ISSN 2664-3987 (Print) & ISSN 2664-6722 (Online)
South Asian Research Journal of Medical Sciences
Abbreviated Key Title: South Asian Res J Med Sci

| Volume-6 | Issue-1 | Jan-Feb -2024 | **DOI: 10.36346/sarjms.2024.v06i01.002**

Original Research Article

Prevalence of Anemia in Chronic Kidney Disease

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Article History
Received: 19.12.2023
Accepted: 24.01.2024
Published: 29.01.2024

Abstract: ***Objective:*** Chronic kidney disease is usually associated with anemia and the level of anemia correlates with the severity of the renal failure. The kidneys help in maintaining electrolyte balance and blood pressure. They produce the active form of vitamin D and a substance called erythropoietin, which stimulates production of red blood cells. Chronic kidney disease has adverse consequences on almost all body systems resulting in high rate of complications i.e. anemia, cardiac, vascular pulmonary etc. This study was carried out to evaluate the prevalence of anemia in chronic renal failure patients. ***Material and Methods*****:** It is across sectional study and the data was collected from department of pathology and dialysis unit of Dr. Akbar Niazi Teaching Hospital, Islamabad from January 2021 to December 2021. All the patients who presented with sign and symptoms of chronic kidney disease were included in the study. Data was recorded in specially designed proforma and statistical analysis was performed using SPSS version 21. ***Results*****:** Total 89 chronic kidney disease patients were included in the study among them 58 (65%) were males 31 (35%) were females. The average age of patients was 55 ± 16.409. Based on eGFR values the CDK patients that belonged to stage 1-5 were 5% (n=4), 6% (n=5), 9% (n=8), 18% (n=16) and 63% (n=56) respectively. The prevalence of anemia in chronic kidney disease patients was 95.5% (n=85) among which 62% (n=56) were males and 32% (n=29) were females. Normocytic normochromic anemia was the most common type with prevalence of 72% (n=64). Mild anemia was recorded in 41(46%) of the CKD patients while severe anemia was recorded in 3(3%) of patients. Besides CDK, diabetes mellitus was present as a comorbid feature in 4 (5%) of the patients, 16 (18%) had positive history of hypertension and 1 (1%) was positive for cardiovascular disease. ***Conclusion*****:** Mild degree of anemia was seen in CKD patients. Most common type of anemia was normocytic normochromic. Most of the patients presented at stage 5. Comorbidities associated in CKD patients were hypertension, diabetes mellitus and cardiovascular disease.

Keywords: Chronic Kidney Diseases, Creatinine, uric Acid, Urinary Protein, Microcytic Anemia, Hypertension.

1. INTRODUCTION

The kidneys functions as filters of blood, removing waste products, and controlling the balance of fluids and electrolytes (sodium, potassium, chloride, calcium, phosphorus, magnesium and sulphate). Kidney is also an important component of endocrine system and produces erythropoietin which is involved in the production of red blood cells and 1,25-dihydroxycholecalciferol (calcitriol) and plays an important role in bone formation.

The filtration process in kidney occurs through bundles of capillaries called glomeruli [1]. Chronic kidney disease is a global healthcare concern because of its increasing prevalence and is defined as kidney damage or glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m^2 for three or more months [2]. End stage renal disease (ESRD) is the final stage

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of chronic kidney disease characterized by progressive, irreversible deterioration in renal function and body fails to maintain fluid and electrolyte balance resulting in uremia and indicate decrease in glomerular filtration rate [3, 4].

1.1. Classification of Chronic Kidney Disease

According to Kidney Disease Outcomes Quality Initiative (KDOQI) classification, CKD is divided into five stages based on the estimated glomerular filtration rate. A glomerular filtration rate of 90 or above represents normal kidney function, GFR of 60-89 represents mildly reduced kidney function, a GFR of 30-59 represents moderately reduced kidney function, a GFR of 15-29 represents severely reduced kidney function while GFR of <15 represents end stage kidney failure [5].

1.2. Prevalence

Chronic kidney disease has become a major health problem. The prevalence around world is estimated in range of 8-16% [6]. Its prevalence varies from one region of the world to another. A study carried out in the US between 1999-2004 showed prevalence of 13.07% [7]. In France the incidence of end stage CKD is estimated between 100 and 150 per million inhabitants per year [8]. In Africa the prevalence of CKD was reported to be 12% in general population of the demographic Republic of Congo [9]. In cote d Ivoiry, a study carried out from 2005-2009 showed a prevalence of 7.5% [10]. A cross sectional study was conducted in 12 representative communities in Karachi, Pakistan and the outcome of this study showed that as overall prevalence of chronic kidney disease in Pakistan is 12.5% [11, 12]. Some authors have claimed that the incidence of CKD has increased by 3%-7% in the past ten years [13]. This increase is related to rapid population growth, aging of the population with several known risk factor of CKD, and environmental factors [14].

1.3. Risk Factors

The risk factors for developing CKD also varied from one region to another [15]. The risk factors for CKD are due to diabetes, hypertension, heart failure severity, family history of kidney disease, obesity or metabolic syndrome and age. Increased blood pressure is one of the main factors causing kidney failure [16]. It is plausible that hypertension induces kidney failure through impacting the blood vessels within the kidney which in turn has effects on the secretion of waste products. It has been observed that the waste may be secreted into extra cellular fluid leading to more increased blood pressure ending with end stage renal disease [17].

1.4. Clinical Presentation

Chronic kidney disease is typically identified through routine screening with serum chemistry profile and urine studies or as an incidental finding. The clinical presentation of the patients include hypertension, fatigue, poor appetite, nausea, vomiting, metallic taste, unintentional weight loss, pruritis, changes in mental status, dyspnea,, or peripheral edema [18]. Less commonly patients may also present with symptoms such as gross hematuria, nocturia, flank pain, or decreased urine output.

Anemia and electrolyte disturbances are adverse outcomes of chronic kidney disease. Progressive deterioration in kidney function leads to numerous hematological and biochemical dysfunction. Although there is large degree of inter-patient variability, the hematocrit generally begin to fall when the plasma creatinine concentration is above 2mg/dL and gets progressively lower as a result, GFR rate declines further. Chronic kidney disease can lead to metabolic acidosis, hyperkalemia, hyponatremia, hypercalcemia, and hyperphosphatemia resulting in serious adverse outcomes such as bone mineral disorders, vascular calcification, and even mortality. Hypercalcemia is increasingly common with the progression of CKD and is one of the life-threatening electrolyte disorders in CKD patients, with a nearly 10 fold risk of death in stage 4 and 5. CDK patients with hyperkalemia may develop certain clinical manifestations such as muscle weakness, cardiac arrhythmias, and cardiac arrest. Meanwhile hyponatremia is the most common electrolyte abnormality in CKD patients which is likely due to fluid overload and positively correlates with mortality and morbidity. Similarly hypercalcemia and hyperphosphatemia are common bone mineral disorders in CKD patients and have been associated with vascular calcification, CKD progression, cardiovascular events and mortality [19].

1.5. Medication in CKD

The medication prescribed to CKD patients address the symptoms and some of them are prescribed to counteract the dangerous accumulation of different chemical elements. Diuretics help patients (who can still pass urine) to excrete the excess fluid that manifests as edema and swelling [20]. Phosphate binders and Vitamin D is prescribed to patients that show increase in phosphorus and parathyroid hormone levels in blood to prevent osteoporosis [21]. In patients with hypertension, ACE inhibitors, angiotensin II receptor blockers (ARBs), diuretics, beta-blockers, calcium channel blockers, vasodilators and direct renin inhibitors are prescribed [22]. For high cholesterol or fats level, lipid medication such as fibrates, statins and cholesterol absorption inhibitors may be prescribed [23].

2. MATERIAL AND METHODS

2.1. Study Setting/ Study Design

This is a cross-sectional study conducted in the department of pathology and nephrology of Dr. Akbar Niazi Teaching Hospital (ANTH) in Islamabad from January 2021 to December 2021.

2.2. Subjects

2.2.1. Inclusion Criteria

Chronic renal disease and hemodialysis patients of both genders (males and females) with age equal or more than 18 years old suffering from chronic renal disease and hemodialysis patients were included in the study. An informed written consent was obtained from each participant for voluntary involvement in the study (Annexure I).

2.2.2. Exclusion Criteria

Patients less than 18 years old, patients suffering from any disease other than chronic renal disease that could affect their hematological parameters such as malignancy, acute and chronic inflammation, inherited and acquired blood disease, dehydration or recent hemorrhagic episode and pregnant and lactating females were excluded from the study.

2.2.3. Clinical Profile

Chronic kidney disease was divided into five different stages based on GFR. In stage 1 chronic kidney disease (CDK) the GFR is >90 ml/minute/1.73 m2. Stages 2, 3 and 4 chronic kidney disease (CDK) are defined by a GFR of 60 and 89 ml/minute/1.73 m2 and 15 to 29 mL/minute/1.73 m2 respectively. The final stage, stage 5 occurs when the GFR is <15 mL/minute/1.73 m2 at this stage patient require dialysis. According to hemoglobin level anemia was divided into three classes mild (9-10.9), moderate (7-8.9), and severe anemia (<7).

2.3. Ethical Clearance

Ethical clearance of the study was obtained from Institutional review board (IRB) of Islamabad Medical and Dental College (IMDC) (IRB letter No. 51/IMDC/IRB-2021) prior to study conductance. Permission was obtained from Director, Dr. Akbar Niazi Teaching hospital for collection of data from Pathology and Nephrology department. Confidentiality of the data was maintained throughout the study.

2.4. Data Collection

2.4.1. Clinical Data

Total 89 patients were included in this study. Clinical data were collected from the patients, Hospital records, files and wards records through a structured questionnaire (Annexure II) which include demographics and lab findings (Hematological and biochemical tests data).

2.4.2. Laboratory Investigation

Laboratory diagnosis of chronic kidney disease include both hematological and biochemical test. Hematological tests includes, white blood cell count, red blood cell count, RDW-CV, hemoglobin level, hematocrit, MCH, MCV, MCHC and platelets count and these tests are performed on state of art Mindray BC-5000 5 parts Hematological Analyzer from Shenzhen Mindray Biomedicals (M-52DIFFLYSE (Cat No. 2021092401)), M-52LHLYS(Cat No. 2021093001)) China, while biochemical tests includes, renal function tests (creatinine, urea, uric acid), blood urea nitrogen, phosphorus, calcium, bicarbonates these test were analyzed on SELECTRA ProM (ELITechGroup) Innoline. Urinalysis and electrolytes (sodium, potassium, chloride) were analyzed on electrolyte analyzer (ELITE Plus) India. These tests were run on ISO certified equipment's by using standard protocols.

2.5. Data Analysis

The data was analyzed by the statistical software SPSS version 21. The results were presented in number, percent (%), and mean ± standard deviation. Descriptive statistics was applied on qualitative variables as frequencies and percentages. The results were presented in the form of pie and bar charts also.

2.6. Objective: To determine the prevalence of Anemia in Chronic Kidney Disease patients.

3. RESULTS

3.1. Demographic data

A total 89 chronic kidney disease patients were enrolled in the study from Dr. Akbar Niazi Teaching hospital. Out of these 89 patients, 58 (65%) were males and 31 (35%) were females (Figure 4.1) with male to female ratio of 2:1. The average age of the patients was 55 years. The average age of male and female patients is shown in Figure 4.2.

3.2. Hematological findings among study participants

Hematological parameters were analyzed to monitor anemia in the study population. Samples from 89 patients of chronic kidney disease were collected. 2-3 ml of peripheral venous blood was drawn using standard procedure. 2.0 ml of blood was transferred into a EDTA vaccutainer tube (BD, USA) for complete blood count and tests were performed on state of art Auto Hematological Analyzer BS-5000 (Mindray, China). The average hemoglobin in our study population was 9 g/dL ± 1.6 (6-13 g/dL). The mean range of WBCs counts was 9553 /mm3 ± 4160 (3460-22760), the mean value of RBCs count was 3 mil/mm3 ± 1.6 (2-5), the mean value of RDW-CV was 15.5 % ± 3.16 (12-29), the mean value of hematocrit was 27.6 g/dL ± 4.8 (17-40), the mean value of MCH was 28.3 % ± 2.4 (20-34), the mean value of MCV was 84.7 pg ± 7 (61-101), the mean value of MCHC was 33.4 fl ± 1.1 (31-37), and the mean value of platelets was 238370 g/dL ± 177175 (15000-14440000). Red cell indices provide information about the hemoglobin content and the size of red cells. Abnormal values of these indicate the presence of anemia and gives us idea about the type of anemia. Red blood cells indices are helpful in differentiating the cause of anemia. In this study it was found that hemoglobin was slightly reduced than normal and MCV, MCH and MCHC were in normal ranges (Table 4.1).

3.3. Biochemical Profile

Biochemical parameters were analyzed to monitor renal function tests in the study population. Tests were performed on Selectra Bio/Merck/25. The mean value of creatinine was 8.2 mg/dL± 7 (1-18), the mean value of urea was 138.7 mg/dL ± 57.7 (30349), the average value of uric acid was 8.2 mg/dL ± 12.5 (2-122), the average value of BUN was 64.9 mg/dL ± 21.6 (11-143), the average value of phosphorus was 5.9 mg/dL ± 2.2 (2-12), the mean value of calcium was 9 mg/dL ± 2 (6-15), Electrolytes were analyzed on electrolyte analyzer (ELITE Plus) the mean value of chloride was 101.5 mEq/L ± 7.1 (79-118), the mean value of sodium was 137.2 mEq/L ± 5.5 (112-150), the mean value of potassium was 4.7 mEq/L ± 1 (3-7), and the mean value of bicarbonate was 15 mmol/L ± 3.8 (5-26). From total 89 CKD patients, 44 (49.4%) patients had proteinuria as shown in (Table 4.2).

3.4. Stages of chronic kidney disease

Out of 89 CKD patients 4 (5%) of patients had stage 1 eGFR ≥90, 5 (6%) had stage 2 eGFR 60-89, 8 (18%) had stage 3 eGFR 30-59, 16 (18%) patients had stage 4 eGFR 1529, while 56 (63%) had stage 5 eGFR <15. From this study we concluded that majority of CKD patients presented stage 5 (63%) and least at stage 1 (5%) (Table 4.3).

3.5. Morphological type of anemia

The prevalence of anemia in CKD patients was 95.55% (n=89). Out of 89 CKD patients, 64 (72%) had normocytic normochromic type of anemia, 23 (26%) had microcytic type of anemia, while 2 (2%) had macrocytic type of anemia.

In this study it was found that in CKD patient's most common type of anemia was normocytic normochromic type 64 (72%) (Table 4.6). The bar chart also show the frequency of different morphological type of anemia (Figure 4.4).

3.6. Severity and frequency of anemia among different stages of anemia

In our study out of 89 CKD patients 41 (46%) had mild anemia, 25 (28%) had moderate anemia, 3 (3%) had severe anemia, and 20 (23%) patients were non anemic.

It is concluded that the mild anemia 41 (46%) was more prevalent in CKD patients (Table 4.8). Bar chart also show the severity of anemia among CKD patients (Fig 4.5).

3.7. Chronic comorbidities

In our study out of 89 CKD patients, 16 (18%) had hypertension, 4 (5%) had diabetes mellitus, 1 (1%) had cardiovascular disease, 13 (15%) had both hypertension and diabetes mellitus, 1 patient had diabetes and cardiovascular disease, 4 (5%) patients had all of above (hypertension, diabetes mellitus and cardiovascular disease), while 50 (56%) CKD patients show no chronic comorbidities. In this study, hypertension was a comorbid feature in 16 patients (18%) (Table 4.6).

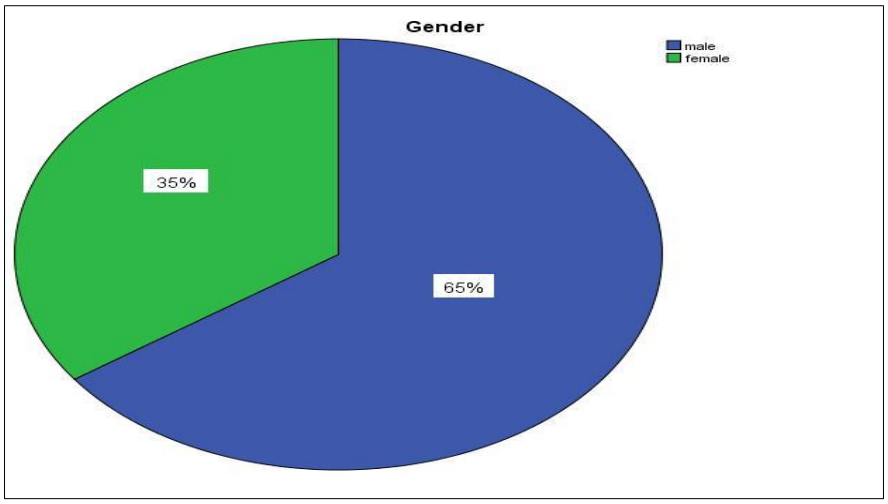

Fig 4.1: Gender distribution among patients of chronic kidney disease

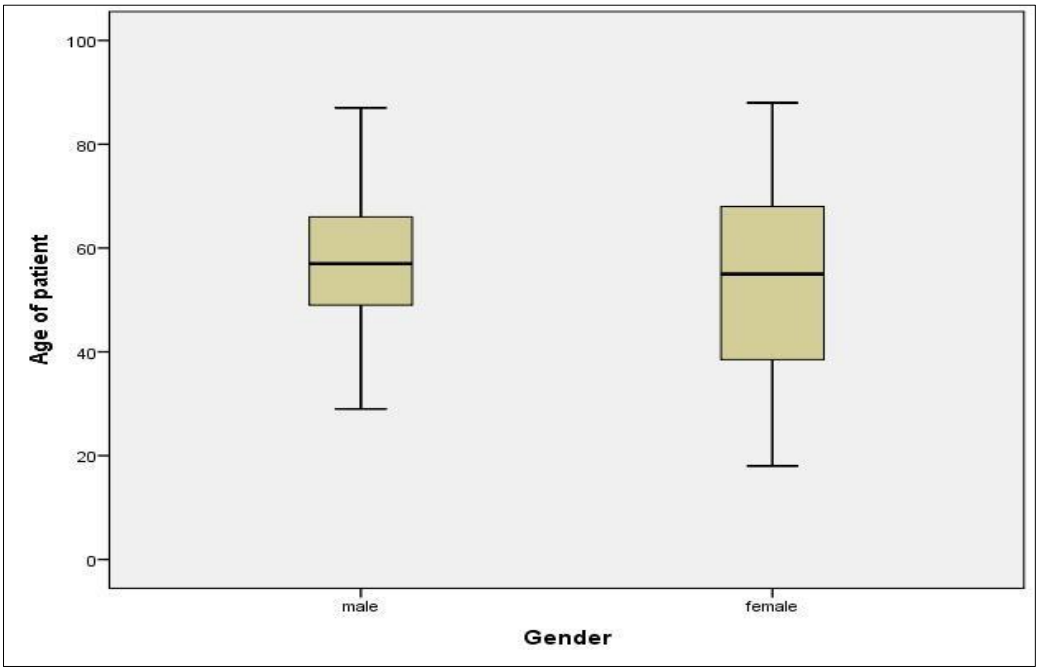

Fig 4.2: Age distribution in males and females

Table 4.1: Hematological parameters of patients with chronic kidney disease

S. No	Parameters (Units)	Mean ± SD (Range)
1	WBC count/mm3	9553 ± 4160 (3460-22760)
2	RBC count Mil/mm2	3 ± 1.6 (2-5)
3	RDW-CV%	15.5 ± 3.16 (12-29)
4	Hemoglobin (g/Dl)	9.23 ± 1.6 (6-13)
5	Hematocrit %	27.6 ± 4.8 (17-40)
6	MCH pg	28.3 ± 2.4 (20-34)
7	MCV fl	84.7 ± 7 (61-101)
8	MCHC g/dL	33.4 ± 1.1 (31-37)
9	Platelets/mm3	238370 ± 177175 (15000-14440000)

Table 4.2: Biochemical parameters of patients with chronic kidney disease

S. No	Parameters (Units)	Mean ± SD (Range)/ Frequency [n (% age)]
1	Creatinine (mg/dL)	8.2 ± 7 (1-18)
2	Urea (mg/dL)	138.7 ± 57.7 (30- 349)
3	Uric acid (mg/dL)	8.2 ± 12.5 (2-122)
4	Blood urea nitrogen (mg/dL)	64.9 ± 21.6 (11-143)
5	Phosphorus (mg/dL)	5.9 ± 2.2 (2-12)
6	Calcium (mg/dL)	9 ± 2 (6-15)
7	Chloride (mEq/L)	101.5 ± 7.1 (79-118)
8	Sodium (mEq/L)	137.2 ± 5.5 (112-150)
9	Potassium (mEq/L)	4.7 ± 1 (3-7)
10	Bicarbonate (mmol/L)	15 ± 3.8 (5-26)
11	Urinary proteins	Present 44 (49%)

Table 4.3: Stages of CKD according to eGFR stages

S. No	Estimated GFR	No (%)
1	eGFR <90 (stage 1)	4 (5)
2	eGFR 60-89 (stage II)	5 (6)
3	eGFR 30-59 (stage III)	8 (9)
4	eGFR 15-29 (stage IV)	16 (18)
5	eGFR <15 (stage V)	56 (63)

Table 4.4: Frequency among different morphological types of anemia in CKD patients

S. No	Type of anemia	No (%)
1	Microcytic anemia	23 (26)
2	Normocytic anemia	64 (72)
3	Macrocytic anemia	2 (2)

Table 4.5: Severity and Frequency of anemia among different stages of anemia

S. No	Severity of anemia	No (%)
1	No anemia (Hb>11)	20 (23)
2	Mild anemia (Hb 9-10.9)	41 (46)
3	Moderate anemia (Hb 7-8.9)	25 (28)
4	Severe anemia (Hb <7)	3 (3)

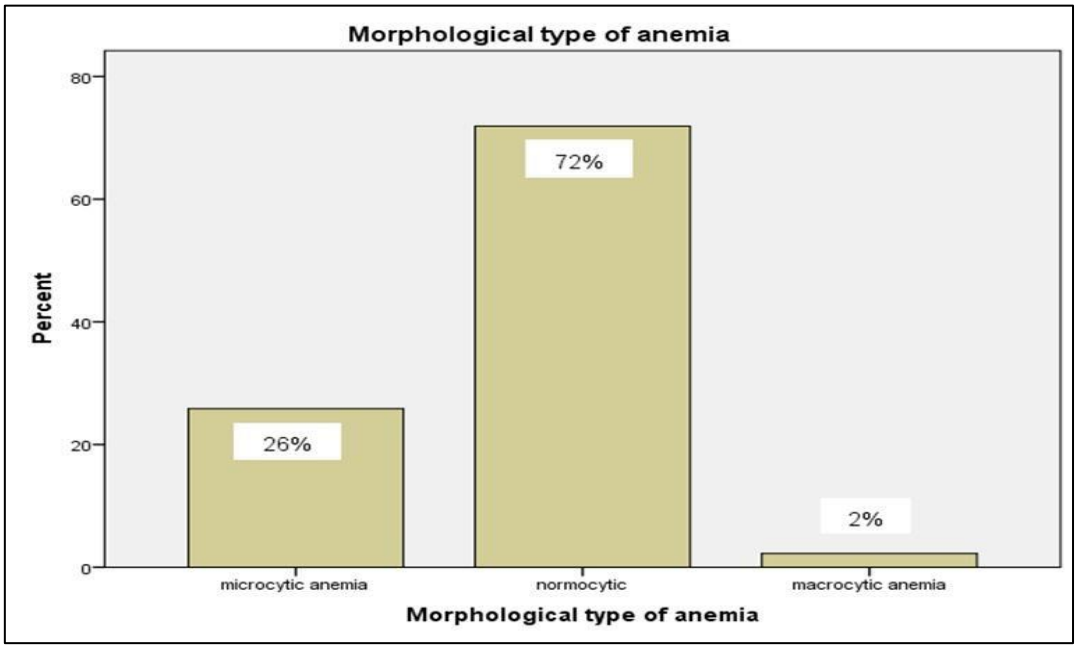

Figure 4.3: Frequency of different morphological types of anemia in CKD patients

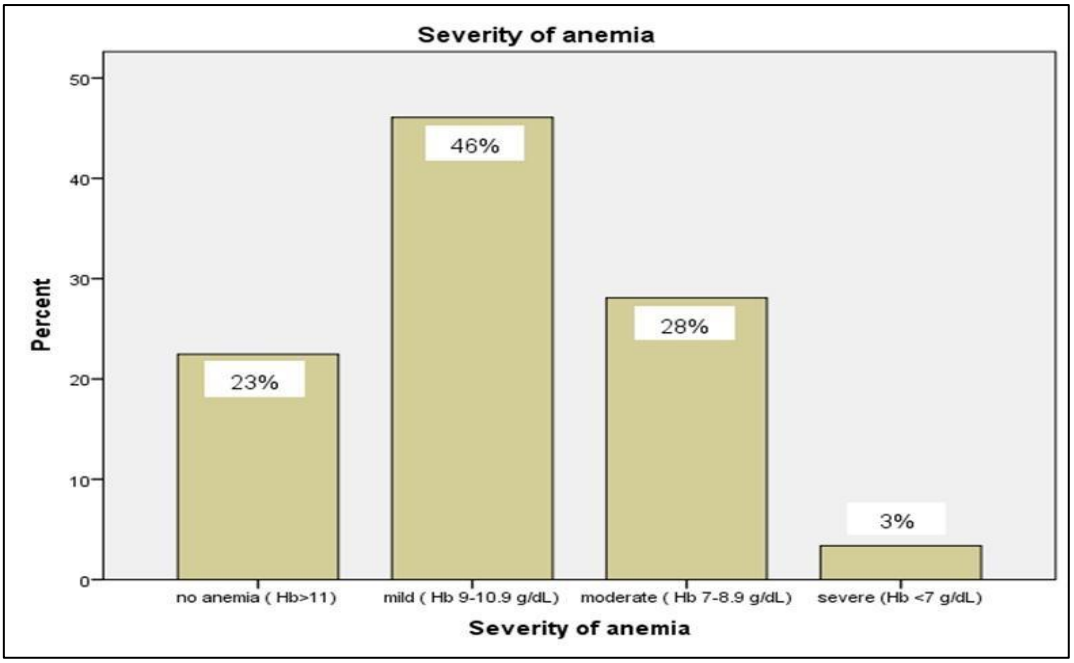

Figure 4.4: Frequency of anemia severity

Table 4.6: Represents the frequency of different comorbidities

S. No	Chronic comorbidities	No (%)
1	Hypertension	16 (18)
2	Diabetes mellitus	4 (5)
3	Cardiovascular disease	1 (1)
4	Hypertension and diabetes	13 (15)
5	Diabetes and cardiovascular disease	1 (1)
6	Hypertension, diabetes mellitus and cardiovascular disease.	4 (5)

4. DISCUSSION

According to WHO Chronic kidney disease is defined a kidney damaged or glomerular filtration rate (GFR) <60 mL/min/1.73 m^2 for three or more months. In this study the prevalence of anemia in chronic kidney disease patients were 95.5% (n=89).

This study included a total 89 CKD patients which were enrolled from Dr. Akbar Niazi Teaching hospital, among them 58 (65%) are male and 31 (35%) are females. The average age of the patients is 55 years, male to female ratio was 2:1. In this study the prevalence of anemia in chronic kidney disease was 95.5% (n=89). Out of 89 CKD patients 4 (5%) of patients had stage 1 eGFR ≥90, 5 (6%) had stage 2 eGFR 60-89, 8 (18%) had stage 3 eGFR 30-59, 16 (18%) patients had stage 4 eGFR 15-29, while 56 (63%) had stage 5 eGFR <15. From this study we concluded that majority of CKD patients presented stage 5 (63%) and least at stage 1 (5%). A study conducted at Medical Department of Lady Reading Hospital Peshawar from July 2015 to December 2015, most of the patients were males n= 231 (70.64%) while females were n= 96 (29.36%), male to female ratio was approximately 2:1. The prevalence of anemia in chronic kidney patients was 48.62% (n=159) [24]. Another study done by Melissa E. Stauffer and Tao Fan which was conducted to determine the prevalence of anemia in subjects with CKD. The prevalence of CKD was 14%. This represents an estimated 31.4 million people in the US population. About half of the people with CKD were at stage 3. A similar proportion was in stage 1-2 combined. Only 4.7% were in stages 4-5. The combined population survey, whether they have CKD or not, showed prevalence of anemia in 7.6% of the study population. The prevalence of anemia in CKD patients was 15.4%. The prevalence of anemia increased with stage of CKD, from 8.4% at stage 1 to 53.4% at stage 5. The prevalence of anemia in people without CKD was 6.3% [25].

In our study, 16 (18%) patients showed history of hypertension, 4 (5%) had diabetes mellitus, 1 (1%) had cardiovascular disease, 13 (15%) had both hypertension and diabetes mellitus, 1 had diabetes and cardiovascular disease, 4 (5%) had hypertension, diabetes mellitus and cardiovascular disease, while 50 (56%) CKD patients showed no chronic comorbidities compared to our study a study conducted at Medical Department of Lady Reading Hospital Peshawar from July 2015 to December 2015 showed that among anemic patients 98 (61.64%) had positive history of diabetes mellitus, 101 (63.52%) had glomerulonephritis, and 76 (47.80%) had positive history of hypertension [26].

In our study the RBCs count, hemoglobin and hematocrit was slightly reduced in CKD patients, while MCH, MCV, and MCHC, were within normal range compared to a cross sectional study carried out in the Hakeem Abdul Hameed Hospital (HAHC) between January 2017 to July 2017.They reported that the RBCs count, hemoglobin levels and platelets count were significantly reduced in the patients of chronic kidney disease patients, and the process of hemodialysis further reduced the all of the above hematological parameters whereas there is slightly increase in leucocyte count [27].

In our study severe anemia (Hb level <7) was present in 3% (n=3) of the study population. The mean hemoglobin level of the study population was 9.2 g/dL. Normocytic normochromic type of anemia was observed in most of the study population 72% (n=64). A study conducted from 2017-2018 in a point G university hospital showed presence of severe anemia (Hb level <5 g/dl) in 2.2% (n=26) of the study population (n=1176). The mean hemoglobin level of the study population was 4.10g/dl ± 0.64 with extremes of 2 and 5 g/dl. Besides CRF, twenty one patients (80.5%) had a history of hypertension. Hypochromic microcytic anemia was observed in every second patient [28]. Another cross sectional study was conducted on 3873 participants aged >40 years in 12 representative communities in Karachi Pakistan. Their findings showed that the prevalence of chronic kidney disease reaches 12.5% in adults aged 40 years or older in Karachi Pakistan, defined as the use of a validated eGFR <60mL/min/7.3m^2 [28]. Another institutional based cross sectional study was conducted on selected public hospitals in Addis Ababa to study prevalence of anemia in CKD patients. A total of 387 participants were included to estimate the prevalence of anemia among CKD patients. The prevalence of anemia was 53.5%. Females were 2 times more likely to develop anemia as compared to their counterparts and hemodialysis history had higher odds of anemia as compared to patients without hemodialysis history [29].

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