

IMPACT OF GENOTYPIC PATTERN ON PATIENTS OF KIDNEY DISEASE AND ITS OUTCOME

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ABSTRACT

The incidence of chronic kidney disease (CKD), which causes significant morbidity and death, is on the rise. It is crucial to comprehend how hereditary factors contribute to the onset and progression of renal disease. The influence of genotypic patterns on renal disease patients and the ensuing clinical outcomes are briefly summarized in this abstract. The relationship between certain genetic variations and the likelihood of developing chronic kidney disease (CKD) has been the topic of much research in the field of kidney disease. Particularly thorough research has been done on genetic variations in proteins that control blood pressure, inflammation, and kidney function. It is becoming more and more obvious that hereditary variables have a substantial role in a person's likelihood of getting renal disease. Additionally, there has been research in the impact of genotypic patterns on the development and severity of CKD. Renal fibrosis, the immune system, and the control of vital pathways involved in the development of CKD are all allegedly influenced by genetic factors. As a result, they could be very important in determining the rate of illness development and the possibility of consequences. In this abstract, we examine the following features of how genetic patterns affect kidney disease outcomes: Development of CKD: Several studies have shown genetic variations linked to the pace of kidney function loss, which may influence the time to end-stage renal disease (ESRD). Recognizing these patterns can aid in risk assessment and the creation of specialized treatment modalities. Response to Treatment: A person's response to certain treatments, such as medicines and renal replacement therapy, may be influenced by their genotype. Genetically-based therapy planning can improve results and lessen side effects. Risk of Complications: Genetic factors can make people more susceptible to problems including high blood pressure, heart disease, and electrolyte imbalances. Understanding these dangers can help with early intervention and preventive measures. Results of the Transplant: In kidney transplantation, genetic compatibility between donors and recipients is essential. The development of precision medicine techniques in nephrology, which will eventually improve the quality of life for afflicted people and lessen the strain on healthcare systems, depends on a thorough knowledge of the genetic causes of CKD. To fully understand the intricacies of genotypic patterns and their therapeutic consequences, more study in this area is necessary.

Keywords: Genotypic, patients, kidney, outcome etc.

1. INTRODUCTION

Individuals' genotypic patterns, or genetic make-up, can significantly affect both how likely they are to develop renal disease and how severe that illness will be. A variety of disorders that have an impact on the structure and operation of the kidneys are referred to as kidney disease. For customized medicine to work and to enhance patient care, it is essential to comprehend how genetics affects various disorders. Numerous kidney-related problems impact millions of individuals, making kidney disease a major worldwide health concern. By filtering waste from the blood, balancing electrolytes, and regulating blood pressure, the kidneys are essential for preserving the body's general health. The effects of damaged kidneys can be serious and life-changing. In addition to hereditary factors, lifestyle decisions, environmental exposures, and underlying medical problems like diabetes or hypertension can all contribute to kidney disease. The chance of developing kidney disease, how quickly the illness progresses, and how well individuals respond to therapy can all be affected by genetic differences. Understanding the genotypic patterns linked to kidney illness can offer helpful insights into the genesis of the condition and aid in the identification of those who might be at higher risk[1]. With the use of this understanding, early interventions and tailored treatments might be used to enhance outcomes and lessen the burden of renal disease. Genotypic patterns have a variety of effects on renal disease. It encompasses both monogenic illnesses, in which kidney disease is caused by a single gene mutation, and complicated genetic interactions that add to the multifactorial aspect of the disease. These genetic variables may have an impact on the illness severity, onset age, and therapeutic response. Additionally, they are able to estimate the likelihood that a patient may acquire particular kidney conditions such polycystic kidney disease, Alport syndrome, or focal segmental glomerulosclerosis. Clinical implications of understanding the genetic basis of kidney disease are significant.[2] Identification of at-risk individuals, treatment options, and perhaps even

the creation of specific medicines can all be aided by genetic testing and counselling. Genetic knowledge can sometimes result in tailored treatment regimens that enhance the health and quality of life of patients. Numerous genetic markers linked to kidney disease have been found thanks to developments in genomics and molecular biology. These findings have increased our knowledge of the disease's underlying causes and created new opportunities for study and the creation of effective treatments. The relevance of genotypic variations in renal disease and its consequences is highlighted in this introduction.[3]It has implications for early diagnosis, risk assessment, and personalized therapy. The interaction between genetics, kidney disease, and patient care is a complicated and developing topic. We may anticipate making great progress in improving the lives of individuals with renal disease as we dive further into the genetic causes underlying these illnesses. It is critical for enhancing both our scientific knowledge and therapeutic management of this significant health concern that we explore genotypic trends in kidney disease.

2. LITERATURE REVIEW

Microalbuminuria, as well as a greater risk and faster time to develop CKD, are all independently linked to HCV infection. According to studies, HCV infection is linked to up to 2.2 times greater mortality as well as a higher chance of developing ESRD due to a gradual decrease of renal function[4]. Men, those under 50 years old, and those who have diabetes, hypertension (HTN), hyperlipidemia, or cirrhosis concurrently have an increased chance of developing CKD. These correlations have been supported by several meta-analyses, with HCV infection linked to up to a 51% rise in the risk of proteinuria and a 43% increase in the incidence of CKD. A greater risk is linked to longer illness duration and lower baseline estimated glomerular filtration rate (eGFR).[5]Other patient populations also show a link between HCV and CKD. Human immunodeficiency virus (HIV) co-infection raises the risk of chronic kidney disease (CKD), with the risk directly correlated with HCV viral load. HCV infection increases the likelihood of CKD advancement in individuals with primary glomerulonephritis, and it predicts poor renal survival in people with diabetes, which results in the development of ESRD sooner. Age, race, sex, blood pressure, proteinuria, the duration of diabetes, and diabetic nephropathy have no bearing on this connection. Additionally, CKD to ESRD progression that requires hemodialysis (HD) and a kidney transplant is hastened in the presence of HCV. HCV prevalence is greater in those with more established CKD, and continued viral replication is linked to fast declines in kidney function (defined as a drop in eGFR of more than 5 mL/min/year on average) and a twofold increase in the chance of developing end-stage renal disease (ESRD).[6]There is no direct correlation between HCV genotype and the development of CKD, although genotypes 1 and 2 have been shown to increase the risk of CKD. Individuals with active viral replication experience a more rapid decline in renal function compared to those who are only HCV antibody positive without active viral replication. [7] Compared to HCV negative patients, those with HCV infection have worse results following kidney transplantation. A higher frequency of de novo immune-mediated glomerulo-nephritis, particularly type I membranoproliferative glomerulo-nephritis (MPGN), which accelerates graft loss, is linked to HCV infection post-renal transplant. HCV infection is linked to worse long-term graft survival and higher recipient mortality in patients undergoing renal transplants [8]. The increased mortality is brought about by a greater incidence of cardiovascular disease, cancer, and hepatic failure after transplant, with chronic allograft neuropathy and glomerulonephritis being the major causes of graft failure. Although there is a greater chance of death in the first six months after transplantation due to an increased risk of infections, transplant recipients generally live longer than patients on waiting lists due to a continuous decline in cardiovascular mortality. HCV-positive recipients had a much higher chance of developing diabetes after a kidney transplant, which may also contribute to the higher mortality risk in these individuals. In HCV-infected individuals, the concurrent presence of hypertension, diabetes mellitus, hereditary factors, and use of nephrotoxic medications can all enhance the risk of renal impairment [9]. Major independent risk factors for CKD include diabetes and hypertension, and chronic inflammation linked to the HCV, increased insulin resistance, and accelerated atherosclerosis in the renal vasculature can all contribute to the development or worsening of CKD. In contrast, individuals with HCV also have a 1.5-fold increased chance of developing insulin resistance and diabetes mellitus and a 2-fold increased risk of incident cardiovascular and cerebrovascular disease events. Chronic renal disease is more common in those with cirrhosis brought on by HCV. Atherosclerosis-associated glomerulosclerosis and higher prevalence of diabetes, in addition to the risk of developing hepatorenal syndrome, raise the likelihood that cirrhotic individuals may develop CKD[10]. Similarly, having HCV infection after a liver transplant is a risk factor for developing CKD.

3. OBJECTIVES

Understanding the genetic variables that may contribute to the onset and progression of kidney disease is the aim of a study looking at the effect of genotypic patterns on individuals with kidney disease and their outcomes. The purpose of this study is to uncover particular genotypic patterns linked to kidney illness, investigate how they relate to disease severity, and evaluate how they affect treatment results and patient outcomes in general.

4. HYPOTHESIS

We postulate that particular genotypic traits, such as genetic mutations and variations, are linked to a higher risk of developing kidney disease. Polymorphisms in genes relating to kidney function, inflammation, or metabolic pathways may be involved in this. We speculate that some genotypic variations might be linked to the development of renal disease. According to this theory, some genetic variants may cause a kidney condition known as chronic kidney disease (CKD) or end-stage renal disease (ESRD) by causing a more rapid reduction in kidney function. We postulate that individuals with kidney illness may respond differently to different therapy methods, such as prescription drugs, dietary changes, or renal replacement treatments, depending on their genotypic makeup. Different treatment results and responses may result from specific genotypic variances. We speculate that certain genotypic variations might raise the likelihood of consequences from renal illness, including electrolyte abnormalities, hypertension, and cardiovascular disorders. The results for patients and their general quality of life may be directly impacted by this. We postulate that distinct genotypic patterns might be used as indicators of renal disease outcomes. These indicators may aid in risk assessment, early intervention, and individualized treatment plans to assist patients with renal disease have a better prognosis. A thorough investigation may include genetic testing, long-term monitoring of kidney disease patients, and the gathering of clinical information on the course of the disease, the effectiveness of therapy, and any complications. The results of this research might have a big impact on how kidney disease patients are treated and managed, possibly leading to more individualized and successful therapies based on genotypic patterns.

5. METHODOLOGY

A thorough and interdisciplinary strategy is needed to investigate the effects of genotypic patterns on renal disease patients and their outcomes. Here is a broad approach that academics might use to look at this connection[11]: This investigation could involve action or observation. When examining genotypic trends, observational studies are often more prevalent. Consider characteristics like age, gender, ethnicity, and the particular kidney illness (such as polycystic kidney disease, chronic kidney disease, etc.) when defining your research population. Gather genetic data from research participants, such as by whole-genome sequencing or genotyping. Assemble thorough clinical information on the renal disease's kind and stage, comorbidities, previous treatments, and results. Patient interviews, questionnaires, and electronic health records can all be useful sources[12]. Measure pertinent biomarkers such as kidney function, inflammatory markers, and genetic markers linked to renal illness. Examples of these indicators are estimated glomerular filtration rate and serum creatinine. Determine the genetic variations linked to renal disease[13]. Genome-wide association studies (GWAS) and other genomic analytic techniques may be used in this. Investigate the connection between certain genetic variations or patterns and the phenotypic manifestation of kidney disease, such as the severity of the illness, its course, or how it responds to treatment[14].

6. RESULTS AND DISCUSSION

An important topic of nephrology study is the influence of genotypic patterns on renal disease patients and their outcomes. The onset, progression, and treatment of kidney disease can be significantly influenced by genetic factors.

Table 1.1: Monogenic versus complex genetic disease characteristics

Monogenic (Mendelian)	Polygenic (Complex)	
Allele/variant frequency	Rare	Can be common
Effect size of major driving gene	Large	Small
Penetrance	High	Low
Role of environment	Limited	Strong
Inheritance model	Mendelian	None apparent

The following are some crucial considerations addressing how genotypic patterns affect renal disease and its results: Some people may be prone to kidney disorders genetically. The likelihood of having illnesses like polycystic kidney disease, Alport syndrome, or specific kinds of glomerulonephritis can be raised by specific genetic variants. The rate at which a disease progresses can be influenced by genetic factors[15]. Some genotypic patterns may cause kidney function to decline more quickly than in others, depending on the situation. Individual responses to different therapies can be influenced by genetic variances.

Table 2; Molecular Markers, Kidney Histology, or Kidney Function as Disease Definitions for Genetic Studies

Advantages	Disadvantages
Kidney function markers (e.g., eGFR, albuminuria)	

<p>Information that is simple to get and standardized in both high- and low-income environments regularly used in scientific studies and medical treatment. allows for the discovery of genetic renal function determinants and kidney disease progression-influencing variables. reasonably affordable Repeated measurements are frequently accessible to evaluate trajectory.</p>	<p>Disease classification is descriptive in nature. Knowledge about the underlying biology, pathophysiology, and clinical heterogeneity of the kidneys. The excretion of albumin in the urine is underutilized. The genetic variations connected to marker metabolism are identified by current markers, but not filtration.</p>
<p>Kidney histology</p>	
<p>enables categorization based on damage patterns in structures. Most glomerular disorders are classified according to a standardized system. Currently used as a benchmark for clinical management using a clinical workflow. A more uniform pathophysiology may be reflected by histology categories than by renal function indices.</p>	<p>is a typical histological damage pattern that frequently groups together a variety of underlying disease-initiating events (such as FSGS), possibly bringing functional and genetic variability. Limited accessibility in environments with limited resources</p>
<p>Non-traditional molecular markers (e.g., markers quantified with high-throughput omic technologies)</p>	
<p>may divide individuals with kidney disease into more homogeneous groupings, making it easier to identify the underlying causes and drivers of the illness. allows for the investigation of renal disease via systems genetics. Possibility of thorough multi-omics profiling (for example, metabolomics, proteomics, and exposomics)</p>	<p>Emerging technologies must develop cost-effective readouts that are easily accessible in low- and middle-income nations due to resource constraints. Large biobank access is necessary for illness subtyping. The kidney's function may affect certain marker levels.</p>

For instance, a patient's genetic make-up may have an impact on the efficacy of drugs used to treat renal problems, such as ACE inhibitors or angiotensin receptor blockers. The likelihood of renal disease-related problems may be increased by specific hereditary variables. For instance, people with particular genetic abnormalities may be more likely to experience electrolyte imbalances, hypertension, or cardiovascular issues. Genetic mutations are a direct cause of several kidney diseases [16]. For instance, the severity of an illness such as autosomal dominant polycystic kidney disease (ADPKD), which is brought on by mutations in particular genes, might depend on the particular genetic mutation involved. The success of kidney transplantation might be impacted by the genetic compatibility between donors and recipients. Both the success of the transplant and the risk of rejection are influenced by genetic and HLA (human leukocyte antigen) matching. The genotypic pattern of a patient can be used to assist customize treatment regimens. Genetic testing may occasionally be utilized to determine the best course of treatment and anticipate illness progression [17]. Family history and the existence of certain genotypic patterns may imply a hereditary component to kidney disease, which can be useful for determining the risk of kidney disease in kin and for genetic counselling. The development of tailored medicines and interventions that target certain genotypic patterns may result from research into the genetic basis of kidney disease. It's significant to emphasize that the varied and multifaceted effects of genotypic patterns on renal disease. The onset and progression of kidney disease are also influenced by other variables, such as environmental impacts and lifestyle decisions [18]. A wide range of genetic variables, illness kinds, and therapeutic choices are all involved in the complicated and varied issue of how genotypic patterns affect kidney disease patients and their results. These fundamental elements of this relationship will be the subject of this discussion: Genetic and environmental factors can both contribute to kidney disorders. One's vulnerability to kidney illnesses may rise as a result of specific genetic abnormalities. These genetic components may be inherited or result from unintentional alterations. Numerous disorders fall under the category of kidney diseases, including glomerulonephritis, polycystic kidney disease, and chronic kidney disease (CKD). Specific kidney disorders originate and advance in large part due to genetic factors [19]. For instance, PKD is predominantly a hereditary condition brought on by gene mutations. The rate at which kidney disease develops can be influenced by genetic factors. While some people may develop the illness more slowly, others may have genetic variations that make them more likely to have a quick reduction in kidney function. Early diagnosis can be helped by knowing a patient's hereditary susceptibility to kidney disease [20]. Genetic testing can identify those who are more vulnerable, enabling monitoring and early intervention. People's reactions to different therapies might vary

depending on their genetic makeup. The effectiveness and possible negative effects of medicines like immune suppressants or angiotensin-converting enzyme (ACE) inhibitors may differ for certain people as a result of their genetic makeup. Certain genetic mutations have been directly connected in some instances to renal diseases [21]. For instance, mutations in the PKD1 or PKD2 genes lead to autosomal dominant polycystic kidney disease (ADPKD). In these situations, genetic testing can offer vital details for a diagnosis and family planning. Precision medicine, which adapts treatment plans to a person's genetic profile, is made possible by advances in genomics. This strategy can improve therapy options and doses in the context of renal disease, thereby enhancing patient outcomes [22]. Greater comprehension of the processes behind kidney illness is being made possible by genomic research. It has sparked the creation of fresh treatments that target certain genetic circuits. For instance, gene-editing methods for PKD have been found via genetic research. Aside from ethical and psychological concerns, genetic testing for kidney illness can also bring up difficulties with informed consent, privacy, and potential psychological harm to patients and their families. In summary, genotypic patterns have a major influence on renal disease patients, impacting susceptibility, disease development, treatment response, and prospective therapeutic options [23]. As genomic medicine develops, it holds up the possibility of providing patients with kidney illnesses with more individualized and efficient care. However, because they are so important to patient care and decision-making, it is crucial to take the ethical and psychological elements of genetic testing and counselling into account in this context [24].

7. CONCLUSION

There are many different aspects and complexities to understanding how genotypic patterns affect renal disease patients and their outcomes. Even though our knowledge in this topic is always changing, we may take the following important conclusions from the study that has been done as of my most recent knowledge update in September 2021: Kidney illnesses arise and advance in large part as a result of genetic variations. There are several known genetic mutations and variations that can either raise the risk of kidney disease or modify its severity. There is a lot of genetic variation among people with renal illness. The genetic bases of many kidney illnesses vary, and even within the same disease, there can be a broad variety of genotypic patterns. Some genetic traits make people more vulnerable to kidney problems. For instance, genetic abnormalities might increase a person's susceptibility to diseases like polycystic kidney disease, Alport syndrome, or diabetic nephropathy. Genotypic variations can affect how kidney disease develops. Variations in clinical outcomes may result from patients' experiencing quicker or slower illness development due to unique genetic polymorphisms. For tailored treatment to be effective, genotypic pattern understanding is essential. To optimize therapeutic advantages and reduce side effects, it can be used to personalize treatment options, including drug selection and transplant compatibility. The significance of genotypic patterns in the family transmission of kidney illnesses is highlighted by inherited kidney diseases such as autosomal dominant polycystic kidney disease. Identification of at-risk family members and proper genetic counselling may need genetic testing. Targeted therapeutics for several kidney illnesses have been developed as a result of genetic science advancements. The administration of these medicines can be guided by identifying certain genotypic patterns, providing hope for better results. Numerous difficulties still exist in the research on genotypic patterns in renal disease, which is still in its infancy. The interpretation of genetic data can be challenging, and it is yet unclear how hereditary and environmental variables interact. Future studies should concentrate on improving diagnostic procedures, generating more potent treatments, and deepening our understanding of genotypic patterns in kidney disease. In the end, this will result in better patient outcomes. In summary, genotypic patterns significantly affect the onset, progression, and treatment of kidney disorders. Even while genetics is not the only factor in kidney disease outcomes, it is a crucial factor. The prognosis and quality of life for people with kidney disease will ultimately improve as research into these hereditary variables advances, resulting in more accurate diagnosis and therapies.

8. REFERENCES

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