ISSN: 2663-9491 e-ISSN: 2789-6897

Correlation between Glomerular Filtration Rate And Serum Erythropoietin Level in Children with Advanced (Stages 3 to 5) Chronic Kidney Disease with Anemia: A Cross-sectional Study

Noor E Zannat[1*], Shireen Afroz[2], Nusrat Jahan[3], Rumana Amin[4], S M Mortaza Ahsan[5]

Received: 21 May 2026
Accepted: 24 May 2026
Published Online: 5 June 2026

Published by:
Gopalganj Medical College, Gopalganj, Bangladesh

*Corresponding Author

DOI: 10.5281/zenodo.20560681

Copyright © 2026 The Insight

This article is licensed under a Creative Commons Attribution 4.0 International License.

ABSTRACT

Introduction: *Advanced CKD (stages 3 to 5) is commonly associated with worsening anemia due to progressive nephron loss and decreased renal EPO synthesis. The optimal glomerular filtration rate (GFR) for initiating anemia treatment with erythropoietin-stimulating agents (ESAs) remains unclear. This study aims to explore the correlation between GFR in advanced CKD with anemia and serum erythropoietin (EPO) levels. Understanding this relationship could facilitate the timely initiation of ESAs and improve the early management of anemia and its associated complications.* ***Aim of the Study:*** *To assess the relation of Glomerular Filtration Rate (GFR) with serum level of erythropoietin (EPO) in children with advanced stages of CKD (Stages 3 to 5) with anemia.* ***Methods & Materials:*** *This cross-sectional study was done in BSH&I on forty children with advanced CKD (Stages 3 to 5) having anemia. The diagnosis of CKD and renal anemia was done according to KDIGO (2012) guidelines. GFR was estimated using the revised Schwartz formula and Serum erythropoietin levels were measured using the enzymatic-chemiluminescent immunometric (CLIA). The Pearson correlation coefficient was used to assess the relationship between GFR and serum EPO levels.* ***Results:*** *Out of 40 study participants 20% had severe anemia. Among them, 12.5% were in CKD Stage 4 and 87.5% in Stage 5. The mean serum EPO levels did not significantly increase in Stage 3 (14.98 ± 4.63 mIU/mL, p< 0.01) in response to anemia as well as hypoxic condition whenever EPO levels decreased in Stage 4 (6.83 ± 2.66 mIU/mL, p< 0.01) and Stage 5 (4.88 ± 1.34 mIU/mL, p< 0.01). The result also showed a significant positive correlation between GFR and serum erythropoietin levels (r= 0.7296, p <0.05). As GFR decreases, reflecting worsening kidney function, serum EPO levels also decline.* ***Conclusion:*** *This study highlighted a significant dysregulation of erythropoietin in advanced CKD with anemia, more in Stage 4 and Stage 5. This correlation may help to optimize anemia management in pediatric CKD patients.*

Keywords: *CKD, Erythropoietin, Glomerular, Anemia, Pediatric, Nephrology, Hemoglobin*

(The Insight 2026; 9(2): 381-387)

1. *Specialist, Department of Pediatric Nephrology, Ashulia Women and Children Hospital , Dhaka, Bangladesh (ORCID: 0000-0002-3920-6861)*
2. *Professor, Department of Pediatric Nephrology, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh*
3. *Specialist, Pediatric& Neonatology Department, Evercare hospital, Dhaka, Bangladesh*
4. *Specialist, Pediatric & Neonatology Department, BRB Hospital LTD, Dhaka, Bangladesh*
5. *Assistant Professor, National Gastroliver Institute and Hospital, Mohakhali, Dhaka, Bangladesh*

INTRODUCTION

Chronic kidney disease (CKD) leads to progressive kidney function loss, often requiring renal replacement therapy.[1] It can lead to life-threatening complications like renal anemia as well as various metabolic challenges, which, if managed effectively, can help to reduce morbidity and mortality.[2] The global burden of CKD disease remains high as it causes irreversible anatomic or functional kidney damage. In a recent meta-analysis, worldwide CKD cases have been increasing continuously, with a 7% increase in ESRD and the prevalence was 13.4% in all five stages and 10.6% in stages 3–5.[3] Another meta-analysis revealed that the prevalence of CKD among the Bangladeshi population is 22.48%,[4] exceeding the global CKD prevalence of 13.4%. The prevalence of CKD in children is not negligible with 74.4 cases per million of the age-related population.[5] The incidence of ESRD in children varies widely across different countries but ranges from 5 to 10 per million children per year among patients under 20 years.[6] Furthermore, children with end-stage kidney disease (ESKD) face a 55 times higher mortality rate than the general pediatric population.[7] A study was conducted at Bangabandhu Sheikh Mujib Medical University (BSMMU), where the incidence of CKD in children was 7.9% in 2013 and thirty-five hundred thousand around the country.[8] In Bangladesh Shishu Hospital and Institute (BSH&I) the yearly prevalence of renal patients in children was 6.9% among them 0.2% of patients had CKD. Anemia is a common complication that affects up to 73% of children with stage 3 CKD and 93% in stages 4 and 5[9] and it can lead to a lower quality of life and an increased risk of cardiovascular disease, hospitalization, cognitive impairment, and mortality.[10] Anemia in individuals with CKD arises from several factors, including both absolute and functional iron deficiency, deficiencies in folate and vitamin B12, and a reduced lifespan of red blood cells, but it is mainly associated with insufficient erythropoietin production as the glomerular filtration rate (GFR) decreases. This condition arises when renal function drops below 50 percent of normal levels.[11] When the estimated GFR drops below 60

ISSN: 2663-9491 e-ISSN: 2789-6897

mL/min/1.73 m^2, categorized as Stage 3a CKD, the kidneys produce less erythropoietin, resulting in the onset of anemia.[12] Another study reports that median hemoglobin levels begin to decline when the GFR decreases below 43 mL/min/1.73 m^2.[13] EPO is synthesized by fibroblast-like cells found in the peritubular capillary network of the renal cortex. Injured fibroblast-like epithelial cells are not the sole reason for reduced EPO production in CKD. Reduced oxygen usage by affected renal tissue disrupts EPO production by elevating tissue oxygen levels, subsequently leading to a decrease in HIF stability. Consequently, this results in reduced EPO transcription, which occurs regardless of any damage to the EPO-producing cells.[14] The goal of managing anemia in patients with CKD is to decrease the morbidity and mortality associated with left ventricular hypertrophy and congestive heart failure, which is now referred to as cardiorenal syndrome.[15] Left ventricular systolic dysfunction was the most common echocardiographic finding in children with chronic kidney disease (CKD). In Bangladesh, hypertension emerged as a primary traditional risk factor for cardiovascular disease (CVD) among these children. Additionally, non-traditional risk factors included anemia, hyperphosphatemia, and hyperparathyroidism. Proper management of hypertension, anemia, hyperphosphatemia, and hyperparathyroidism could help prevent CVD in children with CKD.[16] As deficiency of EPO is the primary cause of this anemia,[17] erythropoietin therapy is considered a treatment modality for anemia in CKD patients. It is well known that there is a positive correlation between hemoglobin and GFR. But, at which level of reduced creatinine clearance or GFR and hemoglobin recombinant erythropoietin treatment should be started is still unclear and is a matter of debate. Although the 2012 guideline from Kidney Disease Improving Global Outcomes (KDIGO) stated that the introduction of ESA therapy should be considered when Hb level decreases below 10 g/dL in patients with non-dialysis-dependent CKD. But in our clinical practices, we routinely administer erythropoietin-stimulating agents (ESAs) to patients with end-stage renal disease (ESRD) and anemia-associated complications. Gouva et al. provide evidence that early intervention with ESAs in anemia can slow the progression of renal disease and delay the initiation of renal replacement therapy.[18] So, should we start ESAs at the early stage (stage 3 of CKD), is also a matter of debate. It is also important to recognize the quantitative relationship that exists between erythropoietin levels and hemoglobin across varying levels of creatinine clearance. There are some adult studies that recommend early initiation of treatment of renal anemia. A study on 395 adult CKD patients demonstrated that a lower threshold for EPO synthesis is evident when creatinine clearance drops below 40 ml/min.[15] Furthermore, another study highlighted a negative correlation between GFR, hemoglobin levels and erythropoietin concentrations in CKD stages 1 to 3 (decreased GFR and hemoglobin then increased EPO level) and a blunt correlation in CKD stages 4 and 5 that is, decreased GFR and hemoglobin but EPO level is not increased according to the degree of anemia, which is known as relative erythropoietin deficiency.[19] There is no definitive guideline in pediatric CKD patients when to start ESAs in CKD is still in a dilemma. Therefore, this study aims to measure serum erythropoietin and to assess the relation of GFR with serum levels of erythropoietin in children with advanced stages of CKD (stage 3–5) with anemia.

METHODS & MATERIALS

This cross-sectional observational study was conducted in the Department of Pediatric Nephrology at Bangladesh Shishu Hospital & Institute, Bangladesh, over a 24-month period from January 2023 to December 2024. Children aged 2–18 years with chronic kidney disease (CKD) stages 3–5 and anemia attending inpatient and outpatient services were enrolled using convenient purposive sampling. The calculated sample size for assessing the correlation between glomerular filtration rate (GFR) and serum erythropoietin level was 45 based on Fisher's Z-transformation formula for correlation studies; however, 40 eligible patients fulfilling the inclusion criteria were included. Children diagnosed with CKD stages 3–5 according to Kidney Disease: Improving Global Outcomes (KDIGO) guidelines with anemia and normal serum iron profile were included, while patients receiving erythropoietin therapy were excluded. Data were collected using a structured questionnaire through guardian interviews, clinical examination, and laboratory investigations. Demographic variables included age, sex, height, weight, and body mass index, while biochemical parameters included complete blood count with peripheral blood film, serum creatinine, and estimated glomerular filtration rate (eGFR). CKD staging was determined using the revised Schwartz formula [0.413 × height (cm)/serum creatinine (mg/dL)]. Clinical assessment included documentation of disease duration, antenatal history, urinary symptoms, renal manifestations, and anemia-related symptoms. Laboratory investigations included serum albumin, blood urea nitrogen, electrolytes, calcium, parathyroid hormone, urine routine examination, ultrasonography of the kidney-ureter-bladder region, and other relevant investigations as indicated. Blood samples were collected, stored at +4°C, and analyzed on the same day. Serum erythropoietin levels were measured by chemiluminescent immunometric assay (CLIA) using IMMULITE/IMMULITE 1000 systems. Renal anemia was assessed clinically and laboratorily according to KDIGO 2012 criteria. Ethical approval was obtained from the Ethical Review Committee of Bangladesh Shishu Hospital & Institute, and written informed consent was obtained from parents or legal guardians prior to enrollment. Data were analyzed using STATA version 17.0. Descriptive statistics were expressed as mean ± standard deviation, frequencies, and percentages. Continuous variables were compared using analysis of variance (ANOVA), categorical variables using chi-square test, and correlations between eGFR and biochemical parameters including hemoglobin, creatinine, blood urea nitrogen, and erythropoietin were assessed using Pearson's correlation coefficient. A p-value <0.05 was considered statistically significant.

RESULTS

This table shows that the study population is evenly distributed, with 30% aged ≤5 years and 35% each in the 6–9 and 10+ years groups. The mean age is 7.38 years (CI: 6.28–8.47).two-thirds of the participants (67%) were male.Regarding gender distribution, male participants constituted the majority (67.0%), whereas females accounted for 33.0% of the study population (*Table I*).

ISSN: 2663-9491 e-ISSN: 2789-6897

Table I: Distribution of participants by age (*n*=40)

Age Group	Frequency (N=40)	Percentage (%)
≤ 5 years	12	30.00
6-9 years	14	35.00
10+ years	14	35.00
Mean Age ± SD (CI)	7.38 ± 0.54 (6.28–8.47)	
Gender		
Male	27	67.00
Female	13	33.00

This table shows that nearly half of the participants (47.5%) belong to the lower middle class, with 32.5% in the lower class category. The majority (60%) have had CKD since birth, and consanguinity is rare (7.5%). A family history of kidney disease is present in 15% of cases. Iron supplementation is used in all patients (100%), and 38.46% have received blood transfusions. Renal biopsy was performed in 25.0% of cases, with FSGS (12.5%) being the most common finding (*Table II*).

Table II: Baseline characteristics of study participants (*n*=40)

Characteristic	Frequency (n=40)	Percentage (%)
Socioeconomic Status		
Lower Class	13	32.50
Middle Class	19	47.50
Upper Class	8	20.00
Duration of Illness		
≤ 3 years	7	17.50
4-7 years	6	15.00
≥ 8 years	3	7.50
Since birth	24	60.00
Consanguinity		
Absent	37	92.50
Present	3	7.50
Family History of Kidney Disease		
No	34	85.00
Yes	6	15.00
Iron Supplementation		
Yes	40	100.00
No	0	0.00
History of Blood Transfusion (H/O BT)		
No	24	60.00
Yes	16	40.00
Renal Biopsy Findings		
C3 GN	1	2.50
C1q Nephropathy	2	5.00
FSGS	5	12.5
IgA Nephropathy	2	5.00
Not Done	30	75.0

This table shows that, among 40 patients, the majority of patients were CKD stage 5 (37.5%), followed by stage 4 (32.5%) and stage 3 (30%) *Table III*.

Table III: Distribution of CKD Stages with Frequency, Percentage

Stage of CKD	Frequency (n)	Percentage (%)
3	12	30.00
4	13	32.50
5	15	37.50
Total	40	100.00

This table presents the distribution of clinical symptoms across CKD stages. Anuria was more frequent in Stage 5 (50%) compared to Stage 3 (33.3%) and Stage 4 (16.7%), though not statistically significant (p=0.649). Hematuria was rare, with only two cases reported. Hypertension was more prevalent in Stage 5 (66.7%). Renal rickets and growth retardation were more common in stages 4 and 5. Anemia showed a significant association (p=0.020), with severe anemia found exclusively in Stage 5 (87.5%), whereas mild anemia was more frequent in Stage 3 (58.3%) *Table IV*.

ISSN: 2663-9491 e-ISSN: 2789-6897

Table IV: Clinical Features of Patients across Different Stages of Chronic Kidney Disease

Variable	Overall (N=40)	Stage 3 (N=12)	Stage 4 (N=13)	Stage 5 (N=15)	P-value
Anuria					
Absent	34 (85.0)	10 (29.4)	12 (35.3)	12 (35.3)	0.649
Present	6 (15.0)	2 (33.3)	1 (16.7)	3 (50.0)	
Hematuria					
Absent	38 (95.0)	11 (28.9)	13 (34.2)	14 (36.8)	0.591
Present	2 (5.0)	1 (50.0)	0 (0.0)	1 (50.0)	
Hypertension (HTN)					
Absent	31 (77.5)	10 (32.3)	12 (38.7)	9 (29.0)	0.105
Present	9 (22.5)	2 (22.2)	1 (11.1)	6 (66.7)	
Renal Rickets					
Absent	36 (90.0)	12 (33.3)	11 (30.6)	13 (36.1)	0.380
Present	4 (10.0)	0 (0.0)	2 (50.0)	2 (50.0)	
Growth Retardation					
Absent	21 (52.5)	8 (38.09)	5 (23.81)	8 (38.09)	0.459
Present	19 (47.5)	4 (21.05)	7 (36.84)	8 (42.11)	
Convulsion					
Absent	38 (95.0)	12 (31.6)	13 (34.2)	13 (34.2)	0.173
Present	2 (5.0)	0 (0.0)	0 (0.0)	2 (100.0)	
Anemia					
Mild	13 (32.5)	8 (61.5)	5 (38.5)	0 (0.0)	0.020
Moderate	18 (45.0)	4 (22.2)	7 (38.9)	7 (38.9)	
Severe	9 (22.5)	0 (0.0)	1 (11.1)	8 (88.9)	

Significant differences were observed in hemoglobin, serum creatinine, BUN, PTH, eGFR, and serum erythropoietin (all P-values <0.01), indicating these parameters reflect disease progression. Serum albumin, serum calcium, ferritin, serum iron, and TIBC showed no significant differences (P-values >0.05) *Table V*.

Table V: Serum Biomarkers and Renal Function Across CKD Stages (*n*=40)

Variable	Stage 3 (N=12)	Stage 4 (N=13)	Stage 5 (N=15)	P-value*
Hemoglobin (g/dl)	9.81 ± 0.84	9.11 ± 1.07	6.93 ± 1.18	<0.01
S. Creatinine (mg/dl)	1.17 ± 0.28	2.13 ± 0.56	6.10 ± 4.01	<0.01
BUN (mmol/L)	8.84 ± 4.40	17.48 ± 6.64	32.54 ± 13.22	<0.01
S. Albumin (g/L)	31.66 ± 6.38	30.27 ± 5.68	30.48 ± 12.25	0.91
S. Calcium (mmol/L)	2.08 ± 0.24	2.00 ± 0.20	1.84 ± 0.43	0.14
Ferritin (ng/ml)	263.19 ± 65.02	242.35 ± 104.54	305.62 ± 209.54	0.51
S. Iron (µg/dl)	92.42 ± 31.21	97.15 ± 37.24	148.73 ± 127.82	0.15
TIBC (µg/dl)	275.17 ± 90.29	264.69 ± 79.83	274.20 ± 103.71	0.95
TSAT (%)	33.91 ± 7.35	37.80 ± 13.07	52 ± 22.85	0.0155
PTH (pg/ml)	97.32 ± 52.45	263.42 ± 253.81	469.36 ± 188.16	<0.01
eGFR (ml/min/1.73m^2)	39.85 ± 11.63	20.72 ± 3.95	9.26 ± 3.24	<0.01
S. Erythropoietin (mIU/ml)	14.98 ± 4.63	6.83 ± 2.66	4.88 ± 1.34	<0.01

** ANOVA Test done.*

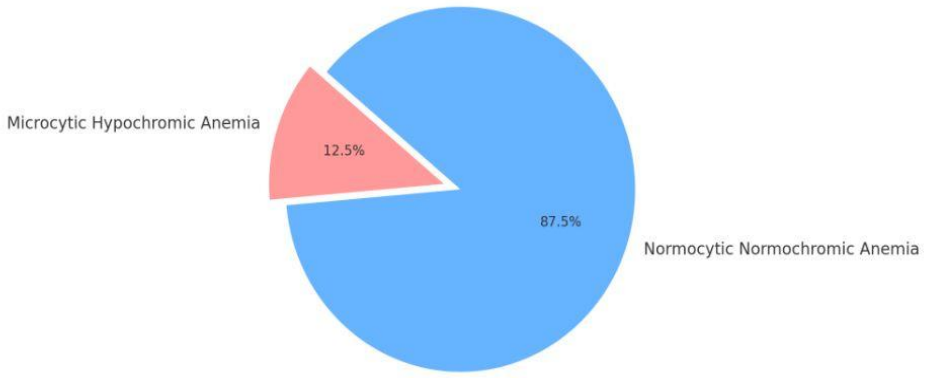

Figure 1: Distribution of anemia by PBF

ISSN: 2663-9491 e-ISSN: 2789-6897

The pie chart illustrates the distribution of anemia types. Normocytic normochromic anemia is the more prevalent (87.5%), followed by microcytic hypochromic anemia (12.5%) *Figure 1*.

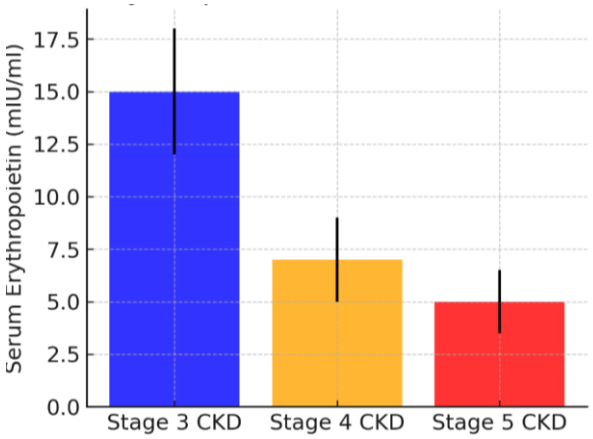

Figure 2: Serum Erythropoietin concentration in Advanced Stages of CKD (3 to 5)

Mean serum EPO levels: Stage 3: 14.98 ± 4.63 mIU/mL; Stage 4: 6.83 ± 2.66 mIU/mL; Stage 5: 4.88 ± 1.34 mIU/mL (*Figure 2*). The p-values for all variables (MCV: 0.424, MCH: 0.823, MCHC: 0.259) are above the significance threshold of 0.05, indicating no statistically significant differences between the stages for any of these parameters (*Table VI*).

Table VI: Distribution of CKD stages by red cell indices

Variable	Stage 3 mean±SD	Stage 4 mean±SD	Stage 5 mean±SD
MCV (fl)	75.26 ± 4.18	77.82 ± 8.17	74.67 ± 6.52
MCH (pg)	25.41 ± 2.24	25.21 ± 2.96	24.74 ± 3.00
MCHC (g/dl)	32.03 ± 0.99	31.30 ± 1.74	32.08 ± 1.17

Congenital Anomalies of Kidney and Urinary Tract (CAKUT) accounted for 65% of CKD cases, with PUV and its complications being the most common (30%). Glomerular diseases represented 35%, with FSGS (12.5%) and SRNS (10%) as major contributors. Non-obstructive congenital anomalies accounted for 32.5%, while PUJ obstruction was rare (2.5%) *Table VII*.

Table VII: Causes of Chronic Kidney Disease (CKD) Distribution (*n*=40)

Category	Cause of CKD	Frequency (n=40)	Percentage (%)
1. Congenital Anomalies of Kidney and Urinary Tract (CAKUT) (n=26)			
a. Obstructive Causes			
	Posterior Urethral Valve (PUV) + Complications	12	30.0
	PUJ obstruction + anomalies	1	2.5
b. Non-Obstructive Causes			
	ARM with Rectovesical fistula	1	2.5
	Bilateral duplex kidney with PUV & recurrent UTI	1	2.5
	Bilateral hypoplastic kidney	1	2.5
	Cystic kidney disease + anomalies	2	5.0
	Neurogenic bladder + anomalies	5	12.5
	Horseshoe kidney, urogenital sinus + anomalies	1	2.5
	Right-sided hypoplastic kidney + HDN	1	2.5
	Pyelonephritis + anomalies	1	2.5
2. Glomerular Diseases (n=14)			
	Focal Segmental Glomerulosclerosis (FSGS)	5	12.5
	C1q nephropathy	1	2.5
	IgA nephropathy	2	5.0
	Steroid-Resistant Nephrotic Syndrome (SRNS)	4	10.0
	C3 GN	1	2.5
	SRNS with nephrocalcinosis	1	2.5

ISSN: 2663-9491 e-ISSN: 2789-6897

eGFR showed a strong positive correlation with hemoglobin (r = 0.6905, p< 0.001) and erythropoietin (r = 0.7296, p< 0.001), indicating that declining renal function is associated with anemia. Serum creatinine (r = -0.6438, p< 0.001) and BUN (r = -0.7002, p < 0.001) had strong negative correlations with eGFR, as expected in CKD progression (*Table VIII*).

Table VIII: Correlations between serum glomerular filtration rate (GFR) and clinical laboratory parameters in CKD

Variables	r	p-value
Hemoglobin (g/L)	0.6905	< 0.001
Creatinine (mmol/L)	-0.6438	< 0.001
Erythropoietin (mIU/mL)	0.7296	< 0.001
BUN (mmol/L)	-0.7002	< 0.001

**r = Pearson correlation coefficient, p = probability.*

DISCUSSION

Hyporegenerative anemia is a common symptom of chronic kidney disease (CKD) that significantly affects the morbidity and mortality of kidney patients. The prevalence of CKD in children is a growing public health issue, which often leads to malnutrition and growth retardation. Many of these children are at an increased risk of anemia-related complications, including cardiovascular mortality and impaired cognitive function. All of these factors severely impact the quality of life for affected children.[19]

Renal anemia mainly develops due to relative erythropoietin deficiency and ESAs are the main treatment modulator of this condition. To avoid life-threatening complications related to anemia it is important to start the ESAs at an appropriate time. This study shows the correlation between erythropoietin levels and advanced (stage 3 to 5) CKD and thus predicts the actual time to start ESAs.

In this study, out of 40 study participants, 70% of patients were between 6 and 10 years of age. Most of the patients were male (male-to-female ratio of 2.03:1). A total of 24 patients (60%) had CKD since birth, and a family history of kidney disease was present only in 6 patients (15%). These baseline characteristics (Tables 1 & 2) are consistent with Ardissino G et al.[5]

The common causes of CKD in this study were obstructive uropathy, ectopic kidney, neurogenic bladder and glomerular diseases. Among them, 65% of patients had Congenital anomalies of the kidney and urinary tract (CAKUT) and 35% had glomerular diseases which is consistent with Ardissino G et al.[5] where they showed about 67.5% of CKD patients had CAKUT. Harambat J & Ku E[16] reported that CAKUT is responsible for 50–60% of CKD cases in children, while glomerular diseases account for 5–15% and hereditary disorders represent 10–20%. Kamath N et al.[20] also found the same results, about 50% of cases were CAKUT and glomerular diseases were 15% which is almost similar to this study.

The clinical features of this study (Table IV) were hypertension and growth retardation which are similar to Roy RR et al.[8] and Kamath N et al.[20] Among the biochemical parameters (Table V), the gradual increase of serum PTH levels and decrease of serum EPO levels occurs as the disease progresses.

In this study, anemia becomes more severe as renal function declines. Overall, 20% of patients experienced severe anemia, with 88.9% of these patients being in CKD stage 5. Notably, no cases of severe anemia were observed in patients with CKD stage 3. Although only patients with anemia and chronic kidney disease (CKD) were included in this study, the prevalence of anemia among pediatric CKD patients remains high. According to the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS), the prevalence of anemia is reported to be 73%, 87%, and over 93% in pediatric CKD stages 3, 4, and 5, respectively, as also noted by Atkinson MA et al.[9]

In normal renal response to anemia, the kidneys rapidly increase EPO production in peritubular fibroblasts, raising serum EPO levels over 100-fold.[21] According to Atkinson & Guzzo,[14] with normal renal function, plasma EPO levels rise exponentially as hemoglobin decreases, from about 15 units/liter to as high as 10,000 units/liter. Panjeta M et al.[19] showed in their study, the median EPO concentration in Stage 1 was 11.0 mIU/mL, Stage 2, 3, 4 and 5 was 15.3 mIU/mL, 13.1 mIU/mL, 10.2 mIU/mL and 8.9 mIU/mL respectively.
The present study showed that serum erythropoietin levels did not significantly increase according to the degree of anemia. The mean EPO concentration in Stage 3 (14.98 ± 4.63 mIU/mL, p <0.001) was not increased significantly whereas EPO concentration in Stage 4 (6.83 ± 2.66 mIU/mL, p <0.001) and Stage 5 (4.88 ± 1.34 mIU/mL, p <0.001) was decreased more markedly. It is important to note that, here the levels of EPO from Stage 3 to Stage 5 were not increased as normal renal response to anemia. Although EPO concentration was decreased in Stage 4 and Stage 5 but remained within the normal range (2.6–19 mIU/mL). This phenomenon is known as a relative erythropoietin deficiency and this also reflects that there is serious damage to kidney tissue and impaired normal EPO biosynthesis, secretion and regulation. So, EPO levels are difficult to interpret in the context of renal failure.
Fehr T et al.[15] showed that above creatinine clearance 40 mL/min, EPO levels increased significantly but below 40 mL/min response to anemia is attenuated. That is EPO levels were not increased according to the degree of anemia though the EPO levels were within their normal range. This finding is similar to the current study.

According to Panjeta M et al.,[19] in patients with renal anemia, below 30 mL/min/1.73 m^2 of GFR (CKD IV and V), the EPO levels were lower than the control group but within the normal range, which is also similar to the present study.
In this study, there is a moderate positive correlation among GFR with serum EPO levels (r=0.7296, p<0.05) and hemoglobin levels (r=0.6905, p<0.001) indicating that as GFR declines, serum EPO and hemoglobin levels also decrease which is similar to Fehr T et al.[15] and Panjeta M et al.[19]
Serum creatinine (r= -0.6438, p<0.001) and BUN (r= -0.7002, p< 0.001) had a moderate negative correlation with GFR which is also consistent with Panjeta M et al.[19]

ISSN: 2663-9491 e-ISSN: 2789-6897

LIMITATION

This study was limited by its single-centre design, small sample size, and the inability to exclude vitamin B12 and folate deficiency anemia due to financial constraints and lack of laboratory support.

CONCLUSION

This study highlights a significant positive correlation between GFR and serum EPO levels. These findings suggest that endogenous EPO production becomes inadequate to compensate for anemia whenever kidney function declines which was more in Stages IV and V. So, ESAs should be started in CKD (Stage 4) patients for early management of anemia and its complications.

RECOMMENDATION

Further multicenter research with a large cohort is needed for a better analysis of EPO levels for correlation with anemia and renal function. Future studies should adopt longitudinal designs to assess the long-term impact of early ESA initiation on disease progression, quality of life, and survival in pediatric CKD patients across all advanced stages. Standardization of EPO measurement protocols and inclusion of diverse geographic and demographic populations will strengthen the evidence base required to formulate definitive guidelines on the optimal timing of ESA therapy in children with CKD.

REFERENCES

1. *Sinha A, et al. Chronic kidney disease and renal replacement therapy. 2016.*
2. *Stack AG. Impact of timing of nephrology referral and pre-ESRD care on mortality risk among new ESRD patients in the United States. American Journal of Kidney Diseases. 2003;41(2):310–318.*
3. *Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, Lasserson DS, Hobbs FDR. Global prevalence of chronic kidney disease – a systematic review and meta-analysis. PLoS One. 2016;11(7):e0158765.*
4. *Banik S, Ghosh A. Prevalence of chronic kidney disease in Bangladesh: a systematic review and meta-analysis. International Urology and Nephrology. 2021;53:713–718.*
5. *Ardissino G, Dacco V, Testa S, Bonaudo R, Claris-Appiani A, Taioli E, Marra G, Edefonti A, Sereni F, ItalKid Project. Epidemiology of chronic renal failure in children: data from the ItalKid project. Pediatrics. 2003;111(4):e382–e387.*
6. *Harambat J, van Stralen KJ, Kim JJ, Tizard EJ. Epidemiology of chronic kidney disease in children. Pediatric Nephrology. 2012;27:363–373.*
7. *Chesnaye NC, Schaefer F, Groothoff JW, Bonthuis M, Reusz G, Heaf JG, Lewis M, Maurer E, Paripovic D, Zagozdzon I, van Stralen KJ. Mortality risk in European children with end-stage renal disease on dialysis. Kidney International. 2016;89(6):1355–1362.*
8. *Roy RR, Al Mamun A, Matin MA, Islam MR. Chronic kidney diseases in children, management difficulties and amelioration in Bangladesh: A review. Journal of Shaheed Suhrawardy Medical College. 2015;7(1):26–32.*
9. *Atkinson MA. Anemia in Chronic Kidney Disease. In: Kher KK, Schnaper HW, Greenbaum LA, editors. Clinical Pediatric Nephrology. 3rd ed. New York: Taylor & Francis Group; 2017. p. 627–638.*
10. *Babitt JL, Lin HY. Mechanisms of anemia in CKD. Journal of the American Society of Nephrology. 2012;23(10):1631–1634.*
11. *Bagga A, et al. Pediatric nephrology and CKD anemia. 2016.*
12. *MacGinley RJ, Walker RG. International treatment guidelines for anaemia in chronic kidney disease – what has changed. Medical Journal of Australia. 2013;199(2):84–85.*
13. *Fadrowski JJ, Pierce CB, Cole SR, Moxey-Mims M, Warady BA, Furth SL. Hemoglobin decline in children with chronic kidney disease: baseline results from the chronic kidney disease in children prospective cohort study. Clinical Journal of the American Society of Nephrology. 2008;3(2):457–462.*
14. *Guzzo I, Atkinson MA. Anemia in Chronic Kidney Disease. In: Emma F, Goldstein SL, Bagga A, Bates CM, Shroff R, editors. Pediatric Nephrology. 8th ed. Switzerland: Springer Nature; 2022. p. 1779–1794.*
15. *Fehr T, Ammann P, Garzoni D, Korte W, Fierz W, Rickli H, Wuthrich RP. Interpretation of erythropoietin levels in patients with various degrees of renal insufficiency and anemia. Kidney International. 2004;66(3):1206–1211.*
16. *Yasmin F, Afroz S, Ferdous T, Tanjila U, Baroi S. Clinical and Biochemical Profile of Children with Chronic Kidney Disease in a Tertiary Care Hospital of Bangladesh. Journal of Bangladesh College of Physicians and Surgeons. 2023;41(2):120–125.*
17. *Bruce G, Schulga P, Reynolds BC. Use of erythropoiesis-stimulating agents in children with chronic kidney disease: a systematic review. Clinical Kidney Journal. 2022;15(8):1483–1505.*
18. *Gouva C, Nikolopoulos P, Ioannidis JP, Siamopoulos KC. Treating anemia early in renal failure patients slows the decline of renal function: a randomized controlled trial. Kidney International. 2004;66(2):753–760.*
19. *Panjeta M, Tahirovic I, Sofic E, Coric J, Dervisevic A. Interpretation of erythropoietin and haemoglobin levels in patients with various stages of chronic kidney disease. Journal of Medical Biochemistry. 2017;36(2):145.*
20. *Kamath N, Iyengar A, George N, Luyckx VA. Risk factors and rate of progression of CKD in children. Kidney International Reports. 2019;4(10):1472.*
21. *Artunc F, Risler T. Serum erythropoietin concentrations and responses to anaemia in patients with or without chronic kidney disease. Nephrology Dialysis Transplantation. 2007;22(10):2900–2908.*