



“TO COMPARE THE CHANGES IN VARIOUS RBC PARAMETERS IN CHRONIC RENAL FAILURE PATIENTS.”

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Abstract-

Background- Chronic kidney disease (CKD) is a major global public health problem. Anaemia is the most common, consistent and severe of the various haematological abnormalities, and has been shown to be a very common condition in Indians. Although anaemia may be found at any stage of CKD, the severity of anaemia increases with CKD progression, (6) resultantly affecting nearly all patients with end-stage renal disease (CKD stage 5).

Aims- the main aim of study is 'To compare the changes in various RBC parameters with stages of chronic renal failure.'

Materials and methods- This was a prospective study done over one and half year (March 2021-Aug 2022) at NSCB Medical College & hospital, India. The study included 256 adult CKD patients [estimated glomerular filtration rate (eGFR) of 60 mL/min/1.73 m²] who underwent anemia evaluation. The eGFR was calculated from serum creatinine levels using the abbreviated Modification of Diet in Renal Disease equation. Anemia was defined as hemoglobin concentration <13.0 g/dL in males and <12.0 g/dL in females.

The anemia was evaluated by RBC count; MCV; MCHC. Kidney function was evaluated using blood urea, and serum creatinine and GFR. The GFR was estimated using MDRD study equation. Estimated Glomerular filtration rate (male) = $175 \times \text{standardized Scr}^{-1.154} \times \text{age}^{-0.203}$. Multiply by 0.742 for women.

Results- Out of 256 CKD patients, Mean age of the patients was 44.83 in patients diagnosed with microcytic anemia while in normochromic anemia mean age was 45.31 with non significance difference statistically.

Majority of the patients (64.5%) with CKD were male. Majority of the patients with CKD were associated with profession of private sector employment, farmer, housewife and shopkeeper. The chief complaint in majority of the CKD patients (86%) was weakness followed by fever (14%). The mean RBC count, Hb level, hematocrit value, MCHC, blood urea and serum creatinine level were statistically significant in different stages of CKD ($p < 0.05$). In present study those patients with advanced stage of CKD (stage 5) had asignificant association with anemia.

Conclusions- Chronic Kidney Disease is a major health problem worldwide. Anemia is a leading cause of morbidity in patients with CKD and it worsens with the stage of the disease. The most common type of anemia is normocytic normochromic anemia due to EPO deficiency and microcytic

hypochromic anemia due to iron deficiency. Evaluation of Hb and RBC parameters in patients with CKD helps in classifying the type of anemia and aids in choosing the correct treatment modalities and avoids unnecessary iron overload in the patients.

Keywords- chronic kidney disease, anemia, health problems, blood parameters.

Introduction- Chronic kidney disease (CKD) is a major global public health problem, (1) estimated to affect more than 10% of the general adult population and up to 50% of some high-risk subpopulations, such as the elderly, (2) those with non-communicable diseases (NCDs), including type 2 diabetes mellitus (T2D) and hypertension, and communicable diseases (CDs), including HIV/AIDS.(3) Haematological parameters, particularly red blood cell (RBC) indices, are most commonly affected,(5) giving rise to anaemia. Anaemia is the most common, consistent and severe of the various haematological abnormalities, and has been shown to be a very common condition in Indians. Although anaemia may be found at any stage of CKD, the severity of anaemia increases with CKD progression, (6) resultantly affecting nearly all patients with end-stage renal disease (CKD stage 5). (5)

Persistent, low-grade inflammation is an essential part of the aetiology of CKD and has been recognised as such since the late 1990s, when it was linked to cardiovascular disease and mortality.(8) Recently, the ratio of neutrophil-to- lymphocyte count (N/L) has been proposed as a novel measure of inflammation in distinct populations and has been shown to have prognostic value; particularly for mortality risk in patients with myocardial infarction and heart failure.(9) However, studies on the relationship of N/L ratio with reduced estimated GFR (eGFR) are limited. Thus, despite recent advances in the aetiology governing the development and progression of CKD, population-based data on the haematological profile of people with CKD in India are scanty.

This analysis assessed the prevalence of anemia in CKD in the adult (>18 years of age) during 2007–2010 using the GFR categories specified by the National Kidney Foundation. We therefore aimed to characterize the haematological spectrum of screen-detected CKD participants, and to correlate the complete blood count measures with CKD stages in tertiary care hospital.

Aims- the main aim of study is 'To compare the changes in various RBC parameters in chronic renal failure patients.'

Materials and methods-

STUDY DESIGN: Prospective observational study

STUDY CENTRE: N.S.C.B. Medical College & Hospital, Jabalpur (M.P.)

DURATION OF STUDY: 1st march 2021 to 31st august 2022

STUDY AREA AND TARGET POPULATION: Study was done at NSCB medical college hospital and target population was indoor and outdoor patients of CKD.

SOURCES OF DATA; The central lab of pathology and biochemistry department, department of general medicine, department of nephrology, NSCB medical college.

INCLUSION CRITERIA; All patients having chronic kidney disease in adult age group(>14 years of age), indoor and outdoor chronic kidney disease.

EXCLUSION CRITERIA; Patients of pediatric age group (<14 Years), Patients not giving consent

SAMPLE SIZE AND SAMPLE TECHNIQUE

Sample size

Sample size was calculated on the assumptions of reported increased anemia from 1% to 9% in CKD

patients with a GFR of 60ml/min/1.73m square to GFR of 30ml/min/1.73m square (Neeta Bahal, 2008). Using formula of simple random sampling the minimum required sample size was estimated as 155 at 95% CI, 5% Alpha and 80% power which was further multiplied with 1.5 as design effect to remove the sample clusterization and this accumulated 233. Further 10% more samples was added to adjust the sample losses due to non- response error. Therefore, finally we planned to study on 256 CKD patients.

Formula

$n = z^2 \times p(1-p) / l^2$ where n = required sample size $z = 1.96$ at 95% CI and 5% alpha $p = 0.09$ $l = 0.045$ (precision or margin of error)

Final Sample size: 256 CKD patients.

Methodology

The study was carried out in the central laboratory of NSCB Medical College and Hospital. Two hundred fifty six diagnosed cases of CKD were analyzed.

Two hundred fifty six diagnosed cases of CKD as per the National Kidney Foundation–Kidney Disease Outcomes Quality Initiative criteria regardless of its primary cause were chosen.

All patients with CKD, either outdoor or admitted to NSCB Hospital were analyzed for the following parameters:

- RBC count;
- Hb;
- hematocrit;
- MCV;
- MCH;
- MCHC;
- blood urea,
- Serum creatinine.

GFR was estimated using MDRD study equation.

Estimated glomerular filtration rate = $175 \times \text{standardized Scr}^{-1.154} \times \text{age}^{-0.203}$ Multiply by 0.742 for women.

Clinical details were collected from the medical record department, and hematological and biochemical data has retrieved from central lab NSCB Medical College, Jabalpur.

Statistical analysis

Data was recorded in Microsoft Excel programme and statistical analysis was performed by the SPSS program for Windows, version 25 (SPSS, Chicago, Illinois). Continuous variables were presented as mean $\pm$ SD, and categorical variables were presented as absolute numbers and percentage. Data was checked for normality before statistical analysis. Descriptive analysis was performed to obtain general characteristic of the study population.

Categorical variables was analysed using either the chi square test or Fisher's exact test. Continuous variables were assessed using ANOVA or independent sample t-test. Pearson correlation (r) was performed to establish the correlation between different parameters. $P < 0.05$ was considered statistically significant.

Observation and results-

Out of 256 CKD patients, 46 patients (18%) had microcytic hypochromic anemia while majority of the patients (82%) had normocytic normochromic anemia. Mean age of the patients was 44.83 in patients diagnosed with microcytic anemia while in normochromic anemia mean age was 45.31 with non- significance difference statistically ($p > 0.05$). Majority of the patients (64.5%) with CKD were male by sex. By anemic type the difference is sex distribution was not statistically significant. ($p > 0.05$). Majority of the patients with CKD were associated with profession of private sector

employment, farmer, housewife and shopkeeper. The difference was statistically significant but nullifies the impact of occupation on type of anemia in CKD patients.

TABLE NO. – 1: DISTRIBUTION OF RBC PARAMETERS IN PATIENTS WITH STAGES OF CKD

RBC parameters		Stage 3		Stage 4		Stage 5		P value
		MH	NN	MH	NN	MH	NN	
RBC Count (million/cumm)	Mean	2.10	3.70	2.15	2.86	2.64	2.51	0.702
	SD	.72	.11	.81	.69	.66	.66	
Hb (g/dl)	Mean	6.23	11.20	6.54	8.77	7.91	7.60	0.564
	SD	1.74	.16	2.52	2.13	1.91	1.96	
Hematocrit (%)	Mean	19.33	34.50	20.27	27.09	24.43	23.36	0.630
	SD	5.50	.57	7.85	6.52	5.71	5.91	
MCV (fl)	Mean	75.23	89.75	69.70	86.46	74.94	85.97	<0.001
	SD	1.078	5.90	5.62	4.92	9.11	6.30	
MCH (pg)	Mean	22.00	28.25	24.91	27.25	24.67	27.19	<0.001
	SD	1.73	.95	2.10	2.40	2.93	2.94	
MCHC(%)	Mean	29.13	29.75	30.88	30.48	32.01	31.29	0.323
	SD	1.02	.50	3.91	1.91	3.51	2.87	

- MH: Microcytic Hypochromic; NN: Normocytic Normochromic
- On comparing hematological parameters between two groups of anemia, mean MCV and MCH values were statistically significant($p < 0.05$).

GRAPH NO. – 1: DISTRIBUTION OF RBC PARAMETERS IN PATIENTS WITH STAGES OF CKD

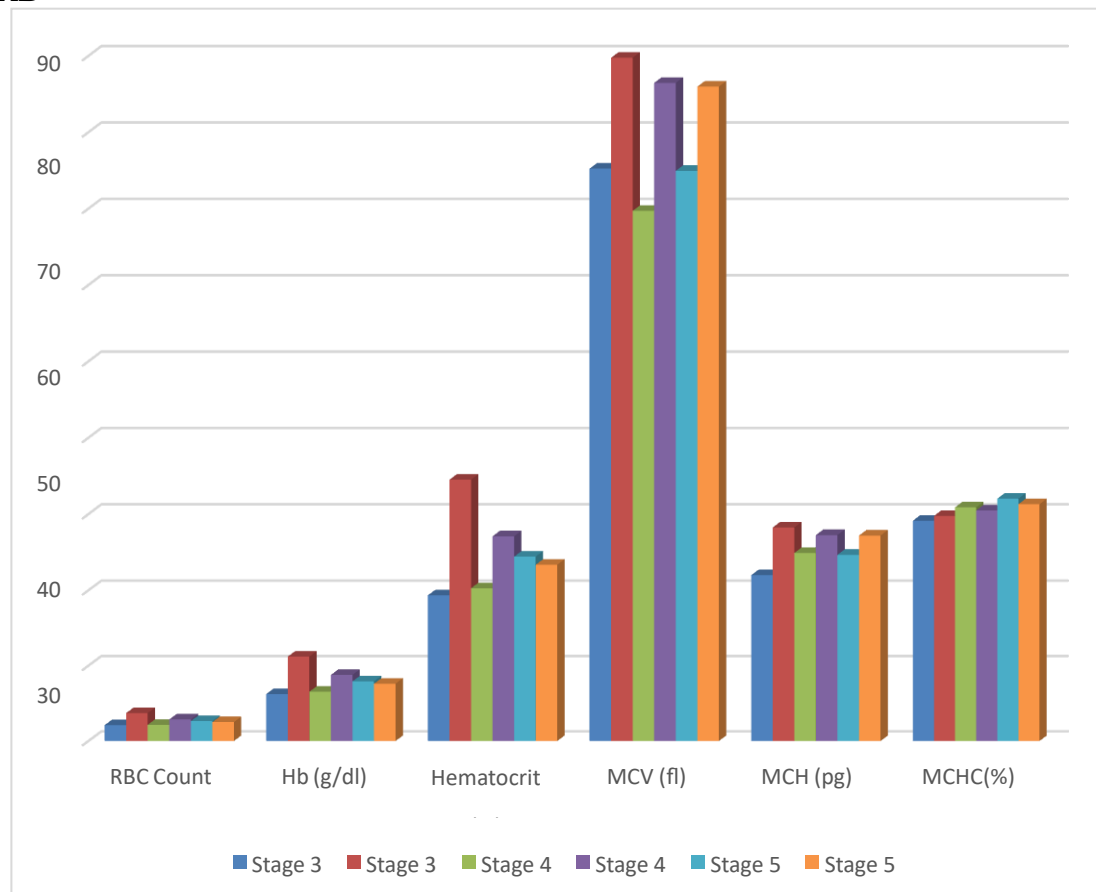


TABLE NO. – 2: PEARSON CORRELATION BETWEEN RBC AND RENAL PARAMETERS WITH STAGES OF CKD

		Stage of CKD
RBC Count (million/cumm)	Pearson Correlation	-.126*
	Sig. (2-tailed)	.045
Hb (g/dl)	Pearson Correlation	-.137*
	Sig. (2-tailed)	.028
Hematocrit (%)	Pearson Correlation	-.146*
	Sig. (2-tailed)	.020
MCV (fl)	Pearson Correlation	.059
	Sig. (2-tailed)	.351
MCH (pg)	Pearson Correlation	.054
	Sig. (2-tailed)	.391
MCHC (%)	Pearson Correlation	.136*
	Sig. (2-tailed)	.030
B. Urea (g/dl)	Pearson Correlation	.391**
	Sig. (2-tailed)	.000
S. Creatinine (mg/dl)	Pearson Correlation	.497**
	Sig. (2-tailed)	.000

-On pearson correlation between RBC parameters with stages of CKD, mean RBC count, Hb level, hematocrit value, MCHC, blood urea and serum creatinine level were statistically significant in different stages of CKD ($p < 0.05$).

Discussion-

In our study mean age of the patients was 44.83 years in patients diagnosed with microcytic hypochromic anemia while in normocytic normochromic anemia mean age was 45.31 with non significance difference statistically ($p > 0.05$). According to the meta- analysis by Shiferaw et al (29), the pooled effects of four studies indicated that those over 50 years of age were 62% more likely to develop anemia compared to those less than 50 years old, although this association was not statistically significant. Another study by Vikrant et al. (28)

In our study we found that mean RBC count, Hb level, hematocrit value, MCHC, blood urea and serum creatinine level were statistically significant in different stages of CKD ($p < 0.05$). Seven (2.7%) patients were CKD Stage 3, 28 (10.9%) patients CKD Stage 4, and 221 (86.3%) patients CKD Stage 5. The mean hemoglobin was 8.2 ± 2.2 g/dL. There was a progressive fall in hemoglobin with increasing severity of CKD, and in CKD Stage 3, 4, and 5 the mean hemoglobin was 9.1, 7.9, and 7.2 g/dL, respectively ($P = 0.001$). A study by Vikrant et al. (28) demonstrated that around 72 (12.3%) patients were CKD Stage 3, 193 (33%) patients CKD Stage 4, and 319 (54.6%) patients CKD Stage 5. The mean hemoglobin was 9.2 ± 2.2 g/dL. By study Vikrant et al. (28). There was a progressive fall in hemoglobin with increasing severity of CKD, and in CKD Stage 3, 4, and 5 the mean hemoglobin was 10 ± 2.2 , 9.4 ± 2.1 , and 8.4 ± 1.9 g/dL, respectively. (28). A study by Shastry et al. (30) found that the mean RBC count was $3.29 \pm 0.79 \times 100/\mu\text{l}$, and a significant fall was noticed as the stage of CKD progressed. 74% and 60% of patients with Stage 4 and 5 CKD, respectively, showed Hb of < 10 g/dl. Correlation of MCV, MCH, and MCHC values with stages of CKD was statistically not significant. In the study by Alghythan and Alsaeed (42) (Saudi Arabia), RBC count, Hb, and PCV levels, although within normal range, were significantly lower when compared with the control population.

A study conducted by Shittu et al. (43) showed comparatively lower MCV and MCH values, but it was not statistically significant because the control population also showed similar values and did not show significant differences in RBC indices in different stages of renal failure. Similarly, in our study, patients in different stages of renal failure did not show significant changes in RBC indices.

In general stage 5 CKD, being male were found to be significantly associated with anemia of chronic kidney disease. Therefore, situation- based interventions and country context-specific preventive

strategies should be developed to reduce the risk factors of anemia in this patient group. In addition, this study may help policymakers and program managers design evidence-based interventions on preventing the occurrence of anemia with CKD patient populations.

Conclusion- Anemia is a leading cause of morbidity in patients with CKD and it worsens with the stage of the disease. The most common type of anemia is normocytic normochromic anemia due to EPO deficiency and microcytic hypochromic anemia due to iron deficiency. Evaluation of Hb and RBC parameters in patients with CKD helps in classifying the type of anemia and aids in choosing the correct treatment modalities and avoids unnecessary iron overload in the patients.

BIBLIOGRAPHY

1. Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, et al. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Annals of internal medicine*. 2003;139(2):137–47.
2. Nitta K, Okada K, Yanai M, Takahashi S. Aging and chronic kidney disease. *Kidney and Blood Pressure Research*. 2013;38(1):109–20.
3. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *The lancet*. 2012;380(9859):2095–128.
4. Hamer RA, El Nahas AM. The burden of chronic kidney disease. *Bmj*. 2006;332(7541):563–4.
5. Babitt JL, Lin HY. Mechanisms of anemia in CKD. *Journal of the American Society of Nephrology*. 2012;23(10):1631–4.
6. Webster AC, Nagler EV, Morton RL, Masson P. Chronic kidney disease. *The lancet*. 2017;389(10075):1238–52.
7. Kazmi WH, Kausz AT, Khan S, Abichandani R, Ruthazer R, Obrador GT, et al. Anemia: an early complication of chronic renal insufficiency.
8. *American Journal of Kidney Diseases*. 2001;38(4):803–12.
9. Stenvinkel P, Heimbürger O, Paulter F, Diczfalusy U, Wang T, Berglund L, et al. Strong association between malnutrition, inflammation, and atherosclerosis in chronic renal failure. *Kidney international*. 1999;55(5):1899–911.
10. George C, Matsha TE, Erasmus RT, Kengne AP. Haematological profile of chronic kidney disease in a mixed-ancestry South African population: a cross-sectional study. *BMJ open*. 2018;8(11):e025694.
11. WHO Scientific Group. Nutritional anemias: Report of a WHO scientific group. *World Health Organ Tech Rep Ser*. 1968;405:5–37.
12. Shaikh H, Aeddula NR. Anemia of chronic renal disease. 2019;
13. Bernhardt WM, Wiesener MS, Scigalla P, Chou J, Schmieder RE, Günzler V, et al. Inhibition of prolyl hydroxylases increases erythropoietin production in ESRD. *Journal of the American Society of Nephrology*. 2010;21(12):2151–6.
14. Agarwal AK. Practical approach to the diagnosis and treatment of anemia associated with CKD in elderly. *Journal of the American Medical Directors Association*. 2006;7(9):S7–12.
15. Bowling CB, Inker LA, Gutiérrez OM, Allman RM, Warnock DG, McClellan W, et al. Age-specific associations of reduced estimated glomerular filtration rate with concurrent chronic kidney disease complications. *Clinical journal of the American Society of Nephrology*. 2011;6(12):2822–8.
16. Hsu C yuan, McCulloch CE, Curhan GC. Epidemiology of anemia associated with chronic renal insufficiency among adults in the United States: results from the Third National Health and Nutrition Examination Survey. *Journal of the American Society of Nephrology*. 2002;13(2):504–10.
17. Stevens LA, Li S, Wang C, Huang C, Becker BN, Bombardier AS, et al. Prevalence of CKD and comorbid illness in elderly patients in the United States: results from the Kidney Early

- Evaluation Program (KEEP). *American Journal of Kidney Diseases*. 2010;55(3):S23–33.
18. Robinson BE. Epidemiology of chronic kidney disease and anemia. *Journal of the American Medical Directors Association*. 2006;7(9):S3–6.
 19. Stauffer ME, Fan T. Prevalence of anemia in chronic kidney disease in the United States. *PloS one*. 2014;9(1):e84943.
 20. Kramer H. The national kidney foundation’s kidney disease outcomes quality initiative (KDOQI) grant initiative: moving clinical practice forward. *American Journal of Kidney Diseases*. 2010;55(3):411–4.
 21. Remuzzi G, Weening JJ. Albuminuria as early test for vascular disease. *Lancet*. 2005;365(9459):556–7.
 22. Patel TV, Singh AK. Anemia in chronic kidney disease: new advances. *Heart Fail Clin*. 2010;6(3):347–57.
 23. Mani MK. The management of end-stage renal disease in India. *ArtifOrgans*. 1998;22(3):182–6.
 24. Agarwal S, Srivastava R. Chronic kidney disease in India: challenges and solutions. *Nephron Clin Pract*. 2009;111(3):c197–203.
 25. Eschbach JW, Egrie JC, Downing MR, Browne JK, Adamson JW. Correction of the anemia of end-stage renal disease with recombinant human erythropoietin. *N Engl J Med*. 1987;316(2):73–8.
 26. Arun S, Prabhu MV, Chowta KN, Bengre ML. The Haematological Pattern of the Patients with Chronic Kidney Disease in a Tertiary Care Setup in South India. *J Clin Diagn Res*. 2012;6(6).
 27. Akinsola A, Durosinmi M, Akinola N. The haematological profile of Nigerians with chronic renal failure. *Afr J Med Med Sci*. 2000;29(1):13–6.
 28. Talwar V, Gupta H. Clinicohaematological profile in chronic renal failure. *J Assoc Physicians India*. 2002;50:228–33.
 29. Vikrant S. Etiological spectrum of anemia in non-dialysis-dependent chronic kidney disease: A single-center study from India. *Saudi J Kidney Dis Transplant*. 2019;30(4):932.
 30. Shiferaw WS, Akalu TY, Aynalem YA. Risk factors for anemia in patients with chronic renal failure: a systematic review and meta-analysis. *Ethiop J Health Sci*. 2020;30(5).
 31. Shastry I, Belurkar S. The spectrum of red blood cell parameters in chronic kidney disease: A study of 300 cases. *J Appl Hematol*. 2019;10(2):61.
 32. Yi SW, Moon SJ, Yi JJ. Low-normal hemoglobin levels and anemia are associated with increased risk of end-stage renal disease in general populations: a prospective cohort study. *PloS One*. 2019;14(4):e0215920.
 33. Ng YH, Myers O, Shore X, Pankratz VS, Norris KC, Vassalotti JA, et al. The Association of Altitude and the Prevalence of Anemia Among People With CKD. *Am J Kidney Dis*. 2019;74(5):715–8.
 34. Al-Khoury S, Afzali B, Shah N, Covic A, Thomas S, Goldsmith D. Anaemia in diabetic patients with chronic kidney disease—prevalence and predictors. *Diabetologia*. 2006;49(6):1183–9.
 35. McFarlane SI, Chen SC, Whaley-Connell AT, Sowers JR, Vassalotti JA, Salifu MO, et al. Prevalence and associations of anemia of CKD: Kidney early evaluation program (KEEP) and national health and nutrition examination survey (NHANES) 1999–2004. *Am J Kidney Dis*. 2008;51(4):S46–55.
 36. McClellan WM, Flanders WD. Risk factors for progressive chronic kidney disease. *J Am Soc Nephrol*. 2003;14(suppl 2):S65–70.
 37. Babitt JL, Lin HY. Mechanisms of anemia in CKD. *J Am Soc Nephrol*. 2012;23(10):1631–4.
 38. Hussain S, Habib A, Najmi AK. Anemia prevalence and its impact on health-related quality of life in Indian diabetic kidney disease patients: evidence from a cross-sectional study. *J Evidence-Based Med*. 2019;12(4):243–52.
 39. Robinson BE. Epidemiology of chronic kidney disease and anemia. *J Am Med Dir Assoc*. 2006;7(9):S3–6.

40. Taliercio JJ. Anemia and chronic kidney disease: What's the connection? *J Fam Pract.* 2010;59(1):14.
41. Moore E, Bellomo R. Erythropoietin (EPO) in acute kidney injury. *Ann Intensive Care.* 2011;1(1):1–10.
42. Singh NP, Ingle GK, Saini VK, Jami A, Beniwal P, Lal M, et al. Prevalence of low glomerular filtration rate, proteinuria and associated riskfactors in North India using Cockcroft-Gault and Modification of Diet in Renal Disease equation: an observational, cross-sectional study. *BMC Nephrol.* 2009;10(1):1–13.
43. Abdullah KA, Abbas HA. Hematological changes before and after hemodialysis. *Sci Res Essays.* 2012;7(4):490–7.
44. Shittu AO, Chijioke A, Biliaminu S, Makusidi M, Sanni M, Abdul Rehman M, et al. Hematological profile of patients with chronic kidney disease in Nigeria. 2013;5:2–10.