

Original Article: Clinical Predictors of Neurocognitive Status in Children With Chronic Kidney Disease



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ABSTRACT

Background and Aim: Chronic kidney disease (CKD) is often associated with a variety of cognitive deficits. This will have significant lifelong implications. Therefore, we measure the clinical predictors of cognitive impairment.

Methods: This cross-sectional study was conducted in a third-level hospital from October 2017 to December 2018. A total of 41 patients with CKD stage III to V and V on dialysis, aged 6 to 14 years of both sexes were included in this study. CKD was staged according to the estimated glomerular filtration rate (eGFR). The Wechsler intelligence scales for children-revised (WISC-R) were provided as an individualized measure of verbal and performance abilities. Then individual score was compared among the study population.

Results: A total of 41 patients were studied. The Mean±SD age was 10.35±2.19 years. The majority were male (56%) and the male-to-female ratio was 1.3:1. Full-scale intelligence quotient (IQ) deficits were found in 31 patients (75.6%) and most of them had mild cognitive deficits (96.8%). Among them, verbal IQ deficit was found in 7 patients (17.1%), performance IQ deficit in 6(14.6%), and combined IQ deficit in 18(43.9%). IQ score did not depend on the severity of the disease. The duration of the disease was longer and the age at initiation of renal replacement therapy (RRT) was lower, for those with the cognitive deficit, was not significant. School attendance and performance were significantly poor in cognitive deficit patients but anemia and hypertension had no significant impact.

Conclusion: The mild cognitive deficit was often associated with childhood CKD but not related to the severity of the disease. Therefore, the cognitive function should be routinely screened and monitored during the evaluation of children with CKD.

Keywords: Chronic kidney disease (CKD), Cognitive deficits, Intelligence quotient (IQ)

Introduction



According to the kidney disease improving global outcome (KDIGO 2012), chronic kidney disease (CKD) is defined as abnormalities of kidney structure or function, persisting for 3 months. The

incidence and prevalence of CKD are reported to be increasing worldwide, regardless of age, sex, and race. In children, the incidence is 3.0-12.1 cases per million child population. On the other hand, the prevalence of CKD among children younger than 16 years old in the Indian population is 1.5-3.0 per million child populations [1]. CKD can be classified into five stages based

on the estimated glomerular filtration rate (eGFR). End-stage renal disease (ESRD) is the most advanced form of CKD and needs renal replacement therapy in the form of dialysis (peritoneal or hemodialysis) or transplantation. In the early stages of CKD (stage I and II), patients may remain asymptomatic. Therefore it does not interfere with the patient's daily activities. But in advanced stages of CKD (stages III, IV, and V), patients develop overt sign-symptoms of disease [2] and complications, such as increased incidence of cardiovascular disease (CVD), hyperlipidemia, anemia, and mineral bone disease (CKD-MBD) [3]. The effects of high stages of CKD on a child's activities, development, and quality of life are complex. Therefore, children with CKD should be assessed for these complications and receive optimal treatment to reduce mortality and morbidity.

Neurocognitive problems have been well documented in children and adults with CKD [4]. The prevalence of cognitive impairment is high in CKD, ranging from 17% to 87% depending on the severity of the disease and involvement of the cognitive domain [5]. Particularly in children, brain development is quite rapid during early childhood and its performance changes as the child grows. Therefore, any disruption of neurodevelopmental processes by kidney disease is likely to affect a variety of cognitive impairments, including lower intellectual function, memory deficits, academic difficulties, and deficits in executive functioning [6]. This will have significant lifelong implications as they move into adulthood. These are commonly seen in any stage of CKD and are generally associated with complications and a poorer prognosis. The mechanisms involved have not been established yet but some factors such as neuronal damage by uremic toxins, cerebrovascular ischaemic lesions, oxidative stress, chronic inflammation, anemia, hyperhomocysteinaemia, and endothelial dysfunction may play a critical role.

In CKD, different longitudinal and cross-sectional studies have shown conflicting data on neurocognitive functions. Some studies have identified lower nonverbal intelligence quotient (IQ) and motor performance in children with kidney disease and some have found no significant differences in memory between children with and without CKD. The extent and patterns of neurocognitive and academic impairment in children may also vary with the progression of CKD. Increased disease severity, longer duration of CKD, poor nutritional status and growth deficit, and early disease onset were identified as potential risk factors for poorer neurocognitive development. Moreover, children with CKD are at risk for CNS problems, such as atrophy and infarcts. The

frequency of these lesions is high in children with a history of vascular insults due to hypertensive crisis or prolonged dependence on dialysis. Lande et al. showed that hypertension and anemia were significantly associated with lower neurocognitive scores indicating problems with short-term memory, attention, and concentration. The overall IQ score for children treated with dialysis seems to be lower than that of children without dialysis and those with kidney transplantation [7]. Therefore identifying patients with cognitive impairment is a crucial step to improve quality of life and mitigate the morbidities caused by this condition. It seems logical that the degree of cognitive impairment may be proportional to the severity of CKD, but the data do not yet support this. To our knowledge, no study in Bangladesh has yet focused on identifying CKD patients who are most at risk for cognitive problems. Therefore, this study was conducted to identify the relationship between clinical aspects of CKD and selected neurocognitive test scores in a sample of pediatric patients. Moreover, this study clarifies specific clinical risk factors for subsequent neurodevelopmental dysfunction in children.

Materials and Methods

This cross-sectional descriptive study was conducted in the department of pediatric nephrology, [Bangabandhu Sheikh Mujib Medical University \(BSMMU\)](#), Dhaka, Bangladesh. Forty-one childhood CKD patients, stage 3-5D (aged 6-14 years of both sexes), newly diagnosed or previously diagnosed, regardless of the cause of CKD, admitted in the inpatient or outpatient department were included in this study from October 2017 to December 2018. Children with cognitive impairment other than renal cause, patients who are medically unfit to perform the cognitive assessment, and with profound developmental delay were excluded from this study.

After a detailed history, physical examination, and relevant investigations, psychological tests were performed. eGFR was calculated by the modified Schwartz equation (Equation 1) and CKD was staged according to eGFR.

Modified Schwartz equation

Equation 1: $eGFR = 0.413 \times (\text{height}/S. \text{creatinine})$,

where height is expressed in centimeter and serum creatinine in mg/dL.

The basic data of patients, including gender, present age, age at onset of CKD, duration of CKD, duration of dialysis (if pt on hemodialysis), hypertensive or nor-

motensive, frequency of dialysis, and treatment history were recorded. All dialysis patients were evaluated in the middle of the week. Neuropsychological evaluation was conducted by Wechsler intelligence scales for children-revised (WISC-R) [8] in the institute of pediatric neuro-disorder and autism (IPNA), BSMMU, Shahbag, Dhaka. This evaluation was conducted by a single psychologist.

It is designed as a comprehensive measure of cognitive ability for children, including verbal intelligence quotient (VIQ), performance intelligence quotient (PIQ), and full-scale IQ (FSIQ) scores. Approximately 50-75 minutes were required to administer a regular battery of 10 tests. The WISC-R is a collection of 10 distinct subtests divided into two scales, a verbal scale and a performance scale. The five verbal scale tests use language-based items, while the five performance scales use visual-motor items that are less dependent on language. Five of the subtests in each scale produce scale-specific IQ scores, and 10 subtest scores produce a FSIQ. These scores have a Mean±SD of 10±3. The scaled scores are combined to produce scores for VIQ, PIQ, and FSIQ. The IQ scores have a Mean±SD of 100±15 (David Wechsler, 1974). FSIQ is the summation of VIQ and PIQ tests. Only VIQ deficit means that the patient has a VIQ deficit and PIQ is borderline or average and a PIQ deficit means that the patient has a PIQ deficit but VIQ is intact. Those patients who had both VIQ and PIQ deficits were called combined IQ deficits.

The verbal scale test includes 5 subtests:

1. Information
2. Similarities
3. Arithmetic
4. Vocabulary
5. Comprehension

Performance scale test includes 5 subtests:

1. Picture completion
2. Picture arrangement
3. Block design
4. Object assembly
5. Coding

Description of Wechsler intelligence scales for children-revised (WISC-R) subtests: verbal scale test:

1. Information: patients were asked to answer questions that address a wide range of general knowledge topics.
2. Similarities: patients were asked to describe how two words representing common objects or concepts are similar.
3. Arithmetic: patients were asked to mentally solve a variety of orally presented arithmetic problems within a specified time limit.
4. Vocabulary: patients were asked to name pictures or provide definitions for words.
5. Comprehension: patients were asked to answer a series of questions based on their understanding of general principles and social situations.

Performance scale test:

6. Picture completion: patients were asked to view a picture and name the essential missing part of the picture within a specified time.
7. Picture arrangement: patients were asked to arrange both a random and a nonrandom arrangement of pictures and mark target pictures within a specified time limit.
8. Block design: patients were asked to replicate a set of modeled or printed two-dimensional geometric patterns using red-and-white blocks within a specified time limit.
9. Object Assembly: Patients were asked to arrange a randomly arranged picture within a specified time limit.
10. Coding: The examinee was requested to copy symbols paired with geometric shapes or numbers using a key within a specified time limit.

As a rule, no one other than the child and the examiner should be in the room during the test. The presence of a stranger or a relative may inhibit the child's spontaneity and result in an invalid assessment of his intelligence. Scores were categorized as:

- § Average (115-85),
- § Borderline (84-70),
- § Mild mental retardation (69-50),

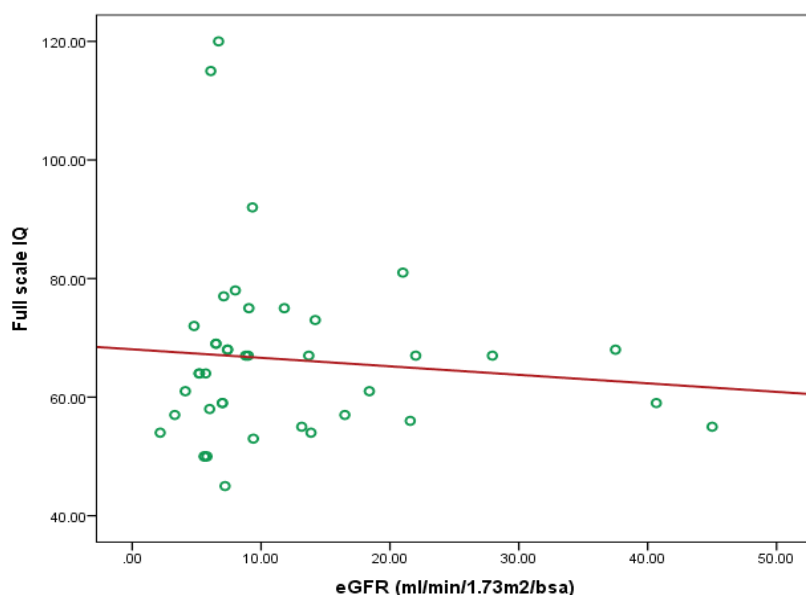


Figure 1. Stage wise distribution of study population

§ Moderate mental retardation (49-35),

§ Severe mental retardation (20-34),

§ <20 indicating profound impairment.

The individual scores were then compared among the study population.

Test score >69 was considered without cognitive deficit. In this study, the cognitive deficit was counted from <69 to downwards. 30

For dialysis

The score was categorized as: average (115-85), borderline (84-70), mild mental retardation (69-50), moderate mental retardation (49-35), severe mental retardation (20-34), <20 indicating profound impairment. Test score > 69 is considered without cognitive deficit. In this study, the cognitive deficit is counted from <69 to downwards.

After case selection informed written consent was obtained from each patient or his/her parents participating in the study. University institutional review board approved this study, including the consent procedure.

Statistical analysis

All variables are presented as Mean±SD. Continuous variables were analyzed using the student's t-test. Qualitative variables and correlations were analyzed using Pearson's chi-square test and Pearson's correlation coefficient analysis (two-tailed probability), respectively.

Non-parametric variables were analyzed using Spearman's rank correlation coefficient analysis. The statistical analysis was performed using SPSS software, version 22. $P \leq 0.05$ was considered significant.

Results

A total of 41 patients were studied. The Mean±SD age was 10.35 ± 2.19 years. The majority were male (56%) and the male-to-female ratio was 1.3:1 (Table 1). Most patients came from rural areas (65.9%). Most patients were from a rural area (65.9%). Anemia and hypertension are present in 80.4% and 63.4%, respectively. Causes of CKD include hypoplastic kidney (34.1%), glomerulonephritis (29.3%), obstructive uropathy (17%), single kidney (4.9%), and others (14.6%). Out of 41 patients, stage III, IV, VND, and VD were 9.8%, 14.6%, 26.8%, and 48.8%, respectively (Figure 1).

FSIQ deficits were observed in 31 patients (75.6%) and most of them had mild cognitive deficits (96.8%). Among them, a VIQ deficit was observed in 7 patients (17.1%), a PIQ deficit in 6 (14.6%), and a combined IQ deficit in 18 (43.9%) (Table 2). In CKD stage III, all 4 patients (100%) had cognitive deficits, among which only VIQ, PIQ, and FSIQ deficits were observed in 50%, 25%, and 100%, respectively. In CKD stage IV, out of 6 patients, 5 patients (83.3%) had FSIQ deficit, among which only 25% VIQ deficit was observed. In CKD stage VND, out of 11 patients, a total of 6 patients (54.6%) had FSIQ deficit. Among them, only PIQ deficit was found in 27.3%. In stage VD, a total of 16 patients (80%) had FSIQ deficit, among which VIQ and PIQ deficits were

Table 1. Demographic and clinical characteristics of the study subjects (n=41)

Variables		No. (%)
Age (y)	≤10	22(53.7)
	>10	19(46.3)
Mean±SD (min-max)		10.35±2.19 (6.33–14.0)
Gender	Male	23(56.1)
	Female	18(43.9)
Residence	Rural	27(65.9)
	Urban	14(34.1)
Father's education	Illiterate	7(17.1)
	Primary	13(31.7)
	Secondary	7(17.1)
	Higher secondary	4(9.8)
	Graduation	10(24.4)
Mother's education	Illiterate	4(9.8)
	Primary	14(34.1)
	Secondary	15(36.6)
	Higher secondary	1(2.4)
	Graduation	7(17.7)
	Anaemia	33(80.4)
Primary diseases	Hypertension	26(63.4)
	Hypoplastic kidney	14(34.1)
	Glomerulonephritis	12(29.3)
	Obstructive uropathy	7(17)
	Single kidney	2(4.9)
	Others	6(14.6)

observed in 20% and 10%, respectively (Table 3). In all stages of CKD, mild mental retardation was observed in 30 subjects (96.8%) out of 31 cognitive deficit patients. Only one patient had moderate mental retardation but the was not significant (Table 4 and Figure 2). No patient had a severe or profound IQ deficit.

The dialysis patients include 20 people and the non-dialytic patients included 21 people. Among dialysis patients, FSIQ deficit was observed in 16 patients (80%) and individual VIQ and PIQ deficits were observed in

4(20%) and 2(10%), respectively. In non-dialytic patients, FSIQ deficit was observed in 15 patients (71.4%) and individual VIQ and PIQ deficits were observed in 3(14.3%) and 4(19%), respectively. Statistical analysis of the cognitive status of dialytic and non-dialytic patients was not significant (Figure 3).

The duration of the disease was more and the age at initiation of renal replacement therapy (RRT) was low, for those with the cognitive deficit, but was not significant (Table 5). School attendance and performance were

Table 2. Cognitive status in study subjects (n=41)

Cognitive Status	No. (%)
Full-scale IQ	31(75.6)
Verbal IQ (only)	7(17.1)
Performance IQ (only)	6(14.6)
Combined IQ	18(43.9)

IQ: Intelligence quotient.

significantly poor in patients with a cognitive deficit but anemia and hypertension had no significant impact (Table 6). The study shows that among all patients, 10 patients did not go to school, and most of the patients whose parents' education level was undergraduate, economical status below average, higher stages of CKD (stage VD, 60%), and frequent dialysis (Table 7).

Discussion

This study examined the current neuro-cognitive profile of children with CKD receiving conservative treatment or dialysis. A total of 41 children aged 6-14 years with CKD were enrolled in this study. No patient was in stage I, and stage II CKD. Out of a total of 41 patients, 4 patients (10%) were in stage III, 6 patients (14.6%) were in stage IV, 11 patients (26.8%) were in stage V (ND), and 20 patients (48.8%) on stage V (D) (Figure 1). This is a tertiary care hospital; therefore most patients with advanced-stage CKD are referred to us. We aimed to include both dialysis and transplant patients but due to the age limit of psychological assessment, which is 6-14 years, we could not include any transplant patients because all our transplant patients were older than 14 years.

The causes of CKD include hypoplastic kidney (34.1%), glomerulonephritis (29.3%), obstructive uropathy (17%), single kidney (4.9%), and others (14.6%),

polycystic kidney disease, nephrocalcinosis, neonatal acute kidney injury, neurogenic bladder (Table 8). Both chronic kidney disease and chronic dialysis are thought to be associated with neuropsychological impairment, including verbal deficits (17.1%) and nonverbal deficits (14.6%) even combined deficits (43.9%).

In the current study, we found a high prevalence of neuropsychological deficits in CKD and hemodialysis (HD) patients without a history of dementia, stroke, or neurodegenerative disease. Among 41 different stages of CKD patients, 31 patients (75.6%) had FSIQ deficit and 10 patients (24.4%) had no cognitive deficit. Combined IQ deficit (43.9%) was higher than individual VIQ (17.1%) and PIQ (14.6%) deficit (Table 2). Mean VIQ, PIQ, and FSIQ are 65.8, 69.02, and 66.34, respectively. In all patients with the cognitive deficit, mild mental retardation (MR) was observed in 30 subjects 30(96.8%) out of 31, but this was not statistically significant (Table 4). One patient had visual impairment due to a bilateral cataract due to steroid toxicity and PIQ test was not performed on this patient. Therefore his IQ score was found to be a moderate IQ deficit.

Brouhard BH et al. found that patients with ESRD have lower IQs than similarly aged siblings. Younger age at diagnosis, increased time spent to develop ESRD, and lower maternal education all predicted lower achieve-

Table 3. Cognitive status in different stages of chronic kidney disease (CKD) patients (n=41)

Cognitive Status	Stage III (n=4)	Stage IV (n=6)	Stage V (ND) (n=11)	Stage V (D) (n=20)	P	
					All	V (ND) vs V (D)
Verbal IQ	2(50.0)	1(16.7)	0(0.0)	4(20.0)	0.141	0.269
Performance IQ	1(25.0)	0(0.0)	3(27.3)	2(10.0)	0.373	0.317
Combined	1(25.0)	4(66.7)	3(27.3)	10(50.0)	0.336	0.275
Full-scale IQ	4(100.0)	5(83.3)	(54.6)	16(80.0)	0.227	0.217

IQ: Intelligence quotient.

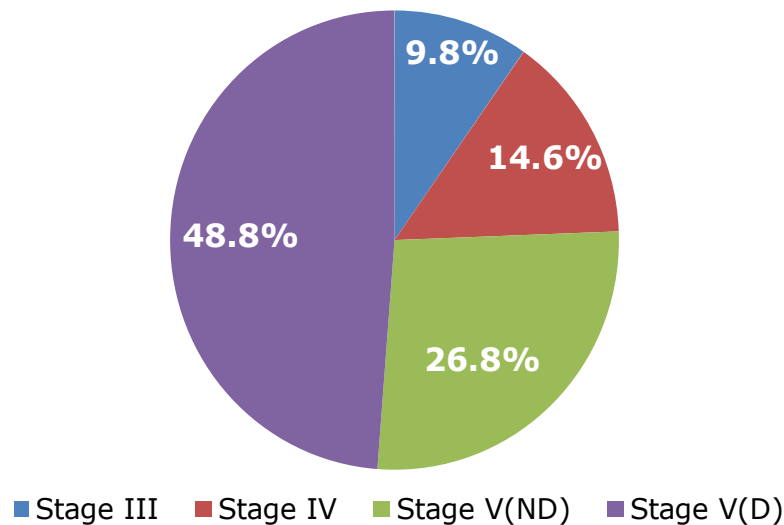


Figure 2. Correlation of estimated glomerular filtration rate (eGFR) with full scale intelligence quotient (IQ) score

ment. Jennifer Slickerss et al. showed that disease severity, represented by the estimated creatinine clearance (eCrCl), yielded the strongest relationship with both IQ ($r=0.57$, $P=0.001$) and memory ($r=0.45$, $P=0.02$), demonstrating that higher estimated creatinine clearance (eCrCl) correlated with higher scores in these cognitive domains. However, eGFR was used to stage CKD, and Spearman’s rho correlation test was performed between eGFR and IQ score (Figure 2). Here Spearman’s rho correlation coefficient (r_s) was -0.095 ($P=0.554$). Therefore a negative correlation was observed between eGFR and IQ score and it was not statistically significant. Hence, no relationship was observed between IQ score and the severity of the disease.

In this study, dialysis and the non-dialysis groups were compared. In dialytic patients, the mean VIQ, PIQ, and FSIQ are 64.25, 67.35, and 65.1, respectively. In non-dialytic patients, the mean VIQ, PIQ, and FSIQ are 67.2,

70.6, and 67.5, respectively. Therefore, in all IQ scores, the mean IQ in patients on dialysis was lower than non-dialytic patients, but the statistical analysis was not significant.

Table 5 presents some clinical predictors, such as age at initiation of RRT, age at disease onset, and duration of CKD between cognitive deficit and normal patients. Here patients with cognitive deficits had early initiation of RRT, younger age at disease onset, and longer duration of CKD but was not significant. Lawry et al found that among 24 children, including dialysis and transplant patients, younger age at ESRD onset correlated with lower IQ scores. Brouhard et al also found that younger age at renal diagnosis was associated with lower achievement scores, although not specifically with lower IQ scores.

Anemia is a crucial predictor of morbidity and mortality, often associated with CVD and possibly neurocognitive dysfunction, and was commonly present early in

Table 4. Cognitive status in different stages of chronic kidney disease (CKD) patients (n=41) according to severity

Cognitive Status	Stage III (n=4)	Stage IV (n=6)	Stage V(ND) (n=11)	Stage V(D) (n=20)	P
Average	0(0.0)	0(0.0)	1(9.1)	2(10.0)	0.668
Borderline	0(0.0)	1(16.7)	4(36.4)	2(10.0)	
Mild MR	4(100.0)	5(83.3)	6(54.5)	15(75.0)	
Moderate MR	0(0.0)	0(0.0)	0(0.0)	1(5.0)	
Severe MR	0(0.0)	0(0.0)	0(0.0)	0(0.0)	
Profound	0(0.0)	0(0.0)	0(0.0)	0(0.0)	

MR: Mental retardation.

Table 5. Comparison of different subtest of verbal and performance IQ between dialysis and non-dialysis patients (n=41)

Variables	Mean±SD		P	
	Dialysis (n=20)	Non-dialysis (n=21)		
Verbal IQ	Information	6.90±3.26	6.05±3.32	0.412
	Similarities	4.55±2.61	3.05±3.09	0.101
	Arithmetic	8.80±2.14	8.52±2.62	0.715
	Vocabulary	15.90±5.00	17.76±7.53	0.359
	Comprehension	12.05±3.62	11.05±4.57	0.442
Performance IQ	Picture completion	9.60±4.78	9.10±3.97	0.715
	Picture arrangement	7.45±5.76	8.33±6.29	0.642
	Block design	15.10±10.32	13.29±8.92	0.550
	Object assembly	15.55±5.60	15.33±5.24	0.899
	Coding	24.05±10.52	29.57±10.06	0.094

IQ: Intelligence quotient.

Table 6. Comparison of age at initiation of RRT, age at disease onset, duration of CKD and school attendance between cognitive deficit and normal CKD patients (n=41)

Variables	Mean±SD/No. (%)		P	
	Cognitive Deficit (n=31)	Normal (n=10)		
Age at disease onset (y)	8.83±3.17	8.55±2.40	0.799*	
Duration of CKD (y)	1.63±2.01	0.95±1.46	0.328*	
Age at initiation of RRT (y)	8.94±2.60	11.20±2.68	0.140*	
Duration of dialysis (y)	1.74±2.59	0.70±0.34	0.446*	
School attendance (day/wk)	3.32±2.33	5.60±1.26	0.006*	
School performance	Good	11(40.0)	9(90.0)	0.027**
	Average	12(36.7)	1(10.0)	
	Bad	3(10.0)	0(0.0)	

CKD: Chronic kidney disease; RRT: Renal replacement therapy.

Table 7. Relation of cognitive deficit with anaemia and hypertension

Variables	No. (%)		P	
	Cognitive Deficit (n=31)	Normal (n=10)		
Anaemia	Mild	6(19.4)	6(60.0)	0.014
	Moderate	14(45.2)	2(20.0)	0.156
	Severe	3(9.7)	1(10.0)	1.000
Hypertension	Hypertensive	21(67.7)	5(50.0)	1.026
	Normotensive	10(32.3)	5(50.0)	1.026

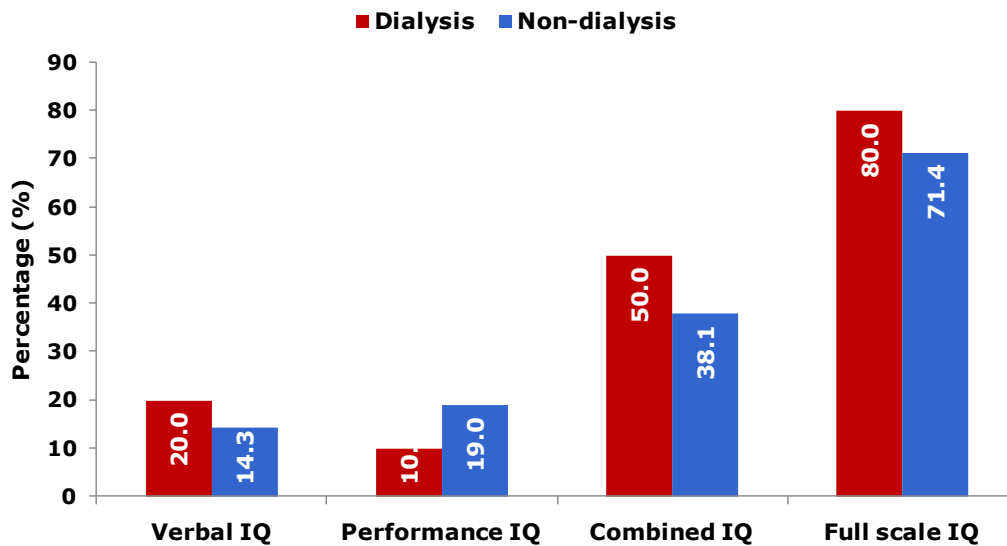


Figure 3. Bar diagram showing cognitive status in dialytic and non-dialytic patients

Table 8. Risk factors of poor school attendance (n=41)

Risk Factors	Parameters	Not Going School	No.(%) Attendance (Days)		P
			<5	≥5	
Parents education	Under graduate	8(80.0)	9(69.2)	13(72.2)	0.840
	Graduate	2(20.0)	4(30.8)	5(27.8)	
Economical status	<20,000tk/month	7(70.0)	4(30.8)	10(55.6)	0.155
	≥20,000tk/month	3(30.0)	9(69.2)	8(44.4)	
Severity of disease	III	1(10.0)	2(15.4)	1(5.6)	0.170
	IV	1(10.0)	1(7.7)	4(22.2)	
	V (ND)	2(20.0)	1(7.7)	8(44.4)	
	V (D)	6(60.0)	9(69.2)	5(27.8)	
Frequency of dialysis	No dialysis	4(40.0)	4(30.8)	13(72.2)	0.113
	<3 times	1(10.0)	4(30.8)	2(11.1)	
	3 times	5(50.0)	5(38.4)	3(16.7)	

the course of CKD [9]. A mean hemoglobin level of less than 10.5 mg/dL is associated with lower memory performance. It was reported that anemia is associated with decreased cognitive function in adult patients with renal disease. Stivelman's review shows that the use of erythropoietin in uremic adults is associated with improved haematocrit and improved cognition. For example, Marsh et al. prescribed erythropoietin in 24 adult patients undergoing hemodialysis to improve their average hematocrit from 23% to 36%. They showed significantly improved

neuropsychological test scores reflecting memory, learning, and attention. In our study, anemia in 33 patients, including mild anemia was more in CKD patients without the cognitive deficit and was significant (P=0.014).

Lande et al. showed that hypertension was significantly associated with lower neuro-cognitive scores indicating problems with short-term memory, attention, and concentration. In this current study, a sample of children with CKD, and hypertension was found in 21 patients

(63.4%) with cognitive deficits. Ten patients (32.3%) had cognitive deficits without hypertension and the P was not significant. Most study samples were under antihypertensive therapy. Some antihypertensive therapies, such as clonidine, have the potential to cause sedating effects in children but can help concentration in other children. The effects of medications on a small number of children can be amplified in this small study sample, and, thus, a true relationship can be obscured. An additional finding in this study found that school attendance and school performance in patients with the cognitive deficit was significantly low and was significant ($P=0.006$). For this purpose, we searched some risk factors of poor school attendance, such as the educational status of parents, economical status, disease severity, and dialysis frequency. Among all, patients 10 patients did not go to school and most patients had parents; education level of bachelor's degree, poor economic status, higher stages of CKD (stage VD 60%), and frequent dialysis, but the significant. Brouhard BH et al. analyzed the type of schooling and found that most patients and their siblings attended school full-time, and most were in regular classes regardless of dialysis or transplant status. But later patients missed more days from school in the previous semester than their siblings (classmates).

Brouhard BH et al. studied 26 dialysis patients, 36 transplant patients, and 62 sibling controls. They showed that patients scored significantly lower than their siblings in all three areas of achievement in spelling, arithmetic, and reading but no difference was observed between dialysis and transplant patients. In this current study, we compared the parameters of VIQ and PIQ between dialysis and non-dialysis patients. All parameters are more or less similar between the two groups. This study has some limitations, such as a single-centre study, a small sample size, and most of the patients in this study presented with the severe stage of CKD because this is a tertiary referral centre in the country.

This study concludes that mild cognitive deficit is often associated with childhood CKD. The severity of the disease does not affect IQ level. Comparing the cognitive status of CKD V and V (D) did not differ in cognition. Patients with cognitive deficits have lower school attendance and school performance.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the institutional review board of [Bangabandhu Sheikh Mujib Medical University](#), and

written informed consent was taken from all patient's guardians (IRB No.: BSMMU/ 2017/ 10192).

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declare no conflict of interest.

References

- [1] Bagga, A and Srivastava, RN. Chronic kidney disease. In: Srivastava RN, Bagga A editors. Pediatric nephrology. New Delhi: Jaypee; 2016. [DOI:10.5005/jp/books/12792_19] [PMID]
- [2] Niemczyk S, Niemczyk L, Romejko-Ciepielewska K. Basic endocrinological disorders in chronic renal failure. Endokrynol Pol. 2012; 63(3):250-7. [Link]
- [3] Khatiwada S, Kc R, Gautam S, Lamsal M, Baral N. Thyroid dysfunction and dyslipidemia in chronic kidney disease patients. BMC Endocr Disord. 2015; 15(1):1-7. [DOI:10.1186/s12902-015-0063-9] [PMID] [PMCID]
- [4] Matta SM, Janaina Matos M, Kummer AM, Barbosa IG, Teixeira AL, Silva AC. Cognitive alterations in chronic kidney disease: An update. J Bras Nefrol. 2014; 36:241-5. [DOI:10.5935/0101-2800.20140035] [PMID]
- [5] Gronewold J, Hermann DM. Cognitive impairment in chronic kidney disease-prevalence, mechanisms and consequences. J Alzheimer's Dis Parkinsonism. 2014; 7:331. [DOI:10.4172/2161-0460.1000331]
- [6] Brouhard BH, Donaldson LA, Lawry KW, McGowan KR, Drotar D, Davis I, et al. Cognitive functioning in children on dialysis and post-transplantation. Pediatr Transplant. 2000; 4(4):261-7. [DOI:10.1034/j.1399-3046.2000.00121.x] [PMID]
- [7] Pliskin NH, Yurk HM, Ho LT, Umans JG. Neurocognitive function in chronic hemodialysis patients. Kidney Int. 1996; 49(5):1435-40. [DOI:10.1038/ki.1996.202] [PMID]
- [8] Wechsler D, Kodama H. Wechsler intelligence scale for children. New York: Psychological corporation; 1949. [Link]
- [9] Marsh JT, Brown WS, Wolcott D, Carr CR, Harper R, Schweitzer SV, et al. rHuEPO treatment improves brain and cognitive function of anemic dialysis patients. Kidney Int. 1991; 39(1):155-63. [DOI:10.1038/ki.1991.20] [PMID]