

Factors Leading To Severe Anaemia In Patients With Chronic Kidney Disease

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Abstract

Objective: Chronic disease of the kidney (CKD) is a lethal malady that usually vitiates the function of the kidney. It often stays unrecognized in the earlier stages but over time it may lead to end-stage renal disease (ESRD). CKD is linked to several complications, such as anaemia and infection which can augment the medical complexities. This study aimed to determine the factors leading to severe anaemia in predialysis CKD patients.

Methods: A Cross-sectional design was selected to conduct a study in the medicine ward at Abbasi Shaheed Hospital, Karachi from 20/08/23 to 20/08/24. Questions were asked about the duration of the CKD, diabetes mellitus (DM), and hypertension (HTN). A venous sample was collected for investigations including serum urea, creatinine, haemoglobin (Hb), hematocrit (Hct), blood urea nitrogen (BUN) and serum albumin level. Glomerular filtration rate (GFR) was calculated. Stages of CKD were classified as per NKF-K/DOQI classification. The information was entered on proforma and analysed through SPSS-23.0.

Results: Among 130 anaemic patients based on haemoglobin, 72 CKD patients had severe anaemia, mean Hb level of 6.59 ± 0.96 g/dl, 49 patients had moderate anaemia with a mean Hb 8.98 ± 0.73 g/dl and only 9 patients had mild type of anaemia, mean Hb 11.96 ± 0.60 g/dl with significant p-value. (p-value=0.000) GFR was 12.00 ± 6.94 ml/min/1.73m² in patients having severe anaemia, 17.20 ± 9.82 ml/min/1.73m² in individuals having moderate anaemia and 18.79 ± 10.22 ml/min/1.73m² in CKD patients having mild anaemia. (p-value=0.001)

Conclusion: The severity of anaemia in advanced stages of CKD is a striking observation. There is a need for early diagnosis and management of kidney disease and nevertheless routine monitoring of kidney function especially in diabetic and hypertensive patients.

Keywords: Creatine, iron deficiency, diabetes mellitus, ocular hypertension, dialysis

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1. Introduction

Renal disorders include chronic kidney disease (CKD) which usually alters the function of the kidney. It often stays unrecognized in the earlier stages but over time it may progress to end-stage renal disease (ESRD).¹ This condition needs kidney replacement therapy (dialysis or kidney transplant) to sustain life. The awareness level of "weak kidneys" is predicted by CKD markers which include (kidney function and albuminuria).² CKD usually arises as a result of a variety of chronic disorders like diabetes mellitus (DM), hypertension (HTN), chronic glomerulonephritis, interstitial nephritis, and polycystic disease, etc, whereas a high level of blood glucose and increased blood pressure are the major reasons for ESRD.³ CKD is linked to many complications, such as anaemia and infection which can augment the medical complexities. Hemolytic anaemia progresses earlier along with CKD, perhaps

it gradually exacerbates as the CKD progresses well before the onset of ESRD.⁴ As the kidney function deteriorates kidney fails to excrete sufficient erythropoietin to arouse adequate hematopoiesis.⁵ Deficiency of iron, folate deficiency, acute and chronic inflammatory conditions, and shortened red blood cell survival, are other factors that may add up to CKD-related anemia. Among the common factors leading to severe anaemia are DM and HTN.⁶ According to the Kidney Disease Improving Global Outcomes (KDIGO) Anemia Work Group, anaemia in CKD occurs when the Hb level is < 13 g/dl for males and 12 g/dl for females and estimated glomerular filtration rate (eGFR) of < 60 ml/min/1.73m² indicate to investigate anaemia in patients with CKD.⁷ Similarly anaemia in patients with CKD is strongly linked to the progression of the disease.⁸ Therefore, this study is planned to explore the above-mentioned issues to generate local data and

appropriate strategies that could be set to decrease morbidity.

2. Materials & Methods

The Descriptive Cross-Sectional study was carried out in the Department of Medicine at Abbasi Shaheed Hospital, Karachi from 20/08/23 to 20/08/24, after institutional review board approval no IBC KU-370/2023. The Non-probability purposive sampling technique was used and the sample size was calculated with the help of the “Practical Manual of Sample Size Determination in Health Studies” by S.K. Lwanga and S. Lemeshow, WHO software, Geneva. Taking the least proportion of severe anaemia in CKD patients as 15% in our population with a 95% confidence interval and 5% absolute precision, the following formula was used to calculate this sample size.

$$N = \frac{z^2 \cdot \frac{1-q}{2} \cdot P(1-P)}{d^2}$$

The sample calculated by the software was 100. On 7% absolute precision. However, we selected 130 CKD patients during a one-year study duration. Participants of either gender, age 18 years or above, and having CKD for >6 months associated with Diabetes Mellitus and Hypertension of more than 2 years duration were included. Whereas the participants with an active gastrointestinal bleed and a history of malignancy were excluded from the study. After the approval by the ethical committee, the study was conducted on the patients admitted to the wards through OPD (Department of Medicine and Nephrology) Abbasi Shaheed Hospital. Written informed consent was taken from all the patients, meeting the inclusion & exclusion criteria for enrolment in the study. A brief history was taken regarding the duration of the CKD, Diabetes Mellitus, and Hypertension. A venous sample was collected for investigations including serum creatinine, hematocrit (Hct), blood urea nitrogen (BUN) and serum albumin level. GFR was calculated. Stages of CKD were classified as stage 1 to stage 5 as per NKF-K/DOQI classification. Anaemia and its severity were labelled as mild anaemia: Hb 10 to 12 g/dL in women and 13.5 g/dL in men, moderate anaemia: Hb 8 to 9.9 g/dL and severe anaemia: Hb < 7.9 g/dL. ⁹ Findings were entered in proforma by the researcher.

A descriptive statistical analysis of continuous and categorical variables was performed. All collected data were entered into a statistical package for social sciences (SPSS) version 23.0. The ratio (male: female) was computed to present gender distribution. Data on continuous variables like age and duration of CKD were presented as mean $\pm$ SD. Categorical variables like gender, the severity of anaemia, HTN, DM and stages of CKD were presented as proportions. Stratification was done about age, gender, duration of CKD, duration, and frequency of DM, HTN, and stage of CKD.

3. Results

A hundred and thirty patients with chronic kidney disease (CKD) were selected during a study duration of one year, having a mean ($\pm$ SD) duration of CKD 7.05 ± 4.35 years. Among these 130 patients, 70 (54%) were males and 60 (46%) were females. The mean age was 56.30 ± 11.95 (Range = 24 – 90) years.

Out of 130 patients, the majority (55.4%) had severe anaemia, followed by 37.7% with moderate anaemia, and 6.9% with mild anaemia. There was no significant association of age and gender with the severity of anaemia ($p > 0.05$). The mean Hct (%) of patients was 35.90 ± 1.81 in mild anaemia, 26.90 ± 2.15 in moderate anaemia, and 19.80 ± 2.87 in severe anaemia which showed a significant difference with $p < 0.001$. There was a significant difference in haemoglobin level with severity of anaemia with $p < 0.001$ (i.e. 11.96 ± 0.60 g/dl in mild anaemia, 8.98 ± 0.73 g/dl in moderate anaemia and 6.59 ± 0.96 g/dl in severe anaemia). Similarly, urea, creatinine, and blood urea nitrogen were significantly associated with the severity of anaemia ($p < 0.05$) while MCV and albumin were not significantly associated with the severity of anaemia ($p > 0.05$). Further, the duration of CKD, diabetes mellitus and hypertension were not significantly associated with the severity of anaemia. Only 9 CKD patients were on erythropoietin treatment, of which 3 (33.3%) had mild anaemia, 4 (44.4%) patients with moderate anaemia, and only 2 (22.3%) were receiving erythropoietin treatment with severe anaemia. This difference was statistically significant with $p = 0.008$. The detailed association of the severity of anaemia with demographic and biochemical characteristics are presented in Table 1. The distribution of the severity of anaemia with the duration of CKD is presented in Figure 1.

Table 1: Demographic and Biochemical characteristics of CKD patients

	Anaemia Severity n (%)			P-Value
	Mild (n=9)	Moderate (n=49)	Severe (n=72)	
Gender				
Male	4(5.7)	26(37.1)	40(57.1)	0.822
Female	5(8.3)	23(38.3)	32(53.3)	
Age(years) ^o	57.11±9.22	57.73±12.16	54.06±13.70	0.146
HCT (%) ^o	35.90±1.81	26.90±2.15	19.80±2.87	0.000
Hemoglobin(g/dl) ^o	11.96±0.60	8.98±0.73	6.59±0.96	0.000
MCV (fl) ^o	89.25±9.61	84.60±8.83	84.57±6.77	0.228
Albumin(g/dl) ^o	2.94±0.65	3.17±0.62	3.08±0.66	0.574
Urea(mg/dl) ^o	79.33±26.19	125.39±39.21	155.40±55.65	0.000
Creatinine(mg/dl) ^o	4.62±2.66	4.48±2.82	6.81±3.85	0.001
Blood urea nitrogen(mg/dl) ^o	37.09±12.22	63.19±21.87	73.58±27.32	0.000
GFR(ml/min/1.73m2) ^o	18.79±10.22	17.20±9.82	12.00±6.94	0.001
CKD duration				
<1 – 4 years	4(7.8)	15(29.4)	32(62.7)	0.366
5-9 years	3(9.7)	11(35.5)	17(54.8)	0.366
>10 years	2(4.2)	23(47.9)	23(47.9)	
Diabetes Mellitus				
Yes	2(4.5)	19(43.2)	23(52.3)	0.562
No	7(8.1)	30(34.9)	49(57)	0.562
Hypertension				
Yes	3(3.9)	27(35.5)	46(60.5)	0.183
No	6(11.1)	22(40.7)	26(48.1)	0.183
On Erythropoietin				
Yes	3(33.3)	4(44.4)	2(22.2)	0.008
No	6(5)	45(37.2)	70(57.9)	0.008

Fisher exact test was applied.

^oMean±SD, ANOVA test was applied.

P-value ≤0.05, considered significant.

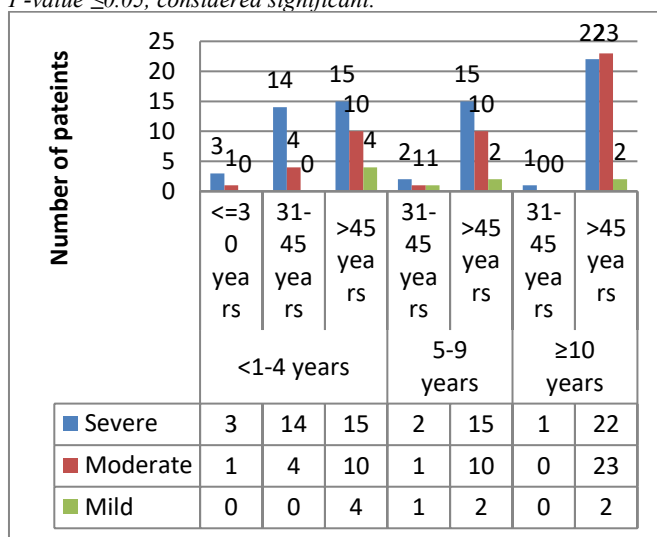


Figure 1: Frequency distribution of severity of anaemia with duration of CKD

4. Discussion

Malfunctioning of the kidney leads to anemia which is the most common complication of CKD. Anaemia is associated with a remarkably raised ratio of death, incorporating a higher probability of left ventricular

hypertrophy and cardiac failure.¹⁰ Even though the fatal sequel of anaemia is found more in patients with advanced chronic kidney disease, therefore, it is suggested that early treatment of anaemia in the case of renal disease could progress a better quality of life and slow down the advancement of renal failure.¹¹ In the case of CKD 60% to 80% of patients are affected by anaemia and this not only affects the quality of life but the risk of an early death rate.¹²

The manifestation of CKF and anaemia has been significantly known for decades. The anaemia exasperates as the function of the kidney declines, and the RBC count reduces to 20% or 15%.¹³ Thus, there is a need to conduct more studies. In our study, there was no significant difference between genders in CKD. A meta-analysis conducted in 2020 stated that females have a 36% higher chance of developing anaemia in CKD patients as compared to males.¹⁴

Haemoglobin and Hct levels were detected to decrease in the CKD patients as the disease advanced in this study. Multiple studies have also shown that the prevalence of anaemia increases as the function of the kidney declines.¹⁵ It is undeniable that a decrease in

kidney function leads to a drop in erythropoietin production.

Blood urea nitrogen, urea and creatinine were raised in our study population and the severity of anaemia increased as the BUN levels increased. A study conducted in a Korean cohort indicated the same results BUN is inversely associated with haemoglobin levels.¹⁶ Another research stated that raised levels of urea, creatinine and BUN can be used for supporting the diagnosis of CKD patients.¹⁷

This is because these laboratory tests are easy to be done and accurately measured.

For more principal findings of the research, regarding anaemia in CKD patients, NKF-K/DOQI guidelines were used to classify CKD. That divides CKD into 5 stages based on GFR and GFR was calculated with the help of the MDRD equation. Our patients lie in stages 4 and 5 of CKD. Anemia was divided into three categories mild, moderate, and severe.

In the conducted study prevalence and the severity of anaemia increased as the GFR declined. Another research analysis specified that anaemia is associated with higher kidney damage.¹⁸

The current study did not show a significant association between the duration of CKD and the severity of anaemia.

Our study indicated that CKD patients were suffering from comorbidities like DM and HTN along in different stages of anaemia but the difference was insignificant. Another study stated diabetes is the most common underlying cause among CKD patients with anaemia.¹⁹ Diabetes mellitus type 2, an inflammatory state, often augments the development of CKD and can also heighten the risk of anaemia in individuals with CKD.²⁰ As CKD is a progressive condition, especially in DM and hypertensive patients kidney function conservation can help in outcome.²¹

There is a need to conduct more research to find the relationship between timely management of anemia on pts with CKD. The results of this study confirm the earlier studies on the clinical course of anaemia of CKD. An optimal treatment program for the management of anaemia during chronic renal insufficiency according to the recommendations detailed in the NKF-DOQI guidelines could potentially improve subsequent outcomes among patients with kidney disease. Further studies are needed to evaluate the impact of the timely correction of anaemia during renal insufficiency on mortality, hospitalization, and costs among patients with

CKD. Although, our study is a single-arm cross-sectional study it serves as important data in local set-ups specifically for patients with chronic kidney disease regarding the prevalence and severity of anaemia and factors leading to it.

5. Conclusion

The severity of anaemia chronic kidney disease of the higher stage is an eye-opening finding. There is a need for early diagnosis and management of kidney disease and nevertheless, routine monitoring of kidney function, especially in diabetic and hypertensive patients.

Institutional Review Board Approval

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Contributions:

E.A, H.F.W - Conception of study

K.M, F.B - Experimentation/Study Conduction

N.P, A.A - Analysis/Interpretation/Discussion

E.A, H.A, S.N - Manuscript Writing

E.A, H.A, H.F.W - Critical Review

All authors approved the final version to be published & agreed to be accountable for all aspects of the work.

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