

# Cognitive Impairment and Associated Factors Among Chronic Kidney Disease Patients: A Comparative Cross-Sectional Study

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**Background:** Cognitive impairment is one of the public health problems affecting 50 million people in the world. Chronic kidney disease (CKD) patients are at high risk to develop cognitive impairment which leads to poor quality of life, difficulty in adhering to medications, increased risk of mortality, and health resource utilization. However, there is no study done on the prevalence of cognitive impairment and associated factors among chronic kidney disease patients in Ethiopia.

**Objective:** This study aimed to assess the prevalence of cognitive impairment and associated factors among chronic kidney disease patients at the University of Gondar Comprehensive Specialized and Felege Hiwot Referral Hospitals in 2020, Northwest Ethiopia, 2020.

**Methods:** An institution-based comparative cross-sectional study was conducted at the University of Gondar Comprehensive Specialized and Felege Hiwot Referral Hospitals in 2020. A systematic random sampling technique was used to select the study participants. Data were collected using standard tools. Data were checked for its completeness and entered into Epi data version 3.0 then exported into STATA 14. Multi-variable logistic regression analysis was employed to identify associated factors of cognitive impairment among CKD patients, and variables having a p-value of  $\leq 0.05$  were declared as significant.

**Results:** In this study, 116 CKD patients and 116 age, sex, and educational level matched controls were included with a response rate of 100%. The prevalence of cognitive impairment was 49.1% [95% CI (40%, 58.3%)] among CKD patients and 28.4% [95% CI (20.9%, 37.5%)] among controls. Independent predictors of cognitive impairment among CKD patients were estimated glomerular filtration (eGFR)  $< 60 \text{ mL/min/m}^2$  [AOR=3.9, 95% CI (1.1–14.74)], proteinuria [AOR=6.0, 95% CI (1.83–20.3)], age greater than 65 years [AOR=4.0, 95% CI (1.12–14.64)], and educational level of grade 8 and less [AOR= 4.7, 95% CI (1.22 -18.47)].

**Conclusion:** The prevalence of cognitive impairment among CKD patients was higher than healthy controls. Cognitive impairment was higher among CKD patients with eGFR  $< 60 \text{ mL/min/m}^2$ , proteinuria, educational level of grade 8 and less, and age greater than 65 years. Therefore, there is a need to have a regular evaluation and follow-up of CKD patients for cognitive impairment.

**Keywords:** cognitive impairment, chronic kidney disease, SMMSE

## Background

Chronic kidney disease (CKD) is characterized by progressive and irreversible damage to the kidney, which leads to the inability of the kidney to perform its function.<sup>1</sup> Recently, the prevalence of CKD has been rapidly increasing as a result of higher prevalence of hypertension, diabetes mellitus, and obesity.<sup>2</sup> A systematic

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review and meta-analysis done in the United Kingdom show that the prevalence of chronic kidney disease is 13.4%.<sup>3</sup> In Africa, a systematic review study done shows that the prevalence of CKD is 13.9%.<sup>4</sup> Institution-based studies in Ethiopia show that the prevalence of CKD ranges from 22.1% to 38.6%.<sup>5-7</sup>

Chronic kidney disease leads to hypertension, anemia, vascular dysfunction, uremia, proteinuria, systemic inflammation, and oxidative stress that are associated with cognitive impairment.<sup>8,9</sup> Cognitive impairment is when a person has trouble remembering, learning new things, concentrating, or making decisions which is a common problem affecting CKD patients.<sup>10</sup> The number of people living with severe cognitive impairment globally was 50 million in 2015. Of those 50 million, 60% of them living in low- and middle-income countries.<sup>11</sup> This severe cognitive impairment prevalence is expected to increase to 82 million in 2030 and 152 million by 2050.<sup>11</sup>

The prevalence of cognitive impairment in CKD patients ranges from 17% to 87% depending on severity.<sup>12-16</sup> Its prevalence among CKD patients is 20% in the United Kingdom,<sup>17</sup> 75.5% in China,<sup>18</sup> and 53.8% in India.<sup>19</sup> A comparative cross-sectional study in Nigeria showed that the prevalence of cognitive impairment CKD patients is 35.3% whereas for the control group it is 6%.<sup>20</sup> Those chronic kidney disease patients with cognitive impairment have an increased risk of death, poor quality of life, difficulty in adhering to medications, and worse quality of emotional well-being.<sup>21-29</sup> It is a major cause of morbidity and a determinant of the quality of life in the elderly chronic kidney disease patients.<sup>30,31</sup> Among hemodialysis patients it is also associated with an approximately two-fold increased risk of both mortality and dialysis withdrawal.<sup>32</sup>

Moreover, cognitive impairment also leads to increase costs for governments, communities, families, and loss of productivity.<sup>11,33</sup> In Ethiopia, there was no study done previously on its prevalence and associated factors among CKD patients. Therefore, this study was conducted to determine the prevalence and predictors of cognitive impairment among chronic kidney disease patients.

## Materials and Methods

### Study Setting and Period

An institution-based comparative cross-sectional study was conducted at the University of Gondar

Comprehensive Specialized and Felege Hiwot Referral Hospitals from February 2020 to April 30, 2020.

### Study Population

All adult CKD patients having follow-up at the University of Gondar Comprehensive Specialized and Felege Hiwot Referral Hospitals with all healthy adult patient's caregivers who came to the University of Gondar Comprehensive Specialized and Felege Hiwot Referral Hospitals matched for age, sex, and educational level were included in the study.

All CKD patients with visual, hearing, speaking difficulty, history of head trauma, AIDS, chronic liver disease, chronic obstructive pulmonary disease, and previous history of stroke were excluded from the study.

### Sample Size Calculation and Sampling Procedure

Sample size was determined by using two population proportion formula by taking

$P_1 = 51.9\%$ <sup>34</sup> and  $P_2 = 33.3\%$ <sup>35</sup> with  $Z_{\alpha} = 95\%$ ,  $Z_{\beta} = 80\%$ .

$$n_1 = \frac{\left[ Z_{\frac{\alpha}{2}} \sqrt{(r+1)\bar{p}\bar{q}} + Z_{1-\beta} \sqrt{rP_1Q_1 + P_2Q_2} \right]^2}{r(P_1 - P_2)^2} = 110$$

Where

$n_1$  = sample size for CKD,  $n_2$  = sample size of control

$P_1$  = proportion of cognitive impairment among CKD patients

$P_2$  = proportion of cognitive impairment among healthy individuals

$Z_{\beta}$  = standard normal variate for power

$Z_{\alpha}$  = standard normal variate for the level of significance

$r$  = the ratio of CKD group to the control group sample size

In this study  $r=1$  since equal sample size for both groups was taken.

$$\bar{p} = \frac{P_1 + P_2}{2}$$

$$n_2 = n_1 \times r = 110$$

By using this formula for each group the sample size was 110. By adding a non-response rate of 5%, the total sample size for each group was 116. During the data collection period 360 and 400 patients were encountered at follow-up clinic of the University of Gondar Comprehensive Specialized and

Felege Hiwot Referral Hospitals, respectively. Using the proportionate random sampling technique 55 and 61 CKD patients were selected from the University of Gondar Comprehensive Specialized and Felege Hiwot Referral Hospitals, respectively, using systematic random sampling techniques with a K value of 7. The first patient was the first one selected using the lottery method; then, every seventh patient was interviewed. For the control group participants matched with age, sex, and educational status were selected using consecutive sampling technique after selection of CKD patients (Figure 1).

## Operational Definitions

Chronic kidney disease is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health.<sup>1</sup>

The estimated glomerular filtration rate (eGFR) was calculated using the cockcroft-gault formula.<sup>36</sup>

Cognitive impairment: we have used the Standardized Mini Mental State Examination (SMMSE) tool.

Using this tool, those participants with educational level of  $\leq$  grade 8 scores 22 and less and participants with educational level of  $\geq$  grade 9 scores 24 and below from the total of 30 scores of SMMSE, had cognitive impairment.<sup>37</sup>

Social support was assessed by the Oslo Social Support Scale which scores out of 14 with 3–8 score poor social support, 9–11 score moderate social support, and 12–14 score strong social support.<sup>38</sup>

Anemia was defined as a hemoglobin concentration below 13 g/dl in men and below 12 g/dl in women.<sup>39</sup>

Khat chewer: individuals who had ever used khat at least once in their lifetime.

Cigarette smoker: individuals who had ever used cigarette at least once in their lifetime.

Alcohol drinker: the proportion of individuals who had ever used alcohol drinks such as tela, tej, katicala/areke, beer, wine, or other drinks that can cause intoxication at least once in their lifetime.<sup>40</sup>

Comorbidity: the presence of one or more of a documented case of the following diseases: hypertension, cardiovascular diseases, and diabetes mellitus.

Underweight: a person having a body mass index (BMI) of  $<18.5 \text{ kg/m}^2$ .

Normal weight: a person having BMI of  $18.5 \text{ kg/m}^2 - 24.9 \text{ kg/m}^2$ .

Overweight: a person having BMI of  $25 \text{ kg/m}^2 - 29.9 \text{ kg/m}^2$ .

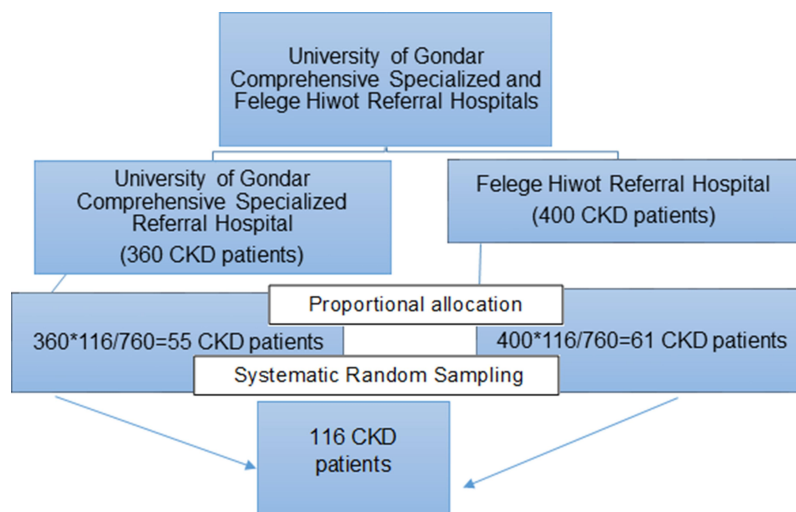
Obese: a person having BMI of  $\geq 30 \text{ kg/m}^2$ .<sup>35,41</sup>

Hypertension: a person having systolic blood pressure of 140 mmHg and/or diastolic blood pressure of 90 mmHg and above<sup>42</sup> or who is on antihypertensive treatment.

Proteinuria: the presence of protein in the urine,  $\geq +1$  in the dipstick.<sup>43</sup>

## Data Collection Procedure and Tools

Data were collected using interviewer-administered structured questionnaire which consists of sociodemographic characteristics, substance use history, Medical Record Review, physical measurements (weight, height, and blood pressure), and Standardized Mini-Mental State Examination tool (SMMSE tool) for cognition



**Figure 1** A flow chart shows the proportion of patients taking from the University of Gondar Comprehensive Specialized and Felege Hiwot Referral Hospitals, 2020.

assessment.<sup>37,44</sup> A SMMSE tool was a cognitive impairment screening tool scored out of 30 which consists of questions that evaluate orientation (10 points), registration (3 points), attention, and calculation (5 points), recall (3 points), language and praxis (9 points).<sup>37</sup> A digital blood pressure machine was used for measuring blood pressure and blood pressure was measured in a sitting position after a rest for 30 minutes. Again, weight and height were measured using height measuring stand with weighing machine.

## Data Analysis Procedure

The collected data were checked for their completeness and coded then entered into Epi data version 3.0 then exported to STATA 14 for analysis. Descriptive statistics; frequency, percentage, and bar graph were used for categorical variables while median, interquartile range, mean, and standard deviation were used for continuous variables. Independent *t*-test was used to compare the mean difference for continuous variables of study groups whereas  $\chi^2$ -test was used to show an association of the categorical variables among study groups. Both bi-variable and multi-variable logistic regression analyses were done. Variables associated with cognitive impairment at *p*-value of  $<0.25$  level in the bi-variable logistic regression were included in the multi-variable regression model. In the multi-variable logistic regression, variables having a *p*-value of  $\leq 0.05$  with a 95% confidence interval were declared as significantly associated with cognitive impairment. Finally, model fitness was checked by Hosmer and Lemeshow test. Using this test the final multiple logistic regression model *p*-value was 0.568, since it was greater than 0.05 the model was fitted. Cronbach's alpha test for the SMMSE tool was done with a reliability coefficient value of 0.78 which shows good reliability of the tool.

## Data Quality Management

To assure the data quality, high emphasis was given to designing the data collection tool. The questionnaire was translated to Amharic language by a language expert and retranslated back to English language by another expert for its consistency. Training regard to SMMSE tool, Medical Record Review, and way of measuring procedure to blood pressure height and weight was given for the data collectors by the principal investigator for one day. One week before data collection, the questionnaire was pre-tested on 12 study participants (6 for each group) at the Tibebe Ghion Specialized Hospital at Bahir Dar city.

Based on the pretest finding, necessary modification of questionnaire was taken. Throughout the data collection period, data collectors were supervised by the supervisor and principal investigator. For prevention of COVID-19 transmission, data collectors used protective materials such as face masks, sanitizers, and gloves with physical distance.

## Results

### Sociodemographic Characteristic of Study Participants

A total of 232 study participants with an equal proportion of CKD patients and healthy controls (116 each) were involved with a 100% response rate. The median age for both CKD patients and healthy control was 57.5 years with interquartile range of 29.5 and 30 years, respectively. The majority of the CKD patients attained primary school or less 72 (62%) were male 75 (64.7%), Orthodox Christianity follower 100 (86.2%), married 69 (59.5%), and employed 63 (54.3%). Similarly, most of the control group participants attained primary school or less 70 (60.3%) were male 75 (64%), Orthodox Christianity follower 87 (75%), married 96 (82.8%), and employed 62 (53.5%). The mean SMMSE score of the CKD patients was 22.3 (SD $\pm$ 5.1) whereas for the control participants it was 24.1 (SD $\pm$ 4.6). The lifetime prevalence of khat chewing, alcohol use, and cigarette smoking among CKD patients were 1 (0.9%), 9 (7.8%), and 1 (0.9%) respectively whereas for control it was 4 (3.5%) for khat chewing, 31 (26.7%) for alcohol intake and 2 (1.72%) for cigarette smoking.

There were no significant differences between the study groups concerning a body mass index, substance use, religion, residence, social support score, income level and occupation. However, marital status, and mean SMMSE scores among study groups had a significant difference. Cognitive impairment also had a significant difference between the study groups ( $\chi^2=10.4563$ , *p*= 0.001) (Table 1).

### Clinical Characteristics of CKD Patients

The mean creatinine and urea level among CKD patients were 2.2 mg/dl (SD $\pm$ 2.6) and 57.3 mg/dl (SD $\pm$ 14.2), respectively. Fifty-eight (50%) patients had proteinuria and 72 (62.1%) of them were anemic. Sixty-eight (59.5%) patients had an eGFR of less than 60 mL/min/m<sup>2</sup> from those, 24 (20.7%) patients had an eGFR of less than

**Table I** Description and Comparisons of Sociodemographic and Clinical Characteristics of CKD Patients and Controls at University of Gondar Comprehensive Specialized and Felege Hiwot Referral Hospitals, 2020 (n=232)

Variables	Category	Study Groups (n=232)		t/X <sup>2</sup> Value	p-value
		CKD Group (n=116) Number (%)	Control Group (n=116) Number (%)		
Age (in Years)	Mean±SD	54.1±17	54.1±17.1	0.011 <sup>c</sup>	0.990
Sex	Male	75(64.7)	75(64.7)	0.000	1.000
	Female	41(35.3)	41(35.3)		
Religion	Orthodox	100(86.2)	87(75)	5.857	0.115
	Muslim	11(9.5)	21(18.1)		
	Protestant	5(4.3)	8(6.9)		
Educational level	≤8 grade	72(62)	70(60.3)	0.128	0.938
	Grade 9–12	19(16.4)	21(18.1)		
	College and above	25(21.6)	25(21.6)		
Marital status	Single	12(10.3)	7(6.0)	15.850	0.001
	Married	69(59.5)	96(82.76)		
	Divorced	15(12.9)	6(5.2)		
	Widowed	20(17.2)	7(6)		
Occupation	Employed	63(54.3)	62(53.5)	3.284	0.350
	Merchant	21(18.1)	28(24.1)		
	Farmer	19(16.4)	11(9.5)		
	Housewife	13(11.2)	15(12.9)		
Monthly Income (ETB)	≤1500	31(26.7)	20(17.4)	4.378	0.223
	1501–2501	8(6.9)	10(8.6)		
	2502–3502	24(20.7)	20(17.2)		
	≥3503	53(45.7)	66(56.9)		
Residence	Urban	79(68.1)	87(75)	10.355	0.244
	Rural	37(31.9)	29(25)		
Social support	Poor social support	24(20.7)	28(24.1)	0.680	0.712
	Moderate support	31(26.7)	33(28.4)		
	Strong support	61(52.6)	55(47.4)		
BMI (Kg/m <sup>2</sup> )	Mean±SD	22.30±2.90	22.09±2.66	−0.559 <sup>c</sup>	0.576
	18.5–24.9	96(82.7)	8(84.5)		
	≥25	61(58.1)	18(15.5)		
SMMSE Score	Mean±SD	22.3±5.1	24.1±4.6	2.779 <sup>c</sup>	0.005
Cognitive	Yes	57(49.1)	33(28.4)	10.456	0.001
Impairment	No	59(50.9)	83(71.6)		

**Abbreviations:** SD, standard deviation; ETB, Ethiopian birr; SMMSE, Standardized Mini Mental State Examination; <sup>c</sup>, t-test.

30 mL/min/m<sup>2</sup>. Forty-seven (40.5%) patients had eGFR 60mL/min/m<sup>2</sup> and above from those patients, 22 (19%) had eGFR 90mL/min/m<sup>2</sup> and above. At the time of data collection, the mean duration of disease was 2.7 years (SD

±2.1) and 81% of CKD patients have been living with CKD for 4 years and lower. Hundred-one (87.1%) CKD patients had comorbidity. With regard to the treatment, all CKD patients had relied on supportive treatment. The blood



**Table 2** Factors Associated with Cognitive Impairment Among CKD Patients at the University of Gondar Comprehensive Specialized and Felege Hiwot Referral Hospitals, 2020

Variables	Category	Total N (%)	Cognitive Impairment		OR (95% CI)	
			Yes (n=57) N (%)	No (n=59) N (%)	COR	AOR
Age (year)	>65	36(31.1)	26(61.2)	10(38.8)	4.1 (1.74–9.68)	4.0(1.12–14.64)*
	≤65	80(68.9)	31(27.8)	49(72.2)	1	1
eGFR	≥60mL/min/m <sup>2</sup>	47(40.5)	9(19.2)	38(80.8)	1	1
	<60mL/min/m <sup>2</sup>	69(59.5)	48(69.6)	21(30.4)	9.7(3.96–23.48)	3.9(1.1–14.74)*
Urea (mg/dl)	Mean ± SD	57.3(±14.2)	60.1±4.4	54.7±2.8	1.0(1.00–1.06)	1.0(0.97–1.05)
Proteinuria	No	58(50)	12(20.7)	46(79.3)	1	1
	Yes	58(50)	45(77.6)	13(22.4)	13.3(5.47–32.17)	6.0(1.83–20.30)*
Comorbidity	No	15(12.9)	4(26.7)	11(73.3)	1	1
	Yes	101(87.1)	53(52.5)	48(47.5)	3.0(0.91–10.17)	1.4(0.21–7.50)
Anemia	No	44(37.9)	10(22.7)	34(77.3)	1	1
	Yes	72(62.1)	47(65.3)	25(34.7)	6.4(2.72–15.04)	2.6(0.82–8.10)
Sex	Male	75(64.7)	40(48.1)	35(51.9)	1	1
	Female	41(35.3)	17(58.8)	24(41.2)	0.62(0.28–1.33)	0.8(0.24–2.49)
Educational level	≤Grade 8	72(60)	42(59.3)	30(41.7)	1.8(0.71–4.46)	4.7(1.22–18.47)*
	Grade 9–12	19(26.7)	4(21.7)	15(78.4)	0.3(0.07–1.32)	0.8(0.14–4.72)
	College and above	25(13.3)	11(44)	14(56)	1	1
Social support	Poor	24(20.7)	14(58.3)	10(41.7)	2.5(0.94–6.51)	2.7(0.78–10.92)
	Moderate	31(26.7)	21(67.7)	10(32.3)	3.7(1.49–9.31)	2.2(0.56–7.26)
	Strong	61(52.6)	22(36.1)	39(63.9)	1	1

Note: \*Statistically significant at P≤0.05.

Abbreviations: AOR, adjusted odd ratio; COR, crude odd ratio; CI, confidence interval; N, number; SD, standard deviation.

pressure of 106 (91.4%) CKD patients was within the normal range at the time of data collection (Table 2).

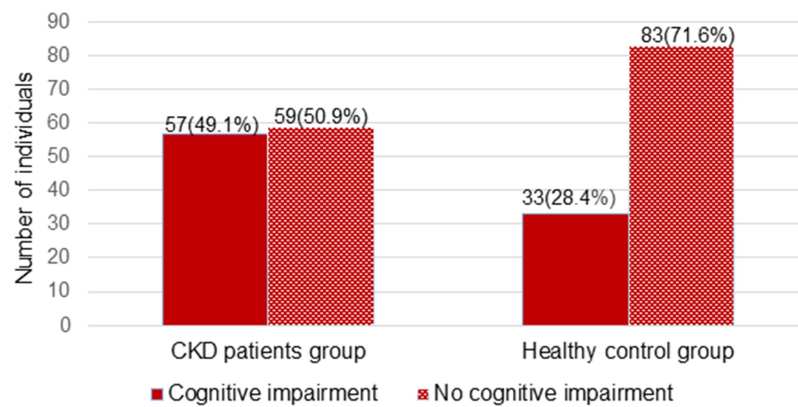
## Comparison of Cognitive Impairment Among CKD Patients and Controls

The overall prevalence of cognitive impairment among CKD patients was 49.1% [95% CI (40%, 58.3%)], and among healthy controls it was 28.4% [95% CI (20.9%, 37.5%)]

(Figure 2). The mean SMMSE score of CKD patients was significantly lower than healthy controls (22.3 versus 24.1,  $p=0.001$ ).

## Predictors of Cognitive Impairment Among CKD Patients

Among variables entered into binary logistic regression age, educational level, social support, sex, eGFR, urea level, proteinuria, anemia, and comorbidity were associated with cognitive impairment at  $p$ -value of  $<0.25$ . However, in multi-variable logistic regression analysis four variables were significantly associated with cognitive impairment at  $p$ -value of  $\leq 0.05$ . Those variables were, low eGFR, proteinuria, educational level, and age. Chronic kidney disease patients with eGFR  $<60$  mL/min/m<sup>2</sup> were 3.9 times [(AOR=3.9, 95% CI (1.1–14.74)]



**Figure 2** Prevalence of cognitive impairment among chronic kidney disease patients and healthy controls at the University of Gondar Comprehensive Specialized and Felege Hiwot Referral Hospitals, 2020.

more likely to develop cognitive impairment than those CKD patients having  $\text{eGFR} \geq 60 \text{ mL/min/m}^2$ . Chronic kidney disease patients with proteinuria were 6 times [AOR=6.0, 95% CI (1.83–20.30)] more likely to develop cognitive impairment than proteinuria negative CKD patients. Chronic kidney disease patients with age  $>65$  years were 4.0 times [AOR=4.0, 95% CI (1.12–14.64)] more likely to develop cognitive impairments relative to CKD patients with age  $\leq 65$  years. Those CKD patients attaining grade 8 and lower were 4.7 times [AOR= 4.7, 95% CI (1.22–18.47)] more likely to develop cognitive impairment than those patients attaining college and above (Table 2).

## Discussion

This research tried to offer insight on the magnitude of cognitive impairment and its significant predictors among CKD patients in comparison with healthy individuals.

In this study, the prevalence of cognitive impairment was 49.1% [95% CI (40%–58.3%)] among CKD patients. It was similar to the study conducted in Nigeria (51.9%) and India (53.8%).<sup>19,34</sup> The possible reason for this cognitive impairment among CKD patients might be due to retention of different neurotoxins. Besides damaging neurons, different waste product accumulation in the blood may result in signaling disturbance in the brain regions, particularly in those involved in cognitive activities.<sup>45–47</sup> However, a cross-sectional study conducted in the United Kingdom reported a lower prevalence (20%) of cognitive impairment than the findings of this research.<sup>17</sup> This difference might be because of a large proportion of participants with a higher educational level were included in the United Kingdom study, which might be lower the prevalence of cognitive impairment.<sup>19</sup> Compare to study done in

China (75.2%) this research finding was low due to the old age of study participants in China.<sup>18</sup> Many studies showed that being an old age was a risk factor for cognitive impairment due to the neurotransmitter derangement during aging.<sup>25,48</sup>

The prevalence of cognitive impairment among healthy controls in this study was 28.4% [95% CI (20.9–37.5%)] which was similar to the study done in Central Africa republic (25%), and Cameroon (33.3%).<sup>35,49</sup> But findings from Nigeria (6.3%), Botswana (9%), and Congo (18.8%)<sup>20,49</sup> reported a lower prevalence of cognitive impairment. The possible reason for this difference might be due to variations in the tool used to assess cognitive impairment and sociodemographic differences of study participants. Community screening interview for dementia tool was used in Nigeria, Congo, and Botswana.

This study showed a higher prevalence of cognitive impairment among CKD patients than healthy controls. This finding was similar to the study done in Nigeria.<sup>50</sup> It might be because of the effect of waste product retention in blood like urea and electrolyte due to a decrement of GFR or abnormality of glomerular capillary. Chronic kidney disease is also associated with many comorbidities that may lead to cognitive impairment like DM, hypertension, and anemia.

Decrease glomerular filtration rate was a significant predictor of cognitive impairment among CKD patients which was similar to other studies.<sup>20,51,52</sup> Patients who had  $\text{eGFR} < 60 \text{ mL/min/m}^2$  were 3.9 times more likely to develop cognitive impairment than those patients with  $\text{eGFR} \geq 60 \text{ mL/min/m}^2$ . This could be due to the effect of neuronal toxic waste product accumulation in blood as glomerular filtration decreases. Specifically, increased

levels of uremic toxins, neuropeptide Y, increased parathyroid hormone, reduced levels of kidney neurotrophin, homocysteine, and vascular damage in the central nervous system may induce cognitive impairment. Noradrenergic, serotonergic, histaminergic neurons, and acetylcholinergic neurons in the encephalic trunk and hypothalamus are responsible for initiating the activity of the cortex and several subcortical regions. Those regions are responsible for sleep-wake cycles, memory, and attention. But those neurons might be sensitive to the concentration of uremic neurotoxins, result alterations in sleep patterns, mood, and attention in CKD which might lead to the development of cognitive impairment in CKD patients.<sup>9,45–47</sup> Anemia which is common in CKD patients was associated with tissue hypoxia and decreased oxygen delivery to the brain which might lead to cognitive impairment. Erythropoietin is a neuroprotective agent so, its decrement in CKD patients might lead to the exposure of neurons to a neurotoxic substance.<sup>20,53</sup> In addition to this electrolyte, and acid-base imbalance in CKD patients might be also the cause of cognitive impairment.<sup>45</sup>

Proteinuria was significantly associated with a decline in cognition. The odds of cognitive impairment was six times higher among CKD patients with proteinuria than patients with proteinuria negative. This result is in line with a systematic review and meta-analysis done in Greece.<sup>54</sup> Proteinuria is a marker of generalized endothelial dysfunction and microvascular disease. It is associated with both brain atrophy and white matter demyelination with axonal loss<sup>55</sup> which might be a possible reason for the risk of cognitive impairment in proteinuria.

Those patients who attained grade 8 and lower were more likely to develop cognitive impairment than those patients attaining college and above, which is in line with the study done in Jamaica.<sup>56</sup> The reason might be due to formal education provides the necessary knowledge, understanding, skills, and competencies which constantly improve cognitive function.<sup>57</sup> Education may create cognitive reserves by increasing synapse number or vascularization.<sup>58</sup>

Increasing age was significantly associated with cognitive impairment. This finding is in agreement with other studies.<sup>20,35,49,51,52,56,58</sup> This might be due to decline in gray matter volume, neurotransmitter, and neocortical synapses during aging which result in cognitive impairment.<sup>59–61</sup>

## Limitation of the Study

The SMMSE tool is used only for screening purposes, so it is impossible to reach a diagnosis using this tool.

## Conclusion

The findings of this study showed a higher prevalence of cognitive impairment among CKD patients than healthy controls. The independent predictors of cognitive impairment among CKD patients were eGFR <60 mL/min/m<sup>2</sup>, proteinuria, educational level of grade 8 and less, and age greater than 65 years. Therefore, there is a need to have a regular evaluation and follow-up of CKD patients for cognitive impairment.

## Abbreviations

BMI, Body Mass Index; CKD, Chronic Kidney Disease; CVD, Cardiovascular Disease; DM, Diabetes Mellitus; eGFR, Estimated Glomerular Filtration Rate; GFR, Glomerular Filtration Rate; SMMSE, Standardized Mini Mental State Examination.

## Data Sharing Statement

The data will be available upon request from the corresponding author.

## Ethics Approval and Consent to Participate

This study was conducted under the Declaration of Helsinki. Ethical clearance was obtained from the Institutional Review Board of the University of Gondar with approval number SOM/1849/06/2012. A permission letter was obtained from the University of Gondar Comprehensive Specialized and Felege Hiwot Referral Hospitals. Written Informed consent was obtained from the study participants to start data collection. The privacy and confidentiality of information were also kept properly.

## Consent for Publication

Not applicable.

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## Author Contributions

All authors made substantial contributions during conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

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## Disclosure

None of the authors have any conflicts of interest for this work to declare.

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