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Role of Iron Deficiency Anemia in Patients with Chronic Kidney Disease

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Abstract:
Background: *Chronic kidney disease (CKD) is a worldwide health problem. CKD is a progressive condition and ultimately end up with kidney failure. A normocytic, normochromic anemia is observed in CKD. The primary cause in patients with CKD is insufficient production of erythropoietin (EPO) by the diseased kidneys. Anemia is both a complication of CKD as a part of uremic syndrome and a risk factor which influences the adverse outcomes of CKD, So evaluation and management of anemia is important to prevent the progress of CKD and for the general well being of the patient. As the renal function worsens, there is a progressive increase in the percentage of CKD patients with anemia.*
Aims and Objectives*: To determine the prevalence of iron deficiency anemia in patient with chronic kidney disease and study the effect of iron deficiency anemia on survival of CKD patients.*
Results: *In present study the overall prevalence of iron deficiency anemia in chronic kidney disease was 42.63% whereas in males, the prevalence of iron deficiency anemia was 44.4% which was less than female patients (55.6%). The observed values of iron deficiency anemia in CKD in relation to age group, hypertension and type of iron therapy have been found satistically nonsignificant, however iron deficiency anemia outcome with sex group, stage of CKD, diabetes and dialysis therapy were found to be satistically significant.*
Conclusion: *Iron deficiency anemia is common in CKD patients (42.63%). Functional Iron deficiency is seen in 39.03%. Iron deficiency is related to stage of CKD, Sex, Diabetes mellitus, erythropoietin therapy and dialysis therapy. There was no relation of Iron deficiency anemia with age, hypertension, and type of iron therapy. However mortality was not related to iron deficiency in CKD patients.*
Keywords: *Chronic kidney disease, Iron deficiency anemia, Hemodialysis, Erythropoietin.*

I. Introduction

Chronic kidney disease is a significant cause of morbidity and mortality world wide[1]. In India, there is a rising incidence and prevalence of kidney failure, with poor outcomes and high cost. The hallmark of CKD is structural and functional damage of the glomeruli of the kidney. The most important outcomes of this kidney damage are loss of kidney function and cardiovascular disease leading to premature death. In CKD, Erythropoietin (EPO)is produced in the peritubular cells of the kidney and is the major hormone involved in the production of red blood cells (erythropoiesis) when erythrocyte cells are produced. Anaemia starves the body of Oxygen and causes decreased capacity, cognitive impairment, and diminished quality of life[2]. Management of anemia in chronic kidney disease involves use of EPO. However EPO is effective only when iron is available in sufficient quantity. Hence evaluation of iron status in patients with chronic kidney disease is very vital. This study is under taken to study haematological profile of iron deficiency anemia in chronic kidney disease.

Defining CKD[3] as Kidney damage for 3 months or more as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifests by either : a) Pathological abnormalities detected by histopathological studies; or b) Markers of kidney damage, including abnormalities in the composition of the blood or urine , or abnormalities in imaging tests. GFR less than 60ml/min/1.73 m^2 for 3 months or more, with or without kidney damage.

Fishbane et al. found high rates of iron deficiency in adult men (57.8 to 58.8%) and women (69.9 to 72.8%) with CKD stages 3-5 in the NHANES 3 and 1999-2004 survey[4].

The prevalence of anemia in stage 3-5 CKD patients aged >64 in 2007-2010 NHANES survey was 24.4%. The prevalence of CKD in the SEEK-India cohort was observed to be 17.2% with 6% have CKD stage 3 or worse. Prevalence of CKD stages 1, 2, 3, 4 and 5 was 7%, 4.3%, 4.3%, 0.8% and 0.8% respectively[5].

National kidney foundation kidney dialysis outcomes quality initiative
(NKF K/DOQI 2012) DEFINES IRON DEFICIENCY ANEMIA[6, 7] :
1. **Absolute Iron Deficiency:** Ferritin <100 ng/ml and TSAT <20%.
2. **Functional Iron Defeciency:** Ferritin > 100 ng/ml and TSAT <20%.

Iron deficiency is common in patients with CRF. 25-37.5% patients of CRF have iron deficiency[8]. The cause's are : Decreased iron absorption as a part of uremic syndrome, loss of RBCs and Fe due to bleeding tendencies in uremic syndrome, dialysis related loss of RBCs and Fe, blood loss due to frequent blood tests.

Serum ferritin reflects body stores of iron[9]. A level of <100 ng/ml indicates absolute iron deficiency in CKD. But this is not very sensitive; it can reflect depleted stores only when the depletion is very low. Serum ferritin values < 30ng/ml indicate severe iron deficiency and are highly predictive of absent iron stores in bone marrow. It is not very specific as serum ferritin is also an acute phase reactant and elevated in conditions such as hyperthyroidism, inflammation/infection, hepatocellular disease, malignancies, alcohol consumption and oral contraceptives[10]. Transferrin saturation reflects the amount of available iron for erythropoiesis. In iron deficiency, elevated transferrin levels maintain the circulating iron pool despite the marked decrement in Tsat. A level of <20% in CKD indicates absolute iron deficiency. Transferrin saturation is decreased only when serum ferritin is decreased in absolute iron deficiency.

The ESRD National Cooperative Anemia Project, a personal communication, J. Wish, April;1997 - 60% of patients were found to be iron deficient. Recent analysis of the National Health and Nutrition Examination Survey 4 suggests that up to 50% of patients with CKD stages 2-5 have absolute or relative (functional) iron deficiency. In CKD, both absolute and relative iron deficiency are common[11].

Aims and Objectives :
- To determine the prevalence of iron deficiency in patient with chronic kidney disease.
- To study the effect of iron deficiency anemia on survival of CKD patients.

II. Material And Methods

It is an open non randomized prospective, cross sectional observational study to determine the prevalence of iron deficiency anemia with CKD and the effect of IDA on survival of CKD patients. The data obtained was studied on 9 parameters and chi-square test was applied and P value was calculated to the attributes to test their significance at 5 % level of significance.
No. Of cases: 190

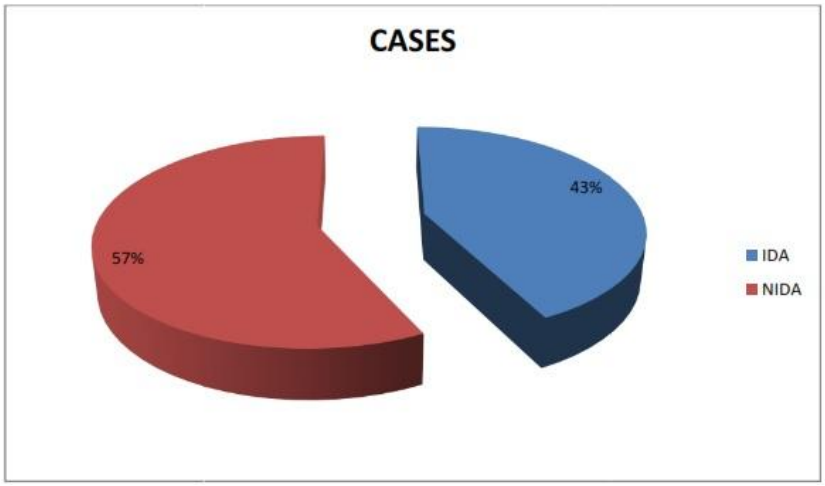
Case definition: Patient was defined as having Iron deficiency anemia in chronic kidney disease if there was: Serum ferritin >100ng/ml and transferring saturation <20%.

Inclusion criteria: All cases diagnosed as chronic kidney disease.

Exclusion criteria: Cases of acute kidney injury, bleeding diathesis, acute bleeding (urological or gastro enterological).
Methodology : The patients under study evaluated as per protocol.
1- **History :** Age, sex, history of hypertension / diabetes mellitus, EPO therapy/ Iron therapy, Hemodialysis.

2. Laboratory investigations :
a) Hemoglobin
b) Serum creatinine
c) Iron studies (serum iron, serum ferritin, TIBC, Transferrin saturation)

Results: Pia chart : showing prevalence of iron deficiency anemia (IDA)



Out of 190 patients, 81(43%) patients were found to have iron deficiency anemia whereas 109(57%) patients were NON-IDA.

Table 1 : Association of different parameters (satistically significant) with iron deficiency anemia (IDA) :

PARAMETERS	IDA	NIDA	TOTAL	CHI-SQUARE	P- VALUE
SEX : MALE	36(44.4%)	73(66.9%)	109	9.6427	0.001 S
: FEMALE	45(55.6%)	36(33.1%)	81	S (>3.84)	(<0.05)
DIABETES	30(37%)	23(21.1%)	53	5.8676	0.015 S
NON-DIABETIC	51(63%)	86(78.9%)	137	S	
EPO THERAPY	55(67.9%)	56(51.4%)	111	5.224	0.022 S
NON-EPO	26(32.1%)	53(48.6%)	79	S	
HEMODIALYSIS	70(86.4%)	78(71.6%)	148	5.9593	0.014 S
NON-HD	11(13.6%)	31(28.4%)	42	S	

The observed values of iron deficiency anemia in CKD in relation to sex group, diabetes and erythropoietin therapy and hemodialysis therapy have been found satistically significant.

Table 2: Association of different parameters (satistically nonsignificant) with iron deficiency anemia (IDA)

PARAMETERS	IDA	NIDA	TOTAL	CHI- SQUARE	P- VALUE
AGE: 21-40	20(24.69%)	26(23.85%)	46	0.0373	0.9981 S
: 41-60	30(37.03%)	40(36.69%)	70	NS	(>0.05)
: > 60	31(38.28%)	41(39.46%)	74	(<3.84)	
HYPERTENSION	54(66.7%)	83(76.1%)	137	2.0763	0.14 NS
NON-HTN	27(33.3%)	26(23.9%)	53	NS	
IRON : ORAL	10(12.34%)	20(18.34%)	30		
: I. V.	27(33.33%)	43(39.445)	70	2.7376	0.6026 NS
NOT ON IRON	44(54.32%0	46(42.22%)	90	NS	
CKD STAGE : 4	8(10.1%)	6(5.7%)	14	1.2485	0.2616 NS
: 5	71(89.9%)	99(94.3%)	170	NS	
DIED	27(33.3%)	36(33%)	63	0.002	0.9612 NS
ALIVE	54(66.7%)	73(67%)	127	NS	

The observed values of iron deficiency anemia in CKD in relation to age group, hypertension and type of iron therapy, CKD staging and prognosis have been found satistically non-significant.

III. Discussion

This study was undertaken in view of prevalence of iron deficiency anemia in chronic kidney disease patients. In the present study, prevalence of iron deficiency anemia, factors responsible for it and its effect on survival of chronic kidney disease patients was studied. Total 190 patients diagnosed as chronic kidney disease were studied. Out of 190 patients, 81 (42.63%) patients were found to have iron deficiency anemia (IDA). The observed values of iron deficiency anemia in CKD in relation to age group, hypertension and type of iron therapy have been found satistically non significant, however iron deficiency anemia outcome with sex group, stage of CKD, diabetes and dialysis therapy were found to be satistically significant.

According to a study by Bowling CB, Inker LA et al[12] , Prevalence of iron deficiency anemia was found more in elderly age group. In this study, contradictory results are found probably because of more young patients developing CKD in Indian population.

According to a study by Singh et al[5] . Prevalence of iron deficiency anemia is higher in males than females. In this study, prevalence of iron deficiency anemia is higher in females than males.

In a a study previously published by New JP, Aung T, Baker PG et al[13] and Fishbane et al[14]. Prevalence of iron deficiency anemia was found to be higher in patients with Diabetes Mellitus. In this study, Prevalence of iron deficiency anemia is found to be higher in patients with Diabetes Mellitus, which is similar to previous studies. According to a study by James B. Post et al[15] and Saul Nurko et al[16] , there was increased prevalence of iron deficiency anemia among the patients receiving erythropoietin. In the present study, there is a direct relation between erythropoietin therapy and IDA i.e. prevalence of IDA is higher in patients receiving erythropoietin therapy, which is similar to previous studies.

According to a study by Melissa E. Stauffer, Tao Fan et al[17] , Prevalence of anemia increased with stage of CKD, from 8.4% at stage 1 to 53.4% at stage 5. In the present study, prevalence of iron deficiency anemia is increased with stage of CKD, which is similar to previous studies.

In a study previously published by Allen R. Nissenson and Jur Strobes et al[18] , 60% of patients were found to be iron deficient on hemodialysis. In our study, There is a direct relation between Hemodialysis and IDA i.e. prevalence of IDA is higher in patients on Hemodialysis, which is similar to previous studies.

IV. Conclusion

Iron deficiency anemia is common in CKD patients (42.63%). Functional Iron deficiency is seen in 39.03%. Iron deficiency is related to stage of CKD, Sex, Diabetes mellitus, erythropoietin therapy and dialysis therapy. There was no relation of Iron deficiency anemia with age, hypertension, and type of iron therapy. However mortality was not related to iron deficiency in CKD patients.

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