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Prevalence of Anemia and its Association with Kidney Function in Pre-Dialysis CKD Patients in Nepal: A Cross-Sectional Study

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Abstract

Background: Anemia, a common complication of chronic kidney diseases (CKD), is involved in significant cardiovascular morbidity. The present study aims to investigate the prevalence and association of anemia with kidney function in pre dialysis CKD patients.

Methodology: This cross-sectional study was conducted at Kathmandu medical college and teaching hospital from 2015 to 2016. The study sample comprised adults aged 18 or above and have had a serum creatinine value between 1.5 mg/dL and 6.0 mg/dL for females or between 2.0 mg/dL and 6.0 mg/dL for males within the past 12 months, and the patients who were stable for 3 months preceding study entry were eligible for the study.

Results: Of total 140 subjects, mean ages of the patients were 52.78 ± 1.54 years. The estimated prevalence of anemia was 53.6%. Anemia was predominantly prevalent (26.425) in stage 3 CKD, followed by stage 4 (18.57%), stage 5 (8.57%), stage 1/2 (7.14%), with their being high tendency towards the association (P<0.001). Prevalence of mild, moderate and severe anemia was 34 (24.28%), 17 (12.14%) and 24 (17.14%) respectively, and the severity of anemia significantly increased with deteriorating the renal function (P<0.001). A significant positive correlation was observed between Hb and GFR (r=0.496, p=<0.01)

Conclusions: Our study indicated that a substantial number of patients with CKD had anemia, and that the severity of anemia increased with the worsening of kidney function. Thus, the study stresses that an earlier intervention and timely management of the anemia in CKD population is essential thereby preventing the complication and improving quality of life.

Keywords: Anemia; Chronic kidney disease; Anemia; Chronic kidney

Introduction

Chronic kidney disease is an increasing worldwide threat to public health issue, and it is estimated to be 10.6% prevalent [1] in Nepalese population. Anemia is predictive of complication from CKD, [2-4], and is the result of several factors including decreased erythropoiesis due to inadequate erythropoietin (EPO) production from the kidneys, iron, B12 and folate deficiency due to nutritional insufficiency or increased blood loss, inflammation and accumulation of uremic toxins [5-9]. Untreated anemia is responsible for cognitive impartment, sleep disturbance, CKD progression, cardiovascular co-morbidities and significant mortality, increased health care cost, and decreased quality of life [9-12]. On the other hand correction of anemia has been shown to improve cardiac function [13], cognitive function [14] and quality of life [15,16]. Despite these benefits, the identification of anemia in Nepalese CKD population, especially on pre-dialysis, is lacking. Therefore, the present study aimed to investigate the prevalence of anemia in patients with CKD not on dialysis, and further to determine its association with kidney function.

Methods

Study design and duration

This cross-sectional study was conducted at Kathmandu medical college and teaching hospital from 2015 to 2016.

Patients' selection

The study sample comprised total 140 patients that satisfied the inclusion criteria. All adults aged 18 years or above and have had a serum creatinine value between 1.5 mg/dL and 6.0 mg/dL for females or between 2.0 mg/dL and 6.0 mg/dL for males within the past 12 months, and the patients who were stable for 3 months preceding study entry were eligible for the study. Patients undergoing dialysis, received treatment with epoetin alfa (including clinical study of epoetin alfa or any investigational forms of erythropoietic therapy), received iron supplementation, or received cytotoxic drug therapy within the past 3 months were excluded from the study. Patients were also excluded if they had a known diagnosis of human immunodeficiency virus, vitamin B12 or folate deficiency, hemolytic anemia, active gastrointestinal bleeding, or current treatment with drugs known to be nephrotoxic (i.e. aminoglycosides).

Data collection

Demographics including age, sex, CKD stage, CKD diagnosis time were approached for analysis. Laboratory data corresponding to anemia (hemoglobin, blood urea nitrogen, serum creatinine, TSAT and ferritin level) were assessed.

Estimation of GFR

GFR were estimated by using MDRD-4 equation [17]:

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- GFR=175 × $(SCr)^{-1.154}$ × $(age)^{-0.203}$ × (0.742) (if female)
- GFR units are mL/min/1.73 m^2.

CKD was classified into five stages defined by the GFR and/or evidence of kidney damage, as recommended by the National Kidney Foundation (Table 1) [18].

Criteria for anemia

Anemia was defined as serum hemoglobin levels ≤ 12 g/dL in women and ≤ 13 g/dL in men, as recommended by KDIGO clinical practice guideline for anemia in chronic kidney disease [19].

Criteria for severity of anemia

Anemic patients were further subdivided into three subcategories based on the severity of the anemia [20]

- **Mild:** males: Hb>12 g/dL and Hb≤13 g/dL, females: Hb>11 g/dL and Hb≤12 g/dL
- **Moderate:** males: Hb>11 g/dL and Hb=12 g/dL, females: Hb >10 g/dL and Hb=11 g/dL
- **Severe:** males: Hb ≤ 11 g/dL, females: Hb≤10 g/dL

Results

Table 2 illustrates the demographic and the clinical parameter of the enrolled patients. Of total 140 subjects, mean ages of the patients were 52.78 ± 1.54 years, with minimum 19 and maximum 89 years, and male population was 100 (71.4%). Mean hemoglobin were 12.39 ± 2.11 g/dl, with minimum 7 g/dL and maximum 17 g/dL. Mean transferrin saturation index (TSI) were 21.87 ± 3.05%, and more than half population 89 (63.6%) subjects had above 20% TSI. Mean ferritin level was 249.47 ± 71.19 ng/ml, with minimum 32 ng/ml and maximum 400 ng/ml.

Forty seven (33.60%) population had history of hypertension and 110 (78.6%) had diabetes mellitus. Mean serum creatine was 2.70 ± 2.24 mg/dL and glomerular filtration rate was 46.76 ± 24.13 ml/min/1.73 m^2. With regards to chronic kidney disease stage, more than half, 72 (51.4%), had stage 3 CKD, 34 (24.3%) had stage 1/2 CKD, 20 (14.3%) had stage 4 CKD and the remaining 14 (10%) had stage 5 CKD.

The estimated prevalence of anemia was 53.6%, with lower bond 47.7% and upper bond 59.5% (Table 3).

As seen in Table 4, mean ages in the anemic subjects were insignificantly higher than the non-anemic subjects (P>0.05). About one fourth (34.28%) male and 19.28% female population had anemia, with the association being statistically significant (p=0.037). Compared with the non-anemic subjects, anemic subjects had significantly higher eGFR (P<0.001), mean Hb level (P=0.001), and mean ferritin level (P=0.011). There were significant differences in TSAT (%) between anemic and non-anemic subjects (P=0.001) Anemia were predominantly prevalent (26.42%) in stage 3 CKD, followed by stage 4 (18.57%), stage 5 (8.57%), stage 1/2 (7.14%), and the tendency towards the association being significantly high (P<0.001).

Stage	Criteria
1	GFR ≥ 90 plus evidence of kidney damage
2	GFR 60-89 plus evidence of kidney damage
3	30-59
4	15-29
5	<15

Table 1: Classification of stage of CKD.

Parameter	Total population (n=140)
Age (years) ± SD (Min-Max) Sex, n(%)	52.78 ± 1.54 (19-89)
Male	100 (71.4)
Female	40 (28.6)
Hb (g/dL) ± SD (Min-Max)	12.39 ± 2.11 (7-17.90)
TSI (%) ± SD TSI (strata), n (%)s	21.87 ± 3.05
<20	51 (36.4)
>20	89 (63.6)
Ferritin (ng/ml) ± SD (Min-Max)	249.47 ± 71.19 (32-400)
HTN (+)	47 (33.60)
Diabetes mellitus (+), n (%)	110 (78.6%)
SCr (mg/dL), mean ± SD: (median)	2.70 ± 2.24: (1.7)
eGFR (ml/min/1.73 m^2), mean ± SD: (median)	46.76 ± 24.13 (43.62)
CKD stage, n (%)	
Stage 1,2	34 (24.3)
Stage 3	72 (51.4)
Stage 4	20 (14.3)
Stage 5	14 (10)

Table 2: Demographics and clinical characteristics.

	95% CI		
Anemia	Prevalence	Lower	upper
	53.6%	47.7	59.5

Table 3: Prevalence of anemia.

	Total (n=140)	Anemia (+)	Anemia (-)	P
Age Sex	140	75 ± 14.75	65 ± 16.33	0.85
Male	100	48 (34.28)	52 (37.14)	0.037
Female	40	27 (19.28)	13 (9.20)	
eGFR		38.11 ± 22.09	56.73 ± 22.62	0.001
CKD	140			0.001
Stage 1,2	34	10 (7.14)	24 (17.14)	
Stage 3	72	37 (26.42)	35 (25.00)	
Stage 4	30	26 (18.57)	4 (2.80)	
Stage 5	14	12 (8.57)	2 (1.40)	
Hb (g/dL)	140	10.92 ± 1.44	14.05 ± 1.44	0.001
TSAT				
<20	51	39 (27.85)	12 (8.57)	0.001
>20	89	36 (25.71)	53 (37.85)	
Ferritin	140	235.32 ± 66.75	265.80 ± 73.14	0.011

Table 4: Patient profile according to presence of anemia.

As presented in Table 5, the prevalence of mild, moderate and severe anemia was 34 (24.28%) 17 (12.14%) and 24 (17.14%) respectively. And the tendency of severity appeared to be significantly increased with decreasing the renal function (P<0.001). The mean Hb, TSAT (%) and ferritin level was 12.37 ± 2.12 g/dL, 21.87 ± 3.08, and 249.47 ± 71.19 ng/mL, respectively. The hemoglobin level was appeared to be decreased as the CKD advanced, with the difference being highly significant (P<0.001).

Similarly, the trend of TSAT (%) was found to be declined as the CKD advanced, except for stage 4 CKD (22.40 ± 4.07), and the tendency towards the association was found to be highly significant (P<0.001). Likewise, a decline pattern was observed for ferritin level as the CKD advanced except for stage 4 CKD (253.50 ± 85.99), and the difference was statistically highly significant (P<0.001).

As shown in Figure 1, Pearson's correlation revealed a significant

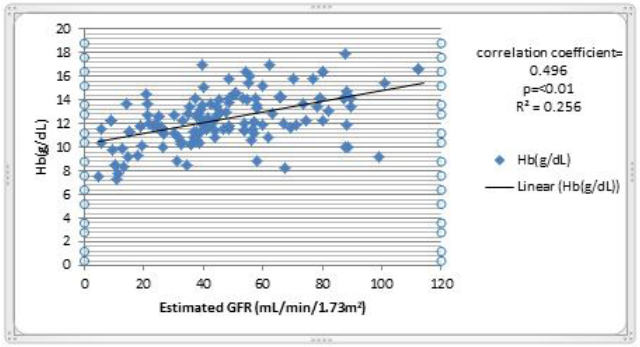

Figure 1: Correlation between hemoglobin concentration and glomerular filtration rate.

positive correlation between hemoglobin concentration and glomerular filtration rate (r=0.496, p=<0.01).

Discussion

This cross-sectional study evaluated the prevalence of anemia in adults with chronic kidney disease. The available literatures indicate a wide variation in prevalence of anemia in CKD patients across the nation. In this study anemia was estimated to be present in 53.57% in any stage of CKD, and the result is somewhat lower than the previous study, 58.5% by Aleix Cases-Amenos [4] and 75.8% by Salman M et al. [21]. Similarly, a higher prevalence of anemia (64.9%; defined as hemoglobin 13 g/dL for men, and 12 g/dL for women) was observed in US nursing home residents aged 64 with CKD stages 3-5 [22].

However, a lower prevalence seen in earlier study reported by McClellan et al. [23] where (47.7%) of patients had hemoglobin ≤ 12 g/dL and 8.9% of patients had hemoglobin ≤ 10 g/d) [4,24]. Similarly, In the MERENA observational multicentre study in Spanish cohort [25], with stages 3 and 4 CKD Patients, anemia prevalence was somewhat lower than our study (51.3% *vs* 53.57%). These wide variations might be explained by the differences in the inclusion and exclusion criteria of the study, the prevalence of the advanced stages of CKD, and some form of treatment provided in earlier studies.

In our CKD patients, more than half 72 (51.4%) subjects had stage 3 CKD, 34 (24.3%) stage 1/2 CKD, 20 (14.3%) stage 4 CKD and the remaining 14 (10%) had stage 5 CKD. The prevalence of CKD in different stages in our study population widely varies with the results reported in the previous studies [4,24].

Our study demonstrated that the prevalence of anemia was gradually increased as the CKD advanced, which corresponds well with the results of earlier studies [4,24]. As far as severity of anemia concerned, majority of the patients in this study was mild anemia followed by severe anemia. However, the prevalence of severity of anemia in this study was inconsistent with earlier: Salman [21] reported that most of the pateints had mild followed by moderate, whereas Reza et al. showed that most of the predialysis patients had moderate anemia followed by mild anemia [26]. We observed that the percentage of severe anemia in the last stage of CKD significantly increased, reflecting that the prevalence of anemia increase with declining renal function.

The mean ages of our study population was incomparable with the results showed in the earlier studies [4,21,23]. In previous report [23], the mean ages of the population were significantly higher in anemic patients than those without anemia (70 ± 14.9 years *vs* 64.7 ± 15.7 years, P<0.001). In our CKD population, however, the mean ages of the patients with anemia were insignificantly higher than those without anemia (75 ± 14.75 years, *vs* 65 ± 16.33 years, P=0.085). In agreement with the earlier reports [4,21], male population were predominantly high and the prevalence of anemia in male population were significantly higher (34.28%) than in female (19.28%).

In this study, mean GFR in anemic patients were notably lower (38.11 ± 22.09) than those without anemia (56.73 ± 22.62), with their being highly significant difference (P<0.001), and the result is in accordance with the previous study [4].

Available literatures [4,21] reported a varying hemoglobin level (10.9 ± 2.4-12.6 ± 1.6) in CKD patients. In our study population, mean Hb level was 12.37 ± 2.12. Similar to the findings of previous studies [4,21], our study showed a significant positive correlation between eGFR and Hb, and the tendency for hemoglobin level appeared to be decreased as the CKD advanced.

Iron stores evaluated in this study revealed that transferrin saturation and ferritin level was important predictors for anemia in pre-dialysis patients, and we noted that the TSAT (%) and ferritin level significantly declined as the kidney function deteriorate, which is in agreement with the results of earlier study [4].

Conclusion

Our study indicated that a substantial number of patients with CKD had anemia, and that the prevalence and severity of anemia increased with the worsening of kidney function. The study highlighted a positive correlation between GFR and Hb. The study provides an understanding of the profile of anemia and unveils that the CKD Patients, particularly at advanced disease, are at great risk for anemia. Thus, an earlier identification and effective management of anemia in pre-dialysis CKD patients seems crucial so as to prevent from the possible cardiovascular complication, and improve the clinical outcome.

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