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A study on the prevalence of anemia, comorbidities, clinical signs and symptoms in the patients with chronic kidney disease of stage 3 to 5

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ABSTRACT

Background: CKD was classified into 5 stages based on the glomerular filtration rate and evidence of kidney damage, in accordance with the guidelines of the national kidney foundation. Anemia was defined as serum hemoglobin levels <12 g/dl in women and <13 g/dl in men. Anemia is a frequent complication of chronic kidney disease (CKD) that increases in prevalence and severity as kidney function declines. Common symptoms of anemia of CKD include low energy, fatigue, and decreased physical function. The prevalence of restless legs syndrome (RLS), in end-stage renal disease (ESRD) patients, is higher than that in the general population.

Methods: A cross-sectional study was done among the patients admitted into the nephrology ward with eGFR <60 ml/min/1.73m^2 in NRI general hospital from December 2019 To March 2020. The study population is 107. Fischer exact test and Pearson chi-square test were used to study the association between categorical variables.

Results: Among the study population, 50.5% belonged to the 51-60 years age group. 55.1% are males and 44.9% are females. It was found that the majority of the study population, 47.6% belonged to CKD stage 3. Among total females with CKD, 41.6% have severe anemia while 18.6% of males with CKD have severe anemia. In this study, the mean (± sd) Hb level prior to a transfusion was 8.2 (± 0.97) gm/dl. In this study the most frequently reported comorbidities among patients with anemia were hypertension (86.9%) and type 2 diabetes/ high blood glucose (19.6%). Among the study population, 41.1% had edema, 35.5% had dyspnea. Among the study population, 39.3% had restless leg syndrome. Among the study population, 24.3% underwent dialysis. Among the study population, 45.8% underwent blood transfusion.

Conclusions: The percentage of the patients with severe anemia, Tsat <20% is more among the patients with CKD stage 5. Clinical features like feeling tired, feeling weak, dyspnea, poor sleep quality, edema, Restless legs syndrome are seen more in patients with CKD stage 5.

Keywords: Chronic kidney disease (CKD), Anemia, End-stage renal disease (ESRD), restless legs syndrome (RLS)

INTRODUCTION

The kidneys function as filters of the blood, removing waste products and controlling the balance of fluid and electrolytes. Filtration occurs via bundles of capillaries called glomeruli (singular, glomerulus). A reduction in glomerular filtration rate (GFR) indicates chronic kidney disease (CKD).[1] Anemia is a frequent complication of chronic kidney disease (CKD) that increases in prevalence and severity as kidney function declines.[2] Common symptoms of anemia in CKD include low energy, fatigue, and decreased physical function, which can negatively affect patients' health-related quality of life (HRQoL).[2]

Anemia has been defined as Hb < 12 g/dL in women and < 13 g/dL in men.[2]

Anemia, a decrease in the hemoglobin (Hb) carried within red blood cells, is a common complication of CKD and is associated with debilitating symptoms, including fatigue, weakness, shortness of breath, dizziness, headaches, and depression.[3]

Anemia in CKD is associated with decreased quality of life and increased risk of cardiovascular disease and mortality.[4]

Anemia in CKD is predominantly caused by a relative deficiency of erythropoietin, a hormone produced in adults primarily by the kidneys[5], although shortened red blood cell half-life and functional iron deficiency also contribute to the anemia of ckd.[6]

Restless legs syndrome (RLS) is a neurological disorder characterized by an irresistible urge to move the legs, with onset at night and at rest and improvement in the symptoms with movement. RLS is considerably more common in adult patients with chronic kidney disease (CKD) than in the general population and is associated with sleep disturbances, depression, cardiovascular events, and increased mortality.[7]

The global burden of disease, injuries, and risk factors study (gbd) 2017 reported the global health burden of CKD with a prevalence of 9.1% (around 700 million cases) of the global population with CKD.[8]

India being home to 115.1 million patients with CKD, comes in the top two countries that contribute to the one-third of global disease burden.[9]

METHODS

A cross-sectional study was done among the patients admitted into the nephrology ward with eGFR below 60 ml/min/1.73m^2 in NRI general hospital. A pre-informed verbal consent was taken from the study group. The study population is 107. The data collected consisted of two parts, which included demographic data (gender, age) and evaluation of the CKD stage, associated symptoms, the severity of anemia, and treatment given to the patients.

eGFR is estimated GFR calculated by the abbreviated MDRD equation:

$186 \times (\text{creatinine}/88.4)^{-1.154} \times (\text{age})^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if black})$.

OBJECTIVES:

1. To study the severity of anemia among the patients with respect to CKD stages.

2. To study the prevalence of clinical features like feeling tired, feeling week, edema, dyspnea, quality of sleep, difficulty in concentration, skin bruising, restless legs syndrome among CKD patients

Inclusion criteria

1. Patients with eGFR below 60 ml/min/1.73m^2 and diagnosed with chronic kidney disease as per NKF/KDOQI guidelines.
2. Patients willing to be a part of the study.

Exclusion criteria

1. Patients with acute kidney injury.
2. Patients not willing to be a part of the study.

Statistical analysis:

Data were analyzed using a statistical package for the social sciences (spss) software, version 23.0. Fischer exact test and Pearson chi-square test were used to study the association between categorical variables.

RESULTS

Table 1 shows the socio-demographic profile of the study population. It was found that 55.1% are males and 44.9% are females. Among the study population, 23.4% belonged to 41-50 years age group, 50.5% belonged to the 51-60 years age group. 26.2% belonged to more than 60 years.

Table 1: Socio Demographic Profile of Study Population

Variable	Number	%
Gender		
Male	59	55.1
Female	48	44.9
Age groups		
41-50	25	23.4
51-60	54	50.5
More than 60 years	28	26.2

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Table 2 shows the distribution of subjects by stages of CKD. It was found that the majority of the study population, 47.6% belonged to CKD stage 3.

Table 2: Distribution of subjects by stages of CKD

Stage of CKD	number	%
CKD stage 3a	17	15.9
CKD stage 3b	34	31.7
CKD stage 4	39	36.4
CKD stage 5	17	15.9

Table 3 shows anemia among the study population. Among total females with CKD, 41.6% have severe anemia while 18.6% of males with CKD have severe anemia which is statistically significant.

Table 3: Distribution of subjects by anemia grading

Anemia grade	male	female	total	*P* value
Moderate	48	28	76	0.008
severe	11	20	31	Statistically significant
total	59	48	107	

Table 4 shows mean ± (sd) of age, creatinine, eGFR, Hb. The mean (± sd) age was 56.79(± 6.4). The mean (± sd) Hb level prior to a transfusion was 8.2 (± 0.97) g/dL. The mean (± sd) of creatinine was 2.56(±1.03) mg/dL. The mean (± sd) eGFR levels was 28.95(±11.9) ml/min/1.73m^2.

Table 4: Mean ± sd of age, creatinine, eGFR, Hb

	Age	Creatinine	eGFR	Hb
Mean	56.79	2.561	28.95	8.269
Standard deviation	6.403	1.0322	11.907	0.9723

Erythropoietin stimulating agent was given to 46.7% of the study population. Oral iron supplements were given to 81.32% of the study population. Iron IV is given 35.5% of the study population. Among the study population, 45.8% underwent blood transfusion and 23.4% underwent dialysis.

Table 5: Distribution of subjects by treatment methods

	NUMBER	%
Dialysis performed	25	23.4
ESA	50	46.7
Oral iron	87	81.32
Iron IV	38	35.5
transfusion	49	45.8

Table 6 shows the prevalence of signs and symptoms in the study population. In this study, patients spontaneously reported symptoms like feeling tired (89.7%) and feeling weak (88.8%).

41.1% had edema, 35.5% had dyspnea, 37.4% had poor sleep quality and 47.7% had difficulty in concentration. Among the study population, 39.3% had restless leg syndrome.

Among the people who underwent dialysis (n=26), 76.92% had restless leg syndrome which is statistically significant (p=0.0001).

Table 6: Prevalence of signs and symptoms in the study population

SYMPTOMS AND SIGNS	CASES	%
Feeling tired		
No	11	10.3
Yes	96	89.7
Feeling weak		
No	12	11.2
Yes	95	88.8
Edema		
No	63	58.9
Yes	44	41.1
Dyspnea		

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No	69	64.5
Yes	38	35.5
Poor sleep quality		
No	67	62.6
Yes	40	37.4
Difficulty in concentration		
No	56	52.3
Yes	51	47.7
Restless legs syndrome		
No	65	60.7
Yes	42	39.3

No	14	13.1%
Yes	93	86.9%
DM		
No	86	80.4%
Yes	21	19.6%
CHF		
No	89	83.2%
Yes	18	16.8%
LUNG DISEASES		
No	98	91.6%
Yes	9	8.4%

Table 7 shows the prevalence of comorbidities among the study population. Among the study population, 86.9% had hypertension, 19.6% had diabetes mellitus type 2.

Among the study population, 23.4% underwent dialysis. Table 8 shows that among the patients with CKD stage 3, 3.9% underwent dialysis. Among the patients with CKD stage 4, 20.5% underwent dialysis while among the patients with CKD stage 5, 94.1% underwent dialysis which is statistically significant (p=0.001).

Table 7: Prevalence of comorbidities among study population

Comorbidity	No.	%
MI		
No	93	86.9%
Yes	14	13.1%
TIA/Stroke		
No	91	85%
Yes	16	15%
HTN		

Among the patients with CKD stage 4, 35.89% had severe anemia while among the patients with CKD stage 5, 94.1% had severe anemia which is statistically significant (p=0.001).

The number of patients with Tsat <20% increased with deterioration of kidney function. Among the patients with CKD stage 5, 100% had Tsat<20% which is statistically significant (p=0.001). Among the patients with CKD stage 3, 7.84% had edema. Among the patients with CKD stage 4, 61.53% had edema while among the patients with CKD stage 5, 94.1% had edema which is statistically significant (p=0.001).

Among the patients with CKD stage 5, 88.23% had poor sleep quality and 94.1% had difficulty in concentration which is statistically significant (p=0.001). Among the patients with CKD stage 3, 11.76% had restless leg syndrome. Among the patients with CKD stage 4, 53.84% had restless leg syndrome while among the patients with CKD stage 5, 88.23% had restless leg syndrome which is statistically significant (p=0.001). Among the study population, 39.3% had restless leg syndrome and 23.4% underwent dialysis. Among the people who underwent dialysis (n=26), 76.92% had restless leg syndrome which is statistically significant (p=0.0001)

Table 8: Prevalence of dialysis, anemia, Tsat, comorbidities, signs and symptoms with respect to CKD Stage

	CKD STAGES			
	CKD STAGE 3	CKD STAGE 4	CKD STAGE 5	*P* Value

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	N=51(47.6%)	N=39(36.5%)	N=17(15.9%)	
Dialysis	2(3.92%)	8(20.5%)	16(94.1%)	0.001
Moderate Anemia	50(98%)	25(64.1%)	1(5.88%)	0.001
Severe Anemia	1(1.96%)	14(35.8%)	16(94.1%)	0.001
Tsat<20	13(24.5%)	37(94.8%)	17(100%)	0.001
Signs and symptoms				
Feeling Tired No Yes	9(17.64%) 42(82.35%)	1(2.56%) 38(97.4%)	1(5.88%) 16(94.1%)	0.053
Feeling Weak No Yes	9(17.64%) 42(82.35%)	2(5.1%) 37(94.9%)	1(5.88%) 16(94.1%)	0.151
Edema No Yes	47(92.1%) 4(7.9%)	15(38.5%) 24(61.5%)	1(5.88%) 16(94.1%)	0.001
Dyspnea No Yes	49(96.1%) 2(3.9%)	18(46.2%) 21(53.8%)	2(11.7%) 15(88.2%)	0.001
Poor sleep quality No Yes	49(96.1%) 2(3.9%)	16(41%) 23(58.9%)	2(11.7%) 15(88.2%)	0.0001
Difficulty in concentration No Yes	40(78.4%) 11(21.6%)	15(38.5%) 24(61.5%)	1(5.88%) 16(94.1%)	0.001
Skin bruising No Yes	46(90.1%) 5(9.8%)	37(94.9%) 2(5.1%)	1(5.88%) 16(94.1%)	0.001
Restless leg syndrome No Yes	45(88.2%) 6(11.8%)	18(46.2%) 21(53.8%)	2(11.7%) 15(88.2%)	0.0001
COMORBIDITIES				
MI	8(15.7%)	5(12.8%)	1(5.88%)	0.637
Stroke	3(5.9%)	7(17.9%)	6(35.3%)	0.01
Hypertension	41(80.4%)	35(89.7%)	10(58.8%)	0.03
Diabetes	5(9.8%)	1(2.56%)	12(70.6%)	0.001
CHF	8(15.7%)	10(25.6%)	11(64.7%)	0.01
Lung Diseases	2(3.9%)	1(2.56%)	6(35.3%)	0.001

DISCUSSION

The present study consists of 107 patients diagnosed with CKD using the MDRD eGFR equation. These patients fulfilled the criteria set by the National Kidney Foundations, Kidney Disease Outcome Quality Initiative for diagnosing CKD.

They were studied and evaluated for clinical symptoms and signs and associated comorbidities by clinical and laboratory investigations. The age of cases was in the range of 41 years to 75 years.

The mean (± sd) age was 56.79(± 6.4). A maximum number of subjects in cases were in the age group of 51-60 years.

In this study, Erythropoietin stimulating agent was given to 46.7% of the study population. 52.3% had stage 4 and stage 5 CKD and erythropoietin

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stimulating agent was given to 46.7%. A similar study was conducted by Susan D. Mathias et al. where Most participants had stage 4/5 CKD (81%) and were being treated with erythropoietin stimulating agent (69%).[10]

In this study, patients spontaneously reported symptoms like feeling tired (89.7%), shortness of breath (35.5%), and feeling weak (88.8%). A similar study was conducted by Susan D. Mathias et al. in which patients spontaneously reported symptoms that included feeling tired (79%), shortness of breath (39%), and weak/lacking strength (36%).[10]

In this study the most frequently reported comorbidities among patients with anemia were hypertension (86.9%) and type 2 diabetes /high blood glucose (19.6%). In a similar study conducted by Chuan-ming hao et al. the most frequently reported comorbidities among patients with Anemia were hypertension (36.5%) and type 2 diabetes/high blood glucose (24.3%).[12]

In this study, the mean (± sd) Hb level prior to a transfusion was 8.2 (± 0.97) g/dl. Among the study population, 45.8% underwent blood transfusion. Among the patients with CKD stage 4, 35.89% underwent transfusion and among CKD stage 5 patients, 41.17% underwent blood transfusion. In a similar study conducted by Kathleen m fox et al. the mean (± sd) Hb level prior to a transfusion was 8.8 (± 1.5) g/dl. Among the patients with CKD stage 4, 21% underwent transfusion and among CKD stage 5 patients, 15% underwent blood transfusion.[13]

In this study, 37.4% had poor sleep quality. In a similar study conducted by Rajeev Kumar Bhatia et al. 50% of the study population had poor sleep quality.[14]

In this study, the total number of patients who met all criteria for the diagnosis of restless leg syndrome is 39.3% and among the people who underwent hemodialysis (n=26), 76.92% had restless leg syndrome. In a similar study conducted by Hamdan h. Al-jahdali et al. the total percentage of patients who met all criteria for the diagnosis of RLS is 50.22% and among the people who underwent hemodialysis, 46.2% had restless leg syndrome.[15]

CONCLUSION:

The percentage of the patients with severe anemia, Tsat <20% is more among patients with CKD stage 5. Symptoms like feeling tired, feeling weak, dyspnea, poor sleep quality are seen more among patients with CKD stage 5. Clinical signs like edema, Restless legs syndrome are seen more in patients with CKD stage 5. While aiming for optimal management of patients with CKD, it is clearly important to monitor Hb levels and be aware of the link between anemia and the patient's overall wellbeing. Thus, there is a need to improve the timing of anemia intervention and the quality of care for these patients. Prevalence of patients with restless leg syndrome is more among CKD stage 5 patients and patients undergoing hemodialysis were confirmed. The sleep quality was significantly impaired among the CKD stage 5 patients with RLS. Comorbidities seen in CKD patients are hypertension, diabetes mellitus type 2, congestive heart failure, etc. Clinical features and comorbidities associated with CKD are important to be treated at earlier stages of CKD to delay progression and reduce associated morbidity and to prevent early mortality.

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