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Anemia profile in Bangladeshi CKD patients: A cross-sectional study

Sushanta Barua [1,*], Nurul Huda [2], Mehdi Hasan [3], Nikhil Chandra Roy [4], Arifur Rahman [5], Shazedur Rahman [6], Uzzal Kumar Sikder [7], Akteruzzaman [8], Rita Rani Barua [9] and Ansari MA Jalil [10]

[1] *Department of Cardiology, National Institute of Cardiovascular Disease, Dhaka, Bangladesh.1207.*
[2] *Department of Nephrology, Chittagong Medical College Hospital, Chittagong, Bangladesh.*
[3] *Department of Cardiology, National Institute of Cardiovascular Disease, Dhaka, Bangladesh.1207.*
[4] *Department of Gastroenterology, BIHS, General Hospital, Dhaka, Bangladesh.*
[5] *Department of Gastroenterology, Upazila Health Complex, Bancharampur, Brahmanbaria, Bangladesh.*
[6] *Department of Cardiology, Sir Salimullah Medical College & Hospital, Dhaka, Bangladesh.*
[7] *Department of Gastroenterology Sheikh Russel National Gastroliver Institute and Hospital,Dhaka,Bangladesh.*
[8] *Department of Cardiology, Sathkira Medical College Hospital, Sathkira, Bangladesh.*
[9] *Department of Pathology, Dr. Sirajul Islam Medical College, Dhaka, Bangladesh.*
[10] *Department of Endocrinology Principal, MH Samorita Medical College, Tejgoan, Dhaka, Bangladesh.*

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Abstract

Background: Chronic kidney disease (CKD) is a growing public health concern worldwide, including Bangladesh. Anemia is a frequent and serious complication of CKD, worsening as the disease progresses. This study aimed to investigate the prevalence and characteristics of anemia according to CKD stage.

Objective: To determine the anemia profile in CKD patients.

Methods: A cross-sectional study recruited 66 CKD patients (stage 1 or above, aged ≥18 years) from the Nephrology unit of Chittagong Medical College Hospital (January 2014-June 2014). Glomerular filtration rate (GFR) was estimated using the MDRD equation, and kidney damage was assessed by abdominal ultrasound. Complete blood count, peripheral blood smear, iron status, vitamin B12, and serum folate levels were measured.

Results: Almost all CKD patients (97%) were anemic. Anemia severity increased with advanced CKD stages. Normocytic normochromic anemia, likely caused by erythropoietin (EPO) deficiency, was the most common type. Iron deficiency (absolute or functional) was present in a significant portion of patients (33.33%). Vitamin B12 and folate deficiency rarely contributed to anemia in this study

Conclusions: This study highlights the high prevalence and severity of anemia in advanced CKD patients at our hospital. Iron deficiency and functional iron deficiency are common, while vitamin B12 and folate deficiency play a minor role. Further research with larger, diverse populations is needed to better understand the complex interplay of factors contributing to anemia in CKD patients in our region.

Keywords: Anemia; Chronic kidney disease (CKD); Erythropoietin (EPO); Iron deficiency; Vitamin B12; Folate deficiency.

* Corresponding author: Barua S

1. Introduction

Anemia refers to a decrease in the total number of red blood cells (RBCs) or the amount of hemoglobin in the blood. It's diagnosed when hemoglobin, hematocrit, or RBC count falls below established levels [1]. Generally, women are more prone to anemia, especially during childbearing years. However, in later life, sex becomes less of a predictor. Interestingly, men with chronic kidney disease (CKD) have a 30% higher risk of anemia compared to women, even though they typically have higher hemoglobin levels. This is likely due to a higher prevalence of advanced CKD in men. Current smokers exhibit a lower prevalence of anemia, possibly due to secondary erythrocytosis [2, 3].Anemia is common in CKD patients. Iron deficiency can be a cause, either absolute (due to poor diet or occult bleeding) or functional (an imbalance between irons needs and supply). Iron deficiency leads to hypochromic microcytic anemia, characterized by small, pale red blood cells [3, 4]. Other culprits in CKD anemia include: Uremic inhibitors (e.g., parathyroid hormone, inflammatory cytokines), reduced lifespan of circulating red blood cells and Deficiencies of folate or vitamin B12 [3, 4].A landmark study by Obrador found that 68% of pre-dialysis patients with advanced CKD requiring renal replacement therapy had a hematocrit level below 30%. Among them, over half (51%) had a hematocrit less than 28% [4]. While less common in early CKD, the prevalence of anemia rises significantly with disease progression. For instance, patients with stage III CKD have a 5.2% prevalence of concurrent anemia, compared to 44.1% in stage IV [5].The etiology of anemia in advanced CKD is often multifactorial. It can involve: Decreased RBC production due to lack of erythropoietin, Increased RBC destruction from hemolysis (intravascular or extravascular) and Increased blood loss from frequent venipuncture procedures [6].This study aims to determine the specific characteristics of anemia in CKD patients and how these characteristics correlate with disease severity. This information is crucial for developing tailored treatment strategies to improve patient outcomes.

2. Material and method

2.1. Recruitment

A cross-sectional study recruited 66 CKD patients (stage 1 or above, aged ≥18 years) from the Nephrology unit of Chittagong Medical College Hospital (January 2014-June 2014. Patients with diagnosed chronic kidney disease (CKD) were informed about the study's aims, objectives, and procedures. Informed consent was obtained, with participants having the freedom to withdraw at any point.

2.2. Inclusion Criteria

Eligible subjects had a documented serum creatinine value within the past 3 months.

2.3. Staging CKD

Stages of Chronic Kidney Disease

- Stage 1: Kidney damage with normal or raised GFR, GFR ≥ 90ml / min /1.73 sq.m.
- Stage 2: Kidney damage with mild decrease in GFR, GFR 60-89ml / min /1.73 sq.m.
- Stage 3: Moderately decreased GFR, GFR 30-59ml/min/1.73 sq.m.
- Stage 4: Severely decreased GFR, GFR 15-29ml/min/1.73 sq.m.
- Stage 5 or ESRD (End stage renal disease): Kidney failure, GFR

2.4. Data Collection

A detailed medical history and physical examination were performed to assess CKD and related complications. Venipuncture was performed on all participants. Approximately 4ml of blood was collected in an EDTA vacutainer for hematological analysis (Full Blood Count and Peripheral Blood Film using Cell DYN 350). Additional blood samples (5ml) were collected in red-top vacutainers for analysis of renal function tests (Comprehensive Chemistry), Serum ferritin, Serum B12 & Folate. Serum iron and transferrin concentration were measured using an Architect c8000 analyzer system (Abbott, USA).

2.5. Data Analysis

Data was checked for consistency, completeness, and cleaned/edited if necessary. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 19.0.New variables were created as needed for analysis.

2.6. Study Variables

- **Qualitative/Discrete:** Age, sex, occupation, socio-economic condition, education level, type of anemia (normocytic normochromic, macrocytic, microcytic hypochromic).
- **Quantitative/Continuous:** Hemoglobin (Hb%), Hematocrit (Hct%), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), Serum creatinine, CKD stage, Serum ferritin, Transferrin Saturation (TSAT), Vitamin B12, and folate.
- **Outcome Variable:** Association between anemia and chronic kidney disease.

3. Result

This study was carried out to determine anemia profile status of CKD patients. Sixty six patients with different stages of CKD were selected for the study. Age ranged from 22 to 68 years, with an average of 52.6 years. More than half (62.1%) were over 50 years old. Males were more prevalent (75.8%) than females (24.2%) with a male-female ratio of 1: 0.32. about one-fourth (28.8%) of the patients' educational status was higher secondary and above whereas about one-fourth (28.8%) patients were illiterate as well. Most of the patients were housewives (24.2%); another important group was industrial workers (21.2%). The economic status of the maximum patients was middle class (37.9%) whereas only 15.2% patients' economic status was very poor. Out of 66 patients of CKD, 64 (97%) were anemic and 2 (3%) were non-anemic clinically. Both clinically non-anemic patients were males. 28 (42.4%) patients out of 66 had edema clinically. Mean systolic and diastolic BP were 133.70±14.95 and 74.34±7.99 mmHg, respectively. (Table 1).

Table 1 Sample Characteristics

Characteristics	Number	Percentage
Age		
Up to 40 years	6	9.1%
41-50 years	19	28.8%
51-60 years	32	48.5%
61-70 years	9	13.6%
Mean age (in years) 52.59 ± 9.028		
Male	50	75.8%
Female	16	24.2%
Education		
Illiterate	19	28.8%
Primary	16	24.2%
Secondary	12	18.2%
Higher secondary & above	19	28.8%
Occupation		
Housewife	16	24.2%
Industrial worker	14	21.2%
Executive	4	6.1%
Service	6	9.1%
Professional	6	9.1%
Teacher	6	9.1%
Farmer	6	9.1%
Business	6	9.1%

Others	2	3.0%
Economic status		
Very poor	10	15.2%
Poor	21	31.8%
Middle class	25	37.9%
Upper class	10	15.2%
Signs	Yes	No
Anemia		
Male	48 (96%)	2 (4%)
Female	16 (100%)	0 (0%)
Edema		
Male	20 (40.0%)	30 (60.0%)
Female	8 (50.0%)	8 (50.0%)
Vital signs	Mean	SD
Pulse	72.52	3.12
Systolic BP	133.70	14.35
Diastolic BP	74.34	7.99

3.1. Anemia Prevalence

A very high prevalence of anemia (97%) was observed in CKD patients. Only 2 (3%) patients were clinically non-anemic, both being male. Severity distribution: Severe anemia: 30.3% Moderate anemia: 40.9% Mild anemia: 27.3% No anemia: 1.5%.Most patients (69.2%) had stage V CKD, followed by stage IV (15.4%), stage III (10.8%), and stage II (4.6%). Hemoglobin concentration decreased with advanced CKD stages. The average hemoglobin level was 8.28 g/dL. Mean haemoglobin concentration, hematocrit level and red cell indices in different stages of CKD are shown in Table II. F test was done to show their association with CKD stages. Hematocrit, MCH and MCHC was found statistically significant with the CKD stage. Haematocrit level decreased with increased stage of CKD. MCH level was lowest (25.08±5.53 pg) in stage iv CKD. MCHC level was lowest (29.18±5.33 g/dL) in stage iv CKD as well.

Table 2 Serum Hb, haematocrit and red cell indices of the patients with CKD (N=66)

Serum level	**CKD**	**Number**	**Mean±SD**	**F**	***P***
Haemoglobin (g/dL)	Stage ii	3	9.80±1.31	1.93	0.134
	Stage iii	7	9.00±1.25		
	Stage iv	10	8.23±2.05		
	Stage v	46	8.08±1.34		
Haematocrit (fl)	Stage ii	3	29.40±3.93	2.63	0.05
	Stage iii	7	28.65±4.82		
	Stage iv	10	24.48±5.98		
	Stage v	46	24.57±4.14		
MCV (fl)	Stage ii	3	75.13±1.21	0.77	0.52
	Stage iii	7	67.97±7.45		
	Stage iv	10	79.33±19.24		

	Stage v	46	74.76±15.12		
MCH (pg)	Stage ii	3	32.00±1.00	3.53	0.02
	Stage iii	7	31.21±2.23		
	Stage iv	10	25.08±5.53		
	Stage v	46	28.37±4.32		
MCHC (g/dL)	Stage ii	3	34.67±0.58	4.54	0.006
	Stage iii	7	34.57±0.77		
	Stage iv	10	29.18±5.33		
	Stage v	46	31.96±2.96		

3.2. Peripheral Blood Film Morphology

Among 66 CKD patients, peripheral blood film was done in 66 patients. Table III shows that Normocytic normochromic cells were observed in stage II and III CKD. Stage IV CKD displayed a mix of cell types: dimorphic, normocytic normochromic, microcytic hypochromic, and macrocytic. Stage V CKD had the highest prevalence of normocytic normochromic cells, followed by dimorphic and microcytic hypochromic cells. The association between peripheral blood film morphology and CKD stage wasn't statistically significant.

Table 3 Peripheral blood film of the patients with CKD(N=66)

CKD	**Normocytic normochromic**	**Macrocytic**	**Microcytic hypochromic**	**Dimorphic**	***P***
	N (%)	N (%)	N (%)	N (%)	
Stage ii	3 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.33
Stage iii	7 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Stage iv	2 (22.22)	1 (11.11)	2 (22.22)	4 (44.44)	
Stage v	30 (65.2)	1 (2.17)	6 (13.0)	9 (19.6)	

3.3. Iron Status

Nine study participants (13.63%) had absolute iron deficiency and female had high proportion (18.75%) whilst functional iron deficiency was seen in (19.70%) of study participants. The gender difference on iron status was not statistically significant, p-value> 0.05 respectively in all categories of iron status except normal iron status (Table IV).

Table 4 Magnitude of iron deficiency among CKD patients (N=66)

Iron Status	**Male n=50**	**Female n=15**	**Total=65**	**p-value**
Normal iron status	36(72%)	7(46.67%)	43(66.15%)	0.0241
Absolute Iron deficiency	6(12%)	3(20%)	9(13.85%)	0.0961
Functional	8(26%)	5(33.33%)	13(20%)	0.1437

3.4. Vitamin B12 and Folate

Levels were measured in patients with macrocytic and dimorphic blood films. Both vitamin B12 and folate levels were higher in patients with dimorphic films compared to macrocytic films.

Table 5 Vitamin B12 and folate in relation to PBF (N=66)

Serum level	PBF	Number	Mean± SD	Z	*P*
Vitamin B12 (pmol/L)	Macrocytic	1	240.00	1.53	0.15
	Dimorphic	13	225.85±8.92		
Folate	Macrocytic	1	2.00	1.83	0.09
	Dimorphic	13	10.92±4.68		

4. Discussion

Present observational study was conducted in the Nephrology department of Chittagong Medical College and Hospital to evaluate the anemia profile in chronic kidney disease (CKD). A total of 100 patients were screened, and 66 consecutive cases of CKD were enrolled. The study population ranged in age from 22 to 68 years, with a mean of 52.59 years. Most patients (62.1%) were over 50 years old, similar to other studies [7, 8]. Males were more prevalent (75.8%) than females (24.2%). This aligns with findings in some studies [7, 8] but differs from others [9]. The data revealed a diverse range of socioeconomic backgrounds, with some patients being illiterate and others working in industrial jobs. This aspect was not explored in the studies compared here. The economic status of the majority of patients was middle class (37.9%), whereas only 15.2% of patients belonged to the very poor category. No other studies compared here highlighted the socioeconomic status of CKD patients with iron profiles. The majority (84.85%) of patients had advanced CKD (stage 4 or 5). This finding aligns with studies from Southeast Asia [10, 11] but differs from an Indonesian study with a higher proportion of earlier CKD stages [9]. This contrasts with studies in developed countries where earlier detection is more common [4, 9]. This might be due to limited early screening programs in our region. A very high prevalence of anemia (98.15%) was observed across all CKD stages. This aligns with studies in India (98%) but is higher than those in the USA (47.75%) or Indonesia (73.1%) [4, 10]. Potential explanations include the high proportion of advanced CKD cases and other environmental factors affecting nutrition. While most studies show a rising prevalence of anemia with advancing CKD stages [7, 12], this study found a different pattern. Here, anemia prevalence was high even in early stages (stage 3: 4.55%). This variation might be due to a small sample size and the possibility of other anemia-contributing factors in early-stage patients compared to later stages. Additionally, improvement in hemoglobin levels of stage 5 patient's already receiving treatment could influence the observed trend. Moderate anemia was the most common type (40.91%), followed by severe (30.30%) and mild anemia (27.27%). This aligns with a study in South India [10].This prevalence pattern is not similar to the findings in our study due most likely to the difference in the population and geographic variation**.** Mean hematocrit level was highest in stage 5 CKD (29.40 ± 3.93 fl) as well. MCV was higher in CKD stage IV, whereas MCH and MCHC were higher in CKD stage II. Similar findings were reported in a study by Akinsola A [13] from Nigeria in that study haemoglobin concentration was highest in stage CKD ii, MCV was more in CKD stage IV, whereas MCH and MCHC were more in CKD stage ii. (30.30%). Normocytic normochromic anemia was the dominant type (65.2% in stage 5), followed by dimorphic anemia (19.6%). This is consistent with other studies [7, 10], suggesting EPO deficiency as the primary cause. Only 66.67% of patients met the NKF-K/DOQI iron sufficiency guidelines. Iron deficiency (serum ferritin <100 ng/ml and TSAT <20%) was found in 13.63% of patients, with functional iron deficiency (serum ferritin >100 ng/ml and TSAT <20%) in 19.70%. These findings are similar to other studies [14].In this study it was evidently noted that, fewer anemic CKD patients (2.2%) had low levels of serum folate and both cases were macrocytic morphologically whilst only (2.2%) of anemic CKD patient had low level of serum vitamin B12 deficiency. Ketut S et al[9] exploring the profile of anemia among CKD patients reported similar results in which also two cases had low level of serum folic acid and all cases had normal level of serum vitamin B12.This result verifies that, folic acid and vitamin B12 were not important contributing factor to anemia in this study.

Limitations

This study acknowledges its limitations, including a relatively small sample size. This could explain some of the observed variations in prevalence and severity compared to other studies.

5. Conclusion

This study highlights the high prevalence and severity of anemia in advanced CKD patients at our hospital. Iron deficiency and functional iron deficiency are common, while vitamin B12 and folate deficiency play a minor role. Further research with larger, diverse populations is needed to better understand the complex interplay of factors contributing to anemia in CKD patients in our region.

Compliance with ethical standards

Acknowledgement

Acknowledges study population and department of nephrology**.**

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of Ethical approval

An ethical clearance was taken from Chittagong Medical College.

Statement of Informed consent

Informed consent was obtained, with participants having the freedom to withdraw at any point.

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