## PREVALENCE OF ANEMIA AND ASSOCIATED FACTORS AMONG STAGE 3-5 CHRONIC KIDNEY DISEASE PATIENTS, JUMC, SOUTHWEST ETHIOPIA



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A RESEARCH THESIS TO BE SUBMITTED TO JIMMA UNIVERSITY, INSTITUTE OF HEALTH, MEDICAL FACULTY, DEPARTMENT OF INTERNAL MEDICINE; IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR SPECIALIZATION IN INTENAL MEDICINE.

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# PREVALENCE OF ANEMIA AND ASSOCIATED FACTOR AMONG STAGE 3-5 CHRONIC KIDNEY DISEASE PATIENTS, IN JIMMA MEDICAL CENTER, SOUTHWEST ETHIOPIA

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#### ABSTRACT

**Background:** Anemia is a common and serious complication of chronic kidney disease (CKD) that starts during the early stage of the disease and worsens as the kidney function deteriorates. It contributes considerably to reduced quality of life of patients with CKD and has been associated with a number of adverse clinical outcomes. Early identification and treatment of anemia may improve cardiovascular morbidity and mortality in CKD patients.

**Objective:** To determine the prevalence of anemia and associated factors among non-dialysis (ND) CKD patients in Jimma Medical Center, Southwest Ethiopia.

**Methods and participants:** An institution based cross sectional study was conducted among 150 CKD patients who were 18 years and above at JMC from September 1 to November 30, 2020 G.C. Two qualified nurses and one medical resident collected the relevant data through an investigator administered pretested questionnaire after taking verbal consent of participants. Data were entered using EPI data manager version 4.6 and analyzed using STATA version 16.0. Bi-variable and multivariable logistic regression analyses were done to identify independent factors associated with anemia among CKD patients. Those variables with a P-value <0.2 in the bivariate analysis was exported to multivariate analysis to control the possible effect of confounders. Adjusted odds ratio (AOR) with 95%CI and P-value <0.05 was used to select variables associated with anemia in CKD patients.

**Results:** Out of 150 ND-CKD patients 128 (85.33%) were anaemic. From 128 anaemic ND-CKD patients, 40.67% had moderate aniemia, 28.67% had mild form of anemia, and 16% had severe anemia. Being in the 18-39 years age group (AOR= 4.05, 95% CI: 1.04-15.73) compared to those in the age group of 40-64 years old, being male (AOR= 4.92, 95% CI: 1.51-16.07), income < 1000 ETB per month (AOR= 4.13, 95% CI: 1.01-17.04) compared to those with income 1000-5000 ETB a month were found to have statistically significant association with anemia among CKD patients in Jimma medical center, Southwest Ethiopia.

**Conclusion:** High number of ND-CKD patients were had anemia and most had moderate anemia. Age category of 18-39 years, male patients, and earning less than 1000 birr a month were independently associated with higher risk of anemia among ND-CKD patients. Further longitudinal studies were required to establish the causal relations of anemia among this population.

Key words- JUMC, CKD, anemia, prevalence, Ethiopia

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## List of abbreviations and acronyms

ACEi: Angiotensin Converting Enzyme Inhibitor

- CCB: Calcium Channel Blocker
- CGN: Chronic Glomerulonephritis
- CKD: Chronic Kidney Disease
- D-CKD: CKD On Dialysis
- DN: Diabetic Nephropathy
- eGFR: Estimated Glomerular Filtration Rate
- ESA: Erythropoesis Stimulating Agent
- EPO: Erythropoetin
- Hgb: Hemoglobin
- IDA: Iron Deficiency Anemia
- KDIGO: Kidney Disease: Improving Global Outcomes
- KNOW-CKD: Korean Cohort Study for Outcome in Patients with Chronic Kidney Disease
- MDRD: Modification of Diet in Renal Disease
- ND-CKD: CKD Not on Dialysis
- HRQOL: Health Related Quality of Life
- PI: Principal Investigator
- RBC: Red Blood Cells
- JUMC: Jimma University Medical center
- TSAT : Transferring Saturation Percentage
- WBC: White Blood Cells
- BMI: Body Mass Index
- NHANES: National Health and Nutrition Examination Survey

#### **CHAPTER-ONE**

#### **INTRODUCTION**

#### **1.1. BACKGROUND**

Anemia is an absolute reduction of the total number of circulating red blood cells (RBC) resulting in a reduction of hemoglobin concentration <13.0 g/dL for adult males and postmenopausal women and an Hgb <12.0 g/dL for premenopausal women (1-3).

Anemia is a common complication of CKD(3, 4). Studies showed that the prevalence of anemia in CKD is different in different population groups. The overall prevalence was 15.4% in USA(5), 30-58.5% in Europe(6-9), 32–82% in Asia(10-14), 50–97% in Africa(15-18) and 30%-64.5% in Ethiopia(19, 20). Anemia presents during the early stage of the disease and increases in prevalence and severity as the kidney function deteriorates (3, 4, 21, 22).

The cause of anemia in CKD is multifactorial. The primary cause is a deficiency of erythropoietin (EPO), which is a hormone responsible for the production of RBCs. Kidney is a major site for EPO production contributing 80-90% of the EPO in circulation. As CKD progresses specialized peritubular cells that produce EPO are partially or completely depleted or injured resulting inappropriately low EPO(23). The other possible causes of anemia in CKD are iron deficiency, shortened red cell life span, uremic environment-induced inhibitors of erythropoiesis and inflammation (3, 4, 22, 24).

Anemia in CKD is associated with cognitive impairment, sleep disturbances, CKD progression and increased risk of cardiovascular and cerebrovascular events(25, 26). In addition, there is an increased hospitalization and all-cause mortality among these patients (4, 27-30).

Since the advent of recombinant human erythropoietin, erythropoiesis-stimulating agents (ESA) have become the cornerstone of anemia treatment in CKD patients and have resulted in reduced requirement for blood transfusion, improved the quality of life, reduced left ventricular hypertrophy, morbidity and mortality in these patients(4, 11, 22, 31-35). According to KDIGO 2012 guideline, the recommended hemoglobin level for CKD patients taking ESA for the treatment of anemia is 10-12 g/dl since the total anemia correction with ESA is not associated with better survival or a significant improvement in quality of life(2). Apart from therapy with ESAs, the other essential management of anemia in CKD patients is iron replacement(4).

Despite all of these advances on understanding of anemia in CKD and its treatments, I couldn't find a published study on prevalence, associated factors and treatment of anemia among CKD patients in the Southwest Ethiopia according to my thorough search. Therefore, the aim of this study is to disclose the prevalence of anemia, its associated factors and treatment among CKD patients in this setting.

#### **1.2 STATEMENT OF THE PROBLEM**

Over the past few decades, there have been major advances in the knowledge of prevalence, causes and natural history of anemia in CKD patients. The advent of effective ESAs in the late 1980s has resulted in major advances in the management of anemia in these patients.

Anemia is a universal complication of chronic kidney disease (CKD). The prevalence of anemia in CKD in USA is 15.4% according to one cross sectional study which was published in 2014(5). The studies from European countries showed 30%-58.5% of CKD patients had anemia (6, 8, 9). Several studies on this topic were published from different Asian countries that showed the prevalence was in the range of 32% (Japan) to 82% (Saudi Arabia) (10-14). The prevalence is even higher in African countries with prevalence of 50%-97% (15-18). After doing a thorough search, I found only two published studies on prevalence of anemia among CKD patients that were conducted in Ethiopia. The first one was done in Tikur Anbesa specialized hospital, Addis Ababa and the other study was done in Gondar, Northwest Ethiopia. Accordingly, the prevalence of anemia in CKD was 30% and 64.5% in Addis Ababa and Gondar respectively(19, 20).

The prevalence of anemia increases with the stage of CKD (5, 7, 11, 17, 19). Several studies demonstrated the association of lower baseline eGFR, significant proteinuria (>1 g/24h), older age and male gender with a higher prevalence of anemia (8, 36-39). The study from Gondar, Ethiopia showed anemia was significantly prevalent in rural residents, patients with non-obese body habitus and in those with a history of hemodialysis(19).Studies from the Western world documented it was significantly associated with diabetic nephropathy (40) while African studies demonstrated it was significantly prevalent in CKD of chronic glomerulonephritis(CGN)(17, 19). Anemia in CKD patients was significantly associated with left ventricular hypertrophy, heart failure, myocardial ischemia and infarction (25, 28, 29, 32, 41, 42). It was also associated with a substantial higher risk of stroke(26, 31) and a lower HRQOL(43). As well, it increased CKD progression, hospitalization, risk of cardiovascular related morbidity and mortality (28-30, 35, 41, 44, 45).

Furthermore, treatments for anemia include iron supplementation and erythropoietin stimulating agents(4, 5, 22). Untreated anemia in CKD patients has been shown to result in negative effects on cardiac, cognitive, and immune functions, as well as survival, while appropriate treatment can significantly improve quality of life, survival and slow disease progression (32-34, 46, 47).

There is shortage of ESA supply in Ethiopia and the price of the drug erythropoietin (EPO) is also expensive. So, most of the patients can't afford to buy the drug. According to my thorough

search, I couldn't find a published study so far in Southwest Ethiopia on prevalence, associated factors and treatment of anemia among CKD patients. I have observed a knowledge gap about anemia among CKD patients in our setup. Therefore, this study is expected to fill this knowledge gap and it is important for clinicians to be aware of the problem in this part of the country. This study has provided us data that will influence the provision of comprehensive and effective management of anemia in CKD patients.

#### **1.3 SIGNIFICANCE OF THE STUDY**

The prevalence of anemia in patients with CKD is said to be high all over the world. I tried to search for any study on prevalence of anemia, its associated factors and treatment among CKD patients in Ethiopia and in southwest Ethiopia in particular. Based on my thorough search, I found only two published studies in Ethiopia that were done in Addis Ababa and Gondar. The first study was conducted in Tikur Anbessa specialized hospital nephrology unit and pharmacy department, Addis Ababa which reported the prevalence of anemia among all stages of CKD patients. This study was primarily done to assess medication adherence and it didn't assess the associated factors. The other study was done in Gondar, Northwest Ethiopia on prevalence of anemia and associated factors among all stages of CKD patients. This study included all patients who had history of hemodialysis and it studied treatment status and options of treatment of anemia in CKD patients but it didn't study the cause of anemia. So far, I couldn't find any study addressing this issue in the Southwest Ethiopia according to my thorough search. The aim of this study is to fill this knowledge gap.

In our hospital, I have seen many CKD patients suffering from anemia and these patients were not thoroughly investigated for its cause and also they were not adequately managed due to the financial limitation of patients. So, I am interested to address this problem in my study.

In this study, we have determined the prevalence of anemia; identify associated factors and treatment gaps of anemia in CKD patients. Since iron deficiency is a common and treatable cause of anemia in CKD patients, we have determined the level of iron store (serum ferritin) in these patients.

The result of this study will build physicians knowledge about these patients in Southwest Ethiopia as well as all over the country. This will improve quality of care to patients, increases adherence and decrease overall cost of medical care. The result will also be a gate way for further study on CKD complications and will advance quality of evidence-based medicine in Ethiopia. It will also bring some data for program developers to concentrate on the problem.

It was therefore justifiable to have this study, which has described the prevalence and associated factors of anemia in CKD patients as the information that was obtained will help in designing the appropriate treatment measures of anemia, so as to reduce complications and morbidity among patients with CKD.

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#### **CHAPTER-TWO**

#### LITERATURE REVIEW

#### 2.1 Prevalence of anemia and associated factors in CKD patients

There are a number of studies about prevalence of anemia worldwide. There is significant difference in prevalence between the studies because of the difference in population under study. It is as low as 15.4% in USA and as high as 64.5% in Ethiopia and 77.5% in Nigerian studies. Prevalence of anemia increase as kidney function decreases.

The Korean Cohort Study for Outcome in Patients with Chronic Kidney Disease (KNOW-CKD) is a prospective nationwide cohort study to investigate natural courses and risk factors for progression of Korean CKD. 2,198 stage 1–5 non-dialysis CKD patients were enrolled from 9 hospitals throughout Korea between June 2011 and February 2016. Overall prevalence of anemia was 45.0% among stage 1 to 5 CKD patients. More than half (51.8%) of female CKD patients had anemia. Diabetic nephropathy (DN) as a cause, CKD stages, body mass index (BMI), smoking, leukocyte count, serum albumin, iron markers, calcium, and phosphorus concentration were identified as independent risk factors for anemia. Diabetic nephropathy (DN) had the highest overall prevalence of anemia (75.9%) than other etiologic subgroups. The lower BMI of 18.5–22.9 was associated with elevated risk of anemia compared with BMI between 23.0 and 24.9 as the reference. Current smoker showed 42.0% reduction of risk for anemia compared with non-smoker(11).

A literature review on burden of anemia in CKD patients in Japan, which was published in 2018, examined relevant manuscripts and abstracts published from 2004 onward. It included CKD patients with anemia, and the outcomes of interest were epidemiology, economic, humanistic, and treatment patterns. The overall prevalence of anemia among patients with stage 3–5 CKD was approximately 32%. The prevalence varied largely (0–95%) based on the different definitions of anemia as well as dialysis status. It increased with CKD severity (lower eGFR) and also among patients who were on HD(12). In other study in Japan, the prevalence of anemia increased in patients with diabetic nephropathy, low serum albumin and along with the progression of CKD stage(36).

There was an analysis of cross-sectional data in USA which was reported in 2014. In this study, data from the National Health and Nutrition Examination Survey in 2007–2008 and 2009–2010

were used to determine the prevalence of anemia in subjects with CKD. Accordingly, from a total of 12,077 adults participated in the interview and examination components of the NHANES surveys, the prevalence of CKD was 14.0% and that of anemia in people with CKD was 15.4%. The prevalence of anemia increased with stage of CKD, from 8.4% at stage 1 to 53.4% at stage 5(5).

In another large cross-sectional survey conducted in many renal centers in USA, anemia was present in 47.7% of 5,222 predialysis patients with chronic kidney disease. Blacks are found to have 3 times increased risk for anemia than white counterpart(38).

In Catalonia study involving 504 patients (56.4% male, mean age of  $67.8\pm15.5$  years): 61.5% had stage 3 CKD, 30.2% stage 4 and 8.3% stage 5. The overall prevalence of anemia was 58.5% (n=295), however, only 14.9% of patients had hemoglobin levels <11g/dl. This study demonstrated significant association of higher prevalence of anemia in CKD with older age, diabetic nephropathy, lower eGFR and stage of CKD (as CKD progresses, a higher presence of anemia is observed)(7).

In the MERENA observational multicenter cohort study, conducted on 1129 patients with stages 3 and 4 CKD tested in outpatient Nephrology clinics in Spain, anemia prevalence was 51.3%. This study did not include patients with stage 5 CKD(6). In another study which was conducted in 1058 patients with CKD not on dialysis in Italy, the prevalence of anemia was 16%, 32% and 51% in stages 3, 4 and 5 respectively(9).

The prevalence of anemia in CKD is even higher in African studies. For example, Chinwuba Ijoma studied 364 patients (mean age 44.8±14.8 years) and 143 control subjects (mean age 43.52±12.00 years, P=0.35) in Enugu Nigerian. Overall, 77.5% of CKD patients and 11.9% (P<0.001) of control subjects had anemia defined as hemoglobin less than 12 g/dL. Anemia increased progressively with declining GFR with mean hemoglobin concentration of 12.91±1.35 g/dL, 12.14±1.96, 10.57±2.42, 8.84±2.19 and 7.33±1.74 for CKD stages 1 to 5, respectively. Chronic glomerulonephritis(CGN), human immunodeficiency/retroviral disease, collagen vascular disease and chronic pyelonephritis were predictor of anemia in CKD(17).

The study in Tanzania revealed the overall prevalence of anemia among 100 CKD patients was 97%(18). Studies from Kenya and Ghana demonstrated prevalence of anemia was 67% and 86.7% respectively(15, 16).

In a study done by Belayneh Kefale, Yewondwossen Tadesse et al in Tikur Anbessa Specialized hospital nephrology unit and pharmacy department involving 256 patients in all stages of CKD, 30% of patients are reported to have anemia out of which 92% are on iron therapy. But the study was primarily done to assess medication adherence and further characterization of the result is difficult(20).

There was a hospital-based cross-sectional study which was conducted from May 1 to September 30, 2018, in university of Gondar hospital, Northwest Ethiopia. Among a total of 251 all stage CKD patients, the overall prevalence of anemia was 64.5%. Anemia was significantly prevalent in patients with chronic glomerulonephritis among other underlying causes of CKD (P-value <0.001). The prevalence of anemia increased with worsening kidney function: stage 1, 2, 3, 4 and 5 CKD were 20%, 44.8%, 46.4%, 81.1%, 93.8% respectively. According to this study, rural residence, BMI of 18.5–24.9 kg/m2 and <18.5 kg/m2 and having hemodialysis history were independently associated with anemia among CKD patients(19).

#### 2.2 Treatment of anemia among CKD patients

Despite high prevalence of anemia in CKD patients, it is usually under diagnosed and under treated condition. Most patients don't have proper work up for their anemia. The proportion of CKD patients being treated for their anemia is strikingly very low. This is also true even in high income countries and tertiary centers.

Among 2,125 CKD patients with anemia in USA total of 22.8% of reported being treated for it. Treatment frequencies were similar at stages 1 and 2 (12.1% and 16.2%; P=0.57; weighted mean 14.6%) and stages 3 and 4 (26.5% and 20.7%; P=0.76; weighted mean 26.4%)(5).

Among 2,127 Korean subjects with CKD stage 1–5 (KNOW-CKD study) with TSAT and ferritin levels available at enrollment, 297 patients (14.0%) had TSAT less than 20.0% and 1,070 (50.3%) had ferritin less than 100 ng/ml. The proportion of patients having TSAT less than 20.0% was higher in patients with anemia than without anemia (20.0% vs. 9.2%; respectively, P<0.001). Of 938 patients with anemia, 44.3% showed TSAT more than 20.0% and ferritin more than 100 ng/ml. Among patients with anemia, the prescription rate of iron agents was 28.7% when TSAT was less than 20.0% and 27.5% when TSAT was higher than 20.0%. Only 6 (1.2%) out of 520 patients who are candidates for intravenous iron supplement according to KDIGO guidelines were managed by intravenous iron. The number of patients having hemoglobin level less than 10 g/dl was 177 (8.1%) out of 2,198 subjects. Among them, 59 patients (33.3%) received ESAs(11).

In another prospective study on anemia management in two visits, performed 6 months apart, in 755 ND-CKD stage 3b-5 patients followed in 19 nephrology clinics. Prevalence of severe (hgb<11gm/dl) and mild (hgb>11gm/dl) anemia was 18.0% and 44.0% at baseline and remained unchanged at Month 6 (19.3 and 43.2%). Iron deficiency was prevalent at both visits (60.1 and 60.9%). There is significant Clinical inertia among physicians to start ESA at baseline and at Month 6 (39.6 and 34.2%, respectively, P = 0.487) and it was less frequent than clinical inertia to iron therapy (75.7 and 72.0%, respectively)(48).

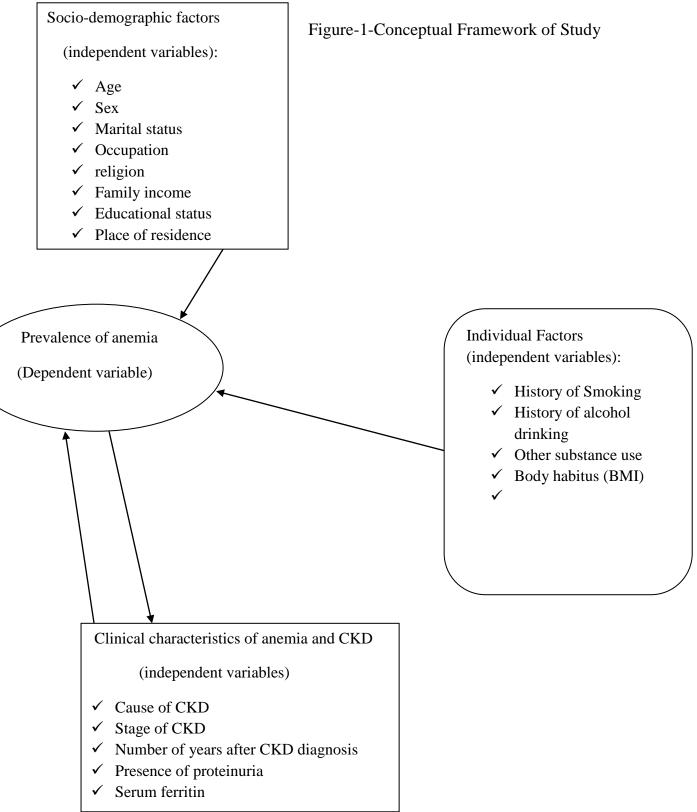
In Catalonia study in Spain, 40.5% of all CKD patients with anemia were receiving some form of treatment for anemia at the time of the visit. Of the patients treated, 68.0% were receiving an ESA, 14.5% were receiving folic acid and 10.0% were receiving vitamin B12. 66.0% of all patients with CKD and anemia were receiving iron supplements at the time of the visit (61% orally and 5% intravenously). The percentage of patients treated increased as the CKD stage increased. ESA was the most frequent treatment as CKD progressed(7).

In Kenyan study, only 41% of the CKD patients with anemia were receiving the treatment for anemia. The treatment modalities used in the management of anemia were erythropoietin derivatives (58%), injectable iron (58%), oral iron (48%) and blood transfusion (24%). Provision of ESA, iron sucrose and blood transfusion as modalities of management were significantly associated with the severity or degree of anemia (p<0.05)(15).

The study in Gondar, Northwest Ethiopia revealed one quarter of patients received therapy among those who had documented anemia. Options of therapy among treated cases were packed blood transfusions (55%), hematinic (55%), and ESA (14.3%)(19).

In summary, anemia is highly prevalent among CKD patients in all studies done all over the world. There are several contributing factors for the development of anemia and also serious complications associated with anemia in CKD patients. Reported treatment rates of anemia in patients with CKD are typically low, regardless of the geographic location of the study. The above studies signify that the problem is understated despite paramount evidence about its effect in quality of life, complications and survival. In Ethiopia, there are still gaps in our current knowledge on the prevalence, associated factors and treatment of anemia among CKD patients in the country as there are only two studies published on this issue. So this study has described the

prevalence, associated factors and treatment of anemia among CKD patients in Southwest Ethiopia as the information that was obtained will help in designing the appropriate treatment measures of anemia, so as to reduce complications and morbidity among patients with CKD.



# **CHAPTER THREE**

# **OBJECTIVE**

# **3.1. General Objective**

✓ To determine the magnitude of anemia and associated factors among stage 3-5 ND-CKD patients in JMC, Southwest Ethiopia.

# **3.2. Specific Objectives**

- ✓ To determine magnitude of anemia among stage 3-5 ND-CKD patients in JMC, Southwest Ethiopia.
- ✓ To identify the factors associated with anemia among stage 3-5 ND-CKD patients in JMC, Southwest Ethiopia.

# **CHAPTER FOUR**

# METHODS AND MATERIALS

## 4.1. Study area and period

The study was conducted in Jimma university medical center (JUMC), which is located in Jimma town, Oromia region, Southwest of Ethiopia. Jimma zone comprises Jimma town and its nearby woredas, with estimated population of 2,486,155. The town is located 346 km from the capital, Addis Ababa.

Jimma University Medical Center (JUMC) is one of the oldest public hospitals in Ethiopia. It is located in Jimma town, Southwest Ethiopia. The hospital is the main referral center in Southwest Ethiopia that gives health services both at inpatient and outpatient levels for about 15 million people. It is also a teaching center that runs both undergraduate and postgraduate programs in several disciplines. The hospital has a medical department that has emergency medical outpatient department (EMOPD), general OPD, subspecialty clinics, dialysis unit and medical ward with sub-specialty units having 120 beds. Patients with CKD are seen at EMOPD and general OPDs, renal clinic, dialysis unit and medical ward.

The study was conducted from September 1 to November 30, 2020 G.C. at EMOPD, general OPD, renal clinic and medical ward.

## 4.2. Study design

An institution based **cross sectional study** was conducted.

## 4.3 Population

## **4.3.1 Source population**

The source population was all adult stage 3-5 CKD patients not on dialysis visiting JUMC.

## 4.3.2 Study population

The study population was all adult stage 3-5 CKD patients not on dialysis visiting JUMC during the study period.

## 4.4 Eligibility criteria

## 4.4.1 Inclusion criteria

- ✓ Stages 3-5 ND-CKD patients
- ✓ Age>18 years.

#### 4.4.2 Exclusion criteria

- ✓ Patients with known malignancy
- ✓ Pregnant patients
- ✓ Patients who won't give their informed consent to participate in the study.

## 4.5 Sample size determination and sampling procedure 4.5.1 Sample size determination

The sample size is calculated by Single population proportion formula. The total population size is considered to be all adult patients with CKD who come to JUMC in the study period. This number is predicted from average number of CKD patients seen every month. According to data from HMIS log book registry found at emergency, OPD, renal clinic and ward, monthly on average 75 CKD patients visit JUMC. Since the study is planned to take 3 months, total number of CKD patients that will be seen in JUMC is 225.

The prevalence of anemia in ND-CKD patients is 64.5% from the study which was done in university of Gonder hospital, Ethiopia (19). So, P- value of 0.65 is taken by the investigator since our setup is similar with the setup of Gondar hospital. A confidence interval of 95% (Z=1.96) and margin of error (w) of 5% are taken.

Single population proportion formula (m) = 
$$\frac{z^2p(1-p)}{w^2}$$
;  
Where: m = sample size necessary for estimating the proportion  
P = prevalence of anemia in CKD  
W= margin of error

That means m= 
$$\frac{1.96^2 0.65(1-0.65)}{0.05^2} = 350.$$

The calculated sample size is 350 using the above single population proportion formula. Because of the small population of CKD patients at JUMC, a population correction formula is used to adjust sample size so that it will provide proportionately more information for small population.

Sample size after correction (n) =  $\frac{m}{1 + \frac{m-1}{N}}$ ,

Where, m = calculated sample size

n = sample size after correction

N= is total number of CKD patients in JUMC in the study period

Then 10% contingency was added on n:

Sample size after correction (n) = 
$$\frac{350}{1 + \frac{350 - 1}{225}} = 137$$
.

From this number 10% non-response rate is added;

137 x 10% = 13.7

137 + 10% non-response rate = 150.

So, the sample size after correction is 150 patients with CKD that are not on dialysis from all ND-CKD patients who visit JUMC during the study period.

## 4.5.2 Sampling procedures

A convenient sampling technique was used taking consecutive patients who come to JUMC until the sample size is reached within study period.

## 4.6 Study variables

## 4.6.1 Dependent variable

- Prevalence of anemia

## 4.6.2 Independent variables

- Age
- Place of residence
- Occupation
- Marital status
- History of smoking
- Number of years after CKD diagnosis
- Stages of CKD
- Presence of comorbidity

- Sex
- Educational status
- Religion
- Body habitus (BMI)
- History of alcohol drinking
- Cause of CKD
- Serum ferritin
- Presence of proteinuria

## 4.7 Data collection procedures

#### 4.7.1 Measurements

Two qualified nurses and one medical resident were trained with the data collection instrument and has collected the relevant data. The data collectors and patients have applied standard COVID-19 infection preventive measures like wearing face mask, hand washing and maintaining adequate distance. Data was collected through an investigator administered pretested questionnaire after data collectors take verbal consent. The questionnaire had three parts. The first section is about the socio-demographic characteristics of the patients. The second part contains questions about CKD and anemia associated characteristics of patients. Last portion was data entry check list for important laboratory findings and medication list.

Patients were interviewed to obtain demographic data, and the patients' medical records were reviewed to obtain information on relevant medical history, laboratory parameters and drug lists. The primary cause of kidney disease was determined based on clinical history, physical examination, ultrasound and laboratory investigations including complete blood count (CBC), urinalysis and blood chemistry.

Data collectors measured the patients' weight (in kilogram) and height (in meter) to calculate the body mass index (BMI). eGFR was calculated from creatinine level using CKD-EPI 2009 formula. A nurse collected about 2-3 ml of blood sample in 5ml of chemistry test tube for each patient with anemia for determination of serum ferritin. The sample was analyzed using Beckman Coulter AU Chemistry Analyzers and the cost of the laboratory for serum ferritin determination was covered by the PI. CBC and peripheral morphology was also determined if the results were not available on the medical record. The cost of the laboratory was covered by the PI as well.

PI had checked all questionnaires before they were filled for completeness and accuracy.

#### 4.8 Operational definitions

**Chronic kidney disease (CKD):** In this study, we used CKD patients that had their diagnosis documented on the chart by treating physicians and having estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73 m<sup>2</sup> as calculated by CKD Epidemiology(CKD-EPI) equation(49).

In this study, we defined stages 3-5 CKD stages as follows

Stages	GFR (ml/min/1.73 m <sup>2</sup> )	
3	30-59	
4	15-29	
5	<15	

Anemia: In this study, we defined anemias as hemoglobin concentration (hgb) < 13.0 g/dl in men and < 12.0 g/dl in women. Hemoglobin level 10 - 12.9 g/dl for men and 10 - 11.9 g/dl for women was used to define mild anemia, hemoglobin 7 - 9.9 g/dl for both genders defined moderate anemia and hemoglobin < 7 g/dl for both genders defined severe anemia.

Anemia of CKD: In this study, anemia of CKD was defined as hemoglobin concentrations of < 13.0 g/dl in men and < 12.0 g/dl in women and that had an isolated normochromic, normocytic anemia (NCNC) RBCs on peripheral morphology.

**Iron study:** in this study, we used serum ferritin level as one of the iron studies to asses iron store of the patient.

**Iron deficiency:** in this study, absolute iron deficiency was defined as serum ferritin of <100ng/ml. Adequate iron store was defined as serum ferritin level of 100-800ng/ml.

**Iron deficiency anemia (IDA):** was defined in this study as serum ferritin level < 100 ng/ml and having microcytic hypochromic RBCs on peripheral morphology.

#### 4.9 Data quality management

The data collectors took onsite training about proper data collection by principal investigator. The data quality was assured by adhering to the inclusion and exclusion criteria and the study protocol. The data was collected by a well-structured questionnaire and from medical records. Incomplete data was rejected.

#### 4.10 Data analysis procedures

All questionnaires were checked daily for completeness by the investigator. Data was entered into computer using EPI Info software version 4.4.1 and then it was transferred to SPSS version 20 for further data cleaning so that to allow consistence and eliminate discrepancies, categorizing of continuous variable and finally analysis. Descriptive statistics, such as means, medians, standard deviations and interquartile ranges was used to compute continuous variables, and counts with percentage for categorical variables. Both bivariate and multivariate logistic regression analyses was used to identify independently associated factors of anemia in CKD patients. Those variables with a P-value <0.2 in the bivariate analysis was exported to multivariate analysis to control the possible effect of confounders. Adjusted odds ratio (AOR) with 95%CI and P-value <0.05 was used to select variables associated with anemia in CKD patients.

#### **4.11 Ethical consideration**

Ethical clearance was obtained from Ethical Review Committee of Jimma university. In addition, permission was taken from the respective heads of Department of Internal Medicine and renal clinic to conduct the study in the clinic. Prior to data collection, patients were informed about the study and verbal consent was obtained from the study participants. Each patient was informed about the objective of the study, procedures of selection, and assurance of confidentiality and their right to refuse was maintained. No identifiers were used to minimize social desirability bias and enhance anonymity. Laboratory cost to determine serum ferritin level was covered by the PI.

#### **4.12 Dissemination plan**

The findings of the study will be disseminated to all relevant stakeholders like Jimma University, Clinicians, researchers and others through presentation Seminars and publication. Copies of the research will be given to Jimma University, Faculty of public health postgraduate program and the department of Internal Medicine. Local and international medical/non-medical journals will be communicated for publication.

## **CHAPTER FIVE**

## RESULT

#### Socio-demographic characteristics of the study participants

Out of 150 study participants, 64.67% were males by sex. The mean (+/-SD) age of the CKD patients were 45.34 (+- 15.17) years old, with 38.67% of them were in 18-39 years age category. From the total study participants, 84 (56.0%) of them never attended formal education, 16% attended elementry school, 14.0% attended highschool and 14.0% attended college and above (Table 1).

 Table 1: Socio-demographic characteristics of CKD patients in Jimma Medical center,

 Southwest Ethiopia.

Variable	Category	Frequency(n=150)	Percent (%)
Sex	Male	97	64.67
	Female	53	35.33
Age	18-39	58	38.67
(in years)	40-64	70	46.67
	$\geq$ 65	22	14.67
Place of residence	Urban	60	40.00
	Rural	90	60.00
Educational status	No formal education	84	56.00
	Elementary school	24	16.00
	High school	21	14.00
	College and above	21	14.00
Monthly Income	Income<1000	53	35.33
(in ETB)	Income1000-5000	72	48.00
	5000-10,000	23	15.33
	>10,000	2	1.33
source of income	patient him/her self	84	56.00
	family support	65	43.33
BMI	BMI<18.5	21	14.09
	BMI 18.5-24.9	77	51.68
	BMI 25-29.9	3	2.01
	BMI≥30	3	2.01
	BMI can't be assessed	45	30.20
Religion	Orthodox Christian	40	26.67
	Muslim	99	66.00
	Protestant Christian	9	6.00
	Other	2	1.33

# **Clinical characteristics of the patients**

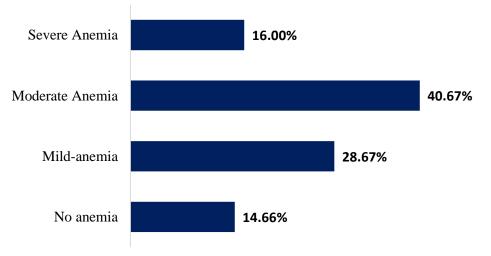
From 150 patients, 85 (56.67%) were in stage 5 CKD by last creatinine, followed by stage 4 (26.0%) and stage 3 (17.33%). Hypertension was found to be the most common (40.82%) cause of CKD, followed by unknown cause (38.1%), and DM (14.97%). Thirty-five (24.48%) patients received blood transfusion (Table 2).

Variable	Category	Frequency(n=150)	Percent (%)
Stage of CKD	eGFR 30-59	26	17.33
	eGFR 15-29	39	26.0
	eGFR <15	85	56.67
Cause of CKD	DM	22	14.97
	HTN	60	40.82
	Glomerular disease	3	2.04
	Obstructive Uropathy	5	3.40
	Unknown	56	38.10
	Other	1	.68
Duration of CKD	<6month	99	66.00
	6 month-1 yr	18	12.00
	01 yr-5 yrs	25	16.67
	>5 yrs	8	5.33
Co morbidity	History of DM	27	18.24
	History of HTN	62	41.89
Anemia related	Symptoms of anemia	67	45.58
	History of transfusion	35	24.48

Table 2: clinical characteristics of CKD patients in Jimma Medical center, Southwest Ethiopia

# Magnitude of anemia among stage 3-5 ND-CKD patients

Overall 128 (85.33%) of the ND-CKD patients were found to be anemic. 61 (40.67%) patients had moderate anemia, and 16.0% of the patients had severe anemia (Figure 1).



 $0.00\% \hspace{0.5cm} 5.00\% \hspace{0.5cm} 10.00\% \hspace{0.5cm} 15.00\% \hspace{0.5cm} 20.00\% \hspace{0.5cm} 25.00\% \hspace{0.5cm} 30.00\% \hspace{0.5cm} 35.00\% \hspace{0.5cm} 40.00\% \hspace{0.5cm} 45.00\% \hspace{0.5cm}$ 

**Figure 1:** Magnitude and severity of anemia among CKD patients in Jimma Medical center, Southwest Ethiopia

#### Patterns of anemia in the stages of CKD based on eGFR by last creatinine

Out of the 128(85.33%) ND-CKD patients who had anemia in the study area, 79(52.67%) of them were in the stage 5, 19.33% in the stage 4 CKD and 13.33% in the stage 3 CKD. Among those who were anemic 128 (85.33%), moderate anemia accounted for 61 (40.67%), mild anemia for 43 (28.67%), and severe anemia 24 (16.0%). Severe anemia across the stages of CKD were 3.33%, 1.33%, and 11.33% among stage 3,4 and 5 CKD respectively (Table 3).

	Frequency n (%)				
eGFR by last creatinine	Mild anemia	Moderate anemia	Severe anemia	No anemia	Total
eGFR 30-59	11 (7.33)	4 (2.67)	5 (3.33)	6 (4.0)	26 (17.33)
eGFR 15-29	16 (10.67)	11 (7.33)	2 (1.33)	10 (6.67)	39 (26.00)
eGFR <15	16 (10.67)	46 (30.67)	17 (11.33)	6 (4.0)	85 (56.67)
Total	43 (28.67)	61 (40.67)	24 (16.00)	22 (14.67)	150 (100.0)

Table 3: patterns of anemia in the stages of CKD based on eGFR by last creatinine

# Factors associated with anemia among CKD patients

A bi-variable logistic regression analysis showed sex, monthly income, occupation, and stages of CKD have statistically significant association with prevalence of anemia among ND-CKD patients. (Table 4)

		COR (95% CI)	P-value
Characteristics			
Age (in years)	18-39	2.65(.893,7.866)	.079
	40-64	1	
	>=65	1.583(.41,6.115)	.505
Sex	Male	2.546(1.017,6.375)	.046
	Female	1	
Educational	No formal education	1	
status	Elementary school	.452(.147,1.386)	.165
status	High school	3.014(.367,24.759)	.305
	College and above	.64(.182,2.258)	.488
Marital status	Married	1	
	Unmarried	.234(.03,1.833)	.167
Monthly	<1000	4.023(1.093,14.807)	.036
income	1001-5000	1	•
(in ETB)	>5000	.869(.275,2.744)	.811
Residence	Rural	1(.989,6.264)	
	Urban	2.489(1.956,6.682)	.053
Occupation	Civil servant	1	
-	Business	3(.698,12.886)	.14
	Farmer	25.636(2.794,235.206)	.004
	Self-employed	2.38(.723,7.832)	.154
Stages of CKD	Stage 3	1	
5	Stage 4	.87(.272,2.779)	.814
	Stage 5	3.95(1.151,13.559)	.029

**Table 4:** Bi-variable logistic regression analysis of factors associated with anemia among ND-CKD patients in Jimma Medical center, Southwest Ethiopia.

A multivariable logistic regression model revealed the age groups, sex, and monthly income were found to have statistically significant association with anemia among CKD patients in Jimma medical center.

After controlling for potential covariates, age was found to have statistically significant association with anemia among CKD patients in Jimma medical center. Participants in the 18-39 years age category were four times more likely AOR 4.05 [95% C.I 1.04, 15.73] to develop anemia as compared to those in the age group of 40-64 years old.

Sex and monthly income were found to have statistically significant association with anemia among CKD patients in Jimma medical center. Being male were about five times more likely AOR 4.92 [95% C.I 1.51, 16.07] to develop anemia as compared to their counterparts. Monthly income < 1000 ETB per month were four times more likely AOR 4.13 [95% C.I 1.01, 17.04] to develop anemia as compared to monthly income of 1000-5000 ETB (Table 3).

**Table 5:** Multivariable logistic regression analysis of factors associated with anemia amongCKD patients in Jimma Medical Center, Southwest Ethiopia.

		AOR (95% CI)	P-value
Characteristics	5		
Age (in years)	18-39	4.05(1.04,15.73)	.043
	40-64	1.0(1.0,1.0)	
	>=65	1.40(.29,6.87)	.672
Sex	Male	4.92(1.51,16.07)	.008
	Female	1.0(1.0,1.0)	
Educational	No formal education	1.0(1.0,1.0)	
status	Elementary school	.28(.07,1.15)	.077
	High school	3.73(.36,38.87)	.270
	College and above	1.66(.21,13.22)	.634
Monthly	<1000	4.13(1.01,17.04)	.049
income	1001-5000	1.0(1.0,1.0)	
(in ETB)	>5000	.56(.09,3.28)	.518
Residence	Rural	2.53(.74,8.67)	.140
	Urban	1.0(1.0,1.0)	

Out of 128 anemic patients, 47.65%(n=61) of them had iron deficiency based on the level of serum ferritin. 42.2% (n=54) of the total anemic patients were taking oral iron therapy and 19.5% (n=25) of them had received blood transfusion.

## Table 6: Treatment of anemia

Treatment of anemia	Frequency(n=128)	Percent (%)
Oral Iron	54	42.2
Blood transfusion	25	19.5
No treatment	74	57.8

**Table 7:** level of iron based on serum ferritin level

Level of iron	Frequency(n=128)	Percent (%)
Iron deficiency	61	47.65
Adequate iron	67	52.35
Total	128	100%

#### CHAPTER SIX

#### DISCUSSION

This study has demonstrated a very high prevalence of anemia among stage 3-5 CKD patients at JUMC with overall prevalence of 85.33%. Monthly income less than 1000 ETB, age group of 18-39 years and male sex were significantly associated with prevalence of anemia among stage 3-5 CKD patients.

In this study, the overall prevalence of anemia among stage 3-5 ND-CKD patients was 85.33%, which is within the range of most African studies(50%-97%) (15-18) but higher than the prevalence of anemia in the study conducted in Gondar(19) and in most Western studies(5, 6, 8, 9). The high prevalence of anemia among ND-CKD patients that was demonstrated in this study may be due to high number of patients having advanced CKD (57.05%).

The study showed prevalence of anemia increased with CKD severity. This finding is similar with several studies that were conducted in other African countries, Asia, USA and Europe(5, 7, 11, 17). In a study which was conducted in 1058 patients with CKD not on dialysis in Italy, the prevalence of anemia was 16%, 32% and 51% in stages 3, 4 and 5 respectively(9). This result was also similar to the study which was done in Gondar, Northwest Ethiopia(19).

The most common cause of CKD that was identified in this study was hypertension. The next main causes identified were unknown causes and diabetes mellitus. This finding is comparable with result of the study that was conducted in Gondar, Northwest Ethiopia. In the Gondar study, hypertension accounted for 45% as a cause of CKD, followed by chronic glomerulonephritis and diabetes(19). The finding is also similar to other African and Western studies(5, 18). The reason for high percentage of unknown causes of CKD in this study may be due to the high number of patients present at advanced stage of CKD that could be attributed to lack of CKD screening and low detection rate of CKD risk factors.

This study demonstrated that anemia was significantly prevalent in ND-CKD patients who were in the age group of 18-39 years. Participants in the 18-39 years age category were four times more likely to develop anemia as compared to those in the age group of 40-64 years old. This is different from Catalonia study where there was significant association of higher prevalence of anemia in CKD with older age. The reason for the significant association of anemia in CKD with the age group of 18-39 years may be due to the concomitant presence of nutritional deficiency and also the small number of study participants in the age group  $\geq$ 65 years (14.67%) might affect the result. This study showed that anemia was significantly prevalent in male ND-CKD patients. Being male were about five times more likely to develop anemia as compared to their counterparts. This may be due to men in developing countries seek treatment more frequently at formal health services as compared to females (50, 51). The Korean Cohort Study for Outcome in Patients with Chronic Kidney Disease (KNOW-CKD) showed a different result. In that study, more than half (51.8%) of female CKD patients had anemia.

There was statistically significant association between ND-CKD patients with monthly income of < 1000 ETB and the development of anemia. Monthly income < 1000 ETB were four times more likely to develop anemia as compared to those patients with monthly income of 1000-5000 ETB and > 5000. The presence of concomitant nutritional deficiencies and helminthic infestation may contribute to the high prevalence of anemia in this group of patients.

This study revealed iron deficiency anemia was present in 47.65% of the total anemic patients. 42.2% of patients received therapy among those who had documented anemia. They received treatment with oral iron therapy and blood transfusion. There was no patient taking Erythropoietin Stimulating Agent (ESA). The result from the Gondar study revealed one quarter of all anemic patients received treatment with iron therapy (55%), blood transfusion (55%) and ESA (14.3%)(19). The Catalonia study showed 68.0% were receiving an ESA(7). In this study, patients were not taking ESA because the drug was not easily available in the setting and due to its high cost.

#### **CHAPTER SEVEN**

## CONCLUSION

There is high prevalence of anemia (85.33%) among ND-CKD patients in the study area where moderate degree of anemia being the most frequent finding. Hypertension, diabetes and unknown causes were commonly identified as causes of CKD. The prevalence of anemia increased with the stages of CKD. Male sex, age group in the 18-39 years of age and monthly income less than 1000 ETB were independently associated with higher risk of anemia among ND-CKD patients in Jimma medical center.

Half of the patients had iron deficiency anemia and more than one third of the patients with anemia and CKD received treatment. The options of treatment were oral iron therapy and blood transfusion.

# CHAPTER EIGHT LIMITATION AND RECOMMENDATION

# Limitation of the study

This study used small study sample size, as a results majority of study population was in advanced CKD stages which might have overestimated the prevalence of anemia among the CKD study population.

The data were cross-sectional, not longitudinal, so that it prevented assessment of whether the associated factors caused or resulted from CKD. Only iron deficiency anemia was determined for the cause of anemia in CKD and the other causes of anemia were not determined due to financial constraints. Proteinuria was assessed using a semiquantitative urine dipstick test due to unavailability of quantitative test and also because of logistic reasons.

# Recommendation

Much have to be done to intervene in prevention of anemia among CKD patients.

**For treating physicians:** they need to give priority for periodic screening and intervention programs for anemia among CKD patients to decrease the high prevalence of anemia as nutritional deficiency anemia was prevalent in these patients.

They also need to give priority for those CKD patients in the age group of 18-39 years, who are male with monthly income of less than 1000 birr.

**For the scientific community:** Further longitudinal studies are required to establish the causal relations of anemia among this population.

# References

1. Anaemias N. Report of a WHO scientific group. World Health Organ Tech Rep Ser1968; 405:5-37.

2. Kliger AS, Foley RN, Goldfarb DS, Goldstein SL, Johansen K, Singh A, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for anemia in CKD. American Journal of Kidney Diseases;62(5):849-59.

3. Nurko S. Anemia in chronic kidney disease: causes, diagnosis, treatment. Cleveland Clinic journal of medicine2006;73(3):289.

4. Floege J, Johnson RJ, Feehally J. Comprehensive Clinical Nephrology E-Book: Elsevier Health Sciences.

5. Stauffer ME, Fan T. Prevalence of anemia in chronic kidney disease in the United States. PloS one;9(1):e84943.

6. MartÃ-nez-Castelao A, GÃ<sup>3</sup>rriz JL, Portolés JM, De Alvaro F, Cases A, Luño J, et al. Baseline characteristics of patients with chronic kidney disease stage 3 and stage 4 in Spain: the MERENA observational cohort study. BMC nephrology;12(1):53.

7. del estudio MICENAS I, Cases-AmenÃ<sup>3</sup>s A, MartÃ-nez-Castelao A, Fort-Ros J, Bonal-Bastons J, Ruiz MP, et al. Prevalence of anaemia and its clinical management in patients with stages 3-5 chronic kidney disease not on dialysis in Catalonia: MICENAS I study. NefrologÃ-a (English Edition);34(2):189-98.

8. Portolés J, Gorriz JL, Rubio E, De Õ Ivaro F, GarcÃ-a F, Alvarez-Chivas V, et al. The development of anemia is associated to poor prognosis in NKF/KDOQI stage 3 chronic kidney disease. BMC nephrology;14(1):2.

9. De Nicola L, Minutolo R, Chiodini P, Zoccali C, Castellino P, Donadio C. at al. TArget Blood Pressure LEvels in Chronic Kidney Disease (TABLE in CKD) Study Group. Global approach to cardiovascular risk in chronic kidney disease: reality and opportunities for intervention. Kidney Int2006;69(538):45.

10. Li Y, Shi H, Wang W-M, Peng A, Jiang G-R, Zhang J-Y, et al. Prevalence, awareness, and treatment of anemia in Chinese patients with nondialysis chronic kidney disease: First multicenter, cross-sectional study. Medicine;95(24).

11. Ryu S-R, Park SK, Jung JY, Kim YH, Oh YK, Yoo TH, et al. The prevalence and management of anemia in chronic kidney disease patients: result from the KoreaN Cohort Study for Outcomes in Patients With Chronic Kidney Disease (KNOW-CKD). Journal of Korean medical science;32(2):249-56.

12. Akizawa T, Okumura H, Alexandre AF, Fukushima A, Kiyabu G, Dorey J. Burden of anemia in chronic kidney disease patients in Japan: a literature review. Therapeutic Apheresis and Dialysis;22(5):444-56.

13. CHATTERJEE TK. PREVALENCE OF ANEMIA IN CKD PATIENTS OF EASTERN INDIA ON MAINTAINED HAEMODIALYSIS. ISHANI ADITYA, SOUMITA GOSWAMI 2, BIPLAB GHOSH 3 AND.

14. Shaheen FA, Souqiyyeh MZ, Al-Attar BA, Karkar A, Al Jazairi AMH, Badawi LS, et al. Prevalence of anemia in predialysis chronic kidney disease patients. Saudi Journal of Kidney Diseases and Transplantation;22(3):456.

15. Maina C, Karimi P, Mariita K, Nyamu D, Mugendi G, Opanga S. Correlates and management of anemia of chronic kidney disease in a Kenyan Tertiary hospita. East Afri Med J;93(10):489-99.

16. Amoako YA, Laryea DO, Bedu-Addo G, Andoh H, Awuku YA. Clinical and demographic characteristics of chronic kidney disease patients in a tertiary facility in Ghana. The Pan African Medical Journal;18.

17. Ijoma C, Ulasi I, Ijoma U, Ifebunandu N. High prevalence of anemia in predialysis patients in Enugu, Nigeria. Nephrology Research & Reviews;2(1):61-5.

18. Juma A. Prevalence of Anemia and its associated factors in patients with Chronic Kidney Disease at Muhimbili National Hospital Dar es Salaam: Muhimbili University of health and Allied Sciences.

19. Adera H, Hailu W, Adane A, Tadesse A. Prevalence Of Anemia And Its Associated Factors Among Chronic Kidney Disease Patients At University Of Gondar Hospital, Northwest Ethiopia: A Hospital-Based Cross Sectional Study. International journal of nephrology and renovascular disease;12:219. 20. Kefale B, Tadesse Y, Alebachew M, Engidawork E. Management practice, and adherence and its contributing factors among patients with chronic kidney disease at Tikur Anbessa Specialized Hospital: A hospital-based cross-sectional study. PloS one;13(7):e0200415.

21. Poudel B, Yadav BK, Jha B, Raut KB, Pandeya DR. Prevalence and association of anemia with CKD: A hospistal based crosssectional study from Nepal.

22. Rivera RF, Lullo L, Pascalis A, Floccari F, Joli G, Pezzini E. Anemia in patients with chronic kidney disease: current screening and management approaches. Nephrol Renal Dis;1(1):1-9.

23. McGonigle RJ, Wallin JD, Shadduck RK, Fisher JW. Erythropoietin deficiency and inhibition of erythropoiesis in renal insufficiency. Kidney international1984;25(2):437-44.

24. Babitt JL, Lin HY. Mechanisms of anemia in CKD. Journal of the American Society of Nephrology;23(10):1631-4.

25. Jurkovitz CT, Abramson JL, Vaccarino LV, Weintraub WS, McClellan WM. Association of high serum creatinine and anemia increases the risk of coronary events: results from the prospective community-based atherosclerosis risk in communities (ARIC) study. Journal of the American Society of Nephrology2003;14(11):2919-25.

26. Abramson JL, Jurkovitz CT, Vaccarino V, Weintraub WS, Mcclellan W. Chronic kidney disease, anemia, and incident stroke in a middle-aged, community-based population: the ARIC Study. Kidney international2003;64(2):610-5.

27. Del Fabbro P, Luthi J-C, Carrera E, Michel P, Burnier M, Burnand B. Anemia and chronic kidney disease are potential risk factors for mortality in stroke patients: a historic cohort study. BMC nephrology;11(1):27.

28. Weiner DE, Tighiouart H, Vlagopoulos PT, Griffith JL, Salem DN, Levey AS, et al. Effects of anemia and left ventricular hypertrophy on cardiovascular disease in patients with chronic kidney disease. Journal of the American Society of Nephrology2005;16(6):1803-10.

29. McClellan WM, Flanders WD, Langston RD, Jurkovitz C, Presley R. Anemia and renal insufficiency are independent risk factors for death among patients with congestive heart failure admitted to community hospitals: a population-based study. Journal of the American Society of Nephrology2002;13(7):1928-36.

30. Langston RD, Presley R, Flanders WD, Mcclellan WM. Renal insufficiency and anemia are independent risk factors for death among patients with acute myocardial infarction. Kidney international2003;64(4):1398-405.

31. Kovesdy C, Trivedi B, Kalantar-Zadeh K, Anderson J. Association of anemia with outcomes in men with moderate and severe chronic kidney disease. Kidney international2006;69(3):560-4.

32. Hayashi T, Suzuki A, Shoji T, Togawa M, Okada N, Tsubakihara Y, et al. Cardiovascular effect of normalizing the hematocrit level during erythropoietin therapy in predialysis patients with chronic renal failure. American Journal of Kidney Diseases2000;35(2):250-6.

33. Portoles J, Torralbo A, Martin P, Rodrigo J, Herrero JA, Barrientos A. Cardiovascular effects of recombinant human erythropoietin in predialysis patients. American journal of kidney diseases1997;29(4):541-8.

34. Revicki DA, Brown RE, Feeny DH, Henry D, Teehan BP, Rudnick MR, et al. Health-related quality of life associated with recombinant human erythropoietin therapy for predialysis chronic renal disease patients. American Journal of Kidney Diseases1995;25(4):548-54.

35. Roth D, Smith RD, Schulman G, Steinman TI, Hatch FE, Rudnick MR, et al. Effects of recombinant human erythropoietin on renal function in chronic renal failure predialysis patients. American journal of kidney diseases1994;24(5):777-84.

36. Akizawa T, Makino H, Matsuo S, Watanabe T, Imai E, Nitta K, et al. Management of anemia in chronic kidney disease patients: baseline findings from Chronic Kidney Disease Japan Cohort Study. Clinical and experimental nephrology;15(2):248-57.

37. Imai E, Matsuo S, Makino H, Watanabe T, Akizawa T, Nitta K, et al. Chronic Kidney Disease Japan Cohort study: baseline characteristics and factors associated with causative diseases and renal function. Clinical and experimental nephrology;14(6):558-70.

38. McClellan W, Aronoff SL, Bolton WK, Hood S, Lorber DL, Tang KL, et al. The prevalence of anemia in patients with chronic kidney disease. Current medical research and opinion2004;20(9):1501-10.

39. Portolés J, LÃ<sup>3</sup>pez-GÃ<sup>3</sup>mez JM, Aljama P. A prospective multicentre study of the role of anaemia as a risk factor in haemodialysis patients: the MAR Study. Nephrology Dialysis Transplantation2007;22(2):500-7.

40. Loutradis C, Skodra A, Georgianos P, Tolika P, Alexandrou D, Avdelidou A, et al. Diabetes mellitus increases the prevalence of anemia in patients with chronic kidney disease: A nested case-control study. World journal of nephrology;5(4):358.

41. Silberberg JS, Barre PE, Prichard SS, Sniderman AD. Impact of left ventricular hypertrophy on survival in end-stage renal disease. Kidney international1989;36(2):286-90.

42. He J, Shlipak M, Anderson A, Roy JA, Feldman HI, Kallem RR, et al. Risk factors for heart failure in patients with chronic kidney disease: the CRIC (Chronic Renal Insufficiency Cohort) study. Journal of the American Heart Association;6(5):e005336.

43. Eriksson D, Goldsmith D, Teitsson S, Jackson J, van Nooten F. Cross-sectional survey in CKD patients across Europe describing the association between quality of life and anaemia. BMC nephrology;17(1):97.

44. Jungers P, Choukroun G, Oualim Z, Robino C, Nguyen AT, Man NK. Beneficial influence of recombinant human erythropoietin therapy on the rate of progression of chronic renal failure in predialysis patients. Nephrology Dialysis Transplantation2001;16(2):307-12.

45. Kuriyam S, Tomonari H, Yoshida H, Hashimoto T, Kawaguchi Y, Sakai O. Reversal of anemia by erythropoietin therapy retards the progression of chronic renal failure, especially in nondiabetic patients. Nephron1997;77(2):176-85.

46. Fink JC, Blahut SA, Reddy M, Light PD. Use of erythropoietin before the initiation of dialysis and its impact on mortality. American Journal of Kidney Diseases2001;37(2):348-55.

47. Xue JL, Peter WLS, Ebben JP, Everson SE, Collins AJ. Anemia treatment in the pre-ESRD period and associated mortality in elderly patients. American journal of kidney diseases2002;40(6):1153-61.

48. Minutolo R, Locatelli F, Gallieni M, Bonofiglio R, Fuiano G, Oldrizzi L, et al. Anaemia management in non-dialysis chronic kidney disease (CKD) patients: a multicentre prospective study in renal clinics. Nephrology Dialysis Transplantation;28(12):3035-45.

49. Levey AS, Coresh J, Bolton K, Culleton B, Harvey KS, Ikizler TA, et al. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. American Journal of Kidney Diseases2002;39(2 SUPPL. 1).

50. Al-Krenawi A, Graham JR. Gender and biomedical/traditional mental health utilization among the Bedouin-Arabs of the Negev. Culture, medicine and psychiatry1999;23(2):219-43.

51. Vlassoff C. Gender differences in determinants and consequences of health and illness. Journal of health, population, and nutrition2007;25(1):47.

# ANNEX: Information sheet and Consent Form (English) Consent form English Patient's information document

Dear participants;

My name is \_\_\_\_\_\_, I am a data collector for a research which is conducted by Dr. Filagot Bishaw on the prevalence of Anemia, associated factors and treatment in patients with chronic kidney disease who are not on dialysis. You are invited to participate on this research.

## Procedure

If you are willing to participate on this study, you will be interviewed by the data collector. Your card will be used to see important laboratory results. You don't need to tell your name to the data collector. You don't have to write or sign, verbal consent is enough.

## **Risk/discomfort**

By participating in this research, you may feel that it has some discomfort especially on wasting time about 20 minutes. We hope you will participate in the study for the sake of the benefit of the research result. There is no risk in participating in this research.

## **Benefits and incentives**

If you participate in this research project, there may not be direct benefit to you but your participation will likely help us to meet the research objective which is intended to improve the treatment of Anemia in non dialytic CKD patients.

You will not be provided any incentives or payment to take part in this project. No payment is requested from you as a fee to participate in the study.

**Confidentiality and privacy:** The information collected from this research will be kept confidential. Information will be stored in a file without your name, only code number is used. It will not be revealed to anyone except the principal investigator.

**Right to refuse or withdraw:** You have full right to refuse from participating in this research. You can choose not to respond to some or all question if you do not want to give your response. You have also full right to withdraw from this study at any time you wish without losing any of your right.

#### Person to contact

If you have any question you can contact and ask the principal investigator any time you want.

Contact address of principal investigator: -Name: Dr. Filagot Bishaw

Name: Dr. Fnagot Bisna

Tell: 0917004064

Email: Filagot\_b@yahoo.com

#### Amharic version of the research consent form

#### የጥናቱ ተሳታፊዎች የመረጃ ቅጽ

በቅድሚያ በዚህ ጥናት **እንዲሳተፉ ስንል በአክብሮት ጥያቂያችንን እያቀረብን ጥናቱ** የሚካሄደው በኩላሊት ታካሚዎች ደም ማነስ ዙሪያ ነው:: **የጥናቱ ዓላማ፡** በኩላሊት ታካሚዎች ደም ማነስ ሁኔታ ማጥናት ነው::

**ሲደርስ የሚችል አደጋ፡-**በዚህ ጥናት ውስጥ አደጋ የሚያደርስ ድርጊት የለም።

<u>የሚገኝበት ጥቅም</u>፡-ይህ ጥናት ለበሽተኞች ልዩና ቀጥተኛ የሚባል ጥቅም የለውም።ይሁን እንጂ ወደፊት የጥናቱ ውጤት በኩሳሊት ታካሚዎች ደም ማነስ ሕክምና አሰጣጥ እንዲሻሻል ከፍተኛ አስተዋጽኦ ያደር*ጋ*ል።

<u>ሚስጥራዊነት</u>፡- የጣንኛውም የጥናቱ ተሳታፊ መረጃ በሚስጥራዊነት ይያዛል። የእያንዳንዱን ማለሰብ መረጃ ከዋናው ተመራጣሪና ከአማካሪዎቹ በስተቀር ጣንም ሲያገኝ አይችልም።

#### *ፌቃ*ደኝነትን ስሰማቋረጥ

በዚህ ጥናት ውስጥ የመሳተፍ መብትዎ ሙስ በሙሉ በፌቃደኝነት ላይ የተመሰረተ ነዉ። በጥናቱ ስመሳተፍ ፌቃደኛ መሆን ወይም ራስዎን ማግሰል ይችሳሉ። እንዲሁም በጥናቱ ባስመሳተፍዎ ምክንያት በአሁን ወይንም የወደፊት የህክምና እርዲታዎ ላይ ተፅእኖ አይኖርም።

#### አድራሻ ማወቅ ካስፈለግዎ፡-

የዋናው ተመራጣሪ አድራሻ :ዶ/ር ፍሳጎት ቢሻው

ስልክ **ቁጥር፡**- 0917004064

ስጥናቱ ቃስመጠይቅ ስማድረግ የግለሰቦች ፍቃደኝነት መጠየቂያ ቅጽ

በቅድሚያ በዚህ ጥናት *እንዲሳተፉ* ስንል በአክብሮት ጥያቄያችንን እያቀረብን ጥናቱ የሚካሄደው በ ኩላሲት ታካሚዎች ደም ማነስ ዙሪያ ነው::

ስምዎ በዚ መጠይቅ ውስጥ የማይጠቀስ መሆኑና በቃለመጠይቁ የሚሰጡትን መረጃ ሁሉ በሚስጥር ተይዞ ለጥናት አንልግሎት ብቻ የሚውል መሆኑን ላረጋግጥልዎ እወዳለሁ። እርስዎ በዚህ ጥናት ላይ የመሳተፍ ያለመሳተፍ ወይንም በማንኛውም ወቅት ቃለመጠይቁን የማቋረጥ ሙሉ መብት አለዎት ነገር ግን እርስዎ በጥናቱ ተሳትፌው የሚሰጡትን መረጃ ጥናቱን ውጤታማ ለማድረግና በአግባቡ ለመሰጠት ከፍተኛ ጠቀሜታ አለው። በጥናቱ ለመሳተፍ ፍቃደኛ ነዎት?

1. አዎ

2. አይደስሁም።

መልሱ አዎን ከሆነ አመሰግናስሁ ቃስመጠይቁን ያካሒዱ።

መልሱ አይደለሁም ከሆነ አመሰግናለው ወደ ሌላ ተጠያቂ ይለፉ፤

ማስሰቡ በቃስመጠይቁ ስማሳተፍ ምንም አይነት ማስገደጃ ወይም ጫና መደረግ የሰበትም።

ቃስመጠይቁ የተካሄደበት ቀን ----- ወር ----- 2011 ዓ.ም

# Annex III. Questionnaire (English version)

Instruction: please Mark " $\sqrt{}$ " in the provided space for the choice questions and for the questions that need direct answer, write the answer in the space provided.

# Part I: Socio-demographic characteristics of respondents

1) Age
2) Sex: Male Female
3) Marital Status (a) Single (b) Married (c) Divorced (d) Widowed
4) Education level
a) Illiterate
b) Elementary school education
c) High school education
d) College and above
5) Occupation (a) Civil servant (b) farmer (c) Self-employed (d) Other
<ul><li>6) Religion</li><li>a) Orthodox Christian</li></ul>
b) Muslim
c) Protestant Christian
d) Other
7) Place of residence
8) Monthly income
A. <1000 birr
B. 1000-5000 birr
C. 5,000-10,000birr
D.>10,000birr
9) Source of income
a) The patient him/her self
b) Family support
c) Other (specify)
10) History of smoking
a) Yes (b) No

11) If yes to question no. 10, how many packs per day did you smoke?

12) If yes to question no 10, for how long did you smoke?\_\_\_\_\_

13) History of alcohol drinking? (a) Yes (b) No

## Part II—CKD and anemia clinical characteristics

14) Number of years since the diagnosis of CKD?

- a) <6 month
- b) 6month 1 year
- c) 1 year-5 years
- d) >5 years

#### 15) Did u have known DM prior to diagnosis of CKD?

- a) Yes
- b) No

16) If yes to the above question, number of years since the diagnosis of diabetes?

17) Did u have known hypertension before the diagnosis of CKD?

a) Yes (b) No

18) If yes to the above question, number of years since the diagnosis of hypertension?\_\_\_\_\_

19) Number of years on treatment for hypertension?\_\_\_\_\_

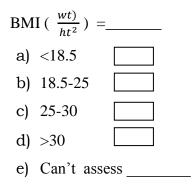
20) Other co-morbid diagnosis \_\_\_\_\_

- 21) Does the patient have any of easy fatiguability, light headedness, tinnitus, or pallor attributable to anemia?
  - a) Yes
  - b) No

22) Does the patient have any history of blood transfusion?

- a) Yes
- b) No

23) Weight of the patient in Kilograms\_\_\_\_\_, and Height in meter\_\_\_\_\_



#### NB. Fill the following information from patient card

1. The last serum creatinine and its eGFR (ml/min/1.73 m<sup>2</sup>) in the last three months.

Serum creatinine = \_\_\_\_\_ eGFR= \_\_\_\_\_ Stage= \_\_\_\_\_

2. Serial proteinuria (spot urine examination/urinalysis) within the last three months.

A. Absent B. Present (+1, ++2, +++3, ++++4)

3. Possible cause of CKD

 $A.\,DM$ 

- B. HTN
- C. Glomerular diseases
- D. Obstructive uropathy
- E. Unknown
- F. Other (specify)\_\_\_\_\_
- 4. CBC results in the last 3 months.
  - A. Hemoglobin\_\_\_\_\_
  - B. MCV\_\_\_\_\_
  - C. MCH\_\_\_\_\_
  - D. MCHC\_\_\_\_\_
  - E. RDW\_\_\_\_\_
  - F. WBC\_\_\_\_\_
  - G. PLT\_\_\_\_\_
- 5. Did the patient have Peripheral morphology result?
  - A. Yes
  - B. No
- 6. If yes to question 5, what was the finding?
- 7. Serum ferritin \_\_\_\_\_
- 8. Stool occult blood test result
  - A. positive
  - B. negative
  - C. patient have overt GI bleeding
  - D. not done

9. Is the patient receiving any treatment for anemia?

A. Yes

B. No

10. Is the patient taking any of the following (tick on the space)

	Yes	No
a) Iron therapy		
b) ESA		
c) Folate		
d) Cobalamine		
e) Other please specify		

# Thank you for your time!!!