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Original Article

Chronic Kidney Disease and Anemia: Exploring Patterns with Creatinine Clearance <30 mL/min/1.73 m²

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Abstract

Objective: This study aims to determine the frequency and patterns of anemia in patients with chronic kidney disease (CKD) who have a creatinine clearance of less than 30 ml/min/1.73 m², in order to inform targeted treatment and reduce adverse outcomes.

Methods: This six-month prospective study at Fatima Memorial Hospital, Lahore, enrolled 156 CKD patients aged 18-60 with a creatinine clearance <30ml/min/1.73m², using nonprobability consecutive sampling. Exclusion criteria comprised of inflammatory diseases, recent blood loss, malignancy, or chemotherapy. Analysis via SPSS 22.0 had been done.

Results: The mean age of our study group was 47.2 ± 8.1years. The average age ranged between 38 and 45 years. Among these, 74.4% participants were males and 25.6% were females. All participants had anemia. The minimum mean hemoglobin level was 7g/dL and maximum were 11g/dL. 64.1% participants had normocytic normochromic anemia, 32.1% had iron deficiency anemia and 3.8% had combined deficiency anemia. These results confirmed the association of different patterns of anemia and CKD.

Conclusion: Present study highlights the prevalence and patterns of anemia in CKD patients with creatinine clearance below 30 ml/min/1.73m². Normocytic normochromic anemia was the most common pattern, followed by iron deficiency anemia and combined deficiency anemia. These findings underscore the multifactorial nature of anemia in CKD and its association with adverse outcomes such as cardiovascular complications and reduced quality of life.

Keywords: chronic kidney disease, Iron deficiency anemia, Normocytic normochromic, Combined deficiency anemia

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Introduction

Chronic Kidney Disease (CKD) is characterized by a glomerular filtration rate of less than 60 mL/min/1.73m², and frequently manifests with anemia, defined as hemoglobin levels below 13 g/dL in men and below 12 g/dL in women by World Health Organization (WHO).[1,2] Anemia accompanying advanced kidney disease usually has a normocytic and normochromic pattern.[3,4] A relative lack of Erythropoeitin (EPO) is considered to be the most common cause of anemia in patients with CKD. Other causes of anemia in CKD include inflammatory processes, blood loss, iron deficiency, folic acid deficiency, other nutritional deficiencies (due to an inadequate diet and defective iron absorption), high levels of hepcidin and uremia.[5,6,7] Several factors contribute to anemia in CKD patients, including gender, individual patient characteristics, CKD stage, treatment modalities, as well as socioeconomic and environmental factors.[7] The prevalence of anemia is greater in females than in males.[8] An inverse relationship exists between GFR <60ml/min/1.73m2 and prevalence of anemia.[9] Several studies have been conducted to determine different patterns of anemia in CKD patients.[10,11] Most common pattern of anemia in CKD patients is determined to be normocytic normochromic where as other less common patterns include microcytic hypochromic and combined deficiency also exist.[11] The prevalence of anemia is highest among blacks and lowest among Asians.[7]

Cross-sectional studies estimated the prevalence of CKD in the United States ranging from 1.5% to 15.6%[7] and a prevalence of 21.2% amongst the Pakistani population.[12,13] According to studies conducted, the prevalence of anemia has been found out to be 9% in patients with GFR less than 30ml/min/1.73m2.[9] Local and international data suggests that the frequency of normocytic normochromic anemia is 70 to 90%,[14] iron deficiency anemia is 60%[10] with remaining being combined deficiency anemia. Cardiovascular complications like angina, left ventricular hypertrophy and heart failure increase morbidity and mortality in CKD patients. The major contributor to these cardiovascular complications is anemia.[15] Anemia adversely affects the quality of life in CKD patients, leading to sleep disturbances, exercise intolerance, cognitive impairment and increased mortality.[16] The rationale of our study is to find frequency of different patterns of anemia in CKD patients with creatinine clearance <30ml/min/1.73m2. So that effective and precise treatment of the exact underlying cause can be employed to treat anemia and reduce the risk of adverse clinical outcomes in CKD patients, as severity of anemia is associated with a greater mortality, hospitalization rate, major adverse cardiovascular events (MACE) and CKD progression.

Methods

Patterns of anemia included iron deficiency anemia (TSAT <20% and serum ferritin <100ng/mL) and normocytic normochromic anemia (MCV 76-96fL and MCHC 32-36g/dL). This prospective study was conducted over six months in the Department of Medicine at Fatima Memorial Hospital, Lahore. The study utilized nonprobability consecutive sampling, enrolling 156 patients aged 18-60 with creatinine clearance < 30ml/min/1.73m². Exclusion criteria included inflammatory diseases (Inflammatory Bowel Disease, Chronic Liver Disease (ALT, AST > 40I U/L), Bronchiectasis, Connective tissue disorders), h/o recent blood loss, active malignancy, or chemotherapy. Data was collected on a structured performa with ethical clearances, IRB approval and informed consent. Venous blood samples (5ml) were drawn and analyzed for hemoglobin levels, RBC indices and iron profile. The data, analyzed using SPSS Version 22, included frequency and percentage for variables like gender and anemia patterns, and mean ± SD for age. Stratification based on age, gender, and duration of CKD was performed, followed by a Chi-square test, with a significance threshold set at P <= 0.05. To ensure participant anonymity, strict protocols, such as data encryption and secure storage, were put in place, adhering to the highest standards of confidentiality and privacy. Participant welfare was given top priority, and precautions were taken to reduce any possible harm.

Results

During the study period, 156 patients were evaluated. The mean is 42.8 with a standard deviation of 11.7. Among these, 116 (74.4%) participants were males and 40 (25.6%) were females.

Total 156 patients that were evaluated, all participants (100 %) had anemia (Figure 1). The data has a mean of 9.12 ± 1.09, with values ranging from a minimum of 7.00 to a maximum of 11.00.

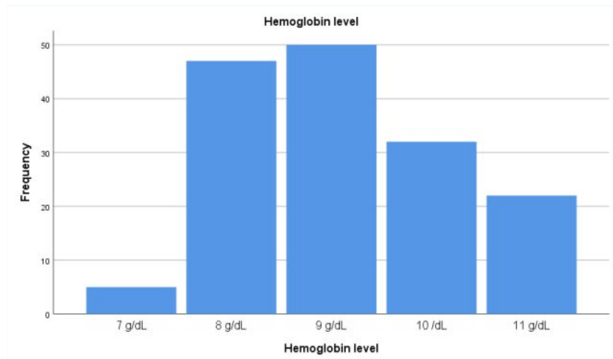

Figure 1: *Frequency of Anemia*

The Mean Corpuscular Volume (MCV) distribution among the study participants revealed that 30 (19.2%) had MCV values between 60 to 70 fL, 48(30.8%) between 71 to 80 fL, 53 (34.0%) between 81 to 90 fL, and 25 (16.0%) between 91 to 100 fL(Figure 2).

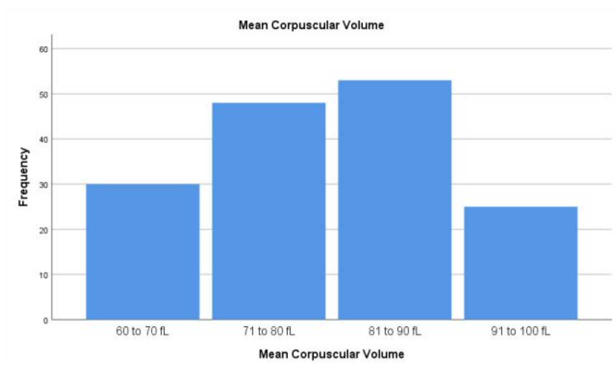

Figure 2: *Frequency of Mean Corpuscular Volume*

The Distribution of Mean Corpuscular Hemoglobin (MCH) levels among the study participants indicates that 50 (32.1%) participants had MCH levels between 20 to 25 pg, 31(19.9%) between 26 to 30 pg, and 75(48.1%) between 31 to 35 pg.

The data illustrates that 50 (32.1%) participants had MCHC levels between 25 to 30 g/dL, while 106 (67.9%) had MCHC levels between 31 to 36 g/dL (Figure 3).

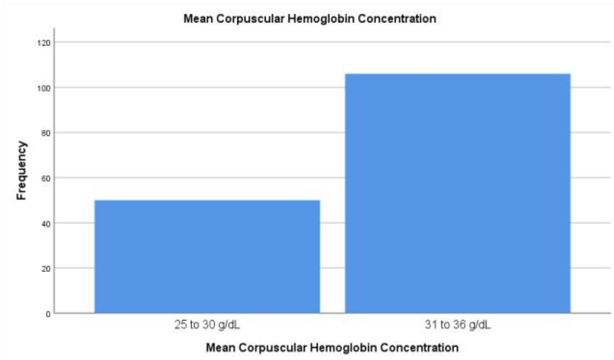

Figure 3: *Frequency of Mean Corpuscular Hemoglobin Concentration*

The frequency of individuals with iron levels ranging from 20 to 30 ug/dL and 31 to 40 ug/dL is approximately equal, both are 22(14.1%). There is a noticeable drop in frequency for the 41 to 50 ug/dL range, with 12 (7.7%). The frequency increases significantly for the 51 to 60 ug/dL range which was 23 (14.7%), followed by a steady rise in the 61 to 70 ug/dL range which was 27 (17.3%). The highest frequency is observed in the 71 to 80 ug/dL category, with over 30 (19.2 %) individuals. Finally, the frequency decreases for the 81 to 90 ug/dL range, with 20 (12.8%). This chart highlights the variation in iron levels within the population, with a significant peak in the 71 to 80 ug/dL range.

Total iron binding capacity (TIBC) is displayed in micrograms per deciliter (ug/dL) amongst the sample population. The 250 to 255 ug/dL range has a frequency of about 34 (21.8%) individuals. The frequency increases slightly for the 256 to 260 ug/dL range, with approximately 38 (24.4%) individuals. The highest frequency is observed in the 266 to 270 ug/dL range, with 52 (33.3%) individuals. Finally, there is a decrease in the frequency for the 276 to 280 ug/dL range, with about 32 (20.5%) individuals.

The lowest category of the distribution of transferrin saturation percentages among the study population is 1 to 10%, has a relatively small frequency with 10 (6.4 %) individuals. The 11 to 20% category shows a significant increase, with about 46 (29.5%) individuals falling within this range. The 21 to 30% range exhibits the highest frequency, with around 80 (51.3%). Finally, the 31 to 40% range shows a decrease, with approximately 20 (12.8%) individuals. Among the respondents, 25 (16.0%) had ferritin levels between 80 to 90 ng/ml, followed by 31 (19.9%) between 91 to 100 ng/ml. The distribution continues with 23 (14.7%) falling within 111 to 120 ng/ml, 28 (17.9%) between 121 to 130 ng/ml, 29 (18.6%) between 131 to 140 ng/ml, and finally, 20 (12.8%) between 141 to 150 ng/ml.

Frequency of different patterns of anemia in chronic kidney disease: Of these 156 anemic patients, 100 patients (64.1%) had normocytic normochromic anemia, 50 patients (32.1%) had iron deficiency anemia and 5 patients (3.8%) had combined deficiency anemia. These results confirmed the association of different patterns of anemia and CKD (Figure 4).

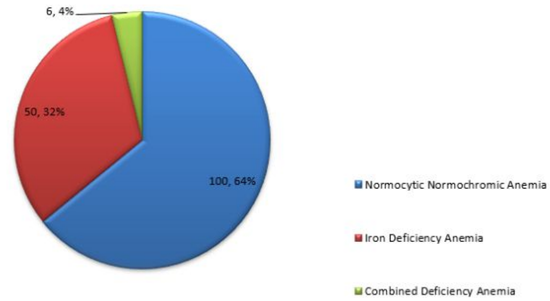

Figure 4: *Frequency of different patterns of anemia.*

Discussion

The global prevalence of CKD is 13.4%.[17] In a study conducted in Australia, the prevalence of CKD was 12.3 % and 6.1 % among women and men respectively.[18] Cardiovascular disease is the leading cause of death worldwide, responsible for 16% of all global deaths.[19] It also is the major cause of mortality and morbidity in chronic kidney disease patients. Left ventricular hypertrophy leading to heart failure occurs early in the course of CKD and is prevalent in about 70 to 80% of the patients. A major contributing factor to these cardiovascular complications is anemia. There are a number of mechanisms by which anemia occurs in CKD patients. These include low synthesis of erythropoietin, iron deficiency, accumulation of uremic toxins and inflammation.[20] The prevalence of anemia in CKD patients is higher among individuals over 60 years old compared to those aged 46 to 60. This increased prevalence is likely due to the higher incidence of CKD in older adults and the lower estimated glomerular filtration rates (GFRs) that accompany aging.[22] The United States Renal Data System (USRDS) 2023 Annual Data Report notes that the percentage of U.S. adults less than 65 years with CKD has remained relatively stable since 2005-2008, with a prevalence of 14.0% in 2017 to March 2020. However, among adults aged 65 and older, the prevalence of CKD has steadily decreased from 38.0% in 2005-2008 to 33.2% in 2017 to March 2020. Additionally, a higher percentage of women (15.4% in 2017 to March 2020) have CKD compared to men (12.6%), a trend that has been consistent since 2005-2008.[23]

Various studies have been conducted to find different patterns of anemia in CKD patients being normocytic normochromic, microcytic hypochromic and combined deficiency anemia. Patients with Chronic Kidney Disease (CKD) often suffer from increased iron losses, particularly those undergoing hemodialysis, losing around 1 to 3 grams per year. This heightened loss is attributed to chronic bleeding caused by uremia-related platelet dysfunction, blood being retained in the dialysis equipment, and frequent blood draws. As a result, individuals with CKD face a high risk of genuine iron deficiency.[24] The prevalence of anemia increases with the progression of CKD. According to the NHANES analysis, 15.4% (approximately 4.8 million people) had anemia associated with CKD. The prevalence of anemia was 17.4% in stage 3 CKD, 50.3% in stage 4 CKD, and 53.4% in stage 5 CKD.[25] Anemia of chronic kidney disease (CKD) is a type of normocytic normochromic, hypoproliferative anemia. A study conducted in Bangladesh in Jan 2022 to June 2021 found that out of 50 study participants, 33 were suffering from normocytic normochromic anemia, 11 were suffering from microcytic hypochromic anemia and the rest 6 were suffering from combined deficiency.[10] In our study, out of 156 anemic patients, 100 (64.1%) had normocytic normochromic anemia, 50 (32.1%) had iron deficiency anemia and just 5 patients (3.8%) had combined deficiency anemia. Anemia worsens the impact of CKD on Health-Related Quality of Life (HRQoL) and is associated with lower productivity in CKD patients.[21] Anemia of inflammation (AI) manifests as a mild to moderate normochromic and normocytic anemia, distinguishing it from the hypochromic and microcytic presentation typical of iron deficiency anemia (IDA). So, it is important to find different patterns of anemia in CKD patients so that precise measures can be employed to treat the cause of anemia and avoid cardiovascular complications, frequent hospitalizations and mortality.

Limitations of the study include; single-center design at Fatima Memorial Hospital Lahore may constrain the broader applicability of its findings, as variations in patient demographics, healthcare practices, and environmental factors across different settings could impact the observed prevalence and patterns of anemia in CKD patients. Additionally, the relatively modest sample size of 156 patients might not fully encompass the diverse spectrum of anemia presentations seen in this population. Furthermore, the study's limited follow-up duration of six months may not capture longitudinal changes in anemia patterns or CKD progression adequately.

Conclusion

So, with all the above discussion, keeping in view different studies conducted in the past, globally and locally, we can draw an inference that anemia has an established association with CKD. Normocytic normochromic anemia emerged as the most prevalent pattern, affecting the majority of patients, followed by iron deficiency anemia and combined deficiency anemia. These patterns underscore the multifactorial nature of anemia in CKD, encompassing factors such as erythropoietin deficiency, iron deficiency, inflammation, and uremia. Our results align with the existing literature, highlighting the association between anemia and adverse clinical outcomes, including cardiovascular complications, reduced quality of life, and increased mortality. Addressing anemia in CKD patients is paramount to mitigating these risks and improving patient outcomes. In clinical practice, our findings emphasize the importance of early detection and tailored management of anemia in CKD patients. Healthcare providers can potentially reduce the burden of anemia and enhance outcomes for this vulnerable patient population by addressing the underlying causes and optimizing treatment strategies.

Ethical Approval: The IRB/EC approved this study via letter noFMH-04-2021-IRB-897-M dated July 12, 2021.

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Authors' Contribution

AT, MKR: Conception

AT, FS: Design of the work

FS, SA: Data acquisition, analysis, or interpretation

AT, FS, SA: Draft the work

MKR: Review critically for important intellectual content

All authors approve the version to be published

All authors agree to be accountable for all aspects of the work

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