Hematological Abnormalities and Comorbidities Are Associated With the Severity of Kidney Disease: A Hospital-Based Cross-Sectional Study in Bangladesh

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ABSTRACT

BACKGROUND: Abnormalities in hematology and comorbidities might have a role in chronic kidney disease (CKD) patients. However, the exact relationships between hematological parameters and the severity of CKD are not well understood. Also, the underlying mechanisms remain under investigation. The present study aimed to evaluate the association of different blood parameters and comorbidities among hospitalized CKD patients in Bangladesh.

METHODS: The present study enrolled admitted CKD patients at Evercare Hospital Ltd, Dhaka, Bangladesh, from January 1, 2021, to August 1, 2021. For this study, the demographic and clinical information of the patients were collected. Then some routine blood tests for the hematological profile of CKD patients were performed. Finally, several statistical methods were performed and data interpretations were done to evaluate the role of hematological changes on CKD patients.

RESULTS: Among 300 patients, early-stage CKD patients (ESCKDP) and advanced-stage CKD patients (ASCKDP) were 153 and 147, respectively. The decreased levels of hemoglobin (Hb) and red blood cell (RBC) in ASCKDP were observed. However, the present study found increased levels of corpuscular Hb in ASCKDP than ESCKDP. Also, the present study noticed correlations between these changes and the severity of CKD. Also, we observed a significant difference in age and body mass index between ESCKDP and ASCKDP.

CONCLUSIONS: Based on our results, lower Hb and RBC levels may use in assessing the severity and the treatment decisions of CKD patients in the hospital setting. Therefore, our findings may assist with developing a treatment protocol for hospitalized CKD patients.

KEYWORDS: Kidney disease, kidney failure, renal insufficiency, renal failure, hematology, hemoglobin, red blood cell

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Background

Chronic kidney disease (CKD) is a long-term dysfunctional renal condition that can cause permanent damage to the renal parenchyma. If this condition remains untreated, it leads to end-stage renal disease (ESRD).[1] Physicians diagnose CKD by a notable reduction in the level of eGFR.[2] CKD is more prevalent than other chronic diseases and one of the 12 leading causes of death globally. In 2017, the world recorded 700 million CKD patients of all stages and 1.2 million deaths. Scientists are projecting 4 million deaths due to CKD by 2040. There is no significant decrease in the death rate caused by CKD compare to other chronic diseases.[3] Moreover, there is a high prevalence of CKD in developed countries like Europe, the USA, Canada, and Australia compared to developing countries like sub-Saharan Africa, India, etc.[4]

A global review reported that the prevalence of CKD is approximately 14% worldwide.[5] A Dhaka-based study in Bangladesh stated 26% CKD prevalence among adults 30 years and older.[6] Also, another study reported that the prevalence of kidney diseases among healthcare providers is at least 7%.[7] Moreover, in rural communities, approximately a third of the rural population had undiagnosed and largely unknown kidney disease.[6] CKD can affect people of all ages, men, women, and people with varying socioeconomic statuses and rates of urbanization.[5] Obesity, diabetes, and hypertension are also risk

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factors for CKD.[6] kidney disease is becoming more prevalent in adults over the age of 55 due to age-related changes in the microanatomical structures and functions of the kidney,[8] resulting in decreased kidney function and increased rates of CKD.[9] There are ethnic disparities, such as an increased blood creatinine level in people of a specific ethnicity due to increased muscle mass.[10] Currently, data on creatinine levels in Bangladeshi populations are insufficient to describe their sex- and age-specific rates of CKD and the prevalence of various stages of CKD.[10]

A significant number of individuals with advanced CKD experience anemia.[11] The prevalence of anemia among CKD patients proportionately increases with the progression of the CKD staging.[11] The end-stage renal disease affects 60% to 80% of CKD patients.[12] Anemia is associated with lowered physical strength, greater susceptibility to infection, impaired cognitive ability, and decreased energy.[13] In pre-dialysis and dialysis patients, anemia exacerbates both their preexisting medical conditions and the quality of their lives.[13] The primary cause of anemia among CKD patients is the failure to produce sufficient erythropoietin by kidneys.[14]Moreover, this condition decreases the quality of life and increases the risk of developing other related health problems.[15] Non-treated anemia can result in hemodynamic and tissue hypoxia changes, all of which accelerate renal function decline.[16] Impaired erythropoiesis due to iron deficiency in CKD patients is the primary cause of developing anemia.[15,17] Significant iron loss occurs in CKD patients due to chronic uremia-related bleeding, repeated phlebotomy, and regular blood trapping in the dialysis machine.[18] Our bodies require iron and erythropoietin to produce red blood cell (RBC) in the bone marrow.[17] Therefore, reduced iron and erythropoietin levels are associated with lowered hemoglobin (Hb) levels.[19] A hormone from the liver named hepcidin regulates iron availability, absorption, and recycling.[20] Several feedback mechanisms of iron and erythropoietin levels regulate hepcidin levels.[21] Hepcidin levels can increase in advanced stage CKD patients presumably due to decreased renal clearance and inflammation-induced induction of hepcidin, which impairs erythropoiesis.[15] Kidney failure is associated with blood loss, RBC lifespan, and impaired erythropoiesis.[15] Scientists observed excess hepcidin levels in CKD patients due to the iron deficiency and reticuloendothelial blockade of cell iron.[22] However, CKD patients may suffer the consequence of iron overload that might affect the major iron storage sites.[23]

Hepcidin hormone primarily regulates systemic iron homeostasis in the human body.[22] Production and secretion of hepcidin in the liver block iron trapping into the plasma.[15] TNF-alpha and interleukin-1 (IL-1) promote hepcidin transcription that might cause iron sequestration, iron deficiency, and anemia. This abnormal iron level is associated with several chronic diseases, including CKD.[15] CKD may affect other hematological parameters that have not been fully characterized.[24] In the late 1990s, scientists observed an associated between inflammation, malnutrition, and cardiovascular disease in patients with CKD.[24] The high ratio of neutrophil and lymphocyte concentrations indicates the inflammatory state in CKD.[14] This ratio is a prognostic indicator of mortality risk in other diseases, for example, myocardial infarction and heart failure.[14] Increased morbidity and mortality from cardiovascular complications may occur in CKD patients due to increased anemia.[25] The progression of renal disease and the development of cardiorenal anemia syndrome might occur in CKD patients.[25] Elevated left ventricular hypertrophy is associated with a decreased survival rate in dialysis patients.[26] Patients with end-stage CKD and left ventricular hypertrophy have a 30% lower 5-year survival rate than other CKD patients with normal cardiac function.[26]

Hypertension is a cardiovascular risk factor linked to an elevated risk of heart attack and stroke in CKD patients.[27] Hypertension increases the risk of cardiovascular events in early-stage CKD patients.[27] However, systolic blood pressure has a link with an elevated risk of cardiovascular death in end-stage CKD patients.[26] Moreover, diabetes is associated with adverse outcomes of CKD patients in any stage.[28] In Bangladesh, studies regarding the evaluation of hematological parameters in CKD patients are limited. Therefore, the present study aimed for hematological profiling of Bangladeshi CKD patients and to find out the association of different blood parameters and comorbidities with the severity of patients.

Materials and Methods

Study population

The present study has been conducted from January 1, 2021, to August 1, 2021, at Evercare Hospital in Dhaka, Bangladesh. At first, CKD patients were screened for hematological evaluation and other comorbidities. The current study enrolled hospitalized CKD patients due to various complications. The present study included CKD patients aged 18 years or above who met the inclusion criteria. Inclusion criteria were newly diagnosed CKD patients who were on conservative management, and patients who were willing to participate and gave consent for their participation. Exclusion criteria were CKD patients with renal replacement therapy, patients with infections, hemoglobinopathies, malignancy, smoking habits, history of blood transfusion in the past month prior to inclusion in the study. The present study also monitored the eGFR levels and the albumin-creatinine ratios to assess the severity of CKD.

Sample collection and analysis

We monitored the dietary restrictions of patients for 6 hours before sample collection. Before collecting the sample, the puncture site was sanitized and cleaned. Blood samples were collected and analyzed for various hematological parameters using a vacutainer tube containing EDTA.[29,30] The routine

procedures for collected blood samples were performed and stored the samples at −80°C until further analyses.[31,32] The present study enrolled CKD patients regardless of their disease severity. A photometric method was performed to evaluate creatinine, Hb, and complete blood count (CBC) using Beckman Coulter, DXE 700 AU, and Sysmex XN 2000. The eGFR was determined by the MDRD equation using serum creatinine value.[33,34] Also, the ion-selective electrode method was applied to calculate Na^+, K^+, CI^-, and HCO_3 using Dimension EXL 200.[35] Thyroid-stimulating hormone (TSH) and HbA1c levels were measured using enzyme-linked immunosorbent assay (ELISA) kits. All the chemicals and reagents of analytical grade were purchased from commercially available recognized sources.

Statistical analysis

Microsoft Excel 2016 was used for data processing and IBM SPSS (version 25.0) was applied for statistical analysis. Independent sample t-tests and fisher's exact test were performed to compare different parameters between early-stage CKD patients (ESCKDP) and advanced-stage CKD patients (ASCKDP). Also, Spearman's rank correlation test was applied to determine the associations among analyzed parameters. Data was presented as mean ± standard deviation. Moreover, severity-specific scatter plot graphs were used to demonstrate associations between altered blood parameters and eGFR of CKD patients. Significant differences or associations among the parameters were considered at a *P*-value of less than .05.

Result

Description of the study population

The general description of the study participants and the severity of CKD patients were presented in Table 1. Among 300 patients, most of them were between 61 and 80 years old in ESCKDP (53.59%) and ASCKDP (58.51%), females in ESCKDP (60.13%) and ASCKDP (58.50%), and obese (BMI above 25) in ESCKDP (67.32%) and ASCKDP (100%). Also, the present study observed an increased BMI in ADCKDP (mean 31.84) compared to ESCKDP (mean 26.62). However, males are more vulnerable to develop advanced-stage-CKD (ESCKDP:ASCKDP = 1:1.041) compared to females (ESCKDP:ASCKDP = 1.028:1). Hypertension, diabetes, hypothyroidism, and hypernatremia were common comorbid diseases in ESCKDP and ASCKDP according to the present study.

Hematological profile of CKD patients

The hematological parameters of ESCKDP and ASCKDP were presented in Table 2. A significant decrease in the level of both Hb (Mean: 10.41 to Mean: 9.22; $P < .001$) and RBC (Mean: 3.54 to Mean: 2.35; $P < .001$) in ASCKDP has been seen compared to ESCKDP. On the other hand, we found a significant increase in the level of both mean corpuscular hemoglobin (MCH) (Mean: 31.29 to Mean: 46.59; $P < .001$) and mean corpuscular hemoglobin concentration (MCHC) (Mean: 36.71 to Mean: 55.32; $P < .001$) in ASCKDP compared to ESCKDP. Also, we noticed a significant decrease of packed-cell volume (PCV) (Mean: 29.68 to Mean: 19.63; $P < .001$) in ASCKDP than ESCKDP. Additionally, total and differential WBC count (neutrophils, lymphocytes, monocytes, eosinophils, and platelets), and different electrolytes (potassium, sodium, chlorine, and bicarbonate) in ASCKDP has been found compared to ESCKDP. However, these differences are not clinically significant.

Correlation among the different research parameters

Significant relationships among different parameters in different stages of CKD have been demonstrated using Spearman's rank correlation coefficient in Table 3. In ESCKDP, RBC is positively correlated with Hb ($r = .666$, $P < .001$), eGFR ($r = .786$, $P < .001$) and PCV ($r = .677$, $P < .001$), whereas it is negatively associated with creatinine ($r = -.739$, $P < .001$), MCH ($r = -.629$, $P < .001$) and MCHC ($r = -.632$, $P < .001$). In ASCKDP, RBC is positively correlated with Hb ($r = .452$, $P < .001$), creatinine ($r = .152$, $P = .066$), eGFR ($r = .126$, $P = .127$) and PCV ($r = .959$, $P < .001$), whereas it is negatively linked with MCH ($r = -.941$, $P < .001$) and MCHC ($r = -.915$, $P < .001$). Again, in ESCKDP, Hb is positively associated with eGFR ($r = .687$, $P < .001$) and PCV ($r = .471$, $P < .001$), whereas it is negatively connected with creatinine ($r = -.657$, $P < .001$), MCH ($r = -.306$, $P < .001$) and MCHC ($r = -.282$, $P < .001$). In ASCKDP, Hb is positively linked with creatinine ($r = .412$, $P < .001$) and PCV ($r = .396$, $P < .001$), whereas it is negatively associated with eGFR ($r = -.318$, $P < .001$), MCH ($r = -.397$, $P < .001$) and MCHC ($r = -.360$, $P < .001$). Moreover, in ESCKDP, MCH is positively associated with creatinine ($r = .471$, $P < .001$) and MCHC ($r = .828$, $P < .001$), whereas it is negatively correlated with eGFR ($r = -.484$, $P < .001$) and PCV ($r = -.464$, $P < .001$). But in ASCKDP, MCH is positively linked with MCHC ($r = .966$, $P < .001$) only and negatively associated with creatinine ($r = -.218$, $P = .008$), eGFR ($r = -.075$, $P = .367$) and PCV ($r = -.932$, $P < .001$). Lastly in ESCKDP, MCHC is positively correlated with creatinine ($r = .490$, $P < .001$) and negatively associated with eGFR ($r = -.522$, $P < .001$) and PCV ($r = -.689$, $P < .001$). But in ASCKDP, MCHC is negatively associated with creatinine ($r = -.230$, $P = .005$), eGFR ($r = -.048$, $P = .566$) and PCV ($r = -.960$, $P < .001$). Severity-specific associations of Hb, RBC, MCH, and MCHC have been presented using scattered plot graphs with fitted line curve (Figure 1).

Table 1. Characteristics and comorbid diseases of CKD patients.

PARAMETERS	ESCKDP (N = 153)			ASCKDP (N = 147)			*P* VALUE
	N	%	MEAN ± SD	N	%	MEAN ± SD	
Age in years			63.28 ± 9.26			65.97 ± 9.68	.014
40-60	62	40.53		46	31.29		
61-80	82	53.59		86	58.51		
Above 80	9	5.88		15	10.20		
Sex							.815
Male	61	39.87		61	41.50		
Female	92	60.13		86	58.50		
BMI (kg/m^2)			26.62 ± 4.06			31.84 ± 1.66	<.001
Below 18.5 (CED)	4	2.61		0	0		
18.5-25 (normal)	46	30.07		0	0		
Above 25 (obese)	103	67.32		147	100		
Hypertension							.031
Yes	124	81.05		103	70.07		
No	29	18.95		44	29.93		
Diabetes							.116
Yes	107	69.93		90	61.22		
No	46	30.07		57	38.78		
Hypothyroidism							.340
Yes	101	66.01		89	60.54		
No	52	33.99		58	39.56		
Dyslipidemia							.257
Yes	9	5.88		4	2.72		
No	144	94.12		143	97.28		
Hypernatremia							.069
Yes	109	71.24		90	61.22		
No	44	28.76		57	38.78		

Abbreviations: ASCKDP, advanced-stage CKD patients; BMI, body mass index; CED, chronic energy deficiency; CKD, chronic kidney disease; ESCKDP, early-stage CKD patients.

Discussion

Altered hematological parameters might help to evaluate the severity and comorbidities of CKD patients. Therefore, present study assessed the hematological parameters and comorbidities among hospitalized CKD patients. We observed some blood parameters altered in CKD patients. Among the parameters, we found a decreased Hb, RBC, and increased MCH and MCHC levels in ASCKDP than ESCKDP. Also, we noticed the degree of alterations directly associated with the severity of CKD patients. The reduced Hb levels may be due to iron-deficiency anemia caused by CKD.[17] Another potential mechanism of developing anemia in CKD patients is the reduced RBC lifespan as the production of erythropoietin reduces in CKD with the progression of the staging.[15] Also, we observed a decrease in PCV levels in ASCKDP than ESCKDP. However, this decrease was not associated with the severity of CKD. Therefore, the change in PCV levels in CKD might have statistical significance but not clinically significant. Without these, the levels of other parameters like different electrolytes, individual precursors of WBC, total WBC remain

Table 2. Hematological parameters of the study cohort at different severity levels of CKD.

PARAMETER	REFERENCE VALUE	ESCKDP (N = 153) MEAN ± SD	ASCKDP (N = 147) MEAN ± SD	*P*-VALUE
Creatinine (mg/dL)	Male: 0.74-1.35. Female: 0.59-1.04	2.33±0.52	4.13 ± 0.62	<.001
eGFR	More than 90	63.92 ± 26.1	17.49 ± 6.45	<.001
Hb (g/dL)	Male: 14-17.5; Female: 12.3-15.3	10.41 ± 1.38	9.22 ± 1.98	<.001
RBC ($\times 10^{12}$/L)	Male: 4.5-5.9; Female: 4.1-5.1	3.54 ± 0.49	2.35 ± 1.03	<.001
PCV (%)	Male: 39-51; Female: 36-48	29.68 ± 4.75	19.63 ± 8.74	<.001
MCV (fl)	80-100	85.37 ± 5.01	84.40 ± 5.26	.104
MCH (pg)	27-31	31.29 ± 4.78	46.59 ± 13.50	<.001
MCHC (%)	32-36	36.71 ± 5.76	55.32 ± 16.42	<.001
RDW-SD (fl)	40-55	44.71 ± 4.39	43.70 ± 5.19	.072
RDW-CV (%)	11-15	14.98 ± 1.85	14.66 ± 1.93	.144
NRBC (10^9/L)	0	0.03 ± 0.1	0.04 ± 0.12	.387
WBC (10^9/L)	4.5-11	8.29 ± 1.82	7.91 ± 2.00	.091
Neutrophils (10^9/L)	2-8	5.52 ± 1.27	5.27 ± 1.42	.115
Lymphocytes (10^9/L)	1.5-4.5	2.06 ± 0.61	2.02 ± 0.62	.606
Monocytes (10^9/L)	0.2-0.8	0.36 ± 0.14	0.32 ± 0.13	.008
Eosinophils (10^9/L)	0-0.4	0.30 ± 0.13	0.27 ± 0.15	.085
Basophils (10^9/L)	0-0.1	0.02 ± 0.01	0.02 ± 0.01	.622
Platelet (10^9/L)	150-450	241.45 ± 52.54	239.88 ± 57.79	.806
MPV (fl)	7.5-12	10.76 ± 0.87	10.74 ± 0.89	.893
PCT (%)	0.22-0.24	0.22 ± 0.005	0.23 ± 0.01	.016
PDW (fl)	8.1-25	12.73 ± 1.66	12.75 ± 1.75	.937
K^+ (mmol/L)	3.5-5.1	4.26 ± 0.52	4.16 ± 0.52	.098
Na^+ (mmol/L)	136-145	150 ± 7.9	148.50 ± 7.86	.098
Cl^- (mmol/L)	Adult: 98-107, elderly (>90 year): 98-111	105.04 ± 4.22	105.07 ± 4.35	.954
HCO_3 (mmol/L)	22-29	25.05 ± 3.58	25.23 ± 3.64	.668
HBA1C (%)	4-5.6	7.41 ± 1.43	7.39 ± 1.45	.876
TSH	0.5-5	4.34±1.28	4.20 ± 1.11	.341

Abbreviations: ASCKDP, advanced-stage CKD patients; Cl, chloride; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; ESCKDP, early-stage CKD patients; Hb, hemoglobin; HBAC1, hemoglobin A1C; HCO_3, bicarbonate; K, potassium; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volumes; MPV, mean platelet volume; Na, sodium; NRBC, nucleated red blood cell; PCT, procalcitonin; PCV, packed cell volume; PDW, platelet distribution width; RBC, red blood cell; RDW, red cell distribution width; TSH, thyroid-stimulating hormone; WBC, white blood cell.
P < .05 (Significant difference between patient and control groups at 95% confidence interval).

unchanged in both stages of CKD. The WBC count, neutrophils, lymphocytes, monocytes, eosinophils, basophils, K^+, Na^+, Cl^- and HCO3 levels have no significant association with CKD severity.

The present study findings are consistent with few earlier studies in different geographical locations and races. One previous research showed a significant decline in RBC indices in CKD.[36] Two studies conducted in Iran and Nigeria stated that

Table 3. Correlations among research parameters in the cohort at different severity stages of CKD.

PARAMETER	ESCKDP (N = 153)		ASCKDP (N = 147)	
	R	*P*	R	*P*
Creatinine and eGFR	−0.816	<.001	−0.754	<.001
Creatinine and HB	−0.657	<.001	.412	<.001
Creatinine and RBC	−0.739	<.001	.152	.066
Creatinine and PCV	−0.557	<.001	.186	.024
Creatinine and MCH	.471	<.001	−0.218	.008
Creatinine and MCHC	.490	<.001	−0.230	.005
eGFR and HB	.687	<.001	−0.318	<.001
eGFR and RBC	.786	<.001	.126	.127
eGFR and PCV	.541	<.001	.089	.283
eGFR and MCH	−0.484	<.001	−0.075	.367
eGFR and MCHC	−0.522	<.001	−0.048	.566
eGFR and HCO3	.075	.358	−0.316	<.001
HB and RBC	.666	<.001	.452	<.001
HB and PCV	.471	<.001	.396	<.001
HB and MCH	−0.306	<.001	−0.397	<.001
HB and MCHC	−0.282	<.001	−0.360	<.001
HB and TSH	.006	.948	.312	<.001
RBC and PCV	.677	<.001	.959	<.001
RBC and MCH	−0.629	<.001	−0.941	<.001
RBC and MCHC	−0.632	<.001	−0.915	<.001
PCV and MCV	.456	<.001	.210	.011
PCV and MCH	−0.464	<.001	−0.932	<.001
PCV and MCHC	−0.689	<.001	−0.960	<.001
MCH and MCHC	.828	<.001	.966	<.001
RDW-CV and PCT	.664	.036	.061	.687
WBC count and Neutrophils	.945	<.001	.960	<.001
WBC and Lymphocytes	.817	<.001	.850	<.001
WBC and Monocytes	.607	<.001	.713	<.001
WBC and Eosinophils	.481	<.001	.549	<.001
WBC and Basophils	.473	<.001	.497	<.001
Neutrophils and Lymphocytes	.640	<.001	.708	<.001

(Continued)

Table 3. (Continued)

PARAMETER	ESCKDP (N = 153)		ASCKDP (N = 147)	
	R	*P*	R	*P*
Neutrophils and Monocytes	.513	<.001	.622	<.001
Neutrophils and Eosinophils	.365	<.001	.444	<.001
Neutrophils and Basophils	.426	<.001	.407	<.001
Lymphocytes and Monocytes	.425	<.001	.628	<.001
Lymphocytes and Eosinophils	.415	<.001	.466	<.001
Lymphocytes and Basophils	.421	<.001	.519	<.001
Lymphocytes and PCT	−0.114	.754	−0.309	.037
Monocytes and Eosinophils	.591	<.001	.555	<.001
Monocytes and Basophils	.374	<.001	.411	<.001
Eosinophils and Basophils	.332	<.001	.363	<.001
Basophils and PCT	−0.266	.458	−0.381	.009
PCT and Na+	−0.798	.006	.243	.104
PCT and HBA1C	.344	.330	−0.324	.030

Abbreviations: ASCKDP, advanced-stage CKD patients; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; ESCKDP, early-stage CKD patients; HB, hemoglobin; HBAC1, hemoglobin A1C; HCO3, bicarbonate; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; Na, sodium; PCT, procalcitonin; PCV, packed cell volume; RBC, red blood cell; RDW, red cell distribution width; TSH, thyroid-stimulating hormone; WBC, white blood cell.
P < .05 (Significant difference between patient and control groups at 95% confidence interval).

individuals with an eGFR less than 60 mL/min/1.73 m^2 had a decreased total RBC count and Hb concentration, regardless of age or sex.[37,38] Reduced renal function results in decreased erythropoietin production, which results in decreased Hb synthesis and a decrease in the total number of RBCs.[39] The patient develops anemia because of this significant decrease in RBC.[40] Iron and erythropoietin produce RBC in the bone marrow.[17] A cross-sectional study among 251 CKD patients in Northwest Ethiopia reported that the prevalence of anemia was 64% which varies from 44.8% to 93.8% with increasing stages of CKD.[41] Another study showed that 19.5% of CKD patients developed severe anemia, and 25% of anemia-affected CKD patients developed anemia even after receiving therapy.[42] Also, a cross-sectional study among 1564 mixed ancestry South African patients showed lowered RBC and Hb levels in the case of CKD participants.[14] A prevalence of anemia ranged from 37.2% (stage 3) to 82.4% (stage 4-5).[14] There is also the prevalence of anemia even after hemodialysis in the case of a patient with CKD.[42] A cross-sectional study on 100 CKD patients revealed that the frequency of anemia among pre-dialyzed patients was 75%, whereas, frequency of anemia among hemodialyzed patients was 85% which contained 25% of severe and 70% of moderate cases.[36] Again, a hematological study on 39 Nigerian CKD patients reveals that 18% of the patients were affected with severe anemia, and 69% of the patients were affected with mild to moderate anemia.[37]

The decreased Hb and RBC levels might cause anemia in CKD patients. Also, we noticed negative associations between Hb and RBC levels with the staging of CKD patients. Several studies showed patients with CKD might suffer from different types of cardiac diseases.[43] Anemia in combination with CKD significantly increases the risk of stroke.[44] Additionally, CKD increases the risk of developing cardiovascular complications such as heart attack or stroke.[45] In our cohort study, we managed to show the relationship between different hematological parameters and different stages of CKD. We observed significant alterations in hematological parameters like RBC, Hb, MCH, MCHC, and PCV with increasing stages of CKD. Also, we have shown a positive and negative correlation among these parameters with eGFR and creatinine that are the primary diagnostic parameters of CKD. Though there are many studies regarding the prevalence of anemia among different CKD stages, there aren't many studies regarding the underlying causes or alterations in hematological parameters like RBC and Hb due to anemia which is a complication of CKD patients.[46-48] Moreover, alterations in hematological parameters like MCH, MCHC, and PCV are new findings that correlate with eGFR and creatinine and are very uncommon. We believe that our

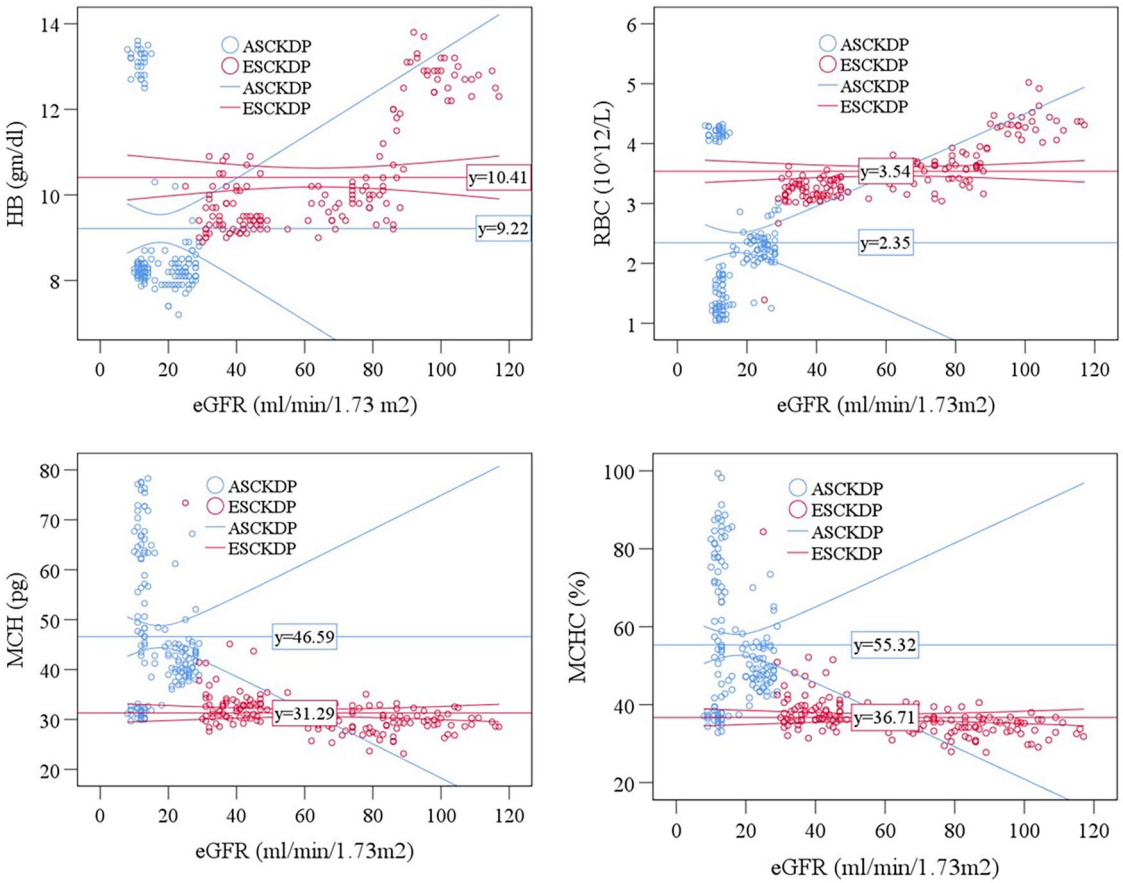

Figure 1. Scatter plot graphs showing association and mean difference of hemoglobin (Hb), red blood cell (RBC), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) with estimated glomerular filtration rate (eGFR) in different stages of CKD patients.
Abbreviations: ASCKDP, advanced-stage CKD patients; ESCKDP, early-stage CKD patients.

study will strengthen the concept of the prevalence of anemia due to changes in levels of RBC and Hb in CKD patients. Here we observed some other hematological parameters in CKD patients that were absent in many earlier investigations. It will open a new field of research concentrating on alterations on different hematological parameters in CKD patients. The present study findings might contribute to developing treatment guidelines, diagnosis, and staging of CKD patients.

The main strength of our study is that this is the first of its kind of study conducted in Bangladesh. As we have differences genetically from other ethnic populations, the outcome might be different from others. So, our study will help diagnose and treat CKD patients of Bangladesh more accurately and precisely. Our study is an observational cohort study. By using a cohort study, we can measure multiple outcomes from a single exposure. In our study, we measured the outcome value of Hb, RBC, MCH, and MCHC values in different stages of CKD. The methods we have used to determine hematological parameters are cost-effective and straightforward. Moreover, we routinely monitored the participants throughout the study timeline, including their hematological changes, dialysis status, so that the reports we get are up to date. We have used the conventional CBC test to determine the HB, RBC, MCH, and MCHC levels.

Potential limitations of the study

There are few limitations of our study. We have conducted this study with only 300 patients in Dhaka city. Using a sample population from a single hospital may not represent the whole scenario of the CKD patients of Bangladesh is another limitation of our study. Thus, the outcome of the present study might be different in those populations of Bangladesh. Another drawback is that this is a cohort study. As the selection of the study participants is not randomized, this leaves a chance of bias in our study though we take adequate measures to conduct the study unbiased. Another drawback of our cohort study is using a single measurement method. To avoid such bias, a randomized controlled trial (RCT) would be preferable in this case. The present study did not assess other hematological parameters such as vitamin-B12, iron, etc. Therefore, the present study findings suggest to conduct a randomized controlled trial with a larger population to get better outcomes with the minimization of biases. Future studies should explore other hematological abnormalities associated with the severity of CKD. The cause and types of anemia in CKD can be a potential field of study in the future. The researcher can also explore the association of anemia in CKD and CVD risk in the Bangladeshi population.

Conclusions

Alterations in hematological parameters in different stages of CKD have always been a center of attraction in diagnosis, treatment guidelines, and staging of CKD patients. Therefore, reduced Hb and RBC levels can serve as potential indicators for the severity of CKD and its treatment decisions. Additionally, our findings may assist with developing a treatment protocol for hospitalized CKD patients. Based on our results, it is recommended that further investigations on a broad range of blood parameters to explore the actual associations between hematology and CKD.

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Author Contributions

MAR, YS, MSA, KD, and MRI Conceptualization, data curation, and formal analysis. MHF, TM, and AAS Investigation, methodology, and writing original draft of manuscript. ZHM, MSR, AR, and MUA performed data analysis, editing the original draft of manuscript. MAR and MRI Supervised the whole work, gave intellectual inputs, and revising the manuscript.

Ethical Approval

The Research Ethics Committee (REC) of the University of Asia Pacific approved the study (REC/UAP/2021/104). We conducted this study following the principle stated in the Declarations of Helsinki. Before sample and data collection, all the participants were briefed about the objective and purpose of this study and their legal representatives. Additionally, we obtained consent from all participants or their legal representatives before they participated in this study.

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