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Corresponding Author

G. Ambedkar,
Department of General Medicine
Government Villupuram Medical
College, India

Author Designation

^{1,3}Assistant Professor

^{2,4}Associate Professor

⁵Junior Resident

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Across-Sectional Study on Hematological Abnormalities in Chronic Kidney Disease

¹Dr. G. Ambedkar, ²Dr. A. Ashok Kumar, ³Dr. R. Satish Kumar, ⁴Dr. C.D. Aranendran and ⁵Dr. M.S. Jegan

¹⁻⁵Department of General Medicine Government Villupuram Medical College, India

ABSTRACT

Chronic kidney disease (CKD) is associated with significant hematological abnormalities, including anemia, leukopenia and thrombocytopenia, which contribute to increased morbidity and mortality. This study aims to assess the prevalence and severity of these hematological changes across different CKD stages. A cross-sectional observational study was conducted among CKD patients at a tertiary care hospital. Hematological parameters, including hemoglobin (Hb), total leukocyte count (TLC) and platelet count, were analyzed across different CKD stages. The data were statistically evaluated to determine associations between CKD severity and hematological abnormalities. Anemia was observed in 97.33% of Stage 3 CKD patients, with all Stage 4 and Stage 5 patients being anemic. The severity of anemia increased with CKD progression, with 16% of Stage 5 patients exhibiting severe anemia (Hb <7 g/dL). Leukopenia was significantly associated with advanced CKD stages, with a decline in mean WBC count from $7.41 \times 10^9/L$ in Stage 3 to $5.09 \times 10^9/L$ in Stage 5 CKD. Thrombocytopenia was more pronounced in late-stage CKD, contributing to an increased risk of bleeding complications. Diabetes mellitus (37.78%) and hypertension (30.67%) were the leading etiologies of CKD. Hematological abnormalities worsen with CKD progression, emphasizing the need for early detection and management. Routine monitoring of hemoglobin, leukocyte count and platelet count is crucial for improving clinical outcomes in CKD patients.

INTRODUCTION

Chronic kidney disease (CKD) is a progressive condition characterized by a gradual decline in renal function, ultimately leading to end-stage renal disease (ESRD) if left untreated. CKD affects millions of individuals worldwide and is associated with significant morbidity and mortality^[1]. The disease is classified into five stages based on the estimated glomerular filtration rate (eGFR), with stages 3-5 representing moderate to severe kidney dysfunction^[2]. Hematological abnormalities are common complications of CKD and contribute to the disease burden. These abnormalities include anemia, leukocyte dysfunction and platelet disorders, which significantly impact patients' quality of life and increase the risk of cardiovascular complications^[3]. Anemia in CKD is primarily due to decreased erythropoietin production, iron deficiency, and chronic inflammation. It is associated with increased hospitalization rates, cardiovascular disease, and mortality^[4,5]. The prevalence and severity of anemia tend to increase with the progression of CKD^[6]. Leukocyte and platelet dysfunction in CKD also contribute to increased susceptibility to infections and bleeding tendencies. CKD-induced platelet dysfunction results from alterations in platelet aggregation and adhesion, which may lead to increased bleeding time and impaired hemostasis^[7]. Furthermore, chronic inflammation and oxidative stress in CKD patients exacerbate hematological disturbances and contribute to disease progression^[8]. Given the clinical significance of hematological abnormalities in CKD, it is crucial to evaluate their prevalence and characteristics in different stages of the disease. Identifying hematological alterations in CKD patients can aid in early diagnosis and targeted therapeutic interventions to improve patient outcomes^[9]. This study aims to assess the hematological abnormalities in patients with CKD and their correlation with disease severity.

MATERIALS AND METHODS

Study Design and Setting: This was a single-center, cross-sectional study conducted at Government Villupuram Medical College and Hospital over a period of two years.

Study Population: The study population comprised patients diagnosed with chronic kidney disease (CKD) attending the outpatient department (OPD) or admitted as inpatients at Government Villupuram Medical College and Hospital. Patients were recruited based on predefined inclusion and exclusion criteria.

Sample Size Calculation: The sample size (n) was determined using the formula:

where:

$Z=1.96$ (for a 95% confidence level).

P =Proportion (expressed as a decimal).

e =Margin of error.

Based on this calculation, a total of 225 patients were included in the study.

Inclusion Criteria:

- Patients diagnosed with CKD.
- Age >14 years.

Exclusion Criteria:

- Pregnant patients.
- Patients with known hematological disorders.
- History of blood transfusion within the last three months.
- Patients on drugs causing bone marrow suppression.

Methodology Patients diagnosed with CKD at Government Villupuram Medical College and Hospital or those presenting to the OPD with a CKD diagnosis were assessed for eligibility. After obtaining informed consent, patients were enrolled in the study. The diagnosis of CKD was established based on serum creatinine levels, disease duration and ultrasound findings. A detailed clinical history was recorded and a general physical examination was performed. Patients were screened for comorbidities such as diabetes mellitus and hypertension. Hematological abnormalities were evaluated through a series of laboratory investigations. Laboratory Investigations Venous blood samples were collected under aseptic precautions. The following hematological and biochemical parameters were analyzed.

Serum Creatinine and Urea: Measured using an automated blood analyzer from clotted blood samples.

Complete Hemogram: Performed using an automated cell counter (Sysmex XP-100), including total WBC count, neutrophils, lymphocytes, RBC count, packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), and mean corpuscular hemoglobin (MCH).

Peripheral Smear Examination: Conducted using Leishman's stain.

Urine Analysis:

- **Urine Albumin:** Estimated manually using 3% sulfosalicylic acid.
- **Urine Sugar:** Analyzed using Benedict's solution.

Coagulation Profile: Prothrombin time (PT), activated partial thromboplastin time (aPTT) and international normalized ratio (INR): Measured using an automated analyzer (Sysmex CA-50). All laboratory investigations were performed in the biochemical and pathological laboratory of the hospital. Data were recorded and

tabulated for statistical analysis. Statistical analysis Data were entered into a Microsoft Excel spreadsheet and analyzed using Stata 14.0 software (Stata Corp LP, College Station, TX, USA). Statistical scrutiny included both univariate and multivariate analyses. A significance level of a <0.05 was considered statistically significant. Binary and multinomial logistic regression analyses were used to evaluate associations between variables. Repeated measurements were analyzed using one-way ANOVA. Dependent variables were analyzed using paired t-tests. Descriptive statistics such as frequencies, percentages, range, mean, standard deviation and p-values were computed. The findings were systematically tabulated for interpretation and discussion at the conclusion of the study period.

RESULTS AND DISCUSSIONS

A total of 225 patients were recruited for the study. The study subjects were sub grouped into 3 groups based on the stage of CKD. Stage 3,4 and 5 were included in the study group with each subgroup having a population of 75 each. There were a total of 149 males 76 females in the study group and across the 3 groups. Majority of the cases were males (66%) and 34% of cases were females.

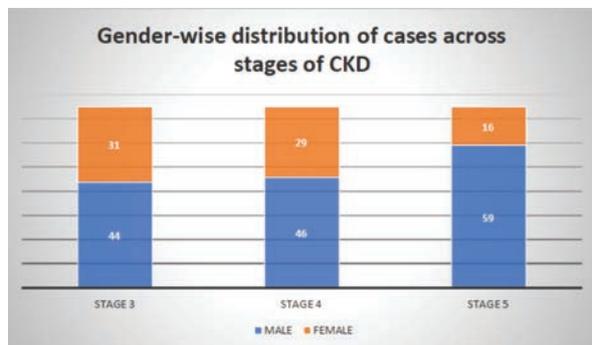


Fig. 1: Stacked Bar Graph Representing the Gender-Wise Distribution of Cases in Each Subgroup

Table 1: Depicting Distribution of Patients with Respect to Age in Each Group

Age Group	Stage 3			Stage 4			Stage 5		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
20-40	8	4	12	14	1	15	16	6	22
40-60	29	18	47	24	15	39	26	8	34
>60	6	10	16	10	11	21	16	3	19
Total	43	32	75	48	27	75	58	17	75

Majority of the patients in the study group (53.33%, n=120) were in the age range between 40 and 60 years. CKD is predominantly a disease of the elderly, But the higher distribution of middle aged population in our study group is an alarming finding. 62.66% (n=47) of the Stage 3 CKD belongs to the age group

between 40 and 60 years. 52% (n=39) of stage 4 CKD belongs to the 40-60 year age group. 45.33%.

Table 2: Depicting the Etiology of CKD Across the Study Groups

Etiology	Stage 3	Stage 4	Stage 5	Total
DM	30	28	27	85
SHTN	19	22	28	69
DM+SHTN	16	20	22	58
CGN	12	13	9	34
ADPKD	1	0	1	2
CKD-U	13	12	10	25
Total Cases	75	75	75	225

Diabetes and hypertension were the commonest causes identified associations among patients with CKD across all stages. 40% (n=30) of patients in Stage 3 CKD had diabetes and resultant diabetic retinopathy. 37.78% of patients (n=85) had diabetic nephropathy across all stages of CKD. Hypertension is also fairly common in all stages of CKD with the maximum prevalence in the stage 5 CKD subgroup (37.33%, n=28). 30.67% of cases (n=69) had hypertension across all stages of CKD. A large proportion of patients has both diabetes and hypertension and cumulative effects of both these modern day epidemics has resulted in renal dysfunction in varying proportions. Chronic glomerulonephritis is also seen in 15.11% (n=34) across all study subgroups. An entity that needs special mention is CKD-U, where the etiology of the CKD is largely unidentified. This is seen in 11.11% (n=25) of subjects in the whole study population.

Table 3: Depicting Distribution of Cases with Respect to Hemoglobin Levels Across Each Subgroup

	Stage 3	Stage 4	Stage 5
No Anaemia	2 (2.67%)	0	0
Mild Anaemia	51 (68%)	42 (56%)	21 (28%)
Moderate Anaemia	21 (28%)	33 (44%)	42 (56%)
Severe Anaemia	1 (1.33%)	0	12 (16%)
Total	75	75	75

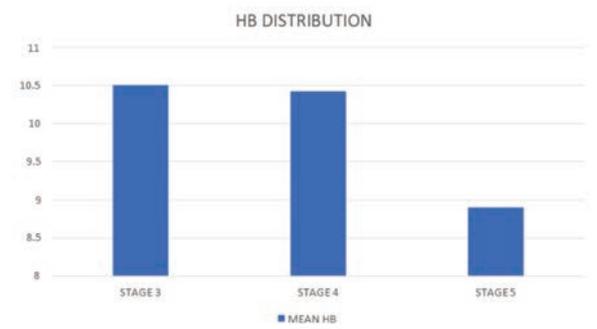


Fig 2: Bar Chart Depicting Mean Hemoglobin Levels in Various Stages of CKD

Table 4: Showing Mean RBC Count Among Various Stages of CKD

Stage of CKD	Mean RBC Count	SD Deviation	P-value
3	3.17	0.626	0.0492
4	2.616	0.318	0.0384
5	1.55	0.253	0.0499

Table 5: Mean WBC Count in Various Stages of CKD

Stage	Total Count Mean	SD
3	7.41	1.36
4	6.09	1.07
5	5.09	0.87

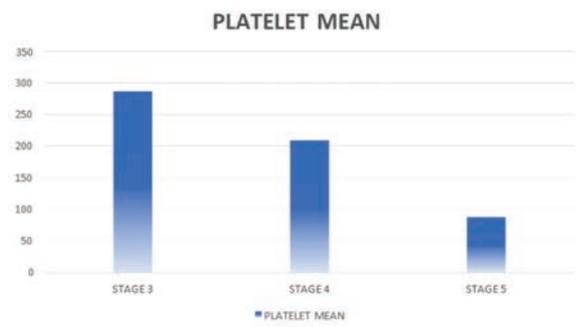


Fig 3: Mean Platelet Count Across Different Stages of CKD

Table 6: Mean Bleeding Time in 3 Subgroups of CKD

Stage	BT Mean	SD
3	3.27	0.817
4	3.228	0.97
5	5.44	0.89

Chronic kidney disease (CKD) is a progressive disorder associated with significant hematological abnormalities, which contribute to increased morbidity and mortality. This study aimed to evaluate the prevalence and characteristics of hematological abnormalities across different stages of CKD. Our findings reveal a strong association between worsening kidney function and increasing severity of anemia, leukopenia and thrombocytopenia.

Prevalence of Anemia in CKD: Anemia is one of the most common complications of CKD, primarily due to reduced erythropoietin production, iron deficiency, chronic inflammation and uremic toxins affecting erythropoiesis. In our study, 97.33% of Stage 3 CKD patients exhibited some degree of anemia, with its severity increasing as CKD progressed. All patients in Stage 4 and Stage 5 CKD were anemic, with 16% of Stage 5 patients having severe anemia (Hb <7 g/dL). This finding is consistent with previous studies reporting an increasing prevalence and severity of anemia with declining kidney function^[1,2]. The progressive reduction in RBC count observed in our study further supports the role of worsening renal function in impaired erythropoiesis.

Leukocyte Abnormalities in CKD: Leukocyte dysfunction in CKD contributes to increased susceptibility to infections due to impaired immune response. We observed a significant decline in total WBC count as CKD progressed. The mean WBC count was $7.41 \times 10^9/L$ in Stage 3 CKD, decreasing to $5.09 \times 10^9/L$ in Stage 5 CKD. This decline may be

attributed to chronic inflammation, uremic toxin accumulation and bone marrow suppression. Previous research has shown that uremia impairs neutrophil chemotaxis, phagocytosis and oxidative burst, thereby increasing infection risk in CKD patients^[3].

Platelet Dysfunction and Bleeding Tendencies: CKD is associated with qualitative and quantitative platelet abnormalities, which contribute to increased bleeding risk. Our study demonstrated a significant reduction in platelet count as CKD progressed. The mean platelet count was significantly lower in Stage 5 CKD, indicating a higher risk of bleeding complications. Platelet dysfunction in CKD is multifactorial, involving uremic toxins, impaired thromboxane synthesis, defective platelet aggregation and altered von Willebrand factor function^[4,5]. These abnormalities explain the prolonged bleeding time observed in advanced CKD stages.

Etiology of CKD and its Association with Hematological Changes: Diabetes mellitus and hypertension were the leading causes of CKD in our study population, consistent with global trends^[6]. 85 patients (37.78%) had diabetic nephropathy, while 69 patients (30.67%) had hypertensive nephropathy. The high prevalence of diabetes and hypertension highlights the importance of early detection and management to prevent CKD progression and associated hematological complications. Chronic glomerulonephritis (CGN) was identified in 15.11% of patients, while 11.11% had CKD of unknown etiology (CKD-U). The presence of anemia was more severe in patients with diabetic nephropathy, possibly due to chronic inflammation and associated microvascular complications^[7].

Clinical Implications: Hematological abnormalities in CKD significantly impact patient quality of life and prognosis. Anemia is associated with fatigue, reduced exercise tolerance, cardiovascular complications and increased hospitalization rates. Leukopenia contributes to recurrent infections, while platelet dysfunction predisposes patients to hemorrhagic complications. Early identification and management of these hematological disturbances are crucial in improving CKD outcomes. Erythropoiesis-stimulating agents (ESAs), iron supplementation and optimal blood pressure and glycemic control play key roles in mitigating these complications^[8,9].

Strengths and Limitations: The strength of this study lies in its comprehensive evaluation of hematological parameters across different CKD stages. The use of standardized laboratory methods enhances the reliability of our findings. However, certain limitations exist:

- **Single-Center Study:** Results may not be generalizable to broader populations.
 - **Cross-sectional Design:** Longitudinal studies are needed to establish causal relationships.
 - **Lack of Assessment of Inflammatory Markers:** Further studies incorporating markers like C-reactive protein (CRP) and interleukins can provide insights into the role of chronic inflammation in CKD-associated hematological abnormalities.
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CONCLUSION

This study highlights the progressive nature of hematological abnormalities in CKD, with worsening anemia, leukopenia and platelet dysfunction observed as kidney function declines. Given their significant clinical implications, regular hematological monitoring and appropriate therapeutic interventions should be integrated into CKD management strategies to improve patient outcomes.

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