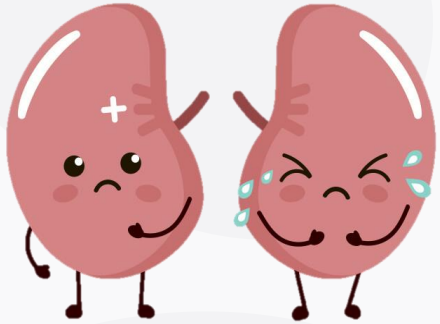
In the name of God

Cognitive Impairment and Brain Atrophy in Patients with Chronic Kidney Disease

Presented by: Shiva Maleki, MD

Chronic kidney disease:



Defined based on the presence of either kidney damage or decreased kidney function (eGFR <60 ml/min/1.73m^2) for three or more months.

CKD is deemed as one of the strongest risk factors for mild cognitive impairment and dementia.

Cognitive impairment:

Definition:

Problems with a person's ability to think, learn, remember, use judgement, and make decisions.

Sign: (impairment)

- memory loss
- trouble concentrating
- completing tasks
- understanding
- remembering
- solving problems

Type:

mild and severe

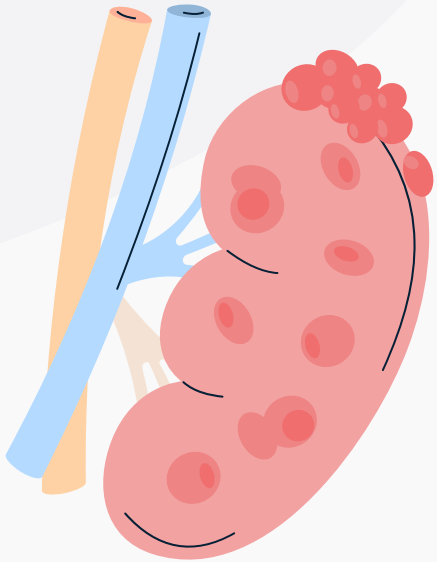
mild impairment, people still be able to do their everyday activities.

severe impairment, that impairs daily living (losing the ability to understand the meaning or importance of something and the ability to talk or write) and independence is typically referred to as dementia.

Previous studies have found a **10%-40%** prevalence of concomitant cognitive dysfunction in patients with CKD by with different CKD stages.

The prevalence of CKD and cognitive impairment (CI) both increase with age.

Patients **aged ≥ 80** years had a higher risk of developing cognitive impairment than patients **aged < 60** years.



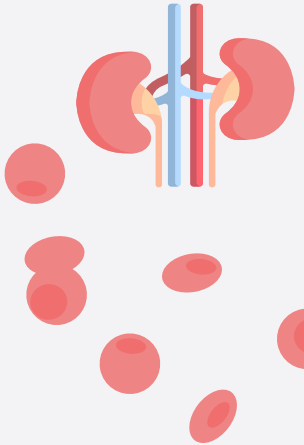
Brain atrophy:

• lose brain cells (neurons), and connections between their brain cells and brain volume often decreases.

• cerebral atrophy progresses rapidly in patients with CKD, especially in dialysis patients.

• Brain atrophy is significantly associated with Cognitive impairment.

Brain Atrophy in Patients with CKD:



1. Brain Atrophy in Patients with Non-Dialysis Dependent CKD (ND):

• The brain volume in ND patients has been shown to have more advanced brain atrophy than in healthy controls.

• the relationship between the higher the urinary albumin excretion and the lower the estimated glomerular filtration rate (eGFR), with the lower the whole brain volume and the faster the progression of brain atrophy was reported.

2. Brain Atrophy in Patients on Hemodialysis (HD):

HD patients have a high frequency of brain atrophy even at a young age , and the mechanism seems to be more complex than ageing.

3. Brain Atrophy in Patients on Peritoneal Dialysis (PD):

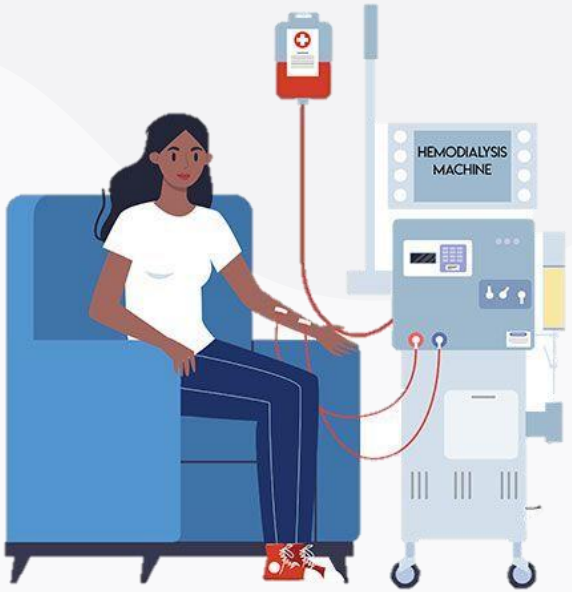
• Comparison between PD and ND Patients:

It has been reported that cognitive function is more impaired in PD patients than in ND patients.

(indicating smaller GMR in PD patients at the same age and brain atrophy progressed more than in PD patients compared to ND patients).

• Comparison between PD and HD Patients:

Studies show that PD patients move through brain atrophy faster than HD patients.



Factors and Pathophysiology Related to CI in Patients with CKD:

Several factors contribute to CI in CKD patients:

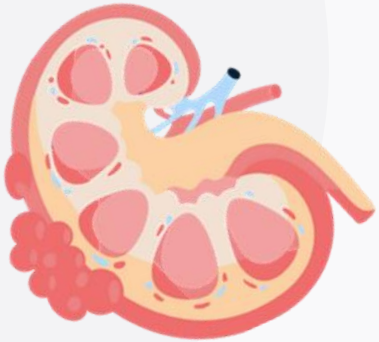
- age
- race (black)
- kidney dysfunction
- anemia
- diabetes
- hypertension
- cardiovascular disease
- oxidative stress
- uremic toxins
- inflammation
- albuminuria
- sleep duration and sleep quality
- malnutrition
- vitamin D deficiency

• A study assessing the level of albuminuria demonstrated that urine albumin/creatinine ratio of 30–299 and ≥300 mg/g is associated, respectively, with 31% and 57% higher risk of cognitive impairment.

• article demonstrates a correlation between mild CI (MCI) and eGFR, with the frequency of MCI increasing as the eGFR decreases.

• Among ND patients, CI is linked to sleep apnea syndrome.

• Vitamin D exerts neuroprotective role in the central nervous system. Vitamin D deficiency was found to be linked with endothelial dysfunction in non dialysis CKD patients. endothelial function may be improved and the cardio cerebrovascular events may be reduced by vitamin D supplementation in CKD patients.



Mechanisms of CI in CKD:

1. Atherosclerosis and Cerebrovascular Disease:

by inducing vascular injury and endothelial dysfunction

- **classical risk factors:**

Hypertension

Diabetes

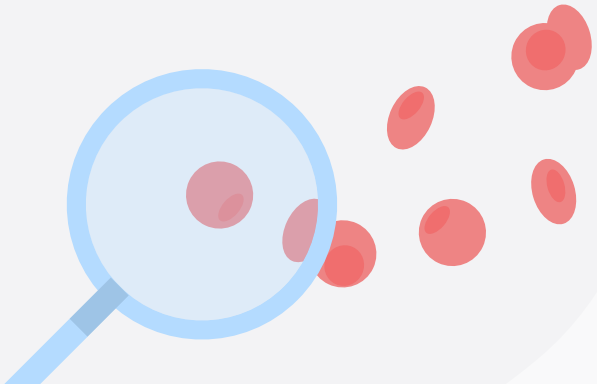
Atrial fibrillation

Carotid artery disease

Heart failure

Obesity

Dyslipidemia



- **Non-classical risk factors:**

Chronic inflammation

Uremic toxins

Reactive oxygen radicals

Anemia

Bone mineral disorders

2. Hypotension and Decrease of Regional Cerebral Blood Flow during HD:

- cerebral hypoperfusion
- blood pressure fluctuations

- mean flow velocity of cerebral arteries has been shown to decrease significantly during HD, leading to transient cerebral ischemia and ischemic white matter lesions.

- One of the factors associated with CI and brain atrophy in HD is a rapid decrease in blood pressure during HD.

- cerebral oxygen saturation (rSO2) decreases at 35 min after the initiation of HD. decrease in mean blood pressure by 10 mmHg during HD increased the risk of cerebral ischemia (rSO2 decreased by 15% or more).

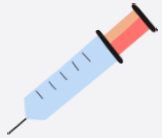
3. Oxidative stress:

• The connection between oxidative stress and cognitive dysfunction has been extensively investigated.

• reactive oxygen species (ROS) production increases and antioxidant function reduces, directly affecting synaptic activity and neurotransmission, leading to cognitive dysfunction.

• In the hippocampus of CKD mice, degenerated cells with nuclear condensation (pyknotic cells) appeared along with the accumulation of 8-hydroxy-2′-deoxyguanosine (8-OHdG). findings suggest that oxidative stress associated with CKD plays a significant role in neuronal damage in the brain and the decline of learning ability in CI in CKD.

Reduce the incidence of CI:



1. RAS inhibitors:

- Telmisartan: angiotensin II receptor antagonist

  administered to mice in a CKD model:

  • Decrease accumulation of 8-OHdG in the brain hippocampus

  • decline in learning capacity were suppressed.

  • decreasing brain oxidative DNA damage

2. Antihypertensive Management:

• a randomized controlled trial (RCT) comparing the incidence of CI between the intensive management group, with a target systolic blood pressure of less than 120 mmHg, and the standard control group with a target of less than 140 mmHg, among hypertensive patients aged 50 years and older with no history of diabetes or stroke.

it has been determined that the incidence of MCI is lower in the intensive management group.

3. Management of anemia:

• recombinant human erythropoietin (rHuEPO) as standard therapy for CKD-associated anemia, has shown a neuroprotective effect and improves brain function.

4. Exercise therapy:

In recent years, concerns regarding frailty have emerged among elderly dialysis patients.
it is characterized by a decline in skeletal muscle mass and strength, and a decline in overall physical and cognitive functions associated with aging.
Exercise therapy has been reported not only to enhance physical function but also to contribute to improvements in cognitive function.
The findings indicated that exercise during or between HD sessions significantly improved cognitive function in HD patients.
the effects were particularly significant when the duration was 30 min or more, performed at least three times a week, and continued for a minimum of 16 weeks.

5. Lifestyle Improvement:

Improve lifestyle in exercise, diet and cognitive training can improve cognitive function.
Cognitive function significantly improved in the lifestyle improvement group, showing a remarkable 25% enhancement compared to the control group.

6. Extension of dialysis session time:

extended HD sessions may contribute to an improvement in cognitive function.
a prospective, case–control study involving 247 patients who consented to 8 h HD sessions three times a week and a control group that consisted of 247 patients receiving 4 h HD sessions three times a week, matched for age, gender, diabetes mellitus, and dialysis history over a 12-month period.
The study compared prognosis, cognitive function, revealing a significant improvement in memory function in the long-hour HD group.

7. PD:

It has been reported that cognitive function is better preserved in PD compared to HD patients.

Dementia was 12.68% in HD patients and 5.62% in PD patients.

8. Melatonin:

a study involving 102 HD patients examined the impact of melatonin administration on sleep quality.

patients were divided into a melatonin group, receiving melatonin, and a control group without melatonin.

Significant improvements in the PSQI were observed in the melatonin group.

9. Kidney Transplantation:

- Cognitive function has been reported to improve with KT.

- compared cognitive function between pre- and post-KTx, and non-KTx patients, and healthy subjects.

- reported an improvement in cognitive function after KTx but noted that it did not reach the level observed in healthy subjects.

10. Prevention: Lowering Blood Pressure and Cerebral Ischemia During and After HD:

• To keep blood pressure from dropping during HD, it is important to set the dry weights correctly and slow down the amount of fluid that is lost each hour.

• Diabetic patients often have significant systemic arteriosclerosis, including stenotic and occlusive lesions in the intra and extra cranial major arteries. They are more likely to experience hypotension during HD and orthostatic hypotension after HD.

• Vasopressor medication may be beneficial in cases where blood pressure drops during dialysis vasopressor drugs can stop the drop in blood flow to the brain that happens because of orthostatic hypotension after HD. The mechanism involves the dilation of cerebral Blood vessels by activating adrenergic receptors, particularly β receptors, In addition to inducing peripheral vasoconstriction.

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Thanks for your attention