# HEMATOLOGICAL CHANGES IN PRE AND POST HEMODIALYSIS IN PATIENTS WITH CHRONIC RENAL FAILURE

By

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**Under the Guidance of**

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## LIST OF ABBREVIATIONS USED

| | |
|---|---|
| CKD | Chronic Kidney Disease |
| CRF | Chronic Renal Failure |
| ESRD | End Stage Renal Disease |
| Hb | Hemoglobin |
| RBC | Red Blood Cell |
| WBC | White Blood Cell |
| TLC | Total leucocyte count |
| HCT | Hematocrit |
| PCV | Packed Cell Volume |
| RDW | Red cell Distribution Width |
| MCV | Mean Corpuscular Volume |
| MCH | Mean corpuscular hemoglobin |
| MCHC | Mean corpuscular hemoglobin concentration |
| ESA | Erythropoietin stimulating agents |
| RRT | Renal replacement therapy |
| HD | Hemodialysis |
| EPO | Erythropoietin |
| ADH | Anti-diuretic hormone |
| GFR | Glomerular filtration rate |
| KDIGO | Kidney Disease Improving Global Outcomes |

| | |
|---|---|
| GN | Glomerulonephritis |
| LMICs | Low middle-income countries |
| PTH | Parathyroid hormone |
| ANA | Antinuclear antibodies |
| CT | Computed tomography |
| MRI | Magnetic Resonance Imaging |
| CVD | Cardio vascular disease |
| LVH | Left ventricular hypertrophy |
| CKD-MBD | Chronic kidney disease- mineral bone density |
| PEW | Protein energy malnutrition |
| CAD | Coronary artery disease |
| CRP | C- reactive protein |
| AVF | Arterio venous fistula |
| AVG | Arterio venous graft |
| WHO | World Health Organization |
| NKF | National Kidney Foundation |
| LDL | Low density lipoprotein |
| VDRL | Venereal Disease Research Laboratory |
| CAPD | Continuous Ambulatory Peritoneal Dialysis |
| MHD | Mulberry Heart Disease |
| BMI | Body Mass Index |

| | |
|---|---|
| BUN | Blood urea nitrogen |
| IgE | Immunoglobulin E |
| EDTA | Ethylene diamine tetra acetic acid |
| PCR | Polymerase chain reaction |
| MCHC | Microcytic hypochromic |
| NCHC | Normocytic hypochromic |
| NCNC | Normocytic normochromic |

# ABSTRACT


## BACKGROUND

Renal diseases are among the major causes of morbidity and mortality in several countries throughout the world. Chronic renal failure (CRF) is a syndrome in which there is progressive and irreversible destruction of kidney function because of gradual damage of parenchyma of kidney. Chronic kidney disease (CKD) is known to be a global public health problem. It may be detected by using simple laboratory tests, and treatment can prevent or delay the complications of decreased kidney function, retard the progression of kidney disease. Hematological parameters like WBC, RBC, Hb, HCT, MCV, MCH, MCHC, RDW and Platelet can be altered after hemodialysis.

So, to evaluate the effectiveness of hemodialysis, it is necessary to test the complete hemogram before and after hemodialysis.

## OBJECTIVES

- To study hematological changes in patients suffering from chronic renal failure before and after hemodialysis.

## MATERIALS AND METHODS

The patients suffering from chronic renal failure admitted in dialysis unit at B.L.D.E. University's SBMPMC, Hospital and Research Centre, Vijayapura were included in this study.

The study period was from 1$^{st}$December, 2015 to 30$^{th}$ June, 2017.

- Two milliliters of blood were collected from chronic renal failure patients before and after hemodialysis, in an ethylene diamine tetra acetic acid (EDTA) vacutainer and immediately analyzed for a complete hemogram, including Hb, RBC count, and RDW, using an automated 5-part differential hematology analyzer.
- A peripheral smear was prepared from the same sample and visually examined for morphological typing of anaemia. All observations were recorded in the proforma sheet as per format.

  Statistical correlation between various parameters was performed and data analyzed.

**RESULTS**

- There was statistically significant difference with changes in values of Hb, WBC, MCH, MCHC and HCT, which got increased after hemodialysis as compared to predialysis cases. Platelet count was found to be decreased after dialysis as compared to predialysis cases.
- The most common type of anaemia was normocytic normochromic type.

**CONCLUSION**

Most of the hematological parameters change after hemodialysis as compared to that of predialysis cases. So, to evaluate the effectiveness of hemodialysis, it is necessary to test the complete hemogram before and after hemodialysis in chronic renal failure patients.

**KEY WORDS**

Anaemia, chronic renal failure, hemoglobin.

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# INTRODUCTION

Chronic Kidney disease (CKD) is a rapidly growing major morbidity worldwide. It leads to progressive destruction of renal tissue with irreversible sclerosis and loss of nephrons. The Kidney Disease Outcomes Quality Initiative designates 5 stages of CKD, with stage 5 being ESRD, the point at which patients' loss of kidney function need dialysis or kidney transplant.[1]

In CKD, hematological parameters are commonly affected. Red cell, WBC, HCT and hemoglobin indices are commonly and severely affected. Several authors noted total white cell count, platelet count and bleeding time of normal ranges but striking eosinophilia and prolonged bleeding time. This is because major part of erythropoietin i.e. 90%, produced in the juxta glomerular apparatus of the kidney and rest i.e. 10 % are produced in the liver and other organs[2].

Most common complication in chronic kidney disease is anemia. The severity of anemia is directly proportional to the degree of renal function. (ESA) Erythropoietin–stimulating agents are used to correct anemia and to maintain hemoglobin level[1].

Increasing rate of chronic renal disease is a huge problem among both healthcare and economy in future years[3]. More than 1.1 million cases are presented with renal failure throughout the world with yearly rise at a rate of 7%. The incidence & prevalence count in USA per million population rise by 32 and 70% from 2000 to 2015 [4], the incidence and prevalence rate in USA are supposed to rise by 44 and 85% respectively. The incidence rate of end stage renal disease as per age was found to be

229 per million population in India and more than one lakh new patients get renal replacement therapy (RRT) yearly[3].

Prevalence of CKD in India, Bangladesh and Pakistan is around or >20% in few communities, and in Nepal and Sri Lanka the prevalence estimates to be between 10-20% in a study conducted in east Asia. Estimates vary from 10 to 19% in the Tibetan region in China which is equivalent to around 120 million cases residing in China and Malaysia with chronic renal disease, the prevalence has been reported to be approximately 10%[5].

Hypertension & diabetes are responsible for >2/3$^{rd}$ of the cases of chronic renal disease in western countries, and 40–60% in India. According to data as per Indian Council of Medical Research, in adult individuals of India, prevalence of diabetes increased to 7.1%, (ranging from 5.8% in Jharkhand to 13.5% in Chandigarh) & in urban population (>40 years age), the prevalence has increased to 28%. Hypertension accounts for 17% prevalence (21.4% in urban and 14.8% in rural) in the adults [6].

At the end of 2011, the number of patients being treated for ESRD globally was estimated to be 2,786,000 with a 6-7% growth rate, continues to increase at a significantly higher rate than the world population. Approximately 2,164,000 were undergoing dialysis treatment and around 622,000 people were living with kidney transplants of these 2,786,000 ESRD patients[7].

In India, the first hemodialysis was performed in 1961.50 years later there are more than 800 centres in the country providing hemodialysis. Hemodialysis was

introduced in Southern India in 1963, at the Christian Medical College and Hospital, Vellore, South India[8].

However, in India the number of patients / pmp on maintenance hemodialysis is far less than in the developed nations, and even countries in southeast Asia[9].

There are many side effects of dialysis on the various blood components. It reduces red blood cell (RBC) count, hemoglobin (Hb) level and; higher in females as compared to males, and in old aged patients due to decreased concentration of erythropoietin. Hemodialysis through removal of juvenile and highly active platelets, reduces the percent of RNA-rich platelets while it does not alter programmed cell death of monocytes or neutrophils. Due to the expensive transplantation and problem in searching a compatible organ donor, the most common type of replacement therapy for kidney is dialysis throughout the world. Nearly, 100 white people per million population (pmp) need replacement therapy for kidney in the United Kingdom every year[10].

## OBJECTIVES

- To study hematological changes in patients suffering from chronic renal failure before and after hemodialysis.

# REVIEW OF LITERATURE

Several authors researched on hematological parameters pre- & post hemodialysis.

Abdullah Khader Alghythan *et al*[4] reported hematological parameters pre- and post-hemodialysis in CRF patients. They noted that many of the hematological parameters got increased after dialysis. The significant rise of Hb, RBC count, PCV and red cell distribution width (RDW) was present in patients after hemodialysis in comparison to before hemodialysis.

Wasti AZ *et al*[1] found that distinction between mean of Hb, RBC count and PCV were significantly reduced both in chronic kidney disease patients and in kidney transplant patients, similarly, MCH and MCHC indices also showed significant fall in both the types of patients. WBC count were raised in CKD patients and marginally raised in kidney transplant patients but not statistically significant, the differential WBC count like lymphocytes reduced in both types of patients but Monocytes reduced in CKD and got increase in kidney transplant patients. MCV, Platelets and granulocytes were normal in both types of patients.

Yassin M. *et al*[7] noted hematological parameters in patients on hemodialysis and observed that platelet and WBC count were slightly increased in hemodialysis patients in comparison to healthy individuals. But Hb, RBC and PCV were observed to be reduced in hemodialysis patients.

Mohd Ali MS *et al*[10]studied hematological indices post hemodialysis in CRF patients in Sudan. They observed that Hb, PCV and RBC count were higher post dialysis. The leucocyte count was also slightly higher post hemodialysis. Prothrombin time and partial thromboplastin time were also higher post hemodialysis.

Suresh M *et al*[11] studied hematological parameters in CRF patients. They observed that there was a significant fall in Hb concentration, RBC count, hematocrit and platelet count. TLC was also reduced but not statistically significant.

Bhatta S *et al*[12]compared hematological indices in chronic kidney disease patients before and after hemodialysis. They observed that there was a fall in levels of Hb and Hct after hemodialysis in comparison to predialysis. Macrocytic normochromic anemia and microcytic hypochromic was more after dialysis as compared to predialysis.

Dorgalaleh Akbar *et al*[13] showed that some red blood cell indices including RBC count and Hb, MCHC and HCT levels were significantly reduced in-patient group as comparison to healthy non- renal affected people($P<0.05$) and anemia was considerable in acute renal failure patients and mild fall in platelet count was also observed in some patients.

S Arun *et al*[14] observed hematological parameters in CKD patients and found that despite most of the anemia was normocytic type, around a third of the patients had microcytic hypochromic and a mixed type of anemia. Those with a microcytic hypochromic picture correlated with a severe degree of anemia.

Dara K M *et al*[15] studied that the RBCs, Hb concentration, PCV and WBCs were significantly more post dialysis.

Kaze FF *et al*[16] observed that at baseline, 75 (79%) patients on chronic hemodialysis got anemia, which was microcytic and hypochromic in 32 (43%).

Aditya I *et al*[17] studied that the anemia was prevalent in CKD patients by 92%. The degree of anemia was severe in females in comparison to males and there was rise in the prevalence of anemia with age. 24% patients were observed to be seropositive with HCV and HBV infections.

Pandian J *et al* [18] studied that the anemia of moderate degree was present before & after hemodialysis, and, the severity of anemia was higher post hemodialysis in most of the cases. Normocytic normochromic was found to be the type of anemia. The reduction was statistically significant in TLC and platelet count ($p < 0.05$). Variations in differential count with a reduction in neutrophil along with monocyte count and higher lymphocyte as well as eosinophil count, found to be significant. The findings of the same study revealed that most of the hematologic indices seen in after dialysis were whether increased or reduced as compared to pre-dialyzed parameters. The current study can guide the clinicians to start taking preventive measures pre- & post-dialysis procedures and thus decreasing anemia, hemorrhage, thrombosis & associated complications.

Daugirdas J T*et al*[19] studied that a number of cases on chronic hemodialysis have been reported in which a marked reduction in platelet count (50% or more) during dialysis was seen, concluding to mild degree of decrease in platelet count before hemodialysis. In only one case, the platelet count was decreased, associated with bleeding. Typically, the platelet count gets slightly reduced during the first hour of dialysis, but most of the times, returns to early values by the end of dialysis.

Bhattacharjee K *et al*[20]studiedthat the anemia was present in all cases. It was observed that the prevalence of anemia was seen in 94% cases, leukopenia was found in 7% cases and thrombocytopenia in 56% cases.

Khanam S *et al*[21] studied that the Hb concentration, RBC, PCV and TC shows significant fall (P<0.001) in mild, moderate and severe Chronic renal failure patients as compared to those of healthy subjects. Again, these parameters were also significantly reduced (P<0.001) in severe CRF than those of mild, moderate and also in moderate than those of mild CRF patients.

Latiwesh OB *et al*[22] observed a significantly reduced (p< 0.05) hemoglobin levels (Hb), RBC count, and hematocrit in CKD patients as compared to healthy controls. Platelet count was reduced (p< 0.05) in hemodialyzed CKD patients than that of predialyzed. The prevalence of anemia in hemodialyzed-CKD patients was markedly increased (96% and 100% for males and females respectively) and double that of the predialyzed CKD patients (53% and 52% for males and females respectively).

Stauffer M E *et al* [23] studied that the prevalence of anemia was higher with the stage of CKD, from 8.4% at stage 1 to 53.4% at stage 5.

Khaswnah N *et al*[24] observed in his study on hematological and biochemical Parameters in Jordanian patients with end stage renal disease that the patients got anemic (hemoglobin 8.99).

Afshar R *et al* [25] studied that in the hemodialyzed patients, the severity of anemia was mild (Hgb > 10 g/dL) in 5%, moderate in 70% and severe (Hgb< 7 g/dL) in 25%, while in pre-dialyzed, it was mild in 45% and moderate in 55%.

Suega K *et al* [26]studied the profile of anemia in pre-dialytic and dialytic CRF patients and observed that majority of the anemic cases were normocytic normochromic.

Hakim Y AH *et al* [27] found that 99.5% of the patients got decreased platelets count post hemodialysis, while 0.5% have stable count of platelets, 98.5% of patients had reduced hemoglobin concentration post dialysis, 83.9% showed higher total white blood cells count post dialysis,14.1% had stable white blood cell count and only 2% got their count reduced from pre-dialysis count.

**KIDNEY**

The kidneys are the main organs of the urinary system. Their main function is to filter blood in order to remove wastes and excess water[28]. The waste and water are excreted as urine. The kidneys also reabsorb and return to the blood needed substances, including amino acids, sugar, sodium, potassium, and other nutrients. About 200 quarts of blood per day is filtered by kidneys and it produce about 2 quarts of waste and extra fluid. This urine flows through tubes called ureters to the bladder. Urine is stored in bladder until it gets eliminated through the body from urethra[29].

**KIDNEY ANATOMY**

Shape of the kidneys is bean-like and they are red in color, situated in the middle part of the back, each on the either side of spinal cord. It is around 12 cm in length and 6 cm in width. The inner renal part has a region known as **renal medulla**. Medulla is comprised of structure known as renal pyramids[30]. P**yramids** of kidney comprise of blood vessels and tube-like structures that collect filtrate. Medulla is dark colored than outer **renal cortex**. Between medulla, cortex gets extended to make sections called renal columns. R**enal pelvis** collects the urine & pass over to the ureter. Renal blood is supplied through the artery called renal artery. Processed blood after removal from kidneys gets returned to the circulation from blood vessels known as renal veins[31].

Every kidney contains > 1 million nephrons. They are extended through cortex and medulla. **They** are responsible for filtering blood. Each nephron consists of a **glomerulus** and a **tubule**. Each glomerulus is a ball-shaped cluster of capillaries. It functions like filter by allowing small waste substance & fluid to pass, whereas inhibiting larger molecules (large proteins, blood cells, etc.) from passing through to the nephron tubule. waste products and excess fluid. The excess fluid and waste products and are removed in the nephron tubule and, needed substances are reabsorbed back into the blood[32].

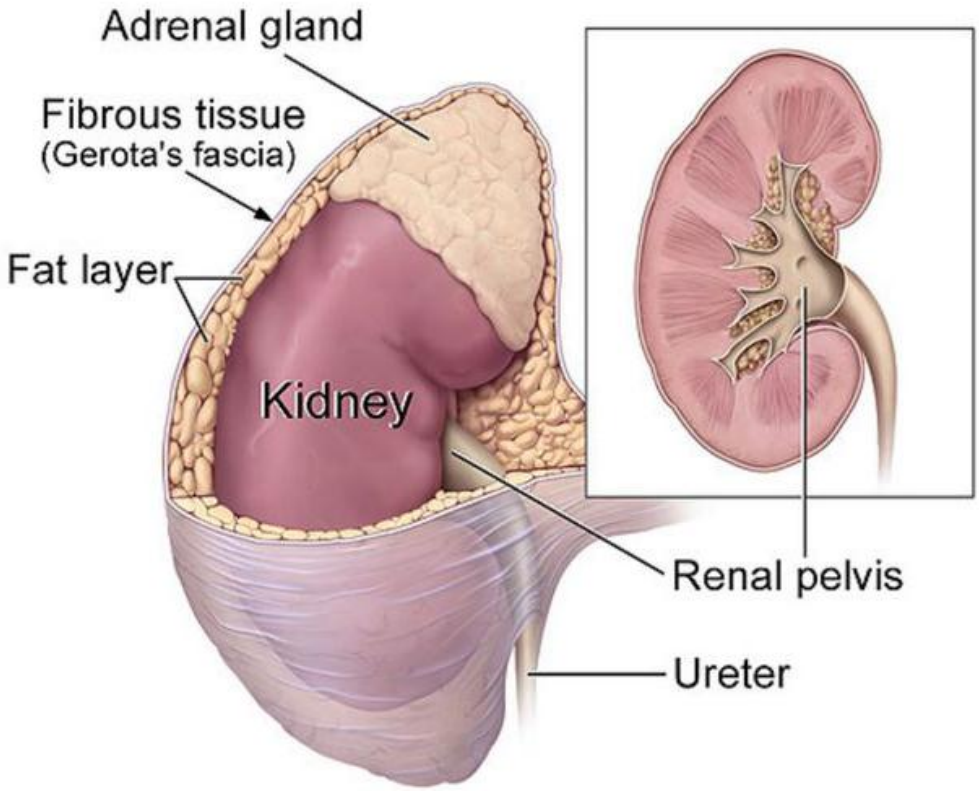


**Fig No.1. Showing structure of kidney**

**KIDNEY FUNCTION**

A. Kidneys remove toxins through the circulation. The kidneys serve many functions which are essential to life[33].

B. The kidneys secrete hormones, essential for normal function. These hormones include:

- **Renin -** controls blood pressure.
- **Erythropoietin (EPO)** - stimulates bone marrow to synthesize RBCs[35].
- **Calcitriol -** active form of vitamin D, maintains calcium for bones and for normal chemical balance[36].

C. The kidneys guide in maintenance of homeostasis of the body through regulation of ion balance, water balance and acid-base levels in fluids[34].

D. Renal function may get affected by adrenal glands. Each adrenal gland is present on both kidneys. They synthesize many hormones, such as hormone aldosterone. Aldosterone makes the kidneys to retain water and sodium & secrete potassium. Aldosterone causes elevation of blood pressure [39].

E. The kidney controls the amount of water excreted from the body by working in conjunction with brain. The hypothalamus produces antidiuretic hormone (ADH), when blood volume is low[37]. ADH is stored in and secreted by pituitary gland. This hormone makes the tubules in the nephrons to get more permeable to water allowing the kidneys to conserve water[38].

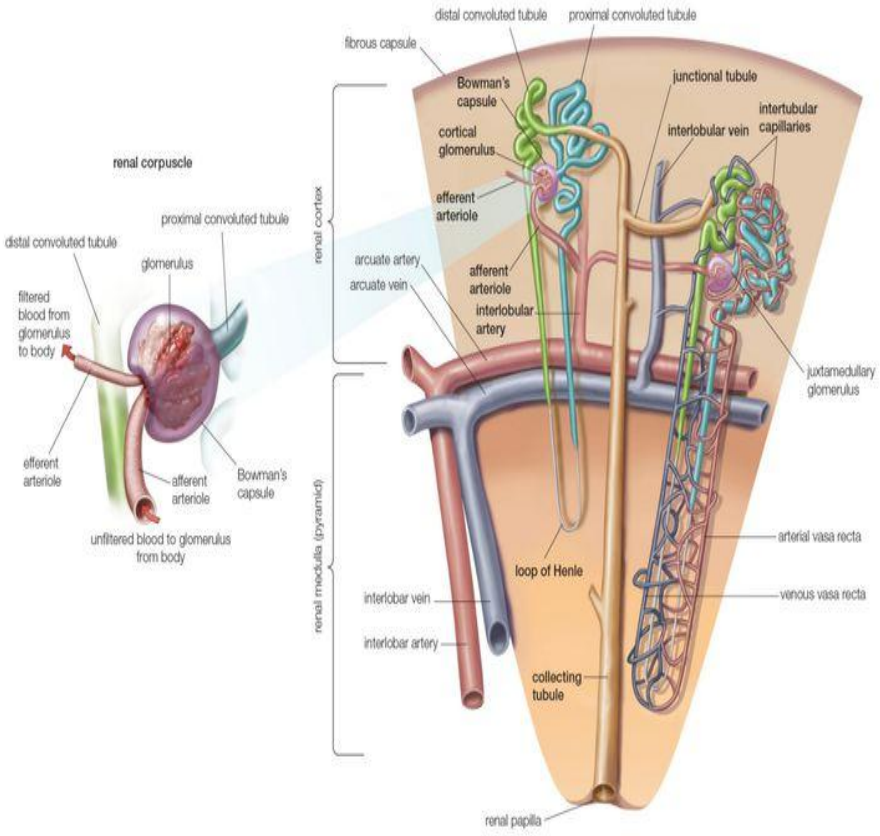


**Fig. No. 2. Nephron and its structure**

F. Nephrons causes the actual filtration of blood . Each nephron comprises of a **glomerulus**, a cluster of capillaries, enclosed by a cup-shaped structure called the glomerular capsule & **nephron tubule** which is surrounded through extra capillary bed. The glomerulus filters waste from the blood through the thin capillary walls. Blood pressure forces the filtered substances into the glomerular capsule and along to the nephron tubule[40]. The nephron tubule is where secretion and reabsorption take place. Some substances such as proteins, sodium, phosphorus, and potassium are reabsorbed into the blood, while other substances remain in the nephron tubule. The filtered waste and extra fluid from the nephron are passed into a collecting tubule, and then to the renal pelvis. From the renal pelvis it goes to the ureter and finally drain to the bladder for excretion[41].

## BLOOD AND ITS COMPONENTS

### The Blood

Blood constitutes about 8% of the human body weight. It is composed of erythrocytes, leucocytes, thrombocytes (platelets) and plasma. Volume percentage of all blood cells is about 45% (hematocrit) and rest consists of liquid plasma which includes water, plasma proteins, electrolytes in an adult human[42].

### Red blood cells:

Red blood cells are disc shape in structure. Their shape helps increase the surface area which enables oxygen and carbon dioxide to diffuse across the red blood cells plasma membrane more readily[43]. Red blood cells contain enormous amounts of a protein called hemoglobin. This iron containing molecule binds oxygen as oxygen molecules enter blood vessels in the lungs. Mature red blood cells do not contain a nucleus, mitochondria, or ribosomes, which enables room for the hundreds of millions of hemoglobin molecules found in red blood cells. Because of their shape, red blood cells pass through tiny blood vessels to deliver oxygen to organs and tissues[44].

Red blood cells are also important in determining human blood type. Blood type is determined by the presence or absence of certain identifiers, called antigens present on the surface of red blood cells. These antigens help the body's immune system to recognize its own red blood cell type[45].

### The white blood cells:

White blood cells are also called leukocytes. Origin of WBCs are stem cells of bone marrow and then they flow in the blood and lymph fluid. They can leave blood vessels to go to the body tissues. White blood cells are classified as granulocyte or an

agranulocyte, by the apparent presence or absence of granules (sacs containing digestive enzymes or other chemical substances) in their cytoplasm[46].

There are three types of granulocytes: neutrophils, eosinophils, and basophils. Granules in these white blood cells are apparent when stained, as seen under microscope. The most prevalent granulocyte in blood is neutrophil, having a single nucleus that appears to have multiple lobes. They are chemically drawn to bacteria and migrate through tissue to the site of infection. Neutrophils are phagocytic in nature. They engulf the target cell (bacterium, diseased or dead cell, etc) and destroy it. Neutrophil granules act as lysosomes to digest cellular macromolecules, when released. Nucleus of eosinophil has two lobes and is usually U-shaped in the smears. They are usually found in the connective tissue of intestine & stomach. They have phagocytic activity and mainly targets complexes of antigen-antibody. During parasitic infections and allergic reactions, eosinophils become increasingly active. Basophil is the least in number out of total WBCs. Their nucleus has many lobes. Their granules have heparin & histamine. Heparin make the blood thin and prevents clot production. Histamine helps to transport leukocytes to infected areas by dilating blood vessels, raises the permeability of capillaries, and blood flow. Basophils are responsible for the body's allergic response[47].

There are two types of agranulocytes: lymphocytes and monocytes. The nucleus of agranulocytes is characteristically large because of the paucity of granules in the cytoplasm. Following neutrophils, the most common type of WBC is lymphocyte. The shape of the lymphocyte is spherical, having enlarged nucleus and scant cytoplasm. The three main classes of lymphocytes are: B cells, T cells & natural killer cells. B cells & T cells are essential for specific response of the immune system.

Natural killer cells give nonspecific immunity. Out of the total WBCs, the largest cell is the monocyte in the blood smear. Their nucleus is solitary, enlarged with kidney shape. They develop into macrophages and dendritic cells, when migrate from blood to tissues. Macrophages are the large cells present in almost all the tissues. They actively participate in the function of phagocytosis. Dendritic cells have been named so because they have projections that are similar in appearance to the dendrites of neurons. Dendritic cells are commonly found in tissue located in areas that come in contact with antigens from the external environment like skin, internally in the nose, lungs, and gastrointestinal tract. Their function is to develop antigen immunity by providing antigenic information to lymphocytes in lymph nodes and lymph organs[48].

**Platelets:**

Out of the three main blood cell types, Platelets are the smallest, are around 20% of diameter of the RBCs. Platelets are produced in the bone marrow Platelets are actually not true cells but merely circulating fragments of cells. But even though platelets are merely cell fragments, they contain many structures that are critical to stop bleeding[49]. Their main function is to form mechanical plugs during normal hemostatic response to vascular injury. In the absence of platelets, spontaneous leakage of blood through small vessels may occur. On their surface, they have proteins which make them to adhere to the breaches in the vessel wall of blood and also to each other. They consist of granules which may secrete other proteins needed for making a firm plug to seal the breach in the blood vessel. Platelets also comprise of proteins same as of muscle proteins which permit them to change shape when they get sticky[50].

**The plasma:**

Plasma carries all blood components throughout the body as the fluid in which they travel. Largest component of the blood is plasma, making about 55% of its overall contents. Blood plasma is light yellow liquid, similar to the color of straw. Along with water, plasma carries salts and enzymes, including electrolytes such as sodium, potassium, chlorine, bicarbonate, magnesium, and calcium, small amount of amino acids, vitamins, organic acids and pigments[51].

## DEFINITION

Chronic kidney disease (CKD) has been defined as "kidney damage lasting for more than 3 months characterized by structural or functional abnormalities of the kidney, with or without decreased glomerular filtration rate (GFR)"[52].

CKD is defined as "abnormalities of kidney structure or function, present for >3 months, with implications for health". CKD is classified based on Cause, GFR category (G1-G5), and Albuminuria category (A1-A3), abbreviated as CGA**. (KDIGO 2016)**[53]

**Table No. 1 showing GFR categories in CKD**

| GFR categories in CKD | GFR category GFR (ml/min/1.73 m2 ) | Terms |
|---|---|---|
| G1 | >=90 | Normal or high |
| G2 | 60–89 | Mildly decreased |
| G3a | 45–59 | Mildly to moderately decreased |
| G3b | 30–44 | Moderately to severely decreased |
| G4 | 15–29 | Severely decreased |
| G5 | <15 | Kidney failure |

**Table No. 2 showing albuminuria categories in CKD**

| **Persistent albuminuria categories**<br>**Description and range** | | |
|---|---|---|
| **A1** | **A2** | **A3** |
| **Normal to mildly increased** | **Moderately increased** | **Severely increased** |
| **<30 mg/g**<br>**<3 mg/mmol** | **30-300 mg/g**<br>**3-30 mg/mmol** | **>300 mg/g**<br>**>30 mg/mmol** |

CKD is defined as "a slowly progressive and irreversible loss of kidney function, leading to a condition in which the kidneys are no longer able to function due to destruction of the nephrons, which reduces the ability of the body to sustain metabolic and hydro electrolytic renal equilibrium"[54].

When the glomerular filtration rate (GFR) decreases less than 60 ml/min/1.73 $m^2$, for more than three months then kidney dysfunction started and, when the glomerular filtration rate gets reduced less than 15 ml/min/1.73 $m^2$ , end stage CKD occurs. In this stage, hemodialysis is done to compensate for the decreased renal function[54].

## AETIOLOGY

- Causes of chronic renal failure:
- Hypertension (5–25%),
- Diabetes mellitus (22–45%)
- Glomerulonephritis (10–23%)
- Adult polycystic kidney disease (2–7%),
- Renal vascular disease (2–7%)
- Chronic pyelonephritis (0.5 to 7%),
- Other known conditions (13–15%), and unknown causes (4–26%)[52].

**Table 3 | Classification of CKD based on presence or absence of systemic disease and location within the kidney of pathologic anatomic findings** [55].

| | Examples of systemic diseases affecting the kidney | Examples of primary kidney diseases (absence of systemic diseases affecting the kidney) |
|---|---|---|
| Glomerular diseases | Diabetes, systemic infections, drugs, systemic autoimmune diseases, neoplasia (including amyloidosis) | Diffuse, crescentic or focal proliferative GN; segmental & focal glomerulosclerosis, membranous nephropathy, minimal change disease |
| Vascular diseases | Hypertension, Ischemia, Atherosclerosis, cholesterol emboli, thrombotic microangiopathy, systemic vasculitis, systemic sclerosis | Fibromuscular dysplasia, ANCA-associated renal limited vasculitis |
| Tubulointerstitial diseases | Systemic infections, drugs, autoimmune, sarcoidosis, neoplasia (myeloma), urate, environmental toxins (lead, aristolochic acid) | Stones, Urinary-tract infections, obstruction |
| Cystic and congenital diseases | Polycystic kidney disease, Fabry disease, Alport syndrome | Medullary cystic disease, Renal dysplasia, podocytopathies |

## RISK FACTORS

Risk factors include diabetes mellitus, childhood obesity, hypertension, advanced age, autoimmune disease, African ancestry, a family history of kidney disease, past history of acute renal injury, & abnormal urinary sediment, or structural abnormalities of the urinary tract, proteinuria, high cholesterol, lack of physical exercise, smoking, and excessive salt intake[56].

Other contributing factors include inappropriate use of medications like aspirin, ibuprofen, and other painkillers; and use of herbal supplements that are known to cause damage to kidneys; infections or inflammatory diseases that affect the kidneys. Also, imaging studies that use iodine contrast substances can have a negative effect on kidneys. Chronic kidney disease sometimes runs in families[57].

Type 2 diabetes mellitus is the major cause of CKD[58]. Other risk factors include Old age, use of mercury‑containing cosmetics, analgesic abuse[59].

According to kottgen studies, CKD has a heritable component Uromodulin (which encodes Tamm–-Horsfall protein in the urine). Mutations are associated with differences in renal function. Another identified mutation is related to APOL1. APOL1 mutations are found exclusively among individuals of African descent and make them more prone to CKD. It is an autosomal recessive pattern of inheritance, associated with a substantially higher risk of ESRD (10-fold higher risk of ESRD due to focal glomerulosclerosis and 7-fold higher risk of ESRD due to hypertension)[60].

Known potential causes of CKD in LMICs are as under: [5]

**Non-communicable diseases**

• Hypertension

• Obesity

• Diabetes mellitus (types I and II)

• Congestive heart failure and cirrhosis

• Malnutrition

• Pregnancy and obstetric complications

• Lupus and primary rheumatologic/immunologic disorders

• Acute renal injuries

• Primary inherited or acquired renal diseases (e.g. polycystic kidney disease, alport's disease and immunoglobulin A nephropathy)

• Microangiopathic hemolytic anemia

• Cancers/malignancies (e.g. myeloma, amyloid, lymphomas, leukemias)

• Sickle cell disease

• Obstructive (e.g. vesicoureteral reflux, nephrolithiasis and tumors)

• Sarcoidosis

**Communicable and infectious diseases**

• Hepatitis B and C

• Leptospirosis

• Human immunodeficiency virus

• Malaria

• Streptococcal and staphylococcal diseases

• Tuberculosis and other mycobacterial diseases (e.g. leprosy)

• Syphilis

• Cystic hydatid (Echinococcus) disease

• Parasitic diseases including schistosomiasis, filariasis, leishmaniasis, toxoplasmosis and onchocerciasis)

• Rickettsial diseases including typhus

• Chronic pyelonephritis

• Enteric and diarrheal diseases (e.g. Escherichia coli, Shigella dysenterae and dengue fever, hantavirus, and yellow fever, typhoid)

• Hemorrhagic fevers & viral vector-borne diseases

**Environmental and occupational exposures**

• Iatrogenic

• Traditional (herbal) medicines (aristolochic acid, Chinese herbs and aloe vera)

• Heavy metals (cadmium, arsenic, gold, lead, uranium, mercury)

• OTCs including nonsteroidal analgesics

• Agricultural pesticides and industrial waste products

• Recreational drugs

• Counterfeit drugs

• Food, milk and personal hygiene dye additives

• Air pollution

• Fertilizers and plastics

**STAGING**[52]

CKD is subdivided into five stages depending on estimated GFR:

- CKD stage 1: eGFR > 90 ml/min (per 1.73 $m^2$) with other evidence of renal disease.
- CKD stage 2: eGFR 60 to 89 ml/min, with other evidence of renal disease.

- CKD stage 3: eGFR 30 to 59 ml/min.
- CKD stage 4: eGFR 15 to 29 ml/min.
- CKD stage 5: eGFR less than 15 ml/min.

CKD 3 may be divided into 3A (eGFR 45–59) and 3B (eGFR 30–44), and the suffix 'p' can be added to any stage to denote proteinuria (ACR >30mg/mmol, PCR >50mg/mmol).

- G1 >90 Normal or high
- G2 60–89 Mildly reduced
- G3a 45–59 Mild - moderately reduced
- G3b 30–44 Moderate - severely reduced
- G4 15–29 Severely reduced
- G5 <15 Renal failure

**SIGNS AND SYMPTOMS[61]:**

Patients are usually asymptomatic in CKD stages 1-3. In stages 4 to 5 (GFR less than 30 mL/min/1.73m²), endocrine/metabolic impairments or disturbances in water or electrolyte get manifest clinically.

In stage 5 CKD, signs of imbalance between salt and water include:

- Hypertension
- Peripheral edema
- Pulmonary edema

In stage 5 CKD, signs of metabolic acidosis include the following:

- Protein-energy malnutrition
- Muscle weakness
- Loss of lean body mass

Anemia in chronic renal disease is associated with the following:

- Fatigue
- Decreased exercise capacity
- Deranged cognitive and immune function
- Decreased quality of life
- New onset of cardiac failure or development of more severe cardiac failure
- Development of cardiovascular disease
- High cardiovascular mortality

Other manifestations of uremia in end-stage kidney disease:

- Pericarditis: may be complicated by cardiac tamponade, possibly leading to death if unrecognized
- Peripheral neuropathy, generally asymptomatic
- Encephalopathy: may progress to coma & death
- Gastrointestinal symptoms: Nausea, vomiting, anorexia, diarrhea
- Platelet dysfunction with susceptibility to bleed
- Restless leg syndrome
- Dermatologic manifestations: Pruritus, Dry skin, ecchymosis
- Erectile dysfunction, reduced libido, amenorrhea
- Malnutrition
- Fatigue, increased somnolence, failure to thrive

  Adult patients with CKD also have symptoms of depression.

**Hematological abnormalities in CRF are**[20]:

1. Anemia.

2. Leukocytopenia.

3. Bleeding diathesis.

4. Hypocellular bone marrow.

5. Shortened RBC lifespan.

6. Splenomegaly/ hypersplenism.

Inadequate synthesis of erythropoietin by the damaged kidneys is the main causative factor of anemia in CKD patients. Other factors include, as a result of nutritional insufficiency (Iron, B12 and folate deficiency) or more blood loss, acute and chronic inflammation with deranged iron utilization, severe hyperparathyroidism with resultant bone marrow fibrosis and reduced red cell life span in the uremic environment.

If anemia is not treated for a long duration, it may result in a number of physiologic impairments, including: cardiovascular complications like reduced tissue oxygenation, raised cardiac output, ventricular hypertrophy, ventricular dilatation and high morbidity and mortality.

In CKD, bleeding tendency as a result of platelet dysfunction due to abnormal platelet aggregation and adhesiveness, along with prolonged bleeding time, reduced activity of platelet factor III and deranged prothrombin consumption.

If there is proteinuria of nephrotic range, then the patients of chronic kidney disease are more prone for thromboembolism, it further leads to hypoalbuminemia and loss of anticoagulant factors, which may result in thrombophilic state.

In chronic kidney disease patients, white blood cell count can be reduced and correction of anemia is followed with raise in natural killer cells and improvement of leukocyte phagocytic function.

**Diagnosis**[61]

*Laboratory studies*

- Complete blood count (CBC)
- Urine analysis
- Basic metabolic panel
- Serum albumin levels
- Lipid profile

Lab test for renal bone disease:

- Serum calcium and phosphate
- Intact parathyroid hormone (PTH) levels
- 25-hydroxyvitamin D Alkaline phosphatase
- Antinuclear antibodies (ANA), double-stranded DNA antibody levels: Screen for systemic lupus erythematosus.
- Serum and urine protein electrophoresis and free light chains: Screen for monoclonal protein probably indicating multiple myeloma
- C-ANCA and P-ANCA levels (Cytoplasmic and perinuclear pattern antineutrophil cytoplasmic antibody): Positive result is useful in diagnosis of granulomatosis with polyangiitis (Wegener granulomatosis); PANCA is also useful in the diagnosis of microscopic polyangiitis.
- Serum complement levels: Results can be reduced with some glomerulonephritides.

- Hepatitis B and C, Venereal Disease Research Laboratory (VDRL) serology, human immunodeficiency virus (HIV): Conditions related to some glomerulonephritides
- Anti–glomerular basement membrane (anti-GBM) antibodies: Presence is mostly indicative of underlying Good pasture syndrome.

*Imaging studies*

- Renal ultrasound: Helpful in case of hydronephrosis, which cannot be seen in early obstruction or dehydrated patients; or for tumor, or diffuse adenopathy; involvement of the retroperitoneum with fibrosis, small, echogenic kidneys are noted in advanced renal failure.
- Retrograde pyelography: Valuable in patients with highly suspicious obstruction in spite of normal ultrasound of kidney, as well as to diagnose nephrolithiasis.
- Computed tomography (CT) scanning: Helpful for better defined tumors and cysts of kidney usually noted on ultrasound; also, the most sensitive test to detect kidney stones.
- Magnetic resonance imaging (MRI): Valuable in cases who need CT scan but who may not get intravenous contrast; helpful in diagnosis of renal vein thrombosis.
- Radionuclide scan of Kidney: Helpful to look for renal artery stenosis when done with captopril administration; also quantitates the contribution of kidney to the GFR
- *Biopsy*- when kidney damage and/or proteinuria encroaching nephrotic range are there, then percutaneous renal biopsy is usually indicated.

## PATHOPHYSIOLOGY[52]

As the renal function slowly deteriorates, compensatory mechanisms usually maintain sustainable health until GFR reaches 10 -15 ml/min. & the patients do not generally die of kidney failure until GFR falls below 5 ml/min. In spite of broad range of single-nephron GFR in diseased kidneys, (the 'intact nephron hypothesis'), glomerular & tubular function gets coordinated in all nephrons. Though the functional accommodations needed to maintain overall homeostasis come at price (the 'trade-off hypothesis'), with the 'hyperfiltration hypothesis' most distinctly expressing how these adaptive changes result in glomerulosclerosis and tubulointerstitial fibrosis and progressive decline in GFR.

Pathophysiological changes—

These include impairment in:

(1) concentration and/or dilution of the urine

(2) excretion and/or conservation of sodium

(3) excretion of potassium, with hyperkalemia often the immediate life-threatening consideration in the management of patients with kidney failure

(4) excretion of acid

(5) calcium/phosphate/vitamin D/bone homeostasis

(6) erythropoietin synthesis, resulting in renal anemia

(7) excretion of many substances and metabolites that act as 'uremic toxins'.

(8) a broad range of endocrine functions.

## COMPLICATIONS[62]

Chronic kidney disease (CKD) is known to be a public health problem worldwide. It may be detected by using simple laboratory tests, and treatment can prevent or delay the complications of decreased kidney function, retard the progression of kidney disease, and decrease the risk of cardiovascular disease (CVD).

CKD may lead to various serious complications:

- Anemia
- Metabolic bone disease
- Hyperlipidemia
- Cardiovascular disease
- Nutritional disorder
- Infections

## ANEMIA

As per WHO, anemia is defined as "a hemoglobin level less than 13 g/dL in men and post-menopausal women, and less than 12 g/dL in pre-menopausal women".

The NKF defines anemia as "a hemoglobin of less than 13.5 g/dL in men and less than 12.0 g/dL in women".

Anemia is defined as "a reduction in one or more of the major red blood cell measurements; hemoglobin concentration, hematocrit, or red blood cell count".

Normochromic, normocytic anemia is commonly seen in CKD, and nearly 50% is the overall prevalence of CKD-associated anemia. Despite anemia can be diagnosed in

cases at any stage of CKD, the strong correlation exists between the severity of CKD and the prevalence of anemia.

The most important and specific etiology causing CKD-associated anemia is reduced synthesis of erythropoietin. Other factors include iron, folate, or vitamin B12 deficiency; gastrointestinal blood loss; severe hyperparathyroidism, systemic inflammation, and reduced RBC life span. Erythropoietin is a glycoprotein, secreted by the renal interstitial fibroblasts and is necessary for the growth and differentiation of red blood cells in the bone marrow. In CKD, tubulointerstitial fibrosis is produced by tubular atrophy, which compromises erythropoietin synthetic capacity of kidney and leads to anemia. Prevalence of anemia has been significantly risen as the creatinine clearance (an estimate of glomerular filtration rate) falls to 70 mL/min or lower among males and to 50 mL/min or lower among females[63].

If anemia is left untreated, it may negatively affect cardiac health, exercise capacity, alter cognitive function, and quality of life among CKD patients. Anemia in CKD raises morbidity & mortality from cardiovascular complications [angina, worsening heart failure and left ventricular hypertrophy (LVH)], which can further deteriorate kidney function and production of vicious cycle called "cardiorenal anemia syndrome". If there is early detection and treatment of anemia, then it can reduce cardiovascular morbidity and mortality. Five-year survival rate of patients with end stage renal disease is 30% decreased with LVH than that of patients lacking LVH. In addition, CKD patients with stable coronary artery disease have anemia as an independent predictor of death[63].

Recombinant human erythropoietin (epo) is used to treat anemia in CKD patients. It improves the level of hemoglobin, quality of life and reduce morbidity and mortality. Erythropoiesis-stimulating agents like epoetin beta, together with epoetin alfa and

darbepoetin alfa, is now available in the market. Administration of epoetin beta to hemodialysis patients once-weekly is as effective as three times-weekly administration in maintaining hemoglobin level at equivalent weekly doses. It rises the probability of decreasing the frequency of administration of rHuEPO therapy, therefore raising the options available for tailoring anemia therapy, and at same time decreasing treatment costs[64]. Transfusions have been replaced by rHuEPO therapy as the main part of treatment and improves the survival of CKD patients with anemia[62].

**METABOLIC BONE DISEASE**

Kidney plays a crucial role in the regulation of mineral metabolism. Control of parathyroid hormone (PTH) & fibroblast growth factor 23(FGF23), along with activation of vitamin D, is done by kidney. So, in chronic kidney disease (CKD), it leads to development of many abnormalities and secondary hyperparathyroidism (SHPT) as the most common. Such dysregulated mineral metabolism in chronic renal disease is known as “renal osteodystrophy” because disease restricted to bone, but it got currently renamed as “chronic kidney disease mineral and bone disorder” (CKD-MBD) as a systemic syndrome. CKD-MBD comprises of bony abnormalities, laboratory derangements, and vascular calcification[65].

In CKD, renal osteodystrophy causes histological alterations in bone architecture. Kidney is the primary site for 1-α-hydroxylation of vitamin D & excretion of phosphate. In CKD, hyperphosphatemia sets in because of insufficient 1, 25 dihydroxy-vitamin D levels that denotes decreased production from scarring of parenchyma. Phosphate removal from kidney is decreased at the same time. Both processes together lead to reduced serum calcium levels, resulting in more parathyroid hormone secretion (secondary hyperparathyroidism). Parathyroid hormone plays role

in phosphaturia. It also raises levels of calcium by escalating resorption of bone and boosting 1-α-hydroxylation of 25-hydroxy vitamin D produced by liver (restricted effect due to decreased renal reserve as a result of scarring). In patients with stage 3 CKD, increasing levels of phosphorus are almost universally noted. Secondary hyperparathyroidism deforms bone; when eGFRs are less than 50 mL/min per 1.73 $m^2$

In CKD patients, four classes of bone phenotypes (renal osteodystrophy) may be diagnosed: osteitis fibrosa cystica (raised bone turnover with secondary hyperparathyroidism), adynamic bone disorder (decreased bone turnover from unrestricted suppression of the parathyroid glands), osteomalacia (reduced bone turnover and insufficient mineralization, mainly associated with reduced vitamin D production), and mixed osteodystrophy (with elements of both raised & decreased bone turnover).

In CKD patients, CKD-associated mineral bone disorders remarkably raise mortality.

**HYPERLIPIDEMIA**

Dyslipidemia raises cardiovascular morbidity and mortality and is common in CKD patients. Prevalence of hyperlipidemia rises as there is reduction in kidney function, with degree of hypertriglyceridemia and increase of LDL cholesterol levels being proportional to severity of derangement of kidney.

Increased synthesis and reduced catabolism of lipoproteins leads to hypercholesterolemia in nephrotic syndrome. The degree of lipoprotein derangement is roughly proportional to the amount of protein in urine and inversely proportional to albumin levels in serum.[62]

## CARDIOVASCULAR DISEASE[62]

Kidney impairment is related with the cardiovascular morbidity. In end stage renal disease, raised cardiovascular risk is a major complication. Even mild to moderate degrees of derangements in the kidney are associated with raised cardiovascular risk. It gets increased earlier in the course of renal disease progression than was initially hypothesized. Cardiovascular death rates are ten to one hundred-fold increase in dialysis patients than age- and sex-matched individuals in the general population. Many traditional cardiovascular risk factors like hypertension results in cardiovascular risk in CKD patients. Szcech and colleagues revealed that patients having hypertension are at more risk for recurrent or new cardiovascular events in patients with stage 2–3 CKD. As a U-shaped relationship present between systolic blood pressure and mortality, Systolic blood pressure is more responsible for cardiovascular death in dialysis patients. In this, increased or decreased systolic blood pressure is associated with raised death rates in stage 5 CKD individuals than either pulse or diastolic pressure.

Diabetes is related to worse outcomes in all stages of Chronic renal disease. Moreover, reduced fasting plasma glucose and /or glycated hemoglobin levels are associated with reduced risk of all-cause mortality and decreased cardiovascular death of borderline significance in patients with moderate to severe renal disease. In CKD, left ventricular hypertrophy (LVH) is also a cardiovascular risk

determinant. It rises in associated with progressively reduced levels of eGFR. Hypertension and anemia have a crucial role in the development of LVH.

Tobacco usage is also related to raised death rates and incidence of cardiac failure in stage 5 CKD patients.

In stage 5 CKD, abnormal parathyroid hormone levels, serum phosphate levels and calcium phosphate ion product, are independent cardiovascular risk factors. In stage 3 or 4 CKD patients and dialysis, raised calcium–phosphate products and the cumulative dose of oral calcium-based phosphate binders correlate with the progression & extent of arterial calcification which leads to clinical morbidity and mortality. Serum phosphate levels are also related to increased mortality & myocardial infarction in stage 3 or 4 CKD. Inadequately controlled metabolic bone disease plays a role in vascular calcification, which elevates arteriolosclerosis and increases stiffness of vessel wall. Aortic stiffness is unrestrained predictor of total & cardiovascular deaths, CAD and fatal stroke in hypertensive patients. In CKD, inflammation has a vital part in developing cardiovascular risk. In CKD, inflammatory markers are usually raised and are predictive of cardiovascular risk. In CKD, C-reactive protein (CRP) level provides prediction of cardiovascular outcomes. Increased CRP is associated with cardiovascular deaths in CKD. Proteinuria, a hallmark of renal derangement, is related to raised risk for cardiovascular morbidity & early cardiovascular deaths in patients with and without hypertension & diabetes.

**NUTRITIONAL DISORDER**

In adult patients on dialysis with stage 5 chronic kidney disease (CKD), nutritional problems may be divided into three types: Obesity, protein–energy wasting (PEW) and diabetes.

PEW is an independent predictor of mortality & morbidity in HD as well as in PD patients. According to a study, twenty-five percent of HD cases shows high-risk malnutrition as estimated from serum albumin & transthyretin (prealbumin) levels.

The prevalence of type 2 diabetes was less, 10% in French HD patients ten years ago, is now seen in ~20% and associated with a 2-fold rise in death rates.

With the progression through stages of CKD, nutritional demands are deranged and metabolism of salt, water, potassium, phosphorous & protein are affected. Despite insufficient intake of protein and carbohydrate substrates, it results in inadequate energy generation. In more severe manifestations it results in "Uremic malnutrition", a syndrome that is different from malnutrition because of insufficient nutrient intake. Both insufficient nutrient intake & ineffective nutrient usage may lead to nutritional impairments in CKD. In CKD cases, uremic malnutrition is very prevalent [66].

**INFECTIONS**

Infections are remarkable factor contributing for deaths in patients with end stage renal disease. Epidemiologic studies denote that infection as a cause is second to cardiovascular disease as the rising cause of mortality in ESRD. Septicemia is one of the most common & serious infections in cases with dialysis. Foley *et al*. observed that admission for septicemia in hemodialysis patients risen by 51% from 1991 to 1999. Septicemia contributes to more than three-fourth of mortality as a result of infections (55). Sarnak and Jaber observed that the annual percent mortality secondary to diabetes mellitus, sepsis and adjusted for age, was at least 50-fold more in dialysis patients as compared to general population. Septicemia encompasses infections with gram-positive staphylococcus organisms, *Staphylococcus epidermidis* & *Staphylococcus aureus* in patients on hemodialysis. Suppressed immunity is major cause responsible for abnormally increased incidence of the bacterial infections in patients on dialysis. In ESRD, risk factor of bacterial infection is vascular access. Infection of the vascular access is primarily responsible for bacteremia, specially

infection as a result of *S. aureus* & coagulase-negative staphylococci. The type of vascular access includes arteriovenous fistula [AVF], dialysis catheter, or arteriovenous graft [AVG]. It shows marked effect on the development of local infections & episodes of bacteremia [67].

**MANAGEMENT OF CHRONIC RENAL FAILURE**

CKD patients suffer from various signs and symptoms affecting many systems. We can treat these manifestations by life style management of CKD patients, by treating underlying cause, by giving medicinal treatment for the manifestations of CRF patients and by giving RRT (renal replacement therapy) which includes hemodialysis and renal transplantation.

The average prevalence values for treated ESRD (not diagnosed ESRD); dialysis and transplant patients in India were 70, 60 and 10 ppm, respectively. Globally, this number is increasing at a rate of 7% every year. Only10–20% of ESRD patients in India continue long-term RRT. In India, it is estimated that in 1 year, there are 3,500 new renal transplants + 3,000 new continuous ambulatory peritoneal dialysis (CAPD) initiation + 15,000 new maintenance hemodialysis (MHD) patients. India has approximately 180–200 renal transplantation centers with the most in the private sector[68].

Management of CRF cases by lifestyle changes include exercise, stopping smoking, alcohol cessation, and including less salt intake.

i) CKD patients generally suffer from hypertension and obesity. So these patients should be advised to do exercise like walking, jogging, cycling and swimming for half an hour daily. Exercise help in lowering blood pressure and also helps in reducing

weight. Patients should be encouraged to achieve ideal BMI which ranges from 18.5-24.9 $kg/m^2$.

ii) CKD patients should be advised to stop smoking as it can deteriorate the health of these patients.

iii) Patients suffering from CRF should be advised less protein intake in their diet as it can be harmful for these patients.

iv) CKD patients should be advised to stop taking alcohol as regular intake may be harmful for kidneys and other organs.

v) CKD patients should be advised to limit salt intake in their diet (< 100 mmol per day) to reduce hypertension[69].

Treatment of manifestations of CRF patients include

A) Treatment of Anemia-

It includes erythropoiesis stimulating agents and iron therapy. Erythropoietin stimulating agents should be administered when Hb level falls below 100 g/L. Iron therapy can be given orally and in intravenous form. When ferritin level falls below 100 ng/ml, iron supplement should be given and when ferritin level more than 100 ng/ml can't be achieved even after giving oral iron supplements then intravenous iron should be administered.

B) Treatment of mineral metabolism

In case of hyperphosphatemia, dietary phosphate should be restricted. If even after the restriction of phosphate in diet, hyperphosphatemia persists then calcium containing phosphate binders like calcium carbonate or calcium acetate should be given. If PTH

(parathyroid hormone) level is more than 53 pmol/L, vitamin D analogues should be taken. If hypercalcemia and hyperphosphatemia in present then vitamin D analogues should not be given and if hypercalcemia is there then calcium containing phosphate binders should not be given.

C) Treatment of cardiovascular risk factors and hyperlipidemia

Cardiovascular risk factors can be prevented by controlling blood pressure. ACE inhibitors and angiotensin receptor blockers are used to treat proteinuria. By reducing serum cholesterol level, cardiovascular risk factors can be prevented. Hyperlipidemia can be controlled by using statin therapy.

**HEMODIALYSIS**

Hemodialysis is defined as a –

- Dialysis technique in which blood is removed from the body, filtered through a dialyzer that removes waste productsand excess fluid, and then returned to body[71].
- A therapeutic procedure for removing low molecular weight toxins by allowing the blood to flow past a semipermeable membrane where the toxins diffuse away from the blood down a concentration gradient, either via an external AV shunt, or a surgically placed AV fistula; hemodialysis is used in renal failure to ↓ BUN, creatinine, hyperkalemia and correct metabolic acidosis[72].
- Removal of certain elements from the blood by virtue of difference in rates of their diffusion through a semipermeablemembrane while the blood is being circulated outside the body. The procedure is used to remove toxic wastes fro m the blood of a patient with acute or chronic renal failure[73].

Most common method used to treat advanced and permanent renal failure is hemodialysis. Simple and more compact dialysis machines have made home dialysis increasingly attractive in recent years. But hemodialysis is still a complicated and inconvenient therapy that requires a coordinated effort from your whole health care team, including your nephrologist, dialysis nurse, dialysis technician, dietitian, and social worker[74].

In hemodialysis, blood is allowed to flow, a few ounces at a time, through a special filter known as dialyzer that removes wastes and extra fluids. The clean blood is then returned to your body. By purifying blood after removal of the harmful wastes and extra salt and fluids, blood pressure gets controlled and balance of chemicals like potassium and sodium in your body can be achieved[75].

Hemodialysis can be done at home or at hemodialysis centre. Hemodialysis is done 3 days in a week and it takes 3-5 hours at centre and 6 hours at home[76]. For hemodialysis, there are three techniques to access to blood i.e. intravenous catheter, arteriovenous fistula and a synthetic graft[77].

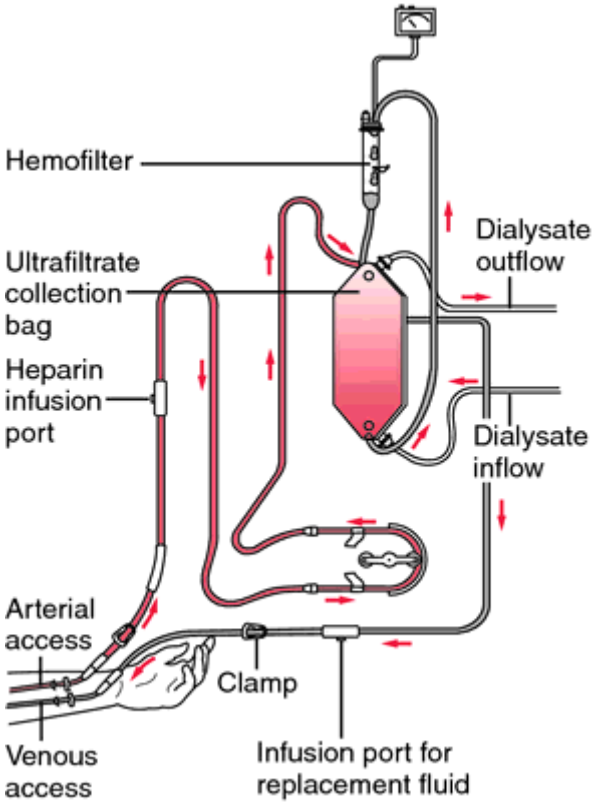


**Fig No. 3.Hemodialysis [78].**

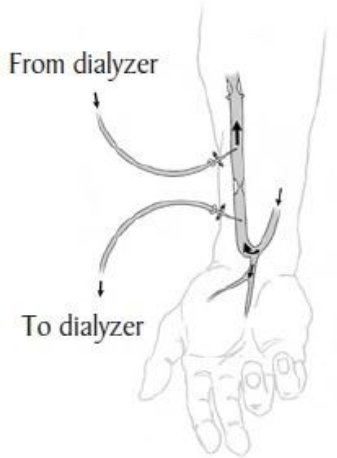


**Fig. No. 4. Arteriovenous fistula.**

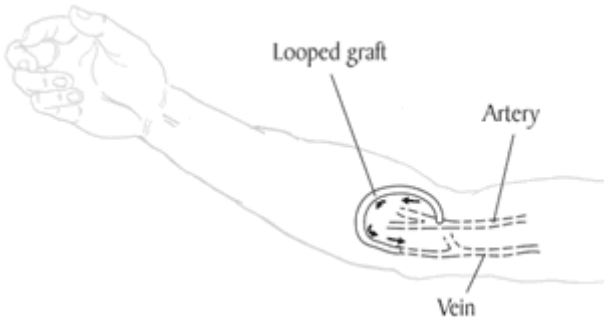


**Fig. No. 5. Graft.**

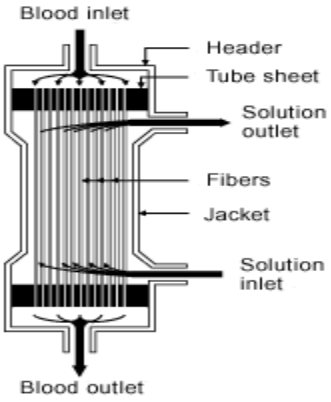


**Fig No. 6. Structure of a typical hollow fiber dialyzer.**

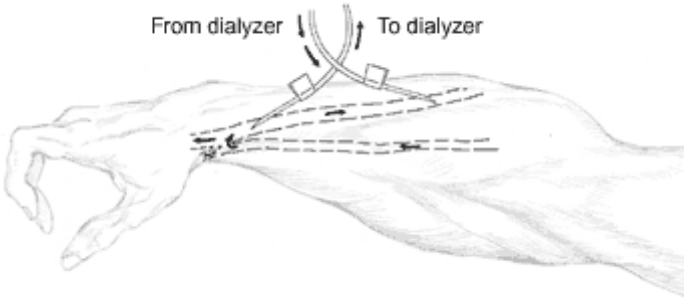


**Fig No. 7. Arterial and venous needles.**

Dialysis machine is used to filter blood of CKD patients. It can be called as artificial kidney as it removes waste products from the blood. Dialyzer contains many small fibers through which blood is passed. In these fibers, dialysate (a dialysis solution) is pumped to remove waste material from the blood[79].

Arterial and venous needles are used in hemodialysis. Venous needles are used to take the impure blood out of the body of patient and arterial needle are used to drain filtered blood back to the body[79].

# MATERIALS AND METHODS

## Source of data

Patients suffering from chronic renal failure admitted in hemodialysis unit at B.L.D.E. University's Shri B M Patil Medical College, Hospital and Research Centre, Vijayapura will be included in this study.

Study period: 1$^{st}$December, 2015 to 30$^{th}$ June 2017.

## Methods of collection of data

Under aseptic precautions, venous blood samples will be collected from renal failure patients before and after hemodialysis after taking informed consent.

A detailed history of renal failure patients will be elicited.

Two milliliters of blood will be taken in an ethylene diamine tetra acetic acid (EDTA) vacutainer and immediately analyzed for a complete hemogram, including Hb, RBC count, and RDW, using an automated hematology analyzer.

A peripheral smear will be prepared from the same sample.

**Sample Size**: With average standard deviation of WBC count in pre- hemodialysis and post hemodialysis 1.8 (6.32±1.82 &7.46±1.87)[8] and at 99% confidence level, considering 90% power in the study, the sample size is ≈ 80.

$$n = \frac{(Z\alpha + Z\beta)^2 \times 2 \times S^2}{d^2}$$

$Z_\alpha$- Z value at 99% confidence level

$Z_\beta$ -Z value at 90% power

S- Common Standard deviation

d - Difference between two parameters

**Statistical analysis:**

Data will be analyzed using following statistical methods:

1. Mean ± SD
2. Paired t test/ Wilcoxen paired test
3. Correlation coefficient
4. Chi square test (if necessary)

**Inclusion criteria:**

Patients with chronic renal failure on RRT in the form of hemodialysis at hemodialysis unit will be included in the study.

**Exclusion criteria:**

1) Patients with other systemic illness without renal failure.
2) Known hematological malignancy causing secondary renal failure.
3) Patients with end stage renal disease treated with renal replacement therapy in the form of renal transplantation.
4) History of blood transfusion during last three months.

## OBSERVATION AND RESULT:

The study Hematological changes in pre- and post hemodialysis patients with chronic renal failure. was undertaken at B.L.D.E. University's Shri B M Patil Medical College, Hospital and Research Centre, Vijayapura during the period from 1st December, 2015 to 30th June 2017.

A total of 80 patients suffering from chronic renal failure were included in this study. The observation and result of the study are as under:

**Table 4: Distribution of cases by sex**

| Sex | N | Percent |
|---|---|---|
| Male | 58 | 72.5 |
| Female | 22 | 27.5 |
| Total | 80 | 100 |

**Table 5: Distribution of cases by Age**

| Age (Yrs) | N | Percent (%) |
|---|---|---|
| 21-30 | 13 | 16.3 |
| 31-40 | 9 | 11.3 |
| 41-50 | 16 | 20 |
| 51-60 | 25 | 31.3 |
| >60 | 17 | 21.3 |
| Total | 80 | 100 |

**Figure 8: Distribution of cases by sex**

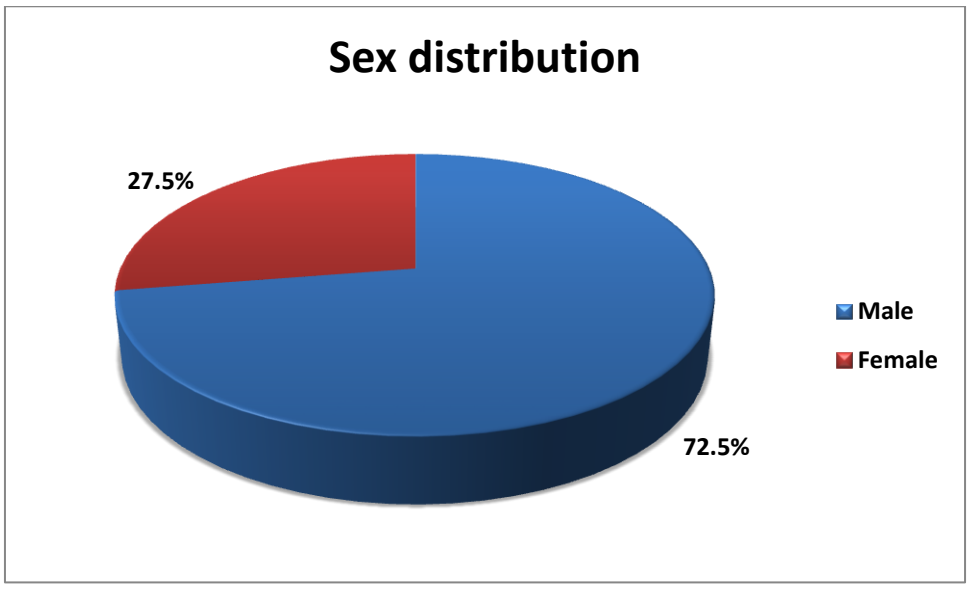

**Figure 9: Distribution of cases by Age**

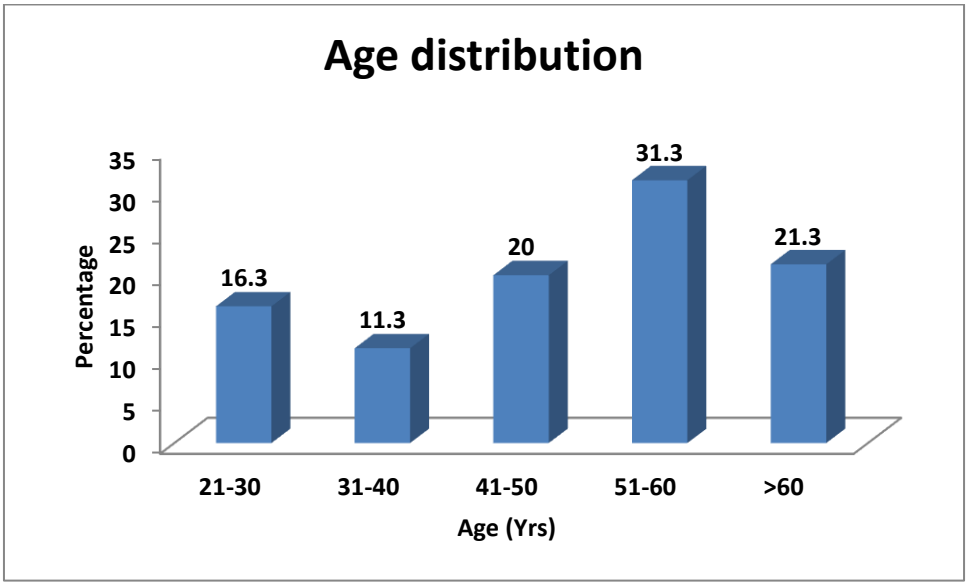

**Table 6: Mean Age of patients**

| Age (Yrs) | Minimum | Maximum | Mean | SD |
|---|---|---|---|---|
| | 23 | 78 | 50.0 | 15.1 |

**Table 7: Distribution of cases by Age and Sex**

| Age (Yrs) | Male | | Female | | t test p value (two tailed) |
|---|---|---|---|---|---|
| | N | % | N | % | |
| 21-30 | 11 | 19.0 | 2 | 9.1 | 0.218 |
| 31-40 | 8 | 13.8 | 1 | 4.5 | |
| 41-50 | 10 | 17.2 | 6 | 27.3 | |
| 51-60 | 15 | 25.9 | 10 | 45.5 | |
| >60 | 14 | 24.1 | 3 | 13.6 | |
| Total | 58 | 100.0 | 22 | 100.0 | |

In present study, out of 80 patients of CRF, 58 patients (72.5%) were male and 22 patients (27.5%) were female. Maximum number of patients i.e. 25 were in age group of 51- 60 years (31.3%), out of which 15 were male and 10 were female.

**Figure 10: Distribution of cases by Age and Sex**

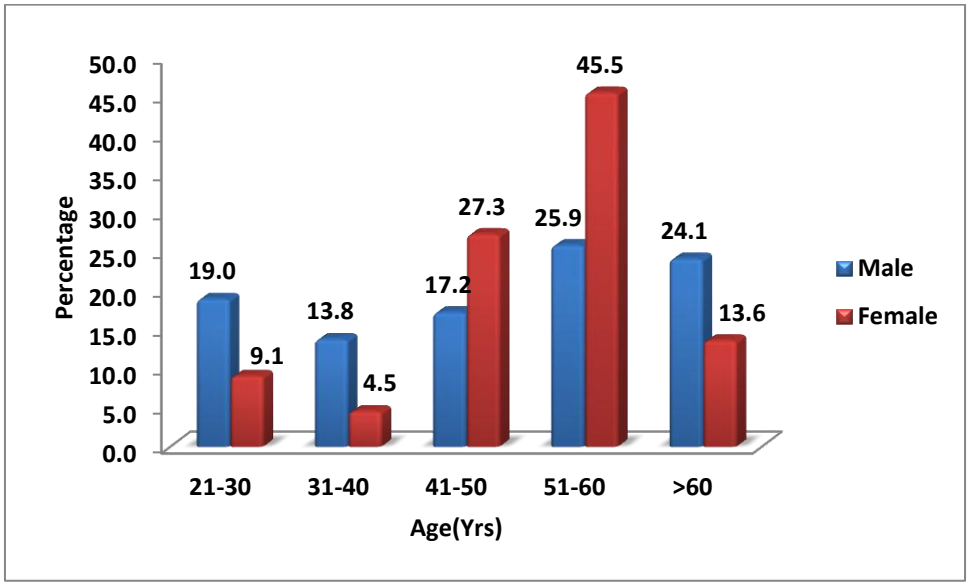

**Table 8: Comparison of the following parameters at different time periods**

| Parameters | Pre | | Post | | t test p value (two tailed) |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| Age | 50.0 | 15.1 | 50.0 | 15.1 | -- |
| RBC | 2.87 | 0.79 | 3.00 | 0.87 | 0.184 |
| WBC | 8.00 | 5.31 | 9.57 | 6.70 | 0.005* |
| Hb | 7.69 | 1.95 | 8.46 | 2.87 | 0.004* |
| Platelet | 2.10 | 0.78 | 1.87 | 0.69 | 0.022* |
| MCV | 88.88 | 10.67 | 88.91 | 10.27 | 0.972 |
| MCH | 27.01 | 2.82 | 27.67 | 2.51 | 0.038* |
| MCHC | 30.48 | 2.77 | 31.09 | 2.33 | 0.040* |
| HCT | 25.21 | 6.49 | 26.94 | 7.10 | 0.038* |
| RDW | 16.13 | 3.14 | 15.92 | 2.45 | 0.519 |

Note: *significantly distributed at 5% level of significance

Mean value of WBC before dialysis was 8 ± 5.31 whereas post dialysis, it was 9.57 ± 6.70 with a significant p value of 0.005.

Mean value of Hb before dialysis was 7.69 ± 1.95 whereas after dialysis, it was 8.46 ± 2.87 with a significant p value of 0.004.

Mean value of platelet before dialysis was 2.10 ± 0.78 which got decreased after dialysis to 1.87 ± 0.69 with a significant p value of 0.002.

Mean value of MCH in predialysis was 27.01 ± 2.82 and after dialysis it became 27.67 ± 2.51with a significant p value of 0.038.

Mean value of MCHC in predialysis was 30.48 ± 2.77 whereas after dialysis it got increased to 31.09 ± 2.33 with a significant p value of 0.040.

Mean value of HCT before dialysis was 25.21 ± 6.49 whereas after dialysis it got increased to 26.94 ± 7.10 with a significant p value of 0.038.

**Figure 11: Comparison of the following parameters at different time periods**

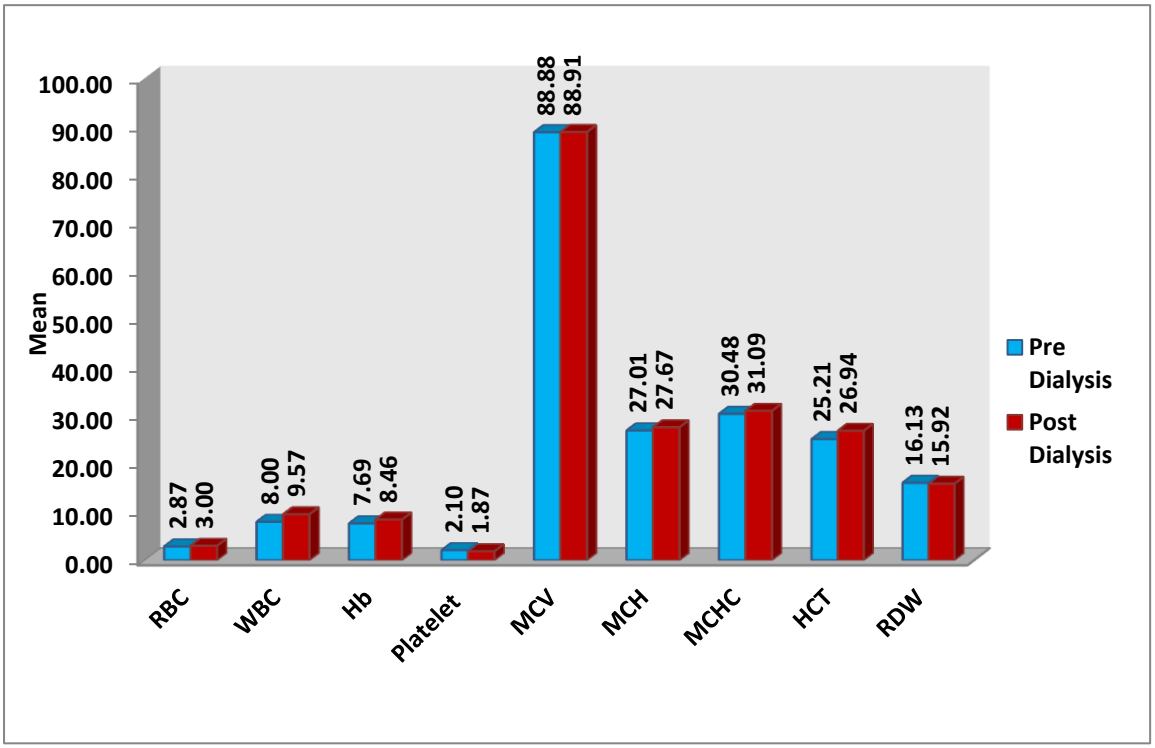

**Table 9: Morphology of Anemia in Pre- & Post Dialysis Patients**

| Anemia | Pre- Dialysis (N=80) | | Post Dialysis (N=80) | | chi sq. test p value (two tailed) |
|---|---|---|---|---|---|
| | N | % | N | % | |
| Macrocytic anemia | 11 | 13.8 | 10 | 12.5 | 0.815 |
| Macrocytic smear | 1 | 1.3 | 0 | 0.0 | 0.316 |
| MCHC anemia | 13 | 16.3 | 14 | 17.5 | 0.833 |
| MCHC smear | 1 | 1.3 | 0 | 0.0 | 0.316 |
| NCHC anemia | 13 | 16.3 | 15 | 18.8 | 0.677 |
| NCHC smear | 1 | 1.3 | 0 | 0.0 | 0.316 |
| NCNC anemia | 39 | 48.8 | 34 | 42.5 | 0.427 |
| NCNC smear | 1 | 1.3 | 6 | 7.5 | 0.053 |
| Dimorphic anemia | 0 | 0.0 | 1 | 1.3 | 0.316 |
| Total | 80 | 100.0 | 80 | 100.0 | |

NCNC anemia was seen in majority of patients. 39 patients before dialysis and 34 patients post dialysis were suffering from NCNC anemia. Macrocytic anemia was seen in 11 patients before dialysis and 10 post dialysis. MCHC anemia was seen in 13 patients before dialysis and 14 after dialysis. NCHC anemia was seen in 13 patients before dialysis and 15 patients after dialysis. Dimorphic anemia was seen only in 1 patient after dialysis.

**Figure 12: Morphology of Anemia in Pre- & Post Dialysis Patients**

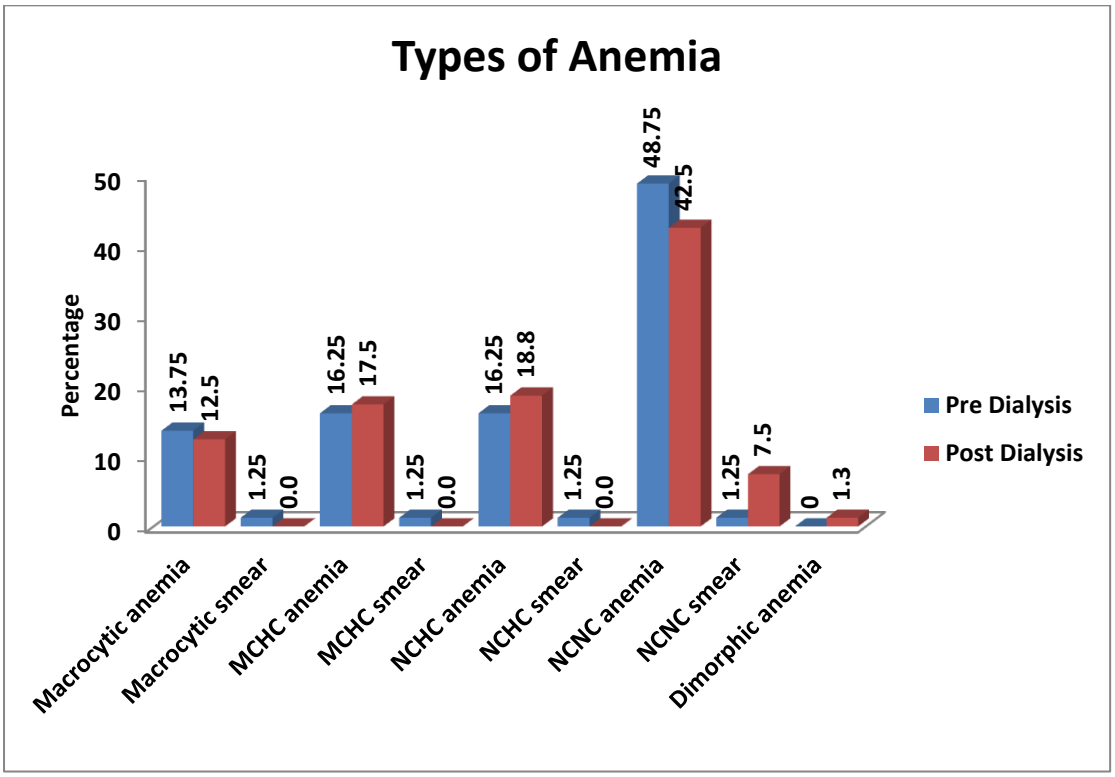

**Table 10: Comparison between RBC count and Pre- & Post Dialysis**

| RBC Level | Pre- Dialysis | | Post Dialysis | | chi sq test p value (two tailed) |
|---|---|---|---|---|---|
| | N | % | N | % | |
| Low | 70 | 87.5 | 69 | 86.3 | 0.843 |
| Normal | 9 | 11.3 | 9 | 11.3 | |
| High | 1 | 1.3 | 2 | 2.5 | |
| Total | 80 | 100.0 | 80 | 100.0 | |

RBC was seen low in 70 patients before dialysis and 69 patients after dialysis. It was normal in 9 patients before dialysis and in 9 patients after dialysis and was found high in 1 patient before dialysis and in 2 patients after dialysis.

**Figure 13: Comparison between RBC count and pre- & post Dialysis**

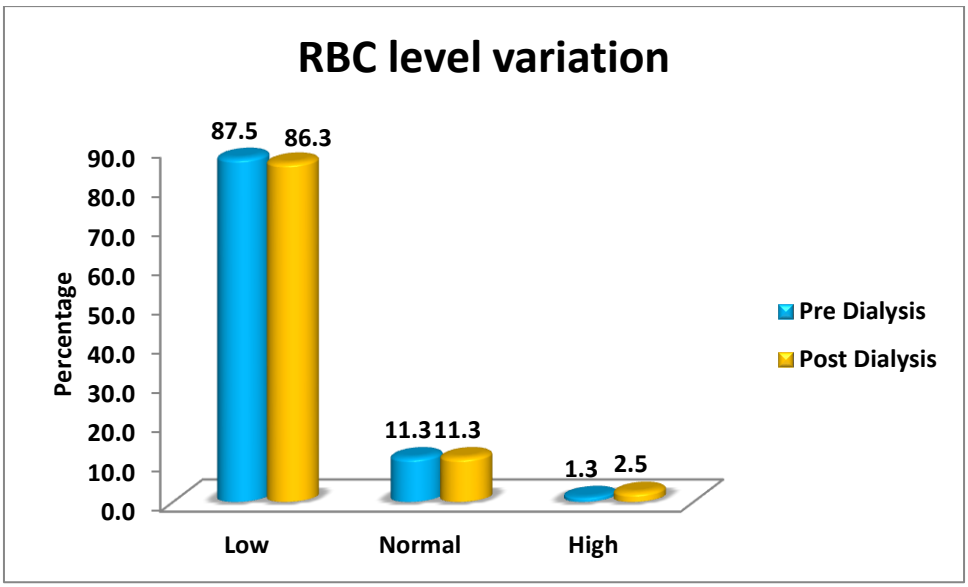

**Table 11: Comparison between WBC count and Pre- & Post Dialysis**

| WBC Level | Pre- Dialysis | | Post Dialysis | | chi sq test p value (two tailed) |
|---|---|---|---|---|---|
| | N | % | N | % | |
| Low | 11 | 13.8 | 11 | 13.8 | 0.324 |
| Normal | 53 | 66.3 | 45 | 56.3 | |
| High | 16 | 20.0 | 24 | 30.0 | |
| Total | 80 | 100.0 | 80 | 100.0 | |

WBC was found normal in 53 patients before dialysis and in 45 patients post dialysis. It was found high in 16 patients before and 24 patients after dialysis. Low WBC count was seen in 11 patients before dialysis and 11 post dialysis.

**Figure 14: Comparison between WBC count and Pre- & Post Dialysis**

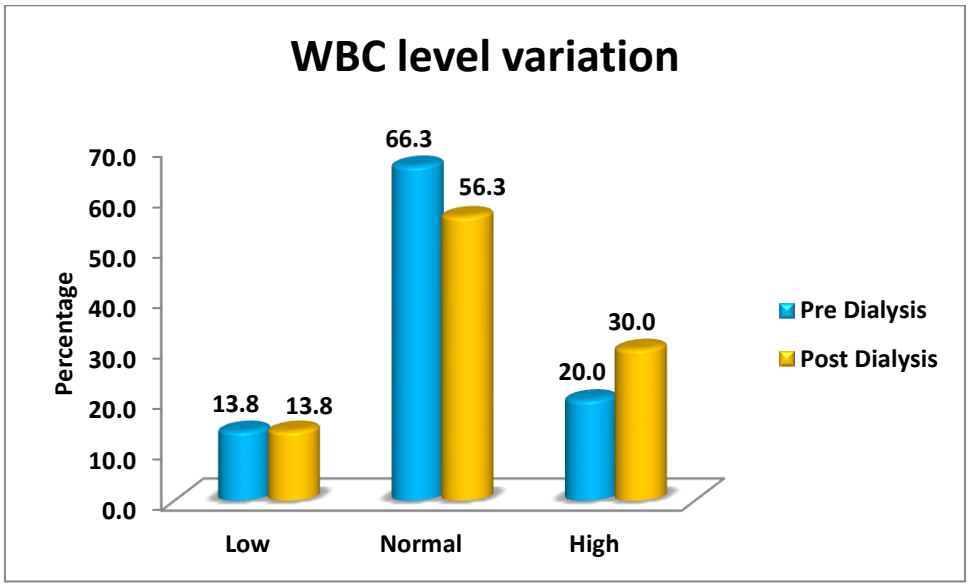

**Table 12: Comparison between Hb level and Pre- & Post Dialysis**

| Hb Level | Pre- Dialysis | | Post Dialysis | | chi sq test p value (two tailed) |
|---|---|---|---|---|---|
| | N | % | N | % | |
| Low | 77 | 96.3 | 72 | 90.0 | 0.263 |
| Normal | 3 | 3.8 | 3 | 3.8 | |
| High | 0 | 0.0 | 5 | 6.3 | |
| Total | 80 | 100.0 | 80 | 100.0 | |

Hb level was seen low in 77 patients before and 72 patients after dialysis. It was normal in 3 patients before and 3 patients after dialysis and was found to be high in 5 patients after dialysis.

**Figure 15: Comparison between Hb level and Pre- & Post Dialysis**

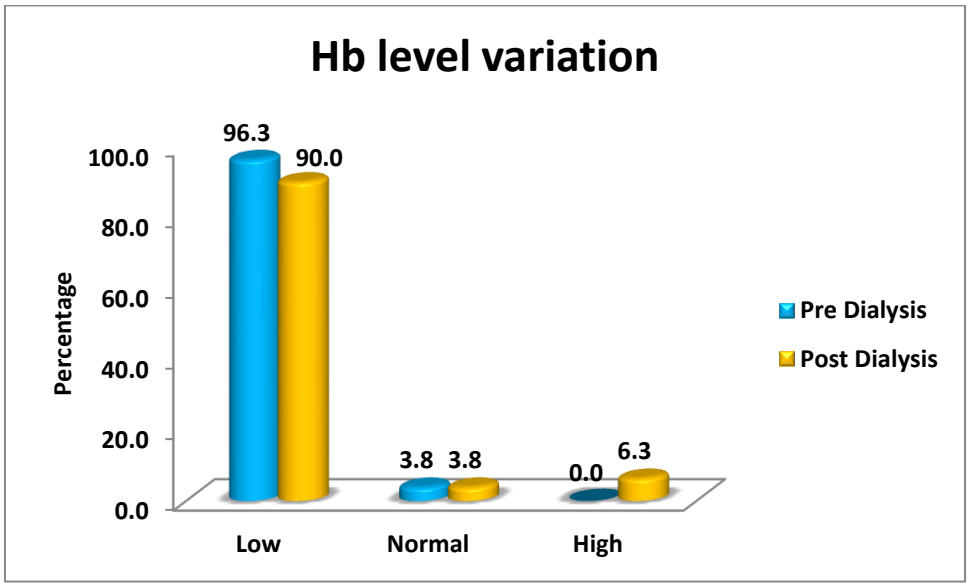

**Table 13: Comparison between Platelet count and Pre- & Post Dialysis**

| Platelet Level | Pre- Dialysis | | Post Dialysis | | chi sq test p value (two tailed) |
|---|---|---|---|---|---|
| | N | % | N | % | |
| Low | 20 | 25.0 | 22 | 27.5 | 0.804 |
| Normal | 58 | 72.5 | 57 | 71.3 | |
| High | 2 | 2.5 | 1 | 1.3 | |
| Total | 80 | 100.0 | 80 | 100.0 | |

Platelets were low in 20 patients before and 22 patients after dialysis respectively. It was seen normal in 58 patients before and 57 patients after dialysis respectively. High platelet count was seen in 2 patients before and 1 patient after dialysis.

**Figure 16: Comparison between Platelet count and Pre- & Post Dialysis**

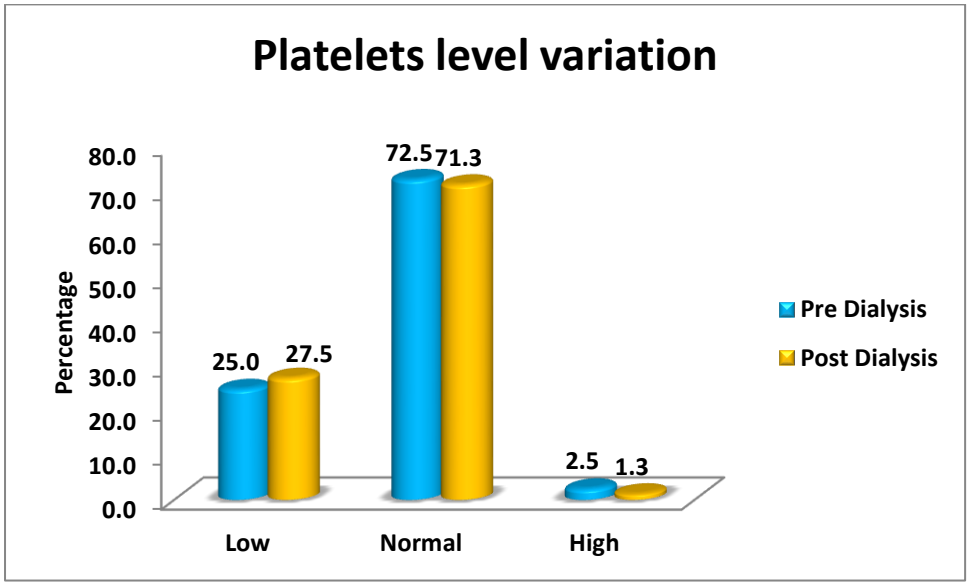

**Table 14: Comparison between MCV and Pre- & Post Dialysis**

| MCV Level | Pre- Dialysis | | Post Dialysis | | chi sq test p value (two tailed) |
|---|---|---|---|---|---|
| | N | % | N | % | |
| Low | 14 | 17.5 | 14 | 17.5 | 0.897 |
| Normal | 54 | 67.5 | 56 | 70 | |
| High | 12 | 15 | 10 | 12.5 | |
| Total | 80 | 100 | 80 | 100 | |

MCV was seen low in 14 patients before and 14 patients after dialysis respectively. It was seen normal in 54 patients before dialysis and 56 patients after dialysis respectively. High MCV was seen in 12 patients before dialysis and 10 patients after dialysis.

**Figure 17: Comparison between MCV and Pre- & Post Dialysis**

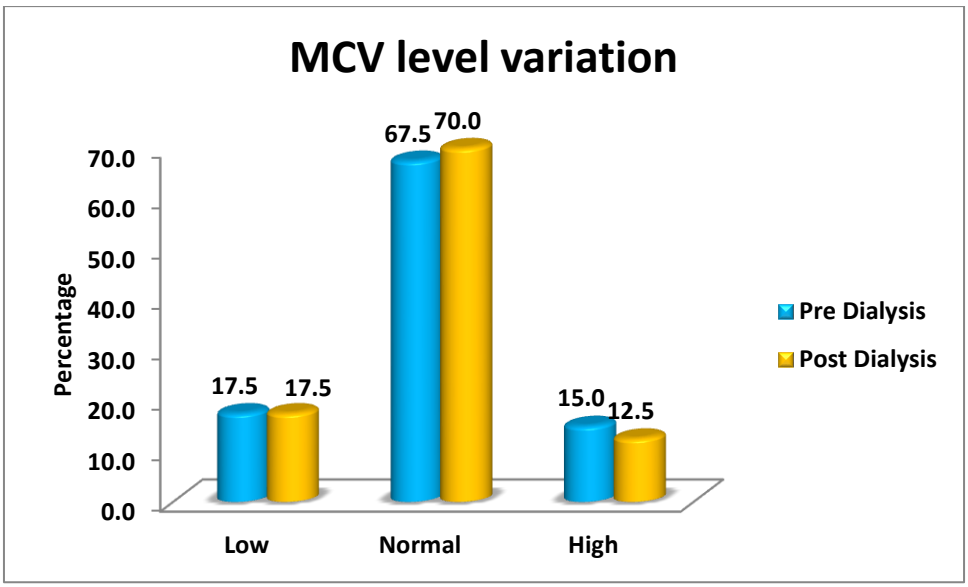

**Table 15: Comparison between MCH and Pre- & Post Dialysis**

| MCH Level | Pre- Dialysis | | Post Dialysis | | chi sq. test p value (two tailed) |
|---|---|---|---|---|---|
| | N | % | N | % | |
| Low | 32 | 40.0 | 33 | 41.3 | 0.12 |
| Normal | 48 | 60.0 | 40 | 50.0 | |
| High | 0 | 0.0 | 7 | 8.8 | |
| Total | 80 | 100.0 | 80 | 100.0 | |

MCH level was seen low in 32 patients before dialysis and 33 patients after dialysis. Normal MCH level was seen in 48 patients before and 40 patients after dialysis. High MCH level was seen in 7 patients after dialysis.

**Figure 18: Comparison between MCH and Pre- & Post Dialysis**

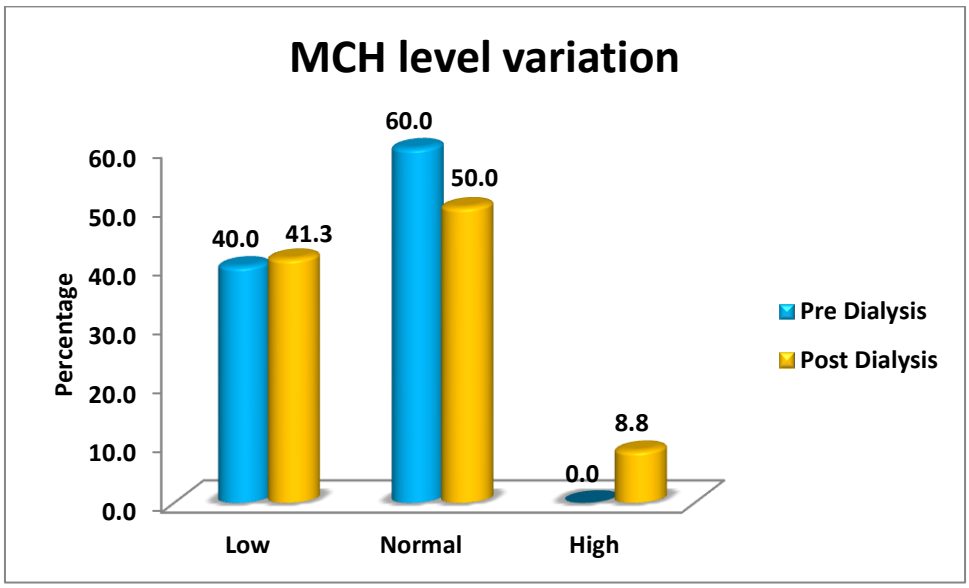

**Table 16: Comparison between MCHC and Pre- & Post Dialysis**

| MCHC Level | Pre- Dialysis | | Post Dialysis | | chi sq. test p value (two tailed) |
|---|---|---|---|---|---|
| | N | % | N | % | |
| Low | 50 | 62.5 | 47 | 58.8 | 0.774 |
| Normal | 26 | 32.5 | 27 | 33.8 | |
| High | 4 | 5.0 | 6 | 7.5 | |
| Total | 80 | 100.0 | 80 | 100.0 | |

MCHC level was seen low in 50 patients before and 47 patients after dialysis respectively. It was seen normal in 26 patients before and 27 patients after dialysis. High MCHC level was seen in 4 patients before and 6 patients after dialysis respectively.

**Figure 19: Comparison between MCHC and Pre- & Post Dialysis**

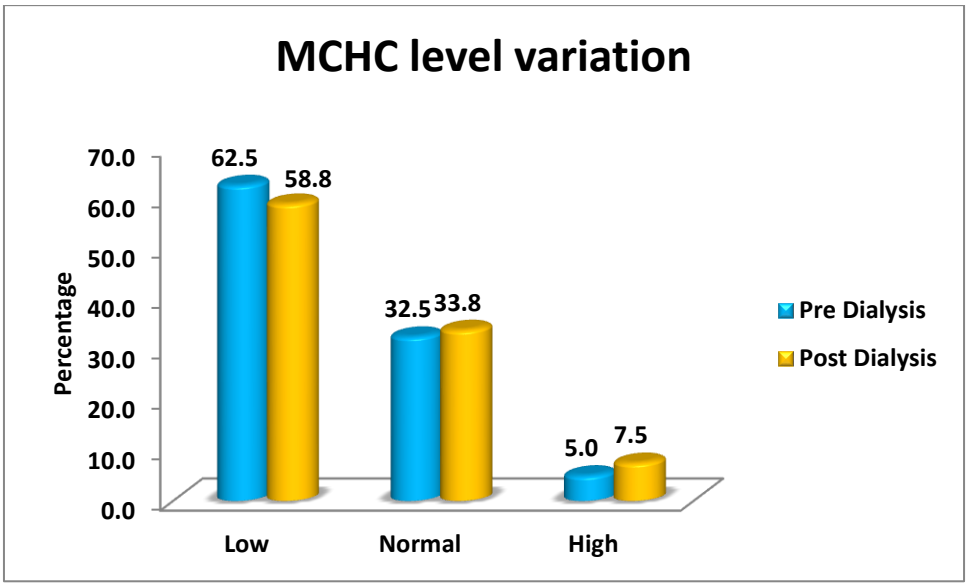

**Table 17: Comparison between HCT and Pre- & Post Dialysis**

| HCT Level | Pre- Dialysis | | Post Dialysis | | chi sq. test p value (two tailed) |
|---|---|---|---|---|---|
| | N | % | N | % | |
| Low | 78 | 97.5 | 72 | 90.0 | 0.093 |
| Normal | 1 | 1.3 | 7 | 8.8 | |
| High | 1 | 1.3 | 1 | 1.3 | |
| Total | 80 | 100.0 | 80 | 100.0 | |

HCT level was seen low in 78 patients before and 72 patients after dialysis. Normal HCT level was seen in 1 patient before and 7 patients after dialysis respectively. High HCT level was seen in 1 patient before and 1 patient after dialysis respectively.

**Figure 20: Comparison between HCT and Pre- & Post Dialysis**

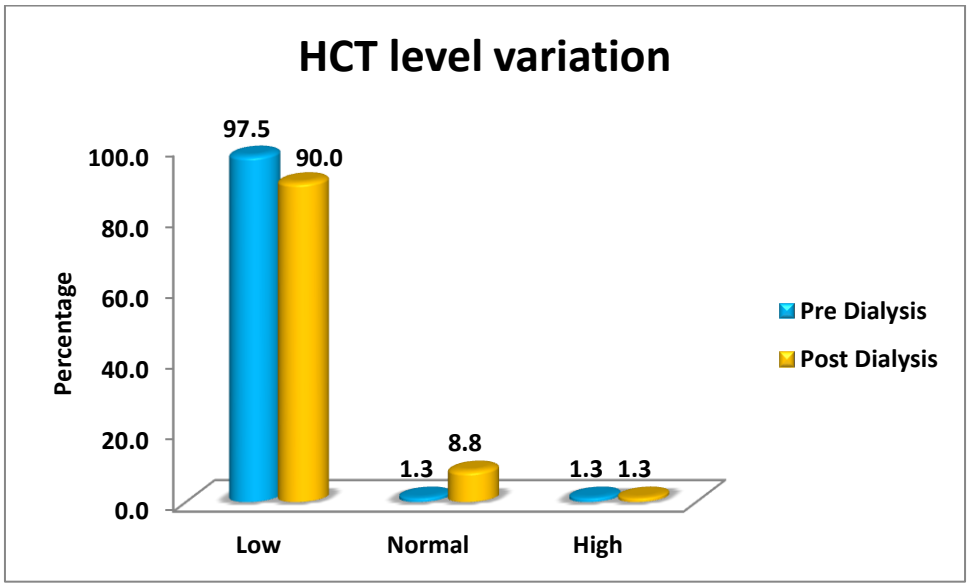

**Table 18: Comparison between RDW and Pre- & Post Dialysis**

| RDW Level | Pre- Dialysis | | Post Dialysis | | chi sq. test p value (two tailed) |
|---|---|---|---|---|---|
| | N | % | N | % | |
| Low | 0 | 0.0 | 0 | 0.0 | 0.633 |
| Normal | 20 | 25.0 | 15 | 18.8 | |
| High | 60 | 75.0 | 65 | 81.3 | |
| Total | 80 | 100.0 | 80 | 100.0 | |

RDW was seen high in 60 patients before dialysis and 65 patients after dialysis. It was seen normal in 20 patients before and 15 patients after dialysis respectively.

**Figure 21: Comparison between RDW and Pre- & Post Dialysis**

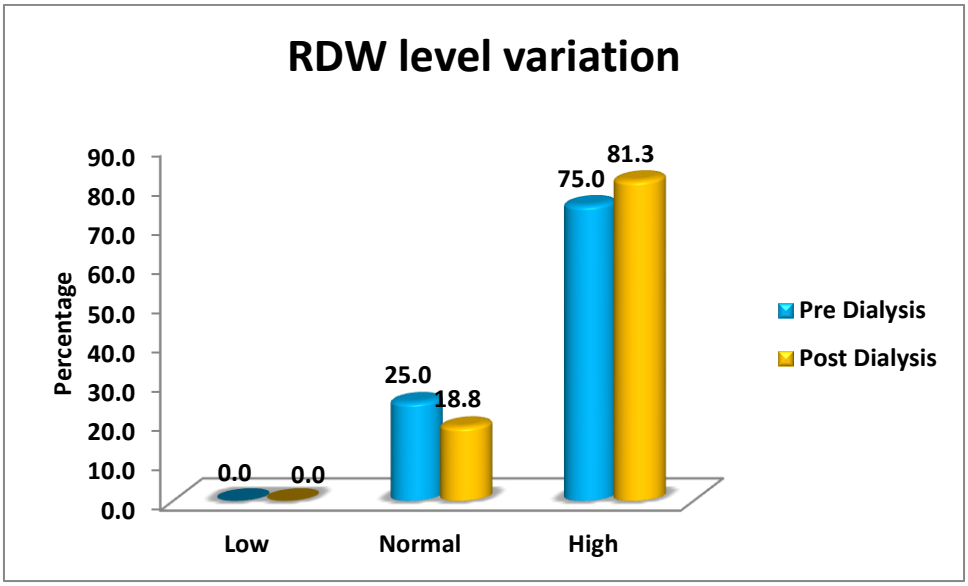


**Figure 22: Automated haematology analyzer (Sysmex XN-1000)**

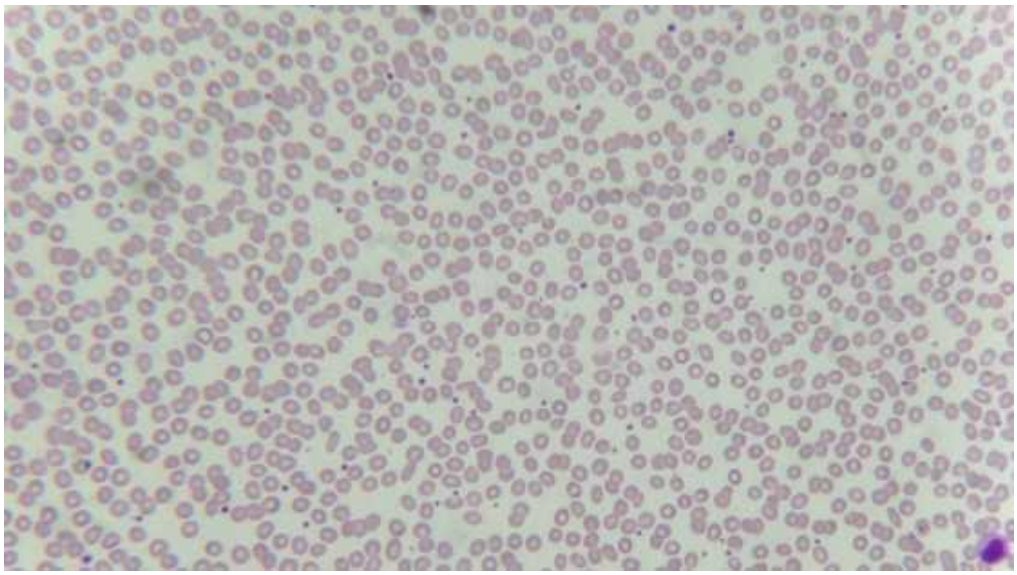

**Figure 23: Photomicrograph of peripheral smear showing normocytic normochromic type of anemia (40x)**

# DISCUSSION

The study Hematological changes in pre- and post-hemodialysis patients with chronic renal failure. was undertaken at B.L.D.E. University's Shri B M Patil Medical College, Hospital and Research Centre, Vijayapura during the period from 1$^{st}$December, 2015 to 30$^{th}$ June 2017.

In CKD, hematological parameters are commonly affected. Red cell, WBC, HCT and hemoglobin indices are commonly and severely affected. Several authors noted total white cell count, platelet count and bleeding time of normal ranges but striking eosinophilia and prolonged bleeding time. This is because major part of erythropoietin i.e. 90%, produced in the juxta glomerular apparatus of the kidney and rest i.e. 10 % are produced in the liver and other organs[2].

In this study, a total number of 80 patients suffering from chronic renal failure were selected. The result of the study shows significant changes in hematological parameters before and after dialysis. The observations were compiled, results statistically analyzed and discussed in comparison with previous studies.

**Table 19: Comparison of Hb level of present study with previous studies before and after dialysis**

| **Studies** | **Hb level after dialysis** |
|---|---|
| Mohd Ali MS *et al*[10] | Increased |
| Alghythan AK *et al*[4] | Increased |
| Bhatta S *et al* [12] | Decreased |
| Hakim Y AH *et al*[27] | Decreased |
| Present study | Increased |

In our study, Hb level was found to be increased after hemodialysis as compared to pre- dialysis. Mean Hb value in pre- dialysis patients was 7.69± 1.95 whereas in post dialysis patients, it was 8.46 ± 2.87 with a significant p value of 0.004.

In a study of Mohd Ali MS *et al*[10], Hb level was also increased in post dialysis as compared to predialysis patients.

In a study of Aghythan AK *et al*[4], Hb level was found to be increased in post dialysis as compared to predialysis patients.

In a study of Bhatta S *et al*[12], Hb level got decreased in post dialysis patients as compared to pre- dialysis.

In a study of Hakim Y AH *et al*[27], Hb level was found to be decreased in post dialysis patients as compared to predialysis patients.

**Table 20: Comparison of WBC level of present study with previous studies before and after dialysis**

| **Studies** | **WBC level after dialysis** |
|---|---|
| Pandian J *et al*[18] | Decreased |
| Mohd Ali MS *et al*[10] | Increased |
| Hakim Y AH *et al*[27] | Increased |
| Present study | Increased |

In our study WBC level was found to be increased after dialysis when compared to pre- dialysis patients. Mean WBC value in pre- dialysis patients was 8± 5.31 whereas in post dialysis patients, it was 9.57± 6.70 with a significant p value of 0.005.

In a study of Pandian J *et al* [18], WBC count was decreased after dialysis when compared to pre- dialysis cases.

In a study of Mohd Ali MS *et al* [10], WBC count was found to be increased in post dialysis patients when compared to pre- dialysis patients.

In a study of Hakim Y AH *et al* [27], WBC count was increased in post dialysis cases when compared to pre- dialysis patients.

**Table 21: Comparison of Platelets level of present study with previous studies before and after dialysis**

| **Studies** | **Platelets level after dialysis** |
|---|---|
| Pandian J *et al* [18] | Decreased |
| Hakim Y AH *et al* l[27] | Decreased |
| Latiwesh OB *et al* [22] | Decreased |
| Daugirdas JT *et al* [19] | Decreased |
| Present study | Decreased |

In our study, platelets were found to be decreased after dialysis as compared to pre-dialysis. Mean platelet value before dialysis was 2.10 ± 0.78 where as it was 1.87±0.69 in post dialysis cases with a significant p value of 0.022.

In a study of Pandian J *et al* [18], platelet count was decreased in post dialysis cases as compared to predialysis.

In a study of Hakim Y AH *et al* [27], platelet count was decreased in post dialysis cases as compared to predialysis.

In a study of latiwesh OB *et al* [22], platelet count was found to be decreased in post dialysis patients when compared to predialysis.

In a study of Daugirdas JT *et al* [19], platelet count was found to be decreased in post dialysis patients when compared to predialysis.

**Table 22: Comparison of HCT level of present study with previous studies before and after dialysis**

| Studies | HCT level after dialysis |
|---|---|
| Bhatta S *et al* [12] | Decreased |
| Present study | Increased |

In our study, HCT level after dialysis was increased when compared to predialysis cases. Mean value of HCT before dialysis was 25.21± 6.49 whereas after dialysis it was 26.94±7.10 with a significant p value of 0.038.

In a study of Bhatta S *et al* [12], HCT was found to be decreased in post dialysis cases when compared to predialysis cases.

**Table 23: Type of Anemia in present study compared with previous studies**

| Studies | Most common type of Anemia before and after dialysis |
|---|---|
| Suega K *et al* [26] | NCNC |
| Pandian J *et al* [18] | NCNC |
| Kaze FF *et al* [16] | MCHC |
| Bhatta S *et al* [12] | MCHC |
| Present study | NCNC |

As per WHO, anemia is defined as a hemoglobin level less than 13 g/dL in men and post-menopausal women, and less than 12 g/dL in pre-menopausal women.

The NKF defines anemia as a hemoglobin of less than 13.5 g/dL in men and less than 12.0 g/dL in women.

Anemia is defined as a reduction in one or more of the major red blood cell measurements; hemoglobin concentration, hematocrit, or red blood cell count.

Normochromic, normocytic anemia is commonly seen in CKD, and nearly 50% is the overall prevalence of CKD-associated anemia. Although anemia can be diagnosed in patients at any stage of CKD, there is a strong correlation between the severity of CKD and the prevalence of anemia.

The most important and specific etiology causing CKD-associated anemia is reduced synthesis of erythropoietin. Other factors include iron, folate, or vitamin B12 deficiency; gastrointestinal blood loss; severe hyperparathyroidism, systemic inflammation, and reduced red blood cell life span. Erythropoietin is a glycoprotein, secreted by the renal interstitial fibroblasts and is necessary for the growth and differentiation of red blood cells in the bone marrow. In CKD, tubulointerstitial fibrosis is produced by tubular atrophy, which compromises erythropoietin synthetic capacity of kidney and leads to anemia. Prevalence of anemia has been significantly risen as the creatinine clearance (an estimate of glomerular filtration rate) falls to 70 mL/min or lower among males and to 50 mL/min or lower among females[63].

In our study also, normocytic normochromic anemia was most commonly seen both in pre- and post-dialysis cases. It was seen in 39 patients before dialysis and 34 patients post dialysis. Macrocytic anemia was seen in 11 patients before dialysis and 10 after dialysis. MCHC anemia was seen in 13 patients before dialysis and 14 post dialysis. NCHC anemia was seen in 13 patients before dialysis and 15 patients after dialysis. Dimorphic anemia was seen only in 1 patient after dialysis.

In a study of Bhatta S *et al*[12], MCHC anemia was most commonly seen both in pre- and post-dialysis.

In a study of Suega K *et al*[26], NCNC anemia was seen in majority of cases both in pre- and post-dialysis.

In a study of Pandian J *et al*[18], NCNC anemia was seen most commonly before and after dialysis.

In a study of Kaze FF *et al*[16], MCHC anemia was seen in majority of cases both before and after dialysis.

As shown in table 8, in our study mean value of RBC before dialysis was 2.87± 0.79 and after dialysis, it got increased 3± 0.87 with a non-significant p value.

In a study of Abdullah Khader Alghythan *et al*[4], mean value of RBC got increased after dialysis as compared to predialysis, with a significant p value.

In a study of Mohd Ali MS *et al*[10], mean value of RBC found to be significantly increased after dialysis as compared to predialysis.

Dorgalaleh Akbar *et al*[13] in their study found that RBC got significantly reduced after dialysis when compared to predialysis.

As shown in table 8, in our study mean value of MCV before dialysis was 88.88± 10 .67and after dialysis it was 88.91± 10.27 with a non-significant p value.

As shown in table 8, in our study mean value of RDW before dialysis was 16.13 ±3.14 and after dialysis it got reduced to15.92± 2.45 with a non-significant p value.

In a study of Abdullah Khader Alghythan *et al*[4] , mean value of RDW got increased after dialysis as compared to predialysis, with a significant p value.

# CONCLUSION

- Most of the hematological parameters like Hb, WBC, MCH, MCHC and HCT increased after hemodialysis as compared to that of predialysis cases. Platelet count was found to be decreased after dialysis as compared to predialysis cases.
- Chronic kidney disease (CKD) is known to be a global public health problem. It may be detected by using simple laboratory tests, and treatment can prevent or delay the complications of decreased kidney function, retard the progression of kidney disease
- So, to evaluate the effectiveness of hemodialysis, it is necessary to test the complete hemogram before and after hemodialysis.

# SUMMARY

A total number of 80 patients suffering from chronic renal failure were included in this study. The study was conducted at B.L.D.E. University's Shri B M Patil Medical College, Hospital and Research Centre, Vijayapura during the period from 1$^{st}$December, 2015 to 30$^{th}$ June 2017. Hematological changes were noted in pre- and post-hemodialysis patients with chronic renal failure.

In this study, maximum no. patients were male. Out of 80 patients of CRF, 58 patients were male and 22 patients were female. Maximum number of patients were in the age group of 51- 60 years.

WBC count was found to be increased after dialysis as compared to predialysis patients. Mean value of WBC before dialysis was 8 ± 5.31 whereas after dialysis, it got increased i.e. 9.57 ± 6.70 with a significant p value of 0.005.

Hb count was found to be increased after dialysis as compared to predialysis patients. Mean value of Hb before dialysis was 7.69 ± 1.95 whereas after dialysis, it was 8.46 ± 2.87 with a significant p value of 0.004.

Platelet count was found to be decreased after dialysis as compared to predialysis patients. Mean value of platelet before dialysis was 2.10 ± 0.78 which got decreased after dialysis to 1.87 ± 0.69 with a significant p value of 0.002.

MCH count was found to be increased after dialysis as compared to predialysis patients. Mean value of MCH in predialysis was 27.01 ± 2.82 and after dialysis it became 27.67 ± 2.51with a significant p value of 0.038.

MCHC count was found to be increased after dialysis as compared to predialysis patients. Mean value of MCHC in predialysis was 30.48 ± 2.77 whereas after dialysis it got increased to 31.09 ± 2.33 with a significant p value of 0.040.

HCT count was found to be increased after dialysis as compared to predialysis patients. Mean value of HCT before dialysis was 25.21 ± 6.49 whereas after dialysis it got increased to 26.94 ± 7.10 with a significant p value of 0.038.

NCNC anemia was seen in majority of patients. 39 patients before dialysis and 34 patients post dialysis were suffering from NCNC anemia. Macrocytic anemia was seen in 11 patients before dialysis and 10 post dialysis. MCHC anemia was seen in 13 patients before dialysis and 14 after dialysis. NCHC anemia was seen in 13 patients before dialysis and 15 patients after dialysis. Dimorphic anemia was seen only in 1 patient after dialysis.

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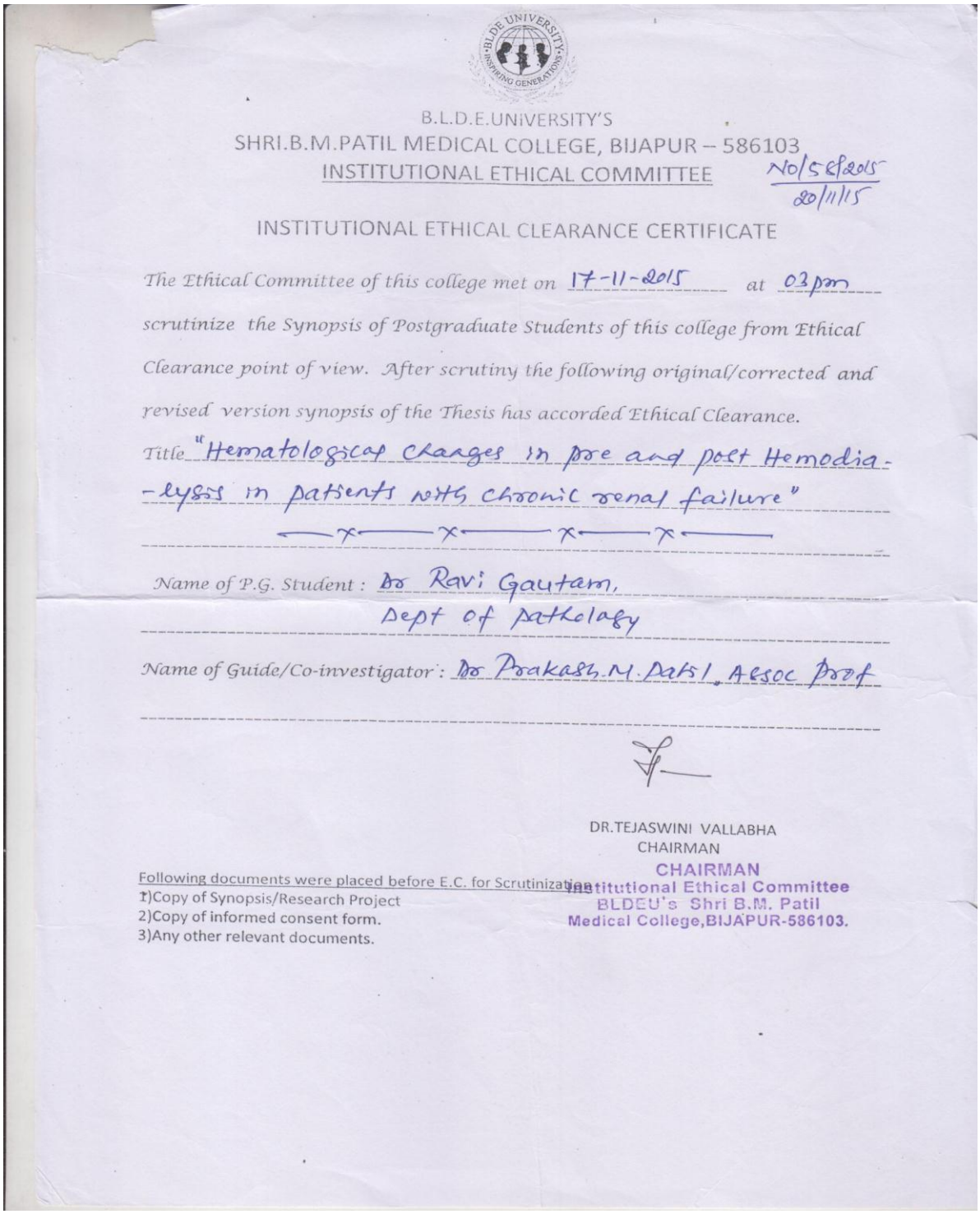
# ANNEXURE – I

# INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE



B.L.D.E.UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR – 586103
INSTITUTIONAL ETHICAL COMMITTEE

No/5 & 2015
20/11/15

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 17-11-2015 at 03 pm scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has accorded Ethical Clearance.

Title "Hematological changes in pre and post Hemodia-lysis in patients with chronic renal failure"

—x—x—x—x—

Name of P.G. Student : Dr Ravi Gautam, Dept of pathology

Name of Guide/Co-investigator : Dr Prakash.M.Patil, Assoc Prof

DR.TEJASWINI VALLABHA
CHAIRMAN

CHAIRMAN
Institutional Ethical Committee
BLDEU's Shri B.M. Patil
Medical College,BIJAPUR-586103.

Following documents were placed before E.C. for Scrutinization
1)Copy of Synopsis/Research Project
2)Copy of informed consent form.
3)Any other relevant documents.

## ANNEXURE – II

## BLDE UNIVERSITY'S SHRI B.M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTER, VIJAYAPURA - 586 103

## RESEARCH INFORMED CONSENT FORM

TITLE OF THE PROJECT : HEMATOLOGICAL CHANGES IN PRE AND POST HEMODIALYSIS IN PATIENTS WITH CHRONIC RENALFAILURE

PRINCIPAL INVESTIGATOR : Dr. RAVI GAUTAM

P.G. DEPARTMENT OF PATHOLOGY,

B.L.D.E. UNIVERSITY'S SHRI B.M.PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA

P.G. GUIDE : Dr. PRAKASH M. PATIL

ASSOCIATE PROFESSOR,

B.L.D.E. UNIVERSITY'S SHRI B.M.PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA

P.G. CO-GUIDE: Dr. R. M. HONNUTAGI

PROFESSOR

DEPARTMENT OF MEDICINE

B.L.D.E. UNIVERSITY'S SHRI B.M.PATIL

MEDICAL COLLEGE, HOSPITAL AND

RESEARCH CENTRE, VIJAYAPURA

**PURPOSE OF STUDY:**

It has been explained to me that the purpose of this study is to analyze the hematological parameters of chronic renal failure patients before and after hemodialysis.

**PROCEDURE:**

I understand that I have to furnish my medical history and undergo relevant clinical examination after which two milliliters of venous blood will be collected from me under all aseptic precautions.

**POTENTIAL RISKS:**

I understand that there are no potential risks or side effects from participating in this study.

**BENEFITS:**

I understand that this study will help in preventing complications in chronic renal failure patients with and without effect of hemodialysis.

**FINANCIAL INCENTIVE FOR PARTICIPATION:**

I understand that I will not receive any payment for participation in this study.

**PRIVACY:**

I understand that the medical information produced by the study will become a part of hospital record and will be subjected to confidentiality and privacy regulations of the hospital.

**AUTHORISATION TO PUBLISH RESULTS:**

It has been explained to me that the results of this study may be published for scientific purposes or presented to scientific groups; however, I will not be identified in any publication or presentation.

**REQUEST FOR MORE INFORMATION:**

I understand that I may ask more information about the study at any time.

**VOLUNTARY PARTICIPATION:**

I understand that my participation is voluntary and that I may refuse to participate or may withdraw from the study at any time without prejudice.

**INSTITUTIONAL POLICY:**

SBMPMC, Hospital and Research Centre in Vijayapura, Karnataka will provide, within the limitations of the laws of the State of Karnataka, facilities and medical attention to me if I suffer any injuries as a result of participating in this study.

**STATEMENT OF CONSENT:**

I volunteer and consent to participate in this study. I have read the consent form or it has been read to me. The study has been fully explained to me and I may ask questions at any time.

---------- ----------

Signature or left-hand thumb impression Date

# ANNEXURE-III

## PROFORMA FOR STUDY

**Name:**

**Age:**

**Sex: M/F**

**OPD/IPD no.**:

**Chief complaints:**

**History of present illness:**

**Past history:**

**Family history:**

**General physical examination:**

**Clinical diagnosis:**

**Hematological investigations before and after hemodialysis:**

| **Parameters** | BEFORE | AFTER |
|---|---|---|
| WBC | | |
| RBC | | |
| HGB | | |
| HCT | | |
| MCV | | |
| MCH | | |
| MCHC | | |
| RDW | | |
| PLATELET | | |

**Peripheral Smear Examination**:

RBCs:

WBCs:

Platelets:

IMPRESSION:

# KEY TO MASTER CHART

| | |
|---|---|
| Hb | Hemoglobin (g/dL) |
| RDW | Red cell distribution width (%) |
| MCV | Mean corpuscular volume (fl) |
| MCH | Mean corpuscular hemoglobin (pg) |
| MCHC | Mean corpuscular hemoglobin concentration (g/dL) |
| RBC | Red cell count (million/cu mm) |
| HCT | % |
| WBC | White blood cell count (cells/cu mm) |
| MCHC | Microcytic hypochromic anemia |
| Dimorphic | Dimorphic anemia |
| NCNC | Normocytic normochromic anemia |
| NCHC | Normocytic hypochromic anemia |
| Macro | Macrocytic anemia |