"IMPACT OF HEMODIALYSIS ON COGNITION"

B.L.D.E (DEEMED TO BE UNIVERSITY) VIJAYAPURA, KARNATAKA

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In partial fulfillment of the requirements for the award of the degree of

DOCTOR OF MEDICINE

IN

GENERAL MEDICINE

"'' IMPACT OF HEMODIALYSIS ON COGNITION''

BY

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ABBREVIATIONS

ACR – Albumin-to-Creatinine Ratio

AER – Albumin Excretion Rate

AKI – Acute Kidney Injury

AKIN – Acute Kidney Injury Network

AVF – Arteriovenous Fistula

AVG – Arteriovenous Graft

AVFs – Arteriovenous Fistulas

BDI – Beck Depression Inventory

CKD – Chronic Kidney Disease

CRIC – Chronic Renal Insufficiency Cohort

CRRT – Continuous Renal Replacement Therapy

CSF – Cerebrospinal Fluid

DSM-IV – Diagnostic and Statistical Manual of Mental Disorders, 4th Edition

DSM-5 – Diagnostic and Statistical Manual of Mental Disorders, 5th Edition

eGFR – Estimated Glomerular Filtration Rate

ESRD – End-Stage Renal Disease

FHN – Frequent Haemodialysis Network

GFR – Glomerular Filtration Rate

HD – Hemodialysis

HDRS – Hamilton Depression Rating Scale

KDOQI – Kidney Disease Outcomes Quality Initiative

KDIGO – Kidney Disease: Improving Global Outcomes

MCI – Mild Cognitive Impairment

MDD – Major Depressive Disorder

PCR – Protein-to-Creatinine Ratio

PD – Peritoneal Dialysis

PHQ-9 – Patient Health Questionnaire-9

RIFLE – Risk, Injury, Failure, Loss, and End-Stage Kidney Disease

RRT – Renal Replacement Therapy

URR – Urea Reduction Ratio

ABSTRACT

Background: Cognitive impairment is a significant yet underrecognized complication among patients undergoing hemodialysis. Studies indicate that up to 30% of hemodialysis patients develop dementia, with many experiencing mild cognitive impairment (MCI) as a precursor. The progression of chronic kidney disease (CKD) to end-stage renal disease (ESRD) requiring hemodialysis is associated with worsening cognitive function, potentially due to factors such as uremic toxin accumulation, haemodynamic instability, and inflammation.

Aimed to assess the presence and extent of cognitive impairment in patients with CKD undergoing haemodialysis and to identify contributing factors.

Material & Method: This cross-sectional study was conducted at BLDE (DU), Shri B.M. Patil Medical College Hospital and Research Centre, Vijayapura, over 18 months (May 2023 – December 2024). A total of 64 patients undergoing maintenance hemodialysis were assessed for cognitive impairment using the Montreal Cognitive Assessment (MoCA). Data were analyzed using SPSS Version 20, with independent t-tests and Chi-square tests applied for statistical significance ($p<0.05$).

Results: The mean age of participants was 52.67±14.2 years, with 62.5% males and 37.5% females. Hypertension (50%) and diabetes (31.3%) were common comorbidities. Cognitive impairment was present in 40.6% of patients. Patients with cognitive impairment had significantly longer CKD duration (2.5 years vs. 1.6 years) and haemodialysis duration (8.6 months vs. 3.5 months) ($p<0.05$).

Conclusion: Cognitive impairment is prevalent in hemodialysis patients and is associated with longer CKD and dialysis durations. Early screening and intervention strategies are essential to mitigate cognitive decline and improve patient outcomes.

Keywords: Cognitive impairment, Hemodialysis, Chronic Kidney Disease, End-Stage Renal Disease, Montreal Cognitive Assessment, Dementia

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INTRODUCTION

Dementia prevalence is alarmingly high in hemodialysis patients, reaching as much as 30%, yet it often goes unrecognized and underdiagnosed.[1,2] "In patients with End-Stage Renal Disease (ESRD), cognitive function is closely linked to the severity of renal disease and the associated risk of dementia. This heightened risk and prevalence of dementia in ESRD patients, particularly those undergoing hemodialysis (HD), are often preceded by mild cognitive impairment (MCI), a transitional stage between normal age-related cognitive changes and dementia.[3,4]

Patients with chronic kidney disease (CKD) on hemodialysis exhibit a notably high prevalence of MCI even when their global cognitive function appears intact. In the early stages of CKD, executive function and attention are the cognitive domains most commonly affected. However, as the disease progresses to ESRD requiring hemodialysis, cognitive impairment becomes more severe and widespread, encompassing multiple domains. This suggests a gradation of cognitive decline that correlates with the severity of kidney dysfunction."[5,6]

Notably, MCI is more prevalent among HD patients compared to those with mild to moderate CKD, with cognitive deficits occurring more frequently and affecting a broader range of cognitive domains. Hemodialysis-related factors, such as hemodynamic instability, toxin accumulation, and inflammation, may contribute to this decline. Despite its significant impact, cognitive impairment in HD patients remains poorly understood and underexplored.

Understanding the scope and mechanisms of cognitive dysfunction in HD patients is crucial, as it may inform early interventions to slow progression, optimize dialysis practices, and improve overall quality of life. This underscores the need for focused studies to substantiate the extent of cognitive impairment in haemodialysis patients and identify modifiable factors contributing to their vulnerability.

REVIEW OF LITERATURE

“Chronic kidney disease (CKD) is defined by the presence of kidney damage or reduced kidney function for 3 or more months, irrespective of the cause.”

Graham (1805-1869), a “Scottish chemical professor, pioneered in vitro solute separation using semipermeable membranes and coined the term "dialysis." In 1924, Haas from Germany became the first to use dialysis in humans. Dr. Willem Kolff, a Dutch physician, applied extracorporeal dialysis to treat patients with acute renal damage in 1944, earning him the title "Father of Hemodialysis." In the early years, hemodialysis faced widespread complications due to technical problems with dialysis equipment and water systems. However, significant technological advancements, particularly in the past 20 years, have reduced these issues. Despite these improvements, complications unrelated to the dialysis machine and water systems remain a major cause of morbidity and mortality in haemodialysis patients.

Brief anatomy

In vertebrates, the kidneys are two reddish-brown, bean-shaped organs located on either side of the retroperitoneal space. Each kidney measures about 12 centimeters (4.5 inches) in length in adults. Blood is supplied to the kidneys by the paired renal arteries, and blood exits through the paired renal veins. The kidneys are connected to the bladder by the ureters, which transport excreted urine. The upper pole of each kidney is positioned at the level of the 12th thoracic vertebra, while the lower pole is

at the level of the 3rd lumbar vertebra. In adult males, each kidney typically weighs between 125 and 170 grams, and in females, between 115 and 155 grams.

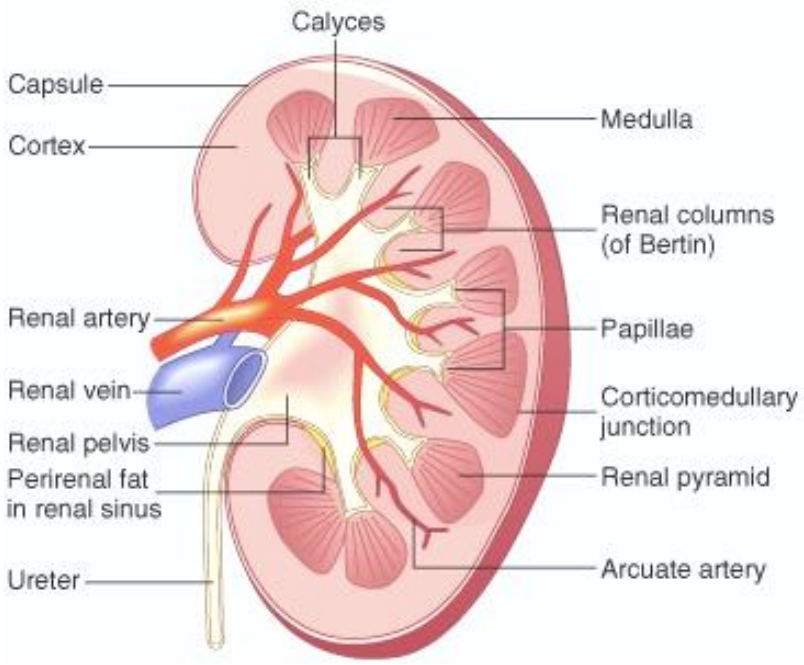


Figure 1: Structure of kidney

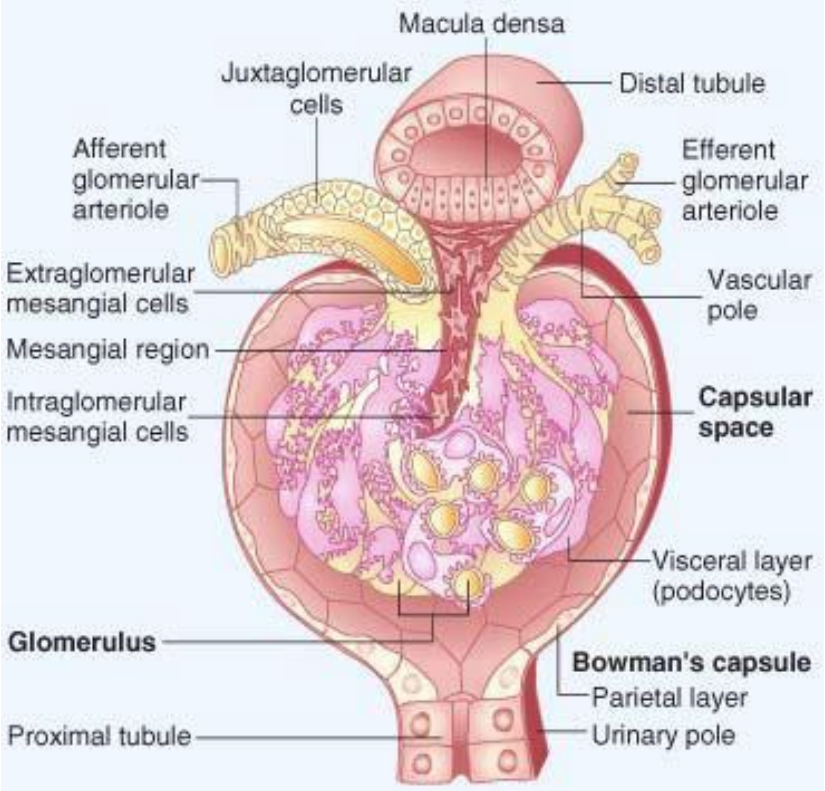


Figure 2: Showing the glomerulus and bowmans capsule

Nephrons

The nephron is the fundamental structural and functional unit of the kidney, with approximately 1 million nephrons present in each adult human kidney and around 12,500 in a mouse kidney." The kidneys play a critical role in regulating various bodily functions, including fluid volume, osmolality, acid-base balance, electrolyte concentrations, and the excretion of toxins. "Filtration occurs in the glomerulus, where about 20% of the blood entering the kidneys is filtered. Compounds like water, sodium, bicarbonate, glucose, and amino acids are reabsorbed, while hydrogen, ammonium,

potassium, and uric acid are secreted. In addition to these functions, the kidneys also contribute to other essential processes, such as converting a vitamin D precursor into its active form, calcitriol, and producing the hormones erythropoietin and renin.

Blood supply

The kidneys receive their blood supply from the renal arteries, which branch off from the abdominal aorta. These arteries account for about 20% of the cardiac output. The renal artery further divides into interlobar arteries, which penetrate the kidney capsule and extend into the renal columns between the pyramids. After filtration, blood drains from the kidneys into a network of small veins, which converge into the interlobular veins. From there, the blood ultimately returns to the inferior vena cava."

Nerve supply

"The renal plexus which course along with the renal arteries to reach the kidney communicate with nervous system. The vasoconstriction in kidney input from sympathetic nervous system, thereby reducing the renal blood flow. Renal system also receives the parasympathetic supply from the renal branches of vagus nerve.

Criteria

Table 1: Various criteria for acute kidney disease or injury

	RIFLE[7]	**AKIN**[8]	**KDIGO**[9]
"Diagnostic criteria*			
		Increase in serum creatinine of ≥0.3 mg/dL or ≥50% within 48 hours OR Urine output of <0.5 mL/kg/hour for >6 hours	Increase in serum creatinine of ≥0.3 mg/dL within 48 hours or ≥50% within 7 days OR Urine output of <0.5 mL/kg/hour for >6 hours
Staging criteria			
Risk (RIFLE) or stage 1 (AKIN/KDIGO)	Increase in serum creatinine to 1.5 times baseline OR	Increase in serum creatinine of ≥0.3 mg/dL or to 150 to 200% baseline OR	Increase in serum creatinine of ≥0.3 mg/dL or 1.5 to 1.9 times baseline OR

	Urine output of <0.5 mL/kg/hour for 6 to 12 hours	Urine output of <0.5 mL/kg/hour for 6 to 12 hours	Urine output of <0.5 mL/kg/hour for 6 to 12 hours
Injury (RIFLE) or stage 2 (AKIN/KDIGO)	Increase in serum creatinine of to 2 times baseline OR Urine output of <0.5 mL/kg/hour for 12 to 24 hours	Increase in serum creatinine to 200 to 300% baseline OR Urine output of <0.5 mL/kg/hour for 12 to 24 hours	Increase in serum creatinine to 2.0 to 2.9 times baseline OR Urine output of <0.5 mL/kg/hour for 12 to 24 hours
Failure (RIFLE) or stage 3 (AKIN/KDIGO)	Increase in serum creatinine to 3 times baseline OR Increase in serum creatinine by >0.5 mg/dL to >4.0 mg/dL OR	Increase in serum creatinine to >300% baseline OR Increase in serum creatinine by >0.5 mg/dL to ≥4.0 mg/dL OR	Increase in serum creatinine to ≥3.0 times baseline OR Increase in serum creatinine of ≥0.3 mg/dL to ≥4.0 mg/dL¶ OR

	Urine output of <0.3 mL/kg/hour for >24 hours or anuria for >12 hours OR Initiation of renal replacement therapy	Urine output of <0.3 mL/kg/hour for >24 hours or anuria for >12 hours OR Initiation of renal replacement therapy	Urine output of <0.3 mL/kg/hour for ≥24 hours or anuria for ≥12 hours OR Initiation of renal replacement therapy
Loss (RIFLE)	Need for renal replacement therapy for >4 weeks		
End stage (RIFLE)	Need for renal replacement therapy for >3 months"		

Kidney damage:

It includes the pathologic abnormalities in the native or transplanted kidney." The damage can be identified with presence of one or more following "clinical markers

- Albuminuria
- Decreased GFR
- Urinary sediment abnormalities
- Kidney transplantation
- Imaging abnormalities
- Pathologic abnormalities

Albuminuria is the most commonly assessed marker of kidney damage in clinical practice. It reflects increased glomerular permeability to macromolecules, indicating the presence of primary kidney disease or involvement of systemic conditions. These conditions often involve widespread endothelial dysfunction, such as hypertension, diabetes, hypercholesterolemia, obesity, smoking, and other related disorders.

Table 2: Categories for albuminuria and proteinuria

	Normal to mildly increased	**Moderately increased**	**Severely increased**
AER (mg/day)	<30	30 to 300	>300
PER (mg/day)	<150	150 to 500	>500
ACR (mg/g)	<30	30 to 300	>300

PCR (mg/g)	<150	150 to 500	>500
Protein dipstick	Negative to trace	Trace to 1+	>1+

Urinary sediment anomalies, such as the "presence of red or white blood cell casts, can indicate glomerular injury or tubular inflammation. Imaging abnormalities, like polycystic kidneys, hydronephrosis, and small, echogenic kidneys, can also aid in diagnosing kidney damage. A kidney biopsy provides direct evidence of glomerular, vascular, or tubule-interstitial disease. Additionally, patients with a history of kidney transplantation are considered to have kidney damage, regardless of the presence of known anomalies on biopsy or markers of kidney damage."

Clinical presentation

Patients with chronic kidney disease (CKD) may exhibit symptoms directly related to reduced kidney function, such as edema or hypertension. "However, many patients do not show any clinical signs, and kidney failure is often identified incidentally. This occurs when elevated serum creatinine, a decreased estimated glomerular filtration rate (eGFR), or abnormal urine analysis results are found during routine evaluations or investigations for unrelated conditions. Additionally, radiographic findings, such as multiple bilateral renal cysts with enlarged kidneys suggestive of polycystic kidney disease, may be detected during imaging performed for other reasons."

Staging of chronic kidney disease

The aim of CKD staging "is to direct management, including risk stratification for CKD progression and complications. Risk stratification is used to direct effective interventions, tracking severity, and patient education.[10,11] When a patient is diagnosed with CKD using the criteria mentioned above, the CKD is staged according to"[12]

- Cause of disease
- Six categories of GFR (G stage)
- Three categories of albuminuria (A stages)

Table 3: CKD classification based upon GFR and albuminuria

"GFR stages	**GFR (mL/min/1.73 m^2)**	**Terms**
G1	≥90	Normal or high
G2	60 to 89	Mildly decreased
G3a	45 to 59	Mildly to moderately decreased
G3b	30 to 44	Moderately to severely decreased
G4	15 to 29	Severely decreased
G5	<15	Kidney failure (add D if treated by dialysis)
Albuminuria stages	**AER (mg/day)**	**Terms**

A1	<30	Normal to mildly increased (may be subdivided for risk prediction)
A2	30 to 300	Moderately increased
A3	>300	Severely increased (may be subdivided into nephrotic and nonnephrotic for differential diagnosis, management, and risk prediction)

Hemodialysis

The Greek words dia, which means "through," and lysis, which means "loosening or splitting," are the origin of the word "dialysis." It is a type of renal replacement therapy where the artificial equipment that removes extra water, solutes, and toxins supplements the kidneys function of filtering the blood. Acute kidney injury (AKI), a sudden loss of kidney function, or chronic kidney disease, a slow, steady loss of function, both require dialysis to maintain homeostasis (a stable internal environment) (CKD). It serves as a stop gap solution for acute renal damage, to buy time until a kidney transplant can be performed, or to maintain individuals who are ineligible for one."[13]

“The prevalence of renal replacement therapy (RRT) is determined by the incidence and prevalence of diseases that cause end-stage renal disease (ESRD), early detection of chronic kidney disease (CKD), and interventions to halt progression to ESRD (ESRD). The systematic identification of patients with a falling estimated glomerular filtration rate (eGFR), severe proteinuria, and a history of acute renal injury episodes enhances the start of planned RRT, reducing the growing trend in emergency RRT occurrence.”

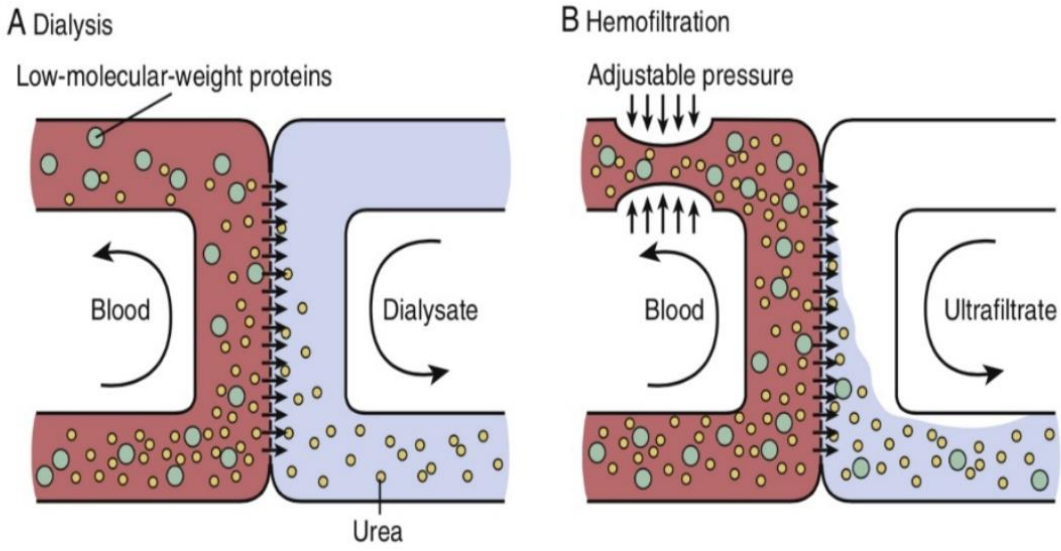
Principle

Haemodialysis operates on the principle of solute diffusion across a semipermeable membrane. The rate of diffusion is determined by factors such as the concentration gradient across the membrane, the membrane's surface area, and its mass transfer coefficient. Smaller molecules diffuse more easily compared to larger ones. In hemodialysis, solute clearance occurs through two primary mechanisms: diffusive clearance, driven by concentration gradients, and convective clearance, which involves solutes moving with water flow during ultrafiltration. The efficiency of solute clearance serves as a key measure of the performance of the dialysis process.

“Dialysis involves the removal of solutes across a semipermeable membrane down the concentration gradient by two mechanisms:

1) Diffusive clearance due to random molecular motion. Small molecules have a higher rate of diffusive transport through the membrane

2) Convective clearance occurs when the osmotic force of the water pushes solutes along with it through the membrane (solvent drag)”



Components of hemodialysis[13,14]

- The dialyzer
- The composition and delivery of dialysate
- The blood delivery system

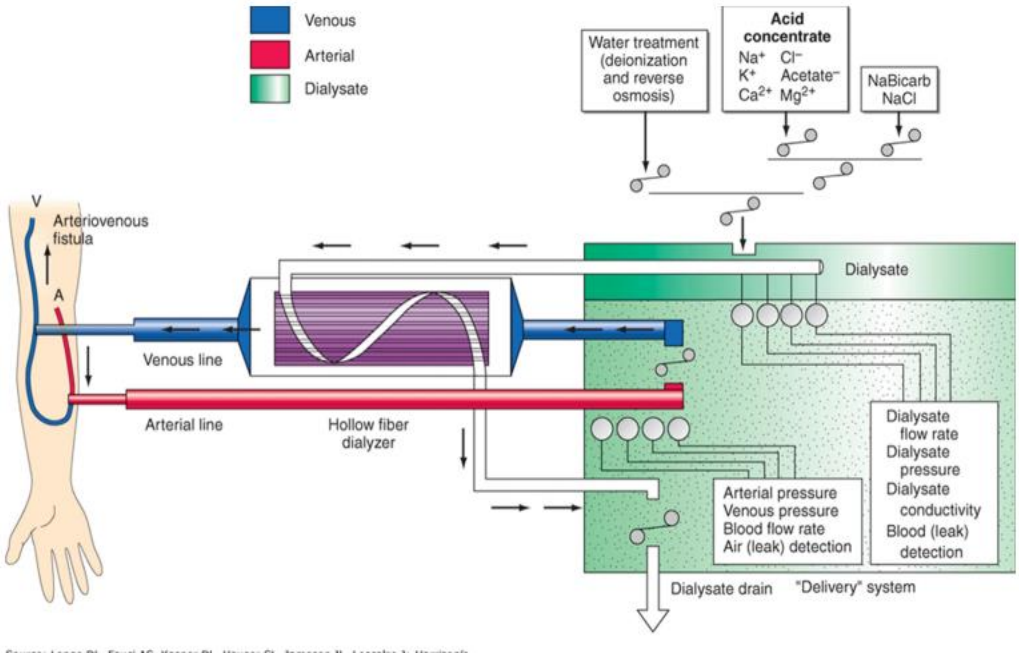


Figure 3: Components of hemodialysis

The dialyzer: “It's a plastic container. A hollow fibre dialyzer is a type of dialysis machine that is extensively used. It is made up of bundles of capillary tubes, and blood flows on the exterior of the fibre bundle.”

The dialysis: “The potassium concentrates ranges from 0.4mmol/l to 2.5meq/lit on average. In hypocalcemia patients with secondary hyperparathyroidism, higher calcium concentrations are utilised. The sodium content is between 136 and 140 mmol/l.”

Blood delivery system: “It is made up of an extracorporeal circuit and a dialysis access. The blood flow rate ranges between 250 and 500ml/min. The most common kind of dialysis access is a native fistula formed by the anastomosis of an artery to a vein (e.g.,

the bresciacimino fistula) in which the cephalic vein is anastomosed end to end to the radial artery."

"Dialysate is composed of highly purified water combined with essential electrolytes and compounds, including sodium, potassium, magnesium, calcium, bicarbonate, chloride, and dextrose. It is intentionally designed to lack low-molecular-weight waste compounds commonly present in uraemic blood. During hemodialysis, when uraemic blood and dialysate are separated by a semipermeable membrane, waste solutes predominantly diffuse from the blood into the dialysate due to the concentration gradient. The flux of these waste solutes from blood to dialysate exceeds the back-flux from dialysate to blood. Over time, the concentrations of permeable waste solutes in the blood and dialysate equilibrate, at which point no further net removal of waste occurs.Broadly three types of dialysis

1) Hemodialysis (HD)
2) Peritoneal dialysis (PD)
3) Continuous renal replacement therapy (CRRT)

Indications

The haemodialysis initiation is needed in the patients with acute illness associated with

1) Uremic encephalopathy
2) Pericarditis
3) Acute kidney injury

4) Life threatening Hyperkalemia
5) Peripheral neuropathy
6) Refractory acidosis
7) Hypervolemia causing end-organ complications
8) Toxic substance ingestion
9) Failure to thrive and malnutrition

These diseases produce cytokine dysregulation and poor clearance, resulting in vasodilation, cardiac depression, and immunosuppression, resulting in end-organ damage, hemodynamic instability, or a delay in renal recovery. In high-cytokine situations such as sepsis, RRT improves cytokine elimination. Catheter problems, electrolyte abnormalities, and intradialytic hypotension all have the potential to cause injury."[13] The National Kidney Foundation's Kidney Disease Outcomes Quality "Initiative (KDOQI) has provided the guidelines (2015 update) for haemodialysis adequacy.[15]

Contraindications

Absolute contraindication to hemodialysis is the inability to secure the vascular access and relative contraindication may included

1) Difficult vascular access
2) Coagulopathy
3) Needle phobia

4) Cardiac failure

Modern approaches are used to enhance the development and preservation of vascular access in individuals with severe vascular disease. Local anaesthetics and nurse support can help overcome relative contraindications like needle aversion. Severe coagulopathy affects anticoagulation management in the extracorporeal circuit."

Preparation

Preparation procedures and related consequences contribute for 25% of chronic uremia hospital admissions. The distal AV fistula is the gold standard.[16] "After a patient's superficial veins have been depleted, the choices include synthetic grafts and tunnelled central venous catheters. The current suggested method is to permanently catheterize only chronic hemodialysis patients who have exhausted their peripheral vascular bed."

Catheters, arteriovenous fistulas (AVFs), and arteriovenous grafts are all options for access (AVGs).[17–20] To get access to circulation, a 15 gauge needle is inserted. In most patients, the "fistula first" strategy stimulates the formation of an arteriovenous fistula to offer stable access to circulation. However, the majority of individuals have an arteriovenous graft.

Vascular access

The radio-cephalic AV fistula is the access of choice otherwise known as Brescia Cimino Access. "The permanent catheter increases the longevity of the HD.

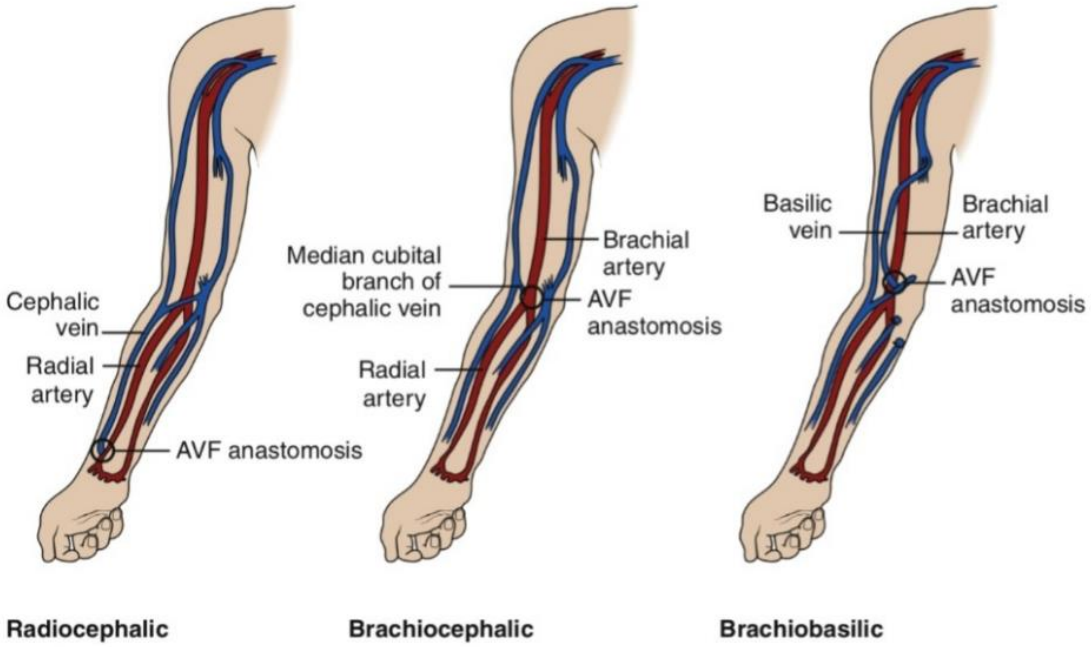


Figure 4: Vascular access

Types of vascular access

1) Arterio venous fistula
2) Arteriovenous graft

AV fistula is created by connecting the vein and artery by two approaches as;

a) End to side anastomosis

b) Side to side approach

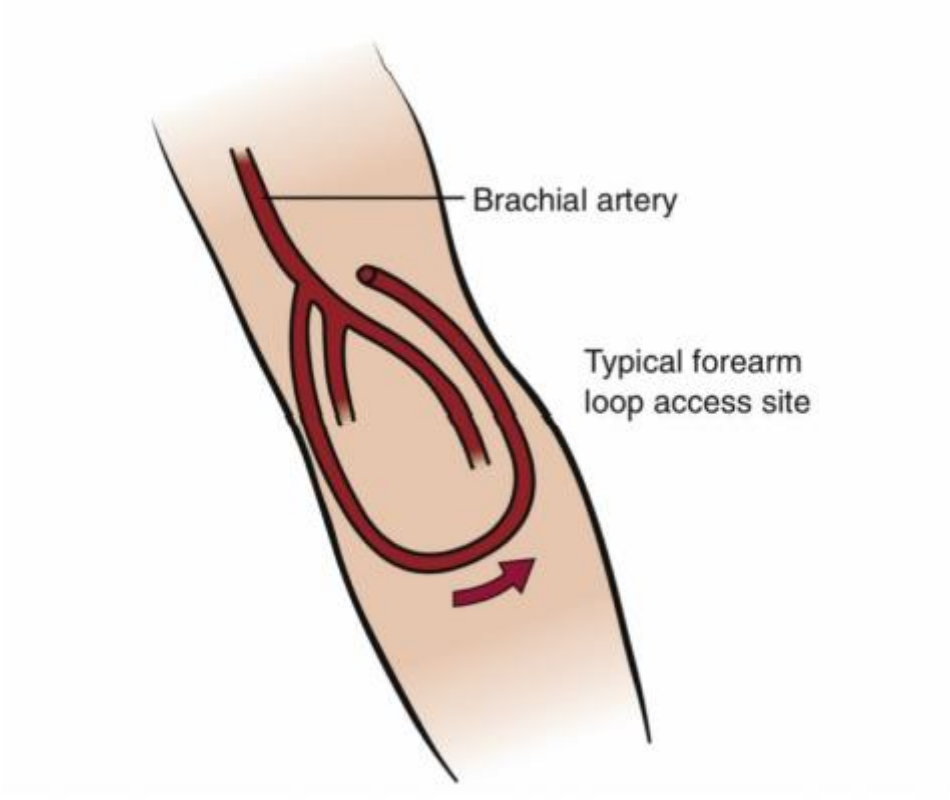


Figure 5: AV fistula

Arteriovenous grafts

Catheters, arteriovenous fistulas (AVFs), and arteriovenous grafts are all options for access (AVGs). To get access to circulation, a 15 gauge needle is inserted. In most patients, the "fistula first" strategy stimulates the formation of an arteriovenous fistula to offer stable access to circulation. However, the majority of individuals have an arteriovenous graft.[17–20]

Complications associated with haemodialysis

Cardiovascular problems are at the top of the list of complications associated with current hemodialysis procedures. The risk of symptomatic intradialytic hypotension ranges between 20% and 50% among cardiovascular problems, and it remains a significant issue. Another source of worry is the rate of arrhythmias related with hemodialysis, which is estimated to be between 5% and 75%. Atrial fibrillation is the second most frequent kind of arrhythmia, accounting for 27% of all cases. Sudden cardiac death is responsible for 62 percent of cardiac-related fatalities and is generally caused by arrhythmias. The first year of hemodialysis is critical in terms of sudden cardiac fatalities, which were assessed in 93 of 1000 patients in the first year of hemodialysis.[21,22]

The most common complications associated with hemodialysis are

1) Muscle cramps
2) Intradialytic hypotension
3) Dialysis disequilibrium syndrome
4)Dialyzer reactions
5)Haemolysis
6)Air embolism
7)Others

Complications associated with haemodialysis instrument

a)Membrane related complications

b)Haemodialysis device related complications

c)Vascular access related complications

d)Water system related complications

1) Intradialytic hypotension: Myocardial stunning during dialysis, characterized by regional wall motion anomalies, is associated with poor long-term outcomes, including elevated mortality." A nadir systolic blood pressure below 90 mmHg is strongly linked to this increased risk. Clinically, it often presents with symptoms such as dizziness, light-headedness, nausea, or other mild manifestations. "Management involves placing the patient in the Trendelenburg position and administering a 100 mL bolus of normal saline rapidly through the bloodline. Additionally, the ultrafiltration rate should be minimized, and the patient closely monitored until vital signs stabilize to ensure proper recovery.

2) Muscle cramps: The exact cause of cramps during dialysis remains uncertain. However, they are often exacerbated by factors such as hypotension, high ultrafiltration rates, hypovolemia, and low-sodium dialysis solutions. These conditions lead to vasoconstriction and reduced blood flow to muscles, resulting in muscular hypoperfusion and impaired muscle relaxation. Treatment, particularly when associated with hypotension, includes administration of 0.9% saline, which has proven

effective. Additionally, forced stretching of the affected muscle can provide immediate relief.[13,23]

3) Dialysis disequilibrium syndrome: This condition most commonly occurs during or shortly after a patient's initial dialysis treatments and is characterized by neurologic symptoms such as restlessness, confusion, headache, occasional muscular twitching, and, in severe cases, coma. It is caused by a significant urea concentration gradient between the cerebrospinal fluid (CSF) and blood, leading to water movement into the central nervous system (CNS) and resulting in increased intracranial pressure. Patients undergoing rapid dialysis are at higher risk for seizures and cerebral edema. To mitigate this, a target urea reduction ratio (URR) of 0.4, equating to a 40% reduction in urea levels within two hours, is recommended. The use of osmotic agents such as sodium, mannitol, high-glucose dialysate, or glycerol can help prevent the formation of the urea gradient. Additionally, adjusting the dialysate's sodium concentration to a higher level during treatment may be beneficial."[24,25]

4) Dialysis Reactions: This condition, which may present within the first 30 minutes of dialysis, includes symptoms such as dyspnea, elevated body and local temperature at the fistula site, a sense of impending doom, itching, urticaria, coryza, watery eyes, stomach cramps, and diarrhea. "These signs are often due to hypersensitivity to ethylene oxide, a chemical used to sterilize dialyzers. Treatment typically involves the administration of intravenous antihistamines, steroids, and epinephrine. To minimize the risk of such reactions, it is crucial to thoroughly rinse dialyzers before use to

remove any residual allergens. Additionally, nonspecific type B dialyzer responses, which are a result of complement activation, can lead to chest or back discomfort between 20 and 40 minutes after dialysis begins. Switching the dialyzer membrane may help prevent this response.

5) Haemolysis: Acute haemolysis during dialysis is characterised by a port-wine look in the venous blood line, a significant drop in the hematocrit, and a pink-colored plasma centrifuged blood sample."

6) Air embolism: "A deadly complication caused by foam in the dialyzer's venous blood line. Chest auscultation may reveal a churning sound. Place the patient in a left lateral recumbent posture, provide 100% oxygen through a mask, then aspirate air from the heart chambers using a percutaneously inserted needle or cardiac catheterization.

Other nonspecific problems include nausea and vomiting (10%), headache (70%), chest and back discomfort (1% to 4%), and itching. These are most likely connected to hypotension or may be an early symptom of disequilibrium syndrome. The symptoms are resolved by treating the accompanying hypotension. A single 5 to 10 mg metoclopramide predialysis dosage is adequate. Acetaminophen can assist with headaches during dialysis. Changing the dialyzer membrane might alleviate itching caused by low-grade hypersensitivity to blood circuit components. Vascular access dysfunction, most typically stenosis of arteriovenous access, is the most powerful factor of a dialysis patient's quality of life. There is decreased blood flow and an increased risk of thrombosis."[26]

Precautions for vascular access: “To prevent additional strain on the dialysis access site, patients should avoid tight clothing or jewelry, heavy lifting, and sleeping on the arm with the access. Blood pressure measurement and blood draws should not be done on this arm. It's also important to rotate the needle insertion site to prevent damage. After needle removal, mild pressure should be applied to stop any bleeding. If bleeding persists for more than 30 minutes, a healthcare provider should be consulted. Hemorrhage is common in dialysis patients due to the use of heparin, and it can be treated with protamine sulfate. Monitoring both venous and arterial pressures is crucial to detect any line separation, and securing needles properly with tape, using moisture detectors for leaks, and employing closed connection devices at tube junctions can help reduce complications. Regular assessments for infection symptoms, such as redness, warmth, and pain, at the access site are necessary. Additionally, loss of normal bruit should be checked for to rule out access site clotting and prevent potential limb ischemia.[13]

Cognitive impairment[27]

Cognitive impairment is frequently observed in individuals with chronic kidney disease (CKD), particularly those undergoing dialysis.[28–30] This impairment may arise from various factors, including metabolic abnormalities associated with kidney failure. However, findings from recent imaging and epidemiological studies suggest that vascular disease is likely the primary contributor. Cognitive impairment in CKD is associated with significant risks, such as depression, reduced quality of life, and increased mortality rates.[31–37] Consequently, understanding its underlying mechanisms and exploring

preventive strategies is essential for improving patient care, especially for those on dialysis."[38–40]

In this context, "two studies published in American Journal of Kidney Diseases (AJKD) provide valuable insights into cognitive function in CKD patients. The first, by Kurella Tamura et al., investigates the impact of frequent dialysis on cognitive function using data from the Frequent Hemodialysis Network (FHN) trials. [41] The second, by Yaffe et al., examines the relationship between retinopathy and cognitive function in individuals with CKD stages 3–4 from the Chronic Renal Insufficiency Cohort (CRIC). This editorial focuses on the findings from the FHN trials while incorporating insights from the CRIC study to highlight the potential role of microvascular disease in cognitive dysfunction among CKD patients, thus providing a broader context for the discussion. [42]

In the general population, vascular dementia is the second most prevalent dementia subtype after Alzheimer's dementia. It is primarily caused by cerebrovascular disease, often involving damage to the microvasculature. Cognitive impairment linked to cerebrovascular disease typically affects processing speed and executive functions—skills crucial for complex attention, task-switching, and action regulation. In contrast, Alzheimer's dementia predominantly impacts memory. [43]

In the Renal REGARDS (Reasons for Geographic and Racial Differences in Stroke) study, Kurella Tamura and colleagues identified a relationship between baseline albuminuria and the onset of cognitive impairment at higher levels of estimated glomerular filtration rate (eGFR). Conversely, in individuals with minimal albuminuria and lower eGFR levels, eGFR itself was a stronger predictor of cognitive risk. This study assessed cognitive

impairment using the 6-item screener, a brief test that emphasizes memory evaluation rather than executive functioning."

Kidney-Brain Axis[27]

The kidney-brain axis describes the physiological and pathophysiological interplay between the kidney and brain, highlighting their shared vulnerabilities to cardiovascular risk factors such as hypertension, diabetes, and smoking.[44,45] "Often referred to as the "neglected kidney-brain axis," this relationship has gained recognition for its role in neurological disease pathophysiology. Both organs are characterized by low vascular resistance systems, allowing for continuous high-volume perfusion. This autoregulation ensures stable cerebral perfusion pressure in the brain and glomerular filtration rate (GFR) in the kidney, despite blood pressure fluctuations.[46,47]

The "strain vessel hypothesis" suggests a shared mechanism for renal and cerebrovascular diseases. Juxtamedullary afferent arterioles in the kidney and cerebral perforating arteries are exposed to high pressure and must maintain steep pressure gradients, making them particularly susceptible to hypertensive injury. Clinically, this manifests as proteinuria and declining GFR in the kidney and as symptomatic stroke, silent cerebral small vessel disease, and cognitive decline in the brain.[47–49]

Inflammatory cross-talk between the kidney and brain is another proposed mechanism linking chronic kidney disease (CKD) to cerebrovascular and neuropsychiatric conditions. CKD and acute kidney injury (AKI) promote the release of cytokines, chemokines, and reactive oxygen species (ROS), leading to neuroinflammation. These inflammatory

molecules can disrupt the blood-brain barrier, interact with neurotrophic factors, and activate the brain's renin-angiotensin system (RAS), exacerbating oxidative stress through angiotensin II. The resulting cascade, involving immune cells, neurons, and glial cells, perpetuates inflammation and contributes to neuropsychiatric disorders."

Mechanisms of susceptibility and risk[27]

The mechanisms underlying the development of mild cognitive impairment (MCI) and dementia in chronic kidney disease (CKD) remain poorly understood, with both vascular and neurodegenerative hypotheses proposed to explain the pathogenesis. "The vascular hypothesis is supported by the high prevalence of cardiovascular risk factors, such as hypertension and diabetes mellitus, in CKD patients, alongside a significant burden of symptomatic and subclinical cerebrovascular disease. In contrast, the neurodegenerative hypothesis highlights the role of uremic toxin accumulation, which can lead to cerebral endothelial dysfunction and contribute to cognitive decline.[50–52]

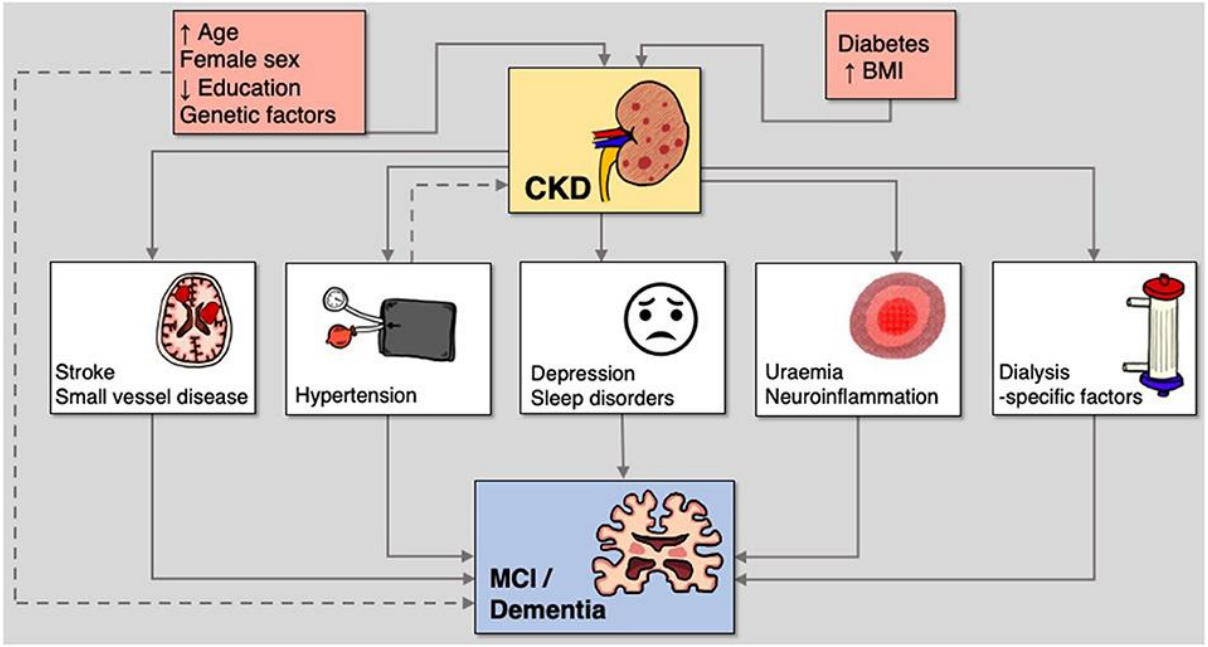


Figure 6: Mechanisms of susceptibility and risk in the relationship between CKD and cognitive disorders.[27]

However, framing these mechanisms as distinct and mutually exclusive may oversimplify a complex, multifactorial process. It is likely that CKD-related neurocognitive disorders arise from an interplay between vascular and neurodegenerative factors. This comprehensive perspective incorporates both shared cognitive risk factors found in the general population and CKD-specific mechanisms, emphasizing the need for further investigation into this multifaceted relationship.

Dialysis-specific factors

Dialysis-specific factors play a significant role in contributing to both acute and chronic brain injury in patients undergoing hemodialysis. Even in clinically stable individuals, intermittent hemodialysis can lead to cerebral edema. This occurs through mechanisms such as increased brain water content and reverse osmotic shifts driven by urea or newly formed brain osmoles. Additionally, global cerebral blood flow has been observed to

acutely decline by approximately 10% during hemodialysis sessions. These changes heighten the risk of secondary brain injury, particularly in the context of acute brain injury, a phenomenon now termed dialysis-associated neurovascular injury (DANI).”[52–57]

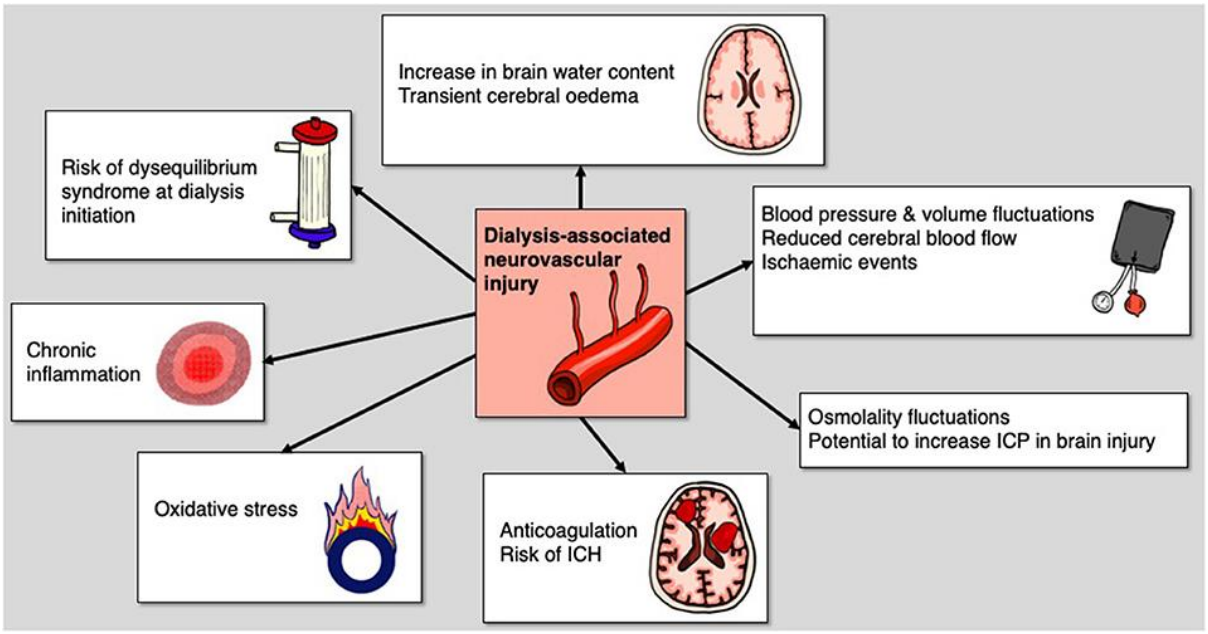


Figure 7: The potential impact of dialysis-associated neurovascular injury on cognition.[27]

In the chronic setting, hemodialysis has been associated with a significant impact on cerebral health. “Research indicates that a 10 mmHg drop in mean arterial pressure during a dialysis session increases the risk of ischemic events by 3%. Notably, nearly 25% of hemodialysis sessions are accompanied by cerebral ischemic events, which have been linked to a decline in executive cognitive function over a 12-month period.[58]

A prospective cohort study involving approximately 100 chronic hemodialysis patients revealed a significant decline in cerebral arterial mean flow velocity (MFV) during dialysis sessions.[59] This intradialytic decline in MFV was strongly associated with both immediate cognitive function impairment and the progression of white matter burden and

cerebrovascular disease at a 12-month follow-up. Hemodialysis appears to induce transient "cerebral stunning," similar to myocardial stunning, which may serve as a primary mechanism of cerebral injury and accelerated cognitive decline in dialysis-dependent patients.

Beta-Amyloid Pathology in CKD and Cognitive Decline[27]

The connection between beta-amyloid (Aβ) pathology and cognitive decline in chronic kidney disease (CKD) remains incompletely understood. Elevated serum Aβ levels in CKD patients may result from reduced renal clearance of Aβ proteins from peripheral circulation. Additionally, cystatin-C, a marker for estimating glomerular filtration rate (GFR), has been found to co localize with beta-amyloid in the brain, suggesting a possible link between renal function and amyloid deposition.[60,61]

Interestingly, emerging evidence from animal models and small human studies suggests that dialysis could play a role in reducing amyloid plaque burden in the brain by enhancing peripheral clearance of Aβ. In one study involving 30 newly diagnosed CKD patients and APP/PS1 transgenic mice, plasma Aβ40 and Aβ42 levels were significantly reduced after peritoneal dialysis (PD). In the animal model, PD also decreased brain interstitial Aβ levels and reduced plaque deposition, with only 10% of Aβ removal attributed directly to the dialysis solution. The remainder appeared to involve efflux transport across the blood-brain barrier (BBB) and activation of endogenous clearance pathways. Treated mice demonstrated lower levels of hyperphosphorylated tau and reduced neuroinflammation, which correlated with slower neurodegeneration and improved cognitive function, as

evidenced by better performance on behavioral tests like the Y-maze and open-field assessments.[62]

In maintenance hemodialysis (HD) patients, brain Aβ deposition has also been observed to be lower. During a single HD session, clearance rates for Aβ42 and Aβ40 were reported at 22% and 35%, respectively. This clearance likely creates a peripheral Aβ sink, stimulating Aβ efflux from the brain and suggesting a potential anti-amyloid therapeutic effect. These findings propose that dialysis, beyond its renal benefits, may hold promise as a strategy to mitigate amyloid-related neurodegeneration in CKD patients."[63,64]

Various articles;

In a study conducted by Kurella M et al., (2006) to "assess the correlation and outcome of dementia among dialysis patients. In a cohort study, 4% of patients had a recorded dementia diagnosis. Cross-sectional analyses identified age, black race, low educational attainment, cerebrovascular disease, diabetes, and modifiable uraemia-related factors such as malnutrition and anaemia as independent risk factors for dementia. After adjusting for confounding variables, dementia was linked to a higher risk of death (RR 1.48, 95% CI 1.32–1.66) and dialysis withdrawal (RR 2.01, 95% CI 1.57–2.57). These findings underscore the association between dementia and adverse outcomes in ESRD patients, highlighting the need for routine cognitive impairment screening in elderly dialysis patients to identify those at higher risk."[65]

In a study conducted by Post JB et al., (2010) to assess the "cognitive profile of CKD and hemodialysis patients. All study participants scored ≥28 on the Mini-Mental State Examination (MMSE), indicating normal global cognitive function. However, executive function deficits were prevalent in at least 25% of subjects in both groups, and memory impairment was observed in 13% of hemodialysis (HD) patients and 15% of chronic kidney disease (CKD) patients. Mild cognitive impairment (MCI) was found in 76% of the study population, with a significantly higher prevalence in HD patients compared to CKD patients (89% vs. 63%). Notably, more than 70% of MCI cases across both groups were classified as non-amnestic MCI. Despite normal global cognitive function as assessed by MMSE, predialysis CKD and HD patients exhibit a high prevalence of MCI, with HD patients showing a greater burden of impairment. The cognitive deficits predominantly

result in non-amnestic MCI, emphasizing the need for targeted strategies to address cognitive health in these populations."[5]

In a study conducted by West MJ et al., (2015) to "assess cognitive dysfunction in hemodialysis patients. Significant declines were observed in cognitive domains, particularly in long-term memory measures, during dialysis sessions ($p<0.05$). A trend toward significance was noted in working memory and mean arterial blood pressure. Changes in hemodynamic variables, including mean arterial blood pressure, hematocrit, and relative blood volume, were correlated with changes in cognitive function, while quality of life and depression questionnaires also showed associations with cognitive performance. These findings indicate that cognitive impairment in hemodialysis patients likely arises from a combination of cerebrovascular issues related to chronic kidney disease (CKD) and the dialysis process itself. Further research is needed to explore the impact on additional cognitive domains and identify the primary mechanisms underlying these impairments."[66]

In a study conducted by Wolfgram DF et al., (2015) to "assess the risk of dementia in peritoneal dialysis patients compared to with hemodialysis patients. An analysis of 121,623 patients, including 8,663 who initiated dialysis on peritoneal dialysis (PD), found that PD was associated with a lower cumulative incidence of dementia compared to hemodialysis (HD). At 1, 2, and 3 years, the incidence of dementia was 1.0%, 2.5%, and 3.9% for PD patients versus 2.7%, 5.3%, and 7.3% for HD patients. The risk of dementia was significantly lower for patients on PD, with a hazard ratio (HR) of 0.46 [0.41–0.53] in an unadjusted model and 0.74 [0.64–0.86] in a matched model. These findings suggest

a potential association between dialysis modality and cognitive outcomes, highlighting the need for further investigation into underlying mechanisms and the impact of dialysis modality on cognitive function."[67]

In a study conducted by O'Lone E et al., (2016) to "assess the cognition in patients with end stage renal disease on hemodialysis. A review of 42 studies involving 3,522 participants, assessed using the Newcastle-Ottawa Scale, revealed that individuals on hemodialysis exhibited worse cognitive performance compared to the general population, particularly in attention (n=22; SMD −0.93; 95% CI −1.18 to −0.68). However, hemodialysis patients outperformed nondialyzed chronic kidney failure (CKF) patients in attention (n=6; SMD 0.70; 95% CI 0.45 to 0.96) and memory (n=6; SMD 0.36; 95% CI 0.08 to 0.63), though their memory was poorer compared to the general population (n=16; SMD −0.41; 95% CI −0.91 to 0.09) and patients with non-dialysis-dependent chronic kidney disease (NDD-CKD) (n=5; SMD −0.40; 95% CI −0.60 to −0.21). Data were insufficient to compare cognitive differences between hemodialysis, peritoneal dialysis, and NDD-CKD patients. Hemodialysis is associated with significant cognitive deficits, particularly in orientation, attention, and executive function, warranting further research to address domain-specific impairments and their implications for patient education and chronic disease management."[68]

In a study conducted by Jayanti A et al., (2016) to "assess the burden of cognitive impairment in patients with end stage renal disease and impact of dialysis. In a study cohort of 204 patients, 90 selected fully assisted hemodialysis, while 114 opted for self-care dialysis. The assisted group had higher median scores on the Modified Mini Mental State

Examination and TMT parts A and B, although metamemory scores did not differ significantly between groups. However, metaconcentration scores were significantly lower in the assisted dialysis group. Higher metaconcentration scores were strongly associated with the choice of self-care dialysis in both univariate and hierarchical regression analyses. Adjusted and unadjusted models revealed a significant correlation between perceived concentration and TMT part B scores ($P < 0.01$), with a 1.6-minute increase in TMT part B score linked to a 1-unit decrease in metaconcentration score. This decrease corresponded to a 20% lower likelihood of selecting self-care dialysis. Self-perceived cognitive ability, particularly metaconcentration, is a critical predictor of self-care dialysis choice and strongly correlates with poorer performance on the TMT part B."[69]

In a study conducted by McAdams DM et al., (2018) to assess the "dementia, alzheimer's disease and mortality after hemodialysis initiation. In patients on hemodialysis, the 1- and 5-year risks of diagnosed dementia were 4.6% and 16% for women and 3.7% and 13% for men, respectively, while the corresponding risks for Alzheimer's disease were 0.6% and 2.6% for women and 0.4% and 2.0% for men. Key independent risk factors for both dementia and Alzheimer's disease included age ≥86 years (HR 2.11), black race (HR 1.70–1.78), female sex (HR 1.10–1.12), and institutionalization (HR 1.10–1.36). A diagnosis of dementia was associated with a 2.14-fold higher risk of mortality, and Alzheimer's disease with a 2.01-fold higher risk. These findings highlight the significant burden of cognitive impairment and associated mortality in older hemodialysis patients.[2]

In a systematic review conducted by Oh H et al., (2019) to assess the correlation of cognitive impairment in patients with CKD on dialysis. A review of 39 studies identified

several factors significantly associated with cognitive impairment in patients with chronic kidney failure (CKF) undergoing hemodialysis. These included advanced age, female gender, history of stroke, greater challenges with daily activities, lower hemoglobin levels, higher levels of pain, sleep disturbances, and depression. Nurses should recognize that these factors can substantially increase the risk of cognitive impairment in this patient population, allowing for more targeted care and interventions."[70]

In a meta-analysis study conducted by Tian X et al., (2019) to "assess the cognitive function and risk of dementia in CKD patients under dialysis. A meta-analysis of 15 cohort or cross-sectional studies compared cognitive functions, including executive function, memory, orientation, and attention, between patients on peritoneal dialysis (PD) and hemodialysis (HD) using neuropsychological tests. Qualitative analysis indicated a trend favoring PD over HD for better cognitive performance. Quantitative analysis showed that PD patients performed better on tests such as the Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), and Stroop interference test, and had a lower risk of dementia compared to HD patients. While the findings suggest that PD is associated with better cognitive function and reduced dementia risk, further large-scale, well-designed prospective cohort studies are needed to confirm these conclusions."[71]

In a study conducted by Joseph SJ et al., (2019) to "assess the cognitive impairment and its correlation with CKD undergoing dialysis. The mean age of patients in the study was 50.32 (±12.4) years, with a mean dialysis duration of 18.8 (±15.11) months. Depression was prevalent in 42% of patients, and cognitive impairment (CI) was observed in 44%. Significant associations were found between education level and the recall ($\chi 2$=31.7,

df=12, p=.002) and orientation ($\chi 2$=29.78, df=8, p=.000) domains of cognition, as well as between socio-economic status and global cognition scores ($\chi 2$=81.13, df=48, p=.002). Longer dialysis duration was negatively correlated with cognition, and depression was significantly linked to various cognitive domains. These findings highlight the high prevalence of CI in hemodialysis patients and its associations with factors like education, socio-economic status, dialysis duration, and depression. Early recognition of CI is crucial for tailoring precise treatment strategies."[72]

In a study conducted by Xu H et al., (2021) to "assess the kidney function and risk of dementia in older patients. Over a median follow-up of five years, 18,983 dementia cases (5.8% of participants) were identified, with incidence rates increasing as estimated glomerular filtration rate (eGFR) declined—from 6.56 cases per 1,000 person-years in individuals with eGFR of 90–104 mL/min to 30.28 cases per 1,000 person-years in those with eGFR <30 mL/min. After adjusting for multiple variables, lower eGFR was significantly linked to higher dementia risk (hazard ratio [HR] 1.71 for eGFR 30–59 mL/min; HR 2.62 for eGFR <30 mL/min) compared to eGFR of 90–104 mL/min. A rapid eGFR decline (>2 mL/min/1.73 m² per year) further increased dementia risk, with the association being stronger for vascular dementia than for Alzheimer's dementia. Notably, up to 10% of dementia cases could be attributed to eGFR <60 mL/min/1.73 m², a higher proportion than that attributed to cardiovascular disease or diabetes, underscoring the significant impact of kidney function on dementia development."[73]

In a study conducted by Karakizlis H et al., (2022) to "assess the cognitive impairment and related risk factors in hemodialysis. Among 479 eligible patients, 408 completed

baseline cognitive tests, with only 25% (n = 102) showing no cognitive impairment. Mild, moderate, and severe impairments were observed in 14% (n = 57), 36.5% (n = 149), and 24.5% (n = 100) of patients, respectively. Cognitive impairment affected all domains, with immediate memory recall being the most impaired and naming ability the least affected. Depression and education level were significantly associated with cognitive performance. No significant changes in cognitive domains were observed after a one-year follow-up. This study highlights the high prevalence of cognitive impairment in hemodialysis patients and underscores the importance of early identification and treatment of depression to potentially improve cognitive outcomes. Education also plays a role in influencing cognitive test results."[74]

In a systematic review by Cao T et al., (2023) to "assess the risk factors and prevalence of cognitive impairment in maintenance hemodialysis. A meta-analysis of 37 studies involving 129,849 cases revealed a cognitive impairment prevalence of 49.1% among maintenance hemodialysis patients. Significant risk factors included older age, female sex, fewer years of education, hypertension, diabetes, cerebrovascular accidents, multiple comorbidities, systolic blood pressure variability, arterial stiffness, and low levels of hemoglobin and albumin. These findings emphasize the need for greater attention to modifiable factors such as cardiovascular disease risks and dialysis-related variables to address cognitive impairment in this population."[75]

AIMS & OBJECTIVES

To determine presence of cognitive deficits in patients with chronic kidney disease undergoing haemodialysis.

MATERIAL & METHOD

Study Type: Cross-sectional study.

Study Place: BLDE(DU), Shri B.M.Patil medical college hospital and research centre, Vijayapura.

Sample Size: 64 patients

Study Duration: 18 months (May 2023 to December 2024).

Source of data:

"Data is collected from the patients who are attending Medicine OPD and admitted with a history of clinical findings and investigation findings suggestive of chronic kidney disease and undergoing haemodialysis where patients are screening for cognitive impairment using MONTREAL COGNITIVE ASSESSMENT (MOCA) in BLDE DEEMED TO BE UNIVERSITY Shri B M Patil Medical College, Hospital and Research Centre, Vijayapura 586103.

Inclusion criteria:

- Patients who underwent maintenance haemodialysis and older than 18 years.

Exclusion criteria:

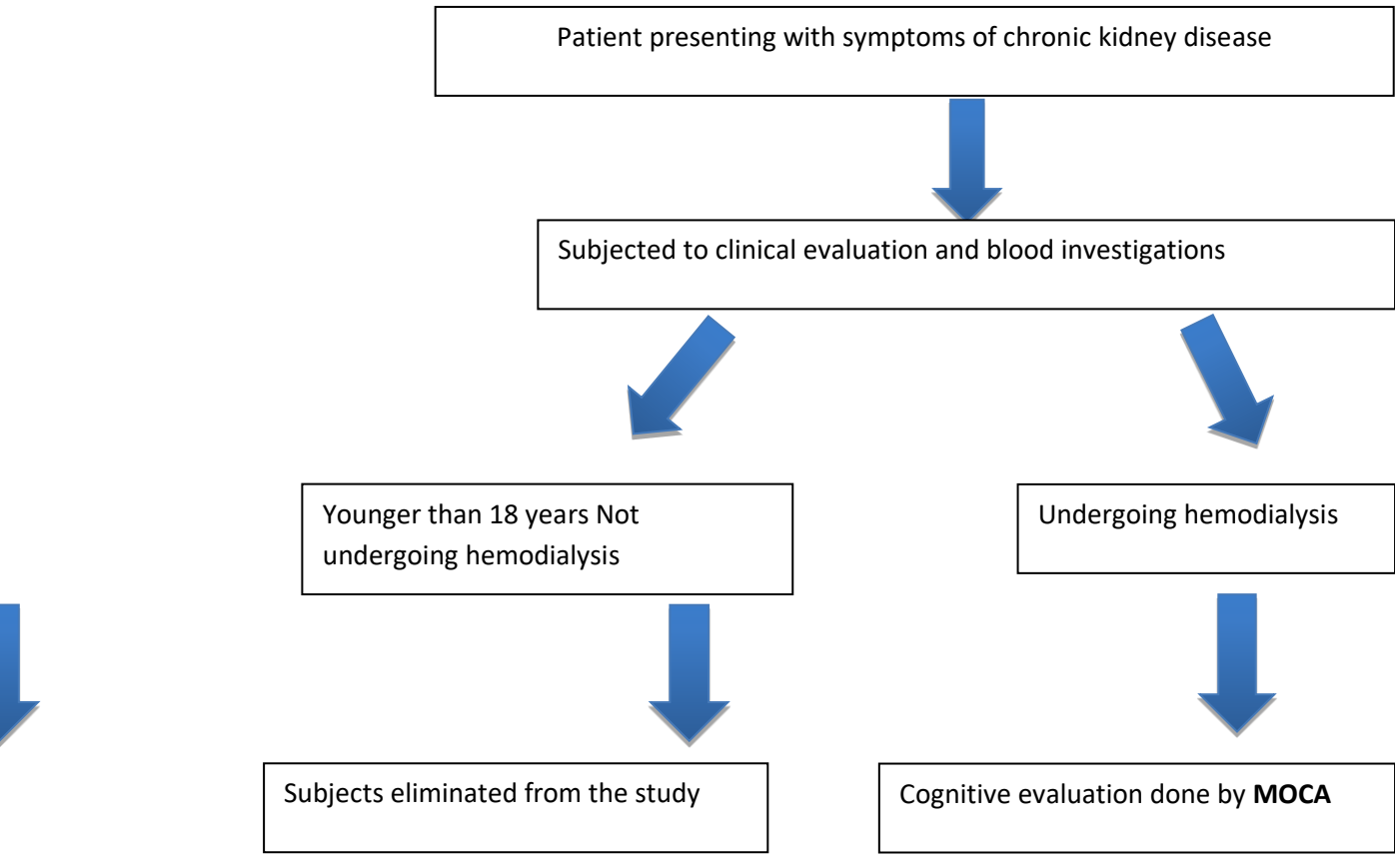
- Patients with a history of dementia.
- Patients with a history of stroke .
- Patients with a history of neurodegenerative disorders are excluded from study.

Method of collection of data:

The data was collected according to proforma in terms of detailed history, clinical examination and necessary investigations of the patient who fulfil the inclusion criteria and exclusion criteria are taken up for study after obtaining consent.

Demographic data, history, and systemic examination were recorded

Patients are assessed clinically using MONTREAL COGNITIVE ASSESSMENT (MOCA)

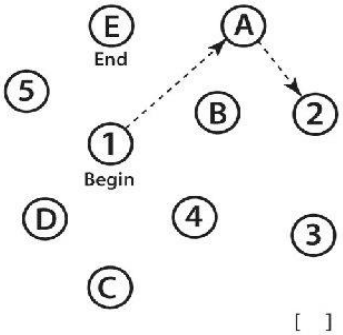


MONTREAL COGNITIVE ASSESSMENT (MOCA)

Version 7.1 Original Version

NAME :
Education : Date of birth :
Sex : DATE :

VISUOSPATIAL / EXECUTIVE



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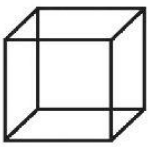


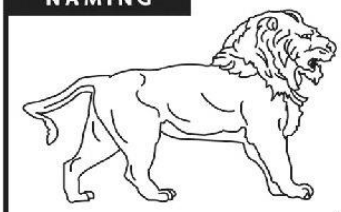
[ ] [ ]

Draw CLOCK (Ten past eleven) (3 points)

[ ] Contour [ ] Numbers [ ] Hands

POINTS ___/5

NAMING



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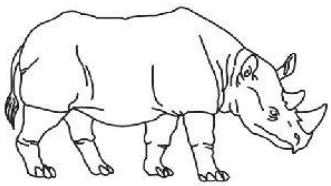

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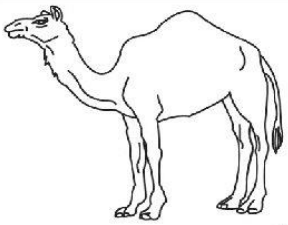

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MEMORY

Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION

Read list of digits (1 digit/ sec.).

Subject has to repeat them in the forward order [ ] 2 1 8 5 4

Subject has to repeat them in the backward order [ ] 7 4 2

___/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

___/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**

___/3

LANGUAGE

Repeat : I only know that John is the one to help today. [ ]

The cat always hid under the couch when dogs were in the room. [ ]

___/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words)

___/1

ABSTRACTION

Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler

___/2

DELAYED RECALL

	Has to recall words WITH NO CUE	FACE [ ]	VELVET [ ]	CHURCH [ ]	DAISY [ ]	RED [ ]	Points for UNCUED recall only
Optional	Category cue						
	Multiple choice cue						

___/5

ORIENTATION

[ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

___/6

www.mocatest.org

Normal ≥ 26 / 30

TOTAL ___/30

Add 1 point if ≤ 12 yr edu

Administered by: _____

STATISTICAL ANALYSIS

The data obtained were entered into a Microsoft Excel sheet, and statistical analysis was performed using a statistical package for the social sciences (SPSS Version 20). Results are presented as Mean (Median) ±SD, counts and percentages, and represented using tables, bar diagrams, pie chart and figures. For normally distributed continuous variables between two groups was compared using the Independent t-test. For not normally distributed variables, Mann Whitney U test was used. Categorical variables were compared using the Chi-square test. A $p<0.05$ was considered statistically significant."

RESULTS

Present study included total of 64 patients with mean age of 52.67±14.2yrs.

Table 4: Showing mean age of the patients

	N	Minimum	Maximum	Mean	SD
Age	64	18	85	52.67	14.283

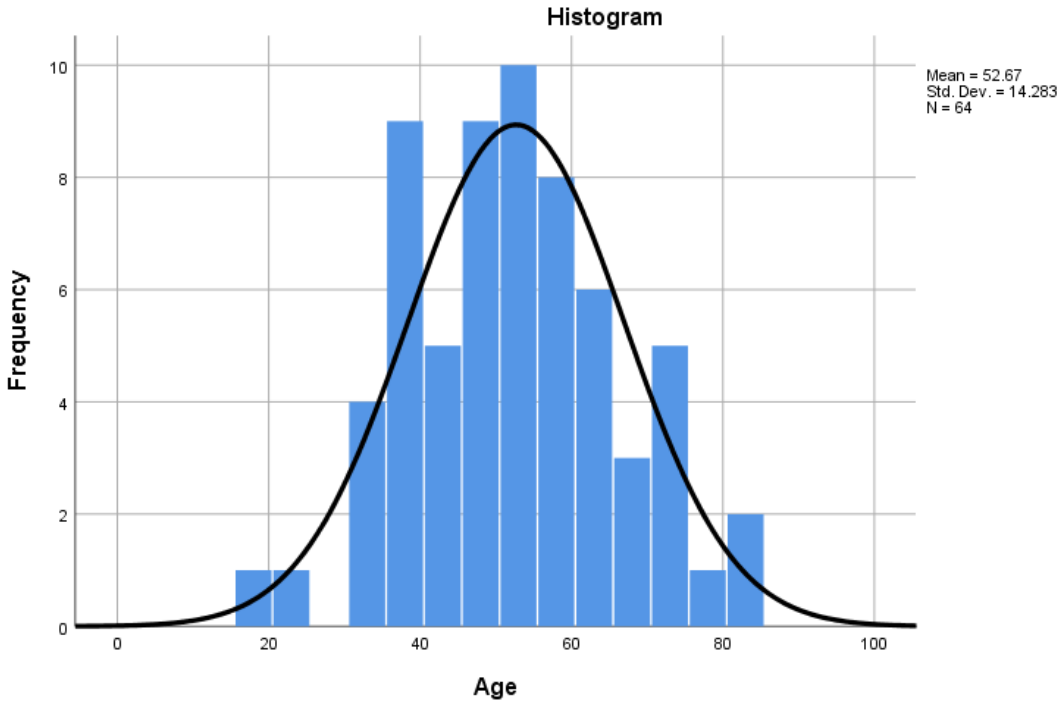

Figure 8: Showing mean age of the patients

Table 5: Gender distribution

		Count	N %
Gender	Female	24	37.5%
	Male	40	62.5%

Among them 37.5% were female and 62.5% were male with male preponderance in study.

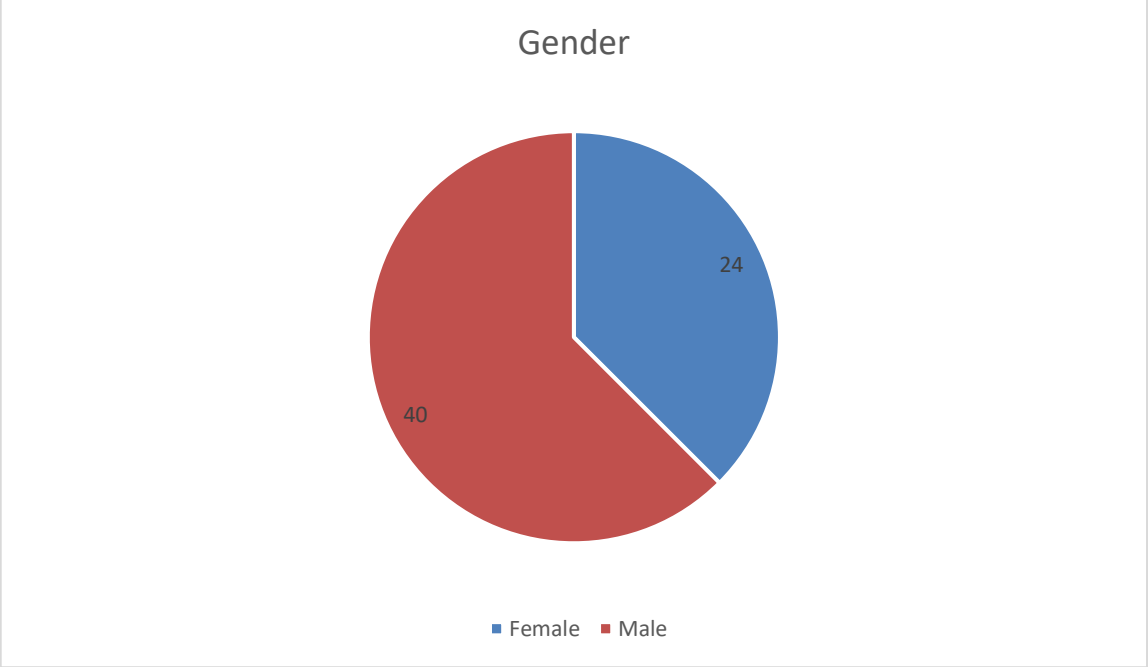

Figure 9: Gender distribution

Table 6: Showing smoking and alcohol habits among patients

		Count	N %
Smoking	No	61	95.3%
	Yes	3	4.7%
Alcohol	No	43	67.2%
	Yes	21	32.8%

Smoking is present in 4.7% and 32.8% alcoholic.

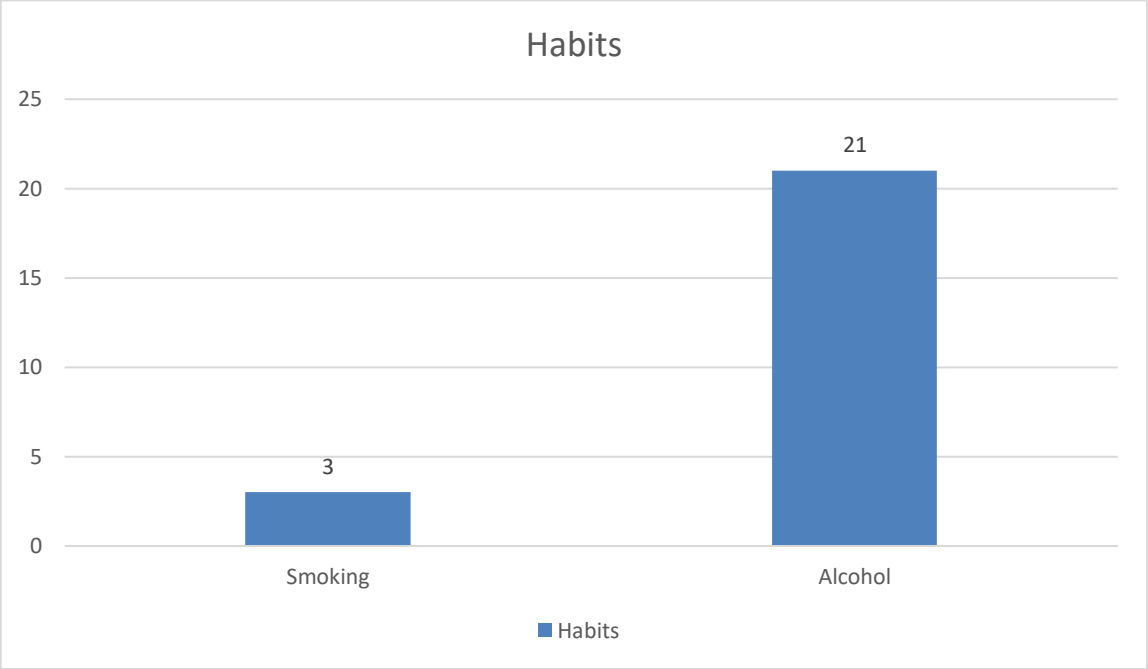

Figure 10: Showing smoking and alcohol habits among patients

Table 7: Distribution of the comorbid conditions among patients

		Count	N %
HTN	No	32	50.0%
	Yes	32	50.0%
DM	No	44	68.8%
	Yes	20	31.3%

Hypertension is present in 50% and diabetes in 31.3% of cases.

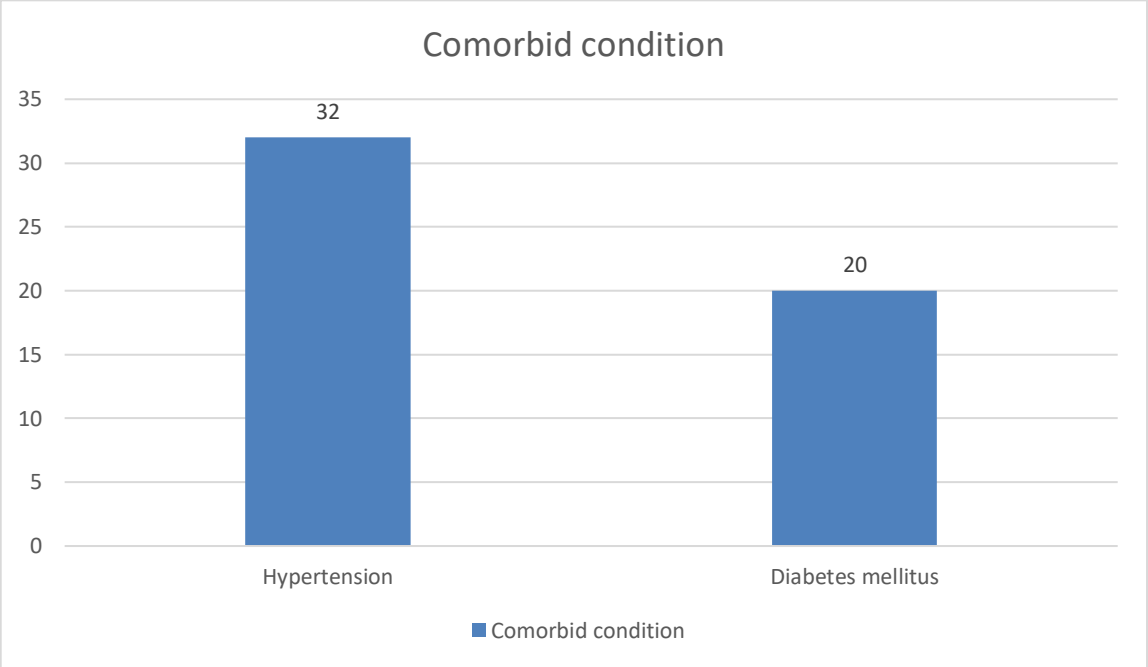

Figure 11: Distribution of the comorbid conditions among patients

Table 8: Showing mean duration of CKD

	Mean	SD
Duration of CKD (yrs)	1.6	1.9

The mean duration of CKD was 1.6yrs.

Table 9: Showing mean blood parameters between the groups

	Mean	SD
Hb	8.9	2.2
TLC	12030.6	7532.9
S. Urea (mg/dl)	117.0	57.2
Creatinine (mg/dl)	8.6	7.8

Table showing the mean blood parameters among the patients.

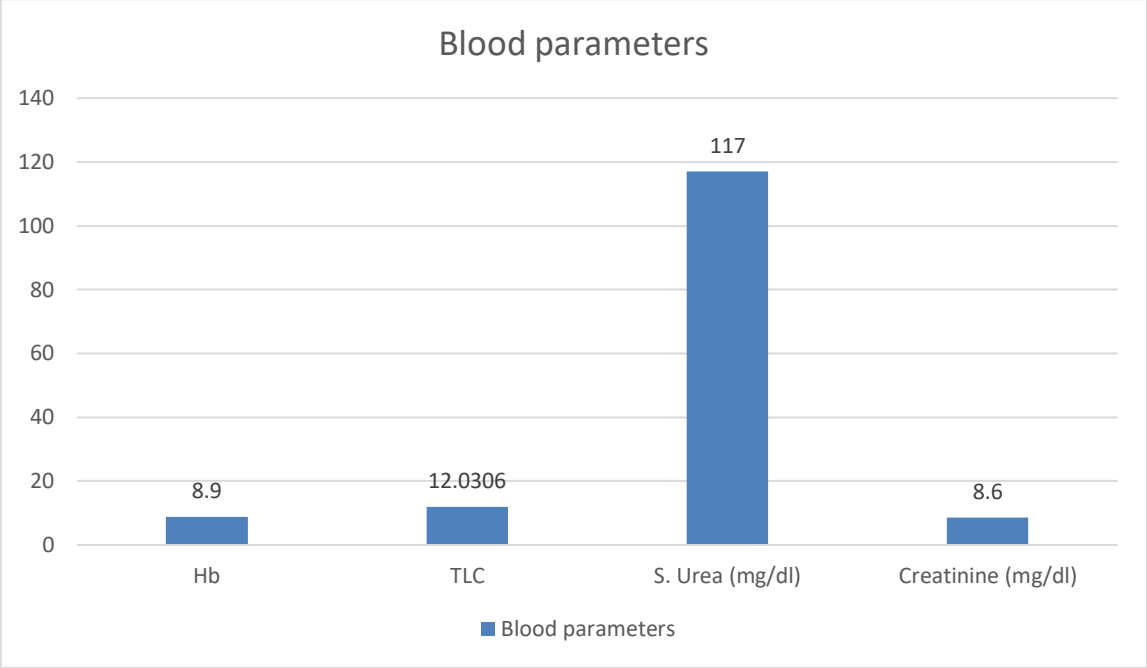

Figure 12: Showing mean blood parameters between the groups

Table 10: Showing the mean scores of MOCA questionnaire

MOCA scoring	Mean	SD
Visuospatial/Executive	3.9	.8
Naming	2.9	.2
Attention	1.7	.5
Read List	.8	.4
Serial 7 substraction	2.2	.6
Language	2.0	.5

Abstraction	2.0	.3
Delayed recall	4.3	.6
Orientation	5.9	.3

Table showing the mean scores of the MOCA questionnaire.

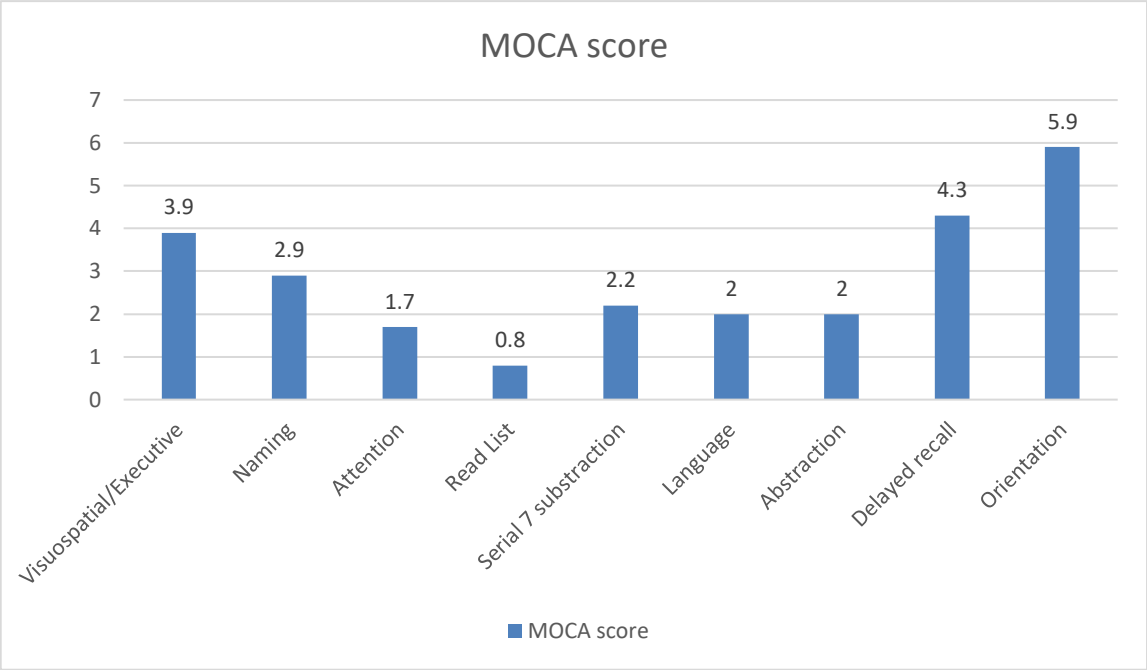

Figure 13: Showing the mean scores of MOCA questionnaire

Table 11: Presence of cognitive impairment

		Count	N %
Cognitive Impairment	Absent	38	59.4%
	Present	26	40.6%

The cognitive impairment is present in 40.6% of the patients on dialysis.

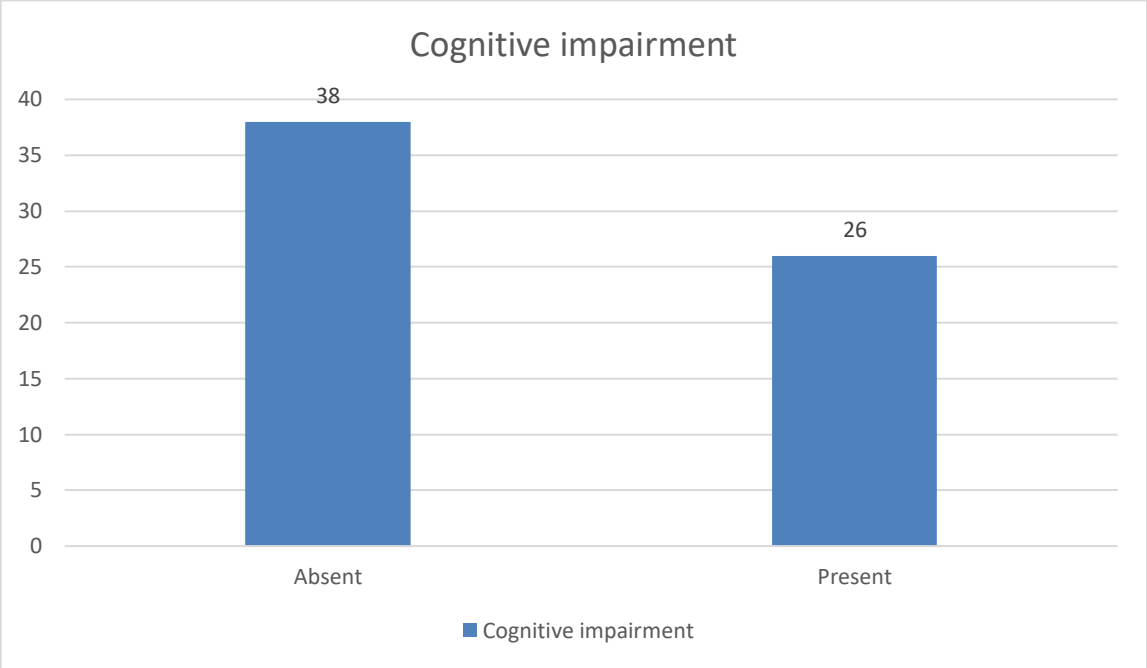

Figure 14: Presence of cognitive impairment

Table 12: Comparison of the duration of CKD with presence of cognitive impairment

	Cognitive Impairment				p-value
	Absent		Present		
	Mean	SD	Mean	SD	
Duration of CKD (yrs)	1.6	0.9	2.5	1.1	0.05*

There is significant longer duration of CKD in patients with cognitive impairment (2.5yrs) compared to patients without cognitive impairment (1.6yrs).($p<0.05$)

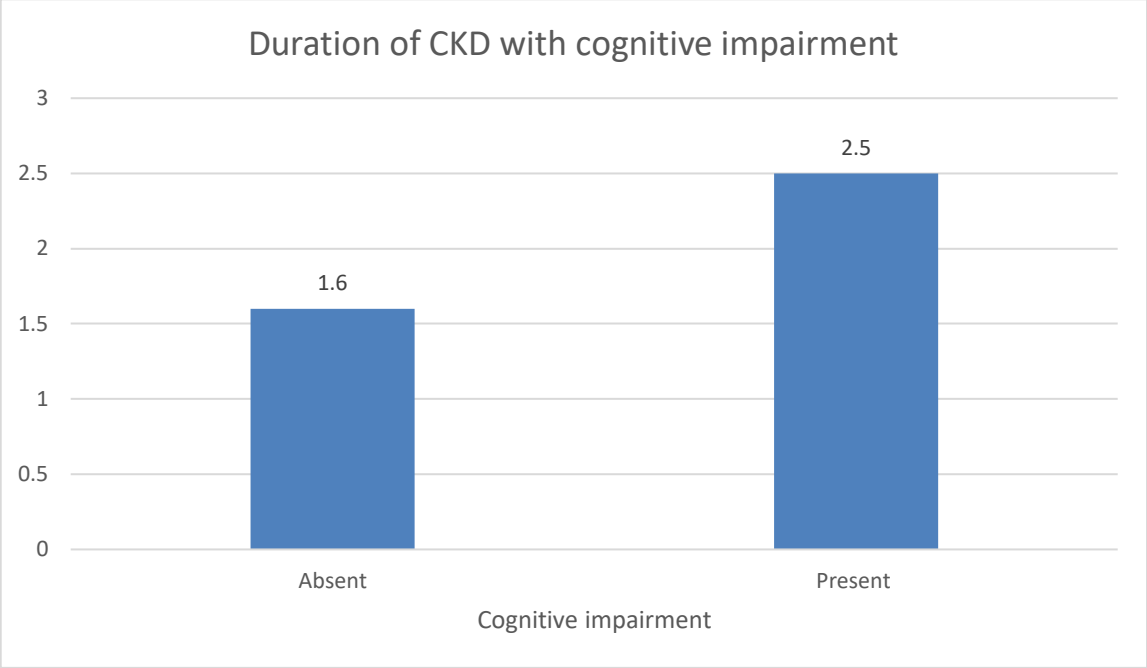

Figure 15: Comparison of the duration of CKD with presence of cognitive impairment

Table 13: Comparison of the duration of hemodialysis with presence of cognitive impairment

	Cognitive Impairment				p-value
	Absent		Present		
	Mean	SD	Mean	SD	
Duration of Hemodialysis (months)	3.5	1.9	8.6	3.6	0.05*

There is significant higher duration of hemodialysis in patients with cognitive impairment (8.6months) compared to patients without cognitive impairment (3.5months).($p<0.05$)

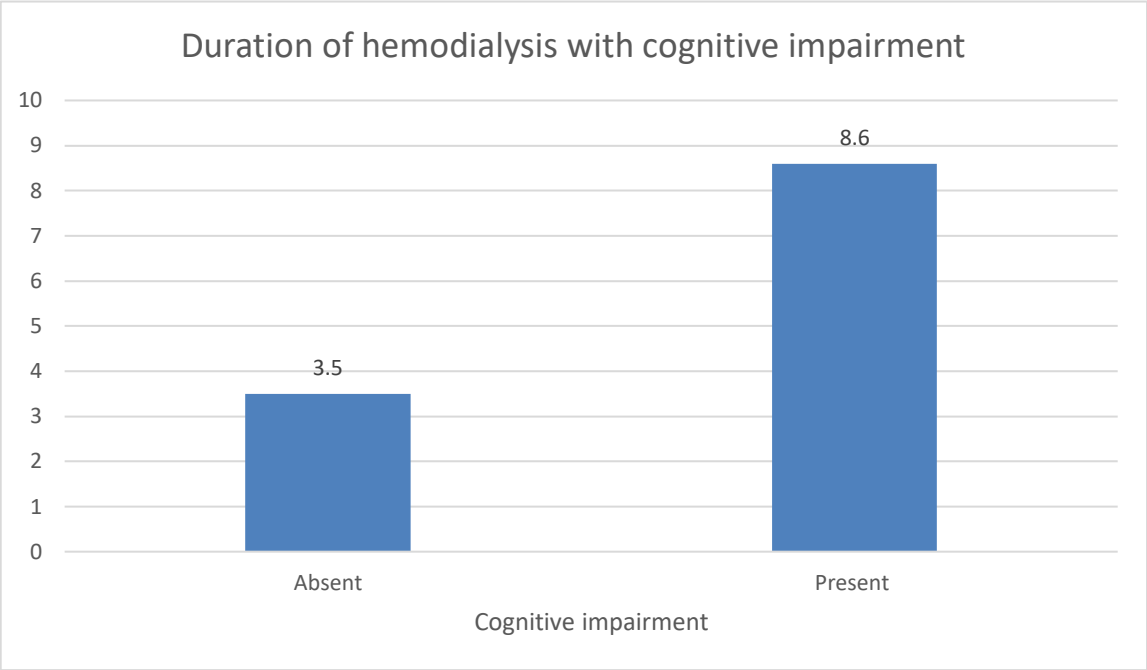

Figure 16: Comparison of the duration of hemodialysis with presence of cognitive impairment

DISCUSSION

Chronic Kidney Disease (CKD) is a growing global health concern, with a significant number of patients progressing to End-Stage Renal Disease (ESRD) requiring hemodialysis (HD) for survival.[76,77] While hemodialysis effectively removes waste products and excess fluids from the blood, emerging evidence suggests that it may have detrimental effects on cognitive function. Cognitive impairment in patients undergoing hemodialysis is a significant yet often underrecognized issue, impacting memory, attention, executive function, and overall quality of life.[77–79]

Several factors contribute to cognitive decline in hemodialysis patients, including long-term exposure to uremic toxins, cerebrovascular disease, fluctuations in blood pressure during dialysis, and oxidative stress. Additionally, comorbid conditions such as hypertension and diabetes—both highly prevalent in CKD patients—further exacerbate cognitive dysfunction. Studies have shown that the prevalence of cognitive impairment in dialysis patients is significantly higher than in the general population, with prolonged dialysis duration and advanced CKD stages being major risk factors.[80]

The underlying mechanisms linking hemodialysis to cognitive impairment remain complex and multifactorial. Hemodynamic instability during dialysis sessions can lead to recurrent episodes of cerebral hypoperfusion, increasing the risk of ischemic injury to the brain. Furthermore, the presence of inflammation, endothelial dysfunction, and metabolic disturbances in CKD patients may accelerate neurodegenerative processes.

Given the increasing burden of cognitive impairment among hemodialysis patients, early identification and intervention are crucial. Routine cognitive assessments, optimized dialysis protocols, and targeted management strategies may help mitigate cognitive decline and improve patient outcomes. Understanding the relationship between hemodialysis and cognitive impairment is essential for developing comprehensive care plans that address both renal and neurological health in this vulnerable population.

Present study included total of 64 patients with mean age of 52.67±14.2 years. Among them 37.5% were female and 62.5% were male with male preponderance in study. Smoking is present in 4.7% and 32.8% alcoholic. Hypertension is present in 50% and diabetes in 31.3% of cases.

In similar Joseph SJ et al., documented with mean age of patients in the study was 50.32 (±12.4) years, with a mean dialysis duration of 18.8 (±15.11) months. [72]

The mean duration of CKD was 1.6 years. The cognitive impairment is present in 40.6% of the patients on hemodialysis. There is significant longer duration of CKD in patients with cognitive impairment (2.5 years) compared to patients without cognitive impairment (1.6 years).($p<0.05$) There is significant higher duration of hemodialysis in patients with cognitive impairment (8.6 months) compared to patients without cognitive impairment (3.5 months).($p<0.05$)

Similar to present study Cao T et al., documented the cognitive impairment in 49.1% of the cases on maintenance hemodialysis. The findings emphasize the need for greater attention to modifiable factors such as cardiovascular disease risks and dialysis-related

variables to address cognitive impairment in this population.[75] Tian X et al., documented with findings suggest that Peritoneal Dialysis is associated with better cognitive function and reduced dementia risk, further large-scale, well-designed prospective cohort studies are needed to confirm these conclusions.[71]

McAdams DM et al., found that patients on hemodialysis, the 1- and 5-year risks of diagnosed dementia were 4.6% and 16% for women and 3.7% and 13% for men, respectively, while the corresponding risks for Alzheimer's disease were 0.6% and 2.6% for women and 0.4% and 2.0% for men. [2] Also in study by O'Lone E et al., the Hemodialysis is associated with significant cognitive deficits, particularly in orientation, attention, and executive function, warranting further research to address domain-specific impairments and their implications for patient education and chronic disease management.[68]

In another study by Karakizlis H et al., the" Mild, moderate, and severe impairments were observed in 14% (n = 57), 36.5% (n = 149), and 24.5% (n = 100) of patients, respectively. Cognitive impairment affected all domains, with immediate memory recall being the most impaired and naming ability the least affected. Depression and education level were significantly associated with cognitive performance. No significant changes in cognitive domains were observed after a one-year follow-up." This study highlights the high prevalence of cognitive impairment in hemodialysis patients and underscores the importance of early identification and treatment of depression to potentially improve cognitive outcomes. Education also plays a role in influencing cognitive test results.[74]

Author	Cognitive impairment (%)
Present study	40.6%
Cao T et al., [75]	49.1%
Karakizlis H et al., [74]	75%
Joseph SJ et al., [72]	44%
Post JB et al., [5]	76%

In concordance the Joseph SJ et al., "documented with Depression was prevalent in 42% of patients, and cognitive impairment (CI) was observed in 44%. Significant associations were found between education level and the recall ($\chi 2$=31.7, df=12, p=.002) and orientation ($\chi 2$=29.78, df=8, p=.000) domains of cognition, as well as between socio-economic status and global cognition scores ($\chi 2$=81.13, df=48, p=.002). Longer dialysis duration was negatively correlated with cognition, and depression was significantly linked to various cognitive domains. These findings highlight the high prevalence of CI in hemodialysis patients and its associations with factors like education, socio-economic status, dialysis duration, and depression. Early recognition of CI is crucial for tailoring precise treatment strategies."[72]

In another study by Xu H et al., found a rapid eGFR decline (>2 mL/min/1.73 m² per year) further increased dementia risk, with the association being stronger for vascular dementia than for Alzheimer's dementia. Notably, up to 10% of dementia cases could be attributed

to eGFR <60 mL/min/1.73 m², a higher proportion than that attributed to cardiovascular disease or diabetes, underscoring the significant impact of kidney function on dementia development.[73] Another study by Post JB et al., documented with executive function deficits were prevalent in at least 25% of subjects in both groups, and memory impairment was observed in 13% of hemodialysis (HD) patients and 15% of chronic kidney disease (CKD) patients. Mild cognitive impairment (MCI) was found in 76% of the study population, with a significantly higher prevalence in HD patients compared to CKD patients (89% vs. 63%).[5]

The Kurella M et al., study findings underscore the association between dementia and adverse outcomes in ESRD patients, highlighting the need for routine cognitive impairment screening in elderly dialysis patients to identify those at higher risk.[65]

Recommendations

Based on the findings of this study, the following recommendations can be made to address the impact of hemodialysis on cognitive impairment:

1. **Early Screening and Monitoring:**
    - Implement **routine cognitive assessments** for all patients undergoing hemodialysis, particularly those with a longer duration of CKD and dialysis treatment.
    - Utilize standardized cognitive screening tools to detect early signs of impairment and track progression over time.

2. **Optimizing Hemodialysis Parameters:**
    - Consider **individualized dialysis protocols** to minimize cognitive decline, including maintaining adequate blood pressure and optimizing ultrafiltration rates.
    - Assess the impact of dialysis frequency and duration on cognitive outcomes to refine treatment approaches.
3. **Managing Risk Factors:**
    - Provide **comprehensive management** for hypertension and diabetes, which are common comorbidities contributing to cognitive decline.
    - Encourage **lifestyle modifications**, such as smoking cessation and reduced alcohol consumption, to improve overall vascular and neurological health.
4. **Nutritional and Pharmacological Interventions:**
    - Promote **nutritional counseling** to prevent deficiencies that may contribute to cognitive impairment.
    - Investigate the potential benefits of **neuroprotective agents** or medications that may support cognitive function in dialysis patients.
5. **Psychosocial Support and Rehabilitation:**
    - Offer **cognitive rehabilitation programs** and mental health support to help patients cope with cognitive decline.
    - Provide educational resources and caregiver support programs to enhance patient adherence and quality of life.

6. **Further Research and Policy Development:**
    - Conduct **longitudinal studies** to explore the long-term impact of hemodialysis on cognitive function and identify modifiable risk factors.
    - Advocate for **integrated care models** that address both renal and neurological health in dialysis patients.

Implementing these strategies may help mitigate cognitive impairment and improve the overall well-being of hemodialysis patients.

CONCLUSION

- The study included 64 patients with a mean age of 52.67±14.2 years, with a male predominance (62.5%). Among the participants, 4.7% were smokers, 32.8% consumed alcohol, 50% had hypertension, and 31.3% had diabetes.
- The mean duration of chronic kidney disease (CKD) was 1.6 years. Cognitive impairment was observed in 40.6% of patients undergoing hemodialysis. Patients with cognitive impairment had a significantly longer CKD duration (2.5 years vs. 1.6 years, $p<0.05$) and a longer duration on hemodialysis (8.6 months vs. 3.5 months, $p<0.05$) compared to those without cognitive impairment.
- To conclude, Cognitive impairment is prevalent among hemodialysis patients and is associated with longer CKD duration and extended time on dialysis. Early identification and management of cognitive decline in CKD patients may improve their quality of life and overall clinical outcomes.

SUMMARY

The present study highlights a significant impact of hemodialysis on cognitive impairment in patients with chronic kidney disease (CKD). Among the 64 patients studied, 40.6% exhibited cognitive impairment, with a notable association between longer CKD duration and cognitive decline. Patients with cognitive impairment had a significantly longer duration of CKD (2.5 years) and hemodialysis (8.6 months) compared to those without cognitive impairment (1.6 years and 3.5 months, respectively) ($p<0.05$). These findings suggest that prolonged CKD and extended hemodialysis treatment may contribute to worsening cognitive function.

Given the substantial prevalence of cognitive impairment in this population, early screening, close monitoring, and potential interventions are crucial to improving patient outcomes and quality of life. Further research is needed to explore underlying mechanisms and develop targeted strategies for cognitive preservation in hemodialysis patients.

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INFORMED CONSENT FORM

BLDE DU'S SHRI B. M. PATIL MEDICAL COLLEGE

HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA-586103

TITLE OF THE PROJECT -

PRINCIPAL INVESTIGATOR - Dr. AKHIL THATI

P. G. GUIDE NAME - Dr R.M.HONNUTAGI, PROFESSOR OF MEDICINE

Dr. A.P.AMBALI , PROFESSOR OF MEDICINE.

P. G. CO-GUIDE NAME - Dr. SANDEEP PATIL, NEPHROLOGIST

CHAIRMAN ETHICAL COMMITTEE

All aspects of this consent form are explained to the patient in the language understood by him/her.

1) PURPOSE OF RESEARCH:

I have been informed about this study. I have also been given a free choice of participation in this study.

2) PROCEDURE:

I am aware that in addition to routine care received I will be asked a series of questions by the investigator. I have been asked to undergo the necessary investigations and treatment to help the investigator in this study.

3) RISK AND DISCOMFORTS:

I understand that I may experience some pain and discomfort during the

examination or my treatment. This is mainly the result of my condition and the procedure of this study is not expected to exaggerate these feelings that are associated with the usual course of treatment.

4)BENEFITS

I understand that my participation in this study will help patients' survival and better outcome.

5) CONFIDENTIALITY:

I understand that the medical information produced by this study will become a part of Hospital records and will be subject to confidentiality and privacy regulation. Information of a sensitive personal nature will not be a part of the medical records but will be stored in the investigator's research file and identified only by a code number. The code-key connecting name to numbers will be kept in a separate location. If the data are used for publication in the medical literature or teaching purposes, no name will be used and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand that I may see the photographs and videotapes and hear the audiotapes before giving this permission.

6) REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time. Dr. AKHIL THATI is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the study, which might influence my continued participation. If during the study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me. I will be given a copy of this consent form to keep for careful reading.

7) REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital. I also understand that Dr. AKHIL THATI may terminate my participation in the study after he has explained the reasons for doing so and has helped arrange for my continued care by my physician or physical therapist if this is appropriate.

8) INJURY STATEMENT:

I understand that in the unlikely event of injury to me resulting directly from my participation in this study if such injury were reported promptly, the appropriate treatment would be available to me, but no further compensation would be provided. I understand that by my agreement to participate in this study, I am not waiving any of my legal rights. I have explained the purpose of the research, the procedures required and the possible risks and benefits to the best of my ability in the patient's language.

_____ _____

DR. AKHIL THATI

(Investigator)

Date :

II) STUDY SUBJECT CONSENT STATEMENT:

I confirm that DR. AKHIL THATI has explained to me the purpose of the research,

the study procedures that I will undergo, and the possible risks and discomforts as well as benefits that I may experience in my language. I have read and understand this consent form. Therefore, I agree to give consent to participate as a subject in this research project.

_____

_____

Participant / Guardian Date:

_____

_____

Witness to signature Date:

STUDY OF IMPACT OF HAEMODIALYSIS ON COGNITIVE IMPAIRMENT

PROFORMA

DOA: Case no

DOD:

Name: I.P. No.:

Age:

Sex: Address:

DOC:

HISTORY

CHIEF COMPLAINT

BRIEF HISTORY OF PRESENTING ILLNESS

PAST HISTORY :

FAMILY HISTORY:

PERSONAL HISTORY:

Diet

Appetite

Sleep

Bowel and bladder

TREATMENT HISTORY:

GENERAL PHYSICAL EXAMINATION

Pulse

BP

Temp.

RR

SYSTEMIC EXAMINATION

Cardiovascular system: -

Respiratory examination: -

Per abdomen examination

Central Nervous examination: -

PROVISIONAL DIAGNOSIS

INVESTIGATIONS

1. HAEMATOLOGY –

1)Hemoglobin	gm. %
2)Total WBC counts	Cells/mm^3
3)Differential counts -	
Neutrophils	%
Lymphocytes	%
Eosinophils	%
Monocytes	
Basophils	

Platelet count	

RENAL FUNCTION TEST

CREATININE	
UREA	
SODIUM	
POTASSIUM	

URINE ROUTINE :

ULTRASONOGRAPHY OF ABDOMEN AND PELVIS

CONCLUSION:

DATE:

SIGNATURE

Azadi Ka Amrit Mahotsav

BLDE

(DEEMED TO BE UNIVERSITY)

Declared as Deemed to be University u/s 3 of UGC Act, 1956

Accredited with 'A' Grade by NAAC (Cycle 2)

The Constituent College

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA

BLDE (DU)/IEC/ 892/2022-23 10/4/2023

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this University met on **Saturday, 18th March, 2023 at 11.30 a.m. in the CAL Laboratory, Dept. of Pharmacology,** scrutinizes the Synopsis/ Research Projects of Post Graduate Student / Under Graduate Student /Faculty members of this University /Ph.D. Student College from ethical clearance point of view. After scrutiny, the following original/ corrected and revised version synopsis of the thesis/ research projects has been accorded ethical clearance.

TITLE: "IMPACT OF HEMODIALYSIS ON COGNITIVE IMPAIRMENT".

NAME OF THE STUDENT/PRINCIPAL INVESTIGATOR: DR.AKHIL THATI

NAME OF THE GUIDE: DR.ANAND AMBALI, PROFESSOR, DEPT. OF MEDICINE

Dr. Santoshkumar Jeevangi
Chairperson
IEC, BLDE (DU),
VIJAYAPURA

Chairman,
Institutional Ethical Committee,
BLDE (Deemed to be University)
Vijayapura

Dr.Akram A. Naikwadi
Member Secretary
IEC, BLDE (DU),
VIJAYAPURA

MEMBER SECRETARY
Institutional Ethics Committee
BLDE (Deemed to be University)
Vijayapura-586103, Karnataka

Following documents were placed before Ethical Committee for Scrutinization.

- Copy of Synopsis/Research Projects
- Copy of inform consent form
- Any other relevant document

Smt. Bangaramma Sajjan Campus, B. M. Patil Road (Sholapur Road), Vijayapura - 586103, Karnataka, In
BLDE (DU): Phone: +918352-262770, Fax: +918352-263303, Website: www.bldedu.ac.in, E-mail:office@bldedu.ac.in
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The Constituent College

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA

Department of Medicine

To
The Registrar
BLDE (Deemed to be University)
Vijayapur

Date: 03.02.2024

Sub: Re-allotment of PG Guides to PGs 2022(March), 2022(Nov) & 2023 batch.

Sir,

Following is the List of re-allotment of PG Guides to PGs of 2022 (March), 2022(Nov) and 2023 batch for information and needful.

Sl. No.	Name of PG	Batch	Name of Previous Guide	Name of Present Guide
1	Dr Somani Gourav	2022(March)	Dr A P Ambali	Dr S T Kalsad
2	Dr Ajaykumar T J	2022(March)	Dr A P Ambali	Dr S T Kalsad
3	Dr Raksha Chandraiah	2022(Nov)	Dr A P Ambali	Dr S N Bentoor
4	Dr Akhil Thati	2022(Nov)	Dr A P Ambali	Dr R M Honnutagi
5	Dr Kommineni Anilkumar	2023	Dr A P Ambali	Dr R C Bidri
6	Dr Ganesh Dad	2023	Dr A P Ambali	Dr V G Warad

Thanking you

Yours sincerely,

Dr S N Bentoor
Professor & Head
Department of Medicine

PROF. & HOD, MEDICINE
BLDE (Deemed to Be University)
Shri B.M.Patil Medical College
Hospital & Research Centre, Vijayapura.

thati akhil

IMPACT OF HEMODIALYSIS ON COGNITION

BLDE University

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MASTERCHART

Sl No	Ip no	AGE	GENDER	SMOKING	ALCOHOL	Duration of CKD (yrs) (months)	HYPERTENSION	DIABETES MELLITUS	PULSE RATE	SYSTOLIC BLOOD PRESSURE	DIASTOLIC BLOOD PRESSURE	HEMOGLOBIN	TOTAL LEKOCYTE COUNT	SERUM. UREA (mg/dl)	CREATININE (mg/dl)	On Hemodialysis (Cycles per week since)	Visuospatial/Executive (Out of 5point)	Naming (out of 3points]	Attention (out of 2points)	Read List (1point)	Serial 7 substraction (3points)	Language (3 points)	Abstraction (2 points)	Delayed recall (5 points)	Orientation (6 points)	Total (out of 30 points)
1	279611	53	M	No	Yes	2yr	Yes	No	88	156	80	8.4	5060	39	5.0	2cy/w/1yr	2	3	1	1	2	2	2	5	6	24
2	13777	55	M	No	No	1yr	Yes	Yes	120	190	100	11.7	28000	137	5.6	2cy/w/8m	3	3	1	1	1	2	2	4	6	23
3	21970	44	M	No	Yes	2y	Yes	No	82	160	90	5.4	5990	70	10.7	2cy/w / 5m	5	3	2	1	2	2	2	5	6	29
4	308964	85	M	Yes	No	3yrs	Yes	No	70	100	70	5.8	4720	153	6.4	3cy/w/2yr	2	2	2	1	2	2	1	4	6	21
5	137483	50	F	No	No	3m	No	Yes	72	130	70	7.2	38000	161	4.8	2cy/w/2m	4	3	2	1	2	2	2	5	6	27
6	143928	50	M	No	No	18m	No	Yes	120	100	70	9.5	13670	232	4.2	2cy/w/5m	4	3	1	1	2	2	2	5	6	26
7	129022	48	M	No	Yes	5 y	Yes	No	78	180	100	13.7	16160	53	3.0	1cy/w/3yr	3	3	1	0	2	2	2	5	6	24
8	239602	31	F	No	No	3m	No	No	86	130	80	10.8	18640	158	7.5	2cy/w / 3 m	4	3	1	1	3	2	2	4	6	26
9	391811	41	M	No	Yes	9 m	Yes	No	110	170	100	8.8	9320	64	6.7	3 cy/w/9 m	5	3	1	0	2	3	2	5	6	27
10	258347	32	F	No	No	5m	No	No	100	90	50	11	14530	107	5.1	1 cy/ w/5 m	4	3	2	1	2	2	2	5	6	27
11	267762	43	M	No	Yes	2.5yr	No	No	72	160	100	10.1	6950	88	7.6	2cy/w/1yr	4	3	1	1	1	1	2	5	6	27
12	14853	34	M	No	No	6 m	No	No	112	200	110	9.5	8000	124	11.3	1 cy/w/ 6 m	4	3	2	1	3	2	2	4	6	27
13	17736	21	F	No	No	2yr	No	No	120	130	90	6.0	5650	12.9	9.5	2 cy/w /6m	3	3	1	1	2	2	2	4	6	25
14	140511	62	M	No	No	5yr	Yes	Yes	86	150	100	7.3	6830	120	13	2cy/w/2yr	3	3	1	1	2	1	2	4	6	23
15	18236	60	M	No	No	2 yrs	Yes	No	70	130	80	6.5	8900	312	15.3	2 cy/w/ 2 yr	4	3	1	1	1	1	2	5	6	24
16	12678	56	F	No	No	1 yr	No	No	80	140	80	6.7	6800	65	5.0	2cy/w/4m	3	3	1	1	2	2	2	4	6	24
17	7818	40	M	No	Yes	6 m	No	No	84	110	80	6.2	4730	94	6.8	2cy/w/3m	4	3	2	1	3	2	2	5	6	27
18	320156	38	F	No	No	6m	No	No	90	130	80	8.2	42000	134	9.3	2cy/w/4m	4	3	2	1	2	2	2	4	6	27
19	17272	48	M	No	Yes	1yr	Yes	No	110	190	100	7.1	5900	128	8.8	2cy/w/6m	5	3	2	1	3	2	2	4	6	28
20	18102	52	M	No	Yes	2m	Yes	Yes	100	180	90	7.2	10000	196	13.7	2cy/w/2m	4	3	2	1	2	2	2	5	6	27

21	197956	35	M	No	No	4m	No	No	92	110	70	11.6	9960	150	7.7	3 cy / w / 2 m	4	3	2	1	2	2	2	5	6	27
22	228847	63	F	No	No	3m	No	No	76	110	80	8.6	16000	40	3.9	2 cy / w / 3 m	4	3	1	0	3	1	2	4	6	24
23	5495	47	M	No	no	5m	Yes	No	90	190	100	10	9000	224	10.2	2 cy / w / 5 m	5	3	2	1	3	2	2	4	6	28
24	5177	41	M	No	yes	1 yr	No	No	82	150	70	10.4	13030	159	10.1	2cy/w/4m	4	3	2	1	2	2	2	5	6	27
25	165498	39	M	No	No	6 m	No	No	70	170	90	8.3	13000	75	9.8	2 cy / w / 6m	4	3	2	1	3	2	2	5	6	28
26	19107	18	M	No	No	1m	No	No	70	120	70	8.3	12340	69	8.1	3 cy/w / 1 m	5	3	2	1	3	2	2	5	6	29
27	20384	43	F	No	No	6 m	yes	Yes	92	130	70	7.5	11210	30	4.9	2 cy / w / 6 m	4	3	2	1	2	2	2	5	6	27
28	13586	51	M	No	No	2 yr	yes	Yes	90	170	80	9.2	6100	42	3.6	2 cy/ w / 2 yrs	4	3	2	1	2	2	2	5	6	27
29	81085	52	F	No	No	3 m	yes	No	72	180	120	10.1	7110	81	5.7	3 cy/w /3 m	4	3	2	0	2	3	2	4	6	26
30	9299	58	M	No	No	2 yrs	yes	No	150	160	110	11.7	1560	147	8.7	2 cy/ w /2 yrs	3	3	1	0	2	2	2	4	6	23
31	8823	70	F	No	No	5yr	No	No	80	110	80	7.9	13370	100	7.4	2cy/w/3yr	4	3	1	1	2	2	2	4	6	25
32	90740	70	M	No	yes	4yr	No	No	110	70	50	1.7	3400	198	6.8	2cy/w/2.5yr	3	3	2	1	3	1	2	4	6	24
33	251286	72	F	No	No	3yrs	yes	Yes	70	110	70	10	9000	40	3.4	2cy/w/2yr	4	3	1	0	2	2	2	4	5	23
34	111014	58	M	No	yes	6 m	No	Yes	80	120	70	11	13000	223	9.0	2 cy/ w /3 m	5	3	2	1	3	2	2	4	6	28
35	240229	50	F	No	No	3 m	No	No	98	124	78	6.6	20000	120	6.6	2 cy/ w / 1 m	4	3	2	1	3	2	2	4	6	27
36	180007	60	M	No	No	2yr	yes	Yes	120	160	90	10.4	13980	151	6.2	3cy/w/1yr	4	3	2	1	2	1	2	4	6	25
37	1013	52	M	No	Yes	6m	Yes	Yes	108	140	80	6.4	7590	143	6.5	2 cy/ w / 4 m	5	3	2	1	2	2	2	5	6	28
38	219349	56	M	No	Yes	2yr	Yes	Yes	112	160	100	8.4	23000	88	9.6	2cy/w/1.5yr	3	3	1	1	2	3	2	4	6	25
39	213221	50	F	No	No	1 yr	Yes	No	92	150	90	5.8	17000	95	6.9	2 cy / w / 4m	4	3	2	0	2	2	2	5	6	26
40	12343	40	F	No	No	1 yr	No	No	108	160	100	7.8	8500	167	8.4	2cy/w/1yr	4	3	2	1	3	2	2	5	6	27
41	166873	73	M	No	yes	3yrs	Yes	Yes	102	160	90	9.5	12320	81	6.1	2 cy / w / 2 yr	3	2	2	1	2	2	2	4	5	23
42	158803	80	F	No	No	5yr	No	No	140	150	70	10.9	17240	140	4.0	2 cy / w / 3 yr	3	2	2	0	2	2	2	4	5	22
43	15165	65	M	No	yes	2yr	No	No	110	130	80	12.1	29000	156	12.7	2cy/w/1yr	4	2	2	1	2	2	2	4	6	25
44	251286	72	F	No	No	3yrs	Yes	Yes	76	140	80	10.4	6330	20	2.0	2cy/w/2yr	4	3	2	1	2	2	2	3	5	24
45	20025	58	M	Yes	yes	6 m	Yes	Yes	80	150	90	7.4	6460	118	7.8	2 cy / w / 5 m	4	3	2	1	3	3	2	3	6	26
46	313005	75	F	No	No	4yr	yes	Yes	130	200	110	7.7	17990	167	6.7	2 cy/ w / 2 m	4	3	1	1	2	2	2	4	6	25
47	180591	36	F	No	No	6 m	No	No	84	180	120	10.1	5900	102	11.9	2 cy/ w /3 m	5	3	2	1	3	2	2	4	6	28
48	131136	54	F	No	No	1 yr	Yes	Yes	102	160	90	8.3	17990	142	9.1	2 cy/w/ 7 m	4	3	2	0	2	3	2	5	6	27
49	43410	54	M	No	No	10yr	Yes	No	100	170	80	9	14000	80	6.5	2cy/w/3yr	4	3	1	0	2	3	2	4	6	25
50	163906	49	M	No	No	8yr	Yes	No	96	150	90	9	14380	90	7.3	2cy/w/3yr	3	3	2	0	2	2	2	5	6	24
51	126165	58	M	No	No	5yr	yes	No	86	170	84	10	13000	70	65	2 cy/ w / 3 yrs	5	3	2	1	2	3	2	4	6	28
52	190544	65	F	No	No	2 yr	No	yes	70	140	80	9	7000	136	13.9	2 cy/w / 4 m	3	3	2	1	2	2	2	4	6	25

53	82058	72	M	No	Yes	5yrs	yes	yes	84	160	90	11	9000	70	5.2	2 cy/ w / 8 m	3	3	2	1	2	2	0	5	6	24
54	151346	70	M	No	yes	3 yrs	No	No	76	140	80	12	8000	77	4.2	2 cy/w / 3 m	3	3	2	0	2	2	2	3	6	23
55	194963	55	M	yes	yes	2 yrs	No	No	72	130	70	11	7200	80	4.9	2 cy/w /2 m	5	3	2	1	3	2	2	4	6	28
56	265985	50	M	No	No	18 m	Yes	No	70	160	90	10	8400	194	9.1	2 cy/w /4m	4	3	2	1	2	2	2	5	6	27
57	77706	53	M	No	No	2 yrs	No	No	80	150	100	11.6	8200	108	10.9	2 cy/ w / 2 m	5	3	2	1	1	2	2	4	6	26
58	209718	65	M	No	yes	3 yrs	Yes	No	84	170	80	12	15000	210	16	2 cy/w / 6 m	4	3	2	1	3	3	2	4	5	27
59	200544	65	F	No	No	5 yrs	No	No	70	140	90	13	18000	98	10.3	2 cy/ w / 1 yr	3	3	2	1	2	2	2	5	6	26
60	20135	38	F	No	No	6 m	no	no	90	140	80	7.1	14000	136	7.7	2 cy/ w / 2 m	5	3	2	1	3	2	2	3	6	27
61	402807	81	F	No	No	5yrs	Yes	Yes	84	170	80	7	6500	90	7.5	2cy/w/3yr	3	3	2	1	2	2	2	3	6	24
62	88594	37	M	No	No	2 yrs	No	No	80	150	70	11	7320	100	6.0	2 cy/ w / 6 m	5	3	2	1	3	2	2	4	6	28
63	78455	67	F	No	No	18m	No	No	80	130	70	9	11000	40	2.8	2cy/w/6m	4	3	2	1	3	3	2	4	5	27
64	73535	30	M	No	No	2 yrs	No	No	72	140	80	11	12000	60	4.5	2cy/w/8m	4	3	2	1	3	3	2	5	6	29