International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Study of Iron Profile in Patients with Chronic Kidney Disease Stage 3 To 5 Not on Dialysis, Presenting to Shree Birendra Hospital

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ABSTRACT

Background: Anemia is a common in many CKD patients who do not require dialysis yet and it is becoming increasingly common as GFR declines. Iron deficiency is one of the contributing factors, which can be problematic especially during erythropoietin therapy. Anemia in CKD is associated with reduced quality of life, increased cardiovascular disease, hospitalizations, cognitive impairment, and mortality.

Objectives: To study the iron profiles and prevalence of anemia in CKD3 to CKD5 not on dialysis.

Methods: It is a cross-sectional study conducted at Shree Birendra Hospital, Kathmandu in Department of Medicine and Nephrology. This study included 146 cases who are diagnosed case of CKD as per standard clinical and laboratory criteria. Patient`s clinical and laboratory parameters were recorded as per predesigned proforma, GFR was calculated by CKD-EPI equation and staging of CKD was done according to GFR. Anemia was defined as hemoglobin ≤10g/dl.

Results: This study shows low level of hemoglobin as severity of CKD increases, The mean hemoglobin in CKD3a was 10.3±1.12, in CKD3b was 10.08±0.61, in CKD4 was 9.20±1.12 and in CKD5 was 8.74±0.64 (P-value <0.001). Anemia was present in 76.71% and mean hemoglobin was 9.25±1.01g/dl. TSAT <20 was found in 81 (55.48%) cases and ferritin <100ng/dl was found in 51 (34.93%) of cases. Iron deficiency was present in 55.48% of patient. Mean TSAT was 21.27±13.21, mean ferritin was 181±147.63 and mean iron was 55±26.29. TSAT and Ferritin had association with CKD (P- value 0.005 and <0.001 respectively). TSAT decreases with increasing age. Normocytic normochromic was in 83.56%, 15.07% had microcytic hypochromic and 2% had macrocytic. Severity of anemia was more in females than male, in male mean hemoglobin was 9.41±1.02g/dl and in female 8.94±0.13g/dl.

Conclusion: This study shows iron deficiency anemia is the most common form of anemia in CKD, prevalence and severity of anemia increases as kidney function decreases and anemia was present in all age group with relatively more common in female gender.

INTRODUCTION

Chronic kidney disease(CKD) is defined as abnormalities of kidney structure or function, present for ≥3 months, with implications for health and is classified based on GFR category(G1-G5) and albuminuria category(1).

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012

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

In Nepal most people cannot afford renal replacement therapy for end stage renal disease due to lack of resources. Early diagnosis of CKD and anemia in CKD can lessen the renal replacement therapy,morbidity,mortality and financial burden to patients and country. In Nepal a door-to-door screening was conducted over 3218 people of age more than 20 years, CKD was found in 10.6% of population.[2]

Anemia is a common feature of patients with CKD who do not yet require dialysis, anemia becoming increasingly common as GFR declines below 60ml/min/1.73m^2.[3]

Anemia of CKD in most of patients, normocytic normochromic and is primarily due to reduced production of erythropoietin by the kidney, to shortened red cell survival, decreased appetite. Anemia in CKD is associated with reduced quality of life and increased cardiovascular disease, hospitalization, cognitive impairment, and mortality.[4]

According to WHO anemia is defined as hemoglobin less than 13g/dl in men and less than 12g/dl in women.[5]

Chronic kidney disease is associated with iron deficiency anemia, which is a common consequence. Both absolute and functional iron deficiencies affect CKD patients. Functional iron deficiency is defined by adequate iron stores but insufficient iron availability for incorporation into erythroid precursors. Absolute iron deficiency is defined as severely reduced or absent iron stores. This is owing to the rising cost of living.[6] Early treatment of anemia is related with a reduced loss of residual renal function and delayed the progression to ESRD , according to various retrospective trial.

It is obvious from above discussions that early detection of anemia in CKD not only reduces morbidity and mortality, but also to prevent renal function loss(GFR) due to anemia and to improve the survival, to

prevent its progression and early management will be more cost effective in nation like Nepal, where most people cannot afford RRT.

RESEARCH OBJECTIVES

General objective:

A. To study the iron profile findings in patients with CKD stage 3 to 5 not on dialysis.

Specific objective:

A. To study the prevalence of anemia in patients with CKD stage 3 to 5 not on dialysis.

B. To study the individual indices of iron profile in CKD stage 3 to 5 not on dialysis.

C. To study about the iron profile findings in CKD stage 3 to 5 not on dialysis patients in relation to gender and age.

REVIEW OF LITERATURE

CHRONIC KIDNEY DISEASE:

Chronic kidney disease (CKD) has become a major public health issue across the world. Developing countries are widely acknowledged as being unable to pay the costs of treatment required to manage patients with end-stage renal disease.

Chronic renal disease is a process in which the number of functioning nephrons in the kidneys continues to decline in an irreversible way, kidney function decrease and it usually corresponds to CKD stages 1-5. End-stage renal disease (ESRD) is a stage of chronic kidney disease in which the accumulation of toxins, fluids, acid base disorder and electrolytes imbalance which are normally filtered and managed by the kidneys. If the toxins are not cleared through renal replacement therapy, such as dialysis or kidney transplantation, this condition leads to death.[7]

DEFINITION OF CHRONIC KIDNEY DISEASE:

Chronic kidney disease is defined as abnormalities of kidney structure or function, present for more than three months, with implications for health and is classified based on GFR category(G1-G5), and albuminuria category.

Criteria for CKD (either of the following present for >3 months)[1]

Markers of kidney damage (one or more):

Albuminuria (ACR ≥30 mg/24 hours; ACR ≥30mg/g [>3 mg/mmol])

Urine sediment abnormalities

Electrolyte and other abnormalities due to tubular disorders

Abnormalities detected by histology

Structural abnormalities detected by imaging

History of kidney transplantation

Decreased GFR: GFR <60 ml/min/1.73 m2 (GFR categories G3a–G5)

Classification of CKD:[1]

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012

GFR categories (ml/min/1.73m²) description and range				Persistent albuminuria categories description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
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	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	<15			

Calculation of GFR:

The CKD-EPI equation, expressed as a single equation,[1]

GFR = 141 × min (Scr/κ, 1)$^{\alpha}$ × max(Scr/κ, 1)$^{-1.209}$ × 0.993^{Age} × 1.018 [if female] _ 1.159 [if black], where Scr is serum creatinine, κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/κor 1, and max indicates the maximum of Scr/κ or 1.

Pathophysiology of CKD:

A series of progressive mechanisms including hyperfiltration and hypertrophy of the viable nephrons that occur because of long-term renal function loss, regardless of the underlying cause. Vasoactive hormones, cytokines, and growth factors are involved in the reactions to a decrease in nephron number. The increasing pressure and flow predisposes to sclerosis and failure of the remaining nephrons, so these short-term adaptations of hypertrophy and hyperfiltration eventually become maladaptive.[7] Even in those with normal GFR, it's critical to identify characteristics that raise the risk of CKD.

Risk factors include:

- Hypertension
- Diabetes mellitus
- Auto-immune disease
- Older age
- Structural abnormalities of urinary tract.
- Family history of renal disease

- A previous episode of acute renal failure
- Presence of proteinuria

Diabetic nephropathy, which is most commonly caused by type-2 diabetes, is the most common cause of CKD. In the elderly, hypertensive nephropathy is a prevalent cause of CKD. Glomerulonephritis is the third most common cause of chronic kidney disease. Albuminuria and even moderate GFR declines in the early stages of CKD are now recognized as substantial risk factors for cardiovascular disease. Other causes of End Stage Renal Disease, such as interstitial nephritis, HIV nephropathy, and so on account for a large fraction of cases.[7,8]

CHRONIC KIDNEY DISEASE HAEMATOLOGICAL ASPECTS:

Anemia is a common complication in chronic kidney disease patients. The cause of CKD-related anemia is multifactorial. However, erythropoietin insufficiency is the most common cause. Even while erythropoietin insufficiency is the cause of normochromic normocytic anemia, other factors such as iron shortage play a significant role, which is more prevalent in dialysis patients.[9]

Anemia is a risk factor for the progression of chronic kidney disease to end-stage renal disease, lowers quality of life and increases morbidity and death. Anemia appears earlier in diabetic patients with CKD, and the severity is more than in non-diabetic patients.[10]

In general, as renal function declines, anemia becomes more common, becoming practically universal in ESRD. Hsu et.al evaluated 12,055 adult ambulatory participants from Boston health clinics and discovered that when creatinine clearance was below 60 mL/min in men and below 40 mL/min in women, mean hematocrit levels fell progressively only when GFR was substantially decreased, less than 30 mL/min in women and 20 mL/min in men, was moderately severe anemia (hematocrit less than 33%) prevalent (occurring in >20 percent of patients). Nearly 90% of cases of anemia are caused by erythropoietin deficit along with an absolute or functional iron shortage.[11]

Etiology of anemia in CKD:

Anemia is a complex condition in chronic kidney disease, with the most common etiology being diminished renal production of erythropoietin, the hormone that stimulates the red blood cells synthesis. Hypoxia-inducible factor (HIF), a transcription factor that regulates erythropoietin gene expression, has recently been linked to decreased erythropoietin. Uremia leads to hemolysis and RBC deformity, folate and vitamin B12 deficiency, iron deficiency, bleeding due to defective platelets, and infrequently blood loss after hemodialysis and damaged renovascular endothelium fragments RBCs in some conditions.[12–14]

Effects of anemia:[8,11]

a. Reduced quality of life
b. Reduced exercise tolerance
c. Impaired cognitive function
d. Hypertrophy of the left ventricle
e. Congestive heart failure
f. Myocardial infarction and angina
g. Disrupted sleep pattern

8) Impaired Immune response

Cardiovascular effects of anemia:

Cardiac disease has a significant influence in CKD patients, lowering their quality of life and increasing the risk of hospitalization and death. The risk of death from cardiovascular disease is more than 15 times higher in hemodialysis patients than in the general population. Congestive heart failure , acute myocardial infarction , and sudden cardiac death account for almost half of all deaths in CKD.[15] Patients with CKD are considerably more likely to die from heart attacks than to develop ESRD.[16]

Anemia causes persistent alterations in the cardiovascular system in CKD patients. A high cardiac output and vasodilated state are part of the body's adaptation for anemia, which somewhat mitigates the effect of diminished oxygen carriage by the bloodstream. Chronic rise of cardiac output may be maladaptive, increasing cardiac work and raising the risk of cardiovascular events by left ventricular hypertrophy.[16,17]

LEFT VENTRICULAR HYPERTROPHY AND ANEMIA:

The most common cardiac problem associated with persistent anemia is left ventricular hypertrophy. Characteristic echocardiographic abnormalities, left ventricular mass index greater than 134g/m^2 and 110 g/m^2 in males and women, respectively, make it easy to diagnose.[18] It's a significant finding because it's a reliable predictor of mortality risk. Hemoglobin levels fall by 1 gm/dL were associated with a 6% increase in the incidence of LVH.[19]

Other Negative Implications of Anemia in Chronic Kidney Disease: Anemia is associated with reduced oxygen carrying and delivery capacity, have negative effects in CKD patients. With worsening anemia, reduced oxygen delivery to damaged kidneys leads to progression of renal disease. Mohanram et al published a post hoc analysis of the RENAAL (Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan) experiment. Initial Hb was an important predictor of renal outcome in 1513 patients with type 2 diabetes mellitus, including time to ESRD and serum creatinine doubling. For every 1g/dL drop in Hb, the risk increased by 11%.

CORRECTION OF ANEMIA HAS BENEFICIAL EFFECTS:[11]

1) **Blood transfusions are used less frequently:**
   - Lower chance of infection with the Human Immunodeficiency Virus/Hepatitis C Virus
   - There are fewer possibilities of alloantibodies forming (transplant rejection)
   - There's a lower chance of iron overload
2) Increased work tolerance and improved quality of life.
3) Regression of left ventricular hypertrophy and congestive heart failure becoming less common.

B. Less frequent angina/myocardial infarction

DIAGNOSTIC EVALUATION OF ANEMIA IN CKD:

Because erythropoietin deficiency is an exclusionary diagnosis, an appropriate history, physical, and laboratory testing should be used to rule out other causes of anemia.

1. Hemoglobin–the severity of anemia is determined by the Hb percent and hematocrit.
2. A complete blood count should be performed to check for any issues in the leukocyte or platelet cell lines.
3. Anemia should be characterized as microcytic, normocytic, or Macrocytic based on red blood indices.
4. Anemia caused by CKD usually results in normocytic erythrocytes. If microcytosis, we should check for iron deficiency, thalassemia, and myelodysplasia. Folic acid and vitamin B12 deficiency must be

ruled out in the case of macrocytosis. Chronic renal failure was assumed to be associated with echinocytes or burr cells. When exposed to a glass surface or incubated uremic plasma, even normal cells undergo a reversible metamorphosis into burr cell-like echinocytes. Upper Gastrointestinal scopy and fecal blood testing[20] (Bini EJ et al) should be performed.

IRON DEFICIENCY IN CHRONIC KIDNEY DISEASE:

The peripheral blood picture is characterized by microcytosis and hypochromia, lower RBC count, MCV, MCH, and MCHC, all of which indicate low hemoglobin owing to iron insufficiency, the severity of which varies with the severity of iron deficiency, which rises as CKD progresses.

DIAGNOSIS OF HYPOPROLIFERATIVE ANEMIA [7]

TESTS	IRON DEFICIENCY ANEMIA	INFLAMMATION	RENAL DISEASE
Anemia	Mild to severe	Mild	Mild to severe
MORPHOLOGY	Normo-microcytic	Normocytic	Normocytic
MCV (fl)	60-90	80-90	90
SERUM IRON(µg/L)	< 30	< 50	Normal
FERRITIN	<15	30-200	115-150
SATURATION %	<10	10-20	Normal
TIBC (µg/L)	> 360	<300	Normal

ERYTHROPOIETIN:

Erythropoietin (E PO) is a 34-kDa glycoprotein hematopoietic growth factor that acts on erythroid precursors in the bone marrow to regulate the red blood cell synthesis. EPO levels in the blood is 4-27 U/L.Peritubular interstitial cells of the kidney produce EPO. The reduction in EPO production in CKD patients is proportionate to the degree of excretory dysfunction.[21]

Anemia and inflammatory cytokines:

CKD patients had higher amounts of inflammatory cytokines. These cytokines limit EPO production and make erythroid cells resistant to EPO activity, resulting in normocytic normochromic anemia.[22,23]

Iron markers in chronic kidney disease

Serum iron, transferrin saturation and serum ferritin are the most often used iron indicators in patients with CKD. Although bone marrow iron staining is the gold standard, it is a semi-quantitative test that is rarely utilized .[24,25]

The Role of Inflammation in Ferritin Synthesis:

Most cells in the body have limited amount of ferritin store in normal condition, however cells in the reticuloendothelial system (RES) may contain more ferritin. Proinflammatory cytokines like IL-1 and TNF-alpha boost ferritin production during the acute-phase response.

Higher levels of ferritin, it is hypothesized, could trap more bodily iron, and prevent the individual from worsening infection, which is almost always preceded by inflammation. As a result, inflammation-induced hyperferritinemia can cause a so-called "functional iron deficiency," which can be beneficial in

"acute" inflammation by containing iron in the RES sites but can be harmful in "chronic" inflammation by causing refractory anemia, as seen in CKD and other chronic disease states.

As a result, a low ferritin level (e.g., 200 ng/ml in hemodialysis patients or 100 ng/ml in non-dialysis CKD patients) is a reliable diagnostic of iron shortage, whereas a normal to moderately high serum ferritin level does not rule out iron deficit or suggest adequate or excessive iron.[26]

HYPERFERRITINEMIA IN CKD:

Increases in serum ferritin associated with inflammation, infection, liver illness, malignancies, and other non–iron-related disorders may make it difficult to determine iron status in CKD when these conditions are present. Neuroblastoma, renal cell carcinoma, and Hodgkin's lymphoma all have high serum ferritin levels. Because the liver is the principal organ for clearing circulating ferritin molecules, hyperferritinemia is also linked to liver impairment. Patients with CKD, glomerular disease, and proteinuria have been reported to have high ferritin levels.

Chronic inflammation is frequent in individuals with CKD, with up to 40% to 70% of patients having elevated C-reactive protein (CRP) levels on a long-term basis. As a result, inflammation is likely to be the most common confounder in CKD-related hyperferritinemia, and it may play a bigger role than iron. Many other chronic illness situations have comparable models of hyperferritinemia, such as rheumatoid arthritis, where iron shortage is present in 50% of patients yet blood ferritin levels are normal or higher.[26]

Hyperferritinemia is related with Erythropoiesis stimulating agents hypo responsiveness and a more severe anemia in patients with CKD. There was a substantial relationship between serum CRP and ferritin that was shown to be irrespective of age, gender, race, and diabetes. CRP and TSAT, independently of each other, were found to have a substantial correlation with serum ferritin in multivariate models. These data imply that a moderately high serum ferritin level in individuals with CKD is more than just a marker of Fe stores, but also a sign of inflammation, malnutrition, and other non–iron related diseases.[26]

MORTALITY IN CKD AND SERUM FERRITIN:

Hyperferritinemia-related morbidity could be attributed to non-iron-related causes. Because serum ferritin is a positive acute-phase reactant, the increased risk of infection and death associated with hyperferritinemia could be a coincidence. As a result, it may be unreasonable to view high ferritin levels as the primary cause of increased mortality in the setting of inflammation or infection, and to avoid appropriate anemia care with intravenous Iron for serum ferritin values of 500 or 800 ng/ml.[26]

IRON MONITORING:

According to the K/DOQI anemia recommendations, iron status should be assessed every month with rHuEPO treatment, who are not receiving iron supplementation. Once rHuEPO dose and iron status have been normalized, monitoring should be done at least every three months Storage iron is measured indirectly by serum ferritin.[27] Serum ferritin's diagnostic usefulness, on the other hand, is restricted by its ability to operate as a powerful acute-phase reactant. Ferritin readings can be high even in the presence of iron deficiency in clinical situations, such as in hemodialysis patients, where the test has a sensitivity of just 41 percent to 54 percent. Iron deficiency in hemodialysis patients cannot be ruled out

by serum ferritin levels more than 100ng/ml due to the extremely high likelihood of false negative results.

TSAT is computed as TSAT = (serum iron/total iron-binding capacity) 100 and is used to determine the availability of circulating iron. As per K/DOQI guidelines a value of less than 20% as an indicator of iron deficiency in patients with kidney disease.

In CKD patients, the percentage of hypochromic red cells has been demonstrated to be a helpful indicator of iron status. One significant flaw in the test is that it is influenced by changes in erythrocyte mean corpuscular volume (MCV). The MCV of samples can be considerably affected when they are stored or delivered.

The content of reticulocyte hemoglobin (CHr) is a direct indicator of iron status at the reticulocyte level. It is unaffected by changes in cell volume because it is a measure of content rather than concentration. Furthermore, because reticulocytes only circulate for about 24 hours, test findings can reveal relatively rapid changes in iron status. A CHr score of less than 29 to 31pg indicates that more severe iron treatment is required.

Hsu et al In the NHANES III study (1988–1994), looked at iron status in people with CKD and found that iron indices indicating of iron insufficiency were present and contributed to anemia in many people.[28]

Serum ferritin 100 ng/ml and TSAT 20% are common iron deficiency indicators used in CKD. These thresholds are frequently used by clinicians to make iron treatment decisions, and K/DOQI guidelines endorse them in nondialysis CKD. If either number is low, then iron treatment is required, according to the K/DOQI criteria.

Steven Fishbane et al., found that between 57.8% and 72.8 percent of CKD patients have serum ferritin less than 100 ng/ml or TSAT less than 20%. In contrast to these relatively high serum ferritins (100 ng/ml) and TSAT (20%) readings that indicate inadequate iron in CKD, lower serum ferritin (15 to 30 ng/ml) and TSAT (15%) thresholds are commonly utilized in the general population. The high prevalence of low iron indices discovered could reflect a problem with iron delivery rather than iron deficiency.[29] However, because the prevalence of gastrointestinal pathology increased in CKD, blood sampling for laboratory testing is common, hospitalizations and surgery for other intercurrent illness could contribute to blood loss, it's possible that iron deficiency is more common than expected. Many patients are also given erythropoiesis-stimulating drugs, which deplete iron stores even further.

Gotloib et al performed sternal bone marrow biopsies on 47 individuals with CKD and hemoglobin levels below 12 g/dl. Surprisingly, 46 of the 47 participants had significant iron deficiency. Patients were then given intravenous iron, with the majority of them improving their Hb concentration, demonstrating that iron deficiency is a prevalent concern in nondialysis CKD patients.[30]

Iron Storage-Serum Ferritin Evaluation:

According to the most recent K/DOQI guidelines, serum ferritin levels for HD patients should be maintained at or above 200ng/ml. The K/DOQI guidelines suggest maintaining serum ferritin levels more than 100ng/mL in patients with CKD who are not yet on dialysis or who are on peritoneal dialysis.

Transferrin Saturation is used to assess iron availability:

For all populations with CKD, the K/DOQI recommended level of transferrin saturation is 20%.

TREATMENT OF ANEMIA:[8,31]

1. Iron supplementation

The following are the objectives of iron therapy:
To maintain a target Hb level,
To prevent stored iron from being depleted,
To avoid iron deficient erythropoiesis,
ESA dose should be kept to a minimum.

2. Dialysis

Dialysis has little effect on correcting anemia, yet the decreased bleeding tendency may result in a slight increase in hemoglobin concentration.

3. Blood Transfusions

To reverse the effects of acute blood loss, packed red cell transfusions are required. In patients who do not respond well to EPO, transfusions may be required to maintain appropriate hemoglobin values.

4. Administration of Recombinant Erythropoietin:

Currently available Erythropoiesis Stimulating Agents are:[11]
Short acting: Epoetin alpha, Epoetin beta
Long acting: Darbepoetin alpha.
Newer erythropoiesis stimulation methods include C.E.R.A (continuous erythropoietin receptor activator), peptide-based ESA hematite, Synthetic erythropoiesis protein (SEP), and EPO gene therapy.
The National Kidney Foundation has developed thorough EPO administration guidelines for individuals with chronic renal disease anemia. In brief, anemia with a hematocrit of less than 33% or hemoglobin of less than 11 gm/dl should prompt a thorough examination for diseases other than impaired EPO production or activity. Folic acid and B12 levels should be checked, with particular attention paid to iron, iron-binding capacity, and ferritin levels. It is not essential to measure EPO levels.
The National Kidney Foundation suggests raising the target hematocrit to 33–36 percent and the target hemoglobin to 11–12 grams per deciliter. In adult patients, the initial EPO dose should be 80 to 120 units/kg/week divided into two or three subcutaneous injections or 120 to 180 units/kg/week given as three intravenous injections to attain the target hematocrit within 3 to 4 months of therapy. At least once every two weeks, hematocrit and hemoglobin should be measured to evaluate the response. When the target hematocrit is achieved, most adult patients can be maintained with a total EPO dose of about 50-100 units/kg/week.
For erythropoiesis to occur, adequate iron levels must be maintained. Before patients are given IV iron, a diagnosis of absolute or functional iron deficiency should be obtained. A ferritin level of less than 100 ng/ml and a transferrin saturation of less than 20% are the most commonly utilized criteria.[32]
Iron-dextran, iron sucrose, and iron-gluconate are the most often used IV iron preparations. Anaphylactic responses can be induced by iron-dextran and iron-sucrose; hypotension can be induced by iron-gluconate.

Common reasons of erythropoietin resistance include:

The following are the most typical causes of a poor response:
Insufficient iron supply,
Chronic iron deficiency,
Infection-related hospitalization,
Catheter insertion, both temporary and permanent
Hypoalbuminemia,
CRP level is high.

In individuals with microcytic red cell indices, aluminum toxic effects should be suspected as a cause of therapy resistance. Pancytopenia, aplastic anemia, hemolytic anemia, prolonged blood loss, inflammatory disorders, infection, and ACE inhibitors are uncommon causes.[11]

Erythropoietin's adverse effects:

Hypertension.

Thrombosis of arteriovenous fistulas, seizures

Hyperkalemia.

Hyperphosphatemia.

Aplasia of the red blood cells pure red cell aplasia. PRCA patients have a low absolute reticulocyte count and are resistant to EPO therapy. The number of erythroid precursors in the bone marrow has decreased.

HEMOSTASIS DISORDERS IN CHRONIC KIDNEY DISEASE[7,8,32,33]

Bleeding has long been recognized as a serious consequence of uremic state. Epistaxis, gastrointestinal hemorrhage, profuse bleeding when brushing teeth, and bruisability are all examples. Rather than occurring spontaneously, more severe bleeding episodes are more likely to occur because of trauma or invasive procedures such as a kidney biopsy. Hemopericardium and subcapsular hematomas of the liver are less common than other types of hemorrhage.

It is known that bleeding occurs in uremic patients despite normal or high coagulation factor levels in the blood. While the number of circulating platelets is usually normal, platelet function is frequently compromised.[11]

In uremia, the most common defect in platelet function is decreased platelet contact with the vascular subendothelial. Platelet adhesion and aggregation are hampered as a result. The bleeding time, a simple approach assessed by cutting a small incision in the skin and counting the time from the first drop of blood to the final pouring of blood from the wound, is the best marker of platelet-vessel wall interaction.

GP1b and GPIIb-IIIa, platelet receptors that play a key role in adherence to the vascular wall and aggregation, are unlikely to be greatly diminished in uremia. The interaction of these receptors with vessel wall proteins, on the other hand, could be abnormal. The activation of GPIIb and IIIa, which aids its adherence to vWF, may be hampered. Finally, the platelet cytoskeleton may be disrupted, resulting in decreased actin incorporation and inefficient intracellular molecular trafficking.[8]

ANEMIA'S ROLE IN PLATELET DYSFUNCTION:

Anemia plays a significant role in uremic platelet dysfunction. During normal circulation, erythrocytes force platelet flow radially, away from the flow's center and toward the endothelial surfaces. Platelets are in closer opposition to the vessel wall when vascular damage occurs, enabling platelet adhesion and activation by vessel wall elements such as collagen. Anemia causes more platelets to circulate in the center of the vessel, away from endothelial surfaces, making platelet activation more difficult. Anemia may also lead to platelet dysfunction because erythrocytes secrete adenosine diphosphate, which normally increases platelet interaction with collagen.[8]

LEUKOCYTES IN CKD:

The total and differential leukocyte counts, as well as the platelet count, are normally normal, but the underlying condition, as with all other hematologic parameters, plays a modifying function. Leukocytes

and platelets may be affected by uremia and dialysis. Granulocyte phagocytic activity may be decreased and complement activation by the hemodialysis membrane may result in pulmonary leukocytosis with granulocytopenia. Infections are more common because cell-mediated immunity is suppressed. Granulocyte migration is reduced, and chemotactic activity is aberrant.[27]

In a cross-sectional cohort, multicenter study by Aleix Cases-Amenós et al.[34] "Prevalence of anemia and its clinical management in patients with stages 3-5 chronic kidney disease not on dialysis in Catalonia: MICENAS I study" 504 patients (56.4 percent male, mean age 67.8 15.5 years) were included in the study; 61.5 percent had stage 3 CKD, 30.2 percent stage 4, and 8.3 percent stage 5 CKD. Vascular and diabetic nephropathy were the leading causes of CKD. Anemia was found in 58.5 percent of patients (n=295), while only 14.9 percent had hemoglobin levels below 11 g/dL. As CKD advanced, mean hemoglobin levels dropped and ESA medication became more common, although there were no significant changes in iron prescriptions according to CKD stages. Darbepoetin alfa, with a median dose of 40 g/biweekly, was the most commonly given ESA, followed by C.E.R.A., with a median dose of 75 g/month, and epoetin beta, with a median dose of 5,000 IU/week, concluded that in a CKD patient group, there is a high prevalence of anemia, which worsens as the disease advances, and it is well controlled. In more than half of anemic CKD patients, moderate doses of ESA and iron supplements are prescribed to achieve this control.

In a hospital-based cross-sectional analytical study by Ikponmwosa OsamudiamenIyawe et al.[35] "Assessment of Iron Status in Predialysis Chronic Kidney Disease Patients in a Nigerian Tertiary Hospital" The iron status of 100 pre-dialysis CKD patients and 90 healthy controls was examined and compared. The patients with CKD were 49.391±4.84 years old on average. In comparison to 3 percent of controls, 14 percent of CKD patients had iron deficiency (P = 0.021). Eleven (85.7%) of CKD patients with ID exhibited functional iron deficiency, whereas three (14.3%) had absolute iron deficiency. Pre-dialysis CKD patients had considerably higher serum ferritin levels (P = 0.001). In CKD patients, there was no significant gender difference in iron indices. Functional iron deficit was found in 11% of the CKD patients, but not in the control group (P = 0.003) and concluded that in predialysis patients, functional iron deficiency is the most common type of iron deficiency, and there was no significant association with age, gender, etiology, or stage of CKD.

In a study by Rumi Deori et al.[36] "Iron status in chronic kidney disease patients' 'The Departments of Medicine and Nephrology of a tertiary care hospital in Assam, India, randomly selected 50 adult patients with CKD who were not taking any hematinic. There were also 50 healthy controls who were age and sex matched. Standard laboratory techniques were used to calculate hemoglobin concentration, serum iron, TIBC, transferrin saturation (TSAT), and serum creatinine. All the CKD patients were anemic, with hemoglobin concentrations < 11 g/dl, and 48% of them had moderate anemia. They had a creatinine level of more than 3 mg/dl in their blood. Diabetes (44 percent) and hypertension were the leading causes of CKD (36 percent). Serum creatinine and total iron binding capacity (TIBC) were significantly (P <0.05) raised in CKD patients while serum iron was significantly lower in CKD subjects than in the control group. Iron deficiency anemia affected 26% of the group (TSAT 20%) and concluded that In CKD patients, anemia is one of the most prevalent and early signs. Iron deficiency anemia may be evident if serum creatinine is greater than 3 mg/dl.

RESEARCH DESIGN AND METHODOLOGY

Place of study:

The study was conducted in Shree Birendra Hospital, Kathmandu.

Research Method:

Quantitative

Type of study:

Cross sectional hospital-based study

Study Population/Sampling Frame:

Diagnosed case of CKD stages 3,4 and 5 not on dialysis coming to OPD as well as those who are admitted in ward of SBH.

Sample size:

$$n_0 = \frac{Z^2 pq}{e^2}$$

Where:
n: sample size
Z: confidence interval (95%)
P: Prevalence
q: 1- Prevalence
e: Error of margin (5%)
So, sample size for the study is minimum of 145.

INCLUSION CRITERIA:

- All diagnosed patients with CKD stage 3 – 5 not on dialysis.
- Age >18 years.

EXCLUSION CRITERIA:

- CKD stage 1 and 2.
- Patient on renal replacement therapy.
- Patients on hematinic.
- Patients on recombinant human Erythropoietin.
- Blood transfusion in last three months.
- Malignancy.

MATERIALS AND METHODS

This study was conducted at Shree Birendra Hospital, during the period of April 2020 to October 2021. One hundred forty-six non dialysis diagnosed case of CKD3 – CKD5 admitted in medicine/nephrology units and presenting to OPD were enrolled in the study.

Clinical examination included:

1. Weight, height, vital parameters
2. Major systems examination

Hematological investigations: Hemoglobin, RFT, sodium, potassium, MCV, MCH, MCHC, Peripheral blood smear, Serum ferritin, Total iron binding capacity, Serum iron, stool OBT were done.

Serum ferritin: The serum ferritin was determined by enzyme linked immunosorbent assay. Iron level was determined by Ferrozine method without deproteinization. Total iron binding capacity (TIBC) was determined by Spectrophotometric Assay.

Transferrin saturation calculated by using formula (TSAT):

TSAT = (serum iron/total iron-binding capacity) × 100

Ethical committee approval: Obtained

Consent	:	Informed consent was obtained
Financial support	:	Nil
Conflict of interest	:	Nil

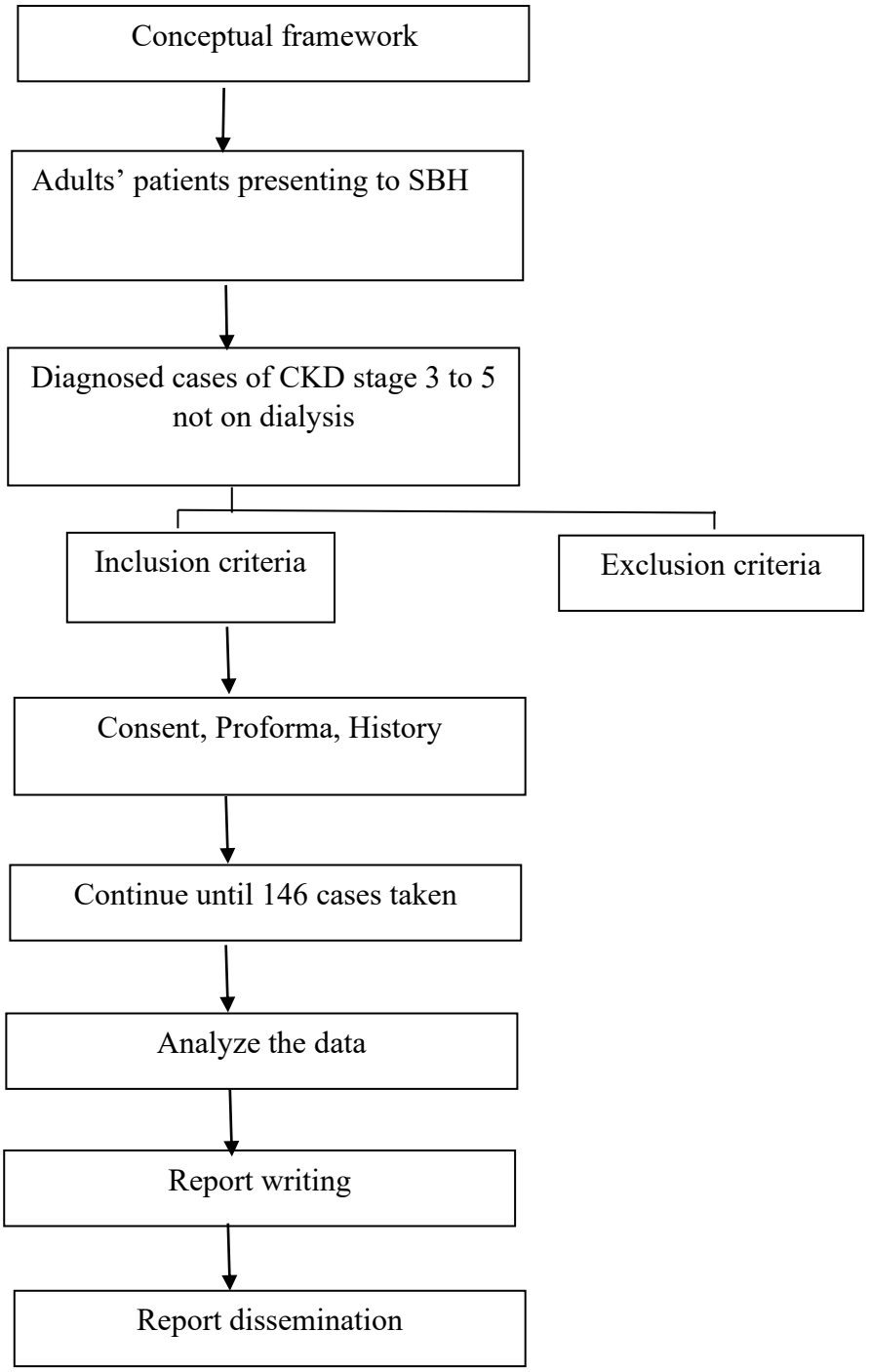
STATISTICAL ANALYSIS

Data were collected using information from the proforma designed for the study. Data presentation was done with tables and figures. Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 21. Qualitative data was demonstrated as number and percentages and association between two group was done using Chi square test.

Quantitative data was presented as mean and SD. Comparison between two group was done by using independent t test, comparison among three or more group with ANOVA test for normally distributed data.

Values in tables were presented in forms of means and standard deviations. Analysis of categorical data and qualitative data was done using Pearson chi square test.

A P-value of less than 0.05 was considered statistically significant.



TABLES AND CHARTS

Table 1: Baseline characteristics of study participants

Variables	Frequency (n)	Percent (%)
Age category		
35-45	9	6.16
46-55	38	26.03
56-65	51	34.93
66-81	48	32.88

Gender		
Male	97	66.44
Female	49	33.56
CKD stage		
CKD3a	2	1.37
CKD3b	30	20.55
CKD4	68	46.58
CKD5	46	31.51

Out of 146 study population, male was 97(66.44%), female was 49(33.56%), in age group 35-45 was 9(6.16%),46-55 was 38(26.03%),56-65 was 51(34.93%) and 66-81 was 48(32.88%); CKD3a was 2(1.37%), CKD3b was 30(20.55%), CKD4 was 68(46.58%) and CKD5 was 46(31.51%).

Table 2: Baseline characteristics of study participants

Stool OB		
Positive	2	1.37
Negative	144	98.63
RBC morphology		
Normocytic normochromic	122	83.56
Microcytic hypochromic	22	15.07
Macrocytic	2	1.37
Tsat		
≤20%	81	55.48
>20%	65	44.52
Ferritin		
<100	51	34.93
100-500	82	56.16
>500	13	8.90

Out of 146 study population stool OBT positive was in 2(1.37%), negative was in 144(98.63%); normocytic normochromic was in 122(83.56%), microcytic hypochromic was in 22(15.07%), macrocytic was in 2(1.37%);Tsat ≤ 20% was in 81(55.48%),>20% was in 65(44.52%) and ferritin <100 was in 51(34.93%),100-500 was in 82(56.16%),>500 was in 13(8.90%).

Table 3: Hematological profile of study participants

Parameters	Mean	SD	Minimum	Maximum
Hemoglobin level gm/dL	9.25	1.01	6.9	11.5
Iron	55.00	26.39	15.18	130
Ferritin	181.75	147.63	10.9	602
TIBC	280.58	63.20	33	385
Tsat	21.27	13.21	6.31	68.42
eGFR	20.63	10.48	5	47

Mean Hb was 9.25g/dl, mean GFR was 20.63 ml/min, mean iron was 55, mean ferritin 181.71 and Tsat was 21.27%.

Table 4: Transferrin saturation and ferritin in different RBC morphology

	Number of cases	Mean Tsat	Mean ferritin
RBC morphology			
Normocytic normochromic	122	23.12	208.34
Microcytic hypochromic	22	10.89	41.94
Macrocytic	2	22.52	98

Out of 146 study population 122 had normocytic normochromic anemia and mean transferrin saturation and ferritin are lowest in microcytic hypochromic anemia**.**

Table 5: Association of ferritin and transferrin saturation with CKD stages

Variables	CKD3 n (%)	CKD4 n (%)	CKD5 n (%)	p-value
Tsat				
≤20%	11 (13.58)	37 (45.68)	33 (40.74)	0.005
>20%	21 (32.31)	31 (47.69)	13 (20)	
Ferritin				
<100	10 (19.61)	18 (35.29)	23 (45.10)	<0.001
100-500	21 (25.61)	47 (57.32)	14 (17.07)	
>500	1 (7.69)	3 (23.08)	9 (69.23)	

Transferrin saturation and ferritin have significant association with CKD stages.

Table 6: Association of iron profile with gender

Variables	Male Mean ± SD	Female Mean ± SD	p-value
Hemoglobin	9.41 ± 1.02	8.94 ± 0.13	0.004
Iron	56.87 ± 28.32	51.29 ± 21.89	0.229
Ferritin	187.47 ± 162.72	170.44 ± 112.64	0.512
TIBC	292.23 ± 57.49	257.53 ± 68.12	0.001
Tsat	21.20 ± 13.46	21.27 ± 12.82	0.930

Hemoglobin and TIBC had significant association with gender.

Table 7: Association of iron profile with age

Variables	35-45	46-55	56-65	66-81	p-value

	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Hemoglobin	8.55 ± 1.35	9.05 ± 1.03	9.10 ± 0.99	9.71 ± 0.78	0.006
Iron	62.66 ± 4.30	60.48 ± 38.0	53.61 ± 22.8	50.70 ± 19.9	0.284
Ferritin	91.86 ± 76.1	233.4 ± 166.4	157.1 ± 156.4	183.8 ± 118.5	0.022
TIBC	216.4 ± 86.9	260.6 ± 51.3	308.4 ± 47.6	278.7 ± 67.7	<0.001
Tsat	35.10 ± 17.3	24.2 ± 18.3	20.3 ± 11.1	17.3 ± 4.9	<0.001

Hemoglobin, TIBC and Tsat have significant association with age.

Table 8: Correlation between hemoglobin level and eGFR

Variable	eGFR	
	Pearson correlation (r)	p-value
Hemoglobin level	0.453	<0.001

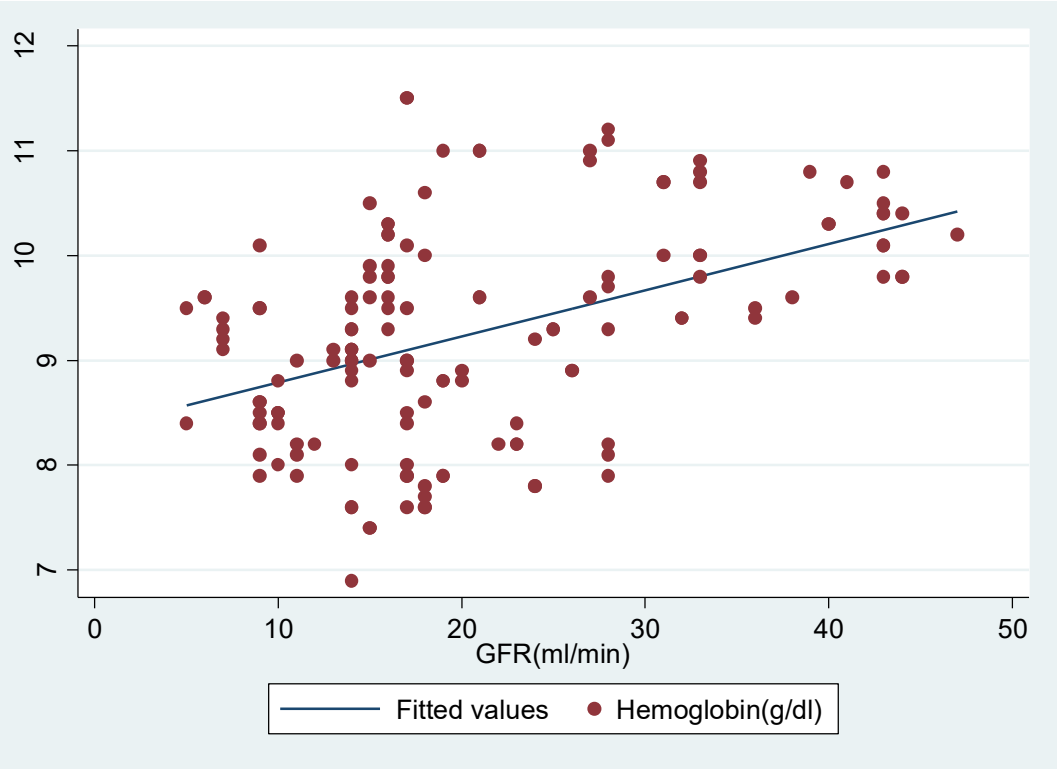


Fig 9: Correlation between hemoglobin level and eGFR

Significant association between hemoglobin and GFR, hemoglobin decreases with decreased in GFR.

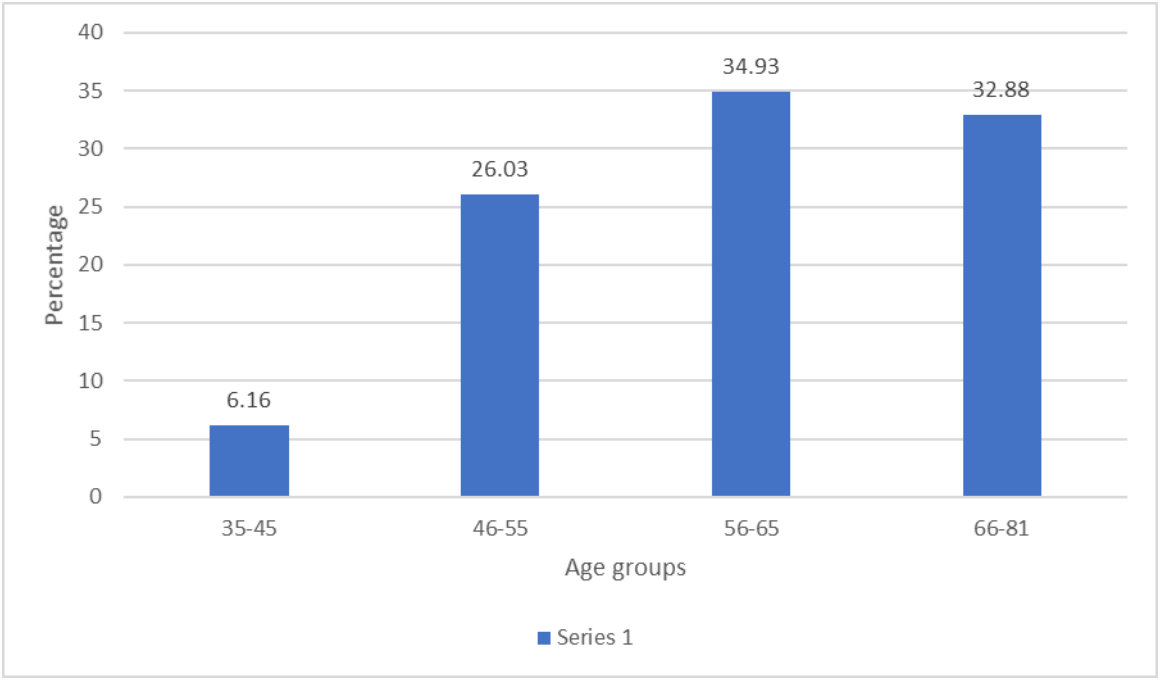


Fig 10: Age distribution

Most of the study population were between the age group of 46 to 81 years**.**

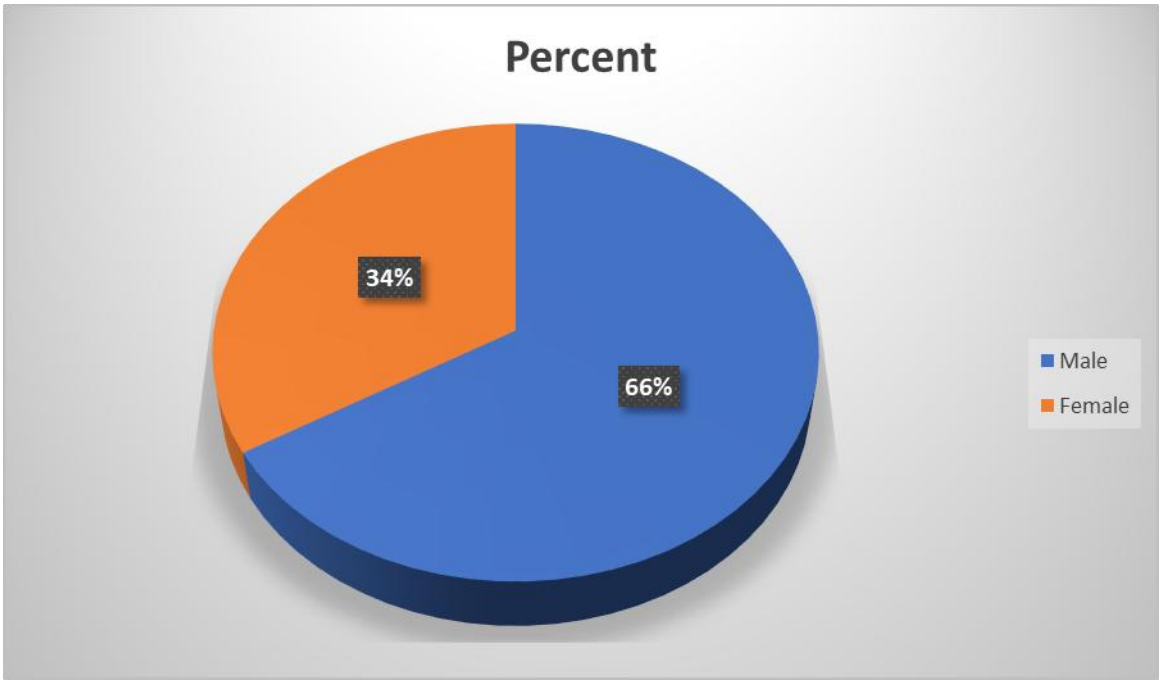


Fig 11: Gender distribution

In our study 34% was female and 66% was male.

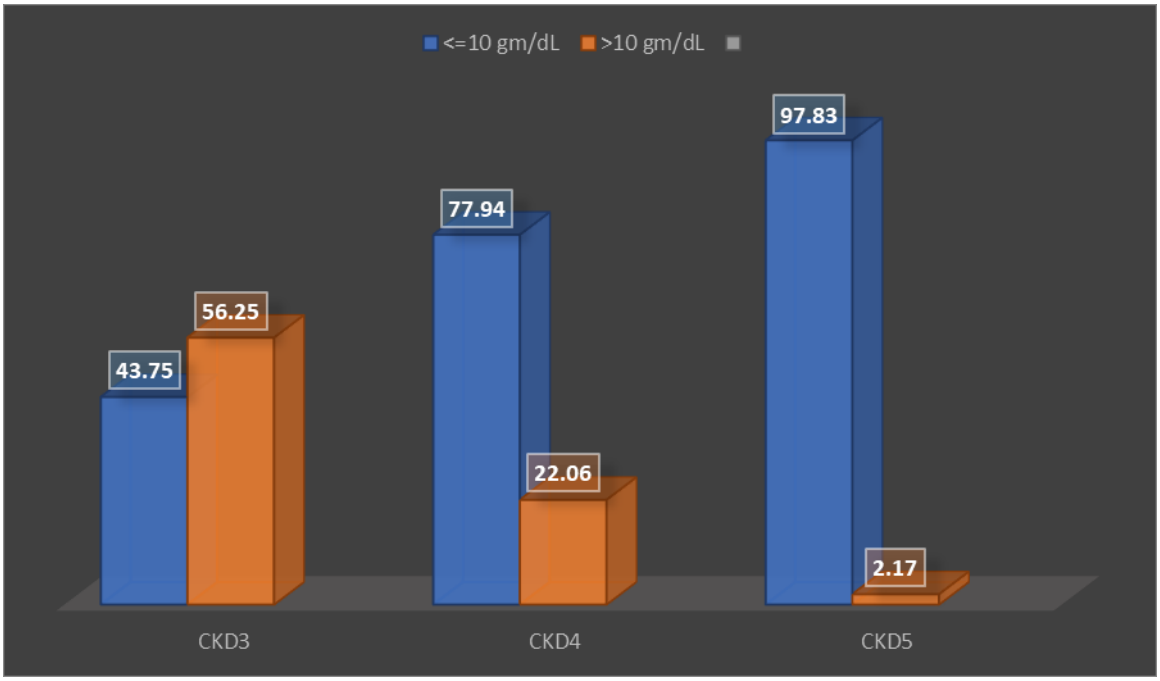
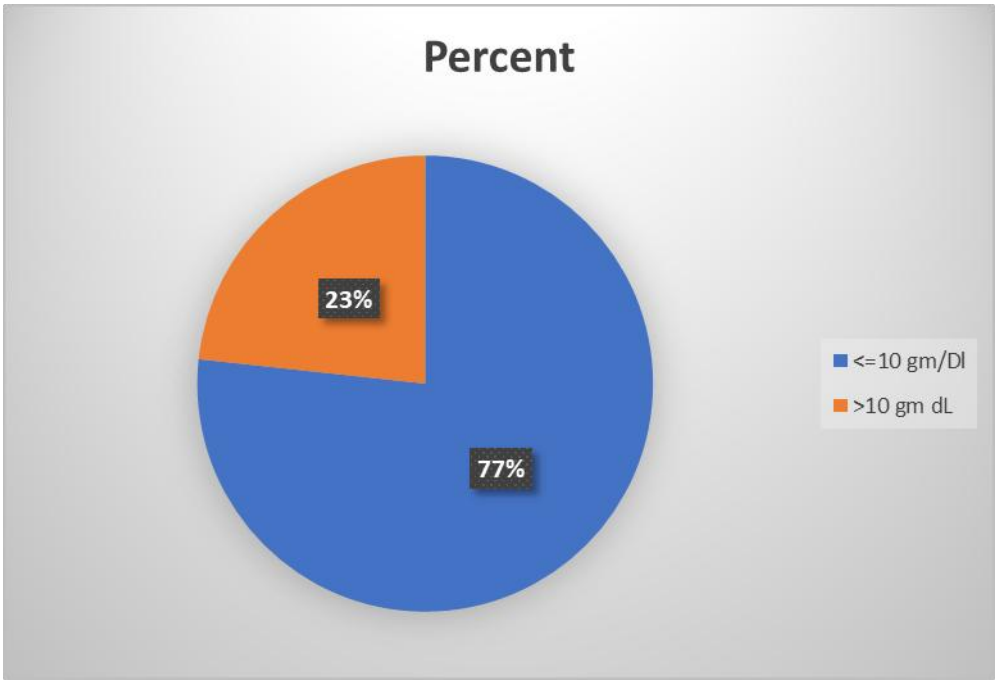


Fig 12: Distribution of anemia severity among chronic kidney disease stages

In CKD3 Hb <10 was in 43.74%, >10 was in 56.25%, in CKD4 Hb<10 was in 77.94%, Hb >10 was in 22.06% and CKD5 Hb <10 was in 97.83%,Hb >10 was in 2.17%s in 56.25%,in CKD4 Hb. Anemia was more common with increasing CKD stages.

Fig 13: Prevalence of anemia



Anemia was present in 77% of study population**.**

OBSERVATIONS AND RESULTS

Characteristics of CKD study population:

A total 146 patients were enrolled in this study out of which 97 (66.44%) were male and 49(33.56) were female. The number of patients in different age group; 6.16% in age group 35-45,26.03% in age group 46-55,34.93%in age group 56-65 and 32.88% in age group 66-81.

The mean GFR was 20.63ml/min±10.48, out of 146 enrolled patients; CKD3a were 1.37%, CKD3b were 20.55%, CKD4 were 46.58, CKD5 were 31.51%.

The mean serum creatinine was 3.49mg/dl ± 1.59 and mean hemoglobin were 9.25±1.01, anemia was present in 76.71 % of patients.

Out of 146 patients 83.56% had normocytic normochromic anemia,15.07% had microcytic hypochromic anemia and 2% had macrocytic anemia.

The mean serum iron was 55±26.39, mean ferritin were 181.75±147.63 and mean TSAT were 21.27±13.21.

Association between iron profile, anemia, and demographics

Sex:

Male patients had mean Hemoglobin of 9.41±1.02 and female had 8.94±0.13 with p-value of 0. 004. Severity of anemia was more in female. TIBC shows significant association with gender mean TIBC in male was 292.23±57.49 and in female 257.53±68.12, P-value 0.001.

Age:

The mean hemoglobin in age group 35-45 were 8.55±1.35, in age group 46-55 were 9.05±1.03, in age group 56-65 were 9.10±0.99 and in age group 66-81 were 9.71±0.78. Anemia was present in all age group and did not demonstrate association with age. Ferritin, TIBC and TSAT had significant association with age. TSAT decreases with age: the mean TSAT in age group 35-45 was35.10±17.3,46-55 was 24.2±18.3,56-65 was 20.3±11.1,66-81 was 17.3±4.9 P- value <0.001.the mean ferritin was 181.75±147.63 P- value 0.022, mean TSAT was 21.27±13.21 P- value <0.001.

Association between iron profile, anemia, and severity of CKD:

Severity of CKD had strong association with prevalence of anemia, demonstrate the association between the prevalence of anemia and GFR that is prevalence and severity of anemia increased as GFR decreases. The mean hemoglobin in CKD3a were 10.3±0.14, in CKD3b were 10.08±0.61, in CKD4 were 9.20±1.12 and in CKD5 were 8.74±0.64, Pearson correlation between GFR and Hb was 0453 with P- value 0. 001.TSAT and Ferritin had significant association with CKD stages-value 0.005 and <0.001 respectively. SAT ≤20 was present in 55.48% and Ferritin <100 was present in 34.93%.

DISCUSSION

Chronic kidney disease is a major public health issue that causes significant morbidity and mortality around the world. The early stages of CKD have a substantially higher prevalence than the latter stages. In clinical practice, however, the prevalence of stage 4 and 5 appears to be higher because the early stages are asymptomatic and people only present when the severity of their symptoms worsens.

Chronic renal disease anemia is caused by a variety of factors. Anemia has long been recognized by the renal community as a factor that can reduce the quality of life, patients' lives and cause irreparable cardiac effects. Anemia, a reversible characteristic of end-stage renal disease, is a risk factor for heart disease and mortality in individuals with end-stage renal disease.[37,38]

Evidence shows that both iron and erythropoietin are required to produce red blood cells; as a result, Erythropoietin will be useless unless appropriate iron is supplied. Although no test is perfect for determining the adequacy of iron stores, the TSAT and serum ferritin are currently the best indications

of the body's iron status. Given the prevalence of iron deficiency in CKD patients and the sensitivity and specificity of TSAT and serum ferritin in detecting iron deficiency, when TSAT is 20% and serum ferritin is 100 ng/mL, the likelihood of iron deficiency is sufficiently high. As a result, all non-dialysis CKD patients should have TSAT and serum ferritin levels of >20 percent and >100 ng/mL, respectively.
Out of 146 patients' anemia was present in 122(76.51%) patients in our study, and it had a direct linear association with GFR decline. The mean hemoglobin in CKD3a were 10.3±0.14, in CKD3b were 10.08±0.61, in CKD4 were 9.20±1.12 and in CKD5 were 8.74±0.64, P- value <0. 001.patients' average hemoglobin level was 9.25 gm/dl. There was a considerable decrease in hemoglobin as the stage of chronic kidney disease progressed.
The same linear association between Hb and GFR was discovered by by Aleix Cases-Amenós et al.[34] , Anemia was found in 58.5 percent of patients (n=295), while only 14.9 percent had hemoglobin levels below 11 g/dL. As CKD advanced, mean hemoglobin levels dropped, Afshar et al[41] and Khanam et al[42] also found a decrease in PCV as GFR decreased. Ijoma et al[43] discovered that mean hemoglobin levels in stage 3 chronic kidney disease were 10.57 gm/dl, 8.84 gm/dl in stage 4, and 7.33 gm/dl in stage 5 chronic kidney disease. According to this, anemia is strongly linked to the severity of chronic renal disease.
Low hemoglobin and hematocrit levels can be caused by lower GFR or EPO synthesis, increased loss of hematopoietic components, and inflammation in CKD patients. Because anorexia, nausea, and vomiting are common in CKD patients, a decrease in food intake of nutrients required for erythropoiesis could be a factor in anemia. Parasitic infestation and low socioeconomic position may play a role in nutritional deficiencies and anemia in developing countries. Furthermore, CKD patients are on a protein-restricted diet, which may play a role in the development of anemia in these patients.[42]
To classify the type of anemia in our patients, a peripheral smear was performed. In the peripheral smear, normocytic normochromic anemia was discovered in 83.56 percent of the patients, microcytic hypochromic anemia was found in 15.07 percent, and 1.37percent in macrocytic. Afsar et al [41]also observed normocytic normochromic anemia in 80% of patients and microcytic hypochromic anemia in 15%. In microcytic hypochromic anemia, serum ferritin levels and transferrin saturation were low.
Iron assays and iron status in hemodialysis patients have long been of great interest. In contrast, little is known about the iron status of nondialysis chronic kidney disease patients. It should be noted that our findings are particularly pertinent to patients with an estimated GFR of less than 60 ml/min, who are more likely to have CKD.
Serum ferritin 100 ng/ml and TSAT 20% are common iron deficiency indicators used in CKD. These thresholds are frequently used by clinicians to make iron treatment decisions, and the NKF-K/DOQI guidelines recommend these in nondialysis CKD.
IkponmwosaOsamudiamenIyawe et.al[35] , found 14 percent of CKD patients had iron deficiency (P = 0.021). 11 (85.7%) of CKD patients with iron deficiency exhibited functional iron deficiency, whereas three (14.3%) had absolute iron deficiency.
Steven Fishbane et al[29] main conclusion was that between 57.8% and 72.8 percent of CKD patients have serum ferritin levels below 100 ng/ml or TSAT levels below 20%. In contrast to this relatively high serum ferritin (100 ng/ml) and TSAT (20%) readings that indicate inadequate iron in CKD, lower serum ferritin (15 to 30 ng/ml) and TSAT (15%) thresholds are commonly utilized in the general population.
In this study TSAT <20 was found in 81 (55.48%) cases and ferritin <100ng/dl was found in 51 (34.93%) of cases. Up to 55.48 percent of patients in our study are iron deficient, according to NKF-

K/DOQI Guidelines(31).TSAT and ferritin have significant association with CKD stages. TSAT decreases with age: the mean TSAT in age group 35-45 was35.10±17.3,46-55 was 24.2±18.3,56-65 was 20.3±11.1,66-81 was 17.3±4.9 P- value <0.001, the mean ferritin was 181.75±147.63 P- value 0.022, mean TSAT was 21.27±13.21 P- value <0.001. TIBC shows significant association with gender mean TIBC in male was 292.23±57.49 and in female 257.53±68.12, P-value 0.001.

Van Wyck et al[44] Iron deficiency is practically universal in hemodialysis patients due to the frequent blood loss. Nondialysis CKD, on the other hand, does not experience dialysis-related blood loss, hence iron deficiency may be less common. The high prevalence of low iron indices reported could indicate that the problem isn't iron deficiency, but rather decreased iron transport along with inflammation, a complex syndrome that develops as CKD progresses. Gotloib et al[45] provides evidence in support of the significant frequency of iron insufficiency reported in CKD, 47 patients with CKD and Hb 12 g/dl, sternal bone marrow biopsies were conducted. Surprisingly, significant iron shortage was discovered in 46 of 47 cases, and these patients were treated with intravenous iron, with most of them improving their Hb concentrations. The average serum ferritin level in our study was 181.75 ng/ml, with 13 cases (8.9%) having serum ferritin levels greater than 500 ng/ml.

Higher levels of ferritin may, hypothetically, capture more bodily iron and protect the individual from worsening infection, which is almost always preceded by inflammation. As a result, inflammation-induced hyperferritinemia can lead to a so-called "functional iron deficiency," which can be beneficial in "acute" inflammation by containing iron in the RES sites, but can be harmful in "chronic" inflammation by causing refractory anemia in patients with CKD or other chronic diseases.[25]

Chronic inflammation is frequent in individuals with CKD, with up to 40% to 70% of patients having elevated C-reactive protein (CRP) levels on a long-term basis. As a result, inflammation is likely to be the most common confounder in CKD-related hyperferritinemia, and it may play a bigger role than Iron.[46]

A low ferritin level (for example, 200 ng/ml in hemodialysis patients or 100 ng/ml in no dialyzed CKD patients) is a reliable marker of iron deficit, but a normal to moderately high serum ferritin level does not rule out iron insufficiency or suggest adequate or excessive Fe on board.[25]

This study shows relationship of ferritin and TSAT with glomerular filtration rate. When compared to patients with normocytic normochromic anemia, those with microcytic hypochromic anemia exhibited lower serum ferritin and lower transferrin saturation (TSAT).

This clearly shows that iron deficiency anemia is a significant aspect of chronic renal disease anemia due to the different reasons mentioned earlier. As a result, every effort should be made to determine the cause of anemia in chronic renal disease patients, treat coexisting iron deficiency anemia in chronic kidney disease patients, and monitor other hematological parameters to detect coexisting abnormalities.

LIMITATIONS OF THE STUDY

- Age below 18 years were not included.
- Folic acid and vitamin B12 were not measured.
- The level of hepcidin was not measured.
- This study was conducted in single center.
- Inflammation was rule out clinically.

STRENGTH OF STUDY

- Study was conducted in tertiary care hospital where the large number of patient of different severity cases admitted and visited out patient department.
- Study population reflects general population as patients came in this hospital from all over Nepal.

CONCLUSION

This study shows iron deficiency anemia is the most common form of anemia in CKD, prevalence and severity of anemia increases as kidney function decreases and anemia was present in all age group with relatively more common in female gender.

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