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ORIGINAL ARTICLE

Iron Status Assessment in Chronic Kidney Disease Patients Preceding Dialysis: An Exploration of Anemia and Iron Deficiency

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ABSTRACT
Objective: The most common kind of anemia, iron deficiency anemia (IDA), is very burdensome for those with chronic kidney disease (CKD). The incidence of IDA rises as renal function deteriorates. The incidence of IDA in CKD patients before the need for dialysis has not been well documented in Pakistan, even though the major cause of anemia in CKD individuals is a shortage of erythrocyte a hormone generated by the kidneys that stimulates red blood cell synthesis. This study's goal is to identify the incidence of IDA in people with kidney failure who are still not receiving dialysis.
Methods: We included 188 pre-dialysis CKD patients, ages 18 to 75, of both sexes. Patients with apparent anemia-related reasons were eliminated. During OPD follow-up, it was then established what proportion of patients had IDA in their pre-dialysis CKD.
Results: The patients who participated in the research had an average age of 46.03 years, with a standard deviation of 12.24 years. There were 188 patients in all, and 102 of them were men, making up around 54.26% of the sample. The study's 1.2 to 1 male-to-female ratio indicates that men were overrepresented. 73 people, or around 38.83% of the total patients in the research, were found to have iron deficiency anemia (IDA) among people with chronic kidney disease (CKD) who had not yet begun dialysis.
Practical Implication: The causes of iron shortage in those with CKD are complicated by several variables, chief among them being decreased nutritional iron consumption and poor gastrointestinal absorption of iron, blood losses brought on by uremia-induced platelet disorder, and persistent inflammation related to CKD. As a result, owing to chronic inflammation causing a reactive rise in ferritin, individuals with CKD have much higher ferritin threshold levels for the absolute iron shortage. As a result, it is advised that patients with CKD before starting dialysis have blood ferritin levels below 100 µg/ml and over 200 µg/ml for those who are already receiving it
Conclusions: According to the study, IDA occurs often in pre-dialysis CKD patients. By paying strict attention to the sources of IDA and replacing it, patients' outcomes may be improved.
Keywords: anemia, dialysis, chronic kidney disease, erythrocyte, iron deficiency, hormone

INTRODUCTION
Chronic kidney disease (CKD) before dialysis sometimes has anemia as a consequence. Anemia usually appears at the beginning of the development of the illness and becomes severe as CKD advances. Around 1.8 billion individuals worldwide suffer from anemia, which is more frequent in kids and females and is caused by an iron shortage [(1)]. The prevalence of anemia increases from 8.4 percent in the initial stage of CKD to 53.4 percent in the fifth stage, making it twice as common among those with CKD as when compared to people in general (15.4 percent vs 7.6 percent) [(2)]. Even among CKD patients who are not yet on dialysis, iron deficiency is a significant risk factor [(3)].

The root causes of iron shortage in those with CKD are complicated by several variables, chief among them being decreased nutritional iron consumption and poor gastrointestinal absorption of iron, blood losses brought on by uremia-induced platelet disorder, and persistent inflammation related to CKD [(4)]. As a result, owing to chronic inflammation causing a reactive rise in ferritin, individuals with CKD have much higher ferritin threshold levels for the absolute iron shortage. As a result, it is advised that patients with CKD before starting dialysis have blood ferritin levels below 100 µg/ml and over 200 µg/ml for those who are already receiving it [(5)].

Pre-dialysis CKD is always associated with iron insufficiency, which is common and significantly correlated with both CKD development and patient survival. According to one research, 39% of CKD patients who were on pre-dialysis had IDA. Another research found that hemoglobin levels begin to fall even in the first stages of renal insufficiency at 70 ml/min eGFR (CKD II) in men and 50 ml/min eGFR (CKD III) in women [(6)]. Iron-restricted IDA and erythropoiesis are caused by elevated hepcidin levels found in those with CKD, which block the uptake of iron from the stomach and iron regeneration from monocytes [(7)]. Patients with CKD have a high prevalence of IDA, the majority of whom do not need dialysis and have creatinine clearances of 60 ml/min (CKD III) [(8)].

Pre-dialysis CKD patients are on the rise, although the frequency is unclear, and accurate identification is sometimes difficult due to underlying inflammation that affects the absorption of iron [(9)]. In this group, timely IDA treatment enhances the quality of life while also lowering cardiac morbidity and death. [(10,11, 12)]

Significance of the study: A thorough review of the medical literature turned up only two studies that referenced microcytic anemia, one from Pakistan and the other merely mentioning it in 14% of pre-dialysis patients with CKD. Determining the prevalence of IDA in CKD patients undergoing pre-dialysis was the study's main goal.

MATERIAL AND METHODS
Study Design: According to the KDOQI recommendations, CKD is divided into 5 phases depending on its severity, irrespective of the root cause. Based on certain hemoglobin (Hb) threshold values, anemia in CKD is identified. Hb values below 13 g/dl are when anemia in males is diagnosed, whereas Hb levels below 12 g/dl are when anemia in women is identified. Transferrin saturation (TSAT) levels may be used to identify iron insufficiency in CKD patients. When TSAT is less than 20% and serum ferritin concentration is less than 100mg/ml, the absolute iron shortage is recognized. TSAT levels below 20% and a serum ferritin level of less than 100 ng/L are signs of functional iron shortage, as are ferritin concentrations that are normal or high.

This research was carried out at the Mayo Hospital in Lahore, Pakistan, in the Nephrology Outpatient Department as a descriptive, cross-sectional study. It will take place between November 2022 and May 2023. Using the WHO sample size calculator, the sample size is determined while accounting for a 95% confidence interval, a 10% margin of error, and the projected incidence of iron deficiency anemia (IDA) in pre-dialysis patients with CKD (39%). 188 represents the estimated sample size.

Patients with CKD who are yet to start dialysis and are between the ages of 18 and 75 are eligible for enrollment in this research. There are both males and females. Individuals with anemia brought on by conditions apart from CKD, like illnesses such as sickle cell leukemia, continuous blood loss, an ongoing febrile disease, hemolytic diseases, pregnancy, a previous diagnosis of cancer, or those using oral iron supplements, are included in the exclusion criteria.

Through outpatient follow-up visits, data on demographic factors, serum iron, total iron-binding capacity (TIBC), hemoglobin levels, and ferritin levels are collected for this research. All studies are carried out at the hospital's laboratory, and the research protocol has been authorized by the ethical committee of the neighborhood hospital. This study's main goal is to quantify the proportion of outpatient follow-up visits with patients who have IDA in pre-dialysis CKD.

Statistical Analysis: SPSS v.27 statistical software was used for data collection and processing. Age-related variables underwent calculations to determine their mean average value and standard deviation, respectively. The frequencies and percentages for categorical variables such as gender, the stages of chronic kidney disease (CKD), and the presence or absence of iron deficiency anemia (IDA) were calculated. The data were categorized to take into consideration the impact of specific characteristics such as gender, diabetes, hypertension, and CKD length. This indicates that the data were broken down into subgroups depending on these variables, enabling a more thorough study within each segment. After stratification, the connection between the variables was investigated using a statistical test known as chi-square. When a p-value was less than 0.05, it was deemed statistically significant, meaning that it was improbable that the observed association between the variables was the result of pure chance.

RESULTS

The patient characteristics included in the research are shown in Table 1. Participants had an average age of 46.03 years, with a standard deviation of 12.24. The patients' ages ranged from 18 to 75, and the majority (54.26%) belonged to the 18 to 45 age range. Figure 2 shows that the male-to-female ratio was 1.2:1 and that the gender distribution was about equal, with 102 patients (54.26%) being male.

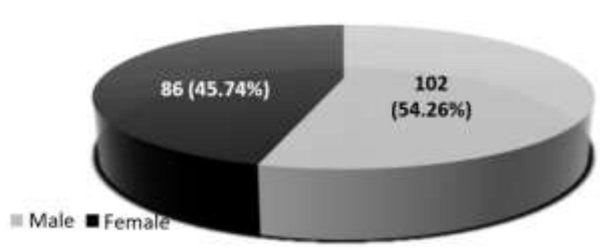

Figure 2: Patients' distribution based on CKD stage

According to the stage of their chronic kidney disease (CKD), the patients are distributed in Figure 3. With a standard deviation of 3.45, the individuals' meantime with CKD was 11.36 months. As seen in Table 1, the majority of patients' CKD was present for less than a year.

The prevalence of iron deficiency anemia (IDA) in CKD patients undergoing pre-dialysis was also examined in the research. Figure 4 shows that 73 people (38.38%) who made up the whole patient group were identified as having IDA.

Table 1: Demographics of the study population

	n	%
Age	46.03± 12.24	
Sex		
Female	86	45.74
Male	102	54.26
CKD		
Stage 5	36	19
Stage 4	68	36
Stage 3	84	45
CKD Duration		
More than 1 year	73	38.83
Less than 1 year	115	61.17
Hypertension		
No	73	38.3
Yes	115	61.17
DM		
No	99	52.66
Yes	89	47.34

Table 2: Iron deficiency anemia frequency

IDA Frequency	n	%	p
Age (Years)			
18 to 45	24/102	24	0.0001
46 to75	49/86	57	
Gender			
Female	38/86	44	
Male	35/102	34	0.17
CKD			
Stage 5	19/36	53	
Stage 4	20/68	29	0.06
Stage 3	34/84	40	
CKD Duration			
More than 1 year	24/73	33	
Less than 1 year	49/115	43	0.18
Hypertension			
No	29/73	40	
Yes	44/116	38	0.84
DM			
No	38/99	38	
Yes	35/89	39	0.99

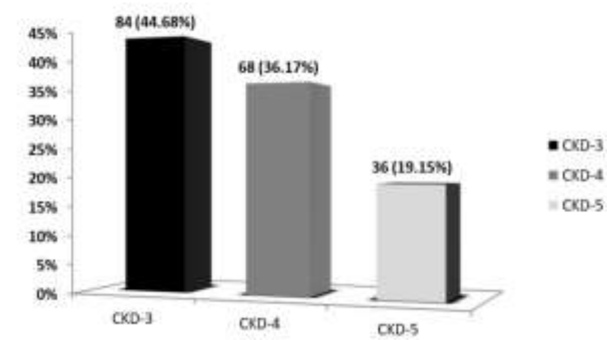

Figure 3: Patients' distribution based on CKD stage

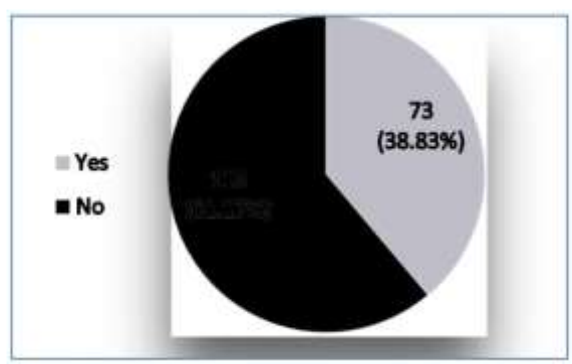

Figure 4: IDA prevalence in patients

These results imply that the research population was made up of people of various ages and a roughly equal number of men and women. The bulk of the patients were between the ages of 18 and 45, demonstrating the occurrence of CKD at younger ages. The distribution of individuals throughout CKD stages suggests that the severity of the illness within the sample spans a wide range. The average length of CKD indicates that the ailment was just recently discovered in the majority of patients.

More than one-third of the study's participants had IDA, which was another notable finding among pre-dialysis CKD patients. This discovery emphasizes the need of taking into account and controlling IDA in people with CKD since it may negatively impact their health and general well-being.

Demographics, disease stage distribution, and the frequency of IDA in pre-dialysis CKD patients are all useful insights that may be gained from the study's extensive patient information. These discoveries add to our understanding of CKD and its consequences, which will help us create effective interventions and treatment plans for this patient group.

DISCUSSION

In the current research, we discovered IDA in over 1/3rd (38.38%) of our study participants with CKD stages 3-5. In recent research, 53% of the 300 CKD patients who were not on dialysis developed IDA [13]. While we had individuals who had pre-dialysis medium to serious stages of chronic kidney disease 3-5, they did not indicate the CKD phases and might have encompassed the initial stages. This frequency is somewhat higher than the anticipated global prevalence of anemia in 2010, which was predicted to be about 33%, with iron deficiency constituting the primary cause in 50% of cases. Women, especially those who are close to having children, are more likely to get anemia [14]. Patients who are female and in pregnancy are more prone to suffer from iron deficiency anemia. Anemia was reported to be 36 percent more prevalent in female CKD patients overall relative to male patients with CKD [15].

The mean age of CKD5-HD in Pakistan is 50 years, which is substantially lower than the average age in wealthy countries [16]. In contrast to our research, where the female-to-male ratio was 1:1, the average age in that investigation was about 45 years old. Therefore, it is reasonable to suppose that the increased incidence of anemia in their research may have been impacted by the larger proportion of females who are of reproductive age. Concurrent anemia was seen in 5.2% of stage 3 CKD patients and 44% of stage IV patients.

Another research indicated that 13.9 percent of 156 patients with chronic kidney disease had microcytic anemia (CKD stage not specified, existence of ESKD not ruled out), but did not offer a full description of IDA [16]. Anemia is a clinically important burden in CKD patients when the glomerular filtration rate (GFR) declines more often. The ground-breaking research found that, amongst pre-dialysis patients with severe CKD needing replacement kidney treatment, 68% had hematocrits of less than thirty percent, and of those, fifty-one percent had hematocrits of less than twenty-eight percent [17].

Anemia is linked to decreased life expectancy and higher cardiovascular morbidity and death. Due to the reduction in renal EPO synthesis, erythropoietin (EPO), insufficiency continues to be the primary cause of anemia in CKD patients. Lack of iron, yet, began to become a significant factor in anemia in CKD patients with the advent of recombinant EPO from humans and the decrease in blood transfusions [18].

Iron deficiency in those on hemodialysis has long been a source of worry, and an iron injection is often given throughout a hemodialysis procedure. According to a recent analysis, several variables, including blood loss from the dialyzer and tubing, routine blood tests, decreased iron from diet digestion, digestive harm, and elevated amounts of hepcidin, have been linked to this recurring iron deficit. The increased erythropoiesis brought on by erythropoiesis-stimulating drugs, such as r. HuEPO results in a decrease of iron in the blood as well.

Our research, which had a nearly equal gender distribution, revealed a greater frequency of IDA among CKD patients who were not yet on dialysis, thus illustrating the load of this curable cause. In contrast to our patients' IDA rate of 38.3% The issue is far less severe in wealthy nations. According to the most recent NHANES research, 15.4% of CKD patients had anemia, with roughly 8% being in Stages 3-5.2. Similar to this, a recent study found that anemia affected 51.5% of individuals with CKD stages I to V [19].

IDA is quite common in the developing countries of our subcontinent. Anemia was shown to be prevalent in pre-dialysis CKD patients overall in that research, with a 47.85% incidence rate [20].

Another study found that 88% of individuals with CKD 5 had anemia just before starting dialysis. [21,22] Their research made no mention of the proportion of IDA. Nevertheless, it does point to Pakistan's subpar care of anemia in the CKD pre-dialysis stage, which is consistent with our findings.

CONCLUSIONS

Our study's results show that pre-dialysis patients with chronic kidney disease (CKD) often have iron deficiency anemia (IDA). Surprisingly, IDA was found in more than one-third of the individuals in our study. These findings support the use of early screening measures to detect and treat iron deficiency in CKD patients undergoing pre-dialysis.

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