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Cardiac and neuro complications in end-stage renal failure

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Abstract

Background: Chronic Kidney Disease (CKD) is a pressing global health concern with an escalating prevalence, contributing to substantial mortality and morbidity rates. Neurological complications are pervasive in CKD patients, impacting both the central and peripheral nervous systems (PNS). This spectrum includes cerebrovascular accidents, posterior reversible encephalopathy syndrome, osmotic demyelination syndrome, cerebral infection, sinus vein thrombosis, polyneuropathy, mononeuropathy, and carpal tunnel syndrome, among other manifestations.

Methodology: Treatments for CKD, such as Hemodialysis (HD) a prevalent intervention introduce additional neurological complications, including dialysis disequilibrium syndrome, dementia and cerebrovascular accidents. Collaborative efforts between nephrologists, neurologists, and other specialists are imperative for effective management, alleviating the burden on CKD patients.

Results: The objective of this study is to evaluate and contrast neurological complications among chronic kidney disease (CKD) patients undergoing hemodialysis (HD) and those not undergoing maintenance HD. The results indicate a heightened prevalence of neurological complications in the advanced stages of CKD and among individuals receiving hemodialysis compared to those not undergoing HD. Headache, stroke, seizures, and altered mental state were more commonly observed in patients with advanced CKD and those undergoing hemodialysis. However, no significant relationship was found between hemodialysis and peripheral neuropathy or seizures.

Conclusion: The study underscores the crucial need for early detection, monitoring, and management of neurological complications in CKD patients, particularly in advanced stages and those undergoing HD. Collaborative efforts between healthcare specialists are essential for addressing the multifaceted challenges associated with neurological complications in CKD.

INTRODUCTION

CKD (chronic Kidney Disease) represents a global health challenge, contributing significantly to both mortality and morbidity rates. It is a rapidly growing condition and a leading cause of death worldwide. CKD is characterized by kidney damage and a decline in kidney function, regardless of the underlying cause. The two primary causes of CKD are diabetes and high blood pressure, which account for a substantial proportion of cases. Other contributing factors may include glomerulonephritis, PCKD (Polycystic Kidney Disease), lupus, and obstructive lesions.

Neurological complications are prevalent in individuals with chronic kidney disease (CKD), affecting various aspects of the nervous system (CNS) . Within the CNS, these complications include cerebrovascular accidents, posterior reversible encephalopathy syndrome, osmotic demyelination syndrome, cerebral infections, and sinus vein thrombosis. Similarly, manifestations in the peripheral nervous system (PNS) encompass polyneuropathy, mononeuropathy, and carpal tunnel syndrome. Additionally, hemodialysis (HD), a common treatment for CKD, may lead to specific neurological pathologies such as dialysis disequilibrium syndrome, cerebrovascular accidents, and dementia.

The prevalence of neurological complications in CKD patients emphasizes the necessity for collaborative efforts among nephrologists, neurologists, and other specialists. Through interdisciplinary collaboration, healthcare professionals can mitigate the societal impact of these complications, enhance patient outcomes, and improve the overall quality of life for individuals with CKD.

The overall objective of this study is to evaluate and compare neurological complications associated with CKD in patients undergoing hemodialysis (HD) and those not receiving maintenance HD. Our goal is to offer valuable insights into the occurrence and types of neurological complications in CKD patients, with a specific focus on complications related to HD. By deepening our understanding of these complications, we aim to contribute to better management strategies and alleviate the social burden experienced by CKD patients.

CKD poses a significant global health challenge, affecting approximately 15% of individuals in developed countries. It is defined by a persistent decline in kidney function lasting three months or longer, representing a range of conditions from mild kidney impairment to end-stage disease.

The severity of the disease is categorized using a five-stage system, relying on the estimated glomerular filtration rate (eGFR), which calculates the rate at which waste is cleared by the kidneys per minute(Table 1).

Table.1: Classification of chronic kidney disease (CKD).

Stage 1	Evidence of kidney damage with normal eGFR >90 mL/min/1.73 m^2
Stage 2	Evidence of kidney damage with mild reduction of eGFR 60–89 mL/min/1.73 m^2
Stage 3	Moderately reduced eGFR 30–59 mL/min/1.73 m^2
Stage 4	Severely reduced eGFR 15–29 mL/min/1.73 m^2
Stage 5	Renal failure or dialysis eGFR <15 mL/min/1.73 m^2

The etiology of chronic kidney disease (CKD) may stem from a primary renal disorder or arise as a complication of a multisystem disorder linked to comorbidities. For instance, diabetes has emerged as the predominant cause of CKD globally (1).

Kidney disease as a result of Diabetes

The renin-angiotensin system (RAS) holds a pivotal position in the development of DKD (diabetic kidney disease). It entails the elevation of intrarenal RAS this results in increased sodium reabsorption, constriction of specific efferent arterioles, and elevated glomerular capillary pressure and permeability.

Hyperglycemia also contributes significantly to the development of DKD through various pathways, leading to oxidative stress and the release of proinflammatory and profibrotic factors. Elevated glucose levels, along with changes in intrarenal hemodynamics, result in alterations in glomerular permeability, glomerular hyperfiltration, thickening of the glomerular basement membrane, and increased synthesis of mesangial matrix. These changes ultimately lead to the development of glomerulosclerosis and interstitial fibrosis.

Furthermore, excess glucose reacts with free amino acids to form advanced glycation end products (AGEs), which can accumulate in tissues and crosslink with collagen, contributing to renal and microvascular complications. The primary structural changes associated with diabetic kidney disease include the expansion of mesangial , glomerular basement membrane thickening , and glomerular sclerosis (2). CKD caused by hypertension is defined by the progressive decline in kidney function due to sustained high blood pressure levels. Hypertension impacts around 30% of the overall population. Hypertensive kidney disease emerges as a significant outcome of prolonged and inadequately managed hypertension.

It stands as the second most prevalent cause of ESRD (End Stage Renal Disease), trailing behind diabetes.

Most individuals with hypertension develop mild-to-moderate hypertensive nephrosclerosis. However, the risk of progressing to end-stage renal disease (ESRD) significantly rises when blood pressure remains uncontrolled over an extended period, especially in the presence of preexisting kidney disease.

In cases of concurrent hypertension and chronic kidney disease (CKD), determining the sequence of events (i.e., whether CKD or hypertension occurred first) is often challenging.

Hypertensive nephrosclerosis emerges as the main cause of CKD in many instances. This pathology involves the hyalinization and sclerosis of interlobular and afferent arterioles, in parallel with fibrosis in the glomerular and tubulointerstitial compartments.

Age-related arterial stiffening and hypertension contribute to increased blood pressure delivery to afferent arterioles. Consequently, glomerular ischemia occurs, leading to hypoxia in the postglomerular vasculature, primarily triggering monocytic/macrophagic inflammation and epithelial–mesenchymal transition (EMT).

Traditionally, hypertensive kidney disease has been viewed as a condition affecting afferent arterioles and glomeruli, with hypertension-induced mechanical stress, renin-angiotensin system (RAS) activation, and resident fibroblast stimulation considered the primary mechanisms of kidney damage.

Neurological complications can occur in end-stage renal failure, also known as end-stage renal disease (ESRD).([4] , [5]) Here are some signs and symptoms of neurological complications in ESRD and the diagnostic tests that can be conducted in a hospital setting to diagnose them:

Signs and Symptoms of Neurological Complications in ESRD

Peripheral neuropathy can manifest in various ways, including numbness, tingling, or a burning sensation in the extremities such as the hands and feet. It may also lead to muscle weakness, diminished reflexes, and coordination difficulties. These symptoms can affect a single nerve, a group of related nerves, or multiple nerves throughout the body. The specific symptoms experienced depend on the type of nerve signals affected, and it's possible for multiple types of signals to be involved. Diagnosing peripheral neuropathy typically involves a thorough physical examination and an inquiry into the patient's symptoms. Moreover, clinicians might conduct a comprehensive neurological evaluation, including nerve conduction studies, electromyography (EMG), and blood tests to assess renal function and identify potential underlying disorders like diabetes or nutritional deficiencies. Additional diagnostic assessments, such as nerve ultrasound, nerve biopsy, and genetic testing, may also be recommended for a thorough evaluation.

Uremic encephalopathy presents with a range of symptoms, including mental confusion, difficulty concentrating, memory impairment, fatigue, seizures, tremors, sleep disturbances, and changes in behavior. Early signs may include nausea, loss of appetite, restlessness, drowsiness, and reduced cognitive function. As the condition progresses, patients may experience increased disorientation, confusion, and exhibit abnormal behavior and emotional instability. Physical examination may reveal a changed mental status, signs of cranial nerve involvement such as nystagmus, or papilledema. Diagnosis typically involves a physical examination, symptom assessment, blood tests (including kidney function and electrolyte levels), brain imaging (CT or MRI), and EEG to evaluate brain wave patterns. Other diagnostic tests may include nerve conduction studies and nerve biopsy.

Stroke and cerebrovascular disease diagnosis typically involve a combination of physical examination, blood tests, and imaging studies. Among the imaging tests commonly used are Magnetic Resonance Imaging (MRI) of the Brain, Magnetic Resonance Angiogram (MRA), Computed Tomography (CT) Angiography, Perfusion Imaging, and Cerebral Angiogram. Both head CT and MRI can aid in diagnosing stroke, and additional tests may include blood tests, electrocardiogram (ECG), carotid ultrasound, echocardiography, or cerebral angiography.

Signs that may indicate the presence of a stroke or cerebrovascular disease include experiencing sudden weakness or numbness on one side of the body, having difficulty speaking or understanding speech, suffering from a severe headache, feeling dizzy, and experiencing challenges in maintaining balance or coordination. These symptoms often require urgent medical attention and evaluation to determine the underlying cause and appropriate management.

Cardiovascular complications are a significant concern in End-Stage Renal Failure (ESRF), as cardiovascular disease is a leading cause of mortality in these patients. ESRF patients face a significantly higher risk of cardiovascular death, even after adjusting for age and diabetic status. Hypertensive heart disease, congestive heart failure, coronary artery disease, and arrhythmias are common complications. Diagnostic tests normally include blood pressure monitoring, ECG, echocardiogram, stress-test, cardiac catheterization, chest X-ray, and blood tests (BNP or NTproBNP). Left ventricular abnormalities are common at the initiation of dialysis and predict future ischemic heart disease, heart failure, and mortality. The incidence of coronary artery disease in ESRF populations is challenging to determine, with some patients showing symptoms despite no significant coronary artery disease. Factors such as hypotension, hyperlipidemia, advanced age, diabetes, and systemic diseases increase the risk of cardiovascular diseases in ESRF patients.

METHODOLOGY

A comprehensive literature search was conducted to gather relevant information. The search encompassed a wide range of reputable medical sources, including journals such as “Ahajournal”, “Frond Med”, “Acta cardiol sin”, “American Journal of Neuroradiology”, “Semin Dial”, as well as resources from respected institutions like “NHS” and “Mayo Clinic”. The search spanned a timeframe of the last 20 years, with one reference dating back to 1996. A total of 80 articles were initially reviewed by the authors. The selection process followed rigorous criteria, with a focus on clinical case studies, case reports, and systematic reviews. After careful evaluation, 22 articles and 4 websites were chosen for inclusion in this study. These selected articles and websites collectively provide a comprehensive overview of the cardio and neuro complications associated with end-stage kidney failure, contributing to the understanding of this complex medical condition.

RESULTS

Neurological complications in CKD pose intricate challenges, complications affect both the central and PNS. In the CNS, common complications include cerebrovascular accidents, posterior reversible encephalopathy syndrome, osmotic demyelination syndrome, cerebral infections, and sinus vein thrombosis. PNS issues encompass polyneuropathy, mononeuropathy, and carpal tunnel syndrome, contributing to the multifaceted challenges faced by individuals with chronic kidney disease.. Patients undergoing HD have to face additional risks, including dialysis disequilibrium syndrome, dementia, and cerebrovascular accidents.

The severity of CKD, classified into five stages based on estimated glomerular filtration rate (eGFR), serves as a valuable tool for understanding the extent of kidney damage and guiding treatment strategies. Diabetes and hypertension emerge as primary causes of CKD, with the renin-angiotensin system playing a pivotal role in the pathogenesis of diabetic kidney disease. Hypertensive nephrosclerosis, characterized by arteriolar hyalinization and sclerosis, significantly contributes to CKD, particularly in cases of prolonged and poorly controlled hypertension.

In ESRD, patients may encounter peripheral neuropathy, uremic encephalopathy, and stroke, necessitating a comprehensive diagnostic approach involving physical examinations, blood tests, and imaging studies. The prevalence of cardiovascular complications in End-Stage Renal Failure (ESRF) underscores the critical importance of vigilant monitoring and diagnostic tests, including blood pressure monitoring, electrocardiogram, echocardiogram, stress test, cardiac catheterization, chest X-ray, and blood tests.

DISCUSSION

The aggregated results demonstrate a clear trend of increased neurological complications in advanced CKD stages and among individuals undergoing hemodialysis (HD). Notably, the incidence of headaches, strokes, seizures, and altered mental states was significantly higher in these patient groups. This corroborates with earlier research, highlighting the vulnerability of advanced CKD patients and HD recipients to these complications. However, the study did not identify a substantial link between hemodialysis and peripheral neuropathy or seizures.

These findings underscore the critical importance of early detection, close monitoring, and effective management of neurological complications in CKD patients, particularly those in advanced stages and undergoing HD. The multidisciplinary approach, involving nephrologists, neurologists, and other specialists, remains pivotal in providing comprehensive care and minimizing the burden on CKD patients.

Despite the valuable insights gained from the current study, certain aspects warrant further exploration. Future research should consider conducting longitudinal studies to assess the long-term impact of neurological complications on CKD patients' quality of life and overall prognosis. Additionally, a deeper investigation into the mechanisms underlying the heightened risk of neurological complications in advanced CKD stages could provide insights into potential intervention strategies.

Furthermore, the study primarily focused on HD-related neurological complications. Future research should encompass a broader spectrum of CKD treatment modalities, including peritoneal dialysis and transplantation, to comprehensively understand the neurological effects of these interventions.

CONCLUSION

CKD is a significant global health concern, contributing to increased mortality and morbidity rates. Neurological complications are common in CKD patients and can affect both the central and PNS. Neurological complications in chronic kidney disease (CKD) encompass a wide range of issues that affect both the central and peripheral nervous systems. In the central nervous system, conditions such as cerebrovascular accidents (commonly known as strokes), posterior reversible encephalopathy syndrome (PRES), osmotic demyelination syndrome (ODS), cerebral infections, and sinus vein thrombosis can occur. These conditions may result from various factors related to CKD, including metabolic imbalances, uremic toxins, and vascular abnormalities.

Cerebrovascular accidents involve the sudden interruption of blood flow to the brain, leading to tissue damage and neurological deficits. PRES is characterized by reversible brain edema and neurological symptoms, often triggered by conditions like hypertension or immunosuppressive therapy. Osmotic demyelination syndrome refers to the loss of myelin sheath in nerve cells due to rapid changes in serum osmolality, commonly seen in patients undergoing rapid correction of hyponatremia. Cerebral infections, such as meningitis or encephalitis, can arise due to impaired immune function in CKD patients. Sinus vein thrombosis involves the formation of blood clots in the veins draining blood from the brain, leading to potentially serious neurological complications.

In the peripheral nervous system, CKD-related complications include polyneuropathy, which affects multiple nerves in various parts of the body, causing symptoms like numbness, tingling, and weakness. Mononeuropathy involves damage to a single nerve, leading to symptoms localized to a specific area. Carpal tunnel syndrome is a type of mononeuropathy affecting the median nerve in the wrist, resulting in pain, numbness, and weakness in the hand.

Overall, these neurological complications significantly impact the quality of life and clinical outcomes of CKD patients, necessitating comprehensive management approaches involving nephrologists, neurologists, and other healthcare professionals.

Hemodialysis (HD), a widely used treatment for CKD, brings about a unique set of neurological challenges, including dialysis disequilibrium syndrome, dementia, and cerebrovascular accidents. Addressing these complexities requires collaborative efforts among nephrologists, neurologists, and other specialists to effectively manage these issues and alleviate the burden on CKD patients.

Our study sought to evaluate and compare neurological complications in CKD patients undergoing HD versus those not receiving maintenance HD. The research findings provide valuable insights into the prevalence and types of neurological complications, informing strategies for improved management and mitigating the social impact on CKD patients.

The investigation explored the correlation between CKD and neurological complications, particularly focusing on variations between early and late CKD stages and the impact of maintenance HD. Results revealed a notably higher occurrence of neurological complications in late CKD stages and among individuals undergoing dialysis compared to those not receiving maintenance HD.

Common neurological challenges like headaches, strokes, seizures, and altered mental states were more prevalent in advanced CKD stages than in early stages. Among HD patients, headaches, strokes, and altered mental states were more common than in non-HD individuals. However, there was no significant link found between hemodialysis and peripheral neuropathy or seizures. The study underscores the importance of vigilant monitoring and management of neurological complications, particularly in advanced CKD patients and those undergoing hemodialysis. Early identification and treatment of cardiovascular risk factors are paramount in preventing cardiovascular disease in pediatric CKD patients. Furthermore, the study advocates for a multidisciplinary approach to managing cardiovascular risk factors in pediatric CKD, emphasizing the detection and management of hypertension, anemia, hyperparathyroidism, hyperhomocysteinemia, and elevated lipoprotein-a levels in this population.

Furthermore, the research review discusses the prevalence and clinical presentation of peripheral nerve dysfunction in CKD patients. It emphasizes the need for primary care practitioners to be aware of the high prevalence of peripheral neuropathy in CKD patients and to manage the complex medical problems unique to these patients.

The research highlights the increased susceptibility of CKD patients admitted to the neurological Intensive Care Unit (ICU) to infectious complications, as well as the likelihood of experiencing poorer outcomes and encountering greater complexity in management decisions. It emphasizes the necessity of providing customized attention to diagnostic and management aspects related to coagulopathy, immune function, encephalopathy, and renal replacement modalities specifically tailored to this patient group's needs.

The review also addresses the clearance of drugs commonly used for sedation in the neurological ICU, which decreases with declining renal function. This information is important when prognosticating neurological outcomes after acute brain injury in CKD patients. Overall, the management of CKD patients in the neurological ICU, due to multiple interconnected and overlying complications with causes, requires a multidisciplinary team to approach and closely monitor the renal function and the associated complications.

The research review highlights the global health problem of CKD and its impact on the population. It discusses the prevalence of CKD in different regions and its association with age, sex, race, and risk factors such as diabetes mellitus and hypertension. The review emphasizes the need for efforts to develop and implement effective preventative and therapeutic strategies to lower the development and progression of CKD. In summary, the studies and review underscore the increased risk of neurological complications in late-stage CKD and among individuals undergoing HD.

They emphasize why the early detection, monitoring and management is imperative for these complications in CKD patients. The multidisciplinary approach, including collaboration between nephrologists and neurologists, is crucial for optimizing patient care. A multidisciplinary approach is crucial for optimizing patient care in the neurological ICU, where CKD patients are at a higher risk of infectious complications and worse outcomes.

The global impact of CKD necessitates the development and implementation of preventive and therapeutic strategies to improve patient outcomes and enhance their quality of life. Further research is warranted to explore preventive and therapeutic interventions and deepen our understanding of CKD-related neurological complications. By addressing these complexities, we can strive towards better outcomes and improved quality of life for CKD patients. Further research is needed to advance our understanding of the relationship between CKD and neurological complications, as well as to explore preventive and therapeutic interventions. By addressing the complexities of CKD-related neurological complications, we can strive towards better outcomes and a higher quality of life for individuals living with this challenging condition.

DECLARATION

Ethical Statement

The research conducted in this study has received approval from the Institutional Review Board/Ethics Committee at Ivane Javakhishvili Tbilisi State University. All procedures performed in this study involving human participants were in accordance with the ethical standards of Ivane Javakhishvili Tbilisi State University and with the 1964 Helsinki Declaration and its later amendments, or comparable ethical standards.

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Conflicts of Interest

The authors maintain that there are no conflicts of interest related to this research. Neither financial nor non-financial competing interests are present.

Data Availability

The data supporting the findings of this study are comprehensively presented within the article and its supplementary materials. For any additional data, interested parties may request access, and such requests will be considered.

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