, and final approval of the version to be published.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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