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Review Article

Effect of Chronic Kidney Disease on Musculoskeletal System: A Scoping Review

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Abstract

Chronic kidney disease (CKD)s one of the global health challenges worldwide. Specially, in Asian countries the incidence of disease is increasing g day by day. With research it was found that kidney disease doesn't affect only the kidney function with affects the musculoskeletal system, cardiovascular system and overall health and wellbeing. The traditional way of treating a patient with kidney disease includes the pharmacological treatments, dialysis and/or kidney transplantation where as in modern treatment trends, rehabilitation is included for improving overall wellbeing of kidney patients and improve quality of life, reducing disease burden. To plan a tailored based rehabilitation approach it is important to understand the effect of disease on patients. So, in this paper the effect of chronic kidney disease on musculoskeletal system are emphasizes. Kidney plays a role in bone mineralization hence it plays vital role in functioning of musculoskeletal system. Effect of CKD on musculoskeletal system can broadly categized as effect on bones, muscles and pain. The primary musculoskeletal problems faced by a patient with CKD are sarcopenia, hyperkalemia, Frequent fatigues and bone disease.

Keywords: Chronic Kidney Disease; Musculoskeletal; Scoping

Introduction

Chronic kidney disease (CKD) is defined as a glomerular filtration rate [GFR] less than 60 mL/min and albumin greater than 30 mg per gram of creatinine for greater than three months, according to the Kidney Disease Improving Global Outcomes (KDIGO) foundation guidelines. End-stage renal disease (ESRD) is defined as GFR of less than 15mL/min. Kidney function decline is gradual and asymptomatic sometimes at the initial stage of disease. Despite the destruction of a few nephrons, the kidneys can maintain the glomerular filtration rate (GFR) through hyperfiltration and compensatory hypertrophy of the remaining nephrons. This compensatory mechanism allows for normal creatinine levels, potentially delaying the detection of renal impairment [1,2].

In Asia, the prevalence of CKD is high. Especially in India, China and Pakistan the prevalence is alarmingly high. CKD patient management is not only socio-economically challenging but medically challenging also as CKD patients demonstrate various systemic problems such as sarcopenia, bone disease, Hyperkalaemia, anaemia and cardiovascular comorbidities. Only managing kidney function may not be sufficient as other associated problems degrade the patient's quality of life. In India, the government is working to establish affordable but significant progress is yet to be made in managing chronic kidney disease (CKD). Hence the need of researches in this area increase to establish better multidimensional treatment strategies. Effect of CKD on musculoskeletal system can broadly categized as effect

on bones, muscles and pain. In the present study, an overview of effect of chronic kidney disease on the musculoskeletal system is discussed further [2-5].

Effect of CKD on muscle:

The effect of CKD is massive on muscles because of several reasons. Sarcopenia is a musculoskeletal disease characterized by the loss of muscle mass, reduced muscle strength, and diminished physical performance. Chronic kidney disease (CKD) accelerates ageing and increases the risk of sarcopenia, especially in end-stage kidney disease, which is linked to severe health outcomes, including higher mortality. The age-related sarcopenia can be differentiated from sarcopenia related to CKD. Muscle protein degradation and Resting energy expenditure Increases in CKD which remains unchanged in Aging patients without CKD. Muscle atrophy in type-I and II both fibres is seen in CKD whereas in CKD patients major muscle atrophy is seen in age-related sarcopenia. In chronic kidney disease (CKD) patients, the dialysis procedure and chronic low-grade inflammation increase protein degradation and decrease protein synthesis, leading to a negative protein balance. Additionally, non-inflammatory factors related to kidney function loss, such as metabolic acidosis, insulin resistance, and vitamin D deficiency, further promote protein catabolism and hinder protein synthesis. Metabolic acidosis, in particular, stimulates protein breakdown by activating caspase-3 and the ubiquitin-proteasome system (UPS) and contributes to insulin and growth hormone (GH) resistance. Sarcopenia is a significant nutritional issue in CKD and end-stage kidney disease (ESKD) that should be routinely screened for in clinical practice. It can develop early and progress quickly due to a negative energy-protein balance, exacerbated by factors like insufficient food intake and increased protein catabolism, particularly in haemodialysis (HD) patients. CKD-related sarcopenia is more prevalent than age-related sarcopenia, especially in HD patients. Sarcopenia in CKD patients can lead to other major problems such as limited functional independence, chances of falls, fatigue and poor Quality of life. Hence it should be managed with rehabilitation approaches such as exercises, physical activity and/or renal rehabilitation [6-9].

Effect of CKD on bone

Chronic kidney disease (CKD) profoundly affects bone health, leading to a condition known as chronic kidney disease-mineral and bone disorder (CKD-MBD). As kidney function declines, the body's ability to maintain calcium, phosphorus, parathyroid hormone, and vitamin D homeostasis becomes impaired, which disrupts normal bone remodelling processes. This dysregulation can result in various bone abnormalities, including osteitis fibrosa (high-turnover bone disease due to secondary hyperparathyroidism), adynamic bone disease (low bone turnover), and osteomalacia (defective bone mineralization). CKD-MBD increases the risk of fractures, contributing to higher morbidity and mortality rates in CKD patients. Studies have shown that patients with CKD, particularly those on dialysis, have a significantly higher incidence of fractures compared to the general population. Additionally, the severity of bone disease in CKD is associated with cardiovascular complications, as vascular calcifications often accompany bone mineral abnormalities, further complicating patient outcomes. Effective management of CKD-MBD requires a comprehensive approach that includes controlling phosphate levels and managing parathyroid hormone levels, all of which have been shown to improve bone health and reduce fracture risk in CKD patients. CKD leads to decreased renal production of active vitamin D (calcitriol), which is essential for calcium absorption and bone mineralization. This deficiency results in secondary hyperparathyroidism, which accelerates bone resorption and contributes to bone loss. Additionally, elevated phosphorus levels in CKD patients can form insoluble complexes with calcium, leading to further bone demineralization and increasing fracture risk. Evidence from studies indicates that CKD patients, particularly those with advanced stages or those on dialysis, have a higher prevalence of osteoporosis compared to the general population. For instance, research has demonstrated that CKD patients experience lower bone mineral density (BMD) and an increased incidence of vertebral and non-vertebral fractures. Effective management of osteoporosis in CKD requires addressing these metabolic imbalances through strategies such as phosphate control, vitamin D supplementation, and, where necessary, the use of medications like bisphosphonates or denosumab, which have been shown to improve bone density and reduce fracture risk in CKD patients [10-13].

Effect of CKD on vitamin D

Chronic kidney disease (CKD) significantly impairs vitamin D metabolism, contributing to various complications including mineral and bone disorders. In CKD, the kidneys' ability to convert

inactive vitamin D to its active form, calcitriol (1,25-dihydroxy vitamin D), is diminished due to reduced renal function. This deficiency in calcitriol impairs calcium absorption in the intestines, leading to hypocalcaemia. Consequently, this stimulates increased parathyroid hormone (PTH) secretion, which can exacerbate bone resorption and contribute to secondary hyperparathyroidism. Studies show that vitamin D deficiency is prevalent among CKD patients, with serum 25-hydroxyvitamin D levels often being markedly low. This deficiency has been linked to worsening bone health, increased risk of fractures, and cardiovascular complications in CKD. For example, research indicates that vitamin D supplementation in CKD patients can help correct deficiencies, improve calcium and phosphate balance, and reduce the risk of secondary hyperparathyroidism. Furthermore, clinical trials have demonstrated that managing vitamin D levels in CKD patients, whether through oral supplements or intravenous administration, can significantly improve bone health outcomes and mitigate some of the adverse effects associated with CKD-MBD (chronic kidney disease-mineral and bone disorder [14-16].

Pain and Other musculoskeletal disorders in CKD

Musculoskeletal disorders linked to chronic kidney disease (CKD) are rising globally, imposing a substantial health burden. These disorders are major contributors to comorbidities, disability, and reduced productivity, significantly impacting individuals' functional status and quality of life. Research indicates that musculoskeletal disorders are moderately common among CKD patients. Factors such as female gender, age between 40 and 49 years, stages III and IV CKD, hypertension, elevated parathyroid hormone (PTH) levels, and low calcium and vitamin D levels are statistically significant in their association with these disorders. Chronic musculoskeletal pain (CMP) is particularly prevalent in patients with advanced CKD and markedly affects quality of life. CMP often accompanies other symptoms of chronic uraemia and is notably common among the elderly, women, those with obesity, and individuals with certain comorbid conditions. Increased inflammatory markers observed in CMP patients may play a key role in its development. The typical profile of patients with CMP includes older females, those with obesity, certain comorbidities, and elevated inflammatory markers. Further research is needed to identify effective, less toxic analgesic treatments and supportive measures for this population. CKD frequently leads to fatigue, a common and debilitating symptom affecting many patients. This fatigue can be attributed to a combination of factors including anaemia, electrolyte imbalances, and the body's reduced ability to clear waste products. The accumulation of toxins and metabolic disturbances in CKD further exacerbate feelings of exhaustion. CKD frequently leads to musculoskeletal pain, which significantly impacts patients' quality of life. The prevalence of musculoskeletal pain increases with CKD severity, particularly in advanced stages. Contributing factors include mineral imbalances, elevated parathyroid hormone levels, and inflammation. This pain often exacerbates functional limitations and disability, complicating the overall management of CKD. Effective management strategies for CKD-related musculoskeletal pain are essential for improving patient outcomes and enhancing quality of life. Renal Rehabilitation is an effective yet unpopular treatment approach for all of the above diseased musculoskeletal problems in CKD patients [17-20].

Conclusion

In the end, it will be appropriate to say, that despite the chronic kidney disease is a systemic disease, it has a massive effect on the musculoskeletal system. CKD not only affects the musculoskeletal system but also has major associated health concerns such as increasing risk of falls, high chances of fracture decreased functional independence, increased hospitalization stay and overall poor quality of life. The rehabilitation approach should be incorporated as a mainstream treatment along with other treatments such as haemodialysis and fluid therapy. Rehabilitation should be primarily focused on the musculoskeletal system, especially sarcopenia and bone health.

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