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# Uncovering the Links Between Hematological and Biochemical Parameters in Chronic Kidney Disease: A Case-Control Study

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## ABSTRACT

**Aims and objectives**- To evaluate the hematological and biochemical parameters in a group of CKD patients compared to normal subjects and to compare the changes in various parameters in different stages of CKD.
**Material & Methods**-This is a 10-month case control study on 150 CKD patients and 150 healthy controls at tertiary care hospital. A group of hematological parameters, such as haemoglobin (Hb), red blood cell count (RBC), mean corpuscular volume (MCV), haematocrit (PCV), total leucocyte count (TLC), platelet count (PL) and erythrocyte sedimentation rate (ESR) were measured. Also, peripheral smear examination was done. Biochemical parameters, such as creatinine, uric acid, Blood Urea Nitrogen (BUN), calcium (Ca), sodium (Na), potassium (K), chloride (Cl), phosphorus (P), C-Reactive Proteins (CRP), and random blood sugar (RBS) were compared with the controls and different stages of CKD.
**Results**- The mean age of presentation was 50 ± 10 years. The male to female ratio was 2.3:1. The mean hemoglobin was 9.5 ± 1 g/dl and mean creatinine was 4.5 ± 0.5 mg/dl. CKD patients exhibited significant drop in Hb, PCV, and RBC count as the disease stage progressed, indicating a worsening of anemia. TLC, differential neutrophil count, ESR, serum uric acid, creatinine, phosphorus, BUN, CRP, and RBS, were elevated while platelet count, and calcium were notably lower in patients compared to the controls ($p < 0.001$).
**Conclusion**-Through a meticulous analysis of hematological and biochemical parameters throughout the different stages of CKD, we can proactively manage and prevent complications, safeguarding the well-being of those afflicted.

***Keywords:*** Chronic kidney disease, Biochemical and hematological parameters, Creatinine, Hemoglobin.

## INTRODUCTION

Chronic kidney disease (CKD) is a life-threatening condition, where there is irreversible and progressive loss of nephrons and at the end stage leads to renal failure. The main causes of CKD are diabetic nephropathy, hypertensive nephropathy, chronic interstitial nephritis, and chronic glomerulonephritis**.** [1]

The number of patients affected by CKD is estimated to be 843.6 million (>10% of world population) worldwide in 2017. [2]
Renal function is monitored and assessed by the glomerular filtration rate which is one of the most important and accurate markers. The estimated glomerular filtration rate (eGFR) for CKD is <60ml/min/1.73 $m^2$ for >3 months as defined by US National Kidney Foundation's Kidney Dialysis

Outcomes Quality Initiative (K/DOQI) guideline. End stage renal disease (ESRD) is stage 5 CKD in which GFR is <15 ml/min/1.73 $m^2$. [3]

Reduced kidney function can influence the rate at which creatinine is filtered by the kidneys. Hence, creatinine can be used as a measure of glomerular filtration rate and thus the kidney function. Hematological and biochemical parameters are commonly affected in CKD, that is more apparent as the stage of CKD progresses. The alterations in hematological parameters are due to marrow suppression by retained uremic products and aluminium toxicity associated with hemodialysis.

Kidneys play a substantial role in the regulation of body fluids, electrolytes, and acid-base stability. Hence in CKD and ESRD there can be hyperkalemia, metabolic acidosis, hypocalcemia, and hyperphosphatemia. This results in severe complications such as bone-mineral disorders, muscle wasting, vascular calcification, azotemia, and clinical uremic syndrome and increased mortality. Derangement in sodium, potassium, calcium, magnesium, and chloride may be life threatening, hence these parameters should be kept within physiological range. [1]

Increasing evidence shows that early detection and therapeutic interventions in the earlier stages may prevent some of these complications and slow down the progression to renal failure.[4]

The aim of present study was to observe the haematological and biochemical parameters changes with the stage of CKD and to assess the type of anaemia.

## MATERIALS & METHODS

A group of 150 CKD patients as per the National Kidney Foundation criteria were chosen with 150 healthy subjects. The study was carried out from August 2022 to May 2023 in a tertiary care hospital.

A group of hematological parameters, such as hemoglobin, RBC count, mean corpuscular volume, hematocrit, TLC, platelet count and ESR were measured. Also, peripheral smear examination was done. Biochemical parameters, such as creatinine, uric acid, BUN, calcium, sodium, potassium, chloride, phosphorus, CRP, and RBS were measured. These parameters were compared with healthy controls and different stages of CKD.

Hematological parameters were measured using Sysmex XN 10 and biochemical data by Vitros 5600.

GFR was estimated using MDRD study equation.

Estimated glomerular filtration rate = $175 \times \text{standardized serum creatinine}^{-1.154} \times \text{age}^{-0.203}$. Multiply by 0.742 for women. [4] The patients were classified into 5 stages using the MDRD equation and the parameters were analyzed in the different stages of CKD.

**Inclusion criteria:** All the patients suffering from chronic kidney disease and > 15 years of age.

**Exclusion criteria:** Patients < 15 years and who didn't have regular laboratory data, were excluded.

## STATISTICAL ANALYSIS

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of frequencies and proportions. Chi-square test or Fischer's exact test (for 2x2 tables only) was used as test of significance for qualitative data.

Continuous data was represented as mean and standard deviation. The independent t test was used as a test of significance to identify the mean difference between two quantitative variables.

P value (Probability that the result is true) of <0.05 was considered as statistically significant.

Statistical software: MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

## RESULT

150 CKD patients and 150 age and sex matched healthy controls were included in the study. The age distribution of the study population ranged from 15 to 70 years. Most patients were between 41 and 60 years of age. There were 104(70%) males and 46 (30%) females.

Hb, RBC count, MCV, PCV and PL were found to be significantly lower($p<0.001$) than in control. 139 patients out of 150 were found to have anemia. Severe degree of anemia was seen in 2% of the cases (Hb<7g%), moderate degree was seen in 68% (7-10g%) and mild in 30%(Hb10-13g%). TLC, differential neutrophil count and ESR were found to be significantly elevated ($p<0.001$) compared to the controls. Creatinine, BUN, uric acid, CRP, RBS were found to be raised compared to the controls.

**Table 1: - Comparison of hematological and biochemical parameters between cases and controls**

| Hematological parameters | CKD (Mean) | Control (Mean) | P-Value |
|---|---|---|---|
| Hb | 9.53 | 12.74 | <0.001 |
| RBC | 3.49 | 4.69 | <0.001 |
| TLC | 13049 | 8186.1 | <0.001 |
| Differential Neutrophil | 85.86% | 61.24% | <0.001 |
| Differential Lymphocyte | 17.82% | 27.89% | <0.001 |
| PL | 1,15,000 | 3,15,000 | <0.001 |
| PCV | 30.12 | 38.42 | <0.001 |
| ESR | 77.03 | 18.24 | <0.001 |
| Biochemical parameters | | | |
| Creatinine | 4.56 | 0.93 | <0.001 |
| Uric acid | 9.09 | 4.54 | <0.001 |
| BUN | 49.55 | 8.84 | <0.001 |
| Na | 136.31 | 136.61 | 0.485 |
| K | 4.37 | 4.28 | 0.255 |
| Cl | 101.81 | 102.65 | 0.332 |
| Ca | 8 | 9.64 | <0.001 |
| P | 5.2 | 1.5 | <0.001 |
| RBS | 220.14 | 97.47 | <0.001 |
| CRP | 17.79 | 0.6 | <0.001 |

**Figure 1: - showing comparison of biochemical parameters between cases and controls.**

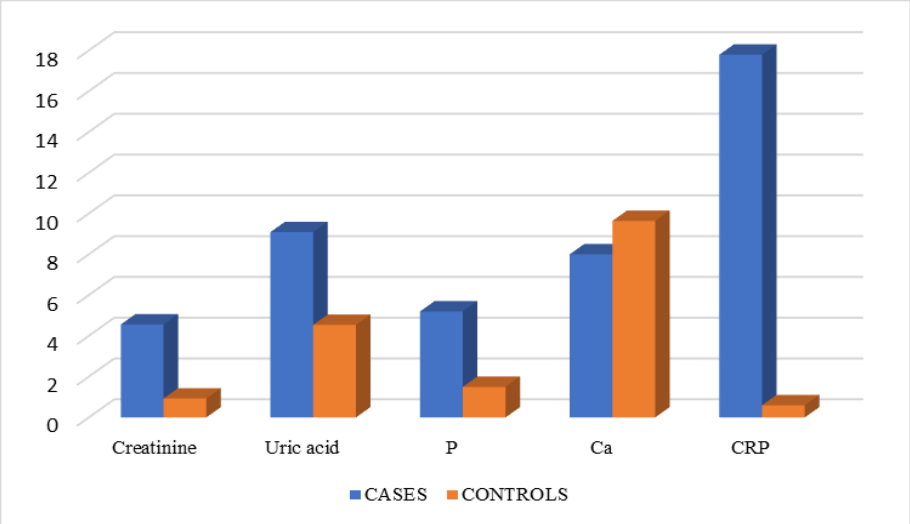


**Table 2: - Comparison of hemoglobin, PCV, MCV, creatinine, uric acid, and BUN across the stages of CKD.**

| CKD | Mean Hb | Mean PCV | Mean MCV | Mean Creatinine | Mean Uric acid | Mean BUN |
|---|---|---|---|---|---|---|
| Stage I | 12.43 | 36.22 | 85.82 | 0.66 | 8.07 | 35.061 |
| Stage II | 11.55 | 33.7 | 83.25 | 1.03375 | 8.72 | 36.45 |
| Stage III | 10.21 | 29.1 | 77.75 | 1.759375 | 9.03 | 38.21 |
| Stage IV | 9.1 | 27.2 | 78.43 | 2.898571 | 9.8 | 49.98 |
| Stage V | 8.14 | 25.1 | 77.88 | 6.7295 | 10.6 | 57.98 |
| P-value | <0.001 | <0.001 | 0.009 | <0.001 | <0.001 | <0.001 |

The degree of anemia was found to increase as the stage progressed. Anemia is said to develop when the creatinine clearance drops to 30 ml/min/1.73 $m^2$ of body surface area. [5] Here we found that anemia developed in stage III of CKD.

Hb, PCV and PL showed progressive decline. The most frequent peripheral smear finding in the patients (95) were normocytic normochromic, 52 had microcytic hypochromic anemia, 1 had dimorphic and 2 had macrocytic anemia. 2 patients with microcytic hypochromic anemia showed hemolytic picture with increased nucleated RBCs, polychromatophils and few fragmented RBCs. Red cell distribution width (RDW) ranged between 15-20. Anisopoikilocytosis was found to be mild to moderate.

TLC, creatinine, BUN, and uric acid were found to be progressively elevated with the stage of CKD. The severity of the anemia showed positive correlation with creatinine levels.

The derangement in the hematological and biochemical parameters with the stage of the CKD was statistically significant($p<0.001$).

**Figure 2: - Graph showing steady decline in the hemoglobin and PCV as the stage of CKD progresses.**

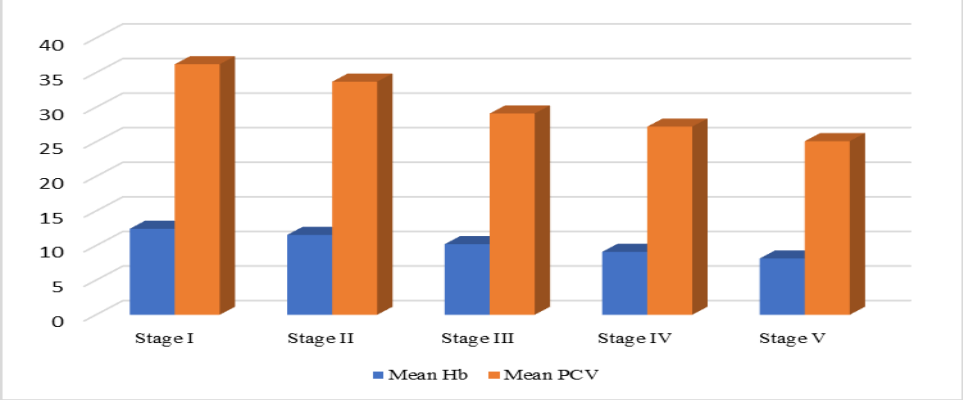



**Fig 3: -Peripheral smear findings in CKD cases**

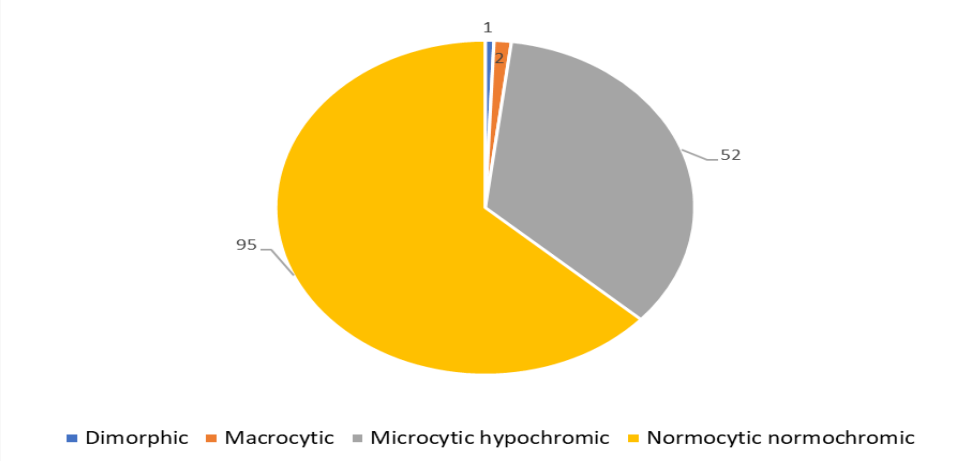
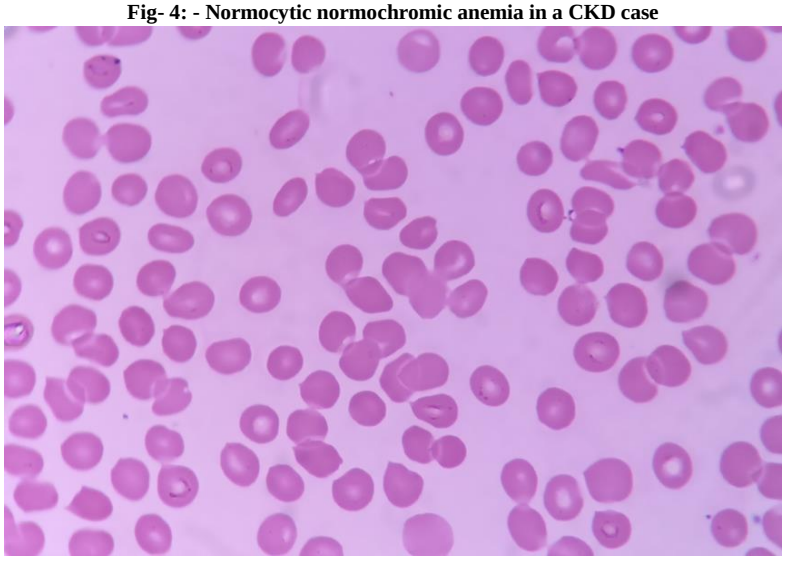


**Fig- 4: - Normocytic normochromic anemia in a CKD case**



## DISCUSSION

Chronic renal failure is progressive renal disease which is associated with various haematological and biochemical abnormalities. Anaemia is the most common haematological abnormality. Anemia in patients with CKD is commonly due to erythropoietin deficiency and iron deficiency. Other causes include increased red cell destruction in uremic patients, vitamin B12/folate deficiency. Anemia is an independent risk factor for the development of cardiac dysfunctions such as increased cardiac output, cardiac enlargement, left ventricular hypertrophy, and congestive cardiac failure. Cardiovascular diseases account for 40%–50% of all deaths in patients with chronic renal failure. [4] The National Health and Nutrition Examination Survey 3 and the Kidney Early Evaluation Program show an increase in the prevalence of anemia in individuals aged >61 years in the presence of Stage 3 CKD or higher. [2]

Many studies have been done to observe the type of anaemia. Anaemia begins to develop when the creatinine clearance drops to approximately 30 ml/min/1.73 $m^2$ of body surface area. As renal function deteriorates further the severity of anaemia also increases. [5] Most of the patients in our study showed normocytic normochromic anemia. Meanwhile Talwar et al. [5] showed a higher incidence of microcytic hypochromic anemia and study by Arun et al. [6] showed features of both normocytic normochromic anemia and microcytic hypochromic anemia.

Our study showed a significant decrease ($p \leq 0.001$) in RBC parameters like Hb, RBC count and PCV levels in comparison with the healthy group. This is comparable with the studies by Shastry et al., [4] and Singh et al. [1] The severity of anemia was found to be directly associated with the stage of the CKD.

TLC and differential neutrophil count were found to be significantly raised in CKD patients, as compared to the control group. Neutrophilic leucocytosis was seen in 73% of the patients. Increase in TLC is due to upregulation and presence of interleukin-6 (IL-6) and cytokines such as tumor necrosis factor –α (TNF-α) in blood which participate to chronic inflammation in the uremic state. [7]

Erythropoietin is said to potentiate the effect of megakaryocyte colony stimulating factors, acetyl hydrolase and paraoxonase. Hence impaired erythropoietin production

leads to reduction in platelet count. [1] Under normal conditions, ADP and serotonin are secreted to attract more platelets. In renal failure patients, their platelet granules have decreased levels of ADP and serotonin. Also, increased destruction of platelets can be drug induced. Heparin given during hemodialysis produces antibodies against platelets. Platelet count and function are both decreased in CKD patients. [8] In our study, thrombocytopenia was significant($p \leq 0.001$) with up to 65% of patients showing less than 1.5 lakh platelet count. This was like the studies by Singh et al., [1] and Khadayate R et.al. [8] This disagrees with the study by Khadim et al. [7] who found increase in platelet count.

ESR and CRP are inflammatory markers. It was found to be significantly raised in the cases compared to the control group. Coronary heart disease risk ratio is associated with high TLC and CRP. [9]

This study showed significant deterioration in renal function tests i.e., creatinine, uric acid, and BUN levels ($p \leq 0.001$) in comparison to healthy group. These parameters were found to be increased in 86% of the cases. In chronic kidney disease when the kidney loses its ability to remove nitrogenous wastes from blood, these substances will accumulate leading to a rise in urea and creatinine levels. [10]

The role of the kidney is to regulate body fluids, electrolytes, and acid-base balance. CKD can lead to electrolyte disturbance in the form hypocalcemia, hyponatremia, hyperphosphatemia, hyperkalemia, and metabolic acidosis. Hyperphosphatemia is due to a decrease in calcium sensing receptors and fat-soluble vitamin D receptor inside the parathyroid glands resulting in hypocalcemia. In the present study we observed significant hypocalcemia in CKD patients compared to the healthy group($p \leq 0.001$). Elevated serum phosphorus has been related to vascular and coronary artery calcification and resulting cardiovascular morbidity. However, unlike the other studies, serum sodium, potassium and chloride levels were normal in this study since most of the patients were already on treatment. Imbalances in key biochemical parameters such as sodium, potassium, calcium, magnesium, and chloride can have life-threatening consequences. Therefore, it is crucial to maintain these parameters within their physiological ranges. [1]

RBS was found to be elevated in 70% of the cases. Thus, proving diabetes as a major causative factor for CKD.

## CONCLUSION

Anemia is the leading cause of morbidity in patients with CKD and it worsens with the stage of the disease. Normocytic normochromic anemia of moderate intensity emerged as the most prevalent form of anemia in our study. Severity of anemia and serum creatinine levels showed negative correlation. Hematological parameters and Renal function test worsened with the progressing stage of CKD.

Notably, there was significant neutrophilic leucocytosis, thrombocytopenia, hyperphosphatemia, and hypocalcemia. All these derangements can result in severe complications like cardiovascular complications, bone-mineral disorders, muscle wasting, vascular calcification, and increased mortality. [1] Monitoring various electrolytes levels across the stages of CKD will reduce these complications and improve their living conditions.

Therefore, by a proper analysis of hematological and biochemical parameters throughout the different stages of CKD, we can proactively manage and prevent

complications, safeguarding the well-being of those afflicted.

### *Declaration by Authors*

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**Conflict of Interest:** The authors declare no conflict of interest.

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