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PREVALENCE OF CARDIORENAL ANEMIA SYNDROME IN CHRONIC KIDNEY DISEASE PATIENTS PRESENTING TO A TERTIARY CARE HOSPITAL IN MAHARASHTRA

General Medicine

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ABSTRACT

BACKGROUND: Cardio-renal-anemia syndrome is a complex self-destructive triad of Chronic Kidney Disease, Cardiovascular Disease and anemia which improves on appropriate intervention and prompt treatment. **OBJECTIVES:** To study Prevalence of cardio renal anemia syndrome in chronic kidney disease (CKD) patients. **MATERIALS & METHODS:** The present cross sectional study was done on 150 study subjects admitted in Government medical college & hospital Aurangabad during period November 2018 to January 2021. **RESULT:** Out of 150 CKD study subjects, prevalence of anaemia was 92.66 % i.e. 139 patients were anaemic.The prevalence of cardiorenal anemia syndrome in patients of CKD in the study population was 57 out of 150 (39%). **CONCLUSION:** There was strong statistically significant association found between Chronic Kidney Disease and anemia and also Cardiovascular Disease.

KEYWORDS

Anemia, Chronic kidney disease, prevalence.

INTRODUCTION:

Acute or chronic dysfunction in one organ may induce acute or chronic dysfunction in the other. The heart and the kidneys both are involved in maintaining hemodynamic stability and perfusion of organ.[1] Chronic kidney disease (CKD) is not a static condition. It is a progressive condition which may ultimately end up with kidney failure. Previous research and literature indicates that identification of chronic kidney disease (CKD) in its earlier stages can prevent its progression.[2]

Anemia is a common co-morbid finding in kidney failure patients and is especially prevalent in those requiring haemodialysis. [3]Anemia in chronic kidney disease (CKD) if left untreated it can negatively affect cardiac, cognitive and immune functions along with renal disease progression and survival rate. It can also aggravate existing comorbidities Timely treatment of anemia in chronic kidney disease (CKD) can improve quality of life and disease outcome[4]

Chronic kidney disease (CKD) is initially without symptoms only an increase in serum creatinine or protein in the urine detected. As the kidney function starts decreasing Blood pressure is increased due to fluid overload and production of vasoactive hormones created by the kidney via the renin–angiotensin system, increasing the risk of developing hypertension and heartfailure. Urea starts accumulating leading to azotemia and ultimately uremia. Potassium starts accumulating in the blood.

Hyperkalemia usually does not develop until the glomerular filtration rate falls to less than 20 to 25 ml/min/1.73 m^2. Fluid overload cause mild edema to life-threatening pulmonary edema. Hyperphosphatemia results from poor phosphate elimination in the kidney which contributes to increased cardiovascular risk by causing vascular calcification. Circulating concentrations of fibroblast growth factor-23 (FGF-23) increase progressively as the kidney capacity for phosphate excretion declines which may contribute to left ventricular hypertrophy. Hypocalcemia resulting from 1,25 dihydroxy vitamin D3 deficiency and resistance to the action of parathyroid hormone. It progresses to secondary hyperparathyroidism, kidney osteodystrophy and vascular calcification which impairs cardiac function[5-6]

National Heart, Lung and Blood Institute defined cardiorenal syndrome as a condition where treatment of congestive heart failure is limited by decline in kidney function. Risk factors associated with Cardiorenal syndrome includes Older age, comorbid conditions like diabetes mellitus, uncontrolled hypertension, anemia, Drugs like anti-inflammatory agents, diuretics etc.[7]

With this perspective the observational cross section study of "Prevalence of cardio-renal anemia syndrome in chronic kidney disease patients presenting to a tertiary care hospital in Maharashtra" was undertaken with objective to assess prevalence of cardiac disease and anemia in chronic kidney disease (CKD) patients.

Materials & Methods:

The present Cross Sectional study was done in department of general medicine of Government Medical College, Aurangabad, a tertiary health care teaching hospital in Maharashtra. The study was conducted during November 2018 to January 2021. Approval of institutional ethics committee was taken prior to commencement of this study.

Chronic Kidney disease patients attending outpatient Department (OPD) / Inpatients Department (IPD) of medicine Department at tertiary care hospital fulfilling inclusion and exclusion criteria were selected for the present study. Patients of age more than 12 years having CKD as per KDIGO guidelines 2012, irrespective of stage and cause were included in the study.

Patients with acute kidney diseases, cases of obstructive uropathy who have not yet progressed to CKD as per KDIGO guidelines 2012. Patients having anemia due to causes not known to be attributable to CKD like gastrointestinal blood loss, hemoglobinopathies etc. Patients having known causes of cardiac disease (rheumatic/ valvular heart disease, ischemic heart disease, cardiac arrhythmiaetc) were excluded from the study.

Considering 0.9% prevalence of cardiorenal anemia in India with 5 % allowable error with 95 % confidence interval sample size came to be 150.

Patients admitted in Medicine wards and satisfying inclusion criteria were selected and complete procedure was explained to the volunteer subjects and proper informed written consents were obtained before the procedure. A detailed history taken regarding complaints, past history, personal history, family history, dietary history and treatment history. Thorough General Examination was done and systemic examination of the cardiovascular, respiratory, abdomen and central nervous system was done. The patients were investigated to assess kidney function & Hematological investigation like hemoglobin, blood sugar, sr. electrolyte and viral markers were done.

Cardiovascular symptom like dyspnea, chest pain, pedal edema, pallor were noted. Blood pressure was measured thrice and the average was taken. Cardiovascular examination was done. Complete hemogram, blood urea, serum creatinine were measured. Patients were also subjected to abdominal ultra-sonogram. Creatinine clearance had been calculated in all patients using the COCKCROFT-GAUL T equation.

Evidence of left ventricular hypertrophy, low voltage complexes, ischemic changes were looked for in electrocardiogram. Echocardiography was done by DM cardiologist on Philips HD11 machine and were looked for Chamber size, Systolic & diastolic function, Left ventricular wall motion abnormalities, Pericardial effusion, valvular abnormalities etc.

Data was entered in Microsoft excel and analysis was done using SPSS software trial version 20. Chi square was applied for qualitative data & t test were applied to quantitative data. Value less than 0.05 were considered as statistically significant.

RESULTS:

In this present study we studied 150 study subjects, the mean age of study subjects were 47.6 ± 16 years. Majority of study subjects were male (63%) while 37% were female. Maximum patients were from the age group > 60 years (28 %) followed by 20 % cases in ≤ 30 years of age. 16 % were in 41 to 50 years of age group while 17 % cases were in 51 to 60 years age groups and 16 % cases were in 31 to 40 years age group. Most of the study subjects (79%) were from rural area as compared to urban (21%).

Most common symptom that brought study subjects to hospital was Breathlessness 73 (49%) followed by Oligourea, which was present in 57 (38 %), Oedema in 66 (44 %), Altered Sensorium in 16 (11 %), Nausea/Vomitting in 10 (7 %)

While considering the risk factors among study subjects, Hypertension was present in the highest number of patients79 (53 %) %) followed by Diabetes Mellitus in 33 (22 %). Addiction (smoking, alcohol) was present in 33 (22%). (Table No.1)

Table 1: Distribution of cases according to Risk Factor and associated Condition

Sr. No.	Risk Factor and associated Condition		Present (%)	Absent (%)
1	Hypertension		79 (53 %)	71 (47 %)
2	Diabetes Mellitus		33 (22 %)	117 (78 %)
3	Obstructive Uropathy		9 (6 %)	131 (94 %)
4	Addiction	Smoking	0 (0 %)	117 (78 %)
		Alcohol	8 (5 %)	
		Tobacco	6 (4 %)	
		Smokong + Alcohol	13 (9 %)	
		Tobacco + Alcohol	6 (4 %)	
5	SLE		3 (2 %)	147 (98 %)
6	Multiple Myeloma		1 (0.6 %)	149 (99.4 %)
7	ADPKD		2 (1.3 %)	148 (98.7 %)
8	Gout		1 (0.6 %)	149 (99.4 %)
9	HbsAg+		1 (0.6 %)	149 (99.4 %)
10	HIV		4 (3 %)	146 (97 %)
11	HCV		1 (0.6 %)	149 (99.4 %)
12	IgA Nephropathy		1 (0.6 %)	149 (99.4 %)
13	PIH		2 (1.3 %)	148 (98.7 %)

On General Examination, oedema was present in the highest number of patients 64 (42.99%), Pallor was present in 56 (37 %), flaps was present in 20 (13 %), Acidotic Breathing was present in 6 (4 %), Raised BP was present in 32 (21 %) and Crepitation was present in 54 (36%). (Table No.2)

Table 2: Distribution Of Cases According To General Examination

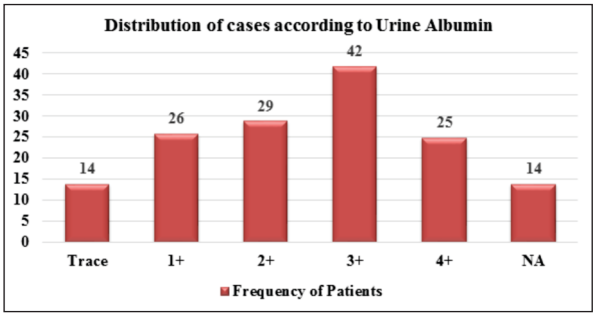
Sr. No.	General Examination	Present (%)	Absent (%)
1	Oedema	64 (42.99 %)	86 (57.01 %)
2	Pallor	56 (37 %)	94 (63 %)
3	Crepitation	54 (36 %)	96 (64 %)
4	Raised BP	32 (21 %)	118 (79 %)
5	Flaps	20 (13 %)	130 (87 %)
6	Acidotic Breathing	6 (4 %)	144 (96 %)

Hemoglobin Concentration (gm/dl) < 7 was present in 33, 7 to 9 was present in the maximum number of patients 69, 9.1 to 12 was present in 37 and >12 was present in 11 case. Mean Hb of the study population was 8.683 ± 2.221 gm/dl. Urea Concentration (mg/dl) ≤ 20 was present in 0, 21 to 100 was present in 41 and >100 was present in 109 cases. Mean urea was 139.44 ± 65.198 mg/dl. Serum Creatinine (mg/dl) ≤ 1.2 was present in 1, 1.3 to 10 was present in 106 and >10 was present in 43 cases. (Table No.3)

Table 3: Distribution Of Cases According To Blood Investigations

Blood Test	Range	Frequency(N)	Percentage(%)
Hemoglobin Concentration (gm/dl)	<7	33	22 %
	7 to 9	69	46 %
	9.1 to 12	37	24.67 %
	>12	11	7.33 %
Urea Concentration (mg/dl)	< 40	0	0 %
	40 to 100	41	27 %
	>100	109	73 %
Serum Creatinine (mg/dl)	≤ 1.2	0	0.66 %
	1.3 to 10	106	70.6 %
	>10	44	28.66 %
Serum Potassium (mmol/dl)	≤ 3.5	20	14 %
	3.6 to 5.2	98	65 %
	>5.2	32	21 %
Blood Sugar Level (mg/dL)	≤ 200	131	87 % %
	>200	19	13 %
Viral Marker	Positive	6	4 %
	Negative	144	96 %

Urine Albumin reading of Trace was present in 14, 1+ was present in 26, 2+ was present in 29, 3+ was present in 42, 4+ was present in 25 and was negative in 14 cases (Graph 1)



Graph No. 1: Distribution Of Cases According To Urine Albumin

While considering Stages of CKD, most of the patients were in stage V (125), Stage I & II was found in none of the patient, Stage IIIa was found in 4 patients, Stage IIIb was found in 1, and Stage IV was found in 20. Mean EGFR= 11.96 ± 10.78 ml/min/1.73mm^2 (Table No.4)

Table 4: Distribution Of Cases According To Stages Of Ckd

Sr. No.	Stage of CKD	EGFR (ml/min/1.73 m^2)	Number of Cases (N)	(%)
1	V	<15	125	83.3
2	IV	15 to 29	20	13.4 %
3	IIIa	45 tp 59	4	3 %
4	IIIb	30 to 44	1	0.6 %
5	I	≥90	0	0 %

6	**II**	**60 to 89**	0	0 %
Total			**150**	**100 %**

ECG Findings were Within Normal Limits in 100 (66.66 %) patients and abnormal findings were found in 50 (33.34 %) patients.

After doing 2 D Echo it was found that ejection fraction was low in 34 patients, in Mid-Range in 23patients and Normal in maximum number of patients (93). Mean ejection fraction was 50.6 ± 14.6%. Dilated cardiomyopathy was present in 16 patients. LVH was present in 68 study subjects. Pericardial Effution was present in 25 patients.

Ultrasonography findings suggested that out of a total of 150 patients, Large kidney was present in 6 (4 %), Small kidney was present in the maximum number of patients107 (71 %) and was absent in 43 (29 %). Poor CMD was present in 99 (66 %) and was absent in 51 (34 %). Obstructive Uropathy was present in 9 (6 %) and was absent in 141 (94 %). ADPKD was present in 2 (1.33 %) and was absent in 148 (98.67 %). HN was present in 4 (2.66 %) and was absent in 146 (97.34 %). HU was present in 4 (2.66 %) and was absent in 146 (97.3%)

Table 5: Distribution Of Cases According To 2 D Echo Finding

2 D Echo Findings	Range (As per 2016 European society of Cardiology guidelines)	Frequency(N)	Percentage (%)
EF	**Low (<40 %)**	34	22.66 %
	Mid-Range (40 to 50 %)	23	15.33 %
	Normal (>50 %)	93	62.01 %
DCM	**Present**	16	11 %
	Absent	134	89 %
LVH	**Present**	68	45 %
	Absent	82	55 %
Pericardial Effution	**Mild**	17	11 %
	Moderate	2	1 %
	Severe	6	4 %
	Absent	125	84 %

While considering the association between stage of CKD and anemia. In Stage IIIa anemic were 4 and non-anemic was none. In Stage IIIb anemic was 1 and non-anemic was 0. In Stage IV anemic was 20 and non-anemic was 0 and in Stage V anemic was 139 and non-anemic was 11. The association was statistically significant (P= 0.027) (Table No.6)

Table 6: Distribution of cases according to Stages of CKD and Anemia

Sr. n	Stage of CKD	Anemic (%)	Non Anemic (%)	Total (%)
1	**V**	114 (76 %)	11 (7.33 %)	125 (83.33 %)
2	**IV**	20 (13.33%)	0 (0 %)	20 (13.4 %)
3	**IIIa**	4 (3 %)	0 (0 %)	4 (3 %)
4	**IIIb**	1 (0.6 %)	0 (0 %)	1 (0.6 %)
Total		**139 (92.66 %)**	**11 (7.33 %)**	**150 (100 %)**
T = 4.8768 ; p Value: 0.02722				

The association between Stages of CKD and Heart Failure was found to be statistically significant (P=0.0015). In Stage IIIa Low EF was found in 1, Mid-Range EF was found in 2 and Normal EF was found in 1. In Stage IIIb Low EF was found in 0, Mid-Range EF was found in 0 and Normal EF was found in 1. In Stage IV Low EF was found in 3, Mid-Range EF was found in 10 and this was the most common finding for stage IV and Normal EF was found in 7 and in Stage V Low EF was found in 30, which was the most common finding, Mid-Range EF was found in 11 and Normal EF was found in 84 patients (Table No.7)

Table 7: Distribution Of Cases According To Stages Of Ckd And Heart Failure

Sr. No.	Stage of CKD	Low EF (%)	Mid-Range EF N (%)	Normal EF N (%)	Total N (%)
1	**I**	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)
2	**II**	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)
3	**IIIa**	1 (0.6 %)	2 (1.33 %)	1 (0.6 %)	4 (3 %)
4	**IIIb**	0 (0 %)	0 (0 %)	1 (0.6 %)	1 (0.6 %)
5	**IV**	3 (2 %)	10 (6.66 %)	7 (4.66 %)	20 (13.4 %)
6	**V**	30 (20 %)	11 (7.33 %)	84 (56 %)	125 (83.33 %)
Total		**34 (22.66 %)**	**23 (15.33 %)**	**93 (62.01 %)**	**150 (100 %)**
T = 10.01 ; p Value: 0.0015					

After considering the association of anemia and 2 D ECHO Findings it was found that amongst the anemic patients, 34 patients had reduced EF, 23 had mid range ejection fraction, 83 had normal ejection fraction. Amongst non anemic patients all 11 patient were having normal EF. The association was found to be statistically significant. (P=0.0274) (Table No.8)

Table 8: Distribution of cases according to Anemia and 2 D ECHO Findings

Sr. No.	Anemia	2 D ECHO Findings			Total N (%)
		Low EF (EF <40%) N (%)	Mid-Range EF (EF 40-50%) N (%)	Normal EF (EF >50%) N (%)	
1	**Patients with Anemia N (%)**	34 (22.66%)	23 (15.33 %)	83 (55.33 %)	**139(92.66 %)**
2	**Patients without Anemia N (%)**	0 (0 %)	0 (0 %)	11 (7.33 %)	**11 (7.33%)**
Total		**34 (22.66%)**	**23 (15.33 %)**	**93 (62.01 %)**	**150 (100%)**
X^2=7.193 ; P =0.0274					

Distribution of cases of patients of chronic kidney disease according to cardiorenal anemia syndrome suggested that, there were no patients in stage I and II. In Stage IIIa anemic was 4, abnormal EF was found in 3. In Stage IIIb anemic was 1, abnormal EF was found in 0. In Stage IV anemic was 20, abnormal EF was found in 13 and in Stage V anemic was 114, abnormal EF was found in 41. Anemia with Heart Failure was found in 57 cases. Hence, maximum cases with anemia and reduced ejection fraction belonged to stage V. (Table No.9)

Table 9: Distribution of cases according to cardiorenal anemia syndrom

Sr. No.	Stage of CKD	Anemic (%)	Heart Failure (%)	Anemia with Heart Failure(%)
1	**I**	0 (0 %)	0 (0 %)	0 (0 %)
2	**II**	0 (0 %)	0 (0 %)	0 (0 %)
3	**IIIa**	4 (3 %)	3 (2 %)	3 (2 %)
4	**IIIb**	1 (0.6 %)	0 (0 %)	0 (0 %)
5	**IV**	20 (13.33%)	13 (8.66 %)	13 (8.66 %)
6	**V**	114 (76 %)	41 (27.33 %)	41 (27.33 %)
Total		**139 (92.66 %)**	**57 (38 %)**	**57 (38 %)**

DISCUSSION:

Progressive damage to kidneys ultimately results in involvement of every organ system of the body. The most common hematological manifestation in patients of CKD is Anemia and CKD is a risk factor for CVD. Present study evaluated the clinical and hematological profile of patients of Chronic Kidney Disease presenting at a tertiary care health centre.

In the present study maximum patients were from the age group > 60 years & maximum no. of cases 98 (63 %) were males. Maximum no. of cases 118 (79 %) were from rural area. Similar results were found in study by **Maria Prothasis et al (2020)**[8] where the majority of patients belonged to the age above 60 years (53.13 %) & males were more in number comprising about 60 % of patients. **Neha Sundhir et al (2018)**[9] found majority (61%) of the patients were belonged to rural background.

In the present Study hemoglobin Concentration (gm/dl) < 7 was present in 33 patients. Mean Hb of the study population was 8.683 ± 2.221 gm/dl. In the similar way study by **Neha Sundhir et al (2018)**[9] found mean hemoglobin level was 8.39 ± 1.71 g/dL in patients of CKD. The most common profile seen on peripheral blood smear was normocytic normochromic anemia (76%) followed by microcytic hypochromic picture seen in 22 % patients.

In the present Study ECG Findings Within Normal Limits were present in 100 (66.66 %) patients and abnormal findings were found in 50 (33.34 %) patients**.** On 2 D Echo ejection fraction low was present in 34, in Mid-Range was present in 23 and Normal was present in 93. Dilated cardiomyopathy was present in 16 and was absent in 134. LVH was present in 68 and was absent in 82. Pericardial Effusion was

present in 25 and was absent in 125.

In the similar study by **Maria Prothasis et al (2020)**[8] found lowest EF in 15 % patients and highest in 65 %.

The association between anemia & CKD was statistically significant (P= 0.027) in this study, similarly study by **Neha Sundhir et al (2018)**[9] they shows the relation between stage of Chronic Kidney Disease and the severity of Anemia. They showed that as the renal dysfunction becomes more severe, there is significant increase in the severity of Anemia ($p<0.05$). More than 95% patients with severe Anemia (Hb < 7 g/dL) belonged to CKD Stage 4-5.

In present study the association between Stages of CKD and Heart Failure was found to be statistically significant (P=0.0015). **Atul V. Rajkondawar et al (2019)**[10] in their study found Hemoglobin levels have been inversely associated with cardiovascular risk in patients with CKD. **Islam MN et al (2015)**[11] in their study found the mean hemoglobin to be as low as 4.96 gm%. This may be indicative of the relatively higher risk of cardiovascular events in CKD patients.

CKD, CVD and especially CHF are common medical problems with high morbidity and mortality. Likewise, anemia occurs frequently as a recognized complication of CKD and cause progression of CKD. Anemia causes and occurs in a large number of patients with CHF. Its prevalence and severity increases as CHF becomes more severe and it is a strong independent risk factor for mortality in CHF patients. The association between the triad of CKD, CVD and anemia has been termed as cardio-renal anemia syndrome [12-13].

Correction of anemia improves cardiac function, reduces ventricular dilatation and hypertrophy, reduces the need and frequency of hospitalization, and prevents further deterioration of CHF and CKD.[14]

CONCLUSION:

The most common risk factor for CKD was hypertension 79 (53%) followed by Diabetes Mellitus 33 (22%). Maximum no. of cases 125 were of CKD stage V with a mean eGFR of 11.69 $\pm$ 10.78 ml/min/1.72mm^2. Maximum no. of cases 139 (92.66%) had anemia with a mean hemoglobin 8.683 $\pm$ 2.221 gm/dl. There was strong statistically significant association found between Chronic Kidney Disease and Cardiovascular Disease. Out of 150 CKD study subjects, prevalence of anaemia was 92.66 % i.e. 139 patients were anaemic.The prevalence of cardiorenal anemia syndrome in patients of CKD in the study population was 57 out of 150 (39%).

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