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Pathology

Anaemic Manifestations in Chronic Kidney Diseases- A Study at a Tertiary Care Centre

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Abstract **Original Research Article**

Kidney disease is ranked 3rd amongst life threatening diseases in India, after cancer and heart disease. Anaemia affects patients with renal impairment and is common in both pre-dialysis and on dialysis patients, leading to decreased exercise tolerance, reduced life quality and additional risk factors for early death. 25 cases admitted in kidney unit at a tertiary care centre were randomly selected for this study between May 2018 to August 2018. All patients were examined and investigated thoroughly as per proforma. The most common type of anaemia was microcytic hypochromic type in 18 patients (72 %), normocytic normochromic with 2 patients(8%), macrocytic in 2 patients(8%) and 3 patients(12%) had haemoglobin overshoot due to treatment &1(4/) had normal Hb. Most common symptoms were facial puffiness, easy fatigability and pedal edema. Most common associated diseases were hypertension, diabetes mellitus, ischaemic heart disease and dyslipidemia. CKD is more common in older age groups. Anaemia is most common complication of CKD and severity of anaemia increases as CKD worsens. In the present study, all patients had anaemia. Both MHD and medical line treatment with EPO have beneficial effect on Hb levels.

Keywords: CKD, ESRD, EPO, MHD, GFR.

INTRODUCTION

The prevalence of CKD is rising worldwide. The worldwide rise in the number of patients with CKD is reflected in the increasing number of patients with ESRD treated by renal replacement therapy- dialysis or transplantation. Two factors are important: first is the ageing of population; the menace of ESRD is higher in elderly people than in general population. The second factor is the global epidemic of type 2 DM.

Community based prevalence rates are not available in India. However, it is estimated that approximately 100,000 new cases of ESRD develop annually in India. Patients with ESRD appear to be the tip of iceberg, and those in the earlier stages of CKD- who are more in number- need attention, to retard progression [1].

Anaemia affects 60-80% of patients with renal impairment and common in both pre-dialysis and on dialysis leading to decreased exercise tolerance, reduced life quality and additional risk factors for early death [2]. Other common causes in people with kidney disease include blood loss from haemodialysis and low levels of nutrients found in food like iron, Vitamin B12, folic acid.

While anaemia in CKD can result from multiple mechanisms (iron, folate, or vitamin B12 deficiency; gastrointestinal bleeding; severe hyperparathyroidism, systemic inflammation, and shortened red blood cell survival), decreased erythropoietin synthesis is the most important and specific etiology causing CKD-associated anaemia. In CKD, tubular atrophy generates tubulointerstitial fibrosis, which compromises renal erythropoietin synthetic capacity and results in anaemia.

A normochromic, normocytic anaemia usually accompanies progressive CKD, and the overall prevalence of CKD-associated anaemia is approximately 50%. Although anaemia may be diagnosed in patients at any stage of CKD, there is a strong correlation between the prevalence of anaemia and the severity of CKD. One quarter of stage 1 CKD patients, half of those stratified to CKD stages 2, 3, and 4 and three quarters of CKD patients starting dialysis suffer from anaemia. Therefore, primary care providers

play an important role in diagnosing and managing anaemia in CKD patients.

In addition to associations of blood haemoglobin with morality and hospitalizations in the CKD population, anaemia is associated with fatigue, weakness, shortness of breath, and a decreased health related quality of life. Furthermore, haemoglobin overshoot may be associated with various safety concerns, including the development of elevated BP with risk for hypertensive encephalopathy, iron deficiency, high platelet count, thrombotic events and accelerated left ventricular dysfunction and hypertrophy.

In 2000, the National Kidney foundation (NKF) and the Dialysis Outcome Quality Initiative (DOQI) advisory board approved the development of clinical practice guidelines to define the chronic kidney disease and to classify stages in the progression of kidney disease [3].

Many people with kidney disease needs iron supplements and EPO to raise their blood cell count to a level that will reduce the need for red blood cell transfusions [4].

Minimizing haemoglobin variability can have important short and long-term clinical consequences. In the short run, fewer fluctuations above 12 g/dl may minimize the occurrence of serious cardiovascular events associated with high haemoglobin levels, whereas fewer fluctuations below 11.0 g/dl provide improved symptomatic relief and maximize survival. The traditional desire to maximize the fraction of patients with CKD and with a blood haemoglobin level >11 g/dl along with recent efforts to minimize the proportion of patients with haemoglobin level >12 g/dl contributes to some of the challenges in the management of haemoglobin variability. Targets that require least frequent ESA dosage adjustment and yet meet the criteria set forth by regulatory or consensus bodies should be pragmatically selected [5].

CKD is defined as

The presence of kidney damage, manifested by abnormal albumin excretion or decreased kidney function, quantified by measured or estimated glomerular filtration rate (GFR) that persists for more than three months.

OR

Kidney damage for >3 months as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifests by either pathological abnormalities or markers of kidney damage[6].

OR

GFR <60ml/min/1.73sq.m for >3 months with or without kidney damage

CKD is not a static condition. It tends to progress and worsen over time to ultimately end up with kidney failure because of progress of disease.

OBJECTIVES

- To study the frequency and extent of anaemia in patients of chronic renal diseases in hospitalized patients in Nagpur
- To know the consequences of anaemia in CKD patients.
- To know exact cause of anaemia in hospitalized patients of CKD and how this helps in definitive management of CKD.

MATERIAL AND METHODS

The study was undertaken after the approval from the institutional ethical committee. The study includes 25 hospitalized patients, both male and female with chronic renal diseases in kidney unit at Lata Mangeshkar Hospital, Nagpur. The frequency of anaemia in different stages of CKD was calculated and the treatment protocol recorded in accordance.

Patients were divided according to stage of their renal disease and severity of anaemia on basis of CBC and biochemical tests, whose anaemia was treated with erythropoietin or mere iron supplementations. Along with this, each patient's laboratory parameters were also studied with their clinical findings. Purpose of study was carefully explained to patients and consent was taken.

Abbreviation	Full form
CKD	Chronic kidney disease
MHD	Maintenance haemodialysis
ESRD	End stage renal disease
DM	Diabetes mellitus
EPO	Erythropoietin
GFR	Glomerular filtration rate

For the purpose of study, the following definitions were used.

- CKD is defined as functional abnormality of the kidney manifested by elevated serum creatinine of >1.5 mg/dl for more than 3 months.
- Anaemia in CKD is defined as Hb<12 g/dl in adult males and postmenopausal females and <11g/dl in premenopausal females and prepubertal persons.
- Anaemia is categorized into mild, moderate and severe with Hb% of 9-11gm%, 7-9gm% and <7gm% respectively as per WHO anaemia classification.

The type of anaemia prevailing in chronic renal diseases was noted in every patient's report and

findings give us the rough idea of importance of its type in disease and treatment.

A history of hypertension, diabetes and any family history of renal disease were noted and relative significance of these complications on anaemia and renal disease were noted in details. For the anaemia evaluation, peripheral smear and CBC was done on patient's blood. A detailed clinical evaluation was noted in the proforma.

OBSERVATIONS AND RESULT

Table-1: Association between haemoglobin and serum creatinine (N=21)

Serum creatinine levels (mg/dl)	No. Of patients on Medical management (Hb levels)			No. Of patients on Maintenance haemodialysis (Hb levels)			Total
	</=7	7-9	9-11	</=7	7-9	9-11	
1.5-5	0	1	1	1	1	0	4
5-10	3	5	3	1	1	1	14
10-15	2	1	0	0	0	0	3
15-25	0	0	0	0	0	0	0
Total	5	7	4	2	2	1	21

1 patient had creatinine value less than 1.5 and had normal Hb level. 3 patients had haemoglobin overshoot due to excessive EPO treatment and were end stage kidney patients.

Therefore, these cases were not included in above chart. The table shows that 16 patients were on medical management and 5 patients were on maintenance haemodialysis. 11 cases were secondary to systemic diseases like DM and hypertension.

Table-2: Association between haemoglobin and complete haemogram (N=21)

Haemoglobin Levels (in g/dl)	Microcytic Hypochromic	Normocytic normochromic	Macrocytic Normochromic	Total
<7	5	0	1	6
7-9	10	0	1	11
9-11	3	1	0	4
Total	18	1	2	21

3 patients had haemoglobin overshoot due to excessive EPO treatment and were end stage kidney patients.

Out of 6 patients with mild anemia, 5 were microcytic hypochromic anaemia and one case is of normocytic normochromic anemia.

Out of 11 cases with moderate anaemia, 10 had microcytic hypochromic anaemia and one with macrocytic normochromic anaemia.

Out of 5 cases with severe anaemia, 3 had microcytic hypochromic anaemia and two had normocytic normochromic anaemia.

CKD was mostly in association with and secondary to hypertension, diabetes and ischaemic heart disease.

DISCUSSION

CKD is characterized by elevation in blood urea nitrogen and serum creatinine concentration with or without decreased urine output. It leads ultimately to functional disorders involving fluid, electrolyte and metabolic disturbances. Haemoglobin concentration was used as baseline parameter for investigation as well as follow up in this study. The lowered transferrin level prevents the proper transport of the iron to the hematopoietic sites, which may be a reason for the low haemoglobin synthesis and also for the development of erythropoietin hypo responsiveness in some of the dialysis patients [7]. The cut off value for haemoglobin level for diagnosis of anaemia in CKD is 12g/dl as set by DOQI guidelines.

Following data was obtained in the present study
Mild anaemia- 5 (20 %)
Moderate anaemia- 9 (36%)
Severe anaemia- 7 (28%)

According to most of the studies conducted worldwide, chronic kidney disease is associated with normocytic normochromic prevalence of anaemia but this study shows predominance of microcytic hypochromic anaemia in patients mostly due to deficient intake of iron in food.

The United States normal haematocrit study evaluated 1,233 haemodialysis patients with clinical evidence of congestive heart failure or ischaemic heart disease. The risk ratio (for death and non-fatal myocardial infarction) was 1.3 for the normal haematocrit group as compared to the low haematocrit group [8].

The study done by Caller SR *et al.* [9] showed that anemia becomes more severe as CKD progresses. This is because as CKD progresses inhibition of bone

marrow, deficiency of EPO, degrees of anaemia and bleeding tendencies increase as a result of increase in circulating toxins.

VK Talwar and HL Gupta [10] in their study found that most of the patients presented with features of anaemia (94%), uraemia (63%) and fluid overload (96%). Severity of anaemia was correlating with degree of azotaemia. Sixty percent of the patients had microcytic hypochromic anaemia, five percent had macrocytic anaemia while 30% had normocytic normochromic anaemia. This study correlates with our present study.

In the present study, the no. of patients receiving treatment for iron deficiency, in the form of oral supplementation / injectable iron were 9 cases. Also, adequate iron replacement could cause a marked improvement in the anemia even without the use of erythropoietin (EPO) [10].

Transfusion was given in 11 cases. It is necessary to detect type of anaemia as it is general tendency to consider anaemia to be of normocytic normochromic type. However in India, a coexisting iron deficiency is also seen [11].

Many studies have shown that correction of anemia can limit the progression of chronic kidney disease and possibly decrease mortality. Patients with plasma ferritin concentrations below 100 ng per ml (100 mcg per L) should be given iron supplements[12, 13].

Lauren BC *et al.* in their study evaluated predictors of anaemia in CKD. They concluded that the probability of anaemia development was greater in local CKD patients with low previous haemoglobin, more advanced CKD, presence of haematological and respiratory disorders, as well as not using iron supplements [14].

CONCLUSION

Iron deficiency anaemia was the most common type of anaemia in CKD patients in our study (72%). Majority of the patients (56%) had mild or moderate degree of anaemia. To minimise the complications, Optimum management of anaemia is in the range of 11 to 12 gm/dl as recommended by current DOQI guidelines is essential. Many of the cases in the study were secondary to systemic diseases like DM & hypertension.

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