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Pathophysiology, Diagnosis, and Management of Chronic Kidney Disease

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Abstract

Chronic Kidney Disease (CKD) is the presence of markers of kidney injury for ≥3 months, as defined by structural or functional malfunctions of the kidney with or without depleted glomerular filtration rate, that can lead to lessen glomerular filtration, manifest by either pathological abnormalities or other markers of kidney injury, involving malfunctions in the composition of blood or urine, or deformity in imaging tests or the presence of glomerular filtration <60 mL/min/1.73 m2 for ≥3 months, with or without distinctive signs of kidney damage as described above. Progression factors cause worsening kidney damage and faster decrement in kidney work after kidney damage has started and modifiable by pharmacological treatment or lifestyle modifications. Examples, higher level of proteinuria, higher blood pressure level, poor glycemic control in diabetes, and smoking. The ultimate familiar pathological manifestation of multiple CKD is renal fibrosis. Treatment goals for all patients include slowing disease progression, identify cause address metabolic abnormalities, education, detecting and managing complications, preventing cardiovascular disease and improve survival and quality of life (QOL). Protein-controlled diet, as well as weight reduction (for patients with an elevated body mass index), may provide some benefit in decreasing proteinuria.

Keywords: Chronic Kidney Disease; Diagnosis; Pathophysiology; Management

Abbreviations: ACEIs: Angiotensin-converting-enzyme inhibitors; ARBs: Angiotensin-receptor blockers; BMI: body mass index: BP: Blood pressure; CCr: Creatinine clearance; EPO: Erythropoietin; ESKD: End stage kidney disease; GFR: Glomerular filtration rate; Hg: Haemoglobin; HgA1c: Glycosylated haemoglobin; KDOQI: Kidney Disease Outcomes Quality Initiative; MDRD: Modification of Diet in Renal Disease; NKF: National Kidney Foundation; NSAIDs: Non-steroidal anti-inflammatory drugs; SCr: Serum creatinine concentration

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Introduction

The definition and categorization of CKD have unfolded over time, but recent international guidelines define CKD as depleted kidney function revealed by glomerular filtration rate (GFR) of < 60 mL/min per 1·73 m², or markers of kidney injury, or both, of at least three months duration, irrespective of underlying cause. When GFR is < 15 mL/min per 1·73m² (category G5), a person has reached ESKD, at which point kidney work is no longer capable to sustain life over the long term. Kidney failure is delineated as a GFR below 15 mL per minute per 1.73 m², usually accompanied by signs and symptoms of uremia, or as the need for initiation of kidney replacement therapy for management of the complications of a diminished GFR [1]. The National Kidney Foundation (NKF) work group defined two principal consequences of CKD: progressive loss of kidney work and advancement of complications, specifically cardiovascular disease. Progressive loss of kidney work over time in further patients with CKD is a well-known consequence. Because of the older age at onset for multiple forms of kidney disease and the slow rate of decrement in kidney function, downgraded kidney function is far more common than kidney failure, for which replacement therapy (dialysis or transplantation) becomes necessary. Diminished kidney function is consociated with complications in nearly entire organ systems [2].

The NKF guidelines emphasize persistent proteinuria as a marker of kidney damage, because proteinuria has been studied most thoroughly and is identified readily using a simple office procedure. A ratio of greater than 30 mg of albumin to 1 g of creatinine in an untimed (spot) urine sample usually is considered abnormal. Distinctive markers of kidney injury involve abnormalities in urine sediment, blood, and urine chemistries, and abnormal results on imaging surveys. Patients who have normal kidney function but have markers of kidney injury are at enhanced pitfall for adverse effects of CKD [3, 4]. Approximately 10–15% of the global population suffer from CKD and its consociated complications, specifically cardiovascular disease, infectious complications, osteoporosis, muscle wasting, frailty and premature ageing. CKD is further familiar among women than men. Greater than thirty five percent of people aged 20 years or older with diabetes have CKD. More than 20% of people aged 20 years or older with hypertension have CKD.

CKD Classification/Staging

CKD is defined as the presence of kidney damage, manifested by abnormal albumin excretion or diminished kidney function, quantified by measured or estimated GFR that persists for greater than 3 months. Both complications and likelihood of progression to ESRD necessitating RRT are further routinely to happen in patients with severe CKD. Additionally, early intervention will further familiarly minimize serious CKD sequelae and minimize CKD progression. To facilitate assessment of CKD severity and, the NKF developed criteria, as section of its NKF KDOQI™, stratify chronic kidney disease patients [5-7].

Stage	Description	Glomerular filtration rate, mL/min/1.73 m2
1	Kidney injury with normal or enhanced GFR	≥ 90
2	Kidney injury with mild depleted GFR	60–89
3a	Moderately diminishing GFR	45–59
3b		30–44
4	Severely depleted GFR	15–29
5	Kidney failure	< 15 (or dialysis)

Table 1: Classification of the stages of CKD

Greater frequency monitoring is recommended for those categories at consummate pitfall of progression of CKD. Less GFR fluctuations in are ubiquitous. Progression is thought-out to be de-escalating in GFR of ≥25% from baseline. Factors consociated with progression involve antecedent of CKD, level of GFR, concentration of albuminuria, acute kidney injury, age, sex, race or ethnicity, raised blood pressure, hyperglycaemia, dyslipidaemia, smoking, obesity, history of cardiovascular disease, andongoing exposure to nephrotoxic agents [1, 8].

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Estimating the GFR

The GFR is an indication of functioning kidney mass; it has implications for treatment goals and for the dosing of renally excreted medications. The KDOQI guidelines delineate stages of CKD depending on an estimated GFR that is calculated from the Scr level. The standard for GFR measurement is the CL rate of inulin, a substance that passes through the kidney unaltered. CCr, as measured by a twenty-four-hr urine collection, ordinarily overestimates the GFR because of the active production of Cr by the kidney and can different with muscle mass. To estimate GFR (estimated GFR or eGFR) from the SCr concentration, using either the Cockcroft-Gault or the MDRD Study estimating equations. Web based tools are available for both estimating equations eGFR: http://www.nkdep.nih.gov/ professionals/ gfr_ calculators/index.htm; Cockcroft-Gault eGFR: http://www.mdcalc.com/cockcroftgault). Significant kidney dysfunction perhaps present despite a normal SCr level. An estimation of the GFR depending on the SCr level correlates better with direct measures of the GFR and detects greater cases of CKD than does the SCr level alone. Additionally, patients with the same SCr level perhaps have distinctive estimated GFRs. Clinically helpful GFR estimates are calculated from the measured SCr level after adjustments for age, sex, and race. A GFR of 100 mL per minute per 1.73 m2 is considered normal for women, and 120 mL per minute per 1.73 m2 is a normal GFR for men. The two most commonly used formulas for GFR estimation are shown in Table 2 [9-12].

Abbreviated MDRD study equation: GFR (mL per minute per 1.73 m^2) = 186 (SCr) $*^{-1.154}$ (age) $*^{0.203}$ *(0.742, if female) *(1.210, if black)
Cockcroft-Gault equation: CCr (mL per minute) = (140 – age) * weight/ 72 *SCr *(0.85, if female)

Table 2: Formulas for estimating glomerular filtration rate in adult. GFR = glomerular filtration rate; MDRD = Modification of Diet in Renal Disease; SCr = serum creatinine concentration; CCr = creatinine clearance. For entire equation, SCr is in mg per dl, age is in years, and weight is in kg. In validation surveys, the MDRD study equation performed as well as versions with further variables; however, a current survey found that the equation underestimated the GFR in patients who did not have CKD [9].

Risk Factors

Much epidemiological and clinical evidence has revealed a link between several factors and the initiation and the progression of CKD. These can be categorized into two distinct categories: those confirmed to be causal (risk factors) and those that are consociated with CKD in the absence of established causal relations (risk markers) [12].

Susceptibility factors: Factors that accelerate susceptibility to kidney injury are not directly confirmed to antecedent CKD. Susceptibility factors are specifically not modifiable by pharmacological treatment or lifestyle modifications. Examples, older age, family history of CKD, reduction in kidney mass, LBW, U.S. racial or ethnic minority status, low income or educational level. Chronic kidney disease familiarly clusters within families, which describes genetic or familial predisposition. Racial factors also have a function in the susceptibility to CKD as revealed by the further prevalence of CKD affiliated to hypertension, diabetes, or both amid African and Native Americans in the USA, as well as Afro-Caribbean and Asian individuals in the UK. LBW and infant malnutrition in certain ethnic minorities might be consociated with a decrement in the number of nephrons, predisposing to hypertension and renal disease in later life. Male and elderly people might also be more susceptible to CKD, which would explain the high proportions of these population groups in renal-replacement-therapy programmes [12, 13].

Initiation factors: Factors that directly initiate kidney damage and modifiable by pharmacological treatment. Examples, Diabetes mellitus, high BP, autoimmune diseases, systemic infections, urinary tract infections, urinary stones, obstruction of lower urinary tract, drug toxicity. HTN, DM, hyperlipidaemia, obesity, and smoking as pitfall factors or markers in the specific population for the advancement of CKD. Common pitfall factors and markers appear to be linked to both renal and cardiovascular diseases in most developed countries. Also, albuminuria itself is a predictor not solely of CKD but also of cardiovascular morbidity and mortality. Impaired kidney function is also a major risk

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factor for patients with cardiovascular disease [12, 14, 15].

Progression factors: Factors that cause worsening kidney damage and faster decrement in kidney work after kidney damage has started and modifiable by pharmacological treatment or lifestyle modifications. Examples, higher level of proteinuria, higher blood pressure level, poor glycemic control in diabetes, and smoking. The progression of established CKD is variable and based on several pitfall factors or markers. Non-modifiable factors involve genetics, race, age, and sex. For example, there is much evidence that the rate of progression of CKD is faster amid patients who are elderly, male, or African-American [16]. Consummate notable amid the modifiable progression factors is systemic hypertension. Proteinuria is a reliable marker of the severity of CKD and a potent and independent predictor of its progression. Metabolic factors have been implicated in the progression of CKD [17]. Obesity is consociated with hypertension, albuminuria, and dyslipidaemia, all of which are potential modifiers of the progression of CKD. Cigarette smoking has been described in the initiation and progression of CKD. A graded increased risk of End Stage Renal Disease was noted in non-diabetic nephropathies with enhancing cigarette smoking; the occurrence of End Stage Renal Disease was increased by 5·9 fold among heavy smokers (greater than 15 pack-years) [12]. Insufficiently restrained diabetes and hypertension enhance the pitfall of progression of CKD to kidney failure. Repeated episodes of acute kidney damage from a variety of causes (e.g., infections, regular and heavy (more than two drinks daily) consumption of alcohol, drugs consumption of analgesics, especially paracetamol and non-steroidal anti-inflammatory agents), or toxins injurious to the kidney) can also contribute to progression of CKD to kidney failure, especially in the elderly. While CKD is further familiar among women, men with CKD are 50% more likely than women to progress to kidney failure [18].

End-stage factors: Factors that increase morbidity and mortality in kidney failure. Lower dialysis dose (Kt/V), temporary vascular access, anemia, low serum albumin level, late referral for dialysis.

Pathophysiology

The ultimate familiar pathological manifestations of multiple CKDs are renal fibrosis. Renal fibrosis represents the unsuccessful wound-healing of kidney tissue after chronic, sustained damage, and is described by glomerulosclerosis, tubular atrophy, and interstitial fibrosis. Glomerulosclerosis is quicker by endothelial injury and dysfunction, proliferation of smooth-muscle cells and mesangial cells, and decrement of podocytes that normally line the glomerular basement membrane. Converting growth factor ß1 and distinctive growth factors (involving platelet-derived growth factor, fibroblast growth factor, tumour necrosis factor, and interferon gamma) enliven mesangial cells to regress to mesangioblasts (immature mesangial cells). Tubular atrophy, interstitial fibrosis, and scarring are closely consociated with GFR and proteinuria.

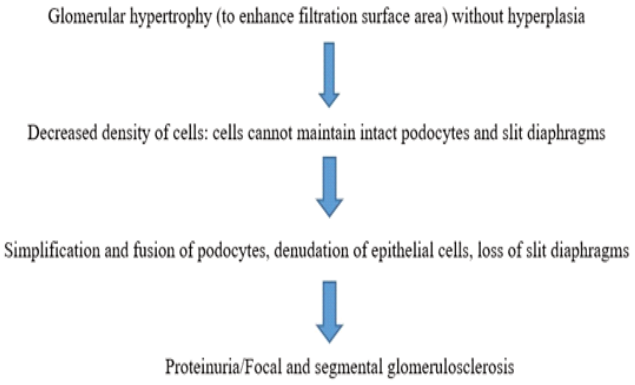

Figure 1: Mechanism of structural alters of kidney in CKD

Tubular epithelial cells are stimulated to secrete inflammatory products involving reactive O_2 species and chemokines by various abnormally-filtered urinary proteins, involving complement, cytokines, and albumin. Kidneys are metabolically mostly active with a more O_2 necessitated. Early in CKD injury, interstitial capillaries become increasingly permeable (the kidney capillary leak syndrome) meaning that more plasma proteins that normally never reach the renal interstitial are capable to do so and trigger an inflammatory reaction [1].

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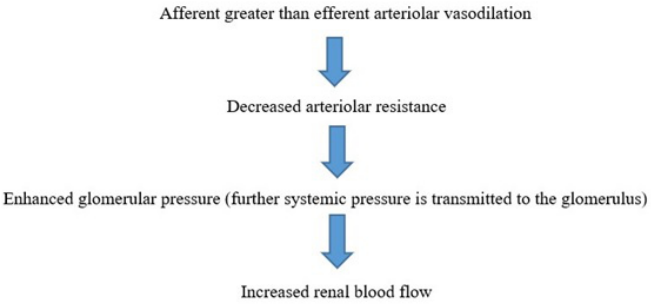

Figure 2: Mechanism of hemodynamic changes in CKD

Diagnostic Evaluation in CKD

Once CKD has been distinguished, goals involve ascertaining the stage of the disease, establishing the antecedent of the disease, and evaluating comorbid situations. All patients with CKD should undergo urinalysis and renal imaging as section of the diagnostic evaluation. Patients with long-standing diabetes, hypertension, and a clinical course consistent with CKD disease 2^{ndry} to these conditions may not require further evaluation. The evaluation of entire patients is guided by the symptoms (e.g., rash, arthritis, or urinary symptoms); family history of kidney disorders (e.g., cystic kidney diseases); and known medical problems. Underlying diseases perhaps distinguished by the physical examination, with special attention bestowed to the skin, joints, and cardiovascular system. Tests for complements three and four are used to screen for collagen vascular disease, hepatitis C–related disease, and infection-related immune complex disease. The antineutrophil cytoplasmic antibody assay distinguishes vasculitis, whereas serum protein electrophoresis and urine protein electrophoresis detect many myelomas [9, 19]. Renal ultrasonography supports to settle the diagnosis and prognosis by documenting the size of the kidneys. Normal size indicates kidney disease that may be amenable to medical treatment. Small kidneys suggest irreversible disease. Asymmetry in kidney size suggests renovascular disease.

Management

The management of CKD based on the particular management of the underlying antecedent, the stage of the kidney disease, and the availability or absence of proteinuria. Management goals for all patients include slowing disease progression, identify cause address metabolic abnormalities, education, detecting and managing complications, preventing cardiovascular disease and improve survival and QOL. Slowing primary disease progression is including glycemic control, BP control and immunosuppressants for 2^{ndry} immune-modulated diseases. Treatment of patients with CKD involves the following: therapy based on the specific diagnosis, evaluation, and management of comorbid conditions; measures to slow loss of kidney function; measures to prevent and treat cardiovascular disease; measures to prevent and treat complications of de-escalated kidney work; preparation for kidney failure and kidney replacement therapy; and replacement of kidney work by dialysis or transplantation if signs and symptoms of uremia are available. Disease management is depending on clinical diagnosis and stage according to glomerular filtration rate and albuminuria.

Non-Pharmacological Treatment

Lifestyle modification: Lifestyle modifications, such as weight reduction, exercise, and dietary manipulations can be effective, as shown in clinical trials in which the incidence of T_2DM in overweight individuals with impaired glucose tolerance was substantially lowered by these means. Approaches to control hypertension by means of dietary salt restrictions and diets rich in fruit and vegetables and low in saturated fat have been recommended [20]. **Education:** Ameliorated public-health education with decrement of excessive bodyweight, regular exercise, and dietary approaches should lead in the long term to a reduction in the growing numbers of person with DMs and hypertension who constitute the major future pool of CKD cases [21]. Avoidance of NSAIDs, phosphorus-based enemas, and iodinated contrast is recommended if possible. **Smoking cessation**: Smoking cessation should be encouraged to decrease the peril of advancing CKD and end-stage renal disease, and to decrease the peril of cardiovascular disease. **Weight reduction**: Obese (BMI > 30.0 kg/m^2) and overweight

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(BMI 25.0–29.9 kg/m^2) people should be encouraged to reduce their BMI to lower their risk of CKD and end-stage renal disease. Maintenance of a health body weight (BMI 18.5–24.9 kg/m^2; waist circumference < 102 cm for men, < 88 cm for women) is recommended to prevent hypertension or to reduce BP in those with hypertension. All overweight people with hypertension should be advised to lose weight. **Dietary protein control**: A protein-controlled diet (0.80–1.0 g/kg/d) is recommended for adults with CKD. Dietary protein restriction of < 0.70 g/kg/day should include careful monitoring of clinical and biochemical markers of nutritional deficiencies. Protein-controlled diet, as well as weight reduction (for patients with an elevated body mass index), may provide some benefit in decreasing proteinuria. **Alcohol intake:** To reduce blood pressure, alcohol consumption in both normotensive and hypertensive people should be in accordance with Canadian guidelines for low-risk drinking. Healthy adults should limit alcohol consumption to two drinks or less per day, and consumption should not exceed fourteen standard drinks per week for men and nine standard drinks per week for women. **Physical exercise:** People without hypertension (to reduce the possibility of becoming hypertensive) or those with hypertension (to lower their blood pressure) should be encouraged to accumulate 30–60 minutes of moderate-intensity dynamic exercise (walking, jogging, cycling or swimming) 4–7 days per week. Higher intensities of exercise are no more effective. **Dietary salt intake restriction:** To prevent hypertension, a dietary sodium uptake of < 100 mmol/day is recommended, additional to a balanced diet. Patients with hypertension should limit their dietary sodium intake to 65–100 mmol/day.

Pharmacological Treatment

Slowing progression of CKD and reduction of albuminuria and protein urea

Proteinuria, a hallmark of renal impairment, is consociated with an enhanced peril for cardiovascular disease and early cardiovascular mortality in patients with and without DM and hypertension. The pitfall consociated with the availability of microalbuminuria escalated progressively with escalating absolute degrees of microalbuminuria [5]. The mean rate of age-related decrement in GFR is 0·75–1·00 mL/min per 1·73 m^2 every year after the age of forty years. Target blood pressure (<130/80 mm Hg vs <140/90 mm Hg) in patients with most accumulations of albuminuria. The most consistent benefit is noted with use of angiotensin-converting-enzyme (ACE) inhibitors and angiotensin-receptor blockers (ARBs), usually in association with diuretic drugs, in patients with most concentrations of albuminuria. ACEIs and ARBs in high doses or with other agents that inhibit the renin-angiotensin system are effective to reduce albuminuria, but have not been tested in long-term trials in populations with CKD [22, 23]. Adults with DMs and persistent albuminuria (ratio of albumin to Cr > 2.0 mg/mmol for men, > 2.8 mg/mmol for women) should receive an ACEI or an ARB to delay the progression of CKD (grade A). ACEIs and ARBs are the drugs of choice for reducing proteinuria (grade A). In carefully selected patients, aldosterone-receptor antagonists may decrease proteinuria (grade D). The doses of ACEI or ARBs are usually increased until proteinuria is reduced by 30% to 50%. ACEI or ARB is first line treatment for proteinuria CKD because these drugs slow the rate of progression of CKD in addition to lowering blood pressure. Second- and third-line treatment in for protein uric CKD: In patients with chronic kidney disease who have proteinuria and edema loop diuretics if preferable for edema. Non-dihydropyridine calcium channel blockers (verapamil and diltiazem) also lower proteinuria. Beta blockers are preferable for hypertensive CKD patients who also have myocardial infraction.

Prevention of complications from decreased GFR

Progression of chronic kidney disease is consociated with a number of serious health complications, involving escalated incidence of cardiovascular disease**.** Controlling BP control using Kidney Disease Outcomes Quality Initiative guidelines (BP goal less than 130/85, less than 125/75 with proteinuria, less than 130/85 in the setting of DMs), usage of angiotensin converting enzyme inhibitor and/or ARBs to minimize proteinuria, titrating insulin and statin therapy to

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achieve proper HbA1c and serum cholesterol levels (<100 mg/dL), respectively will minimize cardiovascular peril and obviate or slow the progression of kidney failure [5].

Hypertension in Patients with CKD

The peril of having a non-fatal myocardial infarction is escalated by 33% when glomerular filtration rate is < 60 mL/min per 1·73 m^2 and by 48% with micro-albuminuria, with peril of both myocardial infarction and cardiovascular death increasing as GFR declines and quantity of albuminuria increases**.** Hypertension is characterized to salt retention and escalated vascular tone owing to a failure to prevent the sympathetic nervous system and renin-angiotensin system, inhibition of sodium-potassium ATPase, and nitric-oxide deficiency. Although restriction of dietary sodium minimizes BP in experimental models, adherence is low in clinical practice. All antihypertensive drugs appear to be effective in lowering BP, but several agents, involving a diuretic, are often necessary to reach the target level. The optimum level of BP and selection of antihypertensive agents to minimize peril of cardiovascular disease are controversial. Guidelines suggest a lower than usual target for blood pressure (less than130/80 mm Hg vs less than 140/90 mm Hg), but no sufficiently powered randomised trials of CKD have been done to test this hypothesis. For patients with proteinuria chronic kidney disease (urine ratio of albumin to creatinine ≥ 30 mg/mmol), antihypertensive therapy should include an ACE inhibitor (grade A) or ARB in cases of intolerance to ACE inhibitors (grade D). Blood pressure should be targeted to < 130/80 mm Hg (grade C). For patients with nonproteinuric chronic kidney disease (albumin to creatinine ratio < 30 mg/mmol), antihypertensive therapy should include an ACE inhibitor (grade B), an angiotensin-receptor blocker (grade B), a thiazide diuretic (grade B), a β-blocker (patients aged 60 years or less; grade B) or a long-acting calcium-channel blocker (grade B). ACEIs and ARBs are currently considered the first line choices in patients with CKD because they reduce intraglomerular pressure up to 35% to 40%. Begin at low doses and increasers the dose at 4 weeks interval to control the level of proteinuria.

Anemia in Patients with CKD

Anemia is delineated as a reduction in one or more of the major RBC measurements; Hg concentration, hematocrit, or RBC count. The WHO delineates anemia as a Hg< 13 g/dL in men and post-menopausal women, and < 12 g/dL in pre-menopausal women. The NKF delineates anemia as Hg < 13.5 g/dL in men and < 12.0 g/dL in women [5]. Anaemia typically normocytic, normochromic and hypo proliferative are a ubiquitous feature of CKD and prevalence accelerates as glomerular filtration rate declines. The kidney is the chief source of EPO, a glycoprotein hormone with a molecular weight of 34 kDa secreted by interstitial fibroblasts around peritubular capillaries and proximal convoluted tubules. EPO stimulates RBC secretion in the bone marrow and drives haemoglobin homoeostasis. The anemia of CKD is treated via recombinant human erythropoietin (epo). However, management with ESA to target Hg concentrations of 130 g/L or greater (achieved mean concentrations greater than 110 g/L or 120 g/L) has been consistently consociated with high rates of cardiovascular disease, particularly in patients who are ESA-hyporesponsive. Iron and recombinant erythropoietin and its synthetic derivatives (epoetin alfa, epoetin beta, darbepoetin alfa, methoxy polyethylene glycol epoetin beta; collectively known as ESAs) are broadly used to manage anaemia and have been shown to reduce the need for blood transfusion in people with CKD, particularly when used in combination [1, 22, 26-29].

CKD Mineral Bone Disease

Mineral bone disease is a ubiquitous complication of CKD and can revealed as any combination of anomalies of calcium, phosphate, parathyroid hormone (PTH), or vitamin D metabolism, which are often recognised on abnormal biochemistry tests such as escalated serum phosphate and PTH concentrations, while amounts of serum calcium might be low, normal, or accelerated; anomalies in bone turnover,

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mineralisation, growth, or strength, which can manifest as bone pain or escalated bone fragility; or extra-skeletal calcification (involving blood vessels and skin) [1]. Mineral and bone disorders in CKD are described by deformity in serum concentrations of calcium, phosphorus, 1, 25-dihydroxycholecalciferol, and parathyroid hormone; deformities in bone morphology; and vascular calcification. Phosphate retention and deficiency of 1, 25-dihydroxycholecalciferol seems to be the main causes of hyperparathyroidism and hypocalcaemia, and can be treated by decreased phosphorus intake (with restriction of dietary protein) and phosphate-binding drugs (calcium carbonate, lanthanum carbonate, and sevelamer). Hyperparathyroidism can also be treated by exogenous 1, 25-dihydroxycholecalciferol and vitamin D analogues, and calcimimetics [22, 30]. Treatment guidelines recommend dietary restriction of phosphate and the use of either calcium or non-calcium-based phosphate binders to obtain serum phosphate concentrations of between 0·87 mmol/L and 1·49 mmol/L [1].

Dyslipidemia in Patients with Chronic Kidney Disease

Dyslipidemias cause atherosclerotic cardiovascular disease. Treatment goal is to decrease the risk of atherosclerotic CKD and to reduce protein urea and decline in kidney function. The prevalence of hyperlipidemia accelerates as renal role decrement, with the level of hypertriglyceridemia and elevation of LDL cholesterol being proportional to the severity of renal impairment. Patients with CKD have a reduction in the activity of lipoprotein lipase and hepatic triglyceride lipase. Specific K/DOQI guidelines on the treatment of hyperlipidemia involve: (1) for patients with LDL cholesterol levels between 100 and 129 mg/dL (2.57 to 3.34mmol /L) lifestyle alters perhaps the initial therapy. If target LDL levels are not achieved (LDL < 100 mg/dL [2.57 mmol/L]), low-dose statin therapy can be instituted. (2) for patients with LDL ≥ 130 mg/dL (3.36 mmol/L), lifestyle alters alone are likely to be ineffective. Statins can use as initial therapy and the dose titrated to achieve target LDL < 100 mg/dL (2.57mmol/L). (3) for patients with TG ≥ 200 mg/dL (3.36 mmol/L), the goal is to achieve non-HDL cholesterol ≤ 130 mg/dL. Primary treatment comprises lifestyle alters plus a low dose statin which is escalated as needed to achieve target levels [5]. Statin therapy should be initiated for patients with stage 1–3 chronic kidney disease according to existing lipid guidelines for the general population (grade A). In patients with stage 1–3 chronic kidney disease, clinicians should consider titrating the dose of statin according to lipid guidelines for the general population (grade B). Clinicians should consider initiating statin therapy for patients with stage 4 chronic kidney disease and titrating the dose to achieve an LDL cholesterol level < 2.0 mmol/L and a ratio of total cholesterol to HDL cholesterol < 4.0 mmol/L (grade B). Gemfibrozil (1200 mg daily) may be considered as an alternative to statin treatment for patients with CKD (stage 1–3) who are at intermediate or high cardiovascular risk with concomitant low levels of HDL cholesterol (< 1.0 mmol/L) (grade B). Fasting triglycerides > 10 mmol/L at any stage of chronic kidney disease should be treated by recommending lifestyle changes and adding gemfibrozil or niacin, as required to reduce the risk of acute pancreatitis (grade D). Current data do not support treating hypertriglyceridemia as a strategy to reduce cardiovascular risk (grade A) [31].

Diabetes in Patients with CKD

The recommended goals in the adult diabetic population are pre-prandial plasma glucose of 90mg/dl to 130mg/dl; peak postprandial plasma glucose of < 180mg/dl; and HgbA1C <7% (grade B). Glycemic control should be part of a multifactorial intervention strategy that addresses blood pressure control and cardiovascular risk, and promotes the use of ACE inhibitors, angiotensin-receptor blockers, statins and acetylsalicylic acid (grade A). Metformin is recommended for most patients with T_2DM with stage 1 or 2 chronic kidney diseases that have stable renal function that has been unchanged over the past 3 months (grade A). Metformin may be continued in patients with stable stage 3 CKD (grade B) [31].

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CNS Damage in Patients with CKD

The neurological complications of CKD can be classified into those that pertain to the peripheral nervous system (neuropathy, myopathy) and those that include the CNS. CKD-induced peripheral neuropathy sequences from a variety of mechanisms. Intracellular accumulation of calcium secondary to hyperkalemia in CKD and reversal of the potassium or calcium pump can antecedent axonal injury and important axonal depolarization (presumably caused by hyperkalemia) has been observed in CKD in the early stages of neuropathy. The relationship between cognitive decline and CKD can be clarified by certain factors, such as traditional peril factors, non-traditional risk factors, increased inflammation, and oxidative stress [32].

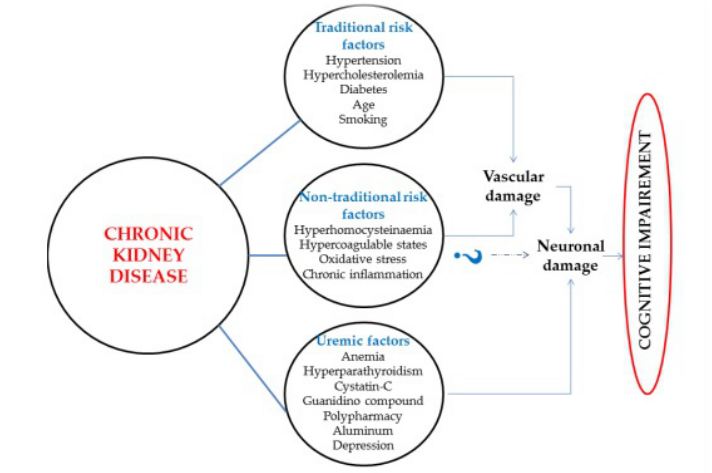

Figure 3: Factors linking chronic kidney disease and Alzheimer's disease

Management of CKD-related peripheral neuropathy is both symptomatic and mechanistic. Painful sensations of CKD-induced neuropathy perhaps respond partially to gabapentin and tricyclic antidepressants [33].

Dialysis and Transplantation

Either hemodialysis or peritoneal dialysis is especially used for management of end stage kidney disease (stage 5) patients. Most person reaching ESKD are managed with either haemodialysis or peritoneal dialysis, with a global prevalence of 280 per million people, analogized with 65 per million people who have a functioning kidney transplant. 5-year survival of person with ESKD on dialysis is between thirteen percent and sixty percent lower than people in the general population of similar ages. Approximately fifty six percent of people with ESKD on dialysis are actively waiting for a kidney transplant, but demand outstrips availability, so solely twenty five percent take a kidney whereas six percent die while waiting for a transplant each year [1].

Conclusion

The NKF guidelines emphasize persistent proteinuria as a marker of kidney damage, because proteinuria has been studied most thoroughly and is identified readily using a simple office procedure. Progression factors cause worsening kidney damage and faster decrement in kidney work after kidney damage has started and modifiable by pharmacological treatment or lifestyle modifications. Examples, higher level of proteinuria, higher blood pressure level, poor glycemic control in diabetes, and smoking. The ultimate common pathological manifestation of multiple CKD is renal fibrosis. Target blood pressure (<130/80 mm Hg vs <140/90 mm Hg) in patients with high concentrations of albuminuria. The most consistent benefit is noted with use of angiotensin-converting-enzyme (ACE) inhibitors and angiotensin-receptor blockers (ARBs), usually in association with diuretic drugs, in patients with high concentrations of albuminuria.

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