Prevalence of Anemia and Its Associated Factors among Chronic Kidney Disease patients at University of Gondar Hospital, North West Ethiopia: a Hospital-based Cross Sectional Study

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Abstract

Background chronic kidney disease (CKD) is a global public health problem associated with progressive decline in kidney function and adverse cardiovascular outcome. Anemia in CKD has substantial adverse outcomes in CKD patients. There is paucity of published data on prevalence of anemia and its associated factors among CKD patients in Northwest Ethiopia. Objective This study aimed to determine the prevalence of anemia and its associated factors among CKD patients at University of Gondar hospital, Northwest Ethiopia. Methods A hospital-based cross-sectional study was conducted from May 1, to September 30, 2018. Consecutive sampling was used to recruit 251 study subjects. Data regarding patient’s socio-demographics, clinical characteristics and laboratory parameters were collected from patients’ interview and medical records. Data was analyzed using SPSS version 20. Bi-variate and multi-variate logistic regression analyses were used to identify predictors of anemia in CKD patients. P<0.05 was used to declare association. Results The prevalence of anemia was high (64.5%), and tended to increase as eGFR declined. Hypertension (45%), chronic glomerulonephritis (24%) and diabetes (20%) were common causes of CKD. Multivariate logistic regression analysis revealed rural residence (AOR=2.75, 95% CI: 1.34-5.65, p=0.006), BMI<18.5 kg/m2 (AOR=6.78, 95% CI: 1.32-34.73, p=0.022) and BMI of 18.5-24.9 kg/m2 (AOR=5.04, 95% CI: 1.26-20.10, p=0.022), and having hemodialysis history (AOR=3.59, 95% CI: 1.24-10.38, p=0.018) were predictors of anemia in CKD patients. Conclusion Prevalence of anemia in CKD patients was high (64.5%). Rural residence, non-obese body habitus and having hemodialysis history were found to be predictors of anemia in CKD patients. Periodic screening and intervention for anemia in CKD patients should be practiced to prevent its sequelae.

Background

Chronic kidney disease (CKD) is progressive, irreversible damage to the kidneys, which leads to inability of the kidneys to perform homeostatic, synthetic and excretory functions. Estimated epidemiological prevalence of CKD in global and Sub-Saharan Africa was reported to be 12–15 % and 10-15% respectively (1-7). The evident reasons for escalating burden of kidney failure in Africa were due to growing urbanization, environmental pollutant exposure, high burden of infectious diseases and increasing rate of non-communicable diseases such as diabetes and hypertension (5-7). Studies from Ethiopia documented institution-based prevalence of CKD in diabetic (high risk) patients were 21-24% (13,14).

Common etiologies of CKD in Africa were hypertension, chronic glomerulonephritis and diabetes. Up to 10% of HIV patients documented to have renal dysfunction. Complications of CKD included anemia, metabolic bone disease, metabolic acidosis, fluid and electrolyte imbalance and uremia, which imposed considerable burden on health care resources (5,7,11,12).

Anemia is a common and significant complication in chronic kidney disease. Study-based estimated prevalence of anemia were 15% in U.S. CKD patients, 45-55% in Asian CKD patients , and 51-87% in African CKD patients (3,4,11,12).
The mechanisms of anemia of CKD include erythropoietin deficiency from reduced renal mass, uremia-induced inhibited erythropoiesis, shortened red cell survival, and disordered iron homeostasis (8,9).

Anemia in CKD patients is significantly associated with worsening CKD, and development of heart failure and stroke. It contributes to impaired physical activity, neurocognitive dysfunction and poor quality of life (9,15,16,22,23).

Documented predictors of anemia in CKD include, but not restricted to, female gender, advanced stage of CKD, diabetic nephropathy as etiology, non-smoking status, non-obese body habit, low serum albumin, abnormal bone minerals level (high phosphorus and low calcium levels), abnormal iron markers (transferrin saturation<20%, serum ferritin level>100 ng/ml), and low leukocyte count (4, 14,17).

Hence, this study was the first of its kind designed to disclose prevalence and predictors of anemia in CKD patients in Northwest Ethiopia.

**Methods**

Study settings and design

A hospital-based cross sectional study was conducted from May 1, 2018 to September 30, 2018 at University of Gondar hospital. The hospital is located in Northwest Ethiopia, which is 750 km away from the capital, Addis Ababa. The hospital has a catchment population of five million people.

Study subjects and variables

Source population was all CKD patients visiting University of Gondar hospital. Patients 18 years and above with an established diagnosis of CKD as per KDIGO criteria regardless of its primary cause was considered as study population. Those study subjects who provided informed consent was included in the study. Patients with known cause of anemia other than renal disease, pregnant women, renal transplant patients and those unwilling to participate were excluded.

Sample size and sampling procedure

The sample size was calculated using Fisher's formula (18) at a prevalence of 80% with a confidence interval of 95% and degree of precision of 5%. Consecutive sampling was used to recruit 251 study subjects.

Data collection

Data were collected through an investigator administered pre-tested questionnaire. Patients were interviewed to obtain demographic data, and the patients records were reviewed to obtain information on relevant medical history like etiology and duration of CKD, medication history, and laboratory parameters including complete blood count (hemoglobin level, leukocyte count and platelet count), urinalysis, blood chemistry (liver function tests, renal function tests and blood sugar level), abdominal ultrasound and HIV.
serology. The hemoglobin level was used to define anemia according to World Health Organization (WHO) criteria (19). The serum creatinine was used to estimate GFR using CKD-EPI equation (20).

Dependent variable: Anemia was the dependent variable, as defined by WHO criteria.

Independent variables: Socio-demographic factors including age, sex, place of residence, educational status and marital status; behavioral factors including smoking and alcohol drinking; and clinical characteristics including cause, duration and stage of CKD, presence of comorbidity, dialysis status, body mass index (BMI), blood pressure level, presence/absence of proteinuria and treatment status for anemia.

Data analysis

Data was entered into EPI Info version 4.4.1 and transported to SPSS version 20 for analysis. Descriptive statistics, such as median and inter quartile ranges (IQR) was used to compute continuous variables, and counts with percentage for categorical variables. Both bi-variate and multivariate logistic regression analysis was fitted to identify predictors of treatment failure. Those variables with a p. value < 0.2 in the bi-variate analysis were exported to multivariate analysis to control the possible effect of confounders. AOR with 95% CI and P-value < 0.05 in multi-variate analysis was used to select variables as predictors of anemia in CKD patients.

Definition of terms

CKD was defined as abnormalities of kidney structure or function present for more than 3 months, with implications for health. CKD is classified based on cause, GFR category (G1-G5) and albuminuria (A1-A3), abbreviated as CAG according to the KDIGO guideline. GFR was calculated by using CKD-EPI equation.

Anemia was defined as hemoglobin level <12g/dl in females and <13g/dl in males in ≥18 years of age.

Chronic glomerulonephritis was defined as presence of loin pain, hematuria, or/and proteinuria with ultrasound-proven reduced kidney size (≤8 cm) and loss of cortico-medullary differentiation.

Hypertension as cause of renal disease was defined as presence of documented history of hypertension predated renal disease (reduced eGFR).

Diabetic nephropathy (DN) was defined as long-standing known diabetes, urinalysis evidence of significant proteinuria and ultrasound-proven normal/increased renal size.

Ethical considerations

Ethical clearance was obtained from the Research Ethical Review Board of College of Medicine and Health Sciences, University of Gondar. Formal letter of permission was obtained from University of Gondar hospital administrative body. Study subjects were recruited only after informed written consent was obtained from them. All data obtained will be treated confidentially. During the data collection
process, those patients who were found to have anemia were taken care of as per the recommendations of CKD guidelines, and advice on preventive measures was given to all participants.

**Result**

**Socio demographic characteristics of study participants**

Among a total of 251 CKD patients, 161 (64.1%) were males and 90 (35.9%) were females. The median age of study subjects was 60 years (IQR=44-69). Majority of patients (61%) were aged from 45 to 75 years. Most of them were non-smoker (95%), non-alcoholic (76%), married (77%), and Orthodox Christian by religion (84%). Majority 142 (57%) were urban dwellers and 118 (47%) joined formal education (Table 1).

6.2. Clinical & Laboratory profile of CKD patients

Hypertension accounted for 45% as cause of CKD, followed by chronic glomerulonephritis (24%) and diabetes (20%). HIV/AIDS was ascertained as etiology of CKD in 2% of cases. Majority of the patients were in KDIGO stage 3 (49%), followed by KDIGO stage 5 (26%) and 4 (21%) (Figure 1). Two-third of patients 180 (71.7%) were positive for proteinuria using urinalysis dipstick. One-hundred four (53.3%) had massive proteinuria (≥2+ proteinuria). One-fifth 51 (20.3%) had ultrasound-proven bilateral shrunken kidneys (≤8 cm), which was evidence for end-stage renal disease (ESRD). Only 32 (12.7%) of patients were having history of hemodialysis (Table 2 and 3).

**Prevalence of anemia among CKD patients**

The overall prevalence of anemia in this study was 64.5% (95% CI: 58.6, 70.5%). The prevalence of anemia increased with worsening kidney function: stage 1 & 2, 3A, 3B, 4 & 5 CKD were 20%, 44.8%, 46.4%, 81.1%, 93.8% respectively (Table 2). Severe anemia (Hgb<8g/dl) was documented in 49/251 (19.5%) CKD patients. Forty-two (25.9%) patients were receiving therapy among those who had documented anemia. The frequent types of therapy were packed blood transfusions 23/42 (55%) and hematinsics 23/42 (55%). Only 6/42 (14.3%) patients received erythropoietin (Figure 2).

**Factors associated with anemia among CKD patients**

Multivariate logistic regression analysis was used to identify potential predictors of anemia among CKD patients. Accordingly, rural residence (AOR=2.75, 95% CI: 1.34-5.65, p=0.006), BMI<18.5 kg/m² (AOR=6.78, 95% CI: 1.32-34.73, p=0.022) and BMI of 18.5-24.9 kg/m² (AOR=5.04, 95% CI: 1.26-20.10, p=0.022), having hemodialysis history (AOR=3.59, 95% CI: 1.24-10.38, p=0.018) were found to be predictors of anemia in CKD patients. Those with diastolic blood pressure (DBP) between 80-89 mmHg (AOR=0.37, 95% CI: 0.16-0.92, p=0.025) were protected from anemia of CKD (Table 4).

**Discussion**
The overall prevalence of anemia among CKD patients was 64.5%, with in the range in African studies report (51-87%) (8,11-13). Recent NHANES report in the United States revealed the prevalence of anemia was twice (15.4%) in CKD patients as compared to non-CKD population (7.5%) (2,3).

A population survey report in the United States showed prevalence of anemia increased with progressive decline in eGFR, from 8.4% at stage 1 to 53.4% at stage 5. (3). Recent Korean cohort revealed similar finding, prevalence of 10% at stage1 to 96.5% at stage 5(4). Similar finding was reported in Ethiopia in high-risk (diabetic) patients (14).

Main etiologies of CKD were hypertension, chronic glomerulonephritis (CGN) and diabetes, congruent with studies from low-and middle-income countries (5,7,10-13). CGN-caused CKD was frequent, as similarly reported in other African countries, possibly related to high prevalence of viral, bacterial, protozoan and helminthic infections/ infestations (10-12). HIV-associated renal disease was low (2%), unlike studies from Sub-Saharan Africa (10).

As in other developing countries, most patients (96%) in this study presented in advanced stage of CKD (stage 3-5), unlike the situation in developed countries (4). Presumed reasons for Patients’ late presentation might be due to low detection and treatment rate of CKD risk factors like hypertension and diabetes, lack of regular CKD screening program and preference to use of alternate treatment (6,7,10,12).

Rural residence was found to be significant predictor of anemia in CKD patients (AOR= 2.75, 95% CI: 1.34-5.65, p=0.006). Rural resident patients might seek health facility late with advanced renal disease. Concomitant presence of nutritional deficiencies, gastrointestinal blood loss or helminthic infestations might contribute to anemia (10).

Those CKD patients with non-obese body habitus was found to be at higher risk of anemia as compared to those with obese body habitus. A cohort study in Korea showed lower BMI was associated with elevated risk of anemia. Lower odds ratio for anemia was reported for higher BMI. Underweight represents the malnourished state, which is closely related with inflammation in advanced renal disease (4).

Anemia of CKD significantly occurred in those who had history of hemodialysis (AOR=3.59, 95% CI: 1.24-10.38, p=0.018). Hemodialysis requiring patients had end stage renal disease (ESRD).

Those CKD patients with DBP (80-89 mmhg) (AOR=0.37, 95%CI: 0.16- 0.92, p=0.025) were protected from anemia of CKD. Normal or controlled blood pressure in CKD patients might indicate early stage renal disease or attenuated renal disease progression respectively (21).

Worsening anemia of CKD leads to adverse cardiovascular events like left ventricular hypertrophy, heart failure, and myocardial ischemia and infarction. CKD and anemia are frequent among stroke patients and are potential risk factors for decreased survival. Anemia of CKD increases risk of cardiovascular related morbidity and mortality (9,15,16,22-25).
Limitation of the study

Prospective study would have been better to identify predictors of anemia in CKD patients. eGFR rather than measured GFR was used to diagnose impaired kidney function.

**Conclusion**

Prevalence of anemia in CKD patients was high (64.5%), and tended to increase as renal function deteriorated. Hypertension (45%), CGN (24%) and diabetes (20%) were common causes of CKD. Rural residence, non-obese body habitus and having hemodialysis history were identified predictors of anemia in CKD patients.

**Recommendation**

Appropriate screening program for early detection of CKD in high risk individuals (patients with hypertension or diabetes) should be practiced. Periodic screening and intervention for anemia in CKD patients should be encouraged to prevent its sequelae.

**Abbreveiations**

CKD: chronic kidney disease; CGN: chronic glomerulonephritis; AOR: adjusted odds ratio; COR: crude odds ratio; eGFR: estimated glomerular filtration rate; ESRD: end stage renal disease; BMI: body mass index, HIV: human immunodeficiency virus; SBP: systolic blood pressure; DBP: diastolic blood pressure; KDIGO: kidney disease/improving global outcomes; WHO: world health organization.

**Declarations**

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**Availability of data and materials**

All data generated and analyzed are included in this research article.

**Authors’ contributions**

HA was actively involved in study design, data collection, statistical analysis and wrote the manuscript. WH, AA and AT contributed in study design, and reviewed and edited the manuscript.
Ethics approval and consent to participate

Ethical approval was obtained from College of Medicine and Health Sciences, University of Gondar. Informed consent was obtained from all study participants in written format.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interest.

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Tables

Due to technical limitations, all Tables are only available as a download in the supplemental files section.

Figures
Figure 1

Stages of CKD by eGFR using CKD-EPI equation
Figure 2

Prevalence rate of anemia across stages of CKD

Supplementary Files

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- Tables.docx