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Research Article

HEMATOLOGICAL PROFILE IN PATIENTS OF CHRONIC KIDNEY DISEASE WITH ITS SEVERITY IN A TERTIARY CARE HOSPITAL, NORTH ODISHA

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ABSTRACT

Objective: Efforts can be made to normalize the hematological parameters and slow the progress of the disease so that the morbidity and mortality in these patients with chronic kidney disease could be effectively reduced.

Methods: The observational study was carried out in the Department of General Medicine, Pandit Raghunath Murmu Medical College Hospital, Baripada, between May 2018 and January 2019. Two hundred seventy patients of chronic kidney disease (CKD) above 15 years of age, satisfying the inclusion and exclusion criteria, were included in the study.

Results: In our study, 179 (66.30%) were male, and 91 (33.70%) were female with M:F of 1.97:1. The average age of the patients in the study was 55.72±12.77 years. About 42.59 % (115) of the patients were between 46 and 60 years of age. About 35.56% of CKD cases had determined etiology and, 64.44% of cases had unknown etiology. Hemoglobin, RBC, and packed cell volume were significantly lower in the patients with CKD compared to the controls (p=0.0001), and RDW was considerably higher in the patients with CKD compared to the controls (p=0.0001). Microcytic anemia was the most prevalent type of anemia. There was a hugely significant association between the prevalence of thrombocytopenia and the severity of CKD (p=0.006).

Conclusion: This study concluded that patients with CKD show abnormal hematological parameters. Evaluation of hematological parameters in these patients helps in classifying the type of anemia, aids in choosing the correct treatment modalities, and decreases mortality.

Keywords: Chronic kidney disease, Anemia, Hemoglobin, Red blood count, Thrombocytopenia.

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INTRODUCTION

Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiologic processes coupled with abnormal kidney function and a progressive decrease in glomerular filtration rate (GFR) [1]. CKD is a universal public health problem, both for the number of patients and the cost of treatment involved, especially in developing countries like India. Internationally, CKD is the 12th cause of death and the 17th cause of disability, respectively [2] with a prevalence of 8–16% [3]. About 6% of the adult populations have CKD Stages 1 and 2, and 4.5% have CKD Stages 3 and 4 (United States population data) [1].

As stated by the National Kidney Foundation in India, renal diseases ranked 3rd among the life-threatening diseases after cancer and heart disease, with about 2 Lakh persons landing into terminal renal failure annually and millions more suffering from lesser forms of renal diseases [4].

The prevalence is high in India, with 229/million population suffering from end-stage renal disease (ESRD) [5]. Community-based studies planned to detect stage 3 CKD or worse show prevalence between 0.16% and 0.79%; with the actual incidence of CKD is higher than the reported number [6-8]. The ESRD incidences have been reported to be 160–232 per million populations (pmp) [5,6] with a projected ESRD prevalence of 785–870 pmp [5,9]. In summary, from the database of CKD registry of India, the yearly incidence of ESRD in India is approximately 150–200 pmp with diabetes mellitus as an important cause of CKD in approximately 30–40% of the cases [10].

There is a proportional increase in the prevalence and severity of hematological impairment with increasing severity of kidney dysfunction. Studies have revealed that anemia begins to noticeable when GFR falls below 60 ml/min/1.73 m^2 (Stage III) [11]. Accordingly, the prevalence of anemia ranges from about 1% in stage 2 of CKD to almost 100% in ESRD patients [12].

Pathophysiologically, anemia is determined by multiple factors in CKD patients [13]. A kidney is a crucial site for EPO production, contributing 80–90% of total EPO in circulation (rest 10–20% produced in the liver). The most significant and crucial factor are the deficient production of erythropoietin (EPO) by the damaged kidneys [14]. Other important factors contributing to the development of anemia in CKD include nutritional deficiencies (Iron, folate, or Vitamin b12), increased blood loss, systemic and chronic inflammatory state, hyperparathyroidism, and shortened red cell survival by uremic toxins and drugs [15].

A load of cardiovascular disease in CKD is further augmented in the coexistence of anemia, particularly in high-risk populations, together with a higher risk of progression of CKD to ESRD and repeated hospitalization [16,17].

Anemia in CKD is associated with disease progression, cardiovascular comorbidities, cognitive impairment, sleep disorder, and higher mortality [18,19]. Direct health-care costs are on the rise in CKD patients with anemia than in those without [20]. Among CKD patients, at all levels of GFR, anemia portends a poor prognosis and is associated with increased mortality compared with those individuals with preserved hemoglobin (Hb) [21].

We come across a large number of patients with CKD with abnormal hematological parameters in our institution of PRM Medical College, Baripada. As these being unpublished facts, we want to carry out a study, first of this type in our new medical college, to assess the array of

hematological abnormalities in our patients with predialysis CKD and associated factors.

METHODS

The observational study was conducted in the Department of General Medicine, Pandit Raghunath Murmu Medical College Hospital, Baripada. The CKD patients who had attended the department of general medicine OPD and who were admitted to the department of general medicine, PRM MCH, Baripada between May 2018 and January 2019 were enrolled in our study.

Inclusion criteria

- All patients of CKD above 15 years of age, satisfying the following criteria, were included in the study. Criteria for diagnosis of CKD were as given by – National Kidney Foundation: K/DOQI clinical practice guidelines for CKD: Evaluation, classification, and stratification [22].

CKD is defined as the presence, for at least 3 months, of evidence of kidney damage with an abnormal GFR or alternatively, by a GFR <60 ml/min/1.73m^2 BSA [22].

Kidney damage is evidenced by:

- Proteinuria >300 mg/day OR
- Pathological abnormality found in histopathological study OR
- Renal imaging study (USG) showing bilateral contracted kidneys <9.0 cm with thinned parenchyma and reduced corticomedullary differentiation.

Exclusion criteria

The following criteria were excluded from the study:

- Patients aged below 15 years of age
- Patients on hemodialysis
- Pregnant and lactating women
- Aplastic anemia
- Known hematological malignancy causing secondary renal failure
- History of blood transfusion during the past 3 months
- History of erythropoietin therapy during the past 3 months
- Patients suffering from recent hemorrhagic episodes were excluded from the study.

Two hundred seventy CKD patients were included in the study, divided into three groups.

- Group A → Mild CKD (n=120) (S. Creatinine =1.5–3.0 mg/dl)
- Group B → Moderate CKD (n=91) (S. Creatinine =3–6.0 mg/dl)
- Group C → Severe CKD (n=59) (S. Creatinine > 6.0 mg/dl).

Investigations

After due consideration into inclusion and exclusion criteria, detailed history and clinical examination were undertaken in all patients. All patients had undergone thorough laboratory investigations such as complete blood counts (Sysmex XS-800i), urine analysis, blood sugar, serum urea, and creatinine. Ultrasonography of the abdomen was done on every patient. The CKD epidemiology collaboration equation, 2009, was used to calculate e-GFR. e-GFR was graded G1, G2, G3a, G3b, G4, and G5 as indicated by the KDIGO 2012 guidelines [1]. Forty healthy persons were taken as controls.

The World Health Organization defined anemia as Hb concentration <12 g/dl (females), <13 g/dl (males) classifying the severity of anemia as mild anemia (Hb concentration between 11–12.9 g/dl for males and 11–11.9 g/dl for females); moderate anemia (Hb concentration between 8 and 10.9 g/dl), and severe anemia (Hb concentration <8 g/dl) [23]. Thrombocytopenia was defined with a value of <150×10^3/µl.

Statistical analysis

The statistical analysis was done using the Statistical Package for the Social Sciences version 21.0. The demographic features of the study population were explained using univariate analysis. Discrete variables were described as frequency and percentages. Continuous variables were presented as means and standard deviation (SD) for unpaired data; the Student's t-test was used to compare mean values (for two groups). Pearson's correlation was used to establish the association between eGFR and other variables. A Chi-square test was used to determine the significant associations between categorical variables. $p<0.05$ was considered statistically significant* and < 0.01 was considered as statistically hugely significant**.

RESULTS

During the study period, 270 CKD patients above 15 years of age, satisfying the inclusion and exclusion criteria were included in the study. All the cases were studied for the clinical presentation, risk factors, and laboratory parameters.

Out of 270 patients, 179 (66.30%) were male and 91 (33.70%) were female with M:F of 1.97:1 (Fig. 1). The average age of the patients in this study was 55.72±12.77 years. The average age of the male and female patients in the study was 55.63±13.24 and 55.89±11.84 years, respectively. The age range was from 20 to 95 years.

Fig. 2 shows that 42.59 % (115) of the patients were between 46 and 60 years of age, and 26.30% (71) of the patients were between 61 and 75 years of age.

Fig. 3 shows that 35.56% CKD cases had determined etiology such as hypertension (32.22%), diabetes (4.07%), adult polycystic kidney disease (1.48%), obstructive nephropathy (1.11%), and medullary sponge kidney (0.37%); and rest of the 64.44% cases had unknown etiology.

Table 1 shows 21.85% (59), 42.59% (115), and 35.56% (96) of the patients in our study group belong to stage 3, stage 4, and stage 5 CKD, respectively.

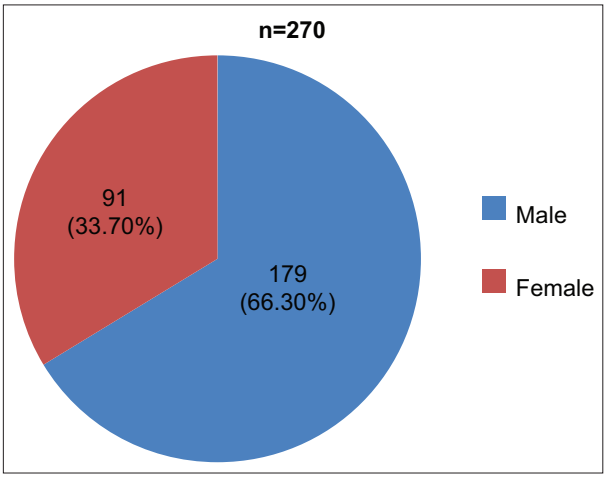

Fig. 1: Gender distribution

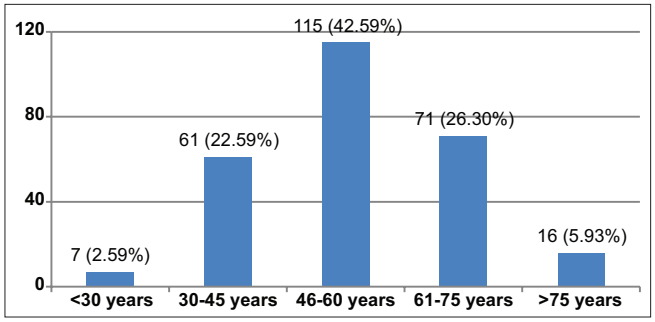

Fig. 2: Age distribution

Fig. 4 show 120 (44.44%) patients belong to mild CKD (Group-A), 91 (33.70%) patients belong to moderate CKD (Group-B), and 59 (21.85%) patients belong to severe CKD (Group-C) in our study group.

Table 2 shows the comparisons between hematologic indices of CKD patients and healthy controls. Hb, RBC, and packed cell volume were significantly lower in the patients with CKD compared to the controls (p=0.0001), and RDW was significantly higher in the patients with CKD compared to the controls (p=0.0001).

Table 3 shows the correlation coefficient of eGFR with different variables in CKD patients. Negative Pearson's correlation coefficient value indicate age, the level of systolic BP, diastolic BP, blood urea, serum creatinine, MCV, MCH, MCHC, and RDW increase with the decline of GFR and positive Pearson's correlation coefficient value indicate the level of hemoglobin, RBC, PCV, and TPC decrease with the decline of GFR. On correlating eGFR with various parameters, statistical significance was observed with systolic blood pressure (r=−0.191, **p=0.0016), diastolic blood pressure (r=−0.140, *p=0.0213), B. Urea (r=−0.729, **p=0.00001), S. Creatinine (r=−0.787, **p=0.00001), hemoglobin (r=0.290, **p=0.00001), RBC (r=0.342, **p=0.00001), PCV (r= 0.315, **p=0.00001), and MCH (r=−0.150, *p=0.0136).

Table 4 shows the prevalence of anemia increased from 96.61% in Stage 3, 97.39% in Stage 4, and 100% in Stage 5 CKD, respectively. There was a hugely significant association between the severity of anemia and the stage of CKD (**p=0.000032).

Table 5 shows that 98.15% (265 cases) of the study population had anemia. The prevalence of anemia increased from 96.67% in mild CKD, 98.90% in moderate CKD, and 100% in severe CKD, respectively. There was a hugely significant association between the severity of anemia and the severity of CKD (**p=0.00001).

Table 6 shows that 80.37% (217) of CKD patients had microcytic anemia. Normocytic anemia was seen in 17.41% (47) of CKD patients and macrocytic anemia was seen in 0.37% (1) of CKD patients. There was no significant association between the type of anemia (PCV) and the severity of CKD.

Table 7 shows that 38.52% (104 cases) of the study population had thrombocytopenia. The prevalence of thrombocytopenia increased from 30.83% in mild CKD, 35.16% in moderate CKD, and 59.32% in severe CKD. There was a hugely significant association between the prevalence of thrombocytopenia and the severity of CKD (**p=0.006).

Table 8 show that there was a hugely significant association between blood urea and serum creatinine level with mild, moderate, and severe CKD (**p=0.0001). There was decrease in level of hemoglobin, RBC, and PCV with severity of disease with hugely significant association between mild to severe and moderate to severe CKD (**p=0.0001).

Table 1: Chronic kidney disease stage based on GFR

Stage of chronic kidney disease (ml/min)	n	f (%)
Stage 1 (GFR > 90)	0	0.00
Stage 2 (GFR 60–89)	0	0.00
Stage 3a (GFR 45–59)	6	2.22
Stage 3b (GFR 30-44)	53	19.63
Stage 4 (GFR 15–29)	115	42.59
Stage 5 (GFR <15)	96	35.56
Total	270	100

DISCUSSION

In our study, out of 270 patients, 179 (66.30%) were male, and 91 (33.70%) were female with M:F of 1.97:1. As per the patients enrolled in the database of "The Indian CKD Registry," a voluntary reporting body of CKD patient's data, initiated in June 2005, 70% of them were males [10]. The patients in the study had an average age of 55.72±12.77 years, ranging from 20 to 95 years. Most of the patients, 74.82% were above 45 years of age, but still, 25.18% of the CKD patients were below 45 years of age, which was significant in number. According to Suhnggwon Kim *et al*. 2009, the average age of the CKD patient was with mean 50.5 years and a SD of 11.1 years [24].

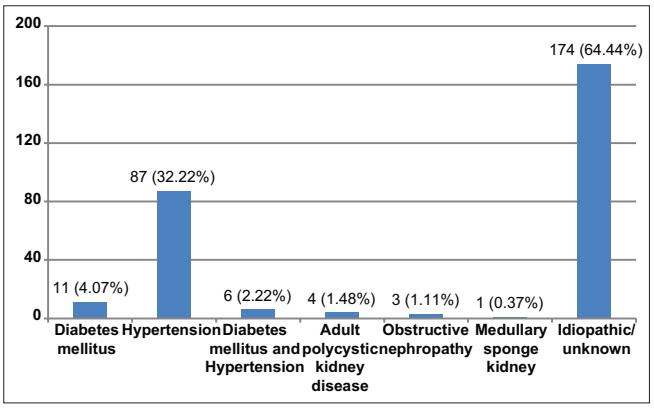

Fig. 3: Etiology of chronic kidney disease

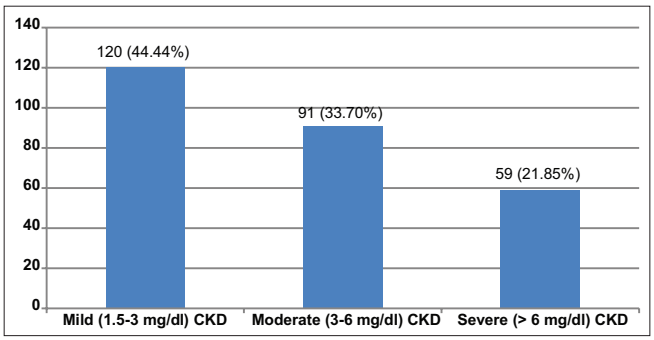

Fig. 4: Creatinine levels with severity of chronic kidney disease

Table 2: Hematologic indices of CKD patients and controls

Indices	CKD patients (n=270) (mean±SD)	Controls (n=40) (mean±SD)	p-value
Hemoglobin (g/dl)	7.76±2.50	13.20±1.03	0.0001**
Red blood count (M=4.7–6.1 million/mm^3 and F=4.2–5.4 million/mm^3)	3.27±1.03	5.64±0.65	0.0001**
Mean corpuscular volume (80–100 fL)	70.53±9.42	71.99±8.67	0.3563
Packed cell volume/hematocrit (M=40.7–50.3% and F=36.1–44.3%)	22.95±7.53	40.13±3.06	0.0001**
Mean corpuscular hemoglobin (27–31 pg)	23.61±3.06	23.56±3.43	0.9244
Mean corpuscular hemoglobin concentration (33.4–35.5 g/dl)	33.51±4.74	32.86±1.49	0.3905
Red blood cell distribution width (RDW) (11.5–14.5%)	16.33±2.46	14.49±2.05	0.0001**
Total platelet count (1.5–4.5 lakh per ml)	1.87±0.89	1.85±0.47	0.8894

*Significance at p <0.05, ** hugely significance at p <0.01

We revealed that 35.56% CKD cases had determined etiology such as hypertension (32.22%), diabetes (4.07%), adult polycystic kidney disease (1.48%), obstructive nephropathy (1.11%), and medullary sponge kidney (0.37%); and rest of the 64.44% cases had unknown etiology; which is an important finding. CKD of unknown etiology has also been documented from other parts of South Asia and among South Asians living in the UK [25].

Table 3: Correlation coefficient of eGFR with different variables in CKD patients

Variables	Pearson correlation coefficient (r)	p-value
Age	−0.002	0.9739
Systolic BP	−0.191	0.0016**
Diastolic BP	−0.140	0.0213*
Blood urea	−0.729	0.00001**
Serum creatinine	−0.787	0.00001**
Hemoglobin	0.290	0.00001**
RBC	0.342	0.00001**
MCV	−0.030	0.6235
PCV	0.315	0.00001**
MCH	−0.150	0.0136*
MCHC	−0.080	0.1900
RDW	−0.062	0.3101
TPC	0.096	0.1155

*Significance at p <0.05, ** hugely significance at p <0.01

In our study, Hb% ranged from 2.8 to 14.3 g/dl, with a mean of 7.76±2.50 g/dl. The RBC count ranged from 1.19 to 5.8 × 10^3 /µl, with a mean of 3.27±1.03. Hematocrit ranged from 7.6% to 43.5%, with a mean of 28.48%±7.8%. These parameters are quite similar to the findings in Shastry *et al*. study [26]. In Shastry *et al*. study, Hb level ranged from 3.6 to 14.2 g/dl with a mean of 9.31±0.52 g/dl, the RBC count ranged from 1.29 to 4.22 × 10^3/µl, with a mean of 3.29±0.79 and hematocrit ranged from 11.6% to 42% with a mean of 28.48±7.8%. Our study recognized that Hb, RBC, and packed cell volume were significantly lower in the patients with CKD compared to the controls (p=0.0001), which was also revealed in Shastry *et al*. study. We found positive Pearson's correlation coefficient value, which indicates the level of Hb, RBC, and PCV decrease with the decline of eGFR, with statistical significance (p=0.00001). We revealed in our study that there was a decline in the level of Hb, RBC, and PCV with the severity of disease with a hugely significant association between mild to severe and moderate to severe CKD (p=0.0001). Singh *et al*. [27], Poudel *et al*. [28], Bueno and Frizzo

Table 4: Associations between the severity of anemia and stage of CKD (with e-GFR)

Severity of anemia	CKD Stage 3		CKD Stage 4		CKD Stage 5		Test statistic
	n	f (%)	n	f (%)	n	f (%)	
Mild (11–12.9 g/dl in males) and (11–11.9 g/dl in females)	9	15.79	13	11.61	6	6.25	χ^2=25.9988 df=4
Moderate (8–10.9 g/dl)	20	35.09	55	49.11	20	20.83	p=0.000032**
Severe (<8 g/dl)	28	49.12	44	39.29	70	72.92	

*Significance at p <0.05, ** hugely significance at p <0.01

Table 5: Associations between the severity of anemia and the severity of CKD (with serum creatinine)

Severity of anemia	Mild (n=120)		Moderate (n=91)		Severe (n=59)		Test statistic
	n	f (%)	n	f (%)	n	f (%)	
Mild (11–12.9 g/dl in males) and (11–11.9 g/dl in females)	17	14.17	8	8.79	3	5.08	χ^2=35.1204 df=4
Moderate (8–10.9 g/dl)	49	40.83	41	45.05	5	8.47	p=0.00001**
Severe (<8 g/dl)	50	41.67	41	45.05	51	86.44	

*Significance at p <0.05, ** hugely significance at p <0.01

Table 6: Associations between types of anemia and severity of CKD

MCV (fL)	Mild (n=120)		Moderate (n=91)		Severe (n=59)		Test statistic
	n	f (%)	n	f (%)	n	f (%)	
Microcytic (<80 fL)	96	80.00	74	81.32	47	79.66	χ^2=0.0786
Normocytic (80–100 fL)	20	16.67	16	17.58	11	18.64	df=2
Macrocytic (>100 fL)	0	0.00	0	0.00	1	1.69	p=0.961459

Table 7: Associations between thrombocytopenia and severity of CKD

Platelet count (lakh/ml)	Total	f (%)	Mild (n=120)		Moderate (n=91)		Severe (n=59)		Test statistic
			n	f (%)	n	f (%)	n	f (%)	
<1.5	104	38.52	37	30.83	32	35.16	35	59.32	χ^2=14.3966 df=4
1.5–4.5	159	58.89	79	65.83	57	62.64	23	38.98	p=0.006131**
>4.5	7	2.59	4	3.33	2	2.20	1	1.69	
	270	100.00	120	100	91	100	59	100	

*Significance at p <0.05, ** hugely significance at p <0.01

Table 8: Associations of hematologic indices with the severity of CKD patients

Hematologic indices	Mild (A) (Mean±SD)	Moderate (B) (Mean±SD)	Severe (C) (Mean±SD)	p-value (A vs. B)	p-value (A vs. C)	p-value (B vs. C)
Blood urea	66.61±22.34	111.49±32.53	191.79±62.02	0.0001**	0.0001**	0.0001**
Serum creatinine	2.24±0.41	3.98±0.78	8.79±2.35	0.0001**	0.0001**	0.0001**
Hemoglobin	8.43±2.38	7.96±2.46	6.10±2.04	0.1629	0.0001**	0.0001**
RBC	3.59±1.01	3.33±0.97	2.54±0.81	0.0610	0.0001**	0.0001**
MCV	70.65±9.63	70.43±9.30	70.44±9.36	0.8677	0.8901	0.9949
PCV	25.21±7.46	23.30±7.04	17.81±5.85	0.0606	0.0001**	0.0001**
MCH	23.36±3.30	23.49±2.88	24.29±2.75	0.7651	0.0634	0.0929
MCHC	33.25±4.62	33.52±4.58	34.04±5.27	0.6735	0.3063	0.5233
RDW	16.29±2.38	16.20±2.61	16.61±2.42	0.7944	0.4015	0.3352
TPC	1.98±0.88	1.82±0.86	1.72±0.946	0.1880	0.0720	0.5055

*Significance at p <0.05, ** hugely significance at p <0.01

[29], and De Francisco *et al*. [30], and Elsayed and Azab [31] studies also showed decreased Hb, low RBC counts, and hematocrit values associated with CKD patients. It has been proposed that in CKD, impaired production of EPO is the foremost reason for the decline in RBC count, Hb concentration, hematocrit, and platelet count with other related factors such as increase hemolysis, suppression of bone marrow erythropoiesis, hematuria, and gastrointestinal blood loss playing their parts in it.

Anemia was observed in 98.15% (265 cases) of the study population with a hugely significant association between the severity of anemia and the severity of CKD (**p=0.00001); comparable to the figures found in studies by Shittu *et al*. and Arun *et al*., who reported the prevalence of anemia to be 94% and 98%, respectively [32,33]. The association of the severity of anemia with the stage of CKD and the severity of CKD (**p=0.000032) were hugely significant, which was similar to Suresh *et al*. study [34]. Microcytic anemia was seen in 80.37% (217) of CKD patients. In India, iron deficiency anemia is widespread. Talwar *et al*. study reported microcytic hypochromic anemia as the predominant type of anemia observed in CKD patients [35]. About 38.52% (104 cases) of the study population had thrombocytopenia. The level of total platelet count was declined, though not statistically significant, with the progression of the stage of CKD. There was a hugely significant association between the prevalence of thrombocytopenia and the severity of CKD (**p=0.006). Arun *et al*. study recorded thrombocytopenia in 29% of the patients with CKD, of which 19 patients had ESRD [33].

CONCLUSION

Our study accomplished that patients with CKD show abnormal hematological parameters; there is a correlation between the progression of CKD and reduction in Hb, red blood count, hematocrit, and platelet count. Anemia is a significant cause of morbidity in patients with CKD worsening with the stage of the disease. The most frequent type of anemia is microcytic hypochromic anemia due to iron deficiency. Measurement of Hb and RBC parameters in patients with CKD helps in classifying the type of anemia, aids in choosing the correct management modalities, and decreasing mortality. Future studies should be made to know the undetermined etiology of CKD in this part of ODISHA. However, timely identification and rectification of anemia in patients with CKD are recommended.

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AUTHOR'S CONTRIBUTIONS

Dr. Bibhu Prasad Behera**,** Assistant Professor in Medicine, Department of Internal Medicine, Saheed Laxman Nayak Medical College and Hospital, Koraput, ODISHA is the primary investigator and the corresponding author. Dr. Bibhu Prasad Behera made the design of the study, data collection, redaction of the manuscript, statistic study, analysis of data, and data interpretation.

CONFLICTS OF INTEREST

None.

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ETHICAL APPROVAL

It is not required.

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