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Clinico Etiological Profile of Anemia in Chronic Kidney Disease and Its Implication to Therapy

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Introduction

Chronic kidney disease (CKD) is a permanent and significant reduction in glomerular filtration rate, or chronic irreversible destruction of kidney tissue.1 CKD is a worldwide public health problem with an increasing incidence and prevalence, poor outcomes, and high cost.2 CKD prevalence is estimated to be 8-16% worldwide.3 The current burden of CKD may be due to a change of the underlying pathogenicity of the disease. Few decades ago glomerulonephritis was the leading cause of kidney disease, though nowadays, infections have become a less important cause for kidney disease, at least in the western world.4 Current evidence suggest diabetes and hypertension to be the major causes of kidney disease worldwide.5,6

In India too, there is a significant burden of CKD although the exact figures vary.7 About 20-30 patients have some degree of renal dysfunction for each patient who needs renal replacement treatment. But less than 10% of end stage renal disease patients have access to any kind of renal replacement therapy.8-9

Chronic Kidney Disease is worldwide public health issue, with an increasing incidence and prevalence associated with poor out comes and high cost.[11] The association of Chronic Kidney disease and anemia has been recognized since the early 19th century, first noted by Richard Bright in 1837 when he observed pallor in the development of Bright's disease.[12] CKD population is much larger than the dialysis population[4].

According to glomerular filtration rate (GFR) and 2006 NKF-K/DOQI guidelines, chronic kidney disease has been divided into 5 stages.[13] Anaemia usually appears at GFR below 60ml/min or stage 3.[14-16]

Anemia, as defined by the NKF, is a hemoglobin (Hb) concentration < 12 g/dl for women and < 13.5 g/dl for men[17]. Anemia is defined in terms of low levels of hematocrit or hemoglobin.[18] Anemia is a common complication of chronic kidney disease which develops quite early in the course of disease. It is common sequelae of the chronic kidney disease, associated with significant morbidity. Anemia of renal failure begins relatively early in the development of kidney disease. As the destruction of the kidney progress, the degree of the anemia increases. Anemia of CKD is a complex disorder determined by a variety of factors. Although, the primary defect is decreased erythropoiesis due to

inadequate erythropoietin (EPO) production from kidneys, a number of other factors may be shortened erythrocyte survival, blood loss, iron and other nutritional deficiency, albumin toxicity and effect of uremic inhibitor on the bone marrow. Severe hyperparathyroidism is one cause of anemia in CKD patients. Non renal and non dialysis factor can also super impose themselves on the anemia of CKD. These include drug induced bleeding, infections and inflammation.[16-19] With this background this study was contemplated in a tertiary care setting of central India to assess hematological profile of Chronic Kidney Disease and its relation to Glomerular Filtration rate and socio-demographic variables.

Iron deficiency anemia is also common in patients with chronic kidney disease. Iron deficiency may be absolute, often due to poor dietary intake or sometimes occult bleeding, or functional, when there is an imbalance between the iron requirements of the erythroid marrow and the actual iron supply. Iron deficiency leads to a reduction in formation of red cell haemoglobin, causing hypochromic microcytic anaemia. Other causes for anaemia in CKD include the presence of uremic inhibitors (e.g., parathyroid hormone, inflammatory cytokines), reduced half-life of circulating blood cells and deficiencies of folate or vitamin B12.[20] As CKD patients commonly presents with anorexia, nausea and vomiting, less dietary intake of nutrients needed for erythropoiesis might also be a factor for anaemia in this group of patients. Moreover, CKD patients are on protein restricted diet which might also have some role for occurrence of anaemia in this series of patients.[21]

Iron deficiency is also accompanied by reductions in serum iron and transferrin saturation (TSAT) and by elevations in red cell distribution width, free erythrocyte protoporphyrin concentration, total serum iron-binding capacity (TIBC), and soluble transferrin receptor (sTfR).[22] TSAT (the ratio of serum iron to total serum iron-binding capacity) is a measure of circulating iron and is <20% in patients with iron deficiency. TSAT fluctuates widely as a result of diurnal variation in serum iron, and transferring is affected by the nutritional status.

Pathophysiology of Anemia In CKD

The anemia of chronic renal failure is due to six mechanisms:

(1) Erythropoetin deficiency

(2) Shortened red cell survival

(3) Retained inhibitors or toxic metabolites that inhibit erythropoiesis

(4) Blood loss resulting from the qualitative platelet defect present in uremia

[5] Iron, B12 and folate deficiency due to nutritional insufficiency or increased blood loss

[6] Hyperparathyroidism, mild chronic inflammation and aluminum toxicity

TREATMENT (a) Iron (oral and intravenous) (b)Recombinant human Erythropoietin(r HU EPO) (c)Erythropoietin stimulating agents (ESA) 1. epoetin alfa 2. epoetin beta 3.Darbopoetin alfa 4. C.E.R.A. (methoxy polyethylene glycol-epoetin-beta) (d)Red blood cell transfusion and blood transfusion (e)Vitamin B12 and folic acid supplements.

Review of Literature

Prevalence and etiology of Chronic Kidney Disease

The Centre for Disease Control and prevention found out that in the US an estimate of 16.8% of adults aged 20 years and older had CKD in the period between 1999 to 2004. In the UK estimates show that 8.8% have CKD.[34]. In Africa, CKD is estimated to affect about 10.4% of some populations.[23-27]

A study done in the US revealed that an estimate of 8.3 million people had CKD stages 3 to 5 and 11.3 million Americans are at risk of developing or have mild decrease in kidney function. It also revealed that the prevalence of these stages of CKD in the US population is as below: 1.8% for stage 1, 3.2% for stage 2, 7.7% for stage 3 and 0.35% for stages 4 and 5. Patients with stage 3 or 4 disease progress to end stage renal disease or stage 5 at a rate of 1.5% per year.[28]

A study done in Ghana gave the following prevalence on aetiology of CKD. Chronic glomerulonephritis (33%), hypertension (21.2%) and diabetes mellitus (22.2%) were found to be the leading causes of CKD.[28] Studies done at KNH revealed that the main causes of CKD are chronic glomerulonephritis, diabetes mellitus and hypertension. [29-31] In one of the studies obstructive uropathy was also found to be a major cause.[29] Herget-Rosenthal et al revealed that currently diabetes is one of the leading cause of CKD worldwide.[30]

Anemia of CKD is due to decreased erythropoietin production from the kidneys, which stimulates RBC synthesis in the bone marrow and it worsens as GFR declines. There is a higher prevalence of anaemia when GFR is less than 60ml/minute/1.73m^2. A significant consequence of anaemia is cardiovascular complications causing increased mortality in CKD patients. The documented causes of anemia in CKD patients include blood loss, shortened life span, erythropoietin deficiency and uremic milleu.[32]

Blood loss is usually due to platelet dysfunction[33], while shortened red cell life span is prominent in haemodialysis where it is reduced by a third[33]. Erythropoietin deficiency is a functional response due to reduced GFR[34] and uremic milieu may explain why level and prevalence of anaemia may correlate with severity of CKD.[35]

A study done in United States revealed that anaemia was twice prevalent in people with Chronic Kidney Disease as compared to the general population. This showed that CKD patients were more at risk of developing anaemia. The same study also revealed that a total of 22.8% of CKD patients with anaemia reported being on treatment within the previous three months. This showed that relatively few CKD patients were being treated for anaemia and therefore screening of anaemia in CKD patients is vital.[42].

Findings from a study conducted in Saudi Arabia revealed that the prevalence of anaemia in CKD patients was slightly lower compared to other studies.[36] This is probably due to differences in population and geographic factors. Like other studies the prevalence of anaemia increased as the Kidney function worsened. The number of people who required treatment with erythropoietin was equally high.

Co-morbidities associated with Anaemia of Chronic Kidney Disease

Anemia is a documented complication in pre dialysis CKD patients. The prevalence of anemia has been shown to increase as the GFR declines particularly among diabetic CKD patients. The prevalence of anemia has been shown to vary depending on the associated co-morbidity. Evidence from literature suggests that there is a high prevalence of anemia in each stage in African American and diabetic patients with CKD.[31] This has been corroborated by a study done to determine the prevalence and severity of anemia. This study revealed that anaemia was more prevalent in diabetic CKD patients followed by vascular diseases and hypertension. Anemia was also evident in CKD caused by multiple myeloma and chronic glomerulonephritis.[37]

Correlation of Anemia in Chronic Kidney Disease

A study done in the United States revealed a strong correlation between anemia and female sex. Female are 2.2 times as likely as males to have values of less than 12g/dl. There was no strong association between severity of anemia and age. The difference in prevalence of anemia in different races was evident. Anemia was observed to be highest in native Americans as compared to Caucasians, African Americans, Hispanics and Asians. The GFR measurements indicated a strong association between prevalence of anemia and severity of CKD[28]. However there is paucity of local data showing correlation of anemia with the several factors.

As kidney functions deteriorates the severity of anemia increases[32]. This has been revealed from a study done in the United States where the prevalence increased gradually in the study population from 8.4% in stage one to 53.4% in stage 5.This has also been corroborated by another study done in Saudi Arabia where there was increase in prevalence of anemia from 21% in stage one to 72% in stage five.[36]

Management of Anemia of Chronic Kidney Disease

Anemia should be managed as per clinical guidelines in CKD patients in order to achieve increase in cognitive and sexual function, exercise capacity and reduce transmission requirements.[57.]A survey done in the United States to determine the prevalence of anemia in CKD patients showed that only 22.8% of CKD patients were being anemia in the previous three months.[24].

Retrospective and prospective studies have observed suboptimal management of anemia among pre dialysis patients with CKD. This inadequate treatment has been seen to negatively impact on cognitive function, cardiac function, and quality of life.

Early intervention in the correction of anaemia has been associated with the reduction of morbidity and mortality.[42]

A study conducted by PRESAM on evaluation management of anemia in CKD study revealed that only 27% of the patients were on ESAs therapy before dialysis. This shows that there is mismanagement regarding anemia of CKD. This observation has been corroborated by report from TRESAM that showed only 10.8% of anemic transplant patients were on ESAs[36].

Treatment Guidelines and Recommendations

The prevalence and incidence of anemia increases as the kidney functions deteriorates. Frequent monitoring of hemoglobin levels is required in order to determine the most appropriate management. The severity of anemia and state of CKD usually determines the choice of intervention from iron administration, ESA therapy or blood transfusion.

According to KDIGO clinical practice guidelines for anemia several recommendations are to be considered when implementing blood transfusion as a haematinic . Red blood cell transfusion is recommended in urgent treatment of anemia, especially where rapid correction of anemia is required to stabilise condition and where rapid pre operative correction of hemoglobin is required40.

Red cell transfusion is also recommended where the benefits outweigh the risks in patients with CKD patients where ESAs therapy risks outweigh benefits and in cases where ESAs therapy is ineffective due to resistance or bone marrow failure. Red cell transfusion may be avoided in order to reduce the risk of allosensitization or to generally reduce risks associated with their use.[41] In hemodynamically stable patients blood transfusion should be considered in very low

haemoglobin levels of less than 7g/dl or levels of less than 8g/dl in post operative surgical patients, ESA resistance, clear symptoms related to anaemia and cardiovascular diseases.[30]

Intravenous Versus Oral Iron Supplementation for the Treatment of Anemia in CKD: Systematic Review and Meta-analysis Benaya Rozen-Zvi,etal .Compared with oral iron, there was a significantly greater Hb level in dialysis patients treated with IV iron (weighted mean difference, 0.83 g/dL; 95% confidence interval, 0.09 to 1.57). Meta-regression showed a positive association between Hb level increase and IV iron dose administered and a negative association with baseline Hb level. For patients with CKD, there was a small but significant difference in Hb level favoring the IV iron group (weighted mean difference, 0. 31 g/dL; 95% confidence interval, 0.09 to 0. 53). Data for all-cause mortality were sparse, and there was no difference in adverse events between the IV- and oral-treated patients. Conclusions: Our review shows that patients on hemodialysis therapy have better Hb level response when treated with IV iron. For patients with CKD, this effect is small.

Iron therapy is recommended when there is benefit of avoiding or minimizing ESA therapy, red cell transfusion or anemia related symptoms. Intravenous iron therapy is recommended for adult CKD patients not on iron or ESA therapy. A one to three month oral iron therapy can be an alternative to non dialysis CKD patients. Intravenous iron therapy is recommended for adult CKD patients on ESA therapy who are currently not taking iron supplements or oral iron therapy for a period of one to three months for pre dialysis patients. The route for pre dialysis patients is based on severity of iron deficiency, availability, side effects with prior oral or intravenous iron, cost and patient compliance.

In initiating ESAs therapy the potential benefits associated with reduction of red cell transfusion, anemia related symptoms should be considered. ESAs therapy should not be initiated in individuals with Hb concentration of more than 10g/dl in pre dialysis patients. In individuals whose Hb is less than 10g/dl in pre dialysis patients, ESAs initiation should be individual based on ESAs risks related therapy, prior iron therapy response and severity of anemia. ESAs therapy is recommended in stage 5 CKD patients to avoid level going below 9g/d [40].

ESAs are regarded as effective agents in correcting and maintaining stable hemoglobin levels. The newer erythropoietin derivatives have longer administration interval due to their longer half life and lower binding affinity to receptor. Complete correction of anaemia has shown no benefit and has been associated with various adverse effects hence a target hemoglobin level of 11-12g/dl has been suggested[23] Stage 5 CKD patients have been shown to require higher ESAs doses than pre-dialysis patients. Hemoglobin levels should increase slowly during the correction phase. Target hemoglobin level rise should not exceed 1g/dl in a two week interval. Higher incremental rates have been associated with cardiovascular and thromboembolic events .

ESAs should be given cautiously in CKD patients with anemia while targeting a hemoglobin level of between 11-12g/dl. Erythropoietin alfa, an ESA has been associated with side effects such as worsening of hypertension and injection site reactions. Recommendation on use of iron supplementation during therapy with ESAs has been encouraged as pharmacologically induced erythropoiesis is limited by iron supply.[31]

Despite the successes of epoetin alfa and darbepoetin alfa, the management of anemia of CKD is poised for

further clinical advancement. Several new anemia therapies are in various stages of development. The agent closest to the market is the third-generation erythropoiesis-stimulating agent continuous erythropoiesis receptor activator (CERA). Phase 3 clinical testing of CERA has recently been completed. The hypothesis being tested is that CERA administered every 3 to 4 weeks is safe and effective for the treatment of anemia associated with CKD (including patients on dialysis and not on dialysis). CERA's long duration of action is attributed to the addition of a large polymer chain into the erythropoietin molecule. The elimination half-life of CERA is approximately 130 hours.Also in the development stages for the treatment of anemia of CKD are the erythropoietin-mimetic peptides. One agent in this class, *Hematide*, is in phase 2 of clinical development. In vitro studies have shown that *Hematide* binds the erythropoietin receptor, triggers intracellular signaling, and causes cell proliferation and differentiation. In vivo studies have shown that *Hematide* is well--tolerated and can stimulate erythropoiesis in multiple species to produce a sustained increase in hemoglobin levels.

Aims and Objectives- 1 To ascertain etiology of Anemia in CKD patients presenting in tertiary care centre in Uttarakhand 2.To ascertain therapeutic response of different treatment strategies in patients of Anemia in CKD.

Materials and Methods

A two year hospital Based Cross-Sectional Observational Study was done in medicine department at Dr. Susheela Government Hospital, Haldwani,, a tertiary care centre in kumaon region of Uttarakhand in northen India. 201 patients aged 18 to 60 years of Chronic kidney disease coming in both OPD and IPD diagnosed on basis of history, physical examination and investigations were included.

Inclusion Criteria: Patients providing informed consent

Aged 18- 60 years

OPD and IPD CKD Patients both Predialysis and Postdialysis

Exclusion Criteria: Age Less than 18 years and more than 60 years

Pregnancy

Acute or chronic inflammation

Malignancy or known cause of haematological disorder

Recent severe hemorrhagic episode.

The patients were subjected to lab and imaging investigation results like Serum creatinine, Hb, GBP, MCHCMCV, Serum iron, Reticulocyte count, ECG. Proforma was prepared in English and Hindi to make it convenient for the population to communicate.

Principle for Hemoglobin estimation: Blood is mixed with N/10 HCL resulting in conversion of hemoglobin to acid hematin which is brown in color. The solution is diluted till it’s color matches with the brown colored glass of the comparator box.The concentration of hemoglobin is read directly.

Automated cell counters calculate the hematocrit by multiplying the red cell number (in millions/ mm3)by mean cell volume in femtolitres.

Creatinine clearance is an estimate of glomerular filtration rate. It is calculated by Cockcroft Gault formula = ([140-age in years] × weight in kg)/(serum creatinine × 72) ,In women multiply by 0.85

RESULTS AND OBSERVATION

Out of 201 patients 107 males 97 females out of which 39 were in CKD stage 3,106 in stage 4 ,56 in stage 5

Table 1: Distribution of patients according to CKD stage

CKD Stage	Frequency (n=201)	Percentage (%)
Stage III	39	19.4%
Stage IV	106	52.7%
Stage V	56	27.9%

About half of the patients had CKD stage IV followed by Stage V and Stage III in 56 (27.9%) and 39 (19.4%) patients respectively. It is shown in Table 1 and Figure No. 1.

Figure 1: CKD stage

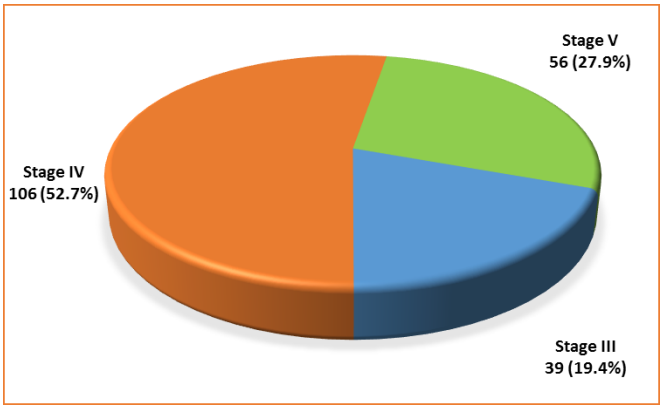

Table 2: Comorbidity

	Frequency(n=201)	Percentage (%)
Hypertension	201	100.0%
Diabetes	44	21.9%

All patients had hypertensive and 44 (21.9%) patients had diabetes. It is shown in Table 2 and Figure No. 2.

Figure 2: Comorbidity

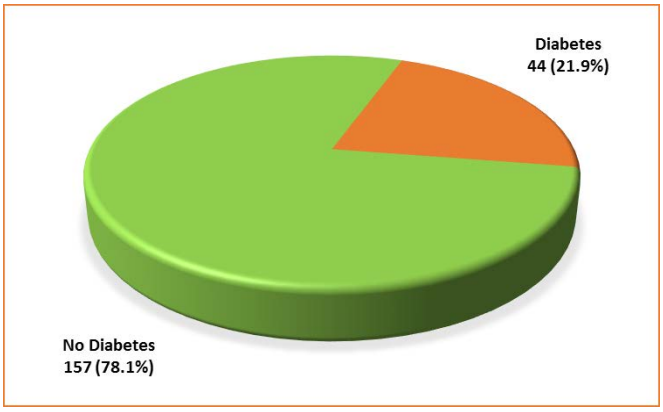

Table 3: Distribution of GBP

GBP	Frequency (n=201)	Percentage(%)
Microcytic Hypochromic	24	11.9%
Normocytic Normochromic	177	88.1%

The morphologic feature of anemia consisted of: microcytic hypochromic 24 (11.9%) and normocytic normochromic 177 (88.1%) patients. It is shown in Table 3 and Figure No. 3.

Figure 3: Distribution of GBP

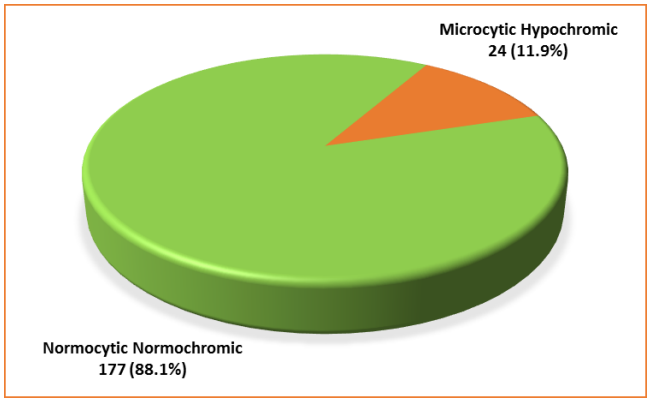

Table 4: Distribution of patients given Iron Supplement

IRON	Frequency (n=201)	Percentage (%)
1000gm sucrose	69	34.3%
500gm sucrose	2	1.0%
Not Given	130	64.7%

136 were found severe anemia and 63 with low serum iron. Patients given iron supplement and erythropoietin. Iron supplement was given to 71 (35.3%) patients. It is shown in Table 4 and Figure No. 4.

Figure 4: Distribution of patients given Iron Supplement

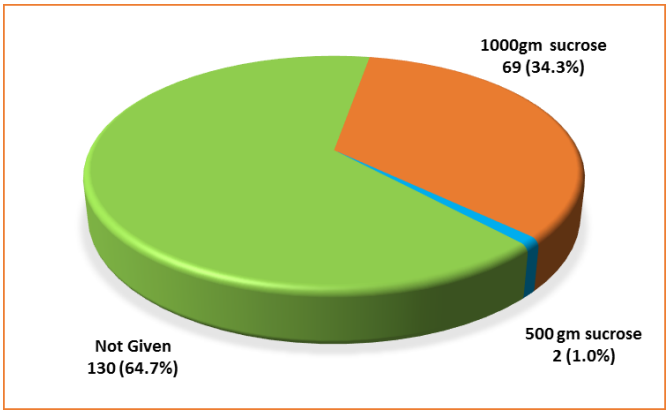

Table 5: Relationship between CKD Stage and severity of Anemia

HB	CKD Stage			
	Stage III	Stage IV	Stage V	Total
< 7.0 (Severe Anemia)	12 (30.8)	70 (66.6)	54 (96.4)	136 (67.7)
7.0 - 9.9 (Moderate Anemia)	27 (69.2)	34 (32.1)	2 (3.6)	63 (31.3)
10.0 - 10.9 (Mild Anemia)	0 (0.0)	2 (1.9)	0 (0.0)	2 (1.0)
Total	39 (100.0)	106 (100.0)	56 (100.0)	201 (100.0)
Chi Square Value	48.187			
p-value	< 0.0001*			

There was significant association observed between severity of anemia and CKD stage. 54 (96.4%) stage V CKD patients were severe anemic. 70 (66.6%) and 12 (30.8%) patients were severe anemic in stage IV and stage III respectively.

Discussion

Among the many comorbidities associated with chronic kidney disease (CKD), anemia and its management remains a challenging endeavor for clinicians. The emergence of recombinant human erythropoietin (rHuEPO) >30 years ago revolutionized the treatment of anemia for CKD patients, but since that time, the mainstays of therapy have remained erythropoiesis-stimulating agents (ESA) and iron supplementation, with a significant number of patients demonstrating persistent anemia despite these interventions. Scientific advances in the understanding molecular regulation of EPO production and the role of the iron-regulatory protein hepcidin in iron metabolism have opened the door for the development of novel ESAs and renal anemia therapies.

Anemia occurs early in the development of kidney disease and worsens with declining kidney function. Many studies have demonstrated an association between the Hb concentration and kidney function. One of the largest, the Third National Health and Nutrition Examination Survey (NHANES III), examined more than 15,000 people in the general U.S. population between 1988 and 1994 and found a inverse relationship between GFR < 60 ml/min/1.73 m^2 and prevalence of anemia. Using estimated GFR, the prevalence of anemia, defined as an Hb concentration < 12 g/dl in men and < 11 g/dl in women, increased from 1% in patients with a GFR of 60 ml/min per 1.73 m^2 to 9% at a GFR rate of 30 ml/min/1.73 m^2 and to 33% for men and 67% for women at a GFR of 15 ml/min/1.73 m^2 [38 37].

In our study, 107 (53.2%) were male and 94 (46.8%) were females. In the study of Mishra et al (2014) 68% patients were males while 32% patients were females . In the study of Afshar et al (2010) 55% patients were males and 45% were females [35]. In the study of Poudel et al (2013) 56.4 % patients were males 43.6% patients were females [38]. However in the study of Deori et al (2016) 72% patients were males and 28% patients were females [49]. In the study of Ahmed et al (2015) 62% were males and 38% were females [36].

About half of the patients had CKD stage IV followed by Stage V and Stage III in 56 (27.9%) and 39 (19.4%)

patients respectively. In the study of Mishra et al (2014), majority of patients are from the stage IV i.e 54.6% (96 patients), 27.4% (48) patients from the stage of V and 15.4% (27) patients from the stage III. In our study, All patients had hypertensive and 44 (21.9%) patients had diabetes. In the study of Afshar et al (2010) The most frequent causes of CKD were diabetes mellitus (49.1%), hypertension (28.3%), glomerular disease (17.1%) and polycystic kidney disease (5.6%) [40]. In the study of Deori et al (2016) ; Diabetes mellitus and hypertension were the most common aetiological cause, seen in 44% and 36% of the CKD subjects respectively [40].

The morphologic feature of anemia consisted of: microcytic hypochromic 24 (11.9%) and normocytic normochromic 177 (88.1%) patients. while In the study of Afshar et al (2010) 80% patients had normochromic-normocytic anaemia ,15% patients had hypochromic-microcytic and 5% patients had macrocytic anemia [39].

In our study, iron deficiency was observed in 63 (31.3%) patients. While in the study of Afshar et al., (2010) The frequency of anemia in hemodialyzed and pre-dialyzed patients were 85% and 75% [33]. In the study of Poudel et al (2013) 47.8% patients had anaemia [39]. In the study of Mc Clellan et al (2004) overall incidence of anaemia in CKD was 47.75% [39]. In the study of Deori et al (2016) 26% patients had anaemia 38].

In our study the severity of anaemia among the patients was mild in 1% patients, moderate in 31.3% patients and severe in 67.7% patients. While in the study of Afshar et al (2010), The severity of anemia among hemodialyzed patients was mild (Hgb > 10 g/dL) in 5%, moderate in 70% and severe (Hgb< 7 g/dL) in 25%, while in pre-dialyzed was mild in 45% and moderate in 55% [38]. In the study of Deori et al (2016) 18% patients had mild anaemia, 48% patients had moderate anaemia and 34 % had severe anaemia. Iron supplement was given to 71 (35.3%) patients [75]. Erythrotoetin was given to 78 (38.8%) patients. In the study of afshar et al (2010) 90.7% of hemodialyzed patients group received erythropoietin.

Our study revealed that there was a correlation between blood transfusion and urea level with CKD stage. As stage increases the level of blood transfusion and urea increases. As per one way ANOVA, blood transfusion and urea level of stage III CKD patients was significantly more than those of stage IV and V. Lower GFR level (12.6±2) was observed in stage V CKD patients followed by stage IV (20±3.6) and stage III (33.5±6.4). Hemoglobin level was significantly raised post dialysis in both patients group who received iron supplement and not. However improvement was better in patients who had received iron supplement.

According to a study by Kathleen M Fox et al., in The mean (± SD) Hb level closest and prior to a transfusion was 8.8 (± 1.5) g/dL [40]. Patients who were hospitalized in the 6 months prior to their first anemia diagnosis were 6.3 times more likely to receive a blood transfusion than patients who were not hospitalized ($p < 0.0001$). Transfusions were prevalent and the trigger hemoglobin concentration was approximately 9 g/dL among ND-CKD patients with anemia. To reduce the transfusion burden, clinicians should consider other anemia treatments including ESA therapy. In a study by Elizabeth V. Lawler et al., in 2010 Among 97,636 patients with CKD and anemia, we observed 68,556 transfusion events (61 events per 100 person years)

Erythropoietin (EPO) has become an essential part of the management of anemic patients with CKD. Numerous randomized, controlled trials have demonstrated that EPO significantly raises hemoglobin

levels, reduces transfusion requirements, and improves quality of life in anemic patients with chronic renal failure. Lefebvre et al conducted an analysis on data from a multicenter, open-label, prospective study of EPO for anemia in patients with CKD not on dialysis to evaluate the relationship between Hb level and quality of life (QOL). The results showed that the maximal incremental gain in QOL occurred when Hb reached 11 to 12 g/dL. This sugges treatment with EPO raised hemoglobin levels, reduced transfusion requirements and improved quality of life. Studies have demonstrated that morbidity and mortality rates are lower when hematocrit values are within the Disease Outcomes Quality Initiative (DOQI) target range (33 to 36%) [41,42].

According to a study by amir hayat et al in 2009 Fatigue is improved somewhat by anemia treatment with EPO [98].

As per the study by Daniel G. Wright et al ., in 2015 Epoetin doses used to achieve equivalent hemoglobin responses in study patients were, on average, 25% higher when epoetin was administered intravenously rather than subcutaneously.

Consider initiating erythropoietin treatment only when the hemoglobin level is less than 10 g/dL.

Conclusion

In 3rd and 4th stages CKD we found anemia (mild to severe). Anemia was observed more in old age than young.

It was found that the diabetes and hypertensions are the etiologies of CKD.

The patients were showing improvement in anemia with blood transfusion, iron replacement and erythropoietin treatment.

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