Introduction

Chronic kidney disease

Chronic Kidney Disease (CKD) is defined as evidence of structural or functional renal impairment for 3 or more months and is usually progressive and irreversible(2). CKD is thus a general term for various disorders affecting kidney structure and function with variable clinical presentation, in part related to cause, severity, and the rate of progression. Abnormalities in kidney structure usually precede abnormalities in function. End-stage kidney disease (ESKD) is traditionally considered to be the most serious outcome of CKD, however, CKD is also associated with substantial cardiovascular disease (CVD), even in the early stages. Thus, many patients with early stages of CKD may die from CVD before they progress to ESKD. The excess cardiovascular (CV) morbidity partly owes to traditional risk factors, such as hypertension, dyslipidemia, diabetes, prediabetes, and insulin resistance, but other CKD-specific metabolic disturbances, such as changes in mineral metabolism, especially hyperphosphatemia, are probably of even greater significance.

CKD is classified according to the glomerular filtration rate (GFR) in CKD stage 1–5 and albuminuria category 1–3 (3). The lower the level of GFR and the higher the level of albuminuria, the higher is the risk for development of ESKD and cardiovascular complications. CKD affects approximately 10-15% of the general population although estimates of the prevalence varies between countries(4). The majority is classified as stage 1, 2, or 3, at which GFR is normal or moderately decreased(5). Patients in stage 4 frequently progress to stage 5, in which renal replacement therapy is usually needed.

Treatment of CKD aims at preventing progression to ESKD and CV complications.

Pathophysiology of chronic kidney disease

The pathophysiology in CKD involves changes in glomeruli, tubular damage and vascular injury. The kidney function can be measured by glomerular filtration rate (GFR), defined as the volume of fluid filtered through the glomerular capillaries per unit time (ml/min). The renal blood flow is enormous, approximately 1200 ml blood is filtered per minute by a large number of nephrons (1

million per kidney) (3). The high renal blood flow also means the kidney tissue is exposed to any potential harmful agents circulating in the blood.

Pathophysiology of CKD leads to several clinical manifestations, like the following:

- Accumulation of creatinine, carbamide and phosphate in the blood/body which are normally excreted in urine
- Failure to maintain an adequate body hydration, fluid osmolality and electrolyte balance leading to fluid accumulation, acidosis and hyperkalemia
- Hypertension which leads to high intra-glomerular pressure impairing glomerular filtration. Damage to the glomeruli leads to increase in protein filtration and proteinuria which is associated with a poor prognosis for both CKD and CVD
- Erythropoietin production declines when the GFR falls below 50% of normal, leading to renal anemia
- Failure to regulate the calcium-phosphorus homeostasis: disturbances in plasma phosphate, magnesia and calcium, activating the phosphorus regulatory axis consisting of parathyroid hormone (PTH), 1α,25-dihydroxyvitamin D and fibroblast growth factor23 (FGF23) and its required co-receptor klotho(6,7). Untreated, this results in hypocalcemia, hyperphosphatemia and secondary hyperparathyroidism (SHPT). This again leads to bone disease and vascular calcifications. Many years of SHPT may stimulate the parathyroid gland to an autonomous (unregulated) function resulting in excessive PTH production and high blood calcium levels
- Hormonal dysfunction including disturbed growth and development, especially in children and increased levels of prolactin inducing gynecomastia in male with CKD (8)
- Nitrogen-containing products from dietary intake and intrinsic protein metabolism accumulate and affects taste and appetite.
- Uremia affects the microbiome and disrupts intestinal epithelia and the gastrointestinal absorption(9)
- As kidney failure advances the nutritional disorder worsens and protein-energy wasting aggravates (10).