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Risk factors for cognitive impairment in chronic kidney disease: A cross-sectional study

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ABSTRACT

Background: Chronic kidney disease (CKD) is a leading public health problem, affecting more than 800 million people worldwide. CKD is frequently associated with complications, including cardiovascular disease, anemia, osteoporosis, and cognitive impairment (CI), which can range from moderate to severe and impact patients' quality of life. This study aims to test the prevalence of CI among patients with CKD and determine associated disease severity measures and elements related to CI.

Methods: This is a cross-sectional observational study done in a tertiary medical center in a developing country's healthcare setting. A cohort of 319 patients with CKD has been recruited. The participants took the Montreal cognitive assessment (MoCA) test. Clinical variables included comorbidities, medications, and laboratory tests from patients' electronic records. Multivariate logistic regression analysis was used to predict factors related to MoCA ratings of < 26 and ≥ 26 after adjusting for applicable covariates.

Results: 41.7% of the individuals had a MoCA score of less than 26, indicating mild CI. Factors significantly associated with cognitive problems included older age, lower educational attainment, reduced estimated glomerular filtration rate, advanced stage of CKD, and use of benzodiazepines.

Conclusion: The study highlights the high prevalence of CI among CKD patients and identifies several modifiable and non-modifiable risk factors. Early screening and targeted interventions should help reduce CKD patients' mental suffering and CI.

Keywords: chronic kidney disease, cognitive impairment, Montreal cognitive assessment, risk factors, cross-sectional study, SGLT2 inhibitors

INTRODUCTION

More than 800 million individuals worldwide suffer from chronic kidney disease (CKD), a major global health threat and one of the world's leading causes of mortality [1-3]. CKD is characterized by gradual kidney function decline, which may lead to complications such as cardiovascular disease, anemia, and bone disorders [4-6]. Furthermore, CKD correlates with cognitive impairment (CI) that involves memory loss, learning deficits, poor concentration, and decision-making capacity [7]. CI goes from mild to severe, affecting the quality of life, self-care, and treatment outcomes for those with CKD [8].

The incidence and risk factors for CI among individuals diagnosed with CKD vary between populations and the methods used in its assessment. Examples of common modifiable risk factors include hypertension (HTN), low educational level, and diabetes mellitus (DM) [9, 10]. A number of these factors can be changed by medical intervention like antihypertensive medications, cognitive training, or lifestyle changes, including physical exercise or diet, and use of some newer oral hypoglycemic medications, as newer studies have shown that the use of sodium-glucose cotransporter-2 (SGLT2) inhibitors have some beneficial effect on the cognitive decline in patients with CKD who have diabetes [10, 11]; however, others cannot be changed like old age [12].

The lack of a standardized and sensitive screening tool is an essential obstacle to studying CI in CKD patients. Despite being widely used, using full words for the mini-mental state examination (MMSE) test has some limitations, such as low sensitivity for use in mild CI and cultural bias [13]. Therefore, more elaborate examinations like the Montreal cognitive assessment (MoCA) are necessary to assess various cognitive domains affected by CKD [14]. The MoCA is more sensitive and

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specific than the MMSE; hence, it may be a promising alternative in other populations, including CKD patients [15].

Several risk factors associated with CKD, such as aging, unemployment, smoking, DM, HTN, cardiovascular diseases, and low HDL, make this condition a significant public health issue [16]. Information about the prevalence and risk factors for CI among CKD patients is sparse in developing countries. This study aims to estimate the prevalence of CI among CKD patients using the MoCA, while considering disease severity and identifying associated factors in such healthcare settings.

METHODOLOGY

Study Design and Participants

In this cross-sectional study, we enrolled 319 CKD patients aged 18 years and above who were following and treated at the nephrology clinics in Jordan University Hospital (JUH) and without a previous diagnosis of dementia. During routine clinic visits, all contributors underwent the MoCA test in private and calm settings.

Health Assessment and Clinical Variables

Participants underwent a 20-25 minute interview, self-reporting comorbidities include HTN, DM, cardiac conditions, hypothyroidism, loss of function (LOF), depression, family history of dementia, and chronic medications like: angiotensin-converting enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARBS), sodium-glucose transporter, thyroxine, diuretics, beta blockers, statins, benzodiazepines, hypoglycemic drugs, erythropoietin, and iron. Additionally, patients' weight, smoking status, and state of dialysis were taken.

Blood Sampling and Analysis

The laboratory results obtained from the JUH electronic system included serum creatinine (mg/dl), with the estimated glomerular filtration rate (eGFR) calculated using the clinical kidney disease epidemiology collaboration method [17]. Other laboratory tests comprised body mass index (BMI), hemoglobin (Hgb) (g/dL), hematocrit (%), mean corpuscular volume (fl), red blood cell count ($\times 10^6/\mu L$), white blood cell count ($\times 10^3/\mu L$), platelet count ($\times 10^3/\mu L$), serum albumin (g/L), and urea (mg/dL). In the comprehensive analysis, other important variables have been included too, like MoCA rating labeled as < 26 and ≥ 26, gender, and age, which was stratified into subgroups.

Cognitive Screening

The MoCA test is a 30-factor screening tool used to assess cognitive functions such as memory, executive functioning, attention, language, visuospatial skills, and orientation. We utilized a validated Arabic form for our patients. MoCA rating < 26 indicates CI. The MoCA version 7.1 used visuospatial capabilities, naming, reminiscence, attention, language, abstraction, and orientation. Tasks include drawing a clock, copying a cube, recalling five words, repeating digit sequences, naming words, and responding to sentences. Abstraction is measured via object similarities, while orientation includes questions about time and place.

Statistical Analysis

Statistical analysis was performed using SPSS version 28, where descriptive statistics were presented for demographic and scientific variables, including means, standard deviations, medians, interquartile ranges (IQR), and frequency distributions. Median (IQR) values were presented solely for non-normally distributed variables. Normality of continuous variables was assessed using the Shapiro-Wilk test, as the variables found to be non-normally distributed are now reported as medians and IQRs instead of means and standard deviations (SDs) (**Table 1**).

The Chi-square test investigated associations among specific variables and MoCA scores, and percentages of MoCA were calculated within each variable. Multivariate logistic regression recognized factors related to a MoCA rating < 26, adjusting for applicable covariates. Odds ratios (OR), 95% confidence interval, and p-values were pronounced, with statistical significance set at $p < 0.05$. The logistic regression model effectively distinguishes between individuals with and without CI (AUC-ROC = 0.81).

We specify that a manual selection approach was used for the multivariate model, and that the specified variables were chosen based on their clinical relevance and statistical significance in the univariate analysis ($p < 0.10$). Sensitivity of (73.2%) correctly identifies 73.2% of those with CI and 82.1% of those without it (specificity [82.1%]). The model explains 39% of the variance in CI, with age, education, LOF, and CKD stage being key predictors. In the login regression model, educational level was considered as a continuous variable. It was calculated based on years of formal education: "elementary or below," which includes those with "illiterate" or "elementary" education, was assigned 6 years, "secondary," which includes "tawjihi" or "secondary" education, was assigned 12 years, "diploma" was assigned 14 years, "bachelor's" was assigned 16 years, and "master's or higher," including "master's" and "doctorate" degrees or exceeding 12 years, was assigned 18 years.

Ethical Considerations

We strictly adhere to ethical recommendations, ensuring the safety and privacy of individuals. Approval from the Institutional Review Board at JUH was secured on March 1, 2023, with decision no. 38/2023, and contributors received comprehensive information emphasizing the study's purpose, procedures, and potential risks. They signed the informed consent form for the study. Before records collection, knowledgeable consent was obtained, emphasizing voluntary participation and the right to withdraw without consequences. Confidentiality measures have been carried out to protect personal information, and information has been anonymized throughout the analysis.

RESULTS

This research included 319 participants with CKD. **Table 1** contains an overview of their clinical and demographic characteristics. The participants' ages varied from 18 to 89 years, with a mean of 61 and an IQR of 49-70. Most of the participants were elderly (30.4% aged 60-69 years and 27.3% ≥ 70 years), only 11.6% of the sample were young (18-39 years).

Table 1. Descriptive statistics and general characteristics of patients with CKD (N = 319)

Variable	Category	N (%)	Median (IQR) or mean ± SD	Range (minimum-maximum)
MoCA score			23.42 ± 4.61	
	< 26	133 (41.7%)		
	≥ 26	186 (58.3%)		
Gender	Female	139 (43.9%)		
	Male	180 (56.1%)		
Age (years)			**61 (49-70)**	18-89
	18-39	37 (11.6%)		
	40-49	39 (12.2%)		
	50-59	59 (18.5%)		
	60-69	97 (30.4%)		
	≥ 70	87 (27.3%)		
eGFR (ml/min/1.73 m^2)			**26.4 (15.2-39.6)**	2.1-87.3
	0-15	96 (30.2%)		
	16-29	77 (24.2%)		
	30-59	126 (39.6%)		
	60-89	19 (6.0%)		
BMI			28.97 ± 5.88	
Hgb	g/dL		**11.6 (10.2-13.1)**	7.0-17.2
Hematocrit	%		36.3 ± 6.3	20.9-56.5
Mean corpuscular volume	fL		86.4 ± 9.1	19.4-130.5
Red blood cell count	×10^6/μL		4.2 ± 0.79	2.4-8.15
White blood count	×10^3/μL		**7.1 (5.6-9.2)**	2.87-80.82
Platelet count	×10^3/μL		239.2 ± 81.2	3.6-546.0
Serum albumin	g/L		**36.0 (33.2-38.6)**	2.2-45.0*
Creatinine	mg/dL		**220 (149-389)**	0.88-14.80*
Urea	mg/dL		66 (48-97)	11.7-220.0

Note. Values in **bold** indicate non-normally distributed variables, reported as median (IQR)

The men created a thin majority of the sample, with 56.1% of the sample male and 43.9% female. The average MoCA score of 23.42 ± 4.61 and 41.7% of cognitive loss (defined as MoCA < 26) indicates that cognitive dysfunction is quite common in CKD patients. With a median eGFR of 26.4 mL/min/1.73 m^2 (IQR: 15.2-39.6), the majority of patients had advanced stages of CKD: a further 24.2% had eGFR between 16 and 29 mL/min/1.73 m^2 (stage 4 CKD), and 30.2% had eGFR <15 mL/min/1.73 m^2 (stage 5 CKD). Only 6% of patients had eGFR values in the stage 2 CKD range of 60 to 89 mL/min/1.73 m^2. A median Hgb level of 11.6 g/dL (IQR: 10.2-13.1) suggested anemia, which is common in CKD patients, and a mean BMI of 28.97 ± 5.88 kg/m^2 indicated that many patients were overweight or obese.

Table 2 shows an important correlation between age and cognitive loss ($p < 0.000001$). Although only 29.7% of individuals were scored at the age of 18-39, the MoCA scores of patients increased rapidly with CI < 26 years of age, which rose to a surprisingly high 78.2% among people aged 70. In individuals with CKD, this pattern emphasizes the close relationship between aging and cognitive decline. The MOCA score was correlated mainly with the progress of CKD steps ($p = 0.031$). Only 4.8% of patients scored under the threshold for cognitive loss in the earlier stages (stage 2), which reflects the lowest rates of cognitive loss. In contrast, as the severity of CKD increased, the prevalence of cognitive loss increased: stage 3A (15%), stage 3B (27.3%), stage 4 (23%), and stage 5 (29.4%).

According to these results, there is a strong relationship between deteriorating kidney function and a high risk of CI, which is also highlighted in **Figure 1**. Additionally, a strong correlation ($p < 0.002$) was found between academic success and MoCA score. Patients with low education levels, such as illiteracy or completion of primary school, have a higher rate of cognitive loss than patients with higher education levels, such as a diploma or a graduate degree. For instance, only 3% of patients with a PhD obtained a MoCA score below 26, whereas 33% of patients with only a secondary education did. These results demonstrate how a higher level of education may prevent cognitive decline.

HTN was a significant factor ($p < 0.05$) associated with CI. Patients with MoCA scores below 26 were more likely to have HTN (87%) than those with scores above 26 (72%). This suggests that uncontrolled HTN may lead to cognitive decline in patients with CKD. Other comorbidities, such as DM, cardiovascular disease, hypothyroidism, and a family history of dementia, were more prevalent in patients with CI than in those without, although they did not show statistically significant correlations with MoCA scores. For example, only 32% of patients with a score of more than 26 had DM, compared to 38% of patients with a score of less than 26.

Multiple logistic regression analysis identified several independent predictors of cognitive loss, including Age: for each year of age, there was a 6% (OR = 1.06; $p = 0.036$) increase in cognitive loss. Educational level: a low risk of cognitive decline was associated with high levels of education (OR = 0.79; $p = 0.005$). LOF: patients with functional loss had significantly higher odds of CI (OR = 3.46; $p = 0.046$). CKD stage: patients in stage 3a were more likely to experience CI than those in stage 2 (OR = 3.45; $p = 0.049$). Other factors, such as eGFR levels and HTN, did not independently predict lower MoCA scores after controlling for confounders.

DISCUSSION

This study provides significant insights into the progression of cognitive decline and its predictors in patients with CKD, highlighting the interaction of demographic, clinical, and socio-economic factors in a cohort of 319 patients. Below, we discuss these findings within the existing literature, explain their implications, and identify areas for future research.

Table 2. Chi-square analysis for factors associated with MoCA score of < 26 and ≥ 26 in patients with CKD (% within each variable)

Variable	Category	MoCA < 26	MoCA ≥ 26	Total (%)	p
Gender	Female	53 (40.2)	87 (46.5)	140 (43.9)	0.259
	Male	79 (59.8)	100 (53.5)	179 (56.1)	
Age	18-39	26 (70.3)	11 (29.7)	37 (11.6)	< 0.000001*
	40-49	24 (61.5)	15 (38.5)	39 (12.2)	
	50-59	23 (39.0)	36 (61.0)	59 (18.5)	
	60-69	40 (41.2)	57 (58.8)	97 (30.4)	
	≥ 70	19 (21.8)	68 (78.2)	87 (27.3)	
eGFR	0-15	40 (41.7)	56 (58.3)	96 (30.2)	0.496
	16-29	32 (41.6)	45 (58.4)	77 (24.2)	
	30-59	49 (38.9)	77 (61.1)	126 (39.6)	
	60-89	11 (57.9)	8 (42.1)	19 (6.0)	
Stage	2	19 (67.9)	9 (32.1)	28 (8.8)	0.031*
	3A	22 (44.0)	28 (56.0)	50 (15.7)	
	3B	23 (31.1)	51 (68.9)	74 (23.2)	
	4	28 (39.4)	43 (60.6)	71 (22.3)	
	5	40 (42.1)	55 (57.9)	95 (29.8)	
Degree	Bachelor's	39 (47.6)	43 (52.4)	82 (25.7)	< 0.002*
	Diploma	22 (50.0)	22 (50.0)	44 (13.8)	
	Doctorate	4 (80.0)	1 (20.0)	5 (1.6)	
	Elementary	1 (4.2)	23 (95.8)	24 (7.5)	
	Illiterate	3 (30.0)	7 (70.0)	10 (3.1)	
	Intermediate	12 (33.3)	24 (66.7)	36 (11.3)	
	Master's	7 (63.6)	4 (36.4)	11 (3.4)	
	Secondary	44 (41.1)	63 (58.9)	107 (33.5)	
Marital status	Married	99 (38.8)	156 (61.2)	255 (79.9)	0.15
	Single	28 (56.0)	22 (44.0)	50 (15.7)	
	Widowed	5 (38.5)	8 (61.5)	13 (4.1)	
Working	Working	29 (48.3)	31 (51.7)	60 (18.8)	0.226
Salary	< 500	79 (39.1)	123 (60.9)	202 (63.2)	0.396
	500-1,000	43 (46.7)	49 (53.3)	92 (28.9)	
	1,000-1,500	7 (36.8)	12 (63.2)	19 (6.0)	
	> 1,500	2 (40.0)	3 (60.0)	5 (1.6)	
Smoking	Smoker	28 (42.4)	38 (57.6)	66 (20.7)	0.696
	FS	24 (46.2)	28 (53.8)	52 (16.3)	
	NS	80 (39.8)	121 (60.2)	201 (63.0)	
Allergy		10 (28.6)	30 (71.4)	40 (12.5)	0.396
Family Hx dementia		10 (62.5)	6 (37.5)	16 (5.0)	0.394
Dialysis		27 (54.0)	23 (46.0)	50 (15.7)	0.154
Depression		1 (16.7)	5 (83.3)	6 (1.9)	0.443
LOF		5 (20.0)	20 (80.0)	25 (7.9)	0.040*
HTN		96 (37.1)	163 (62.9)	259 (81.2)	0.001*
DM		67 (38.3)	108 (61.7)	175 (54.9)	0.216
CVD		44 (37.9)	72 (62.1)	116 (36.6)	0.309
Hypothyroid		17 (43.6)	22 (56.4)	39 (12.2)	0.773
ACEI		15 (34.9)	28 (65.1)	43 (13.5)	0.011*
ARBS		24 (30.0)	56 (70.0)	80 (25.1)	0.004*
Benzodiazepines		12 (20.7)	46 (79.3)	58 (18.2)	< 0.00001*
SLGT2		2 (25.0)	6 (75.0)	8 (2.5)	0.002*
Thyroxine		8 (44.4)	10 (55.6)	18 (5.6)	0.003*
Diuretics		59 (37.3)	99 (62.7)	158 (49.5)	0.002*
Iron		27 (37.0)	46 (63.0)	73 (22.9)	0.551
B blockers		66 (38.8)	104 (61.2)	170 (53.3)	0.468
Statin		66 (50.0)	123 (65.1)	189 (59.2)	0.002*
Vitamin D		74 (46.8)	125 (62.8)	199 (62.4)	0.135
Hypoglycemic drugs		54 (44.3)	68 (55.7)	122 (38.2)	0.453

Note. FS: Former smoker & NS: Non-smoker

Cognitive Impairment (MoCA Score)

The prevalence of CI (MoCA < 26) was 41.7%, which is consistent with earlier CKD studies that found rates between 30 and 60% [8, 9]. The average MoCA score (23.42 ± 4.61) is in line with studies that show a correlation between the severity of CKD and impairments in memory and executive function [18]. There may be a threshold effect where cognitive decline speeds up as kidney function drops below a critical level, as evidenced by the stronger correlations between impairment and advanced CKD stages (e.g., stage 4) than moderate stages (3a/3b) (18). Due to variations in GFR estimation techniques (e.g., updated CKD-EPI equations [17, 19]), it was not found a correlation between CKD stage and cognition in older cohorts [15].

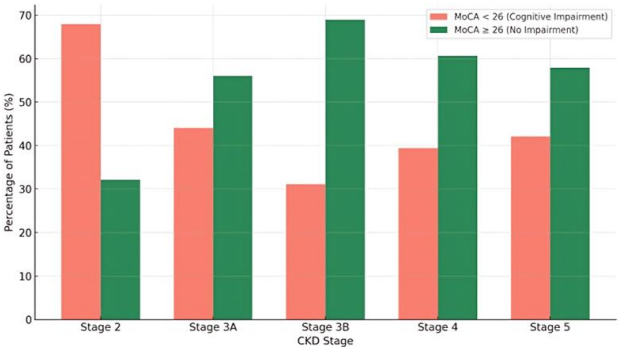

Figure 1. Distribution of cognitive impairment across CKD stages (Source: Authors' own elaboration)

Age

78.2% of patients aged ≥ 70 years showed impairment, making age a significant predictor (OR = 1.06 per year) as presented in **Table 2**. Age-related cerebrovascular changes and CKD-specific mechanisms (such as anemia and uremic toxins) increase the risks for older adults [18]. Remarkably, 70.3% of young adults (18-39 years) also displayed impairment, which most likely reflected early vascular injury from diabetes (54.9%) or HTN (81.2% prevalence) [5, 19]. This is consistent with [8], which found that younger CKD patients with comorbidities experienced an accelerated rate of cognitive decline. In **Table 2**, the relationship between age and cognitive decline can be presented by the unadjusted prevalence of MoCA < 26. It appears higher in younger age groups (e.g., 18-39 years) due to a small sample size in this subgroup (11.6% of the cohort) and confounding by comorbidities such as HTN (81.2%) and diabetes (54.9%). On the contrary, the multivariate regression model in **Table 3** is adjusted for CKD stage, education, and comorbidities. It specifically demonstrated a significant independent association between older age and CI (OR = 1.06 per year, p = 0.036).

CKD Stage and eGFR

As CKD progressed, the prevalence of CI increased: 4.8% in stage 2 vs. 29.4% in stage (**Table 2**). However, it was contended that early CKD starts neuropathological processes (like endothelial dysfunction) before overt uremia, while stage 3a independently predicted impairment (OR = 3.45; **Table 3**) [9]. Paradoxically, closer clinical supervision (e.g., dialysis) may help advanced-stage patients (e.g., stage 5) reduce cognitive risks [2, 17]. This indicates that kidney disease may impact cognitive function, suggesting that the highest degree of CI appears while kidney function drops beneath a threshold. At the same time, one can expect variability in CKD patients and the effect of other elements like comorbidities, medications, and lifestyle on cognitive functioning [20, 21]. Regression models' lack of eGFR significance (OR = 0.99) emphasizes that CKD stage accounts for multifactorial risks that go beyond glomerular filtration [22].

Table 3. Multivariate logistic regression analysis for factors associated with a MoCA score of < 26 in patients with CKD

Variable	Type	Exposure vs. reference	OR	95% confidence interval	P-value
Age	Continuous	Per year increase	1.06	[1.01-1.12]	0.036*
Educational level	Continuous	Higher vs. lower	0.79	[0.67-0.93]	0.005*
LOF	Categorical	Yes vs. no	3.46	[1.02-11.73]	0.046*
CKD stage 3a	Categorical	Stage 3a vs. stage 2	3.45	[1.01-11.79]	0.049*
CKD stage 3b	Categorical	Stage 3b vs. stage 2	1.68	[0.45-6.27]	0.449
CKD stage 4	Categorical	Stage 4 vs. stage 2	2.01	[0.51-7.92]	0.319
CKD stage 5	Categorical	Stage 5 vs. stage 2	2.35	[0.04-125.26]	0.608
eGFR	Continuous	Per unit increase	0.99	[0.97-1.01]	0.452
HTN	Categorical	Yes vs. no	1.22	[0.72-2.05]	0.457
ACEI	Categorical	Yes vs. no	0.79	[0.32-1.97]	0.610
ARBs	Categorical	Yes vs. no	1.45	[0.55-3.83]	0.447
Benzodiazepines	Categorical	Yes vs. no	2.21	[0.56-8.72]	0.259
SGLT2 inhibitors	Categorical	Yes vs. no	1.55	[0.21-11.45]	0.668
Thyroxine	Categorical	Yes vs. no	0.68	[0.09-5.10]	0.707
Diuretics	Categorical	Yes vs. no	1.13	[0.54-2.38]	0.725
Statins	Categorical	Yes vs. no	1.18	[0.55-2.54]	0.677
Erythropoietin	Categorical	Yes vs. no	0.67	[0.08-5.62]	0.720

Note. *Statistically significant at $p < 0.05$

Level of Education

Strong protection was provided by higher education (OR = 0.79; **Table 3**). Stern's cognitive reserve hypothesis was supported by the fact that only 3% of PhD holders showed impairment, compared to 33% of patients with secondary education (**Table 2**) [23]. Mendelian randomization studies have demonstrated that education may improve neural adaptability to insults related to CKD [24]. In contrast, it highlighted regional differences in CKD management by reporting weaker educational effects in European cohorts with universal healthcare [2].

Medications

Benzodiazepine use was linked to CI (p<0.00001; **Table 2**), which is consistent with [25], which cautioned against sedatives in CKD due to cumulative toxicity and delirium risks. SGLT2 inhibitors were associated with higher MoCA scores (p = 0.002; **Table 2**), consistent with the neuroprotective mechanisms proposed in [26]. This exciting result is of mental merit potential for patients with diabetes, contrary to other hypoglycemic medications, which can be recognized to affect cognitive function, and future research is needed to affirm these associations and discover underlying mechanisms. Impairment was predicted by thyroxine use (p = 0.003; **Table 2**), which may be a result of untreated hypothyroidism or over-replacement that exacerbates the cardiovascular strain [16]. ACEI, ARBS, beta-blockers, and statins did not show any significant associations, which may be because proper blood pressure management obscures the risks of HTN [16, 19].

Comorbidities and Loss of Function

Although HTN was common (81.2%; **Table 2**), it was not significant in adjusted models (OR = 1.22; **Table 3**). Antihypertensive medication confounding or cohort-wide blood pressure control could be the cause of this paradox (16) as the reasonable use of antihypertensive medications by most of our patients, which includes ACEI, angiotensin second receptor blockers, and beta-blockers, which may also reduce the effect of high blood pressure on cognitive function. The reason we did not find a significant impact in the regression model could be due to the confounding effects of other medications or inadequate facts on medicine adherence and dosing, as the data was retrieved from the electronic records for patients with inadequate information about medication adherence. In contrast to the polyvascular disease that was emphasized in [12], DM (54.9%) and CVD (36.6%) showed nonsignificant trends. The high baseline burden of comorbidity may limit the ability to detect incremental risk [5, 20]. LOF independently predicted impairment (OR = 3.46; **Table 3**), consistent with studies that associate frailty with inflammation and sarcopenia in CKD [21, 27]. Functional decline may exacerbate cognitive deficits by reducing cerebral perfusion or social engagement [15].

Socio-Economic Factor

Similar to [1], which highlighted the disproportionate burden of CKD in low-resource settings, lower income (< 500 JD) was associated with higher impairment rates (39.1%; **Table 2**). Occupational engagement was suggested as a buffer for cognitive reserve by the lower impairment rates of working patients (48.3% vs. 60.2% in non-workers; **Table 2**) [23].

This study is subject to several limitations. First, due to its cross-sectional design, it is impossible to establish causal relationships between the risk factors that have been identified and CI. Second, the results may not be as applicable to larger CKD populations, particularly those in different medical or geographic contexts, due to the single-center sample. Third, although the MoCA is a widely used screening tool, it does not provide a comprehensive neuropsychological evaluation, and its sensitivity may be influenced by cultural and educational factors. Finally, potential confounding variables such as depression, socio-economic status, and nutritional status that could have impacted this cohort's cognitive performance were not assessed.

CONCLUSION

Clinicians should be mindful of factors associated with CI in CKD patients and offer appropriate interventions to prevent or delay cognitive decline. For instance, patients with lower education levels may benefit from cognitive training and educational programs. In contrast, those with lower eGFR and higher CKD stages may benefit from optimal management of kidney function and related complications. Additionally, our study suggests that SGLT2 inhibitors may positively impact

cognitive function in CKD and DM patients, warranting further investigation through randomized controlled trials. This study emphasizes the importance of tailored interventions for patient care and the need for continued investigation of the complex association between CKD and cognitive function.

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Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

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