"EVALUATION OF DERIVED INDICES OF PERIPHERAL WHOLE BLOOD CELL COUNTS IN NON-DIALYSIS CKD PATIENTS – ONE YEAR CROSS SECTIONAL STUDY IN A TERTIARY CARE HOSPITAL"

By

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With reference to the above, we wish to inform you that your proposed research project titled **"EVALUATION OF DERIVED INDICES OF PERIPHERAL WHOLE BLOOD CELL COUNTS IN NON-DIALYSIS CKD PATIENTS – ONE YEAR CROSS SECTIONAL STUDY IN A TERTIARY CARE HOSPITAL."**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee.

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LIST OF ABBREVIATIONS USED

CKD	-	Chronic Kidney Disease
ESRD	-	End Stage Renal Diseases
NLR	-	Neutrophil-Lymphocyte Ratio
PLR	-	Platelet-Lymphocyte Ratio
MLR	-	Monocyte-Lymphocyte Ratio
LMR	-	Lymphocyte-Monocyte Ratio
HTN	-	Hypertension
DM	-	Diabetes mellites
DN	-	Diabetic Nephropathy
HD	-	Hemodialysis
GFR	-	Glomerular Filtration Rate
eGFR	-	Estimated Glomerular Filtration Rate
CKDu	-	CKD of Unknown Origin
HIV	-	Human Immunodeficiency Virus
BMI	-	Body Mass Index
ECM	-	Extracellular Matrix
RAS	-	Renin-Angiotensin System
IDF	-	International Diabetes Federation
AGEs	-	Advanced Glycation End-products

DKD	-	Diabetic Kidney Disease
ESKD	-	End-Stage Kidney Disease
ESC/ESH	-	European Society of Cardiology and the European Society of Hypertension
eGFR	-	Estimated Glomerular Filtration Rate
CVD	-	Cardiovascular Disease
NKF	-	National Kidney Foundation
MCD	-	Minimal Change Disease
FSGS	-	Focal Segmental Glomerulosclerosis
IgAN/IgAV	-	IgA Nephropathy/IgA Vasculitis
MPGN	-	Membranoproliferative Glomerulonephritis
ADPKD	-	Autosomal Dominant Polycystic Kidney Disease
ACR	-	Albumin-to-Creatinine Ratio
IQR	-	Interquartile range
CRP	-	C-reactive Protein
Hs-CRP	-	High sensitivity C reactive protein
ESR	-	Erythrocyte Sedimentation Rate
ANC	-	Absolute Neutrophil Count
ALC	-	Absolute Lymphocyte Count
AMC	-	Absolute Monocyte Count

AEC	-	Absolute Eosinophil Count
NK cells	-	Natural Killer cells
ROS	-	Reactive Oxygen Species
SIRS	-	Systemic Inflammatory Response Syndrome
CAD	-	Coronary Artery disease
MCV	-	Mean Corpuscular Volume
MCH	-	Mean Corpuscular Hemoglobin
MCHC	-	Mean Corpuscular Hemoglobin Concentration
CBC	-	Complete Blood Count
RDW	-	Red Cell Distribution Width
RDW-CV	-	Red Cell Distribution Width - Coefficient of Variation
RDW-SD	-	Red Cell Distribution Width - Standard Deviation
MPV	-	Mean Platelet Volume
CKD-EPI	-	Chronic Kidney Disease Epidemiology Collaboration

ABSTRACT

Background: Chronic kidney disease (CKD) is marked by declining kidney function and high mortality rates, particularly in India. It predominantly affects lower socio-demographic regions. Routine blood tests, including hemogram and inflammatory markers, can provide cost-effective prognostic benefits.

Objectives: To evaluate neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR) and monocyte-lymphocyte ratio (MLR) or lymphocyte-monocyte ratio (LMR) as a biomarker to assess the severity of inflammation in different stages of CKD and to study the pattern of NLR, PLR, MLR in different types of CKDs

Methodology: We collected blood samples and clinical data from adult non-dialysis CKD patients at the Nephrology OPD of KLE's DR. Prabhakar Kore Hospital and MRC, Belagavi. 140 participants provided 3ml venous blood samples in EDTA and plain tubes for CBC, hs-CRP, and RFT analysis. NLR, PLR, and LMR values were calculated for each patient using the collected data.

Results: As CKD stages advanced, NLR, PLR, MLR (with lower LMR), RDW, and hs-CRP levels increased, while ALC and platelet counts decreased. NLR had the strongest correlation with hs-CRP (Spearman correlation 0.72), LMR showed a moderate inverse correlation (-0.51), and PLR had a weak correlation (0.35).

Conclusion: Our research shows that NLR, PLR, MLR, and RDW increase with CKD progression, while ALC and platelets decrease. These biomarkers can assess inflammation severity and monitor disease progression, indicating the need for personalized diagnostic and therapeutic approaches.

Keywords: Chronic kidney disease (CKD), neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR) and monocyte-lymphocyte ratio (MLR), inflammation

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INTRODUCTION

Chronic kidney disease (CKD) constitutes a major health problem and is one of the leading causes of death worldwide, with rising incidence, high costs, and a high morbidity and mortality rate. According to World Health Organization reports, chronic kidney disease ranks 10th in the world as a cause of death, with 1.3 million deaths reported by 2019 with a significant increase in the last 20 years.[1] Patients with CKD have higher mortality and morbidity rates than the general population, with cardiovascular disease being the primary cause of death, accounting for roughly 50% of all-cause mortality in those with Ends stage renal diseases (ESRD).[2]

Inflammation plays a crucial role in the development of kidney disease. Commonly used diagnostic and monitoring markers for inflammation include C-reactive protein, erythrocyte sedimentation rate, ferritin, tumor necrosis factor, interleukin-1, and interleukin-6. However, considering the current socioeconomic conditions, there is a growing need for more cost-effective biological markers. Recently neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR) and monocyte-lymphocyte ratio (MLR) or lymphocyte-monocyte ratio (LMR) which are established in other medical fields, have been introduced for use in kidney patients. These ratios are valuable as they reflect inflammation, endothelial damage, and can predict mortality.[3]

In recent research, derived indices of peripheral whole blood cell counts, such as NLR, PLR and MLR (LMR) have gained attention for their ability to indicate systemic vascular and inflammatory conditions. These ratios, along with other markers, serve as novel indicators of inflammation.[1,4]

Assessing NLR, PLR, and MLR (LMR) at hospital admission strongly predicts 30-day mortality in ESRD patients requiring renal replacement therapy for at least six months.

Higher ratios correlate with longer hospital stays and more frequent dialysis sessions. NLR, particularly, reflects inflammation in ESRD patients on hemodialysis (HD). PLR also correlates with inflammation and mortality prediction in HD patients. However, their relevance in assessing inflammation in advanced stages of non-dialysis CKD patients remains uncertain.[1,5]

In this study we aim to evaluate the use of these indices as biomarkers to assess the severity of inflammation in different stages of CKD patients who are not on dialysis.

AIMS AND OBJECTIVES

PRIMARY OBJECTIVE:

To evaluate neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR) and monocyte-lymphocyte ratio (MLR) or lymphocyte-monocyte ratio (LMR) as a biomarker to assess the severity of inflammation in different stages of CKD.

SECONDARY OBJECTIVE:

To study the pattern of NLR, PLR, MLR in different types of CKDs

REVIEW OF LITERATURE

CHRONIC KIDNEY DISEASE

Chronic kidney disease (CKD) involves a range of physiological issues related to impaired kidney function, frequently leading to a gradual decrease in glomerular filtration rate (GFR). The likelihood of CKD worsening is strongly tied to both GFR and the level of albumin in the urine [6]. CKD is identified by a persistent abnormality in kidney structure or function lasting more than three months, as indicated by criteria such as a GFR below 60 mL/min/1.73 m^2 or albuminuria levels equal to or exceeding 30 mg per 24 hours [7].

EPIDEMIOLOGY

The Global Burden of Disease collaboration highlights CKD as a significant cause of illness and death worldwide. From 1990 to 2017, there was a notable rise in both the prevalence and mortality rates of CKD globally. In India specifically, the proportion of deaths linked to kidney failure surged by 38% from 2001-03 to 2010-13 [8 9].

The occurrence of CKD spans a wide range across different regions, varying from less than 1% to as high as 13%. Recent findings from the International Society of Nephrology's Kidney Disease Data Center Study have indicated a prevalence of 17% [10 11]. CKD's causes vary significantly across India, with certain areas in Andhra Pradesh, Odisha, and Goa experiencing elevated rates of CKD of unknown origin (referred to as CKDu). This condition is characterized by a chronic form of kidney damage with a gradual onset and slow advancement [10 12].

Patients tend to seek medical attention for CKD only when symptomatic, often in the advanced stages of the condition. Early detection of CKD typically occurs incidentally during evaluations for other health conditions or, less commonly, through routine

screenings [8] [13]. Considering that CKD disproportionately affects regions with lower socio-demographic indices [8] [14], effective identification and management of CKD risk factors are crucial for global health outcomes. Tailored strategies that address the unique challenges of these regions are essential for achieving widespread success in combating CKD [8].

RISK FACTORS FOR CKD

The primary factors contributing to the onset and advancement of CKD are diabetes and hypertension. CKD resulting from these conditions affects approximately 5-7% of the global populace, with a higher prevalence observed in developing nations and among socioeconomically disadvantaged and minority groups [15] [16].

Understanding the factors associated with CKD is vital for its prevention, early detection, and management. These factors can be grouped into several categories, including chronic nonrenal (systemic) diseases, demographic and geographical factors, childhood and

adolescent conditions, adult-onset factors, genetic influences, viral infections, and lifestyle components.

Chronic Nonrenal (Systemic) Diseases: Chronic illnesses like diabetes and metabolic syndrome, autoimmune disorders such as lupus and vasculitis, and infections like HIV, hepatitis B, and hepatitis C elevate the likelihood of developing kidney disease. Hypertension is also closely linked to kidney issues.

Demographic, Anthropomorphic, Ancestry, and Geographic Factors: Age, gender, population ancestry, and family history influence disease prevalence. Regional differences also affect risk, with higher rates in Central America, Sri Lanka, and among indigenous communities in Australia and New Zealand.

Childhood and Adolescent States and Diseases: Premature birth, low birth weight, higher BMI during childhood, persistent microscopic hematuria, and elevated childhood blood pressure increase future kidney disease risk. Previous childhood kidney conditions and cancer treatments also contribute.

Adult Onset: A history of acute kidney injury, preeclampsia, and kidney donation or other nephrectomies heighten the risk of developing chronic kidney conditions.

Genetic Factors: Both monogenic Mendelian inheritance and complex polygenic inheritance can predispose individuals to kidney disease.

Viral Infections: HIV infection and SARS-CoV-2 infection significantly increase the risk of developing chronic kidney issues.

Lifestyle: Smoking, dietary choices, and physical activity levels play crucial roles in determining susceptibility to kidney disease.

Each category highlights specific factors that contribute to the development and progression of chronic kidney disease in adulthood.[6]

PATHOPHYSIOLOGY OF CKD

CKD is a broad term encompassing various disorders, often linked to factors like diabetes, nephritis, hypertension, and immune system dysfunction. Despite diverse causes, CKD typically results in common renal pathologies such as glomerulosclerosis and interstitial fibrosis. Recent advancements in understanding the cellular and molecular mechanisms underlying CKD have significantly improved our comprehension of its pathophysiology. These developments pave the way for the potential development of effective therapies targeting CKD. [17]

The hallmark pathological features of CKD involve the depletion of renal cells and the accumulation of extracellular matrix (ECM). Regardless of the initial causes, the progression of renal disease is marked by morphological transformations, including renal inflammation, glomerulosclerosis, tubular atrophy, tubulointerstitial fibrosis, and capillary rarefaction. The development of renal fibrosis, encompassing glomerulosclerosis and interstitial fibrosis, is a gradual process culminating in end-stage renal failure, a severe condition necessitating renal replacement therapy such as dialysis or transplantation.[17] [18]

The development of CKD involves two primary mechanisms of harm:

1. Specific triggers related to the underlying cause, such as genetic anomalies in kidney development, immune reactions leading to complex deposition and inflammation in certain forms of glomerulonephritis, or exposure to toxins affecting renal tubules and interstitium.

2. General mechanisms involving hyperfiltration and hypertrophy of the remaining functional nephrons, which are typical outcomes of long-term reduction in renal mass regardless of the underlying cause. Responses to nephron reduction are orchestrated by vasoactive hormones, cytokines, and growth factors. Over time, the short-term adaptations of hyperfiltration and hypertrophy to sustain glomerular filtration rate become counterproductive, leading to distortions in glomerular architecture, abnormal podocyte function, and disruption of the filtration barrier, ultimately resulting in nephron sclerosis and loss.

Increased activity of the renin-angiotensin system (RAS) within the kidney seems to contribute to both the initial compensatory hyperfiltration and the subsequent harmful effects of hypertrophy and sclerosis. This process elucidates why a decrease in renal mass from an isolated injury may cause a gradual decline in renal function over many years and

underscores the effectiveness of pharmacological interventions aimed at mitigating this response.[6]

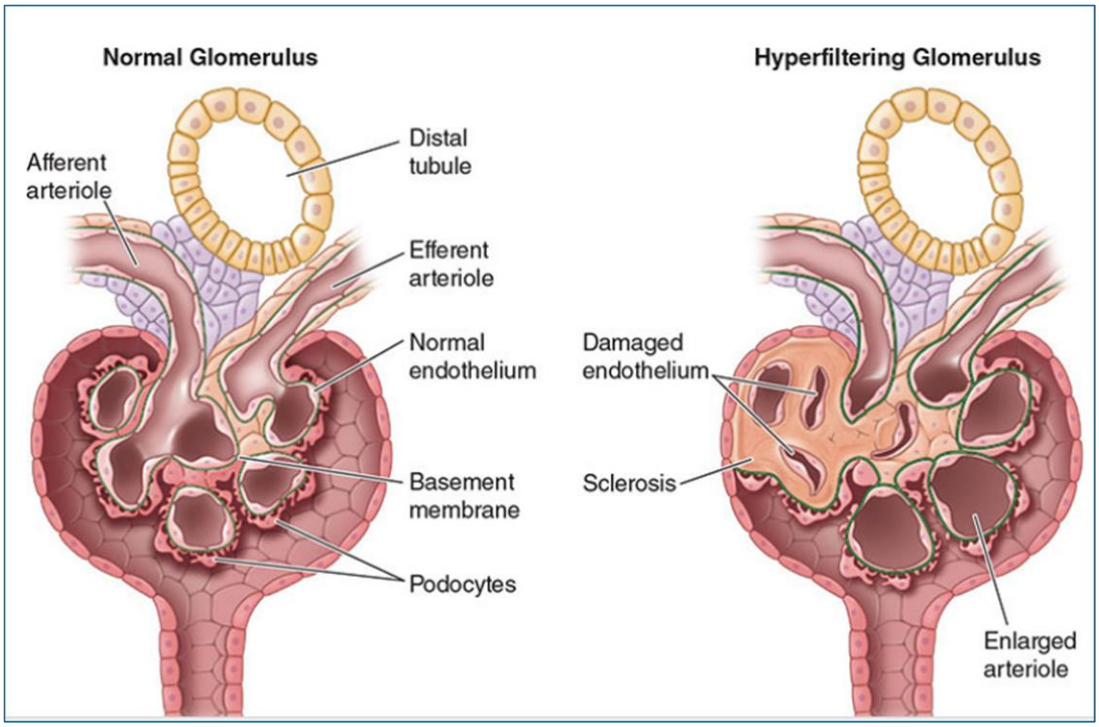

Figure 1. **Left**: Diagram of normal glomerular structure. **Right**: Secondary changes in the glomeruli due to a decrease in nephron number, including enlarged capillary lumens and focal adhesions, likely resulting from compensatory hyperfiltration and hypertrophy in the remaining nephrons. *Image taken from Loscalzo J, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL, editors. Harrison's principles of internal medicine. 21st edition. New York: McGraw Hill; 2022.* [6]

NATURAL HISTORY OF RENAL DISEASE

Following kidney injury, the clinical presentation can range from asymptomatic to requiring long-term renal replacement therapy. Nephrons adapt to injury by adjusting filtration rates, a process known as adaptive hyperfiltration. While initially beneficial, this can lead to nephron and glomerular damage, presenting as proteinuria and progressive renal failure, with chronic changes including tubular atrophy, interstitial fibrosis, and glomerulosclerosis. In CKD patients, the decline in kidney function is nonlinear and influenced by various factors such as underlying etiology, comorbidities, socioeconomic status, genetics, ethnicity, and episodes of Acute Kidney Injury (AKI), which can accelerate CKD progression to ESRD. [19] [20].

As people age, their kidneys undergo significant changes, including structural and functional alterations. These changes involve kidney volume fluctuations, cyst formation, cortical thinning, nephron loss, glomerulosclerosis, tubular atrophy, and interstitial fibrosis. They collectively lead to a decline in Glomerular Filtration Rate (GFR). [19]

DIABETES MELLITUS IN CKD

Diabetes mellitus has become a significant global health challenge, impacting a considerable number of individuals worldwide. As per estimates by the International Diabetes Federation (IDF), roughly 463 million adults aged 20 to 79 were diagnosed with diabetes in the year 2019 [21] [22].

Diabetes poses a substantial risk factor for kidney disease, particularly in the form of diabetic nephropathy. Estimates suggest that a considerable proportion, ranging from 20% to 40% of individuals with diabetes may develop diabetic nephropathy, emphasizing its clinical significance.

The pathogenesis of diabetic nephropathy is characterized by chronic hyperglycemia, leading to progressive damage to the renal microvasculature [21] [23].

It is theorized that the elevated blood sugar levels in diabetes trigger the development of advanced glycation end-products (AGEs), along with an increase in reactive oxygen species. These byproducts subsequently provoke inflammation within the kidney tissues, resulting in damage and fibrosis at various levels including the glomerulus, its capillaries, tubules, and interstitium, thus contributing to CKD. The deposition of these glycosylation byproducts within the matrix was extensively documented by Drs. Kimmelstiel and Wilson in 1936 [24], leading to the identification of what is now referred to as Kimmelstiel-Wilson nodules, classic lesions found in the glomerular mesangium. AGEs can activate molecular pathways that further intensify local inflammation within the kidneys in cases of Diabetic Kidney Disease (DKD), consequently promoting tissue fibrosis[25]. Additionally, mesangial cell activation and expansion via the TGFβ pathway complicate the situation[26]. This process involves an increase in pro-inflammatory and pro-fibrotic factors, which in turn attract macrophages to the kidneys, exacerbating inflammation and worsening kidney tissue damage. The persistent injury to kidney tissue ultimately drives the progression of DKD to end-stage kidney disease (ESKD).[24] [27]

HYPERTENTION IN CKD

Hypertension, as described by the European Society of Cardiology and the European Society of Hypertension (ESC/ESH), is indicated by a blood pressure measurement of 140/80 mmHg or higher. It affects roughly 30% of the general adult populace and can be observed in up to 90% of those diagnosed with CKD [28] [29] [30]. Hypertension serves as both a contributing factor to and a consequence of CKD, exacerbating its advancement [28] [31] [32]. As the estimated Glomerular Filtration Rate (eGFR) decreases, there is a notable rise in both

the frequency and intensity of hypertension (21). Moreover, hypertension and CKD independently heighten the risk of cardiovascular disease (CVD). Their coexistence significantly amplifies the likelihood of morbidity and mortality due to CVD [28 33].

Hypertension stands as the second most common cause of kidney failure after diabetes mellitus [34 35]. While the majority of hypertensive patients experience only mild to moderate hypertensive nephrosclerosis, the incidence of renal failure due to high blood pressure (BP) is escalating due to its pervasive occurrence in the general population. Traditionally, hypertensive kidney disease has been associated with nephroangiosclerosis and hyalinosis, resulting in glomerular damage. However, recent evidence suggests that elevated BP can also harm tubular cells, leading to epithelial-mesenchymal transition and tubulointerstitial fibrosis. It is widely agreed upon that both accelerated and malignant hypertension can rapidly progress to renal failure and end-stage renal disease (ESRD). Moreover, the cardiovascular outcomes of individuals with CKD are frequently intertwined with hypertension. [34]

GLOMERULAR DISEASES

Glomerular diseases represent a significant contributor to CKD and end-stage kidney disease (ESKD) across age groups. The prevalence of specific glomerular diseases varies throughout different stages of life. In children, the most common glomerular diseases include Minimal Change Disease (MCD), Focal Segmental Glomerulosclerosis (FSGS), and IgA Nephropathy/IgA Vasculitis (IgAN/IgAV) [36 37], although regional differences exist. While MCD and IgAV predominate in childhood cases, IgAN and FSGS are predominantly diagnosed in adulthood. The epidemiological patterns further diverge regionally, as evidenced by a large international study of 42,603 biopsy-proven cases.

FSGS emerged as the primary glomerular disease in the United States/Canada, accounting for 19.1% of cases, while in Europe and Asia, IgAN/IgAV predominated [36 38] .

IgA Nephropathy

IgA Nephropathy (IgAN) stands out as one of the most commonly occurring forms of glomerulonephritis (GN) worldwide. Studies have indicated a wide-ranging prevalence for IgAN, spanning from 5% to 40%. Over a ten-year period, approximately 15% to 20% of IgAN patients progress to ESRD, with this figure increasing to 30% to 40% over a 20-year follow-up period. Diagnosing IgA Nephropathy (IgAN) usually requires renal biopsy, but this isn't consistently done, affecting prevalence assessment. IgAN isn't considered rare or benign. Its progression is tied to factors like proteinuria (<1 g/day), hematuria, hypertension, elevated serum creatinine, and specific microscopic lesions noted in the Oxford classification at diagnosis. Immunofluorescence microscopy commonly reveals notable IgA deposits within the mesangium, a characteristic feature of IgA Nephropathy (IgAN). [39]

Focal segmental glomerulosclerosis (FSGS)

Focal segmental glomerulosclerosis (FSGS) is a kidney condition marked by glomerular scarring, causing protein leakage into urine and potentially leading to kidney failure. In the US, it constitutes 20-25% of clinical kidney biopsy diagnoses and up to 40% of glomerular disease patients progressing to kidney failure. FSGS presents diverse histological categories—collapsing, tip, cellular, perihilar, and not otherwise specified (NOS)—each with unique clinical features and outcomes, highlighting their prognostic importance. Diagnosis relies on kidney biopsy, facilitating prompt treatment. Additionally, FSGS is suspected with a 24-hour urinary protein level surpassing 3.5 g/day, serum albumin below 3.0 g/dL, particularly with diffuse foot process effacement. [40]

Minimal change disease

Minimal Change Disease (MCD) is the primary cause of nephrotic syndrome in children but a smaller proportion in adults (10–16%). It's characterized by normal or nearly normal glomerular appearance on light microscopy and immunofluorescence, with podocyte foot process effacement observed on electron microscopy. The hallmark features include sudden-onset proteinuria and widespread swelling (anasarca), with unclear mechanisms of protein leakage, possibly involving circulating factors from T cells. Some patients may progress to advanced stages of CKD, transitioning from MCD to Focal Segmental Glomerulosclerosis (FSGS). This raises questions about whether MCD and FSGS are distinct diseases or different stages of the same condition. [41]

Membranoproliferative Glomerulonephritis (MPGN)

Membranoproliferative glomerulonephritis is a rare kidney disorder distinguished by the proliferation of mesangial cells and changes in the structure of the glomerular capillary walls.[42] MPGN can be idiopathic, but it is more often secondary to systemic inflammatory conditions such as chronic infections (especially hepatitis C), autoimmune diseases, plasma cell dyscrasias, and cryoglobulinemia.[43]

Three types of MPGN—Type I, Type II, and Type III—are classified based on pathological characteristics. Although all three types involve hypocomplementemia, they differ in their mechanisms of complement activation. Type II, also called "dense deposit disease," is linked to the presence of C3-nephritic factor. MPGN mainly affects children and young adults, who may present with nephrotic or nephritic syndrome or asymptomatic renal disease. This form of glomerulonephritis often advances slowly to end-stage renal disease and tends to recur after kidney transplantation, especially in Type II cases. [42]

AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD)

Autosomal Dominant Polycystic Kidney Disease (ADPKD) is the most common inherited kidney disorder, affecting 1 in 500 to 1 in 1000 people globally. In the United States alone, it affects over 600,000 individuals, and worldwide, about 12 million people are impacted. Around 70% of ADPKD patients develop end-stage renal disease (ESRD) by age 58, making it the fourth leading cause of ESRD globally and in the US. ADPKD is characterized by the gradual development and enlargement of multiple cysts in the kidneys, leading to complications, primarily declining renal function. Despite ongoing kidney damage, remaining glomeruli compensate by increasing filtration, maintaining normal kidney function for many years. Only when a significant portion of nephrons are compromised does renal function begin to decline, usually leading to ESRD after the age of 40. [44]

CRITERIA AND STAGING OF CKD

CRITERIA

CKD is characterized by persistent kidney structure or function abnormalities lasting over three months[7 45 46] . These abnormalities include:

(1) Glomerular filtration rate (GFR) below 60 mL/min/1.73 m²,

(2) Albuminuria (with urine albumin levels equal to or exceeding 30 mg per 24 hours or a urine albumin-to-creatinine ratio [ACR] of 30 mg/g or higher),

(3) Indications of kidney damage based on urine sediment, histology, or imaging,

(4) Tubular disorders of kidney

(5) History of kidney transplantation [45].

To differentiate CKD from acute kidney injury (which occurs within 2-7 days) and acute kidney disease (lasting ≤3 months), repeat assessments may be necessary if the duration of kidney disease is unclear. Evaluating the underlying cause of CKD should be based on a patient's clinical history, physical examination, and urinary findings.[7] [47]

STAGING

After diagnosing CKD, the next step involves determining its staging, which is determined by GFR and albuminuria. [47]

Glomerular Filtration rate (GFR)

Glomerular Filtration Rate (GFR) estimates kidney function by calculating the fluid filtered through the renal glomeruli per unit time, reflecting the total filtration of all kidney glomeruli. Inulin, which is freely filtered and neither reabsorbed nor secreted, can be used to measure GFR by determining the blood volume cleared of inulin per minute, calculated as urine concentration times urine flow divided by plasma concentration. Clinically, creatinine often substitutes inulin because it is naturally occurring and doesn't require injection.[48] GFR serves as the primary assessment tool for kidney function and has traditionally been evaluated in routine clinical settings through estimated GFR (eGFR) using serum creatinine levels [49].

For screening purposes, it is recommended to perform tests for serum creatinine, commonly included in basic and comprehensive metabolic panels (BMP and CMP). The equations used to estimate Glomerular Filtration Rate (GFR) from creatinine levels have been revised multiple times to improve accuracy and reduce bias. It is now advised to calculate the estimated GFR (eGFR) using the latest CKD-EPI creatinine equation from 2021. This updated equation no longer includes race as a factor, promoting a more equitable approach

in the United States. [50] [51] [52] Clinicians can access an **eGFR calculator on the National Kidney Foundation (NKF) website** for convenience.[50]

While creatinine currently serves as the primary endogenous biomarker for estimating GFR in clinical practice, it is affected by numerous factors beyond GFR, leading to potential over or underestimation of kidney function [53] [54]. Cystatin-C has emerged as an alternative biomarker for estimating GFR, as it is not subject to the same limitations as creatinine. When combined with creatinine, cystatin-C results in a more accurate estimation of GFR [51].

G1	**GFR (> 90 mL/min/1.73 m²)**
G2	**GFR (60–89 mL/min/1.73 m²)**
G3a	**GFR (45–59 mL/min/1.73 m²)**
G3b	**GFR (30–44 mL/min/1.73 m²)**
G4	**GFR (15–29 mL/min/1.73 m²)**
G5	**GFR (< 15 mL/min/1.73 m²)**

Table 1. CKD staging based on GFR [47]

Proteinuria/Albuminuria

Proteinuria denotes an increase in the excretion of various urinary proteins, encompassing albumin, other serum proteins, as well as proteins synthesized within the tubule (such as Tamm-Horsfall protein) or within the lower urinary tract. Conversely, albuminuria specifically refers to elevated excretion of albumin alone. In healthy individuals, there's typically a small amount of protein excretion in urine. However, persistent elevation in protein excretion commonly indicates kidney damage. Elevated albumin excretion serves as a sensitive and specific indicator for CKD associated with diabetes, hypertension, and glomerular diseases.[55]

Ideally, urine albuminuria should be quantified using a urine albumin-to-creatinine ratio (ACR). This categorizes albuminuria into three stages:

A1 (urine ACR <30 mg/g),

A2 (30–300 mg/g), and

A3 (>300 mg/g). [45]

Guidelines recommend urine ACR for staging CKD instead of urine protein-to-creatinine ratio due to better standardization and precision of assays, especially at lower levels of albuminuria[56]. The most accurate measurements are obtained from either a first morning sample or a 24-hour urine collection, as there is significant biological variability in urine albumin excretion throughout the day [45 57 58].

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/ 1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

Figure 2. CKD prognosis based on GFR and albuminuria. Image taken from Inker LA, Astor BC, Fox CH, Isakova T, Lash JP, Peralta CA, et al. KDOQI US Commentary on the 2012 KDIGO Clinical Practice Guideline for the Evaluation and Management of CKD. Am J Kidney Dis. 2014 May;63(5):713–35. [47]

OTHER INDICATORS OF RENAL DAMAGE

The decision to test for additional markers of kidney damage to detect CKD should be based on clinical judgment. This may involve considering imaging studies, alternative urine or serum markers, or even kidney biopsy. For instance, individuals with a family history of polycystic kidney disease should undergo ultrasound screening to identify cysts, while those with a family history of Alport syndrome should undergo urinalysis to detect the presence of blood in urine (hematuria).[55]

CLINICAL MANIFESTATIONS

Early stages of CKD typically manifest without symptoms, with signs becoming noticeable in stages 4 or 5. Diagnosis often occurs through routine blood or urine tests. Symptoms and signs that may emerge during these later stages include nausea, vomiting, loss of appetite, fatigue, weakness, disrupted sleep patterns, reduced urine output (oliguria), diminished mental clarity, muscle twitches, cramps, swelling in the feet and ankles, persistent itching (pruritus), chest discomfort due to uremic pericarditis, and breathing difficulties from pulmonary edema due to fluid retention. Additionally, hypertension may become challenging to manage. Physical examination may not yield significant findings, but patients may exhibit changes in skin pigmentation, scratch marks from itching, a friction rub over the pericardium due to uremic pericarditis, uremic frost resulting from high blood urea nitrogen levels, and hypertensive changes in the retina indicating chronicity.[59]

INFLAMMATION IN CKD

In CKD, inflammation was acknowledged as a pivotal aspect in the late 1990s, particularly due to its correlation with cardiovascular disease, protein-energy wasting, and mortality. Subsequently, there has been a substantial surge in interest surrounding inflammation in CKD and ESRD. This heightened focus has transformed our understanding of

inflammation from a novel concept to a firmly established risk factor for morbidity and mortality among CKD patients. [60]

Numerous factors contribute to immune dysregulation and inflammatory activation in CKD. Some of these factors may stem from the primary disease itself rather than solely from uremia. Additionally, modifiers originating from genetic predispositions, as well as influences from diet, lifestyle, and environmental factors, also play a role, representing epigenetic influences. Elevated levels of circulating cytokines are partly attributed to decreased renal clearance, although increased production has also been observed[60 61]. The uremic milieu induces oxidative stress and carbonyl stress, both of which are highly inflammatory. [60]

A clear inverse relationship between GFR and inflammation has been established. In the Chronic Renal Insufficiency Cohort (CRIC) study, various biomarkers of inflammation such as IL-1β, IL-1 receptor antagonist, IL-6, TNF-α, CRP, and fibrinogen exhibited an inverse correlation with measures of kidney function and a positive association with albuminuria [62]. Notably, inflammation is evident not only in adult but also in pediatric patients with CKD/ESRD. Moreover, intriguingly, the erythrocyte sedimentation rate (ESR) in adolescents has been identified as predictive of ESRD in middle-aged men.[60 63]

C-REACTIVE PROTEIN (CRP) AS INFLAMMATORY MARKER

C-reactive protein (CRP) is a member of the pentraxin protein family, primarily synthesized by the liver. Its levels in the blood rise significantly in response to acute infections, inflammation, and trauma. During such clinical scenarios, CRP levels typically increase rapidly, often surpassing 10 mg/l along with a simultaneous elevation in erythrocyte sedimentation rates (ESR)[64 65]. Due to its stable pentraxin structure, CRP has a relatively extended half-life of approximately 18 to 20 hours.[64]

In recent years, advanced techniques for measuring C-reactive protein (CRP) levels with high sensitivity and rapid results have emerged. These include immunonephelometry, immunoturbidimetry, high-sensitivity enzyme-linked immunosorbent assay (ELISA), and resonant acoustic profiling (RAP), capable of detecting CRP within a sensitivity range of 0.01 to 10 mg/l. [64] [66]

These high-sensitivity assays are particularly valuable for quantifying subtle levels of systemic inflammation, even in the absence of clear signs of systemic inflammatory or immunologic disorders. Hs-CRP has been extensively studied as a biomarker in the search for an optimal predictor of global cardiovascular disease (CVD) risk. [64]

It's widely known that CRP poses a risk for CKD, and increased levels of CRP in the bloodstream are linked to higher mortality and illness rates in CKD cases [67] [68]. In individuals with CKD, elevated CRP levels indicate a likelihood of cardiovascular issues, and in stages 3 and 4 of CKD, it independently heightens the risk of death from all causes. [67]

A genetic inclination toward elevated CRP levels might increase the likelihood of CKD advancement in patients. There's a strong likelihood that heightened CRP levels could facilitate the influx of inflammatory cells and the secretion of cytokines, chemokines, and TGF-β1 from the affected kidney, leading to the gradual onset of renal inflammation and fibrosis.[67]

Elevated levels of high-sensitivity C-reactive protein (hs-CRP) not only indicate inflammation but actively contribute to it. When hs-CRP levels are high, they can adhere to damaged kidney cells, including those in the glomeruli, tubules, and surrounding blood vessels. This attachment triggers an inflammatory response within the kidney tissues. Moreover, increased hs-CRP levels can exacerbate oxidative stress, a significant factor in

the development of kidney disease and its complications. This stress leads to the peroxidation of phospholipids in the glomerular capillary basement membrane, causing it to become more permeable. Ultimately, these processes contribute to the progression of kidney disease. [69]

Patients' hs-CRP levels should be indicated in milligrams per liter (mg/l). If the concentration is below 3 mg/l, there is no need for repeated measurements. However, if the value exceeds 3 mg/l, it should be retested after at least two weeks, when there is no sign of active systemic inflammation. The lower of the two results should be utilized. Values surpassing 10 mg/l indicate a robust acute phase response, which, if not attributed to cardiovascular causes, necessitate further investigation into their etiology. [70]

HEMATOLOGICAL INDICES:

NEUTROPHILS

Neutrophils, often referred to as the "soldiers of our innate immune system," are the frontline defenders against infections. They swiftly migrate to sites of infection, where they engulf and neutralize invading microorganisms through a process involving the production of reactive oxygen species. [71] [72] Beyond their role in combating infections, neutrophils are also key players in both acute and chronic inflammatory conditions, as well as autoimmune disorders. [71] [73]In adults, the normal range of white blood cell (WBC) count typically falls between 4000 to 11,000 cells/microL, with mature neutrophils comprising 60% to 70% of these circulating cells in peripheral blood. [71]

An absolute neutrophil count (ANC), representing the percentage of neutrophils in the bloodstream among adults, typically ranges from 2500 to 7000 neutrophils/microL. Leukocytosis is characterized by a WBC count exceeding 11,000 cells/microL. Neutrophilia, the most common form of leukocytosis, is identified by an increase in the

absolute neutrophil count to approximately over 7700 neutrophils/microL (calculated as 11,000 cells/microL multiplied by 70 percent, or two standard deviations above the mean). [71]

Neutrophils, constituting the largest proportion of white blood cells, are implicated in chronic meta-inflammatory conditions like obesity, insulin resistance, type 2 diabetes, gestational diabetes mellitus, and coronary artery disease.[74]

Increased neutrophil levels may play a role in the onset and progression of CKD through various mechanisms. Research by Mahfouz et al and Bolignano et al has highlighted neutrophil gelatinase-associated lipocalin (NGAL), primarily produced by neutrophils, as a potential predictor of CKD and its advancement.[74] [75] [76] However, it's worth noting that NGAL synthesis isn't exclusive to neutrophils; other cells, including epithelial cells, are involved. [74] [77] Additionally, studies indicate that elevated blood sugar levels, as seen in hyperglycemia, can trigger an increase in circulating neutrophils. These neutrophils are then drawn to sites of glomerular basement membrane injury through chemokines, initiating an inflammatory cascade that involves further recruitment of mononuclear macrophages.[74] [78] Neutrophils may also contribute to CKD progression via the secretion of neutrophil elastase (NE) upon activation. NE's proinflammatory properties have been observed in various disease models, and previous research has linked neutrophils and NE to insulin resistance by degrading insulin receptor substrate 1. NE can also directly damage renal cells, exacerbating CKD progression in individuals with type 2 diabetes. Collectively, these findings suggest that neutrophils likely play a role in the pathogenesis of CKD. [74]

LYMPHOCYTES

Lymphocytes typically comprise approximately 20% to 40% of the total white blood cell count and the absolute lymphocyte count (ALC) is determined by multiplying the total

white blood cell count (WBC) by the percentage of lymphocytes present in the peripheral blood. [79]

Lymphocytes play a vital role in the immune system by influencing responses to infectious microorganisms and other foreign substances. Natural killer (NK) cells, T cells, and B cells represent distinct types of lymphocytes, each playing a crucial role in the functioning of the immune system. These cells influence the immune system's responses to various foreign substances, including invading microorganisms, tumor cells, and transplanted tissues.[80]

Lymphocytosis, characterized by an elevation in the absolute lymphocyte count (ALC) to over 4000 lymphocytes/microL in adult patients, is a frequently observed hematologic anomaly.[79] Causes of lymphocytosis include viral infections bacterial and protozoal infections, certain medications and hematological malignancies. [80]

Lymphopenia is characterized by a reduction of ALC (usually below 1.0 x 10^9 cells/L) in the circulating in the blood. [81] Lymphopenia has emerged as a widely acknowledged indicator of increased severity in COVID-19 cases. It is linked with a greater occurrence of established risk factors for COVID-19, including advanced age, male gender, hypertension, chronic obstructive pulmonary disease (COPD), CKD, coronary heart disease, and obesity.[82]

Lymphocytes, especially T cells and innate lymphoid cells (ILCs), are vital in the inflammation associated with chronic kidney disease (CKD). CKD is characterized by a continuous low-grade inflammatory state, which not only advances the disease but also leads to complications like cardiovascular issues and higher mortality rates.[83,84]

T cells, including subtypes like Th1, Th17, and regulatory T cells (Tregs), play a significant role in inflammation. Th1 and Th17 cells are typically pro-inflammatory, releasing cytokines like IFN-γ and IL-17, which worsen inflammation and kidney damage. In

contrast, Tregs usually help suppress inflammation, but their function can be impaired in CKD's chronic inflammatory environment, potentially worsening the disease. Innate lymphoid cells (ILCs), such as ILC1, ILC2, and ILC3, also participate in the inflammatory processes of CKD. These cells quickly respond to tissue damage and produce cytokines that can either enhance or mitigate inflammation. For example, ILC2s generally have anti-inflammatory effects, while ILC1s and ILC3s can be pro-inflammatory, depending on the situation.[84]

MONOCYTES

Monocytes constitute 5–10% of all immune cells in the blood, originating from the bone marrow as mononuclear cells with a lifespan of approximately 1–3 days [85,86]. Under normal conditions, they contribute to homeostasis and possess the capacity to differentiate into tissue macrophages. However, during inflammation, monocytes are recruited to the inflammatory site where they differentiate into either inflammatory macrophages or dendritic cells. Monocytes and macrophages serve as integral components of the innate immune system, crucial for orchestrating inflammation. They play essential roles not only in producing inflammatory mediators and regulating both innate and adaptive immunity but also in resolving inflammation and restoring equilibrium. Consequently, dysfunction in these cells often underlies the pathophysiology of chronic infections and numerous severe sterile inflammatory and autoimmune disorders. [85]

Monocytes represent a significant element of the innate immune system and have been increasingly linked to complications and advancement of CKD. This association is logical, considering their notable capacity to swiftly migrate from the bloodstream to sites of inflammation and their robust reactions to inflammatory triggers.[87] Monocytes exhibit particular cytokines and adhesion molecules pivotal in the development of inflammation

associated with CKD. These cytokines facilitate the activation and migration of immune effector cells across endothelial barriers, resulting in a persistent pro-fibrotic inflammatory infiltration in the kidneys and other tissues.[87–89]

PLATELETS

Platelets are tiny, non-nucleated cell fragments found in the bloodstream, essential for maintaining vascular integrity and regulating hemostasis. A typical platelet count in the blood ranges from 150,000 to 400,000 per microliter. Megakaryocytes found in the bone marrow are responsible for creating platelets. Each megakaryocyte has the capacity to produce between 5,000 and 10,000 platelets. On average, a healthy adult generates approximately 100 billion platelets daily. The removal of old platelets occurs through phagocytosis by cells in the spleen and liver. [90]

Platelets primarily play a crucial role in initiating blood clotting processes, particularly when there's damage to blood vessels, which exposes the underlying tissue (subendothelial surface). They help in establishing hemostasis by adhering to this damaged area. Various triggers, known as platelet agonists, further stimulate platelet adhesion to the subendothelial surfaces. During this process, platelets change shape, release granule contents, and form aggregates by sticking together, all aimed at minimizing blood loss.[90,91]

While their main function is to regulate hemostasis and thrombosis, platelets also have significant roles in various disease processes. Understanding platelet interactions and their involvement in the progression of cardiovascular diseases (CVD) has been a longstanding challenge.[90,92] Notably, the tendency for platelet hyper-aggregation in diabetic patients with cardiovascular disease presents an area worthy of investigation. In several diseases, platelet hyperactivity can have adverse effects, particularly in conditions like coronary artery disease, where excessive aggregation can impede blood flow.[90]

Thrombocytopenia (low platelet count) and thrombocytosis (high platelet count) can develop in CKD. These variations lead to unusual clotting and bleeding tendencies. Platelet irregularities in CKD patients are associated with disrupted hemostasis, influencing both thrombotic and hemorrhagic risks.[93,94] CKD patients frequently show elevated platelet activation, which makes them more prone to clot formation and raises their risk of cardiovascular events, including heart attacks and strokes. Studies reveal that platelets in CKD patients are more reactive to different agonists, indicating a state of increased blood clotting.[93,95]

NEUTROPHIL- LYMPHOCYTE RATIO (NLR)

The neutrophil-to-lymphocyte ratio (NLR), determined by comparing neutrophil and lymphocyte counts in peripheral blood, serves as a biomarker that encompasses both aspects of the immune system: the innate response, primarily mediated by neutrophils, and the adaptive immunity, supported by lymphocytes. Neutrophils act as the frontline defense against pathogens, employing various mechanisms such as chemotaxis, phagocytosis, and release of reactive oxygen species (ROS), granular proteins, as well as cytokine production. Additionally, neutrophils contribute significantly to the regulation of adaptive immunity and serve as the principal effector cells during the systemic inflammatory response (SIRS).[96]

An increase in neutrophil count, leading to a higher NLR, can occur in various conditions, including bacterial or fungal infections, acute stroke, myocardial infarction, atherosclerosis, severe trauma, cancer, post-surgery complications, and any situation involving tissue damage triggering systemic inflammatory response.[96] SIRS leads to the inhibition of neutrophil apoptosis, enhancing neutrophil-mediated destruction as a component of the

innate response.[97] Consequently, NLR typically exhibits elevated neutrophil levels alongside decreased lymphocyte counts. [96]

Furthermore, NLR has the potential to forecast mortality in the general populace. It showed a significant correlation with increased overall mortality as well as with specific causes of death, including heart disease, chronic lower respiratory diseases, influenza/pneumonia and kidney diseases. Conversely, no notable correlations between NLR and mortality resulting from cancer, cerebrovascular disease, accidents, or diabetes mellitus were observed. [96 98] Additionally, findings from the Rotterdam study revealed that NLR levels were autonomously and significantly linked to a heightened risk of mortality from all causes . [96 99]

Nonmicrobial inflammation contributes to the progression of CKD and fibrosis. Neutrophil count reflects inflammation, while lymphocyte count indicates general stress and nutritional status. The neutrophil-to-lymphocyte ratio (NLR) in CKD patients offers insight into inflammation levels. NLR is proposed as an additional prognostic marker for assessing cardiovascular risk in CKD3-5 patients. Studies have shown that an increase in neutrophil count alongside a decrease in lymphocyte count predicts mortality in hemodialysis and peritoneal dialysis patients. Additionally, NLR indicates the progression rate of stage 4 CKD to dialysis. However, research on NLR's prognostic potential for end-stage renal disease (ESRD), cardiovascular disease (CVD), and all-cause mortality in patients with CKD stages 1–4, apart from stage 5 CKD, is limited. Given that NLR can be easily calculated from complete blood count tests, its predictive capacity should be explored in a large cohort of patients with CKD stages 1–4. [100]

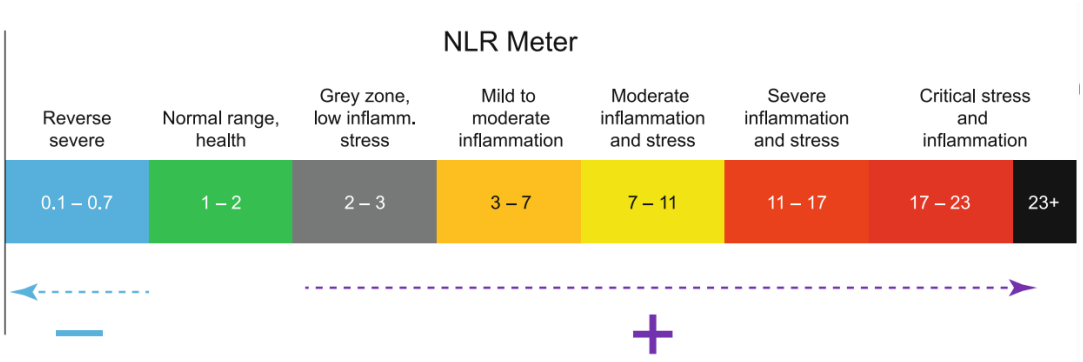

Figure 3. The NLR-meter evaluates immune-inflammatory responses and stress levels. The "grey zone" (NLR 2.3–3.0) suggests mild inflammation, while NLR 3–7 indicates mild-to-moderate inflammation. NLR 7–11 suggests moderate to severe inflammation, and NLR 11–17 indicates severe conditions like sepsis. NLR 17–23 signifies critical immune-inflammatory reactions, while NLR ≥ 23 indicates severe systemic inflammation, seen in conditions like major surgery or terminal cancer. *Image taken from Zahorec R. Neutrophil-to-lymphocyte ratio, past, present and future perspectives. Bratisl Med J. 2021;122(07):474–88.* [101]

MONOCYTE-LYMPHOCYTE RATIO (MLR) OR LYMPHOCYTE-MONOCYTE RATIO(LMR)

The monocyte-to-lymphocyte ratio (MLR) represents the ratio of absolute monocyte count to absolute lymphocyte count and has been identified as a new hematological and inflammatory indicator. [102]

The monocyte–lymphocyte ratio (MLR) [or lymphocyte-monocyte ratio (LMR)] serves as a straightforward, cost-effective, and reproducible measure reflecting the levels of monocytes and lymphocytes in peripheral blood. Monocytosis, indicating an elevated monocyte count, holds clinical significance across various conditions such as acute and chronic infections, tumors, auto-inflammatory disorders, iatrogenesis, and non-specific stress [102,103]. Conversely, lymphopenia, denoting a decreased lymphocyte count, is associated with conditions like severe combined immunodeficiency [102,104], autoimmune disorders (e.g., systemic lupus erythematosus), type 2 diabetes mellitus [102], end-stage renal disease [102,105], tumors, iatrogenesis, and viral or bacterial infections. Given that inflammation is a common factor influencing both peripheral monocytes and lymphocytes,

an elevated MLR (reduced LMR), resulting from increased monocyte and/or decreased lymphocyte counts, is frequently utilized as an inflammatory marker in various clinical scenarios. Notably, elevated MLR (reduced LMR) , has been observed in conditions such as non-affective psychosis, coronary artery disease (CAD), preeclampsia, and stroke-associated pneumonia, among others. Furthermore, MLR (LMR) has shown prognostic value in tuberculosis and cancer.[102]

Inflammation typically leads to a decrease in lymphocyte count, which has been linked to increased cardiovascular risk and mortality. Low lymphocyte levels, along with high monocyte counts, have been associated with unfavorable cardiovascular outcomes in individuals with coronary artery disease. The combination of high monocyte and low lymphocyte counts is considered a marker of inflammation, with the MLR (LMR) potentially serving as a more effective predictor of vascular risk in atherosclerosis patients. MLR (LMR) has also been proposed as a prognostic indicator for assessing the severity of coronary artery blockage prior to intervention. [106]

Chronic low-grade inflammation, characterized by increased levels of proinflammatory substances in the bloodstream, plays a significant role in causing vascular problems and elevating CVD risk in both the general population and individuals with CKD. [107,108] Since monocyte count correlates with levels of these proinflammatory substances [107,109], it can be considered a proxy marker for inflammation, contributing to the heightened CVD risk. Moreover, the MLR (LMR) has emerged as a valuable indicator for predicting CVD risk. While monocytes participate in the inflammatory response, lymphocytes, including T cells, B cells, and natural killer cells, regulate the immune system. Therefore, an elevated MLR (reduced LMR) may suggest increased inflammation and compromised immune function.[107]

Increasing evidence suggests that the uremic milieu in individuals with CKD promotes vascular inflammation by stimulating monocytes to adopt a proinflammatory phenotype. This indicates that CKD-related factors contribute to an inflammatory state in monocytes, potentially exacerbating vascular complications [107,110,111]. Monocytes from CKD patients show heightened responsiveness to inflammatory signals, such as increased expression of TNF receptor. They also exhibit increased adhesion and potential migration to the vascular endothelium, as evidenced by elevated expression of CD11b. Furthermore, these monocytes are prone to releasing proinflammatory cytokines like TNF-a, IL-1b, and IL-6. [107]

PLATELET LYMPHOCYTE RATIO (PLR)

The Platelet-Lymphocyte Ratio (PLR) is determined by dividing the platelet count by the lymphocyte count, both extracted from the same blood sample. Platelets discharge proinflammatory agents like chemokines and cytokines. When activated, platelets encourage the formation of blood clots in reaction to the rupture of atherosclerotic plaques or the erosion of endothelial cells, fostering atherothrombotic conditions. [112]

The PLR serves as a new marker for systemic inflammation. Elevated platelet count typically indicates heightened platelet activity, leading to increased thrombosis and the release of various mediators fostering inflammation and atherosclerosis. This heightened platelet activity correlates with more severe inflammation. Research suggests that a higher PLR, even without absolute thrombocytosis, is linked to increased thrombosis and inflammation, likely due to increased platelet activity. Furthermore, a lower lymphocyte count relative to a high PLR may signal the impact of elevated endogenous cortisol levels resulting from inflammation. [113]

MCV, MCH AND MCHC

Wintrobe introduced mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) in 1929 to characterize the size (MCV) and hemoglobin content (MCH, MCHC) of red blood cells. These parameters, collectively known as red cell indices, are valuable for diagnosing various types of anemias. Nowadays, electronic cell counters routinely measure red cell indices alongside other blood count parameters. [114]

MCV measures the size of red blood cells and is typically expressed in femtoliters (fl) or cubic microns (μm3) and its normal range is around 80 -95 fl. MCH evaluates the hemoglobin content per individual red blood cell its normal value falls within 27- 31 picograms (pg) per cell. MCHC reflects the concentration of hemoglobin within red blood cells in relation to their volume. Unlike MCH, MCHC considers hemoglobin content relative to cell volume. It is commonly expressed as grams per deciliter (g/dl) or as a percentage with normal range about 32 - 36 g/dl. [114]

MCV, which measures the average size of red blood cells, has been linked to mortality across various clinical contexts. Elevated MCV levels, typically exceeding 100 (fL), often indicate underlying conditions such as nutritional deficiencies, substance abuse[115,116], vitamin B12 deficiency, certain medications, or bone marrow disorders. In patients with stage 3 or higher of CKD, elevated MCV has been associated with increased risks of all-cause mortality, cardiovascular disease mortality, and mortality related to infections. Some researchers have found MCV to predict composite cardiovascular events in CKD patients.[115] Additionally, a study involving over 100,000 incident hemodialysis patients found that those with higher MCV levels (>98 fL) faced elevated risks of all-cause mortality, cardiovascular mortality, and mortality associated with infections.[115,117]

RED CELL DISTRIBUTION WIDTH (RDW)

Convenient and reasonably priced, the red blood cell distribution width (RDW) is a biochemical metric that represents the diversity in size of circulating erythrocytes and may be acquired from a standard complete blood count (CBC). Many hematological system disorders, such as iron-deficiency anemia and bone marrow dysfunction, have been identified over the past few decades using RDW with mean corpuscular volume (MCV).[118] RDW-CV, which is based on the mean red cell volume and the coefficient of variation of the red blood cell distribution volume, is the most popular method of reporting RDW. The red blood cell distribution curve width, or RDW-SD, is a measurement that is independent of the mean red cell volume and can be expressed as RDW. Typically, labs include RDW-CV in full blood count (FBC) results as part of the red blood cell indices. [119]

Most laboratories employed an RDW with a typical reference range of 11–15%.[118]

Inflammatory cytokines can prevent erythropoietin-induced erythrocytes from maturing by suppressing the bone marrow, which is partially reflected in an increase in RDW. By reducing the lifespan of red blood cells and disrupting iron metabolism, inflammation and oxidative stress in MI can raise RDW levels and alter the bone marrow's reaction to erythropoietin. [118]

Yoon et al.'s study [118,120] showed that a steady increase in RDW can independently predict death and cardiovascular events in patients with ESRD. A research has also established a link between low glomerular filtration rate, microalbuminuria, and elevated RDW levels.[118,121]

MEAN PLATELET VOLUME (MPV)

The mean platelet volume (MPV) is an accurate assessment of platelet size, determined by hematological analyzers through volume distribution in standard blood morphology tests. Typically, MPV falls within the range of 7.5 to 12.0 fl, with large platelets constituting approximately 0.2% to 5.0% of the total platelet count.[122] Under normal physiological circumstances, mean platelet volume (MPV) tends to decrease as platelet count increases. This relationship is linked to the regulation of hemostasis and the consistent maintenance of platelet mass.[122,123]

In healthy individuals, increased platelet count suppresses Tpo synthesis, prompting platelet release by megakaryocytes to maintain constant platelet mass. However, inflammation, driven by IL-6, can trigger platelet release by stimulating thrombopoietin production and affecting megakaryocytes. This results in increased platelet production and a higher percentage of large platelets. Concurrently, during inflammation, platelets migrate to inflamed sites, undergo activation, and eventually wear out, leading to a drop in MPV.[122]

Mean platelet volume (MPV), a readily accessible indicator of platelet activity, is linked to numerous prothrombotic and proinflammatory illnesses. Elevated MPV levels are associated with various established risk factors for cardiovascular and cerebrovascular disorders, as well as low-grade inflammatory conditions that predispose individuals to arterial and venous thromboses. Conversely, high-grade inflammatory diseases like active rheumatoid arthritis or familial Mediterranean fever often exhibit reduced MPV levels, which can be reversed with anti-inflammatory treatment.[124]

RETICULOCYTE COUNT

Reticulocytes, originating from erythroblasts, are immature red blood cells that travel through the bloodstream for about 1 to 4 days before maturing into erythrocytes. They offer a real-time assessment of erythropoiesis function, making them valuable for diagnosing anemias and monitoring how the bone marrow responds to treatment. [125]

Reticulocytes serve as a valuable clinical marker for anemias and the bone marrow's reaction to anemic conditions. In a healthy individual, the normal range for reticulocyte count is typically 0.5 to 2.5%. If a patient experiences anemia and the bone marrow fails to respond adequately, the reticulocyte count will decrease. Conversely, when the bone marrow is able to respond effectively, the reticulocyte count will rise.[126]

METHODOLOGY

Source of Data: Blood samples and clinical history of non-dialysis CKD patients visiting Nephrology OPD (Outpatient department) at KLE's Dr. Prabhakar Kore Hospital and MRC, Belagavi.

Study Design: A cross-sectional study

Study Period: January 1st, 2023 to December 31st ,2023.

Sample Size: 140

Inclusion criteria:

Adult patients diagnosed with CKD.

Exclusion criteria:

1. Patients who are unwilling to participate.

2. Patients on dialysis, liver failure, chronic consuming diseases (e.g., cancer, severe heart failure, and acquired immunodeficiency syndrome), and/or infectious diseases are all excluded from the study.

3. Patients with a history of hospitalization and surgeries in the three months prior to the start of data collection.

4. Patients with only one kidney.

5. History of kidney transplantation.

6. Pregnant Women.

Data collection procedure:

Blood samples were obtained from non-dialysis CKD patients via phlebotomy, adhering to strict aseptic protocols. A 3 mL venous blood sample was collected in both EDTA and plain tubes. These samples were analysed for hemogram, serum creatinine, serum urea, and hs-CRP levels.

Relevant clinical history was collected from patients and from OPD records

Automated hematology analyzer - The Sysmex XN-1500 automated hematology analyzer employs Fluorescence Flow Cytometry alongside a hydrodynamically focused impedance method. This hydrodynamic focusing technique enhances the precision and consistency of blood counts. By ensuring blood cells pass through the aperture in a single file, it also reduces the likelihood of generating abnormal blood cell pulses.

The machine performs a variety of tests, including RBC(Red blood cell) count, Hb (hemoglobin), HCT (Hematocrit), MCV (Mean corpuscular volume), MCH (Mean corpuscular hemoglobin), MCHC (Mean corpuscular hemoglobin concentration), RDW (Red cell distribution width), Reticulocyte count, WBC (White blood cell) count, ANC(Absolute neutrophil count), ALC (Absolute lymphocyte count), AMC (Absolute monocyte count), AEC (Absolute eosinophil count) , Platelet count, and MPV (Mean platelet volume).

SYSMEX XN1500

Serum creatinine was tested using COBAS C 503 analyzer

This colorimetric assay, based on the Jaffé method, detects creatinine levels by forming a yellow-orange complex with picrate in an alkaline solution. Interference from bilirubin is minimized using rate-blanking. Results for serum or plasma are adjusted downward by -26 µmol/L (-0.3 mg/dL) to correct for non-specific reactions caused by various pseudo-creatinine chromogens.

Normal range:

Females: 0.51‑0.95 mg/dL

Males: 0.67‑1.17 mg/dL

Serum urea tested using COBAS C 503 analyser

A kinetic assay utilizing urease and glutamate dehydrogenase (GLDH) was conducted. Initially, urea is broken down by urease into ammonium and carbonate. Subsequently, ammonium reacts with 2-oxoglutarate in the presence of GLDH and NADH coenzyme to produce L-glutamate. Each mole of urea hydrolyzed results in the oxidation of two moles of NADH to NAD+. The rate of NADH concentration decline is directly proportional to the urea concentration in the sample and is assessed photometrically.

Normal range:

Adults (18‑60 years): 12.6‑42.6 mg/dL

Adults (60‑90 years): 17.4‑49.2 mg/dL

COBAS C 503

Hs-CRP measured using Erba EM 200

The hs-CRP assay is based on a latex enhanced immunoturbidimetric assay. When an antigen-antibody reaction occurs between CRP in a sample and anti-CRP which has been sensitized to latex particles, agglutination results. This agglutination is detected as an absorbance change (546 nm) with the magnitude of the change being proportional to the quantity of CRP in the sample. The actual concentration is then determined by the interpolation from a calibration curve prepared from calibrators of known concentration.

Expected values: <6 mg/L

ERBA EM 200

Calculation of eGFR

Estimated glomerular filtration rate (eGFR) was calculated using CKD-EPI Creatinine equation (2021) formula, which is the preferred method for calculating eGFR for adults. Developed in 2021 the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) and recommended by the National Kidney Foundation and American Society of Nephrology Task Force. It estimates GFR from serum creatinine, age and sex. The eGFR was calculated from the mobile application named **"eGFR Calculators"** developed by National Kidney Foundation.

Equation used by **"eGFR Calculators"**:

$eGFR_{cr} = 142 \times \min (S_{cr}/\kappa, 1)^{\alpha} \times \max (S_{cr}/\kappa, 1)^{-1.200} \times 0.9938^{Age} \times 1.012$ [if female]

where: S_{cr} = standardized serum creatinine in mg/dL

$\kappa = 0.7$ (females) or 0.9 (males)

$\alpha = -0.241$ (female) or -0.302 (male)

$\min (S_{cr}/\kappa, 1)$ is the minimum of S_{cr}/κ or 1.0

$\max (S_{cr}/\kappa, 1)$ is the maximum of S_{cr}/κ or 1.0

Age (years)

Inflammatory marker ratios were calculated as follows:

NLR (Neutrophil to Lymphocyte Ratio): Absolute neutrophil count / Absolute lymphocyte count

PLR (Platelet to Lymphocyte Ratio): Platelet count / Absolute lymphocyte count

LMR (Lymphocyte to Monocyte Ratio): Absolute lymphocyte count / Absolute monocyte count

Data processing and analysis/statistical analysis:

The data entry for the values was done in the Microsoft excel spreadsheet and the results were obtained with Kruskal-Wallis test, Oneway ANOVA test, Mann-Whitney U test and Spearman correlation for different parameters. The statistical analyses were done using Stata software (version 17).

For statistical significance, p value of less than 0.05 was considered statistically significant.

RESULTS

Table 2. Age distribution among the study participants (N=140)

Age groups (in years)	Frequency	Percentage (%)
21-40	24	17.2
41-60	58	41.4
61-80	58	41.4
Total	**140**	**100**

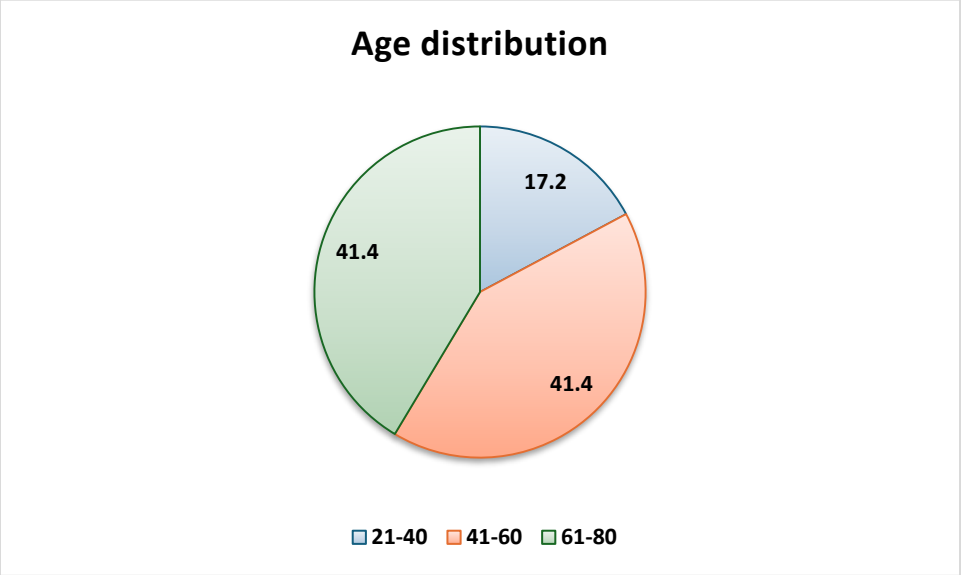

Figure 4. Age distribution among the study participants

Table 2 and Figure 4. depicts age distribution among the study participants. Of total, 41.4% (n=58) belonged to age group 41-60 years and 61-80 years. 17.2% (n=24) belonged to 21-40 years of age.

Table 3. Gender distribution among the study participants (N=140)

Gender	Frequency	Percentage (%)
Male	94	67.1
Female	46	32.9
Total	**140**	**100**

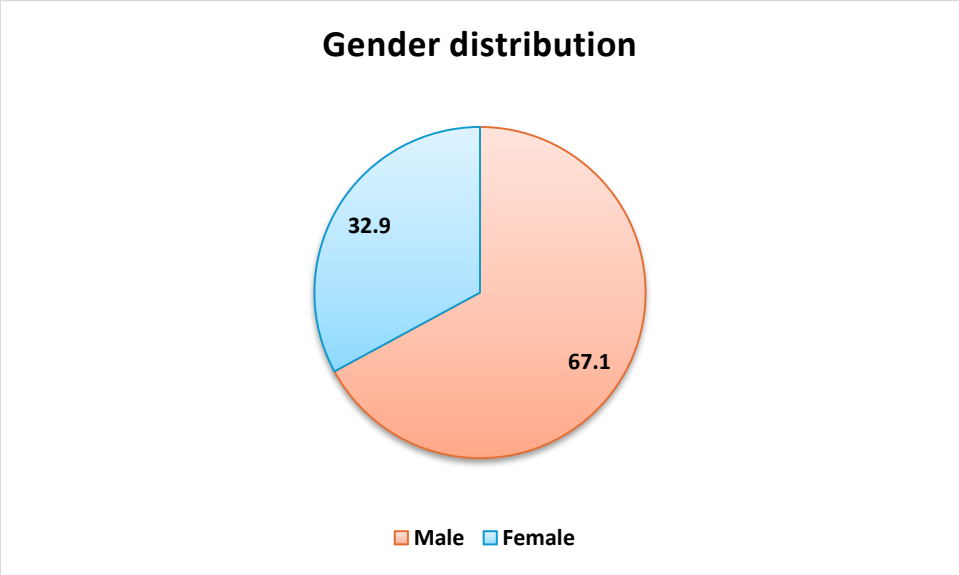

Figure 5. Gender distribution among the study participants

Table 3 and Figure 5 depicts gender distribution among the study participants. Of total, 67.1% (n=94) were males and 32.9% (n=46) were females.

Table 4. Hypertension distribution among the study participants (N=140)

Hypertension	Frequency	Percentage (%)
Yes	106	75.7
No	34	24.3
Total	**140**	**100**

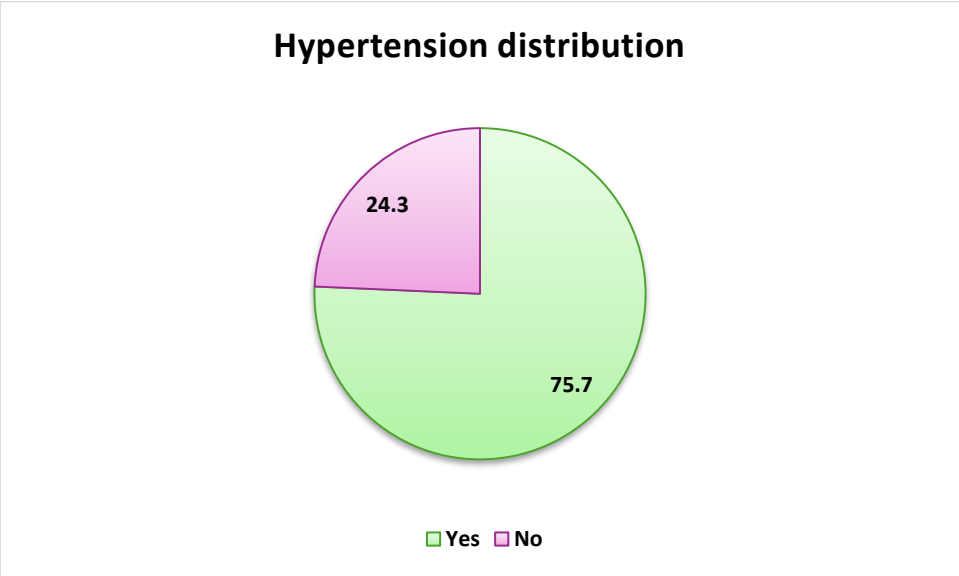

Figure 6. Hypertension distribution among the study participants

Table 4 and Figure 6 shows hypertension distribution among the study participants. of total, 75.7% (n=106) were hypertensive and 24.3% (n=34) were non-hypertensive.

Table 5. Diabetes Mellitus distribution among the study participants (N=140)

Diabetes Mellitus	Frequency	Percentage (%)
Yes	75	53.6
No	65	46.4
Total	**140**	**100**

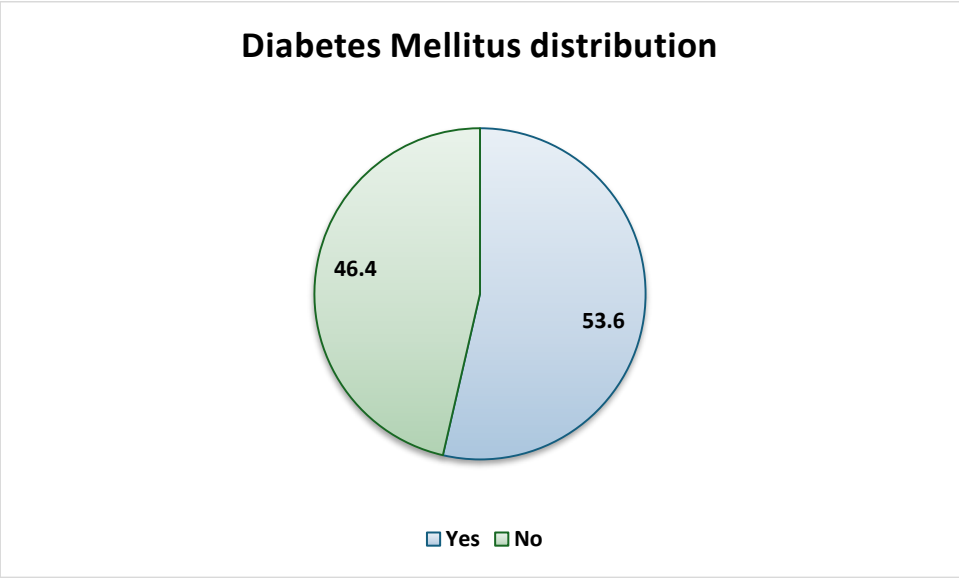

Figure 7. Diabetes Mellitus distribution among the study participants

Table 5 and Figure 7 shows diabetes mellitus distribution among the study participants. of total, 53.6% (n=75) had diabetes mellitus and 46.4% (n=65) did not have diabetes mellitus.

Table 6. Grades of CKD distribution among the study participants (N=140)

Grades of CKD	Frequency	Percentage (%)
G2	7	5.0
G3	36	25.7
G4	20	14.3
G5	77	55.0
Total	**140**	**100**

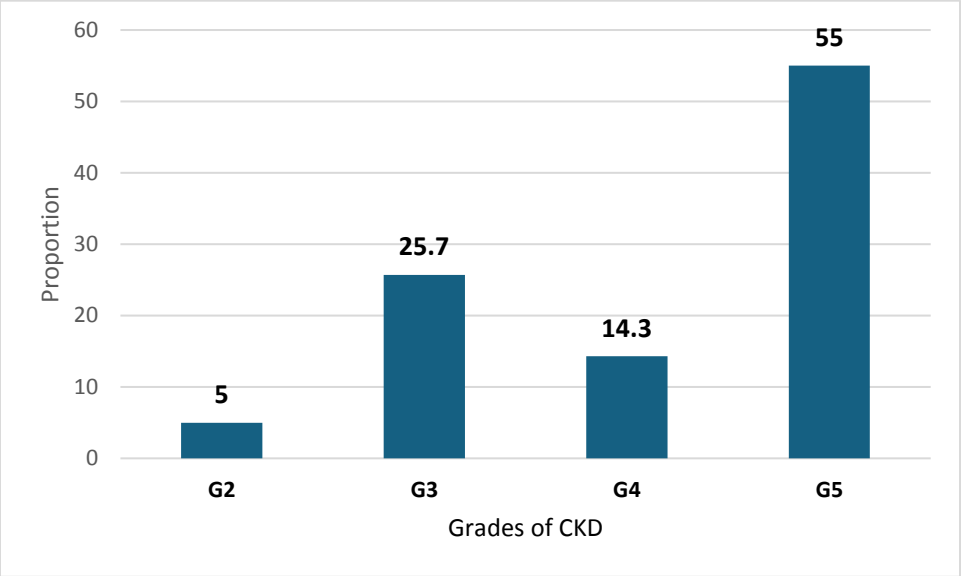

Figure 8. Grades of CKD distribution among the study participants

Grades of CKD distribution among the study participants is described in Table 6 and Figure 8. Among all, 55% (n=77) belonged to grade 5, 25.7% (n=36) belonged to grade 3, 14.3% (n=20) were grade 4 and 5% (n=7) were grade 2 of CKD.

Table 7. Clincal profile of the study participants (N=140)

Variables	Mean/ Median	SD/ IQR
S. UREA (mg/dL)	81.4	31.3
S. CREATININE (mg/dL)	3.9	1.8
EGFR (ml/min/1.73m^2)	14	11-36
HB (g/dL)	9.9	2.2
HCT %	32.2	6.8
MCV (fL)	88.4	9.9
MCH (pg)	27.8	2.8
MCHC (g/dL)	31.6	4.6
RDW %	15.2	2.2
RBC COUNT x 10^6/uL	3.5	0.8
RETIC %	1.2	0.8
WBC COUNT x 10^3/uL	8.6	3.6
PLATELET x10^3/uL	231.1	90.5
MPV (fL)	9.5	8.7-10.4
ANC x 10^3/uL	6.1	3.0
ALCx 10^3/uL	1.7	0.8
AMCx 10^3/uL	0.6	0.2
AECx 10^3/uL	0.3	0.1

Clinical profile of the study participants is described in Table 7. The mean (SD) serum urea, serum creatinine and haemoglobin were 81.4 (31.3) mg/dL, 3.9 (1.8) mg/dL and 9.2 (2.2) g/dL respectively. The median (IQR) EGFR was 14 (11-36) ml/min/1.73m^2. The mean (SD) level of HCT%, MCV, MCH, MCHC, RDW%, RBC count, and retic % were 32.2 (6.8) %, 88.4 (9.9) fL, 27.8 (2.8) pg, 31.6 (4.6) g/dl, 15.2 (2.2) %, 3.5 (0.8) x 10^6/uL, and 1.2 (0.8) % respectively. The mean (SD) ANC, ALC, AMC and AEC were 6.1 (3.0) x 10^3/uL, 1.7 (0.8) x 10^3/uL, 0.6 (0.2) x 10^3/uL and 0.3 (0.1) x 10^3/uL respectively.

Table 8. Distribution of inflammatory biomarkers among the study participants (N=140)

Variables	Median	IQR
NLR	3.8	2.5-5.5
PLR	146.6	108.9-200.8
LMR	2.8	1.8-4
hs- CRP (mg/L)	7.9	4.9-11.9

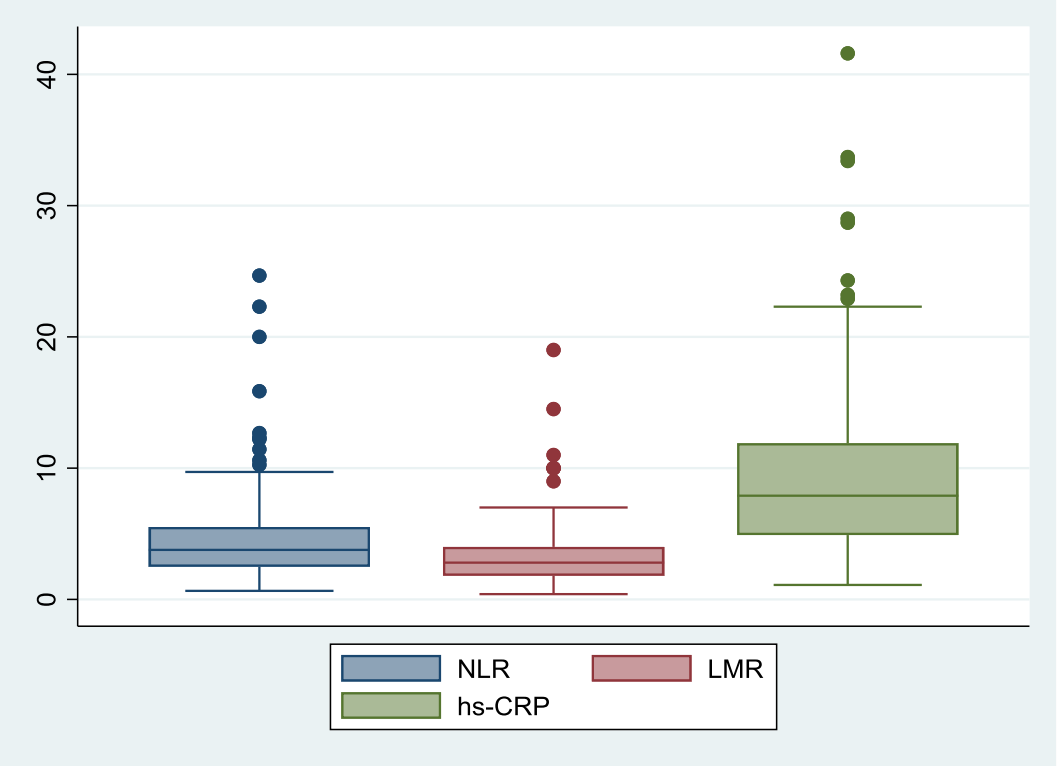

Figure 9. Box plot depicting NLR, LMP and hs-CRP levels among the study participants

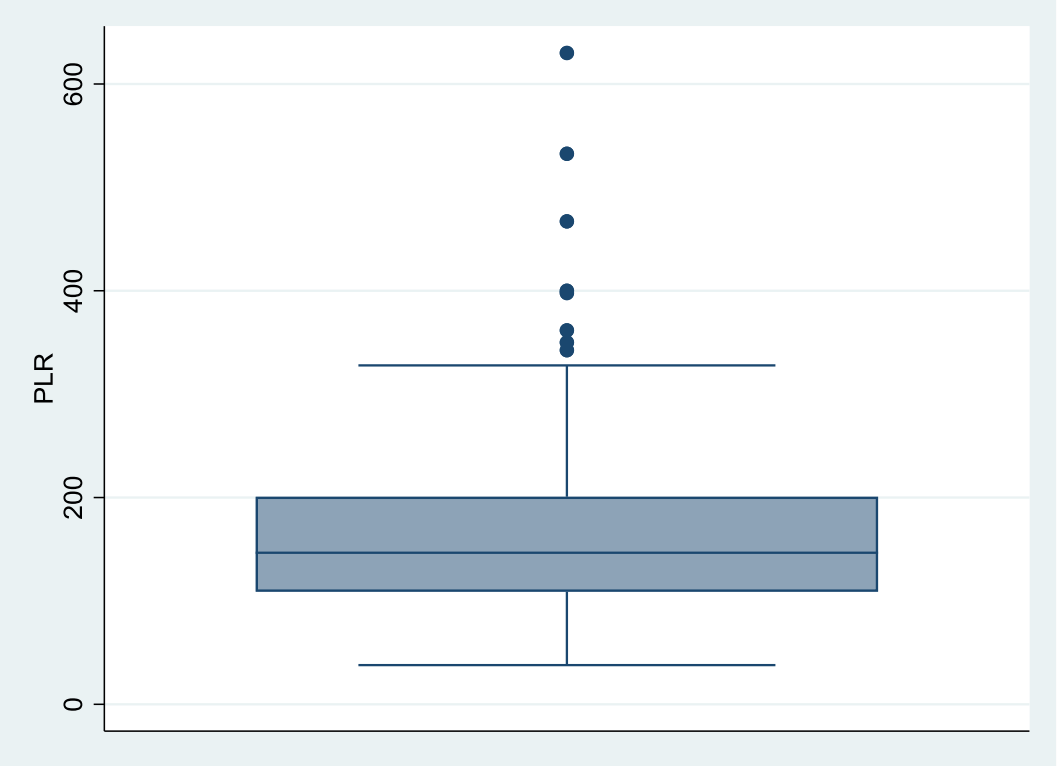

Figure 10. Box plot depicting PLR level among the study participants

Distribution of inflammatory biomarkers among the study participants is depicted in Table 8 and Figure (9,10). The median (IQR) levels of NLR, PLR, LMR and hs-CRP were 3.8 (2.5-5.5), 146.6 (108.9-200.8), 2.8 (1.8-4) and 7.9 mg/L (4.9-11.9) respectively.

Table 9. Comparison of NLR across the grades of CKD among the study participants (N=140)

Grades of CKD	NLR		P value*
	Median	IQR	
G2	2.2	1.7-2.5	<0.001
G3	3.0	2.2-3.8	
G4	4.1	2.5-5.5	
G5	4.4	3.3-5.7	

*Kruskal-Wallis test

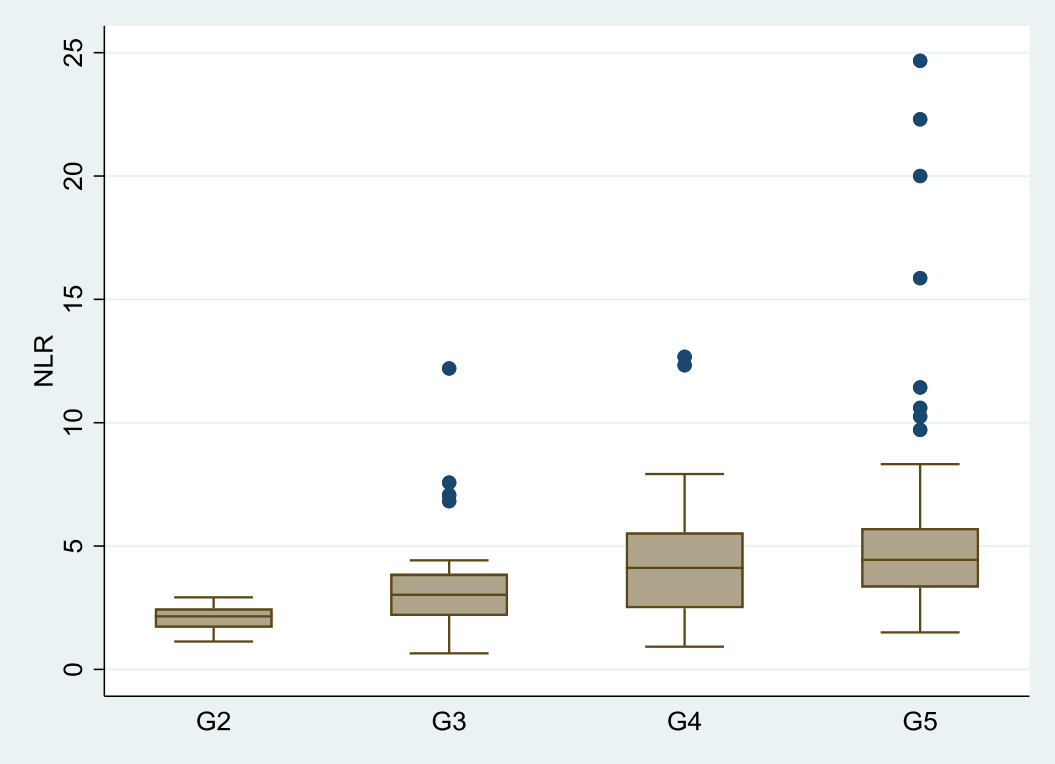

Figure 11. Box plot depicting comparison of NLR across the grades of CKD among the study participants

Table 9 and Figure 11 shows comparison of NLR across the grades of CKD among the study participants. The median level of NLR significantly increased as the grades of CKD progressed (p<0.001). The median (IQR) of NLR among grade 2 patients was 2.2 (1.7-2.5), grade 3 was 3.0 (2.2-3.8), grade 4 was 4.1 (2.5-5.5) and grade 5 was 4.4 (3.3-5.7).

Table 10. Comparison of PLR across the grades of CKD among the study participants (N=140)

Grades of CKD	PLR		P value*
	Median	IQR	
G2	108.8	93.2-132.2	0.07
G3	132.9	105.6-184.4	
G4	141.5	96.1-179.2	
G5	161.1	113.7-209.1	

*Kruskal-Wallis test

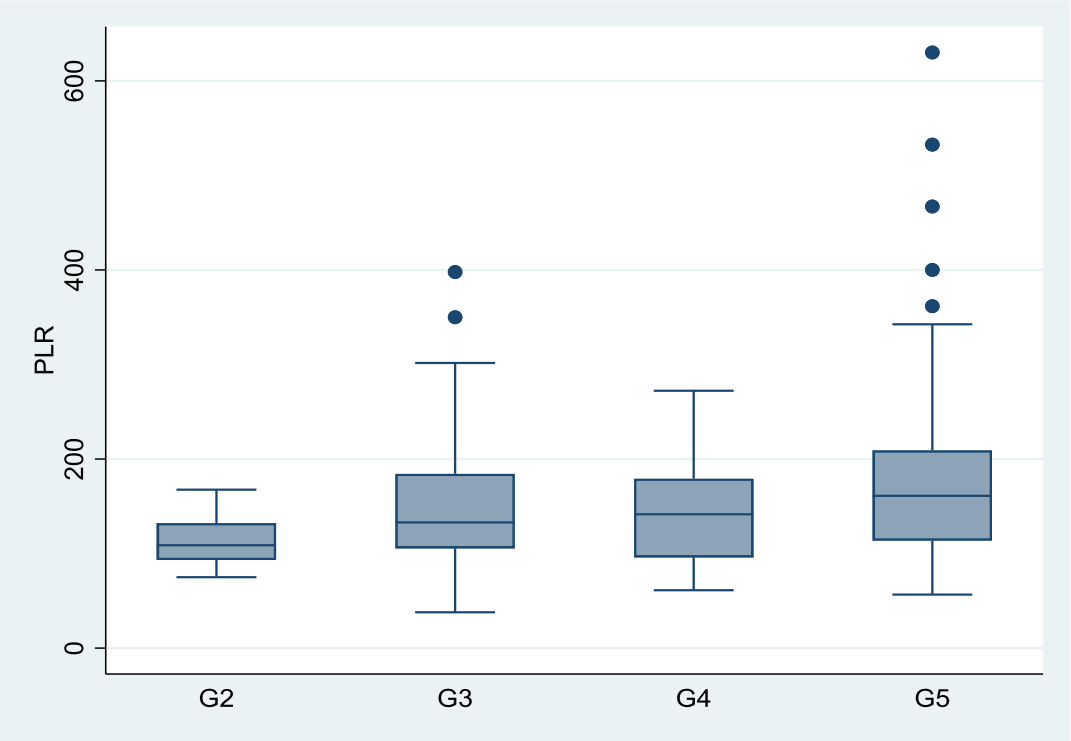

Figure 12. Box plot depicting comparison of PLR across the grades of CKD among the study participants

Table 10 and Figure 12 shows comparison of PLR across the grades of CKD among the study participants. The median level of PLR increased as the grades of CKD progressed but it was not statistically significant (p=0.07). The median (IQR) of PLR among grade 2 patients was 108.8 (93.2-132.2), grade 3 was 132.9 (105.6-184.4), grade 4 was 141.5 (96.1-179.2) and grade 5 was 161.1 (113.7-209.1).

Table 11. Comparison of LMR across the grades of CKD among the study participants (N=140)

Grades of CKD	LMR		P value*
	Median	IQR	
G2	4.5	3.4-5.8	0.005
G3	3.1	2.3-4.8	
G4	2.6	1.9-3.8	
G5	2.6	1.6-3.5	

*Kruskal-Wallis test

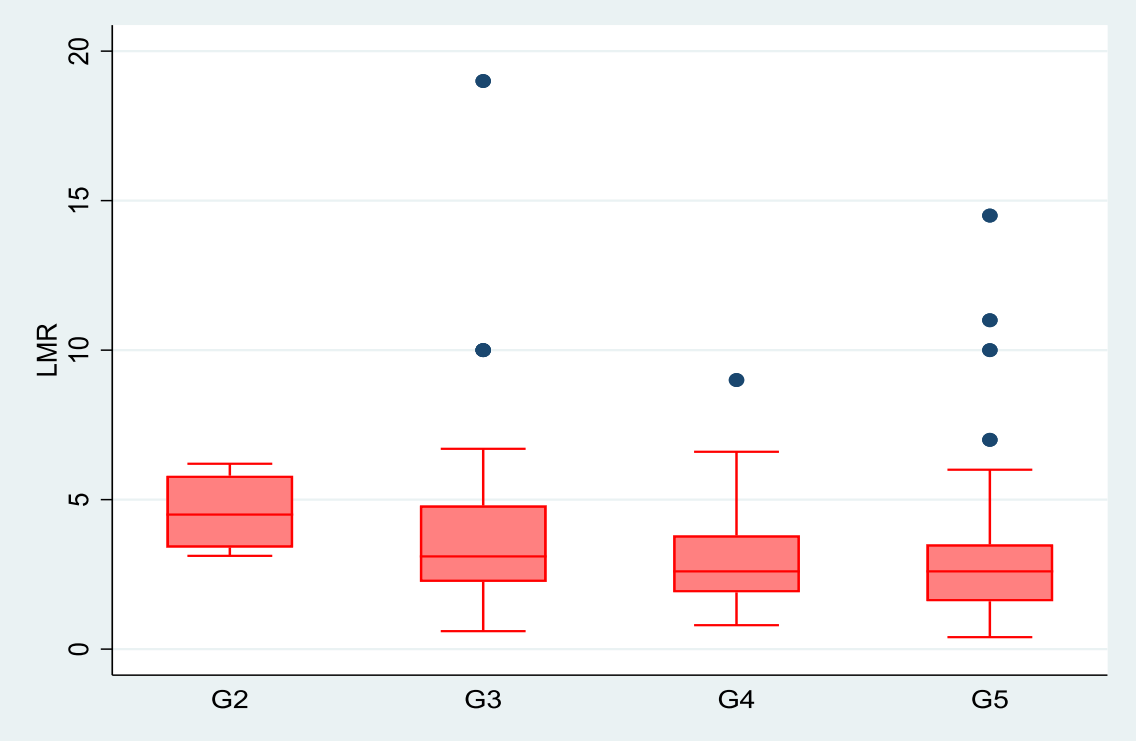

Figure 13. Box plot depicting comparison of LMR across the grades of CKD among the study participants

Table 11 and Figure 13 shows comparison of LMR across the grades of CKD among the study participants. The median level of LMR significantly decreased as the grades of CKD progressed (p=0.005). The median (IQR) of LMR among grade 2 patients was 4.5 (3.4-5.8), grade 3 was 3.1 (2.3-4.8), grade 4 was 2.6 (1.9-3.8) and grade 5 was 2.6 (1.6-3.5).

Table 12. Comparison of hs- CRP across the grades of CKD among the study participants (N=140)

Grades of CKD	hs- CRP (mg/L)		P value*
	Median	IQR	
G2	2.8	1.7-3.4	<0.001
G3	5.2	3.2-8.1	
G4	8.9	5.1-11.2	
G5	9.9	6.9-15.1	

*Kruskal-Wallis test

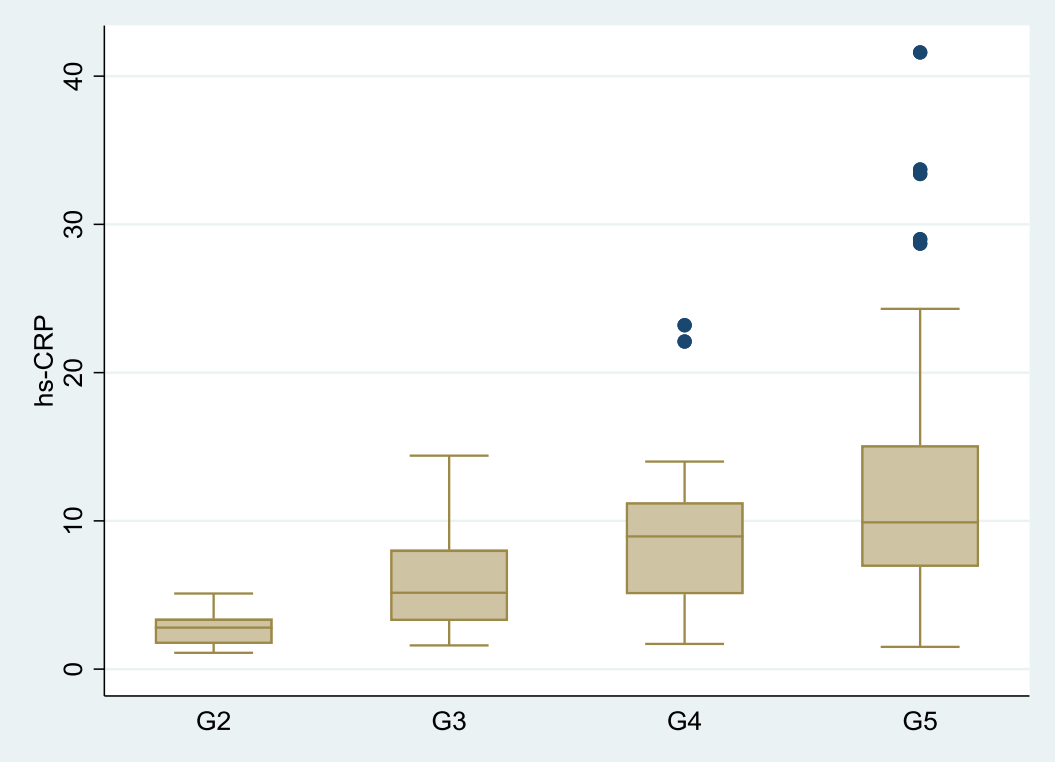

Figure 14. Box plot depicting comparison of hs-CRP across the grades of CKD among the study participants

Table 12 and Figure 14 shows comparison of hs-CRP across the grades of CKD among the study participants. The median level of hs-CRP significantly increased as the grades of CKD progressed ($p<0.001$). The median (IQR) of hs-CRP among grade 2 patients was 2.8 (1.7-3.4), grade 3 was 5.2 (3.2-8.1), grade 4 was 8.9 (5.1-11.2) and grade 5 was 9.9 (6.9-15.1).

Table 13. Comparison of ALC across the grades of CKD among the study participants (N=140)

Grades of CKD	ALCx 10^3/uL		P value*
	Mean	SD	
G2	2.8	0.8	<0.001
G3	2.1	0.9	
G4	1.7	0.8	
G5	1.4	0.7	

Oneway ANOVA test

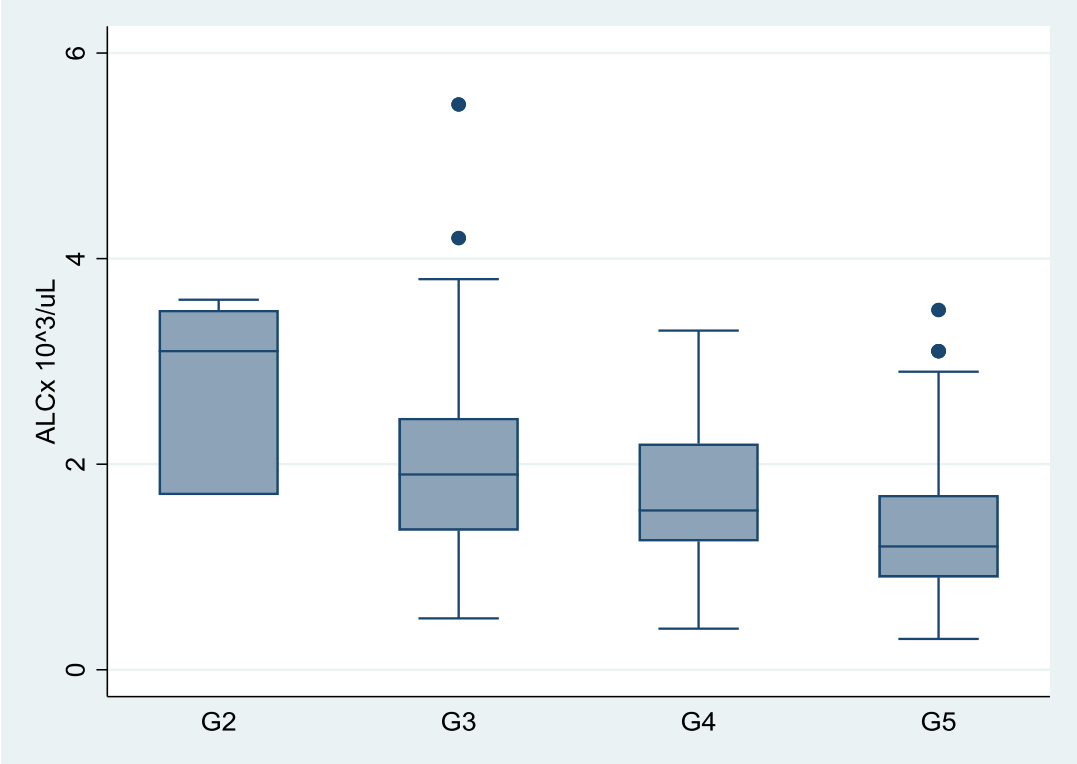

Figure 15. Box plot depicting comparison of ALC across the grades of CKD among the study participants

Table 13 and Figure 15 shows comparison of ALC across the grades of CKD among the study participants. The mean level of ALC significantly decreased as the grades of CKD progressed (p<0.001). The mean (SD) of ALC among grade 2 patients was 2.8 (0.8), grade 3 was 2.1 (0.9), grade 4 was 1.7 (0.8) and grade 5 was 1.4 (0.7) x 10^3/uL.

Table 14. Comparison of platelets across the grades of CKD among the study participants (N=140)

Grades of CKD	PLATELET x10^3/uL		P value*
	Mean	SD	
G2	298.6	61.5	<0.001
G3	272.4	98.8	
G4	218.4	72.2	
G5	209.0	84.4	

Oneway ANOVA test

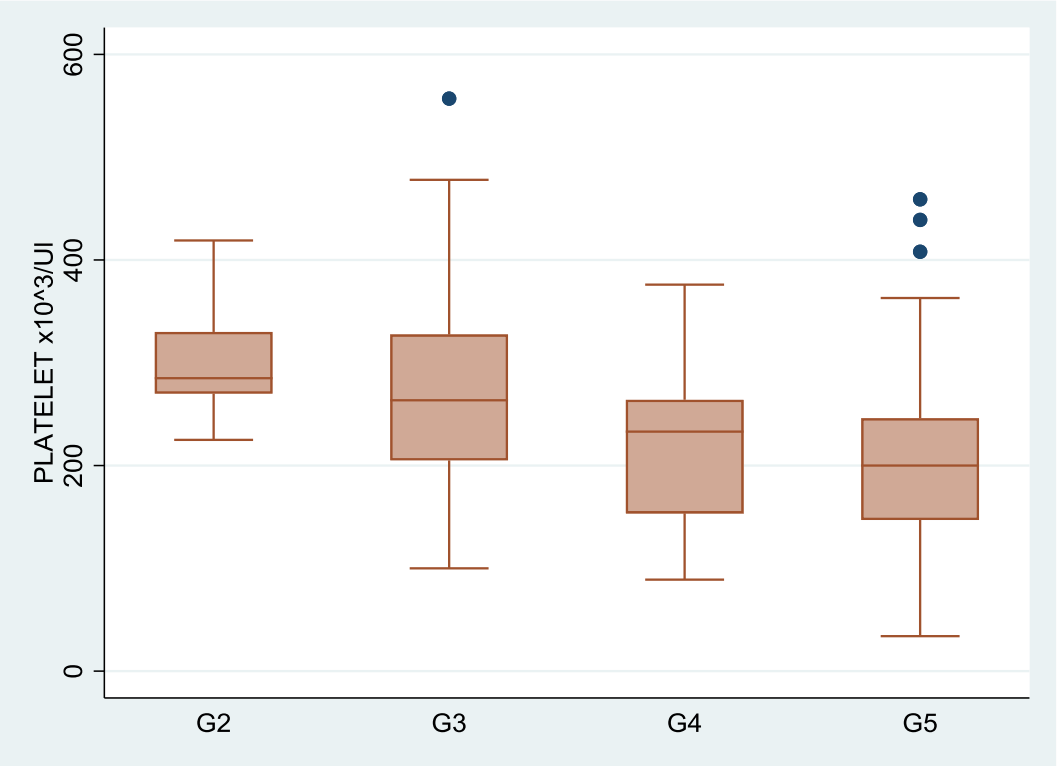

Figure 16. Box plot depicting comparison of platelet across the grades of CKD among the study participants

Table 14 and Figure 16 shows comparison of platelets across the grades of CKD among the study participants. The mean level of platelets significantly decreased as the grades of CKD progressed (p<0.001). The mean (SD) of platelets among grade 2 patients was 298.6 (61.5), grade 3 was 272.4 (98.8), grade 4 was 218.4 (72.2) and grade 5 was 209.0 (84.4) x 10^3/uL.

Table 15. Comparison of RDW across the grades of CKD among the study participants (N=140)

Grades of CKD	RDW %		P value*
	Mean	SD	
G2	13.9	0.9	0.04
G3	14.6	1.5	
G4	15.1	2.4	
G5	15.6	2.4	

Oneway ANOVA test

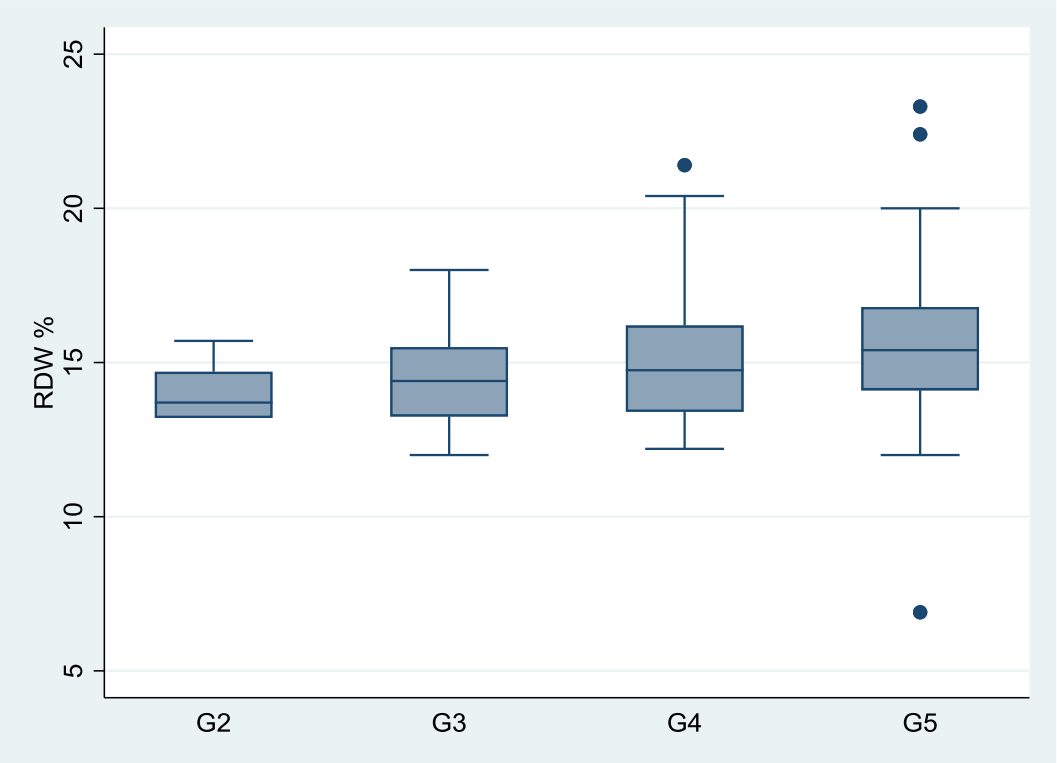

Figure 17. Box plot depicting comparison of RDW % across the grades of CKD among the study participants

Table 15 and Figure 17 shows comparison of RDW across the grades of CKD among the study participants. The mean level of RDW significantly increased as the grades of CKD progressed (p=0.04). The mean (SD) of RDW among grade 2 patients was 13.9 (0.9), grade 3 was 14.6 (1.5), grade 4 was 15.1 (2.4) and grade 5 was 15.6 (2.4) %.

Table 16. Correlation between hs-CRP and NLR among the study participants

		NLR
hs- CRP	Spearman Correlation	0.72
	P value	<0.001
	N	140
Correlation is highly significant (p value = <0.001)		

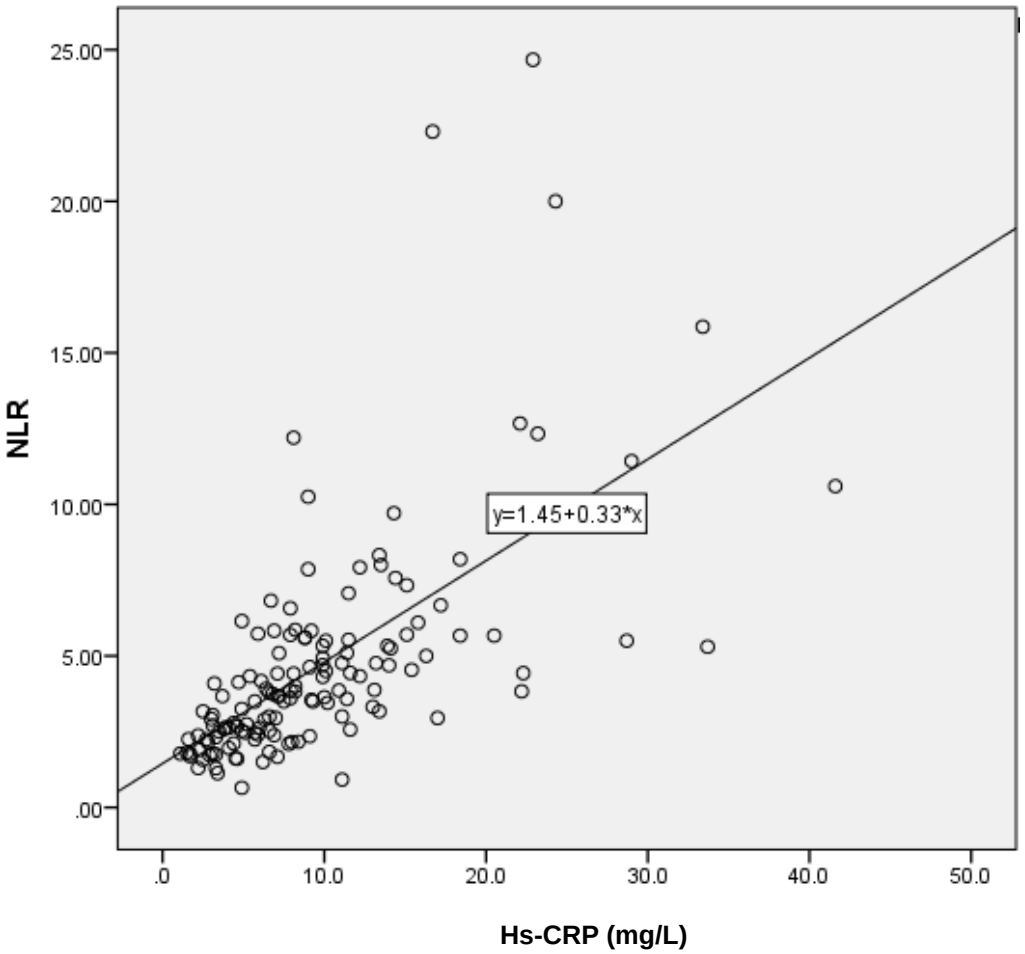

Figure 18. Scatter diagram showing correlation between hs- CRP and NLR among the study participants

Correlation between hs-CRP and NLR among the study participants is described in Table 16 and Figure 18. Spearman correlation coefficient is 0.72 (strong correlation) and it is statistically significant (p<0.001).

Table 17. Correlation between hs- CRP and PLR among the study participants

		PLR
hs- CRP	Spearman Correlation	0.35
	P value	<0.001
	N	140
Correlation is highly significant (p value = <0.001)		

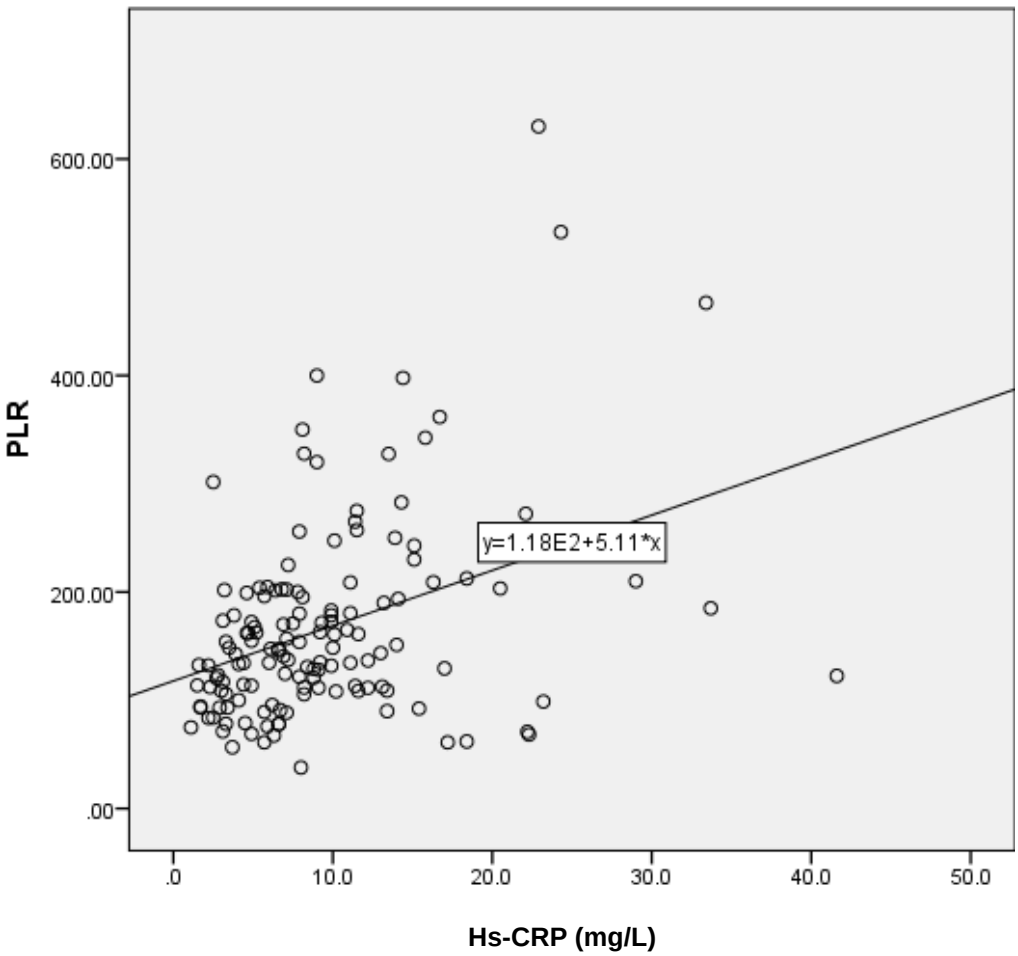

Figure 19. Scatter diagram showing correlation between hs- CRP and PLR among the study participants

Correlation between hs-CRP and PLR among the study participants is described in table 17 and shown in Figure 19. Spearman correlation coefficient is 0.35 (weak correlation) and it is statistically significant (p<0.001).

Table 18. Correlation between hs- CRP and LMR among the study participants

		LMR
hs- CRP	Spearman Correlation	-0.51
	P value	<0.001
	N	140
Correlation is highly significant (p value = <0.001)		

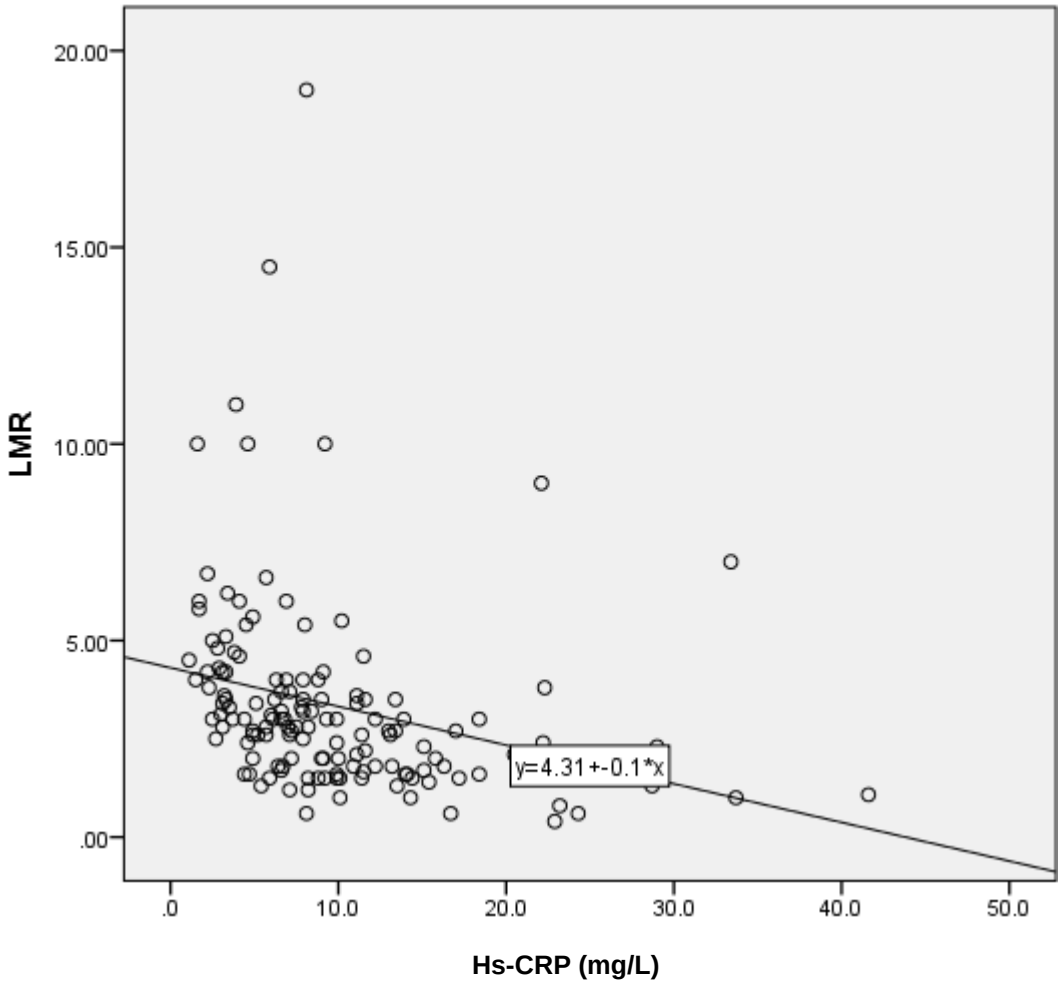

Figure 20. Scatter diagram showing correlation between hs- CRP and LMR among the study participants

Correlation between hs-CRP and LMR among the study participants is described in Table 18 and plotted in Figure 20. Spearman correlation coefficient is -0.51 (moderate correlation) and it is statistically significant (p<0.001).

Table 19. Comparison of PLR across the hypertension status among the study participants (N=140)

Hypertension	PLR		P value*
	Median	IQR	
Yes	138.6	105.5-196.2	0.04
No	162.7	130.8-225	

Mann Whitney U test

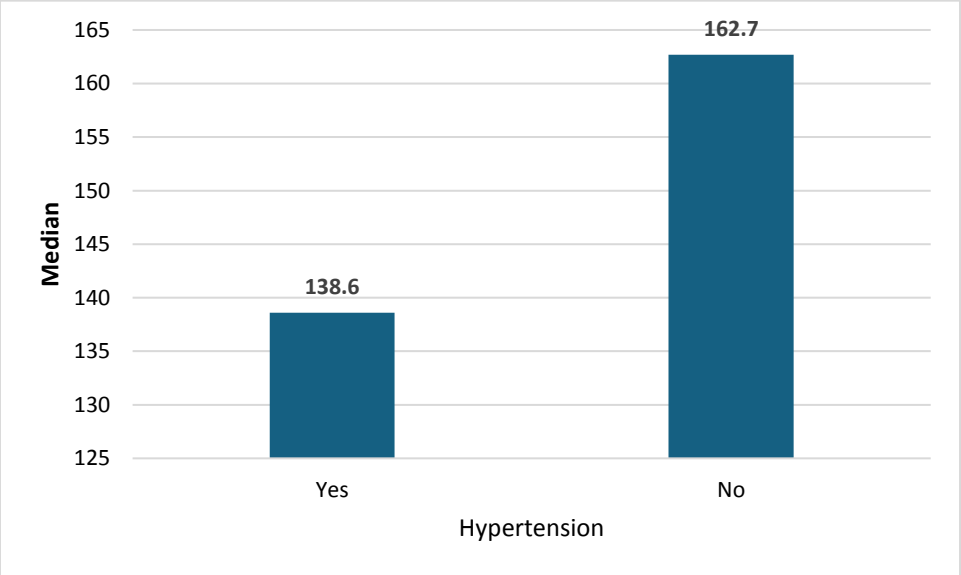

Figure 21. Comparison of PLR across the hypertension status among the study participants

Table 19 and Figure 21 shows comparison of PLR across the hypertension status among the study participants. The median level of PLR was significantly lower among the participants with hypertension as compared to participants with normal blood pressure (p=0.04). The median (IQR) of PLR among the participants with hypertension was 138.6 (105.5-196.2) and 162.7 (130.8-225) among participants with normal blood pressure. However, the median levels of NLR, LMR and hs-CRP was not significantly different across the hypertension status among the study participants.

Table 20. Comparison of NLR across the IgA nephropathy status among the study participants (N=140)

IgA nephropathy	NLR		P value*
	Median	IQR	
Yes	2.4	2.1-3.3	0.03
No	3.9	2.6-5.6	

Mann Whitney U test

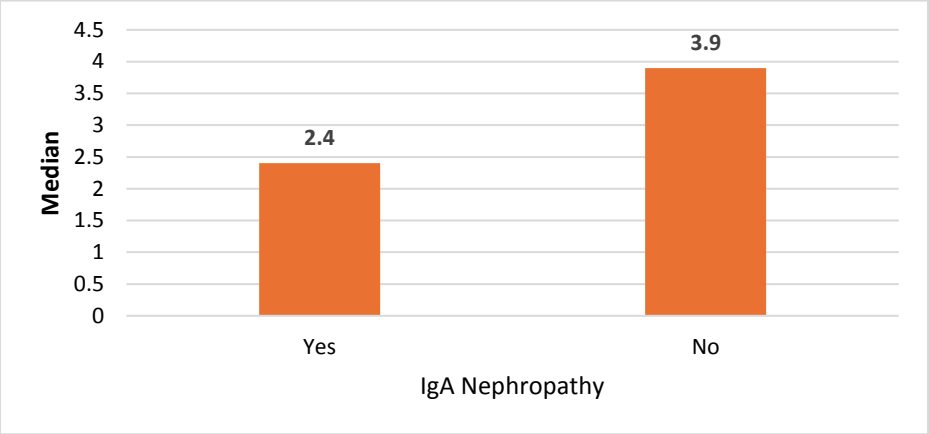

Figure 22. Comparison of NLR across the IgA nephropathy status among the study participants

Table 20 and Figure 22 shows comparison of NLR across the IgA nephropathy status among the study participants. The median level of NLR was significantly lower among the participants with IgA nephropathy as compared to participants without IgA nephropathy (p=0.03). The median (IQR) of NLR among the participants with IgA nephropathy was 2.4 (2.1-3.3) and 3.9 (2.6-5.6) among participants without IgA nephropathy.

Table 21. Comparison of hs- CRP across the IgA nephropathy status among the study participants (N=140)

IgA nephropathy	hs- CRP (mg/L)		P value*
	Median	IQR	
Yes	4.1	2.7-8.4	0.007
No	8.1	5.4-12.2	

Mann Whitney U test

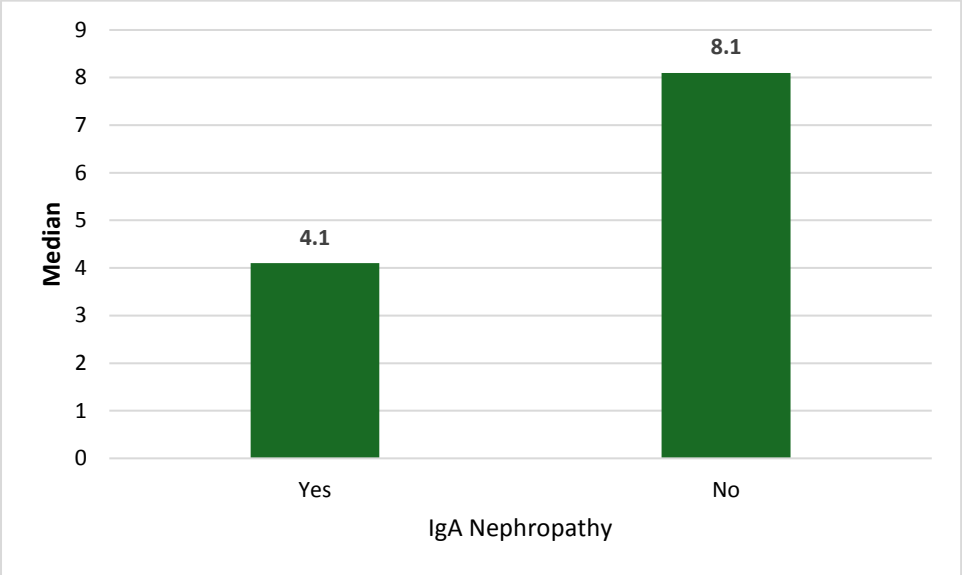

Figure 23. Comparison of hs- CRP across the IgA nephropathy status among the study participants

Table 21 and Figure 23 describes comparison of hs-CRP across the IgA nephropathy status among the study participants. The median level of hs-CRP was significantly lower among the participants with IgA nephropathy as compared to participants without IgA nephropathy (p=0.007). The median (IQR) of hs-CRP among the participants with IgA nephropathy was 4.1 (2.7-8.4) and 8.1 (5.4-12.2) among participants without IgA nephropathy. However, the median levels of LMR and PLR was not significantly different across the IgA nephropathy status among the study participants.

DISCUSSION

CKD is a progressive and irreversible loss of kidney function characterized by a gradual decline in the GFR. This decline leads to a group of clinical complications, including electrolyte imbalances, metabolic acidosis, anemia, and cardiovascular disease.[59,127] In recent years, chronic inflammation has emerged as a critical factor not only in the pathogenesis of CKD but also in its progression. Inflammatory mediators and immune cell infiltration have been implicated in damaging kidney structures and impairing renal function.[60] The infiltration of these cells leads to the accumulation of extracellular matrix, glomerular collapse, and the development of fibrosis, ultimately contributing to the progression of CKD. Moreover, CKD is associated with immune system dysfunction, including changes in the apoptosis rates and activation of immune cells like neutrophils, monocytes, and T cells. These alterations in the immune system further exacerbate the chronic inflammatory state and increase the risk of infection and cancers in CKD patients.[60,128,129]

Neutrophils play a crucial role in the innate immune response, while lymphocytes are central to the adaptive immune system. The NLR serves as a reflection of the balance between these two immune arms, with higher values indicating a pro-inflammatory state.[101] Monocytes have the ability to differentiate into macrophages, influencing both inflammation and tissue repair. On the other hand, the MLR (LMR) offers insights into the potential interplay between monocytes and lymphocytes.[107,130] Platelets, in addition to their role in hemostasis, contribute to inflammatory processes. The PLR may suggest a connection between heightened inflammation and altered platelet function in CKD.[112,124] By examining these ratios across different stages of CKD, our study investigates the potential of readily available peripheral blood markers, specifically the NLR, PLR, and

MLR (LMR), as biomarkers to assess the severity of inflammation in different stages of CKD.

The socio-demographic profile of the participants revealed that the majority were within the age ranges of 41-60 years and 61-80 years, each representing 41.4% of the study population. Our study had a higher proportion of males (67.1%) compared to females (32.9%). This distribution aligns with the higher prevalence of CKD among older adults and a slightly greater incidence in males, consistent with existing literature.[131–133]. But contradicts the higher global prevalence of CKD among females as reported by MD J N et al.[134] A high prevalence of comorbidities like hypertension (75.7%) and diabetes mellitus (53.6%) was observed among the participants. Similar to our findings a higher prevalence of hypertension (87%) than diabetes (37%) was reported in Indian Chronic Kidney Disease Study (ICKD) by Kumar V et al.[8] Another study in Andhra Pradesh by Kanyari SS et al. reported similar pattern with hypertension prevalence of 74.2% and diabetes prevalence of 41.2% among CKD patients.[135] Since these conditions are known to contribute to inflammation and CKD development, it strengthens the rationale for exploring inflammatory markers in this population.

The distribution of CKD stages among our study participants reveals a significant predominance of advanced CKD, with over half of participants having grade 5 CKD. This skew towards more advanced stages reflects the typical clinical scenario where patients are often diagnosed late due to the asymptomatic nature of early CKD.[59] The high prevalence of grade 5 CKD signifies critical renal function decline, necessitating intensive management. This contradict the CKD scenario in India reported by Singh et al. where lower prevalence of advanced grade CKD was reported.[136] This discrepancy shows the potential for regional variations in CKD presentation and diagnosis patterns. Thus, our

findings highlight the urgent need for early detection and intervention strategies to prevent progression, especially in high-risk populations such as those with hypertension and diabetes. Enhanced clinical strategies focusing on early intervention and rigorous monitoring of inflammation are vital for improving outcomes and quality of life for CKD patients.

The clinical profile of our study participants highlights key biochemical and hematological parameters characteristic of CKD. The mean serum urea and creatinine levels were elevated (81.4 mg/dl and 3.9 mg/dl, respectively), reflecting significant renal impairment consistent with advanced CKD stages. The median eGFR of 14 ml/min/1.73m² underscores the severe reduction in kidney function among the participants. These findings align with the known progression of CKD, where declining eGFR and rising urea and creatinine levels mark worsening renal function as outlined by Chen et al.[7] The Indian CKD study reported higher mean eGFR (40.5 ml/min/1.73m²) and lower serum urea (45 mg/dl) and creatinine (1.7 mg /dl) levels.[8,132] This difference could be due to several factors. The studies might have enrolled participants at different stages of CKD progression due to variations in inclusion criteria. Additionally, the specific CKD subtypes present in each population and the demographics such as age, ethnicity might have influenced the results. Sample size could also play a role as ICKD study had 4056 participants

Mean hemoglobin level was 9.9 g/dl, indicating prevalent anemia, a common complication in CKD due to reduced erythropoietin production and iron deficiency.[137,138] The hematocrit, mean corpuscular volume (MCV), and mean corpuscular hemoglobin (MCH) values were also indicative of this anemic state. Additionally, the increased red cell distribution width (RDW) of 15.2% suggests anisocytosis, often seen in CKD-related anemia.[139] The elevated white blood cell (WBC) count (8.6 x 10^3/µL) and neutrophil count (ANC of 6.1 x 10^3/µL)

may reflect a chronic inflammatory state, which is frequently observed in CKD due to persistent immune activation and infections. The median platelet counts of 231.1 x 10^3/µL was within normal range, yet the slight reduction in advanced CKD stages might indicate platelet dysfunction or bone marrow suppression The data collectively highlight the multifaceted pathophysiological alterations in CKD, including metabolic imbalances, anemia, and inflammation, emphasizing the need for comprehensive management strategies in these patients.[140]

The analysis of inflammatory biomarkers among our study participants reveals a clear association between inflammation and the progression of CKD. The median NLR significantly increased with advancing CKD stages, from 2.2 in grade 2 to 4.4 in grade 5 ($p<0.001$). This trend is consistent with existing literature that identifies elevated NLR as a marker of systemic inflammation and a predictor of adverse outcomes in CKD patients.[101,141] In our study, the increase in NLR with CKD severity suggests an escalating inflammatory response as renal function deteriorates, which could be attributed to the accumulation of uremic toxins that activate immune responses.[142] Aneez F A et al reported similar findings, indicating a significant increase in NLR with CKD progression: from 1.62 in stage II to 3.26 in stage IV ($p<0.001$).[143] Higher NLR values have also been significantly associated with increased all-cause mortality in CKD patients. This association is consistent across various studies, indicating that NLR is a reliable marker of systemic inflammation and a predictor of adverse outcomes in CKD patients. For example, Muresan AV et al. reported that mortality at 30 days was significantly higher in ESRD patients with high NLR values (40.12% vs. 1.97%; $p < 0.0001$).[1,144,145]

Similarly, the PLR also showed an upward trend, although there was no statistical significance ($p=0.07$). The median PLR increased from 108.8 in grade 2 to 161.1 in grade

5. Aneez F A et al. also found an increase in PLR with CKD stages, with values rising from 101.11 in stage II to 150.0 in stage IV, although this increase was statistical significance ($p<0.001$).[143] Elevated PLR has also been associated with inflammation and poor prognosis in CKD, and like NLR, higher PLR values have been significantly positively associated with all-cause mortality in CKD patients as reported by Muresan AV et al. and Chen Y et al.[1,112,144] However, the lack of statistical significance in our study suggests that while PLR may be less sensitive or specific compared to NLR in reflecting inflammatory status, it remains an important prognostic marker.

The lymphocyte-to-monocyte ratio (LMR) significantly decreased (or MLR significantly increased) with worsening CKD, from 4.5 in grade 2 to 2.6 in grade 5 ($p=0.005$). Lower LMR has been linked to higher inflammatory states in CKD patients.[144] The decrease in LMR with CKD progression may indicate an imbalance in immune cell populations, reflective of the chronic inflammatory state and immune dysfunction associated with advanced CKD.[146] Aligning with our results a cohort study by Zhang M et al. has reported that LMR (MLR) was associated with risk of CKD (hazards ratio- 16.12 (4.5-57.6, $p<0.001$).[147] Also Ester S OH et al has reported that CKD patients with higher MLR (lower LMR) had higher risk of cardiovascular events.[107]

Hs-CRP levels also showed a significant increase across CKD stages, from 2.8 mg/dL in grade 2 to 9.9 mg/dL in grade 5 ($p<0.001$). This aligns with findings by Jalal B et al and Heidari D et al. highlighting hs-CRP as a reliable marker of inflammation and cardiovascular risk in CKD patients.[148,149] The rising hs-CRP levels indicate heightened systemic inflammation, which is a critical factor in the pathogenesis of CKD-related complications, including cardiovascular disease and anemia.[150] These findings underscore

the relevance of monitoring inflammatory biomarkers in CKD patients as indicators of disease severity and potential predictors of adverse outcomes.

The absolute lymphocyte count (ALC) significantly declines as CKD progresses, with mean ALC values decreasing from 2.8 in grade 2 to 1.4 in grade 5 ($p<0.001$). This decrease in ALC reflects the impaired immune function often seen in advanced CKD stages, which may be due to chronic inflammation and uremia-induced immunosuppression. Aneez F A et al also reported similar pattern with a decrease from 2.3 (2.0-3.4) among stage 2 to 1.8 (1.5-2.1) among stage 4 (p value-0.001).[143]

There is also a significant reduction in platelet counts across CKD stages, with mean platelet levels dropping from 298.6 in grade 2 to 209.0 in grade 5 ($p<0.001$). This thrombocytopenia can be attributed to factors such as increased platelet destruction, decreased production, and the dilutional effect of fluid overload common in CKD patients. Reduced platelet counts are clinically relevant as they contribute to bleeding tendencies and can complicate the management of CKD patients.[151] This also aligns with findings by Bladel E R V et al. where reduced platelet reactivity was reported among CKD patients.[94] However, it's important to acknowledge conflicting findings, like study by Aneez F A et al. where he found increase in platelet count across stages with 249.0 (202.0-268.0) among stage 2 to 277.0 (256.5-390.0) in stage 5 (p value-0.013).[143] This discrepancy might be due to several factors. The underlying causes and severity of CKD can vary greatly between patients, leading to differences in platelet counts. Additionally, studies with smaller sample sizes or specific patient populations might not capture the full range of platelet count changes in the entire CKD population.

RDW significantly increases with CKD progression, from a mean of 13.9% in grade 2 to 15.6% in grade 5 ($p=0.04$). Elevated RDW in CKD patients is indicative of anisocytosis,

often resulting from chronic inflammation, malnutrition, and erythropoietin resistance, which are prevalent in advanced CKD. Adding to our findings Deng X et al. reported that higher RDW is associated with increased mortality and cardiovascular events in CKD patients, emphasizing its prognostic value.[152] Lu YA et al. also reported a linear trend towards higher RDW among patients with worsening renal function.[153]

A strong positive correlation exists between hs-CRP and NLR with a Spearman correlation coefficient of 0.72 ($p<0.001$). This strong correlation suggests that both markers are reflective of systemic inflammation and can be used interchangeably to some extent to assess inflammatory status in CKD patients . Elevated hs-CRP and NLR are both associated with higher mortality and cardiovascular risks in CKD.[144] A weak but significant positive correlation exists between hs-CRP and PLR with a Spearman correlation coefficient of 0.35 ($p<0.001$). Despite the weaker correlation compared to NLR, PLR still serves as an indicator of inflammation and has been linked to adverse outcomes in CKD patients. A moderate negative correlation exists between hs-CRP and LMR with a Spearman correlation coefficient of -0.51 ($p<0.001$). The inverse relationship suggests that as inflammation increases (indicated by higher hs-CRP), LMR decreases (MLR increases), reflecting the protective role of higher LMR (lower MLR) values in CKD patients. Lower LMR (higher MLR) is associated with worse clinical outcomes, highlighting its relevance as a prognostic marker.

These findings underline the importance of routinely monitoring these biomarkers in CKD patients to assess inflammation, immune function, and hematological status. Understanding these correlations and their clinical implications can aid in better risk stratification, early intervention, and improved management of CKD patients to mitigate complications and enhance patient outcomes. This could include the use of anti-inflammatory medications,

lifestyle modifications, and careful management of comorbid conditions to improve overall patient outcomes and slow the progression of CKD.

A significant difference emerged in PLR between hypertensive and normotensive CKD patients (p=0.04), with lower PLR observed in the hypertensive group. This suggests a potential link between hypertension and altered PLR levels. While the exact mechanism remains unclear, hypertension often involves systemic inflammation, endothelial dysfunction, and altered platelet function.[154] These factors might influence PLR, reflecting the complex interplay between inflammation, hemostasis, and cardiovascular risk in hypertensive individuals.[155]

The comparison of NLR levels among study participants with and without IgA nephropathy reveals a significant difference, with median NLR levels lower in those with IgA nephropathy (2.4, IQR: 2.1-3.3) compared to those without (3.9, IQR: 2.6-5.6), with a p-value of 0.03. This indicates a reduced inflammatory response in individuals with IgA nephropathy. This contradicts existing literature, where NLR has been established as a potential predictor of poor prognosis in IgA nephropathy. A study by Li et al. found that NLR was higher for IgA nephropathy patients than healthy controls and was an independent risk factor for IgA nephropathy progression, even after adjusting for well-known risk factors.[156] Another study by Wang S et al. also reported that a high NLR was an independent risk factor for IgA nephropathy and that NLR was negatively correlated with eGFR and positively correlated with urine protein and serum creatinine levels.[157] These discrepancies highlight the need for further investigation into the role of NLR in IgA nephropathy. The variations in findings could be attributed to differences in study populations, methodologies, or stages of disease among participants. Further research is necessary to clarify the relationship between NLR and IgA nephropathy and to determine the underlying

mechanisms that may influence NLR levels in this patient population. Understanding these factors is crucial for the development of reliable biomarkers for disease prognosis and management.

The comparison of high-sensitivity C-reactive protein (hs-CRP) levels among study participants with and without IgA nephropathy reveals a significant difference, with median hs-CRP levels being lower in those with IgA nephropathy (4.1 mg/L, IQR: 2.7-8.4) compared to those without (8.1 mg/L, IQR: 5.4-12.2), with a p-value of 0.007. This suggests a less pronounced systemic inflammatory response in individuals with IgA nephropathy. This is consistent with findings of Baek et al. where there was no significant differences in hs-CRP levels between controls and patients with IgA nephropathy, indicating that hs-CRP may not closely reflect the inflammatory pathogenesis in IgA nephropathy.[158] While hs-CRP is a general marker of inflammation, it may not accurately reflect the localized inflammatory processes occurring in the kidneys of IgA nephropathy patients. The lower inflammatory biomarker levels observed in those with IgA nephropathy may reflect differences in disease pathophysiology, immune response, and renal inflammation characteristic.[155]

CONCLUSION

- Our research offers an evaluation of inflammatory biomarkers such as NLR, PLR, MLR (LMR), RDW, ALC and hs-CRP across various stages and types of CKD. We have observed notable correlations between these biomarkers and the severity of CKD. Specifically, as CKD stages progress, NLR, PLR, MLR (with LMR decreasing) and RDW demonstrate consistent increases, with decrease in ALC and platelets, indicating their potential as valuable indicators of inflammation in renal pathology.
- NLR, PLR, and MLR (LMR) emerge as promising biomarkers for assessing severity of inflammation, with variations across CKD stages indicating their utility in disease monitoring. Moreover, distinct patterns of these biomarkers across different CKD types mark the heterogeneity of inflammatory responses, emphasizing the need for personalized diagnostic and therapeutic approaches.
- Correlation analysis further strengthens the link between known inflammatory biomarker like hs-CRP and novel hematological indices like NLR, PLR, MLR (LMR), offering insights into the systemic inflammatory response in non-dialysis CKD patients and its implications for disease management. Overall, these findings highlight the clinical relevance of inflammatory biomarkers in CKD assessment.

SUMMARY

This cross-sectional study aimed to assess the utility of NLR, PLR, and MLR (LMR) as biomarkers for evaluating inflammation severity across different stages and types of chronic kidney disease (CKD. It was conducted between January 2023 and December 2023; we enrolled 140 individuals diagnosed with CKD who were not on dialysis. Majority of participants fell within the age groups of 41-60 years and 61-80 years, with males comprising a higher proportion. Hypertension and diabetes mellitus were prevalent among the participants. The distribution of CKD stages showed a higher prevalence of grade 5 CKD (55%). Clinical profiles exhibited elevated serum urea and creatinine levels, indicative of renal impairment, and prevalent anemia. Analysis of inflammatory biomarkers revealed median levels of NLR, PLR, MLR (LMR), and hs-CRP, demonstrating their association with CKD severity. NLR, PLR, and hs-CRP levels increased significantly with advancing CKD stages, while LMR exhibited a significant decrease (increased MLR). Correlation analysis showed strong associations between hs-CRP and NLR, moderate correlation between hs-CRP and MLR (LMR), and a weak correlation between hs-CRP and PLR. Our study highlights the potential of NLR, PLR, MLR, and hs-CRP as biomarkers for assessing inflammation severity in CKD. Further research is warranted to validate these findings and exploring the complex links between inflammation and CKD progression. Additional investigations into the utility of these biomarkers in predicting clinical outcomes and guiding therapeutic interventions in CKD management are warranted.

LIMITATION

- **Nature of study**: The present study is a cross sectional study. Longitudinal studies may be better to investigate temporal relationships and assess the predictive value of inflammatory biomarkers for disease progression and outcomes over time.
- **Potential Confounders**: Our study may not have adequately accounted for all potential confounding variables that could influence inflammatory biomarker levels, such as medication use, comorbidities, and lifestyle factors. Failing to adjust for these confounders could introduce bias and affect the accuracy of the associations observed.
- While exploring the etiology of CKD, the clinical data for IgA nephropathy though included, was limited in our study in comparison to more common etiological factors like diabetes and hypertension.

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INFORMED CONSENT FORM

"Evaluation of Derived Indices of Peripheral Whole Blood Cell Counts in non-dialysis CKD patients- One year cross sectional study in a tertiary care hospital"

Principal Investigator: Reg no: BN0121007

Name of Guide: _____

Objective: We aim to evaluate if NLR (Neutrophil to Lymphocyte ratio), PLR (Platelet to Lymphocyte ratio), MLR (Monocyte to lymphocyte ratio) can be used as an inflammatory biomarker for different stages of CKD and to study the pattern of NLR, PLR, MLR in different types of CKD

Explanation of procedure: During this study, a complete blood count will be done to detect blood parameters. The principal investigator of this study is Dr. Karan Khatri (PG) under the guidance of Dr. Reshma Karishetti (Guide).

Withdrawal from participation in the study: Participation in this study is voluntary. You will be free to decide whether to participate in this study or continue participation once enrolled. In case you decide to withdraw your participation, you are free to do so. However, please convey the decision to the principal investigator.

Possible benefits from participating in the study: You will not have nor get any benefits by participating in this study. The data gathered will help the population at large.

Possible risks from participating in the study: There are no risks involved in participating in this study.

Privacy and confidentiality: The information collected from you will be coded, to prevent any person from identifying you. Your Identity will never be revealed. The data collected from you will be kept confidential and only processed or aggregated data will be used for publication.

Financial incentives: You will not receive any payment for participating in this study.

Authorization for publication of aggregated data: Results obtained after processing of the aggregated data will be published for scientific purposes and /or presented to scientific groups. However, your identity will never be revealed.

Questions: In case of any questions with regard to this study, you are free to contact: Reg No: BN0121007, Department of Pathology, Jawaharlal Nehru Medical college, Belagavi If you have any question or complaints with regards to your right as a study participant you may contact Dr Harsha Hegde, Chairperson, Ethical committee of JNMC, 0831-2473777 Extension 4052.

Legal rights: By signing this consent form, we are not waving any of your legal rights.

CONSENT STATEMENT

I am making a voluntary decision to participate in the study "Evaluation of Derived indices of Peripheral Whole Blood Cell Counts in Non-Dialysis CKD Patients – One year Cross Sectional Study". My signature below indicates that I have decided to participate and I have read the information provided above or the information provided above has been read to me in the language that I understand best. I was given the opportunity to ask questions and that they have been answered to my satisfaction.

Name of the participant:

Signature or left thumb impression of the participant:

Name of the witness:

Signature or left thumb impression of the witness:

Name of the investigator:

Signature of the investigator

PROFORMA

Name: Sample ID:

Age: Sex: Male/Female/Other

IP no:

Brief clinical history:

(with duration of illness)

Medication history:

(with duration of treatment)

Co morbid conditions:

Hypertension	Yes/No
Diabetes Mellitus	Yes/No
Coronary artery disease	Yes/No
Hepatic/ renal failure	Yes/No
Evidence of active infection	Yes/ No

INVESTIGATION DETAILS

CBC

Hemoglobin (g/dL):

RBC count ($x10^6$ / uL):

Hematocrit (%):

Mean corpuscular volume (MCV) (fL):

Mean corpuscular hemoglobin (MCH) (pg):

Mean corpuscular hemoglobin concentration (MCHC) (g/dL):

Retic count (%):

Total WBC Count ($x10^3$ /mm^3):

Absolute neutrophil count (cells/mm^3):

Absolute lymphocyte count (cells/mm^3):

Absolute monocyte count (cells/mm^3):

Absolute eosinophil count (cells/mm^3):

Platelets ($x10^3$ /dL):

RENAL FUNCTION TEST

Sr. Creatinine:

Sr. Urea:

eGFR:

Hs-CRP (C reactive Protein):

KEY TO MASTERCHART

OP. NO	-	Out patient number
HTN	-	Hypertension
DM	-	Diabetes
ADPKD	-	Autosomal Dominant Polycystic Kidney Disease
FSGS	-	Focal segmental glomerulosclerosis
S. Urea	-	Serum Urea
S. Creatinine	-	Serum Creatinine
EGFR	-	Estimated glomerular filtration rate
HB	-	Hemoglobin
HCT	-	Hematocrit
MCV	-	Mean Corpuscular Volume
MCH	-	Mean Corpuscular Hemoglobin
MCHC	-	Mean Corpuscular Hemoglobin Concentration
RDW	-	Red Cell Distribution Width
RBC	-	Red Blood Cell
WBC	-	White Blood Cells
MPV	-	Mean platelet volume
ANC	-	Absolute Neutrophil Count
ALC	-	Absolute Lymphocyte Count
AMC	-	Absolute Monocyte Count
AEC	-	Absolute Eosinophil Count
NLR	-	Neutrophil to Lymphocyte Ratio
PLR	-	Platelet to Lymphocyte Ratio
LMR	-	Lymphocyte to Monocyte Ratio
Y	-	Yes
N	-	No

OP. NO.	NAME	AGE	SEX	HTN	DM	IgA NEPHROPATHY	ADPKD	FSGS	S. UREA (mg/dl)	S. CREATININE (mg/dl)	EGFR (ml/min/1.73m^2)	CKD STAGE	HB (g/dl)	HCT %	MCV (fL)	MCH (pg)	MCHC (g/dl)	RDW %	RBC COUNT x 10^6/uL	RETIC %	WBC COUNT x 10^3/uL	PLATELET x10^3/Ul	MPV (fL)	ANC x 10^3/uL	ALCx 10^3/uL	AMCx 10^3/uL	AECx 10^3/uL	NLR	PLR	LMR	hs- CRP (mg/dl)
7144971	BASAVANNEPPA	70	M	Y	N	N	N	Y	87	2.2	31	G3	9	27	85.4	24	30	15	3.16	0.5	10	342	7	7	2	0.7	0.3	3.5	171	2.8	7.5
6787807	RAJSHREE	37	F	Y	N				71	1.3	73	G2	10.3	33.5	66.7	20.5	30.7	15.7	5.02	3.5	11	272	10.4	7.3	2.5	0.8	0.4	2.92	108.8	3.12	3
7131919	ABDUL	49	M	Y	Y				130	3.5	21	G4	9.1	27.3	79	25.2	28.9	14.5	4.1	0.6	8.5	145	8.4	6.8	1.2	0.3	0.2	5.6	120.83	4	8.8
7138611	BIBI BASHIR	64	F	Y	Y				28.5	1.6	36	G3	8.5	25.5	78.2	23.6	29.8	16	3.1	0.5	6.1	123	7.7	4.2	1.1	0.7	0.1	3.82	111.82	1.5	8.2
5907322	BASAPPA	70	M	Y	N				48.5	2.4	28	G4	10	32.2	92	28.6	31.1	14.4	3.5	1.8	8.3	376	9.8	5.4	1.8	0.5	0.6	3	208.8	3.6	11.1
7101697	KALLAVVA	52	F	Y	Y				67.7	4.65	11	G5	5.6	16.8	72	22.5	27.1	19	1.87	0.5	5.3	119	7.2	3.8	1.1	0.2	0.2	3.45	108.1	5.5	10.2
4467605	BASAVRAJ	21	M	N	N	Y	N	N	68.4	6.54	15	G5	9.6	31.4	78.8	24.1	30.6	22.4	3.99	2.1	9.1	273	7.3	6.3	1.9	0.7	0.2	3.32	143.6	2.7	13
7154559	BHIMAPPA	81	M	Y	N				66	2.18	30	G3	11	33	82	30.2	31.5	13	4.2	0.8	9.4	326	8.2	7.1	2	0.2	0.1	3.55	163	10	9.2
7159167	YALLAPPA	69	M	Y	Y				99	3.27	20	G4	11.6	34.8	84.2	29.6	30.8	12.2	4.58	0.7	10.3	242	9.1	7.5	1.6	1	0.1	4.69	151.2	1.6	14
6601773	ASHOK	40	M	Y	N				90	5.3	13	G5	14.3	48.8	105	30.9	29.2	13.7	4.6	0.8	7.6	208	7.4	5.1	1.4	0.7	0.4	3.64	148.5	2	10
6605285	SHANKAR	79	M	Y	N				127	5.1	11	G5	11.4	38.4	80.8	24	29.7	15.8	4.75	0.6	8.6	246	8.6	5.6	1.9	0.7	0.4	2.95	129.4	2.7	17
2818653	TUKARAM	64	M	Y	Y				47	1.6	48	G3	16.5	56.9	100	29.2	29.1	14.4	5.67	0.8	13.2	144	8.4	8.2	3.8	0.7	0.5	2.16	37.89	5.4	8
7083050	DEEPAK	63	M	Y	N				123	6.4	9	G5	5.2	17.1	92.9	28.3	30.4	14.4	1.84	2.1	9.2	147	10.5	8	0.7	0.3	0.2	11.43	210	2.3	29
6796425	ALLAMAPRABHU	49	M	Y	Y				74	1.82	45	G3	13.9	43.4	90.6	29	32	13.1	4.7	1	7.1	226	9.6	3.5	2.7	0.4	0.4	1.3	83.7	6.7	2.2
3547182	SHIVANAGOUDA	56	M	Y	N				66	1.5	54	G3	13.6	44.1	91.9	28.3	30.8	13.3	4.8	1.6	7.7	307	8.8	4.5	2.3	0.5	0.4	1.96	133.4	4.6	4.1
4383702	KALINDRA	50	M	N	Y				91.5	4.83	14	G5	8.3	26.1	98.5	31.3	31.8	14.1	2.65	1.6	6.4	270	11.5	4.4	1.2	0.6	0.2	3.67	225	2	7.2
2351201	MAHADEV	45	M	Y	Y				42.4	2.23	36	G3	14.6	45.6	90.3	29	32	12.4	5.04	1.5	8.1	262	9.6	5.1	1.3	0.7	1	3.92	201.5	1.8	6.4
6164065	MAHADEV R	65	M	Y	N				52	2.9	23	G4	12.2	37.1	80.5	26.5	32.9	16.1	4.6	0.7	7	260	6.7	4.4	1.6	0.6	0.4	2.75	162.5	2.6	5.2
7203320	NARAYAN	76	M	Y	N				42.9	1.64	43	G3	11.9	37.7	84.4	27.1	32.1	13.3	4.34	1.2	12.9	557	9.2	10.6	1.4	0.9	0.5	7.57	397.8	1.5	14.4
7059013	TARANUM	40	F	Y	N	N	N	Y	41.1	1.1	65	G2	14.8	43.4	86.9	29.7	34.1	13.2	4.99	0.5	7.4	289	9	3.5	3.1	0.5	0.3	1.13	93.2	6.2	3.4
6505149	SAMPAT	22	M	N	N				117	6.5	12	G5	9.5	29	110.3	36.1	32.8	14.1	2.63	2.4	7.6	256	12.5	5	1.9	0.6	0.1	2.63	134.7	3.1	6
7182531	MANISHA	56	F	Y	Y				173	5.05	9	G5	10	32.6	90.6	27.8	30.7	13.5	3.6	1.6	11.1	305	10.3	8.5	1.5	0.7	0.3	5.67	203.3	2.1	20.5
4467210	IRAGOUDA	38	M	Y	N				58.2	5.51	13	G5	10.7	35.3	85.7	26.2	30.6	16.1	5.86	0.78	10.2	348	8.2	5.9	3.1	0.8	0.2	1.9	112.2	3.8	2.3
7131583	BASAPPA	70	M	N	Y				133	5.3	11	G5	9.1	27.5	77.7	25.8	33.2	15.5	3.54	1.2	7.5	339	7.6	4.9	1.9	0.4	0.2	2.58	178.4	4.7	3.8
7079291	JAGDISH	52	M	Y	N				65.5	4.85	14	G5	9.2	30	71.8	21.8	30.3	19.5	3.119	1.47	10.9	408	9.7	11.5	2.6	1	0.3	4.42	156.9	2.6	7.1
4050061	SUCHITA	52	F	Y	Y				75.2	4.55	11	G5	10	30.4	90.9	30	33	14.9	3.35	1.7	8.5	255	8.4	6.8	1.2	0.4	0.1	5.67	212.5	3	18.4
7204675	RAMAPPA	65	M	Y	Y				114	5.35	11	G5	11.2	37	81.8	26.2	31.9	18.4	4.45	0.51	20.2	239	10.6	15.5	3.5	0.9	0.3	4.43	68.29	3.8	22.3
7296767	FATIMA	75	F	Y	Y				125	3.78	12	G5	8.3	27	82.3	25.3	30.7	16	3.28	1.2	10.4	307	11.1	8.1	1.7	0.5	0.1	4.76	180.5	3.4	11.1
7280152	SHIVAPPA	81	M	Y	N				74	2.3	28	G4	10.8	33.3	96.8	31.4	32.4	13.6	3.44	0.5	11.4	202	11.6	7.4	3.3	0.5	0.1	2.24	61.2	6.6	5.7
5933050	PARVATI	67	F	Y	N				30	1.3	45	G3	11.3	36.7	100	30	30.8	14	3.67	1.5	8.1	314	10.4	5.6	1.6	0.6	0.3	3.5	196.2	2.6	5.7
6900765	SHASHIKANT	65	M	Y	N				69.4	3.75	17	G4	8.9	26.6	86.1	28.7	33.3	15.6	3.15	1.11	13.2	89	7.5	11.1	0.9	1.1	0.1	12.33	98.8	0.8	23.2
5860178	SIDDAVVA	42	F	N	N	Y	N	N	78.1	5.61	9	G5	9.2	30.6	93.3	28	30.1	15	3.28	1.3	4.2	157	8.6	2.9	1.1	0.1	0.1	2.64	142.7	11	3.9
5909422	BASAVANNI	70	M	Y	Y				127	3.2	20	G4	9.8	32.6	96.4	29.3	30.4	20.4	3.44	1.6	7.8	131	10.8	4.8	1.9	0.7	0.4	2.53	68.95	2.7	4.9
7326265	MANING	30	M	Y	N				160	7.1	10	G5	8.2	25.9	82.1	26.1	31.6	17.3	2.5	0.6	8.9	243	9.8	6.2	1.5	0.9	0.3	4.13	162	1.6	4.7
7324696	SAMEER	54	M	Y	Y				98	5.8	11	G5	8.1	25.5	76.1	24.2	31.7	16.9	2.33	1.1	11	459	8.4	8.2	1.4	1.1	0.2	5.86	327.8	1.2	8.2
7314985	ARJUN	43	M	Y	N				101	6.9	9	G5	8.4	27	81.8	25.8	31.5	13.2	2.99	1.94	3.1	34	9.1	2.2	0.6	0.2	0.1	3.67	56.6	3	3.7
7235414	SAGAR	38	M	Y	Y				67.3	2	43	G3	9.9	32.2	83.9	25.9	30.8	15.5	3.29	0.75	11.6	385	9.5	9.9	1.4	0.3	0	7.07	275	4.6	11.5
7307483	MALLIK	55	M	Y	N				126	5.5	11	G5	9.2	29	96.7	30.7	31.7	17.1	3.21	1.5	15.6	147	11	12.8	1.2	1.1	0.5	10.6	122.5	1.08	41.6
803675	DODAPPA	47	M	Y	Y				114	6.6	10	G5	7.7	25.7	71.6	21.4	30	20	3.59	0.77	10.2	439	11.2	6.7	2.4	0.8	0.2	4.7	182.9	3	9.9
7085892	PADMAVATI	63	F	Y	Y				84	5.9	8	G5	9.4	29.1	81.7	26.3	32.2	13.7	3.52	0.96	12.3	363	7.2	8.5	2.2	1.2	0.4	3.86	165	1.8	10.9
7145972	BASSAPPA	70	M	Y	Y				94	1.66	44	G3	9.8	30.2	94.7	30.4	32.1	15.7	3.33	1.02	11.4	329	9.9	5.4	4.2	1	0.8	1.29	78.33	4.2	3.3
7145087	KALAPPA	46	M	Y	N				77.6	3.69	20	G4	10.9	34.4	87.6	27.6	31.5	13.2	3.95	0.6	7.9	297	8.6	5	2	0.6	0.2	2.5	148.5	3.3	3.5
7145913	HARIBHAV	76	M	Y	N				64	1.25	60	G3	13.1	41.4	85.2	26.1	30.7	13.8	4.6	0.52	6.5	222	9.4	4.5	1.1	0.3	0.6	4.09	201.8	3.6	3.2
7148034	SAVITA	40	F	N	N				111	6.07	8	G5	10.2	32.9	94.3	30.7	32.5	13.9	4.14	1.85	5.6	108	9.5	3.5	1.6	0.4	0.1	2.9	67.5	4	6.3
7139135	BALAGOUDA	65	M	Y	N				125	5.9	10	G5	8.1	25.1	80.5	25.5	31.7	15.4	2.86	1.84	5.1	239	7.6	3.2	1.2	0.5	0.3	2.67	199.1	2.4	4.6
7131225	DIVENRAPPA	75	M	Y	N				104	5.2	11	G5	9.2	29.4	87.4	30.5	31.3	13.7	3.14	0.76	8.4	120	10.5	5.9	1.3	0.9	0.3	4.54	92.3	1.4	15.4
7129714	VISHWANTH	44	M	Y	N				135	6.4	10	G5	6.1	19.9	92.3	28.5	30.9	18.8	2.15	2.1	4.3	90	9.1	3.1	0.8	0.3	0.1	3.88	112.5	2.6	13.1
6112898	HIMANTH	53	M	Y	Y				108	5.9	11	G5	8.1	26.7	85.5	25.8	30.6	18.5	2.6	2.17	5.9	117	7.5	3.8	1.5	0.4	0.1	2.53	78	3.7	6.6
5874536	ANASUYA	43	F	N	Y				58.4	2.04	30	G3	9.9	31.2	77	24.2	31.4	18	3.36	3.21	11.1	371	9.6	8.4	1.9	0.1	0.7	4.42	195.2	19	8.1
7123478	SHOBHA	64	F	Y	Y	N	Y	N	79.4	4.4	11	G5	8.9	30.2	88.8	26.2	29.5	16.6	3.07	3.23	30.9	192	9.4	25.4	3.1	1.9	0.2	8.19	61.9	1.6	18.4
7117593	RAMESH	32	M	Y	Y				27.1	2.34	37	G3	13.7	42.5	88.5	26.3	30.6	12.9	4.63	0.51	8.8	249	8.3	5.9	2	0.7	0.2	2.95	124.5	2.8	7
7211611	WASIM	49	M	Y	N				88.4	5.3	12	G5	6.9	20.7	106..7	35.1	32.9	23.3	2.9	6.5	15.3	110	10.7	12	1.8	1.2	0.3	6.67	61.1	1.5	17.2
5755828	GANESH	23	M	N	N				84.7	7.03	10	G5	8.3	25.7	95.5	30.9	32.3	15.4	2.69	0.45	4.57	162	10	3.49	0.63	0.38	0.06	5.53	257.1	1.66	11.5
5806470	ARIF	31	M	Y	Y				137	6.1	9	G5	10	30.7	96.2	31.3	32.6	13	3.19	1.6	7.6	179	9.9	4.2	2.3	0.7	0.3	1.83	77.8	3.2	6.6
6443864	SUBBIAH	74	F	Y	N				22.7	2.51	20	G4	10.5	34.4	103.6	31.9	30.8	16.4	3.75	1.14	6.4	162	9.5	1.2	1.3	0.6	0.3	0.92	134.6	2.1	11.1
6486393	MARUTI	49	M	Y	Y				131	5.8	11	G5	10.1	30.6	89.3	29.6	33.1	16	3.4	1.9	3.6	200	7.8	2.1	1	0.3	0.2	2.1	200	3.3	7.8
7148893	GURUNAIK	82	M	N	N				36	1.83	37	G3	11.5	33.9	90.6	30.7	33.9	16.6	3.74	0.62	5.97	150	11.3	3.66	1.31	0.8	0.17	2.79	114.5	1.6	4.4
6972524	MARUTI	56	M	Y	Y				87.4	6.4	10	G5	7.7	23.6	95.4	31.1	32.6	14.1	2.47	0.71	4	131	10.5	3.2	0.4	0.3	0.1	8	327.5	1.3	13.5
7109353	BHARTI	52	F	Y	N				47	2.5	23	G4	10.2	31.7	85.5	27.4	82.1	15.1	3.71	0.44	12.5	245	7.4	11.4	0.9	0.1	0.1	12.67	272.2	9	22.1
6736527	UMESH	45	M	Y	N				114	5.4	13	G5	8.8	26.1	84.8	28.5	33.6	16	3.08	0.66	5.7	179	10.5	4.6	0.7	0.2	0.2	6.57	255.9	3.5	7.9
7182498	KRISHNA	64	M	Y	N	N	N	Y	123.5	6.4	9	G5	6.9	24.9	92.2	26.3	28.5	15.1	2.13	0.6	6.7	136	82	4.3	1.2	0.8	0.4	3.58	113.3	1.5	11.4
7187132	NIVRITI	60	M	Y	Y				27.7	1.82	42	G3	11.6	37.2	85.7	26.7	31.2	14.4	4.34	1.9	11.4	211	9.6	8	2	0.7	0.6	4	105.5	2.8	8.2
7181117	SATVEER	72	M	Y	Y				94.5	3.22	20	G4	11.5	35.6	85.4	27.6	32.3	14.7	4.17	0.7	3.3	99	11	2.2	0.4	0.4	0.3	5.5	247.5	1	10.1
7181027	VIJAYLAKSHMI	25	F	N	N	Y	N	N	97.4	5.02	12	G5	9.6	33.4	93	27.3	29.3	14.5	2.91	1.04	6.8	177	10	5	1.2	0.4	0.2	4.17	147.5	3	6.1
7180632	BARAKU	73	M	N	Y				42	1.67	43	G3	9.5	31.5	71.1	21.4	30.2	17.4	4.43	1.9	11	367	11.2	7.8	1.8	1.3	0.1	4.33	203.8	1.3	5.4
7179946	TUKARAM	74	M	Y	Y	N	N	Y	88.3	5.3	11	G5	11.9	33.3	84.6	30.2	35.7	12.8	4.04	1.3	8.7	189	8.1	7.4	0.3	0.7	0.2	24.67	630	0.4	22.9
7179910	MAHADEVI	52	F	Y	Y				87.4	3.49	15	G4	11.6	35	97.8	30.7	31.4	12.9	3.9	1.8	9.9	224	9.5	8	1.3	0.5	0.1	6.15	172.3	2.6	4.9
7178899	NAMDEV	60	M	Y	Y				71.9	3.08	22	G4	11.7	33.8	78.6	27.2	34.6	12.4	4.3	1	9.3	250	10.2	6.9	1.4	0.9	0.1	4.93	178.5	1.5	9.9
7178698	NAGRAJ	23	M	N	N	N	N	Y	48	1.2	87	G2	14.8	47.9	81.8	27.8	34	14.7	5.14	0.46	6.2	225	9	4	1.7	0.4	0.1	2.37	132.2	4.2	2.2
7176809	JAYANTI	81	F	Y	N				64.8	1.5	35	G3	8.9	30.2	88.8	26.2	29.5	16	2.9	0.8	12.8	254	9.2	8.9	2.8	0.8	0.3	3.17	90	3.5	13.4
7112762	SARASWATI	62	F	N	Y				84.4	4.19	11	G5	8.6	28.1	84.1	25.7	30.5	14.3	3.3	1.3	6.2	206	8.9	4.36	1.2	0.4	0.08	3.5	171.6	3	9.3
7293907	CHANNAVVA	50	F	N	Y				101	4.2	12	G5	8.5	27	81.8	25.8	31.5	13	3.01	1.2	9	200	9.1	7.4	1.3	0.4	0	5.69	153.8	3.2	7.9
7293004	SHOBHA	52	F	Y	N	N	N	Y	74	1.3	49	G3	10.5	32.3	81	25.1	31	15.5	4.03	0.61	11	478	11.7	7.2	3.1	0.6	0.2	2.32	154.1	5.1	3.3
7292851	YASHODHARA	50	F	Y	N				124	5.5	9	G5	4.1	25.7	95.5	27.9	30.3	15.1	1.47	0.77	6.4	218	10.1	4	1.7	0.4	0.3	2.35	128.2	4.2	9.1
7291461	SURYAKANT	66	M	N	Y	Y	N	N	64	1.83	40	G3	9	29.9	89	30.5	30.8	15.2	3.14	0.72	6.3	242	9.3	3.8	1.8	0.6	0.1	2.11	134.4	3	4.4
7291270	GAYATRI	48	F	N	Y				78.5	4.11	13	G5	9.5	33.8	78.4	22	28.1	16.4	3.23	0.8	8.2	198	9.9	6.8	0.7	0.7	0.1	9.71	282.8	1	14.3
7288825	NISHAD	60	M	Y	Y	N	Y	N	135	5.9	10	G5	9.2	29.4	95.8	30	31.3	14	3.07	1.9	9.3	207	11.5	6.3	1.9	0.7	0.4	8.32	108.9	2.7	13.4
7283414	MALAGOUDA	73	M	Y	Y	N	Y	N	77.1	2.97	22	G4	9.5	25.8	98.8	36.3	36.7	21.4	2.61	0.8	10.9	250	9	6.9	2.8	1	0.2	2.46	89.2	2.8	5.7
7282214	MALAPRABHA	66	F	Y	N	Y	N	N	47.7	1.2	50	G3	8.7	28.1	84.1	25.7	30.5	14.3	3.3	0.9	6	362	8.9	3.8	1.2	0.4	0.5	3.17	301.6	3	2.5
7150492	YANKAVVA	60	F	Y	N	Y	N	N	97.8	3.8	13	G5	8.8	29.1	80.3	24.4	30.8	18.3	3.6	2.3	5.1	182	8.4	2.9	1.6	0.4	0.1	1.81	113.7	4	1.5
7263917	PANDURANG	61	M	Y	Y				63.4	1.5	53	G3	6.4	24.4	92.1	25.7	27.9	13.3	2.5	0.8	9.2	100	9.1	7.5	1.1	0.6	0.1	6.82	90.9	1.8	6.7

7280595	HEMANTH	63	M	Y	Y				48.5	3.16	21	G4	10.5	33.4	99.7	31.3	31.4	14	3.35	2.6	7.8	270	8.7	5.4	1.5	0.6	0.3	3.6	180	2.5	7.9
7277649	FARUK	48	M	Y	Y	N	Y	N	57.4	4.02	17	G4	14.4	43.2	85.2	27.9	35.2	14.9	4.8	0.5	15	268	9.7	11.1	2.4	1.2	0.3	4.63	111.6	2	9.1
7277621	LAXMI	30	F	N	Y				53.7	1.4	52	G3	9.9	32.2	83.9	25.9	30.8	15.5	4.14	0.7	9.4	240	9.5	6.3	2.4	0.4	0.2	2.63	100	6	4.1
7274041	PARVATI	70	F	Y	N	Y	N	N	63.3	4.9	12	G5	9.4	28	91.1	30.5	33.5	18.2	3.07	1.8	9.1	173	7.9	8	0.4	0.6	0.1	20	532.5	0.6	24.3
7272804	ZAMEER	62	M	N	N	N	Y	N	107	4.2	15	G5	8.1	27.9	99.6	28.9	29	15.3	2.8	3.3	11.9	327	9.2	11.1	0.7	0.1	0	15.86	467.1	7	33.4
7258685	KASTURI	72	F	N	Y	N	N	Y	66.5	3.99	11	G5	9.7	31.8	96.7	30.1	31.1	17	3.2	0.64	10.1	340	9.3	8	1.4	0.6	0.1	5.7	242.8	2.3	15.1
7258429	SHANTAVVA	53	F	Y	N	N	Y	N	73.9	4	13	G5	5.4	19.5	92.9	25.7	27.7	15.4	2.1	2.1	2.8	162	10.8	1.6	1	0.1	0.1	1.6	162	10	4.6
7255471	PREMA	35	F	Y	N				30.9	1.1	67	G2	8.1	27.9	77.7	22.6	29	13.7	3.5	1.2	10.2	330	11.1	5.9	3.5	0.6	0.2	1.69	94.2	5.8	1.7
7252987	SANAVVA	55	F	Y	N	Y	N	N	77.9	1.75	34	G3	11.8	39.6	97.1	28.9	29.8	13.1	4.08	1.8	8.8	296	10.4	4.9	2.8	0.8	0.4	1.75	105.7	3.5	3.3
7252059	SHAVARAB	58	F	Y	Y				72.2	6.1	10	G5	9.5	29.1	81.7	26.3	32.2	13.7	3.4	0.9	6.1	225	7.2	3.8	1.6	0.4	0.2	2.38	140.6	4	6.9
7251229	SUVARNA	34	F	Y	N	Y	N	N	28.8	1.1	68	G2	12.2	35.9	97.6	31.5	32.3	13.2	4.6	1.5	6.7	285	11	4.2	1.7	0.5	0.2	2.47	167.6	3.4	5.1
7260103	GURUBADAPPA	52	M	Y	N				68.1	1.14	58	G3	9.8	29.5	96.7	32.1	33.2	13.6	3.05	2.6	3.7	193	10.5	1.1	1.7	0.3	0.6	0.65	113.5	5.6	4.9
6854665	MANJUNATH	32	M	Y	N				105	2.8	30	G3	8.9	29.1	23.9	28.7	30.6	14.3	3.1	0.6	5.4	175	10.5	3.6	1.2	0.4	0.2	3	145.8	3	6.6
4461634	MAHANANDA	52	F	Y	Y				79.4	5.3	9	G5	10.2	33.1	97.6	30.1	30.8	6.9	3.3	1.4	5.3	133	10.6	2.5	1.5	0.4	0.8	1.67	88.6	3.7	7.1
3491836	SHIVAJI	65	M	N	Y				112.5	5.5	11	G5	9.3	30.5	93	28.4	30.5	18.3	3.2	1.8	7.8	185	9.8	5.3	1	1	0.5	5.3	185	1	33.7
6329196	GURUSIDAPPA	72	M	Y	Y				77	4.29	14	G5	10.6	35.8	101.7	30.1	29.6	14.4	3.52	1.5	4.1	134	11	2.1	1.4	0.4	0.2	1.5	95.71	3.5	6.2
3556107	NAGOJI	73	M	N	Y				78	5.8	10	G5	7.3	20	82.3	25.9	31.5	13.3	3.37	1.2	15.2	217	9	13.4	0.6	0.9	0.3	22.3	361.67	0.6	16.7
7341433	VIKRANT	56	M	Y	N				107	5.3	12	G5	9.1	29.5	92.8	28.6	30.8	15.3	3.18	1.5	12.8	170	12.9	9.2	2.4	1	0.3	3.83	70.83	2.4	22.2
5933058	OMANI	77	M	Y	Y				86.2	7	8	G5	9.2	28.8	95.7	30.6	31.9	15.3	3.01	0.9	5.3	123	10.4	3.9	0.9	0.3	0.2	4.33	136.67	3	12.2
7172358	RODRIGUE	59	M	N	Y				93	5	13	G5	9.3	29.3	100	31.8	30.8	13.3	2.9	0.5	7.6	151	9.5	5.6	1.1	0.4	0.15	5.09	137.27	2.7	7.2
4923051	SANTOSH	40	M	Y	N				67.1	5.1	14	G5	9.5	31.1	93.1	28.4	30.5	15.8	3.3	0.8	5.5	182	10.3	3.3	0.9	0.7	0.5	3.67	202.22	1.2	7.1
7370983	YALLAPPA	56	M	Y	Y				45	4.5	15	G5	10.3	33	103.4	32.3	31.2	13.7	3.19	0.5	9.19	228	10.4	5.4	2.1	0.6	0.18	2.57	108.57	3.5	11.6
6940951	GANGAPPA	61	M	N	Y				65	4.2	15	G5	7.6	22.6	101.1	32	31.7	14.9	3.9	0.8	8.5	225	10.5	6.3	1.1	0.7	0.4	5.73	204.55	1.5	5.9
5137099	VANDANA	51	F	N	Y				97	3.8	14	G5	10.6	35.4	91.2	29.6	32.5	12	3.3	1.2	6.6	280	8.7	5.5	0.7	0.2	0.2	7.86	400	3.5	9
7241925	BASSAPPA	65	M	N	Y				38.6	1.6	48	G3	9.5	33	86.6	24.9	28.8	17.8	3.81	2.5	16.9	392	10.9	9.8	5.5	1.3	0.3	1.78	71.27	4.2	3.1
7240326	JAKKAPPA	75	M	Y	N				62.9	2.9	22	G4	9.4	29.9	92	28.9	31.4	14.8	3.2	1.1	7.9	213	9.9	4.4	2.7	0.5	0.2	1.63	78.89	5.4	4.5
7239638	RATIK	22	M	N	N	Y	N	N	34.9	2.44	38	G3	16.6	49.9	82.4	27.6	33.5	13.2	6.01	1.8	9.4	301	10.2	5.6	2.5	1	0.2	2.24	120.4	2.5	2.7
7238861	SADU	55	M	Y	Y				56.1	2.5	30	G3	13.3	45.9	97.6	31.5	32.3	13.2	4.7	1	11	280	11	7.2	1.9	1.1	0.7	3.79	147.37	1.7	6.6
7237797	JOTIBA	82	M	N	Y				81.1	1.78	38	G3	11.6	35.7	89.4	27.6	30.9	15.5	3.4	1.1	7.5	175	10.5	6.1	0.5	0.8	0.1	12.2	350	0.6	8.1
7235252	SUSHILA	82	F	Y	Y				71	2.14	23	G4	7.6	25.9	82.1	26.1	32	16.3	2.78	0.9	12.4	145	9.8	10.3	1.3	0.7	0	7.92	111.54	1.8	12.2
7232954	ARVIND	67	M	Y	Y				38.1	1.5	51	G3	13.8	44.4	89.2	27.9	33.2	15.2	4.5	0.8	8.5	252	9.2	4.7	3	0.6	0.1	1.57	84	5	2.5
7232940	BASAVRAJ	60	M	Y	Y				50.1	1.7	46	G3	9.9	31.8	82.6	25.7	38.1	14.4	3.8	1.4	3.8	124	10.4	2.6	0.8	0.4	0	3.25	155	2	4.9
6760629	GOPAL	64	M	Y	Y				155	5.1	12	G5	7.3	27.8	86.9	26.9	30.9	15.3	2.3	0.7	11.3	276	10.7	8.8	1.2	0.7	0.6	7.33	230	1.7	15.1
7123302	MAHADEVAPPA	62	M	Y	Y				98	6.08	10	G5	9	30.2	84	25.6	30.5	13.2	3.5	1.2	9.6	211	11.9	6.9	1.6	1	0.1	4.31	131.88	1.6	9.9
5243811	SHRISHAIL	60	M	Y	N				78	5.2	12	G5	10	35.4	89.3	27.6	30.5	14.6	3.4	1.2	5.5	145	8.7	4	0.9	0.4	0.2	4.44	161.1	2.2	11.6
6285438	BHIMAPPA	58	M	Y	N				128	4.5	14	G5	9.3	31.7	98.1	28.8	29.3	15.5	3.2	0.9	5.7	155	9.8	4.2	0.8	0.5	0.2	5.25	193.7	1.6	14.1
6368759	GIRUADEVI	73	F	Y	Y				103	4.6	10	G5	10.8	36.9	99.7	29.2	29.3	16.5	3.7	1.5	7.3	230	10.6	5.5	1.1	0.6	0.1	5	209.09	1.8	16.3
7212023	BABLOO	55	M	Y	N				83	5.1	11	G5	9.7	31.7	70.5	21.6	30.6	16.1	4.2	1.2	4.3	102	8.3	3.5	0.6	0.1	0	5.83	170	6	6.9
7210515	NINGAPPA	44	M	Y	Y				106	4.8	14	G5	10.1	35.8	99.4	28.1	28.2	16.7	3.8	1.3	6.2	243	8.9	4.5	1.2	0.4	0.1	3.75	202.5	3	6.8
6977218	SHILPA	28	F	N	Y				102	6.1	9	G5	10.5	34.6	91.1	27.8	30.5	14.6	3.79	0.5	6.19	274	9.4	4.88	0.8	0.4	0.11	6.1	342.5	2	15.8
4881180	SHAILAJA	45	F	Y	N				67	3.9	14	G5	8.1	29.1	104.4	29.1	27.8	16.8	2.7	0.5	8.4	207	8.6	6.4	1.2	0.5	0.3	5.33	172.5	2.4	9.9
7307504	MURUGESH	51	M	Y	Y				113	5.9	11	G5	8.1	24	88.2	29.9	34	17.6	2.7	1	2.9	100	8.8	2.2	0.4	0.3	0	5.5	250	1.3	28.7
6770861	GIRAMALLA	60	M	Y	Y				67	3.2	16	G4	8.4	31.3	105	28.2	26.8	17.1	2.9	0.5	5.5	212	9.5	4.08	0.8	0.3	0.1	5.1	265	2.6	11.4
7180950	RAVINDRA	46	M	Y	N	Y	N	N	98	7.1	9	G5	6.6	19	93.6	29.1	31.1	17.9	2.4	0.89	4.8	128	8.3	4.1	0.4	0.2	0	10.25	320	2	9
6019086	BASSAPPA	58	M	Y	Y				125	5	13	G5	12.4	40.4	94	28.8	30.7	14.8	4.3	2.1	6.8	116	9	5.1	0.9	0.6	0.2	5.6	128.8	1.5	8.8
7075819	PUPSHLATA	56	F	N	N	Y	N	N	89	1.3	48	G3	11.6	38.1	88.8	27.7	31.2	15.1	3.8	1.04	8.3	301	11.9	5	2.3	0.7	0.3	2.17	130.8	3.2	8.4
7075117	MALLAPPA	68	M	N	Y				37.5	1.8	40	G3	12.8	41.2	93.6	29.1	31.1	12.7	4.4	1.1	8.1	199	10.1	5.2	1.7	0.6	0.4	3.05	117.06	2.8	3.1
7057052	MARIYAM	54	F	Y	Y				93.4	4.9	10	G5	6.8	24.4	92.1	25.7	30.9	16.3	2.5	0.7	14.6	341	9.6	10.8	2.8	0.7	0.3	3.86	121.7	4	7.9
7072053	TANGEVVA	65	F	Y	Y				105	3.5	14	G5	10.5	34.8	79.4	25.3	31.8	14.6	3.4	0.68	10.8	220	9	7	2.9	0.2	0.6	2.41	75.86	14.5	5.9
7071632	RAVEENDRAGOUDA	27	M	Y	N	Y	N	N	47.1	1.5	65	G2	12.8	40.7	88.7	27.9	31.4	13.2	4.5	1.9	11	270	10.3	6.4	3.6	0.8	0.2	1.78	75	4.5	1.1
7070429	PREMANAND	65	M	Y	Y				80.1	4.5	14	G5	11.6	37.1	83.4	24.5	29.4	12.1	3.6	1.18	8.4	242	9.7	4.5	2.6	0.6	0.6	1.73	93.08	4.3	2.9
7062616	JANUBAI	66	F	N	Y				45.7	2.5	21	G4	12.4	42.5	88.5	26.3	29.6	12.9	4.1	1.2	9.4	289	8.5	5.5	3.1	0.5	0.3	1.77	93.23	6	1.7
7060274	GAJANAND	50	M	Y	N				123	5.6	12	G5	9	38.9	81.9	25.7	31.4	17.9	3.1	0.98	7.5	193	8.2	5.4	1.2	0.8	0	4.5	160.8	1.5	10.1
7059751	GURUPADAPPA	64	M	Y	Y				38.9	1.5	52	G3	11.5	35.4	91.2	29.6	32.5	12	3.8	0.9	6.7	265	8.9	4.5	2	0.2	0	2.25	132.5	10	1.6
7051005	PRAKASH	31	M	N	N	N	Y	N	91.8	6.2	12	G5	8.1	26.3	82.4	26.3	31.9	17.1	3.88	1.1	11.3	323	9.3	8.1	1.7	0.9	0.5	4.76	190	1.8	13.2
7093592	SHANKAR	64	M	Y	N				71.4	6.1	10	G5	5.2	28.9	88.9	26.8	30.1	15.4	1.7	1.5	4.9	81	9.8	3.5	0.6	0.4	0.4	5.83	135	1.5	9.2
7093513	SWATI	29	F	N	N	Y	N	N	34.6	1.2	63	G2	13.2	48.1	89.4	27.7	31.5	13.7	5.1	0.95	12.1	419	9.1	7.3	3.4	0.7	0.7	2.15	123.24	4.8	2.8
7073815	NEELLAVVA	51	F	N	Y				47.1	1.4	45	G3	11.2	38	80.3	25.8	32.2	16.7	4.7	0.8	7.2	294	8	4.6	1.7	0.5	0.3	2.71	173.53	3.4	3.1
7126270	SAROJINI	55	F	Y	Y				107	4.8	10	G5	8	26.8	83.2	26.1	31.3	16.7	3.6	1.1	4	150	8.2	3.2	0.6	0.2	0	5.33	250	3	13.9