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Chronic Kidney Disease: From Etiology to Personalized Interventions - An In-Depth Review

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Abstract

This review delves deeply into the various facets associated with chronic kidney disease (CKD). This thorough analysis explores the several aetiologies and contributing variables of chronic kidney disease (CKD), providing insight into the condition's intricate history. The content that has been abstracted offers insights into the customized interventions that are covered in the article. It implies that the book or article addresses patient-specific tactics and techniques, highlighting the significance of personalized medicine in the management of chronic kidney disease. It may be noted how precision medicine, tailored treatment regimens, and the application of cutting-edge medical technology may improve the prognosis of patients with chronic kidney disease. The goal of personalized medicine is to detect a person's predisposition to illness, determine the optimum therapeutic strategy for each patient at the right time, and/or provide timely and focused prevention by utilizing their unique phenotypes and genotypes. Based on unique characteristics and requirements, it has the power to drastically change patient treatment in the context of renal illnesses. Approaches to personalized medicine specifically target chronic kidney disease (CKD) and try to customize treatment plans according to genetics, underlying causes, disease progression rate, and other personalized characteristics. Acute renal injury is a common cause of chronic kidney disease (CKD), while it can also come from other pathogenic causes. The rate and degree of renal function recovery following acute renal injury may have an impact on the onset and course of chronic kidney disease (CKD).

Keywords: Chronic kidney disease (CKD), personalized medicine, customize treatment plans.

1. Introduction:

The degenerative illness known as chronic kidney disease is marked by changes to the kidney's structure and function that can arise from a variety of sources. Reduced kidney function, an estimated glomerular filtration rate (eGFR) of less than 60 mL/min per 1.73 m², or indicators of kidney damage, such as albuminuria or hematuria, or abnormalities found through laboratory

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testing or imaging that have persisted for at least three months are the standard definitions of chronic kidney disease (appendix p 5) (Willig and Warady 2023). An estimated 10% of individuals worldwide suffer from some kind of chronic kidney disease, which causes 1.2 million deaths and 28.0 million years of life loss annually. The global burden of chronic kidney disease is significant and continuing (Bikbov et al. 2020)(Xie et al. 2018). One of the biggest predicted rises of any major cause of death by 2040 is chronic renal disease, which is predicted to rise to the fifth position in the world's top causes of death (Foreman et al. 2018). Regional differences exist in the frequency of several chronic kidney disease etiologies. Although there are several causes of chronic kidney disease, including well-known and studied ones like diabetes, glomerulonephritis, and cystic kidney disorders, the exact mechanism underlying chronic kidney disease is still unknown. For example, there is debate on the causal relationship between chronic renal disease and hypertension, even though the two conditions are closely related (Ku et al. 2019). Another example is chronic kidney disease, which is found in some agricultural communities in south Asia and Central America but whose etiology is unknown and for which there is no known treatment. Recurrent volume depletion has been suggested as a possible cause, particularly in light of the increasing frequency of heat waves linked to climate change (Pearce and Caplin 2019). This unidentified potential cause of chronic kidney disease emphasizes the need of being well hydrated as a kidney-preserving tactic. Air pollution has also been linked to the worldwide burden of chronic kidney disease, which is disproportionately experienced by various parts of the world (Bowe et al. 2020). The degree of chronic kidney disease also varies, ranging from normal function kidney damage to kidney failure, also known as end-stage renal disease, which usually happens when eGFR falls below 15 mL/min per 1.37 m^2. Chronic kidney disease generally becomes more frequent with age and is more common in high-income nations in those who are obese, diabetic, or have high blood pressure (Cockwell and Fisher 2020)(Silverwood et al. 2013). The rate at which kidney function is lost varies depending on the etiology, exposures, and therapies; nonetheless, kidney failure usually progresses over months to decades. If kidney failure is not treated, it will eventually end in death. Signs and symptoms of kidney failure include progressive uremia, anemia, volume overload, electrolyte abnormalities, mineral and bone diseases, and acidemia (Zarantonello et al. 2021). For those with kidney failure, renal replacement therapy—either in the form of kidney transplantation or chronic dialysis—is a life-sustaining procedure.

Due to the lack of available kidney donors and the age-related comorbidities that frequently make kidney transplantation impossible (Cano et al. 1987)(Song 2016). The main objective of kidney-preserving treatment, a life-sustaining conservative management strategy, is to prevent the need for dialysis as long as feasible or, ideally, never need it by delaying the course of chronic renal disease and maintaining kidney function. By effectively treating renal and non-renal comorbidities and the symptoms they cause, this strategy aims to maximize survival, enhance cardiovascular health, and improve health-related quality of life (Rhee et al. 2020)(Kalantar-Zadeh et al. 2021). The use of conservative management is increasing, with a greater focus on kidney-preserving strategies, despite variations in definitions, the provision of

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(or access to) care, patient demographics, and socioeconomic status across different domains of the conservative management of chronic kidney disease (Brown et al. 2015)(Carson et al. 2009)(Chandna et al. 2011)(Da Silva-Gane et al. 2012)(Hemmelgarn et al. 2012)(Joly et al. 2003)(Kamar, Tam-Tham, and Thomas 2017)(Murtagh et al. 2007)(Reindl-Schwaighofer et al. 2017)(Seow et al. 2013)(Shum et al. 2014). The goal of primary preventative treatment is to establish optimal control of the risk factors for chronic kidney disease by treating high blood pressure, high blood sugar, smoking, physical inactivity, and obesity (Stengel et al. 2003). While there is debate on the cost-effectiveness of doing population-wide screening for chronic kidney disease, it is advised to test those with risk factors (such as obesity, diabetes, and hypertension) specifically by routinely measuring their eGFR and albuminuria (Komenda et al. 2014).

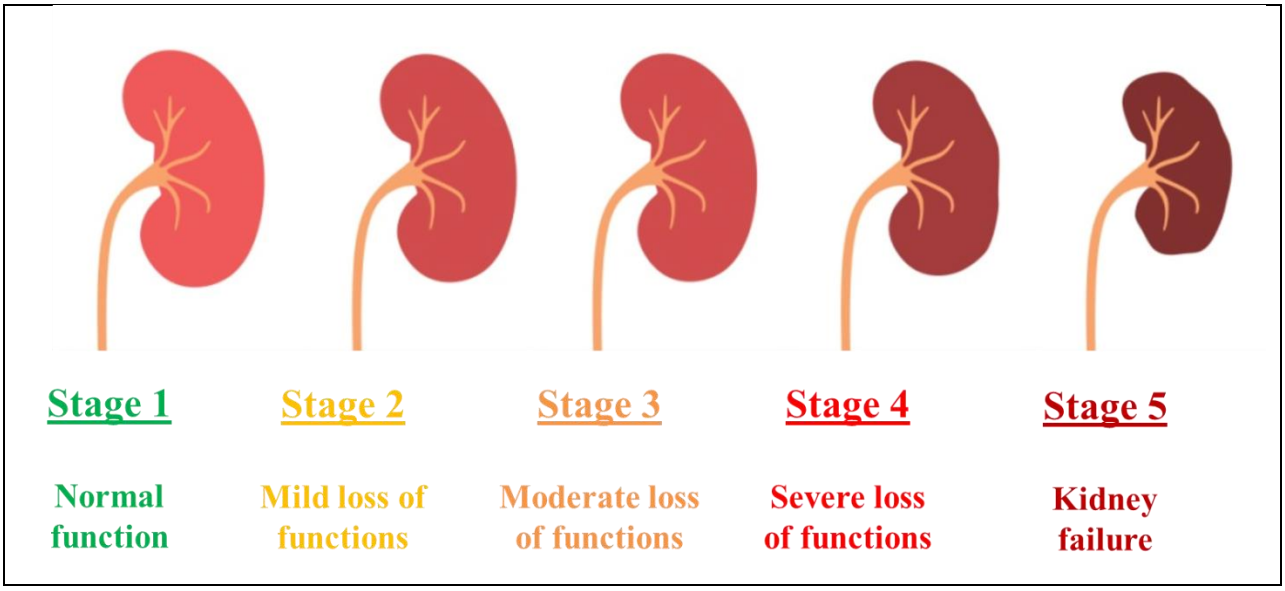

Fig. 1: Stages of chronic kidney disease

2. Etiology of Chronic Kidney Disease:

Progression to end-stage kidney disease (ESKD) is the most visible concern, since it forces patients to undergo dialysis and/or renal transplantation, commonly known as renal replacement therapy (RRT). However, the risk of ESKD is generally minimal in many populations; instead, it is more crucial to take into account other concerns such as increased hospital admissions, acute kidney injury (AKI), and morbidity and mortality from cardiovascular disease (Kerr et al. 2012).

2.1 Risk factors:

To focus screening programs on high-risk populations, it is critical to identify characteristics linked to an increased risk of developing chronic kidney disease (CKD). Factors that enhance the chance of developing CKD and those that increase the chance of CKD progressing to ESKD are the two primary categories of risk factors associated with CKD (Table 1).

Table 1: Risk factor for CKD

S.no.	Contributing and triggering elements	Recurring elements
1.	Increasing Age	African-American race
2.	Gender	Proteinuria

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3.	Ethnicity	Hypertension
4.	Family history of CKD	High dietary
5.	Lower socioeconomic status	protein intake
6.	Metabolic Syndrome	Obesity
7.		Anemia
8.		Dyslipidemia
9.	Nephrotoxins (NSAIDs, antibiotics, radiological contrast)	Nephrotoxins
10.	Urological Disorders (obstruction, recurrent urinary infections)	
11.	Cardiovascular disease	Cardiovascular disease
12.	Diabetes mellitus	Diabetes mellitus
13.	AKI (Acute kidney injury)	AKI

Genetic components - A very tiny percentage of cases are hereditary renal disorders caused by abnormalities in a single gene. More important are the genetic variables that raise an individual with a family history of CKD's chance of developing complex CKD. For instance, it has been demonstrated that the risk of ESKD increases 1.3 times (95% confidence interval (CI) 0.7e2.6) for a single first-degree relative with the disease, and 10.4 times (95% CI 2.7e40.2) for two.

Composition - Due to its correlation with other socioeconomic status-related confounding variables, ethnicity is a challenging risk factor to isolate. However, even after accounting for socioeconomic characteristics, ethnicity is still a major risk factor in epidemiological research. According to the US Renal Data System, Native Americans and African-Americans had an annual incidence of ESKD that is 1.6 and 3.4 times higher, respectively, than that of white Americans. The high frequency of the risk alleles in the African-American population can be explained by the interesting fact that these alleles also confer resistance to the tsetse fly-borne parasite Trypanosome brucei, which causes "sleeping sickness" in some parts of Africa. As a result, they would confer survival advantage in endemic areas (Kruzel-Davila et al. 2016).

The socioeconomic elements - The incidence, prevalence, and development of chronic kidney disease (CKD) are influenced by socioeconomic variables such as income, education, and environmental factors. These factors can be changed. Comparably, white Americans in the USA who fall into the lowest economic quintile had an 86% higher chance of developing chronic kidney disease (CKD) than those in the top.

Age - Age-related increases in the frequency and incidence of CKD suggest that nephron loss may be a "normal" aspect of ageing. According to one research, 6207 glomeruli are lost annually. According to some research, the rate of GFR loss increases with age; nevertheless, the danger of dying off concurrently reduces the likelihood that ESKD would precede. As a result, the majority of elderly CKD patients pass away from other reasons prior to developing ESKD.

Sex - The most reliable conclusion is that males are more likely than women to have CKD and ESKD, despite significant heterogeneity between research. The finding that men often have a

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greater incidence of CKD risk factors helps to partially explain this. In comparison to women, men also show higher rates of progression for various forms of renal disease. Women's postmenopausal state may have an impact on the risk, although more research is needed on this.

High blood pressure - In addition to being a nearly ubiquitous side effect of CKD, hypertension also speeds up the disease's development. Though it is still debatable whether hypertension in and of itself causes kidney disease, population-based studies have shown that hypertension is an independent risk factor for end-stage kidney disease (ESKD). Treatment of hypertension is necessary to limit the pace of development of CKD, and all patients with recently diagnosed hypertension should be examined for CKD as a potential cause.

Low blood sugar - In both industrialized and developing nations, diabetes mellitus is the most frequent cause of chronic kidney disease (CKD). Every patient with diabetes should have their GFR and UACR evaluated yearly because about 40% of them develop CKD. The two most crucial therapies to halt the course of CKD are achieving adequate glycemic control and treating hypertension early with an angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker.

Glomerular nephropathy - The phrase "glomerulonephritis" describes a broad spectrum of primary and secondary disorders that inflame and harm the glomerulus. Most of the time, the immune system plays a role in the pathogenesis, although the precise processes are still poorly understood. Hematuria along with proteinuria is a characteristic of glomerulonephritis. So, every patient who presents with CKD or AKI should have a urine dipstick test done. Usually, a renal biopsy is necessary to arrive at a precise diagnosis. The prognosis, progression rate, and exact diagnosis all influence the course of therapy.

Hereditary illnesses - The most frequent monogenic ailment causing CKD in adults is adult polycystic kidney disease. It usually manifests in the third and fourth decades of life and is inherited in an autosomal dominant manner. Extra-renal symptoms such as cysts affecting other organs (liver, spleen), brain aneurysms, and abnormalities in the heart's valves are often linked to it.

Heart-related illnesses - CKD and cardiovascular disease are commonly linked. Atherosclerosis can impact the smaller intracranial arteries and arterioles to create ischemic nephropathy or constrict the larger renal arteries to cause renal artery stenosis. Reduced renal perfusion from cardiac failure is accompanied by a further reduction in GFR from diuretics used to address fluid retention. Cardio renal syndrome is the term used to describe the combination of cardiac and renal dysfunction.

Urological circumstances - The most common cause of reflux nephropathy, which arises from repeated infections brought on by vesico-ureteric reflux, is childhood. Examining children who have recurrent UTIs should help identify any signs of vesico-ureteric reflux. Prostatic hypertrophy, renal calculi, or pelvic cancers are some of the major, possibly treatable causes of urinary tract blockage, which can result in AKI/CKD.

Infections -Although it can develop with any infection, streptococcal infection is usually linked to post-infectious glomerulonephritis. Although it is not a common cause of chronic kidney

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disease (CKD) in wealthy nations, it is a significant cause in developing nations. Malaria, HIV, hepatitis B and C, TB, and other diseases can also result in chronic kidney disease (CKD). Every infection has a unique pathogenesis and course of treatment.

Short-term renal damage - AKI is becoming better acknowledged as a CKD risk factor that can both initiate and persist. Remaining damage and fibrosis following an incomplete AKI recovery might worsen over time. Those who recover from AKI have a much higher chance of going on to develop CKD (hazard ratio 8.8) and ESKD (hazard ratio 3.1) in observational studies. An additional increased risk of ESKD is seen in those with CKD prior to AKI development. Therefore, patients who exhibit inadequate recovery following AKI should undergo routine GFR and UACR monitoring in addition to clinical follow-up.

3. Diagnosis and Staging of Chronic Kidney Disease

3.1. Renal function measured by glomerular filtration rate

By measuring the renal clearance of exogenous filtration indicators, one can indirectly determine GFR. Inulin is the reference standard marker. Inulin is promptly eliminated into the urine via glomerular filtration because it is inert, does not bind to plasma protein, is freely filtered by the kidney, and does not undergo metabolism, tubular secretion, or reabsorption. Since inulin is costly and cumbersome, it is seldom utilized in practice. Instead, different filtering markers are employed, with the majority of the selection being influenced by local availability(Salgado et al. 2010)(Choudhary, Bundela, and Bharang 2023). GFR is defined as the amount of exogenous marker that is cleared following a single bolus injection of the marker. It can be calculated using examinations of plasma and urine concentrations (commonly referred to as renal or urinary clearance) or just measurements of plasma concentrations (commonly and somewhat misleadingly called plasma clearance). The use of plasma measurement eliminates the need for scheduled urine collections as well as the hazards and inconvenience of indwelling bladder catheters; nevertheless, there are trade-offs, such as higher bias and much lower clearance estimate accuracy(Trevisani et al. 2020)(Isakov et al. 2022).

The glomerulus freely filters creatinine, which is a byproduct of muscle metabolism that is typically generated at a fairly consistent pace. Though more muscle mass also contributes to an increase in concentrations, GFR declines with time. Age, sex, ethnicity, and body size are included in eGFR estimation equations as imprecise proxy measures of muscle mass variance among groups, in an effort to represent the variability in creatinine induced by muscle mass(Luis-Lima et al. 2019)(Hayes et al. 2016). Aside from the consumption of meat or the usage of protein supplements, other variables that affect creatinine concentration include tubular secretion, extra-renal excretion, physical activity, and creatinine breakdown, the effects of which may vary as GFR decreases. These effects make it difficult to accurately identify genuine variations in GFR across individuals as well as changes over time within individuals, and they are sometimes difficult to anticipate from readily acquired demographic or clinical factors. Hyperthyroidism can be caused by several drugs. For the lower ranges of GFR, using a combination of creatinine and cyclostatin C may increase accuracy in eGFR estimation(Facenda et al. 2011)(Yuan, Bruzelius, and Larsson 2022).

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3.2. Analyzing endogenous filtration markers-derived eGFR

The percentage of eGFR values that fall within 30% of measured GFR for estimating equations can reach, at most, 75–85%. Stated differently, estimations will range more than 30% above or below the observed GFR in up to 25% of the population. A measured GFR of less than 7 or more than 13 mL/min per 1·73 m² will be present in up to 25% of individuals with an eGFR of 10 mL/min per 1·73 m². A quarter or less of individuals with an eGFR of 60 mL/min/1·73 m² will have a measured GFR of less than 42 or more than 78 mL/min per 1·73 m². The physician may consider some non-GFR determinants of creatinine when interpreting eGFR findings (e.g., variations in creatinine can be estimated for extremes in muscle mass)(Filler, Huang, and Yasin 2012)(Soveri, Berg, Björk, et al. 2014)(Eppenga et al. 2015). But since some elements, like nutrition and metabolism in particular, are impossible to measure, there will always be some random fluctuation and imprecision. Measurements of the creatinine concentration in serum and timed urine collections can also be used to calculate renal creatinine clearance. Nonetheless, this approach lacks practicality, as there is compelling proof that, over the full range of GFR and regardless of patient attributes, creatinine clearance significantly overestimates GFR and is less accurate than alternative techniques for estimating GFR solely from serum creatinine concentration(Soveri, Berg, Bjö Rk, et al. 2014)(Hasan et al. 2018)(Levey, Becker, and Inker 2015).

3.3. Proteinuria as an indicator of renal impairment

Less than 150 mg of protein and less than 30 mg of albumin are lost daily in the urine of healthy persons. Losses that persist above these thresholds may indicate injury to the kidneys, as greater glomerular permeability permits the filtration of macromolecules that ought to stay in the bloodstream. Menstrual blood contamination, urinary tract infections, intense physical activity, upright posture (orthostatic proteinuria), and other illnesses that raise vascular permeability, such sepsis, can all cause momentary increases in albuminuria(Masaki et al. 2021)(Carretón et al. 2020). Greater early reductions in proteinuria are related with slower kidney disease development, but proteinuria itself is linked to an increased risk of ESKD and early mortality. To calculate total albumin loss or total protein loss, one can measure the whole amount of urine protein or simply the albumin portion using a variety of different techniques. Spot urine tests normalize albumin concentration for urinary creatinine concentration to estimate 24-hour albumin or protein loss, taking into consideration urinary concentration and hydration state(Abdeldayem 2022)(Skrzypczyk et al. 2021). Individuals with a body surface area of 1.73 m² and normal kidney function filter around 1 g of creatinine every 24 hours. Therefore, in an average-sized person, 1 g of protein for every 1 g of creatinine equals roughly 1 g of proteinuria in 24 hours. A muscular individual excreting 2 g creatinine in 24 hours may have nephrotic-range proteinuria of 4 g per day, which is represented by a ratio of 2 g protein to 1 g creatinine. In a similar vein, the spot ratio would exaggerate the actual proteinuria of a frail elderly lady with renal disease whose daily excretion of 0·5 g of creatinine may represent 1 g of protein. Morning samples are preferred because of the significant variation in urine protein loss that occurs during the day(Ouyang et al. 2021)(Bramham and Rajasingham 2012).

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3.4. Kidney biopsy and pathology guided by percutaneous ultrasonography

A percutaneous kidney biopsy may be necessary in a patient who presents with suspected chronic kidney disease (CKD) in order to make a diagnosis, inform treatment decisions, and gauge the severity of acute and ongoing alterations. Kidney biopsy carries risks, similar to any invasive procedure. These risks include the possibility of severe bleeding (1 in 1000 patients), the need for angiographic intervention (1 in 2000 patients), unilateral nephrectomy (1 in 10,000 patients), and in a small number of cases, death (1 in 5000 patients). As always, benefits and risks should be balanced(Dündar et al. 2021)(Gomes et al. 2021). For those with a high risk of bleeding during kidney biopsy procedures, transjugular or laparoscopic techniques may be suitable substitutes. During the kidney biopsy operation, samples are taken from the lower pole of the left kidney under direct visualization, usually via ultrasonography, using a needle gauged between 14 and 18. Two tissue cores are extracted during the process using disposable, automated, spring-loaded devices under local anaesthesia(Ojalehto et al. 2002)(Tang et al. 2002). The tissue cores are then put into a medium and sent to the laboratory for analysis. Light microscopy, electron microscopy, and immunofluorescence or immunohistochemistry are used in the processing and examination of biopsy specimens. The specimen for light microscopy is embedded in paraffin, thinly sliced into 2-3 μm pieces, and stained with many standard stains to provide complementary information regarding the state of the glomeruli and interstitium(Fortuño Andrés et al. 2010)(Horvatic et al. 2007).

3.5. Urine sediment; haematuria and pyuria

A crucial part in determining the underlying causes of chronic kidney impairment is the automated or human microscopic analysis of the urine sediment, which is done in addition to measuring GFR and proteinuria. Under high power microscopy, normal urine contains up to four red blood cells and five white blood cells per field(Ayoub et al. 2019)(Siu et al. 2022).

The reasons of underlying renal illness may be revealed by the presence of cells, casts, and crystals in the urine sediment. Red blood cells in the urine from glomerular illness can be seen or unseen to the naked eye, whereas white blood cells can be observed in tubulointerstitial nephritis or in conjunction with haematuria in different types of glomerulonephritis(Valls Sanchez et al. 2019).

3.6 Imaging studies

Renal ultrasonography is usually regarded as the first-choice imaging modality when evaluating individuals with renal impairment that has not yet been identified. Kidneys with acute renal damage can be distinguished from those with chronic kidney disease by their enhanced echogenicity and small size. Additionally, ultrasound can distinguish between obstructive diseases that induce hydronephrosis and intrinsic causes of kidney disease(Matsuda-Abedini et al. 2018)(Rudnick et al. 2021).

Additionally, congenital or inherited kidney illnesses such as cystic kidney disease can be detected with this approach. A duplex can also help evaluate renal artery stenosis and blood flow. Other imaging methods, such as CT, MRI, and isotope scans, are not frequently utilized to

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diagnose chronic kidney disease (CKD), but they may be useful in some circumstances(Schneider et al. 2019)(Zhao et al. 2023).

4. Staging

Staging is decided upon depending on GFR, albuminuria, and CKD aetiology when a diagnosis of CKD has been obtained(IRIS 2019).

5 Staging of GFR is classified as:

- G1 (GFR 90 mL/min/1.73 m2)
- G2 (GFR 60-89 mL/min/1.73 m2)
- G3a (45-59 mL/min/1.73 m2)
- G3b (30-44 mL/min/1.73 m2)
- G4 (15-29 mL/min/1.73 m2)
- G5 (<15 mL/min/1.73 m2)

The establishment of estimating equations (such as the Chronic Kidney Disease Epidemiology Collaboration and Modification of Diet in Renal Disease Study equations) has largely replaced the need for direct measurement in clinical practice, even though GFR can be directly measured by the clearance of agents like iohexol or iothalamate(Elliott and Watson 2017). These days, clinical labs frequently provide estimated GFRs (eGFRs) derived from filtration indicators. Creatinine, a 113 Dalton consequence of creatine metabolism, is the most often used filtration marker. Since 2003, laboratory procedures for this marker have been standardized. Since the CKD-EPI 2009 creatinine equation is more accurate than the previous MDRD equation, especially for eGFR levels larger than 60 mL/min/1.73 m2, it is the recommended estimating equation in the United States and much of the rest of the globe(Winearls and Glassock 2009)(Gunawan et al. 2023). Cystatin C and creatinine can be substituted in the CKD-EPI 2012 creatinine-cystatin C equation when more accuracy and precision are needed.

For those with altered creatinine production and/or metabolism (such as those with abnormally high or low body size or muscle mass, limb amputation, high-protein diets, creatinine supplements, or medications that impact tubular secretion of creatinine), adding cystatin C may be especially helpful(Lamprea-Montealegre, Shlipak, and Estrella 2021).

Ideally, a urine ACR should be used to measure albuminuria. The stage of albuminuria is categorized as:

- A1 (urine ACR <30 mg/g)
- A2 (30-300 mg/g)
- A3 (>300 mg/g)

Urine ACR is preferred by guidelines over urine protein-to-creatinine ratio for the staging of chronic kidney disease (CKD) due to the former's tests' higher likelihood of standardization and accuracy at lower albuminuria levels. The best results are obtained from a 24-hour collection or first-morning sample since urine albumin excretion varies greatly during the day due to biological variability(Pettitt et al. 2020).

5. Personalized Medicine and Chronic Kidney Disease

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Personalized medicine makes use of an individual's genotype and phenotype to determine a patient's risk for a disease, to choose the best course of treatment for them at that particular moment, and/or to give timely and focused prevention. Based on unique characteristics and requirements, it can drastically change patient treatment in the context of renal illnesses. Personalized medicine techniques specifically target treating chronic kidney disease (CKD) by customizing care plans according to genetics, underlying causes, disease progression rate, and other personalized characteristics("Personalized Medicine and Chronic Kidney Disease in Sub-Saharan Africa: Advances and Challenges" 2021)(Connaughton and Hildebrandt 2020)(Ali et al. 2023). Personalized medicine emphasizes customized lifestyle modifications and creates treatment programs that are appropriate for each patient. The specific needs and risk factors of each patient must be taken into account when choosing blood pressure control, exercise, diet, and stopping smoking, among other things. Furthermore, while selecting and delivering drugs, this approach considers specific patient characteristics such renal function, comorbidities, and medication tolerance. Pharmacogenomics approaches may be very helpful in this situation for identifying genetic variants that impact medication metabolism and response(Zhang et al. 2016)(Cao, Zhou, and Liu 2019).

Nutrition, exercise, stress reduction, and other lifestyle choices are examples of environmental variables that should be taken into account during a patient's personalized therapy for chronic kidney disease (CKD). To produce personalized lifestyle therapies in this context, a bespoke strategy considers patient preferences, socioeconomic situations, and cultural considerations. To stop the advancement of CKD and associated comorbidities, prevention is very crucial. Avanafil and Vardenafil have been shown to have a possible renoprotective effect in contrast-induced nephropathy in an animal model, which is in line with lowering the risk of AKI and the progression to renal failure. Their research might open the door to more methodical investigations into renoprotective techniques to stop contrast-induced kidney damage(Tye, Denig, and Heerspink 2021)(Yao et al. 2021)(Poh and De Lusignan 2011).

6. Management and Interventions

The goals of treating chronic kidney disease (CKD) are to delay the onset of end-stage renal disease (ESRD) and to get the patient ready for ESRD. Therapy for continuously progressive kidney failure (CKD) is often focused on an asymptomatic illness that can only be identified by laboratory testing, as the symptoms of this condition grow slowly. That is, basic preventive strategies including nutrition, weight control, and exercise can help prevent the major causes of ESRD, hypertension, and type 2 diabetes to some extent. The idea that chronic kidney disease (CKD) is a single process is supported by studies indicating that shared physiological mechanisms ultimately drive the course of CKD regardless of the initial insult, as well as by the success of treatment across a variety of primary conditions (Hostetter 2003)(Zandi-Nejad and Brenner 2005)(Remuzzi, Benigni, and Remuzzi 2006). With chronic kidney disease (CKD), cardiovascular disease (CVD) is now widely recognized to be widespread and frequently deadly (Go et al. 2004)(G. et al. 2017).

Renin–angiotensin–aldosterone system:

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In 1993, Lewis et al. discovered that angiotensin-converting enzyme (ACE) inhibitors were the first medication to effectively delay the development of diabetic nephropathy. The research was conducted after various laboratories, most notably Barry Brenner's in the 1980s, conducted animal investigations (Weidenbusch and Vielhauer 2017)(Zatz, Anderson, and Meyer 1987). Standard medications for primary hypertension include angiotensin II receptor blockers (ARBs) and ACE inhibitors. Nonetheless, they are all very good in halting the CKD patient's GFR's steady decline (T. H. Jafar et al. 2001)(Lewis et al. 2001)(Remuzzi et al. 1996)(Brenner et al. 2001). According to a recent metaanalysis, individuals with proteinuria of 41000 mg/day had the greatest evidence for the advantages of RAAS inhibition on the course of chronic kidney disease (CKD) in nondiabetic renal disorders (Tazeen H. Jafar et al. 2003).

Blood pressure:

While there is some overlap in the advantages of RAAS inhibition and blood pressure management, it is crucial to recognize them as distinct therapy objectives. The ideal goal arterial pressure in chronic kidney disease, however, is mostly a matter of opinion. According to current guidelines, individuals with CKD should aim for a goal of 130/80 mm Hg, which is a stricter control than the 140/90 mm Hg advised for the general population (Lewandowska et al. 2023)(Cuffee et al. 2019). When comparing a goal systolic blood pressure of 140 mm Hg with one of 120 mm Hg in type 2 diabetes, the ACCORD study revealed no overall advantage to the lower goal (Carriazo et al. 2022). Although albuminuria decreased with decreasing pressure, this group's eGFR also decreased by the study's conclusion. The experiment did not specifically target individuals with chronic kidney disease (CKD), and the initial eGFR were, on average, 490 ml/min per 1.73 m2 with lower albumin excretion than microalbumuria. The current recommendation of 130/80 mm Hg appears fair until these data are obtained, particularly for those with greater levels of proteinuria. The choice of the second medication is also primarily subjective if the goal of 130/80 is not reached after first-line therapy with an ACE inhibitor or ARB, which it frequently does not (Carpio et al. 2022)(Cheung et al. 2019)(Yan et al. 2022).

It is advised to aim for a blood pressure of 130/80 mm Hg, however this frequently calls for two or more medications.

Diabetic glycemic control:

In both Type 1 and Type 2 diabetes, reducing the development of increased albuminuria is a measure of how well glucose management is doing. Strict glycemic control, as opposed to conventional management, for instance, slowed the transition from micro albuminuria (30–299 mg albumin per g creatinine) to macro albuminuria (4300 mg albumin per g creatinine) in the DCCT for Type 1 diabetes (“Effect of Intensive Therapy on the Development and Progression of Diabetic Nephropathy in the Diabetes Control and Complications Trial” 1995)(Bilous 2008)(Ismail-Beigi et al. 2010)(“Intensive Blood Glucose Control and Vascular Outcomes in Patients with Type 2 Diabetes” 2008).

Lipid-lowering management:

Renal failure is frequently accompanied with abnormal lipid metabolism. Hyperlipidemia may hasten the course of chronic kidney disease (CKD), even if it does not appear to be the cause of

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primary renal disease. The lipid nephrotoxicity theory was initially proposed by Moorhead et al (Moorhead et al. 1982). The suggested pathways are similar to the occurrences of damage that cause atherosclerosis in other arterial beds. Meningeal cells are triggered to produce chemokine's in the presence of lipids, which attract macrophages. Oxidized low-density lipoproteins result from the production of oxygen radical species by activated mesangial cells and aggregated macrophages. It has been demonstrated that these oxidized low-density lipoproteins increase profibrotic and proinflammatory cytokines (Rovin and Tan 1993)(Keane 2000). As a result, there is a lot of interest in the nephrology community on lipid-lowering treatment as a means of slowing the course of chronic kidney disease. While several classes of these drugs have been investigated, the relevant information focuses on HMG-CoA (3-hydroxy-3-methyl-glutaryl-CoA) reductase inhibitors, also known as statins. This family of drugs appears to have additional anti-inflammatory effects in addition to lowering the lipoprotein load in tissues, which may be beneficial. Statin treatment has been demonstrated in animal trials to decrease fibrosis and mesangial cell growth, restrict the production of inflammatory markers such as chemokine's, cytokines, and adhesion molecules, and diminish macrophage recruitment into the glomerulus (Fried 2008)(Ota et al. 2003).

Conclusion

The goal of personalized medicine ought to be to ascertain a patient's susceptibility to a particular ailment, implement prompt and focused illness prevention, and ascertain the best course of treatment for each patient at the appropriate moment. In this regard, the Special Issue "Personalized Medicine in Kidney Disease" presents interesting new perspectives and emphasizes the significance of customized approaches for every person, considering that therapies may differ significantly based on particular kidney illnesses and personal traits. Developing treatment strategies that maximize results and reduce the chance of problems requires the application of precision medicine. Through routine clinical evaluations, laboratory testing, and imaging examinations, it is important to regularly evaluate disease activity and response to treatment. This makes it possible to identify illness progression or flare-ups early on and modify the treatment strategy as necessary. It is possible to evaluate disease activity and forecast therapy response by using biomarkers, such as proteinuria, complement levels, or genetic markers. Interstitial macrophages' prognostic and predictive function in kidney biopsies from patients with IgA nephropathy was reported by Aiello et al. in this Special Issue.

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