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Original Research Article

Prevalence of iron deficiency anaemia in chronic kidney disease patients not on renal replacement therapy: a cross-sectional observational study

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ABSTRACT

Background: Chronic kidney disease (CKD) is a leading cause of mortality in India. Iron deficiency anaemia (IDA), both absolute and functional, is prevalent among CKD patients, especially in developing countries. Timely diagnosis and treatment are essential to reduce associated morbidity and mortality.
Methods: A cross-sectional observational study was conducted from August 2022 to July 2024 at Indira Gandhi Government Medical College, Nagpur. The study included 100 diagnosed CKD patients (stages 3–5) not on renal replacement therapy, fulfilling specific inclusion and exclusion criteria.
Results: Among the participants, 35% were in stage 4 and 38% in stage 5 CKD. The majority (37%) were aged 51–60 years. A significant association was observed between mean haemoglobin levels and CKD stages in males. All females were anaemic, indicating a significant link between gender and anaemia status. Regarding red blood cell morphology, 51% exhibited a normocytic normochromic pattern, while 29% had a microcytic hypochromic pattern. A statistically significant correlation was found between serum iron profile and CKD stages. Of the 91 anaemic patients, 31 (34.06%) had IDA.
Conclusions: CKD predominantly affects older adults, with the highest prevalence in the 51–60 age group and a male predominance. Serum iron profiles deteriorate as CKD stages advance, correlating with increased prevalence and severity of IDA.

Keywords: Absolute iron deficiency, Chronic kidney disease, Iron deficiency anaemia, Relative iron deficiency

INTRODUCTION

The world is currently facing global pandemic of chronic kidney disease (CKD). Kidney diseases are ranked 3rd amongst life threatening diseases in India, after malignancy and heart disease. The disease and its treatment puts not only physical but also an economical burden on the society and the healthcare system.[1] Anaemia is defined as haemoglobin level less than 13 g/dl in males and less than 12 g/dl in females.[2] Although relative deficiency of erythropoietin production is the major driver of anaemia in CKD, iron deficiency stands out among the mechanisms contributing to the impaired erythropoiesis in the setting of reduced kidney function. Iron deficiency plays a significant role in anaemia in CKD. This may be due to a true paucity of iron stores (absolute iron deficiency) or a relative (functional) deficiency which prevents the use of available iron stores.[3] Most common cause of anaemia in CKD is given to be normocytic normochromic (anaemia of chronic disease); but as India being a developing country, nutritional factors such as iron deficiency play an important role in etiopathogenesis of anaemia.[4] As anaemia is an important factor in increasing mortality and morbidity in patients with CKD, prompt diagnosis and treatment of anaemia is essential. Studying prevalence and correlation of iron deficiency anaemia in a developing and resource limited country such as India will help in deciding treatment modalities and curb morbidity and mortality due to anaemia in patients with CKD and to improve survival.

METHODS

A cross-sectional observational study was conducted amongst 100 diagnosed cases of chronic kidney disease (stages 3-5) who were not on renal replacement therapy from in-patient and out-patient department of Indira Gandhi Government Medical College, Nagpur from August 2022 to July 2024 who fulfilled inclusion and exclusion criteria. Institutional ethical committee clearance was obtained before commencement of the study.

Inclusion criteria: Males and females of Age>18 years of age who are diagnosed cases of CKD with sr creatinine more than 1.5 mg/dl for more than 3 months and eGFR less than 60 ml/min/ 1.73 m^2 who have given written and informed consent.

Exclusion criteria

Patients with sr creatinine less than 1.5 mg/dl, HIV, pregnant females, bleeding disorders, haematological malignancies, worm infestation, acute kidney injury, chronic disorders like SLE, Arthritis, tuberculosis etc, chronic liver disease, evidence of acute infection or trauma in last 4 weeks, history of parenteral iron injection in last 14 days, history of blood transfusion in last one month, patients on renal replacement therapy.

Patients were evaluated by relevant history taking, general examination and systemic examination after taking a written informed consent. Blood samples were drawn for complete hemogram, renal function test (Sr creatinine and Blood Urea Nitrogen), iron profile including Sr iron, Sr ferritin, TIBC and TSAT in appropriate vacutainer bulbs. Peripheral smear was made from a fresh finger prick sample. USG KUB was performed to look for kidney sizes, corticomedullary differentiation and other renal pathologies. eGFR was calculated according to 2021 CKD-EPI creatinine equation using age, sex and serum creatinine values. Patients were categorised into CKD stages according to eGFR values.

Statistical analysis

All the data were tabulated and then analysed with appropriate statistical Software 'SPSS 27th version'. Data were presented as distribution into various categories and mean with standard deviation was calculated by applying following statistical significance tests. 'Chi–square Test', 'One way ANOVA Test' and 'Fisher's exact test' were used for statistical significance testing.

RESULTS

Table 1 shows prevalence of CKD amongst the 100 participants was 27% in stage 3, 35% in stage 4 and 38% in stage 5. Also, 37% of the participants out of 100 were in the age group of 51-60 years, followed by 25% in the age group of 61-70 years and 20% in the age group of 41-50 years. Table 2, shows 37% of the participants had both diabetes and hypertension, 21% had hypertension alone, while 16% had diabetes alone. Other causes included CGN (5%), ADPKD (1%), SCD (2%) and unknown aetiology (17%). In almost half, 52% of study subjects, CKD was diagnosed in less than 6 months. Only in 3% of participants the duration since diagnosis of CKD was more than 5 years. In 97% of the participants, CKD diagnosis was done in the last 5 years.

The mean Hb decreased from 12.4 g/dl in stage 3 to 8.01 in stage 5 in male participants. A significant association was observed between mean Hb in males and CKD stages. In female participants mean Hb decreased from 9.61 g/dl in stage 3 to 8.09 in stage 5. No significant association was observed between mean Hb in females and CKD stages. Out of 91 subjects who had anaemia, 49 were males and 42 were females. All the females were anaemic. A significant association was observed between sex and anaemic status. Table 3 out of 21 participants with hypertension, 10 males were anaemic (47.6%) while 2 were not anaemic (9.5%), while all 9 females (42.9%) were anaemic. Out of 16 with DM, 5 males were anaemic (31.3%) while 5 were non-anaemic (31.3%); all 6 females were anaemic (37.4%). Out of 37 patients who had both hypertension and DM, 56.8% were anaemic among males and 40.5% were anaemic among females. Out of 5 patients who had CGN, all had anaemia (4 males and a female).

Also, all patients with unknown aetiology and 2 SCD patients had anaemia. Out of the 2 with ADPKD, 1 male did not have anaemia, while 1 female was anaemic. 51% of participants had predominantly normocytic normochromic pattern followed by 29% with predominantly microcytic hypochromic, then normocytic hypochromic picture in 17%. There was a progressive decline in MCV and total red blood cell count noted amongst participants as the CKD stage progresses, which was found to be statistically significant. Majority (64%), of the study participants had high RDW-CV value followed by (34%) with normal values. Association between RDW-CV and CKD stage was found to be significant. Mean serum iron was 93.3, 79.8, 64.2 in stages 3, 4 and 5 respectively. Association between serum iron and CKD stages were found to be statistically significant. Mean serum ferritin was 93.3, 79.8, 64.2 in stages 3, 4 and 5 respectively.

Association between serum ferritin and CKD stages were found to be statistically significant. Mean serum TSAT was 25.7, 21.1, 18.4 in stages 3, 4 and 5 respectively. Association between serum TSAT and CKD stages were found to be statistically significant. Mean serum TIBC was 366.3, 373.2, 338.9 in stages 3, 4 and 5 respectively. Association between serum TIBC and CKD stages were not found to be statistically significant. 39% of the study subjects had shrunken kidneys and CMD partially maintained. Followed by 26% with shrunken kidneys with lost CMD. 1% had bulky kidneys with multiple cysts. As shown in Table 4, out of 4 participants (all female) with

functional/absolute iron deficiency anaemia, 2 had functional while 2 had absolute iron deficiency (50% each) in CKD stage 3. 9 participants had functional iron deficiency and absolute iron deficiency each (50% each) in stage 4, while 20 participants (74.07%) had absolute iron deficiency out of 27 participants having stage 5 CKD. Out of 91 anaemic patients, 31 (34.06%) had iron deficiency anaemia.

Table 1: Distribution of study participants according to age and CKD stage.

CKD					P value
Age (in years)	Stage 3	Stage 4	Stage 5	Total	
≤20	0	1	0	1	0.590
21-30	0	2	3	5	
31-40	2	3	1	6	
41-50	7	5	8	20	
51-60	10	15	12	37	
61-70	8	16	11	25	
>70	0	3	3	6	
Total	27	35	38	100	

Table 2: Distribution of study participants according to etiology.

Etiology	CKD			Total	%
	Stage 3	Stage 4	Stage 5		
Hypertension	9	7	5	21	21
Diabetes mellitus	12	3	1	16	16
HTN+DM	5	14	18	37	37
CGN	0	2	3	5	5
ADPKD	0	1	1	2	2
Others	1	8	10	19	19
Total	27	35	38	100	100

*others: 2 scd, rest unknown etiology.

Table 3: Distribution of study participants according to etiology, sex and anaemic status.

Etiology	Male (n=58)		Female (n=42)		Total
	Anemia	Non-anemia	Anemia	Non-anemia	
Hypertension n=21	10 (47.6%)	2 (9.5%)	9 (42.9%)	0	21
Diabetes mellitus n=16	5 (31.3%)	5 (31.3%)	6 (37.4%)	0	16
HTN+DM n=37	21 (56.8%)	1 (2.7%)	15 (40.5%)	0	37
CGN n=5	4 (80%)	0	1 (20%)	0	5
ADPKD n=2	0	1 (50%)	1 (50%)	0	2
Others n=19	8 (42.1%)	0	11 (57.9%)	0	19

Table 4: Distribution of study participants according to types of iron deficiency anemia.

CKD stage	Iron deficiency anemia	Sex		Total
		Male	Female	
Stage 3 (n=27)	Functional iron deficiency	0	2 (50%)	2 (50%)
	Absolute iron deficiency	0	2 (50%)	2 (50%)
	Total	0	4	4
Stage 4 (n=35)	Functional iron deficiency	2 (40%)	7 (53.84%)	9 (50%)
	Absolute iron deficiency	3 (60%)	6 (46.15%)	9 (50%)
	Total	5	13	18
Stage 5 (n=38)	Functional iron deficiency	6 (37.5%)	3 (27.27%)	9 (33.33%)
	Absolute iron deficiency	10 (62.5%)	8 (72.72%)	20 (74.07%)
	Total	16	11	27

DISCUSSION

Out of 100 participants with CKD, 27% belonged to stage 3, while 35% to stage 4 and 38% to stage 5. The actual prevalence of initial stages of CKD is much more than the later stages. Coresh et al, have reported a population prevalence of 3.3%, 3.0%, 4.3%, 0.2% and 0.2% in stages 1, 2, 3, 4, 5 of CKD, respectively.5 However in clinical practice, the prevalence of stage 4 and 5 appear to be more as initial stages are asymptomatic and people seek medical attention when severity of symptoms worsens. Also, the prevalence is high compared to western literature probably as the patients seek treatment only at later stages when the severity of symptoms increases and CKD stage has progressed.

Economic constraints also play a role. Coresh et al and Viswanathan et al, have indicated that the prevalence of CKD is higher in older age groups with a male preponderance. The former has also reported that 11% of individuals older than 65 years have CKD.[5] This older age and male predominance can be explained by underlying disease entities causing CKD. Diabetes and Hypertension, both of which are major etiological factors for CKD are more prevalent in older age group and male sex.[6]

In our study, there was preponderance of cases in the age group of 51 to 70 years. 37% of the participants were in the age group of 51-60 years, followed by 25% in the age group of 61-70 years. Out of the 100 participants, 58% were male while remaining 42% were female. However, there was no significant association found between age and sex with CKD stage. It could be because of a smaller sample size, convenience sampling.

Among the aetiology of CKD, as per the DOQI advisory board guidelines, diabetes is the most common cause followed by hypertension, vascular diseases, glomerular diseases, cystic diseases and tubulointerstitial diseases.[7] In this study, 37% of the participants had both diabetes and hypertension, 21% had hypertension alone, while 16% had diabetes alone. This discrepancy could be because of a smaller sample size and convenience sampling in a limited setting like a tertiary care centre and medical college which might not reflect trends in the entire population.

A study done by Callen IR et al, showed that anaemia becomes more severe as CKD progresses.[8] This is because, as CKD progresses, inhibition of bone marrow, deficiency of EPO, deficiency of iron and bleeding tendencies as a result of an increase in the circulating uremic toxins. In our study, the mean Hb decreased from 12.4 g/dl in stage 3 to 8.01 in stage 5 in male participants.

Almost one third 21 (36.2%) participants had mild anaemia followed by 17 (29.3%) had moderate anaemia. A significant association was observed between mean Hb in males and CKD stages. While in female participants mean Hb decreased from 9.61 g/dl in stage 3 to 8.09 in stage 5. Almost one third 21 (36.2%) participants had mild anaemia followed by 17 (29.3%) had moderate anaemia. No significant association was observed between mean Hb in females and CKD stages. That could be because of a smaller sample size and convenience sampling. Also, in higher prevalence of anaemia in females in general population due to reasons like nutritional causes, menstrual loss, which could be additive to the underlying CKD.[9] In our study, out of 91 subjects who had anaemia, 49 were males and 42 were females. All the females were anaemic. A significant association was observed between sex and anaemic status. Overall, as the CKD stage is progressing, anaemia is more severe.

Out of 21 participants with hypertension, 10 males were anaemic (47.6%) while 2 were not anaemic (9.5%), while all 9 females (42.9%) were anaemic. Out of 16 with DM, 5 males were anaemic (31.3%) while 5 were non-anaemic (31.3%), all 6 females were anaemic (37.4%). Out of 37 patients who had both hypertension and DM, 56.8% were anaemic among males and 40.5% were anaemic among females. Out of 5 patients who had CGN, all had anaemia (4 males and a female). Also, all patients with unknown aetiology and 2 SCD patients had anaemia. Out of the 2 with ADPKD, 1 male did not have anaemia, while 1 female was anaemic. This is in compliance with ADPKD being known to be associated with higher Hb levels at least in initial stages of CKD, as reported by a study by Edgar et al, female with ADPKD could have a nutrition cause exacerbating the anaemia.[10]

In this study, almost half, 51% of participants had predominantly normocytic normochromic pattern followed by 29% with predominantly microcytic hypochromic, then normocytic hypochromic picture in 17%. Similar prevalence is reported by Callen et al and in a study by DOQI advisory board.[11,28]

In our study, there was a progressive decline in MCV and total red blood cell count noted amongst participants as the CKD stage progresses, which was found to be statistically significant. This can be explained by a corresponding reduction in the synthesis and serum levels of erythropoietin which is the major drive for erythropoiesis in the bone marrow.

Barring TIBC, other variables constituting iron profile (serum ferritin, serum iron, TSAT) in this study showed a positive correlation between progression of CKD stage and prevalence of iron deficiency. As CKD stage progresses, iron deficiency became more prevalent and severe.

In our study, out of 4 participants (all female) with functional/absolute iron deficiency anaemia, 2 had functional while 2 had absolute iron deficiency (50% each). 9 participants had functional iron deficiency and absolute iron deficiency each (50% each) in stage 4, while 20 participants (74.07%) had absolute iron deficiency out

of 27 participants having stage 5 CKD. That is, as CKD stage progressed, more participants had absolute iron deficiency anaemia, which was defined as iron deficiency anaemia in the study. As described in a study by Anat Gafter-Gvili et al, iron deficiency anaemia is a common complication of CKD patients. Absolute iron deficiency in CKD patients is commonly defined when TSAT is ≤20% and the serum ferritin concentration is ≤100 ng/ mL among patients not on haemodialysis. Functional iron deficiency, also known as iron-restricted erythropoiesis, is characterized by TSAT≤20% and elevated ferritin levels.[12] The same study mentioned that the severity of anaemia was a predictor of ESRD, increased rate of mortality and cardiovascular hospitalizations. In our study, similarly, as the CKD stage progressed, more participants had iron deficiency anaemia.

A study by Bishaw et al, conducted in Ethiopia, describes that there is wide variation in the prevalence of anaemia in CKD across regions.[13] For instance, the reported prevalence of anaemia in CKD is 14% in the USA, 39.36% in India, 51.5% in China, 43.18% in South Africa and 79% in Cameroon. Moreover, the prevalence increases with the CKD stage, with an overall prevalence of 22.4%, 41.3% and 53.9% in CKD stages 3, 4 and 5, respectively. The same study also showed that iron deficiency anaemia was present in nearly half (47.65%) of the patients with anaemia.

This is higher than the results reported in other studies, like 39% in India. In our study, total prevalence of anaemia out of the 100 CKD participants was (stage 3, 4 and 5), 91%. Which is much higher than mentioned in the literature, which might be because of other contributing factors like low socio-economic status, malnutrition, societal traditions, access to healthcare etc, which are outside the scope of this study. Out of 91 anaemic patients, 31 (34.06%) had iron deficiency anaemia, while others had either functional iron deficiency or other types of anaemia like anaemia of chronic disease. Out of a total of 100 CKD patients, 31% had iron deficiency anaemia, which similar to the prevalence given in the literature.[14]

CONCLUSION

CKD is prevalent in adult population in older age group with maximum prevalence in the age group of 51-60 years, with a male predominance. Hypertension and diabetes are the commonest aetiological factors for CKD. Anaemia is a common complication of CKD and the degree of anaemia increases as CKD stage progresses. Anaemia prevalence was higher in females, with all females with CKD having anaemia irrespective of the stage. Predominant blood picture was normocytic normochromic followed by microcytic hypochromic.

There was a progressive decline in Hb, MCV and RBC count as CKD stage progressed, while RDW-CV progressively increased with worsening CKD stage. Serum iron profile including serum iron, ferritin and TSAT all showed progressively worsening iron deficiency as CKD stage progressed; except for TIBC, which failed to show any significant correlation. As the CKD stage progressed, kidney sizes were smaller. As the CKD stage progressed, prevalence and severity of iron deficiency anaemia increased.

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