ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF MEDICINE

DEPARTMENT OF INTERNAL MEDICINE

THE BURDEN AND DETERMINATES OF ANEMIA AMONG PREDIALYSIS CHRONIC KIDNEY DISEASE PATIENTS FOLLOWING IN RENAL UNIT AT TIKUR ANBESSA SPECIALIZED HOSPITAL

A THESIS REPORT TO BE SUBMITED TO THE DEPARTEMENT OF INTERNAL MEDICINE, ADDIS ABABA UNIVERISTY COLLEGE OF MEDICINE AND HEALTH SCIENCE, IN PARTIAL FULFILEMENT OF THE REQUIREMENTS FOR SPECIALITY CERTEFICATE IN INTERNAL MEDICINE

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Abbreviations and Acronyms

AAU: Addis Ababa University

TASH: Tikur Anbessa Specialized Hospital

CKD: Chronic Kidney Disease

BP: Blood Pressure

DKD: Diabetic Kidney Disease

LMIC: Low and Middle Income Countries

KIDGO: Kidney Disease/Improving Global Outcomes

WHO: World Health Organization

eGFR: Estimated Glomerular Filtration Rate

NHANES: National Health and Nutrition Examination Survey

ESA: Erythropoiesis Stimulating Agent

APCKD: Adult Polycystic Kidney Disease

HIV: Human Immune Deficiency Virus

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ABSTRACT

Background: Anemia is common and significant complication of chronic kidney disease (CKD). Anemia of chronic kidney disease is associated with significant cardiovascular morbidity mortality and poor quality of life. However, its prevalence and management has not been studied thoroughly at local and national level.

Objective: To assess the prevalance, severity and management of anemia among predialysis chronic kidney disease (CKD) patients on follow up at Tikur Anbessa Specialized hospital (TASH) renal clinic.

Methods and Materials: A hospital based cross sectional hospital study was conducted from April 1 to July 30, 2020. Consecutive sampling was used to recruit 100 study participants. participants were interviewed using structured questionnaire, and their medical records were reviewed to obtain information on relevant medical history and laboratory parameters. Serum Iron panel was determined for all enrolled patients. Data was analyzed using SPSS version 26. Continuous variables were presented as means ± standard deviations and compared by t-test. Categorical variables were expressed as count with percentage and compared by Chi-square. Bivariate and multivariate logistic regression analyses were used to identify independently associated factors of anemia. P-value <0.05 was used to declare association.

Results: the burden of anemia in CKD was high (48%) and its prevalence increased with worsening kidney function. Diabetes (40%) and hypertension (25%) were the leading causes of CKD. CKD stage, iron marker and BMI were found to be independent determinant of anemia among CKD patients. Among patients with anemia, only 35.4% were treated, only 27% of patients were managed with iron agent and only 8.3% were managed with ESA.

Conclusion: Screening and intervention programs should be implemented to improve the outcome of CKD patients with anemia.

Grant source: Addis Ababa University, college of health sciences, school of medicine

Key words: chronic kidney disease, anemia, Ethiopia.

CHAPTER1: INTRODUCTION

1.1. 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. CKD which was once thought to be a disease of the industrialized world is now increasing alarmingly in Low and Middle Income (LMIC) like Ethiopia.[4-7] All stages of CKD are associated with increased risks of cardiovascular morbidity, premature mortality, and decreased quality of life. Other common complication of CKD includes hematological, metabolic bone disease, metabolic acidosis, and fluid and electrolyte imbalance.[4-7]

Anemia is the most common hematologic complication associated with CKD and it is the result of several factors including decreased erythropoiesis due to inadequate erythropoietin (EPO) production from the kidneys, iron, vitamin B12 and folate deficiency due to nutritional insufficiency or increased blood loss, inflammation and accumulation of uremic toxins.[9] Anemia in CKD is associated with CKD progression, cardiovascular comorbidities, and higher mortality. It also contributes to poor quality of life, sleep disturbances, and cognitive impairment.[21-25]

Timely treatment of anemia with an emphasis on raising hematocrit to at least 33% can improve patient's quality of life, decrease the need of blood transfusions, and improve cognitive function, and decrease hospitalizations and mortality.

1.2. Statement of the problem

The global burden of CKD is increasing at an alarming rate, which is associated with significant morbidity and mortality, necessitating special attention as one of the growing public health problems. According to the global burden of disease 2015 study, CKD was the 17th leading cause of global years loss of life and one of the fastest rising major causes of death, overall mortality due to CKD has increased by 31.7% from 2005 to 2015. [2] The burden posed by CKD disproportionately affects Low and middle income countries like Ethiopia because of increasing rate of noncommunicable diseases such as Diabetes and hypertension combined with risks associated with poverty like: high burden of infectious disease, enviromental pollution. [4-7]

Anemia is common in chronic kidney disease (CKD) and contributes to adverse clinical outcomes. The burden of anemia among CKD patient is higher in Low and middle income countries than developed countries this may be related to late presentation of patient with CKD, high prevalance of helminthic and other parasitic infestations and malnutrition. [10-13, 15-17] Studies done in both high income and LMIC have shown that the treatment of anemia in CKD patient is lower than what's expected according to the recommendations. Different factors have been identified to contribute to suboptimal treatment of anemia in these studies. [3, 8, 10-11, 17]

If untreated anemia in CKD patient is significantly associated with progression of CKD, and development of heart failure and stroke. It also contributes to impaired physical activity, neurocognitive dysfunction and poor quality of life. [21-25] These make it important to prevent, identify and treat CKD patients with anemia.

However, the prevalence, severity and management of anemia of CKD in Ethiopia have not been fully investigated. Therefore, this study aimed to determine the prevalence, severity and management of anemia among predialysis CKD patient following at renal clinic at TASH, Addis Ababa, Ethiopia.

1.3. Significance of the study

This study is expected to fill the gap in information on in the extent, severity, and determinants of anemia among predialysis CKD patients in Ethiopia. It also provides an insight on the practice of anemia management and assessment of iron deficiency. Due to the similarities in the population the results of this study could also be extrapolated to other Sub Saharan African countries.

CHAPTER2. LITERATURE REVIEW

2.1. The Epidemiology of chronic kidney disease

Chronic kidney disease (CKD) is a major public health problem across the world. The estimated global prevalance of CKD was reported to be 13%.[1] chronic kidney diseases (CKD) is on the rise worldwide including in Low and Middle Income countries (LMIC). As has been experienced in LMIC in other continents, the prevalence of chronic kidney disease (CKD) is dramatically increasing in the African continent with its complicationss overwhelming the poorly developed health infrastructure of most of those countries. According to recent report, the African region has a CKD prevalence of 10-15 %.[4-7] the reasons for escalating burden of CKD in Africa were due to rapid urbanization, life style change, environmental pollutant exposure, high burden of infectious diseases and increasing rate of non communicable diseases such as diabetes and hypertension.[4-7] Common etiologies of CKD in Africa were hypertension, chronic glomerulonephritis and diabetes.[4-7]

In Ethiopia, recently published hospital based studies have clearly demonstrated high prevalence rates of CKD. According to this study the prevalence of CKD was found to be 18% from southern part of Ethiopia, 20.9% from Gondar and 26% from Jimma.[18-20]

2.2. Prevalence and severity of anemia among CKD patient

Anemia is common in chronic kidney disease (CKD) and contributes to adverse clinical outcomes. The prevalence of anemia among CKD patient varies from one region to another. Recent NHANES report in United States revealed the prevalence of anemia was twice (15.4%). in CKD patients compared to the non CKD population (7.5%).[3] Recent Korean and Chinese cohort studies reported the prevalence of anemia to be 45% and 51% respectively.[8] Compared to developed countries, the burden of anemia among CKD patient is higher in Low and middle income countries. Report from several African studies revealed prevalence of anemia ranging from 51-87 %.[10-13, 15-17] Comparable trend was also observed from recent Ethiopian study with overall prevalence of anemia among CKD patient to be 64 %.[10] The prevalance of anemia increases with progression of CKD, becoming almost universal in patient with stage 4&5 CKD.[3, 8, 10-13, 15-17]

Various clinical factor and laboratory parameter are were identified as independent risk factors for anemia in CKD patient, which include, but are not restricted to, female gender, advanced stage of CKD, diabetic nephropathy as etiology, nonsmoking status, non obese body habitus, low serum albumin, abnormal bone minerals level (high phosphorus and low calcium levels), abnormal iron markers (transferrin saturation<20%), and low leukocyte count. [8, 13]

2.3. Treatment of anemia among CKD patients

Treatment of Anemia in CKD when indicated may involve iron therapy, blood transfusion, and use of erythropoiesis stimulating agents, and correction of anemia to a target hemoglobin concentration of 11-12 g/dl. [26] Early detection and optimal management of anemia has been shown to reduce morbidity and mortality among CKD patients. Untreated anemia in CKD patient is significantly associated with progression of CKD, and development of heart failure and stroke. It also contributes to impaired physical activity, neurocognitive dysfunction and poor quality of life.[21-25] despite these adverse effects, the identification and treatment of anemia among CKD patients had been reported to be suboptimal. [3, 8, 10-11, 17]

CHAPTER 3.METHODS

3.1. Study area

The study project was conducted in Tikur Anbessa specialized hospital which is the largest hospital in Ethiopia located in the capital Addis Ababa. The hospital is a teaching hospital for the Addis Ababa University, College of Medicine and Health sciences and is involved in undergraduate, postgraduate and fellowship trainings in different fields of clinical medicine. It has its own renal unit that's responsible for care of CKD patients both as inpatients and outpatients. The care to patients who are on follow-up at the renal clinic is provided by internal medicine residents in consultation with Nephrology consultants. Renal patients visit the clinic three times per week.

3.2. Study period

The study was conducted on CKD patients having follow-up in renal unit at Tikur Anbessa specialized hospital (TASH) over a period of four month from April1, 2020 to July 30 of 2020.

3.3. Study Design

A cross sectional hospital based study was conducted to assess the burden and determinants of anemia among predialysis chronic kidney disease patients following in renal clinic at Tikur Anbessa Specialized hospital (TASH).

3.4. Source Population

All CKD patients who have follow up at the renal clinic of Tikur Anbessa Specialized hospital.

3.5. Study population

All patients with an established diagnosis of CKD as per KIDGO eGFR criteria regardless of its primary cause were considered as study population.

3.6. Inclusion and exclusion criteria for patients

3.6.1. Inclusion criteria

- ✓ All Patients 18 years and above with an established diagnosis of stage 3 CKD and above and not on dialysis

3.6.2. Exclusion criteria

- ✓ Patients with causes of anemia other than kidney disease that is confirmed or suspected by treating physician, such as bleeding, active malignancy, hematologic causes
- ✓ Pregnant women
- ✓ Patient with prior history of dialysis
- ✓ Patient with incomplete medical record
- ✓ Those unwilling to participate

3.7. Study Variables

3.7.1. Dependant variables

- ✓ Anemia
- ✓ Severity of anemia
- ✓ Iron status

3.7.2. Independent variables

- ✓ Sociodemographic factors including age, sex, place of residence, educational status and marital status; behavioral factors including smoking and alcohol drinking
- ✓ Blood pressure level
- ✓ BMI
- ✓ Comorbidity and medication used for treatment of comorbidity
- ✓ Stage and causes of CKD
- ✓ Proteinuria/Albuminuria
- ✓ eGFR
- ✓ Hemoglobin
- ✓ Anemia treatment status and treatment modality

3.8. Operational Definitions

Chronic kidney disease (CKD): abnormalities of kidney structure or function present for more than three months, with implications for health. CKD is classified based on cause and GFR category (G1–G5). GFR was determined by using CKD-EPI equation for eGFR

Stages of CKD	Estimated GFR (ml/min/1.73/m2)
Stage 3a	45–59
Stage 3b	30–44
Stage 4,	15–29
Stage 5,	<15

LMIC: Gross national income per capita of less than$10 066 US dollars per annum in 2004.

Anemia: hemoglobin level <12g/dL in females and <13g/dL in males in patients aged 18 years of age and above. Severity of anemia was classified as mild (11–11.9 g/dL (females), 11–12.9 g/dL (males)), moderate (8–11 g/dL), and severe (<8 g/dL).

Hypertension: persistently elevated systolic blood pressure ≥140 mmHg and/or diastolic blood pressure≥90 mmHg in patients aged 18 years of age and above, history of hypertension, or the use of antihypertensive drug(s)

Hypertensive kidney disease: history of hypertension and physician diagnosis of hypertensive kidney disease

Diabetes: history of diabetes, or use of antidiabetic medication.

Diabetic kidney disease (DKD): type one diabetes mellitus for more than 5 years or type two diabetes mellitus of any duration, and urinalysis evidence of significant proteinuria.

Chronic glomerulonephritis: physician diagnosis of chronic glomerulonephritis and persistent proteinuria for 3 or more months.

Adult polycystic kidney disease: documented imaging evidence of polycystic kidney disease.

Obstructive uropathy: documented imaging evidence of obstructive uropathy.

3.9. Sample size and Sampling technique

Sample size is calculated using a single proportion formula at a prevalence of 80% with a confidence interval of 95% and degree of precision of 5%. Consecutive sampling was used to recruit 100 study participants.

3.10. Data collection

Data were collected through an investigator administered pretested questionnaire. Patients were interviewed to and their medical records were reviewed to obtain information on

relevant medical history and laboratory parameters. Serum iron panel (serum iron, total iron binding capacity, transferrin saturation and ferritin level) was determined for all study participants. The presumed cause of CKD was taken from clinical history, physical examination, and laboratory investigations including complete blood count, urinalysis, blood chemistry and ultrasound.

The hemoglobin level was used to define anemia according to WHO criteria. The serum creatinine was used to estimate GFR using chronic kidney disease epidemiology collaboration (CKD-EPI) equation.

3.11. Data analysis

All analyses were performed in IBM SPSS Statistics version 26. Continuous variables were presented as means ± standard deviations and compared by t-test. Categorical variables were expressed as count with percentage and compared by Chi-square. Both bivariate and multivariate logistic regression analyses were used to identify independently associated factors of anemia in CKD patients.

Those variables with a P-value <0.05 in the bivariate analysis were exported to multivariate analysis to control the possible effect of confounders. Odds ratio (OR) with 95%CI and P-value <0.05 were used to select variables associated with anemia in CKD patients.

4. Ethical consideration

Ethical clearance was obtained from the Research ethical review committees of Department of Internal medicine and Addis Ababa University, college of medicine and health sciences. Written informed consent was obtained from participants, and confidentiality of information obtained was maintained by coding and restricting access to the questionnaire.

5. Limitation of the study

This is a single centered hospital based study and as such the results cannot be generalized to the general population since patients that present to this hospital may not represent patients in the whole country. As this study is partially based on review of medical record, the data obtained will be incomplete for some associated factors

CHAPTER 4. Result and Discussion

4.1. Result

4.1.1. Sociodemographic characteristics of study participant

Among a total of 100 CKD patients, 73(73%) were male and 23(23%) were females. The mean age was 54.9 ± 15.6. Most of them were from Addis Ababa (86%), non-smokers (94%) and non-alcoholics (81%). Majority of them were Orthodox Christian followers (78%) and have joined formal education (66%).

4.1.2. Clinical and laboratory profile of CKD Patients

Diabetes was the leading cause of CKD, it accounted for 40% of cases, followed by Hypertension (25%). Majority of patients were in Stage 3 CKD (52%), followed by Stage 4 CKD (26%) and Stage 5 CKD (22%). albuminuria using urinalysis dipstick was documented in 71 patients, 59 of them had massive proteinuria (≥2+ albuminuria). 21% study subjects had ultrasound proven shrunken kidney.

Table1. Sociodemographic characteristics of CKD patients (N=100)

Variables	Frequency	Anemia		P-Value
		Present(N=48)	Absent (N=52)	
Age(years)				
18-34	14	8	6	0.486
35-49	17	11	6	
50-64	40	17	23	
65-79	27	11	16	
≥80	2	1	1	
Sex				
Male	73	33	40	0.487
Female	27	15	12	
Address				
Addis Ababa	86	40	46	0.49
Oromia	11	7	4	
Amhara	3	1	2	
Marital Status				
Single	16	12	4	0.134
Married	74	32	42	
Divorced	6	4	2	
Widowed	4	0	4	

Occupation				
Civil servant	12	6	6	0.867
Merchant	3	2	1	
Farmer	1	1	0	
Self employed	18	7	11	
Housewife	5	2	3	
Student	5	3	2	
Daily laborer	7	4	3	
Others [a]	49	23	26	
Religion				
Orthodox	78	39	39	0.607
Protestant	8	4	4	
Muslim	14	5	9	
Education				
Unable to read and write	11	2	9	0.054
Able to read and write				
Primary education	13	8	5	
Secondary education	23	9	14	
College and above	26	17	9	
	27	12	15	
Smoking				
Never	94	47	47	0.207
Former	5	1	4	
Current	1	0	1	
Alcohol drinking				
Never	81	40	41	0.844
Former	14	6	8	
Current	5	2	3	

Note: a= retired or no job

Table2: Clinical Characteristics of CKD Patients (N=100)

Variables	Frequency	Anemia		P-Value
		Present (N=48)	Absent (N=52)	
Family history of CKD				
Yes	10	3	7	0.223
No	90	45	45	
Presence of commorbidity				
Yes	63	27	36	0.216
No	37	21	16	
Taking other Medications[a]				
Yes	92	43	49	0.391
No	8	5	3	
CKD stage				
Stage 3a	23	4	19	<0.001
Stage 3b	29	11	18	
Stage 4	26	14	12	
Stage 5	22	19	3	
Causes of CKD				
Diabetes	40	19	21	0.813
Hypertension	25	9	16	
Unknown	12	7	5	
Obstructive uropathy	8	5	3	
Chronic GN	6	3	3	
PCKD	4	2	2	
Others	5	3	2	
BMI category				
<18.5	8	7	1	0.014
18.5-24.9	42	19	23	
25-29.9	37	13	24	
≥30	13	9	4	
SBP category				
<90	1	1	0	0.518
90-119	22	13	9	
120-139	34	14	20	
140-159	24	11	13	
≥160	19	9	10	

DBP category				
<60	3	3	0	0.305
60-79	44	21	23	
80-89	25	12	13	
90-99	25	11	14	
≥100	3	1	2	
Degree of albuminuria				
Negative	26	10	16	0.24
Trace to +1	12	2	10	
+2 or more	59	35	24	
Renal Ultrasound				
Normal	20	12	8	0.151
Shrunken	21	12	9	
Obstructive	6	4	2	
Polycystic	4	2	2	
Others	3	0	3	

Note: a= ACE inhibitors, calcium channel blockers, diuretics, insulin, oral antidiabetic drugs (metformin, glibenclamide), ASA and statins

Table 3: Comparisons of laboratory data between patients with and without Anemia (N=100)

Variables	Without Anemia	With Anemia	P-value
WBC, 10^6/L	7535 ± 2692	7162 ± 2326	0.937
Hemoglobin, g/dl	14.9 ± 1.6	11 ± 1.42	<0.001
Platelet, 10^9/dl	232 ± 63	274 ± 123	0.41
Serum Creatinine, mg/dl	2.13 ± 0.95	4 ± 2.4	<0.001
eGFR with race factor	42.7 ± 14.7	25.2 ± 14.7	<0.001
eGFR without race factor	36.8 ± 15. 7	21.7 ± 12.7	<0.001
Serum iron, microgram/dl	82.3 ± 35.8	62.8 ± 26.5	0.001
TIBC, ng/ml	303.7 ± 50.8	304 ± 82	0.53
Ferritin, ng/ml	200.3 ± 157	351 ± 462	0.045
TSAT, %	27.8 ± 12.8	23 ± 13	0.021
Calcium, mg/dl	8.7 ± 0.63	8.1 ± 1.5	0.22
Phosphorus, mg/dl	3.7 ± 1.02	4.6 ± 1.7	0.007
PTH	274.5 ± 318.2	372 ± 359.6	0.644

4.1.3. Prevalence of Anemia among CKD Patients

Among 100 non-dialysis CKD stage3–5 patients, 48 patients (48%) had anemia. The prevalence of anemia increased with worsening renal function, 4(17.4%) in Stage 3a, and 11(48%) in Stage 3b, 14(54%) in Stage 4 and 19(86.4%) in stage 5 CKD (Figure 1). With respect to the etiologic disease subgroups, subgroups with DN had the highest overall prevalence of anemia (47.5%) than other etiologic subgroups. Anemia was mild in 27 patients, moderate in 19 patients and severe in 2 patients. The severity of anemia also increased as the kidney function declined (Figure3).

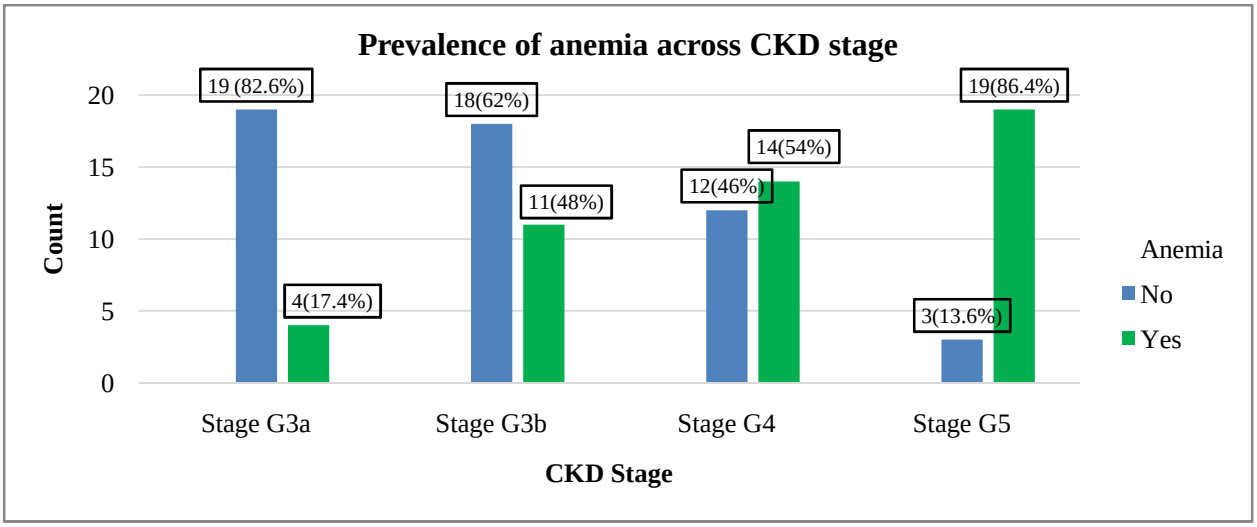

Figure 1: prevalence of anemia across CKD stage

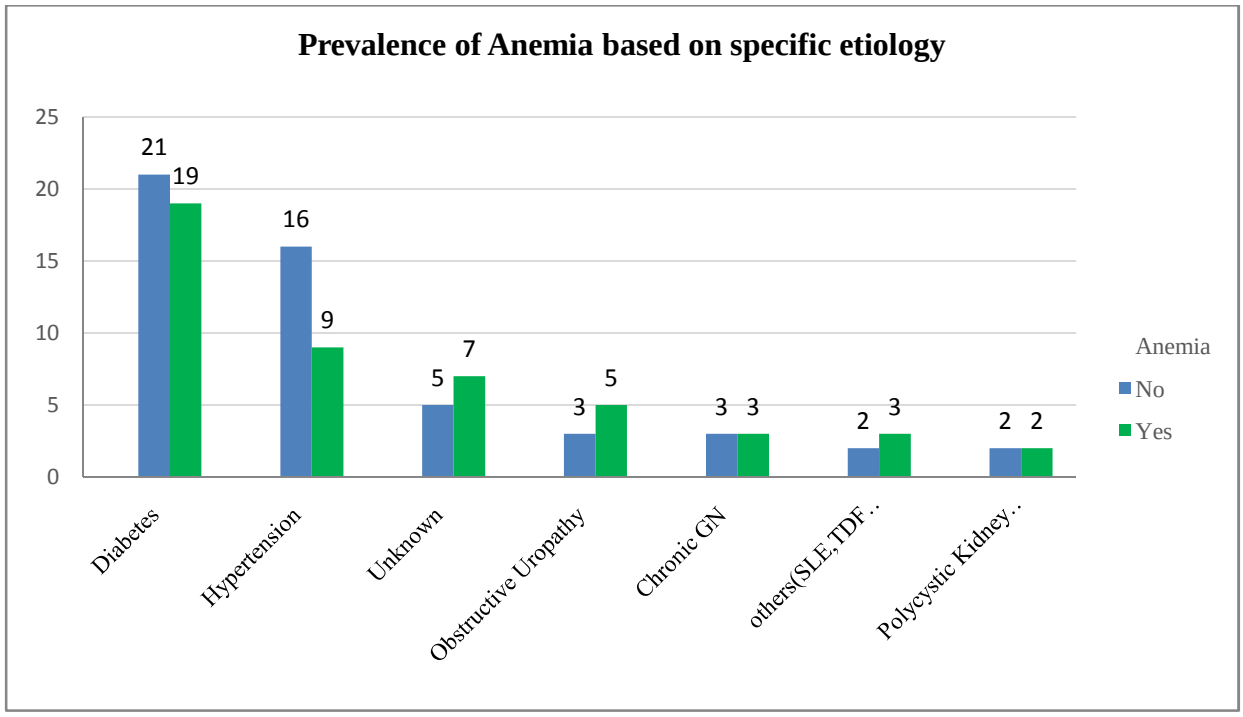

Figure 2: Prevalence of anemia across underlying cause of CKD

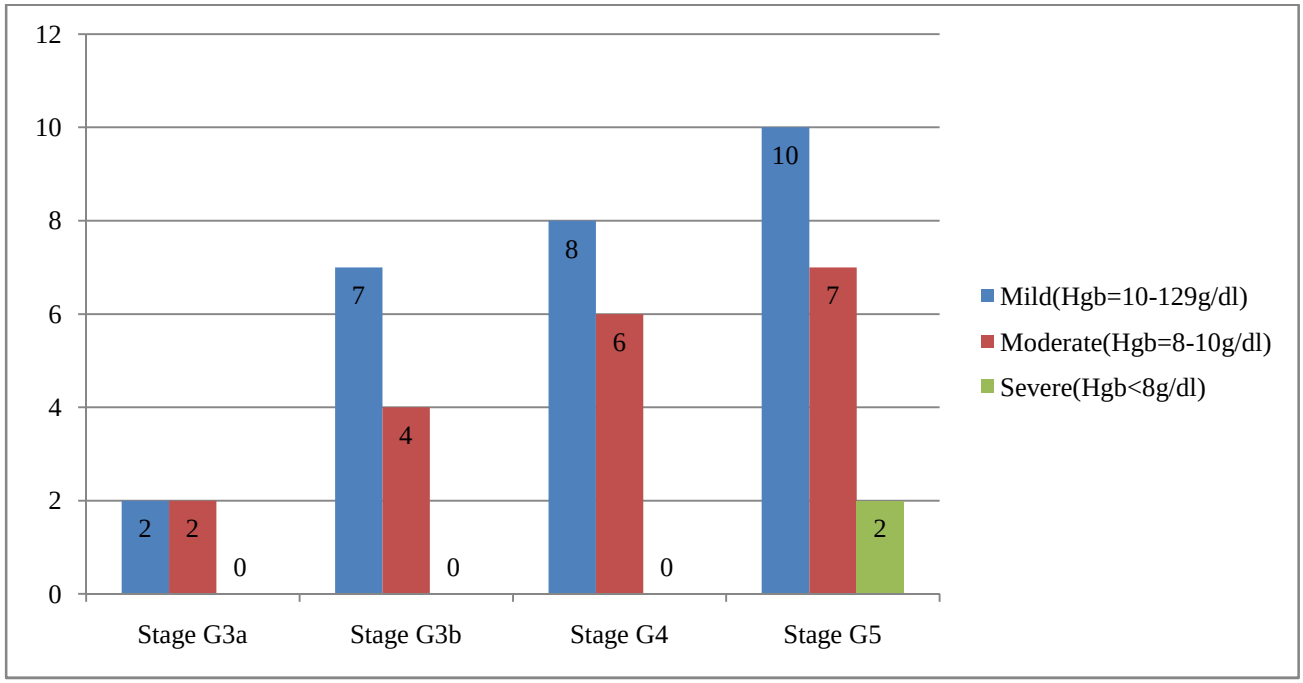

Figure 3: Severity of Anemia across CKD stage

4.1.4. Factors Associated with Anemia among CKD patients

The association of various clinical factors and laboratory parameters with anemia was examined using a bivariate logistic regression analysis. Among them, all the significant variables were included in the multivariate logistic regression model (Table 4). The risk for anemia increased with stage of CKD in stepwise manner (OR of 3.97 for stage 3b, OR of 11.6 for stage 4 and OR of 68.47 for stage 5, stage3a as the reference). The risk of anemia were lower among those with BMI of 18.5-24.9kg/m2 (OR=0.039, 95%CI; 0.003-0.552, P=0.016) and BMI of 25-29.9 kg/m2 (OR=0.046, 95%CI; 0.003-0.637, P=0.022).

With regard to iron markers, 6.1-fold increased risk was observed in the group with TSAT< 20.0% (OR=6.143, 95%CI, 1.72-21.938, P=0.005), while 14.7% reduction of OR was shown in the group with ferritin ≥ 500ng/Ml.

Table 4: Bivariate and Multivariate Logistic Regression Analysis of Factors Associated With Anemia among CKD Patients at TASH, April1, 2020 to July 30, 2020 (N=100)

Variables	Anemia		Bivariate		Multivariate		
	Present	Absent	OR	95%CI of OR	OR	95%CI of OR	P-value
Sex							
Male	33	40	1				
Female	15	12	1.515	0.623-3.682			
Smoking							
Never	47	47	1				
Former	1	4	0.25	0.027-2.321			
Current	0	1	0.25	0.027-2.321			
BMI category							
<18.5	7	1	1		1		
18.5-24.9	19	23	0.118	0.013-1.046	0.039	0.003-0.552	**0.016**
25-29.9	13	24	0.077	0.009-0.669	0.046	0.003-0.637	**0.022**
≥30	9	4	0.321	0.029-3.556	0.168	0.009-3.155	
CKD stage							
Stage 3a	4	19	1		1		
Stage 3b	11	18	2.9	0.781-10.796	2.487	0.484-12.784	
Stage 4	14	12	5.54	1.472-20.86	11.846	2.142-65.531	**0.005**
Stage 5	19	3	30.08	5.915-152.922	51.992	5.123-527.68	**0.001**

Causes of CKD							
Diabetes	19	21	0.402	0.098-1.643			
Hypertension	9	16	0.646	0.175-2.382			
Unknown	7	5	0.714	0.1-5.118			
Obstructive uropathy	5	3	1.071	0.128-8.977			
Chronic GN	3	3	0.714	0.074-6.922			
PCKD	2	2	1.19	0.19-7.456			
Others	3	2	1				
Ferritin category							
≥500 ng/ml	39	49	1		1		
<500 ng/ml	9	3	3.769	0.955-14.873	0.147	0.023-0.949	**0.044**
TSAT category							
≥20%	22	11	1		1		
<20%	26	41	3.154	1.315-7.564	6.143	1.71-21.938	**0.005**
Calcium, mg/dl	Mean= 8.4 ±1.2		0.605	0.403-0.908	1.262	0.598-2.665	
Phosphorus, mg/dl	Mean= 4.14 ± 1.5		1.765	1.184-2.629	1.091	0.645-1.844	
PTH	Mean= 321.34 ± 340.5		1.001	1-1.002			

4.1.5. Iron status and management of Anemia

Among 48 subjects with anemia, baseline iron panel study was done only for 7(14.6%) patients. After enrollment into study iron study was determined for all study participant and among patients with anemia, 22(45.8%) had TSAT <20% and 39 (81.25%) had Ferritin <500 ng/ml. while 26 (54.2%) had TSAT ≥20%. and 9(18.75%) had ferritin ≥500ng/ml. (Table 5). Among 48 patients with documented anemia, only 17(35.4%) were treated. Options of therapy were oral iron agent 13/48, ESA 1/48, iron agent and blood transfusion 1/48 and B12 and folate 2/48 (Table 6).

Among patients with anemia, iron agents was prescribed for 6/22 when TSAT was less than 20.0%, and for 7/26 when TSAT was higher than 20.0%. None of them received IV iron (Table 7). According to 2012 KIDGO guideline, we found 12 patient who were eligible for ESA, but only 1 received ESA.

Treatment target (Hgb of 10-11g/dl) was achieved only in 9 of 17 treated cases and the median change in hemoglobin was 1.4 g/dl (range 0.3-5.4g/dl).

Table 5: Comparison of iron status between patients with anemia and without anemia (N=100)

Iron marker	Without Anemia (N=52)	With Anemia (N=48)
TSAT ≥20% or ferritin ≥500ng/ml TSAT ≥20 Ferritin ≥500 ng/ml	 41 3	 26 9
TSAT < 20% or ferritin < 500 ng/mL TSAT <20% Ferritin <500ng/ml	 11 49	 22 39

Table 6: Treatment of patient with anemia (N=48)

Type of treatment	Number
Oral iron agent	13
ESA only	1
Oral Iron and blood transfusion	1
Other(folate and B12)	2
Not treated	3

Table 7: Treatment with iron agents in patients with anemia

Treatment	TSAT <20%(N=22)	TSAT ≥20(N=26)
Iron agent	6	7
Oral iron only IV iron	6 0	7 0

4.2. Discussion

In this study, the overall prevalence of anemia in non-dialysis patients with CKD stage 3–5 was 48%. This is comparable with recent Korean and Chinese cohort studies which reported 45% and 51% of non-dialysis CKD stage 1-5 had anemia respectively.[8] In the United States, the prevalence of anemia in CKD patients was 15.4% in a NHANES study including 410 CKD stage 1–5 subjects older than 18. [3] Report from several African studies revealed prevalence of anemia ranging from 51-87%. [10-13, 15-17] A report from study conducted in Northwest Ethiopia showed that 64.5% of 251 patients with CKD stage 1-5 were diagnosed with anemia.[10] The

variation in the prevalence of anemia could be due to the differences in the severity of CKD in the study population, the overall prevalence of anemia in adults without CKD in that population, and the differences in the nutritional status.

We examined the contributing factors to anemia using a bivariate and multivariate logistic regression analyses. The study demonstrated prevalence of anemia increased with stage of CKD. Similar finding was reported from Korean cohort with prevalence of 10% at stage 1 to 96.5% at stage 5.[8] Comparable trend was also observed from recent Ethiopian study with prevalence of 20% at stage 1 and 2 to 93.8% at stage 5.[10] In contrast, gender or age or smoking status was not significant factors associated with anemia.

The main etiologies of CKD were diabetes and hypertension. Which reflect a consequence of growing epidemic of chronic non-communicable disease in developing countries [4-7]. However, in our study there was no significant association between anemia and etiology of CKD. This might be due to small sample size of our study.

Patients with normal and overweight body habitus was associated with lower risk of anemia compared. A Korean study showed that higher BMI was associated with lower risk for anemia, while lower BMI was associated with higher risk for anemia.[8] underweight may represent the malnourished state, which is closely related with chronic inflammation in CKD and it's one of the indicator of advanced CKD.

In terms of blood pressure, higher systolic blood pressure, lower diastolic blood pressure, was not significant factors associated with anemia. High phosphorus was associated with anemia in a bivariate model. However, when we included high phosphorus into the multivariate model, its statistical significance disappeared.

The 2012 KDIGO Anemia guidelines recommend that TSAT and ferritin level should be determined in all pt with CKD and anemia. And recommend trying intravenous iron when TSAT is less than 30.0% and ferritin is less than 500 ng/ml. also suggests physicians to make a decision whether to initiate ESAs considering the risk and benefit in adult non-dialysis CKD patients with hemoglobin less than 10.0 g/dl.[26]

In our study only 7 (14.6%) patients with anemia were screened for iron deficiency before enrollment into study. After enrollment into study iron panel was done for all participants and among patients with anemia, 22(45.8%) had TSAT <20% and 39 (81.25%) had Ferritin <500

ng/ml. In contrast, 26 (54.2%) had TSAT ≥20%. and 9(18.75%) had ferritin ≥500ng/ml. In those subjects' causes of anemia other than iron deficiency, such as erythropoietin deficiency, uremia related inhibition of erythropoiesis, and short life span of the red blood cell may be responsible. In a multivariate analysis, TSAT lower than 20.0% was associated with 6-fold increased risk of anemia, but ferritin < 100 ng/mL showed negative association with anemia. The poor correlation of ferritin level and anemia in CKD patients could be explained by hepcidin as well as uremic inflammation. Hepcidin inhibits the iron usage by degradation of iron transporter ferroportin, and its serum level is increased in CKD patients.[10] in that condition, ferritin could be elevated in spite of poor usage of intracellular iron.

The rate of prescription with iron agents was lower than expected in this study. In patients with anemia and TSAT less than 20.0%, iron agents were supplemented in only 27%. Out of 12 patients with hemoglobin<10g/dl and TSAT<20% and ferritin <500ng/ml, only 1 received ESA and none was given IV iron. Suboptimal treatment of anemia with ESA and iron agent was noticed in this study, possibly explained by unavailability or high cost of drugs.

CHAPTER 5. Conclusion and Recommendation

5.1. Conclusion

In this study, the overall burden of anemia was substantial. The proportion of patients with anemia and its severity increases as the CKD stage worsens. Additionally low serum ferritin, low transferrin saturation, and low BMI were independently associated with the presence of anemia.

Iron studies were not done in the majority of patients with anemia as part of their routine care. Treatment of anemia was also nor provided to the majority of patients which require treatment as per evidenced based treatment guidelines.

5.2. Recommendation

We recommend, screening and intervention program for anemia of CKD should be implemented to improve the outcome of CKD patient with anemia. Longitudinal population based studies are required to determine the burden and actual determinant of anemia in CKD patients.

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Appendix

Appendix 1: Declaration

I, the undersigned, declare that this postgraduate thesis is my original work, has not been presented for degree in this or any other university and that all sources of material for the thesis have been duly acknowledged.

Post graduate candidate: Semir Abdi (MD, Internal Medicine Resident)

Signature: ……..

Date of submission: January 8

This thesis has been submitted with my approval as advisor

Advisor: Addisu Melkie (MD, Internist and Consultant in Nephrology)

Lissane Seifu (MD, Internist and Consultant in Nephrology)

Signature: …….

Date: …….

Place: Addis Ababa, Ethiopia

Appendix 2: QUESTIONNAIRE **(For Patient interview)**

This is a questionnaire prepared to undergo a study on the prevalence, severity and management of anemia among predialysis CKD patients on follow-up at the Tikur Anbessa Specialized Hospital (TASH) renal follow up clinic. You will be asked a series of questions about your chronic kidney disease and other aspects associated with your health. We would like to assure you that none of the information obtained here will be used for any other purpose except for this study. You can refuse if you want not to be included in the study either at the start or at any time during the interview. We highly appreciate your contribution.

Date: _____ MRN/ICARE NUMBER: _____ Study ID: _____

1. Sociodemographic characteristics

1.1. Age: _____

1.2. Sex: A) Male B) Female

1.3. Address: A) Addis Ababa b) Oromia C) Amhara D) SNPPR E) others (specify)

1.4. Marital status: A) Single B) Married C) Divorced D) Widowed

1.5. Occupation: A) Civil servant B) Merchant C) Farmer D) Housewife E) self-employed

F) Daily laborer G) student H) others (retired, no job) specify

1.6. Educational status: A) unable to read and write B) Able to read and write C) primary education D) secondary education E) college and above

1.7. Religion: A) Orthodox Christian B) Catholic Christian C) Protestant Christian

D) Muslim

2. Clinical profile of CKD patient

2.1. Smoking status: A) Never B) former C) Current D) unknown

2.2. Do you have a sibling, parent or offspring who has chronic kidney disease?

A) Yes B) No

2.3. Symptoms of anemia

Symptoms/ ምልክቶች	Yes	No
Fatigue/ የድካም ስሜት		
Dizziness/ የማዞር ስሜት		
Tinnitus/ በጆሮ ላይ መÄህ		
Palpitation/ የልብ ምት መሰማት		
Shortness of breath/ትንፋሽ ማጠር		

CHECKLIST (FOR CHART REVIEW)

2.5. Comorbidities (other than cause of CKD): A) Yes B) No

A) Coronary Artery Disease (CAD)

B) Heart Failure

C) Cerebrovascular disease

D) Peripheral arterial disease

E) Others (specify) _____

2.6. Any medication prescribed for treatment of commorbidity

A) No B) Yes (specify what medication was prescribed)

2.7. Stage of CKD: A) stage G3a B) stage G3b C) stage G4 D) stage G5

2.8. Presumed etiology of CKD

A). Hypertension B) Diabetes C) Chronic glomerulonephritis D) HIV E) polycystic kidney disease F) obstructive uropathy G) Unknown H) others (specify)

2.9. Most recent vital sign

1) BMI (kg/m^2): _____

2) Blood Pressure: Systolic blood pressure: _____ Diastolic blood pressure: _____

3. Laboratory profile of CKD patient

3.1. Most recent Creatinine (in mg/dl): _____

3.2. eGFR (ml/min/1.73m^2) using CKD-EPI(calculate both with and without race factor):

- With race factor _____ without race factor ----------

3.3. Urine protein on dipstick

A) Negative

B) Trace to +1

C) +2 or more

3.4. CBC profile: (current value)

CBC profile	values
WBC count (10^6/L)	
Hemoglobin (g/dl)	
MCV (fl)	
MCHC (pg/dl)	
RDW	
Platelet count (10^9/L)	

3.5. Number of Hgb determined and value of each Hgb determined in the past 6month

Number of Hgb determined	Values of each Hgb determined in the past 6month			

3.6. Iron study:

Iron study	Available	Not available
Serum iron		
TIBC		
Ferritin		
Transferrin saturation		

3.7. Iron study current value:

Iron study	Current value
Serum iron (microgram/dl)	
Serum ferritin (nanogram/dl)	
Total iron binding capacity (microgram/dl)	
% Transferrin saturation	

3.8. HIV serology: A) reactive B) non reactive C) unknown

4. Management of Anemia

The following should be filled for those patients with diagnosis of Anemia hemoglobin less than or equal to 10gm/dl

4.1. was the patient started on treatment for anemia: A) Yes B) No

4.2. If the answer to above question is yes, what type of treatment was started?

Types of treatment	Tick the types of treatment given
Iron only	
Blood Transfusion only	
Erythropoietin Stimulating agent (ESA) only	
Iron and blood transfusion	
Iron and ESA	
Iron + ESA + Blood transfusion	
Others (specify- Folic acid, Vitamin B12)	

4.3. Was target of treatment achieved A) Yes B) No

4.4. Current Hgb value----------

Appendix 3: Consent form

RESEARCH PROJECT PARTICIPATION CONSENT FORM: FOR PATIENTS

Information to study participants (Patients)

Title of the study project: **The prevalence, severity and management of anemia in predialysis CKD parents following renal clinic at Tikur Anbessa Specialized Hospital (TASH), Addis Ababa, Ethiopia.**

Principal Investigator: Dr Semir Abdi (MD, Internal medicine resident)

Procedure of the study: The study primarily involves data collection with interview using semi structured questionnaire and review of medical records of patients attending follow up clinic at Tikur Anbessa Specialized Hospital (TASH) renal clinic.

Benefits, Risk or possible discomfort

Benefit: There is no direct benefit patients get as a result of being involved in the study. The participants will not be provided any payment and/or other incentives to take part in the study.

Risks: There is no risk associated with the study. No procedures will be done on patients during this study except for Blood pressure, Pulse, weight and height measurement.

Confidentiality and right to withdraw

Participants' information will be stored in a locked file to be only accessible for the purpose of the study only. The file will be organized and coded so that patients' specific identifiers will not be revealed at any point during the study.

Patients have the full right of refusing to withdraw at any point during the study.

Consent form

Dear Participant,

My name is_____. I am one of the members of the group who are conducting this study. I am conducting a research project titled: The prevalence, severity, management of anemia and biochemical Mineral Bone Disease abnormalities among predialysis CKD patients on follow-up at the Tikur Anbessa Specialized Hospital (TASH), Addis Ababa, Ethiopia. Accordingly, I am grateful to inform you that you are selected to be a participant of the study. By participating in the study, you will provide us about 30 minutes of your time in answering certain questions related to your disease.

All the information you provide us will be kept confidential. There is no risk associated with the study to you. You have full right to decline involvement in the study or withdraw from the study at any point during the interview. Finally, we kindly ask you to give as a genuine response.

Once you decide to involve in the study please put your signature in the space provided below to describe that you willingly decided to participate in the study.

Signature of participant: _____ Date: _____

Signature of the interviewer: _____ Date: _____

Contact information

This research project will only be carried out after approval from the Ethical review committee of department of internal medicine and of Addis Ababa University. If you have any questions and concerns you can contact Dr Semir Abdi by any of the following addresses

Mob: 0936115271

Email: semirabdi61@gmail.com

ስጥናቱተሳታፊዎችየመረጃቅጽ

በአዲስአበባየኒቨርሲቲጤናሳይንስኮሌጅበድህረምረቃትምህርትንርግፊምየሙስጥደዌትምህርትክፍል፡፡

ከዚህበታችእንደተመለከተዉበአዲስአበባየኒቨርሲቲበድህረምረቃትምህርትንርግፊምየሙስጥደዌትምህርትክፍልየኩላሊትሕመምተኞችንበሚመለትአነስተኛጥናትበጥቁርአንበሳሆስፒታልየኩላሊትክፍልእያካሄድንነዉ፡፡

የዚህጥናትተሳታፊለመሆንእርስዎተጋብዘዋል፡፡በጥናቱሳይከመሳተፍበፊትጥናቱንበተመለከተለስፈላጊየሆኑመረጃዎችንማግኘ ተያስፈልግዎታል፡፡ስለሆነምበጥናቱሳይለመሳተፍምሆነሳለመሳተፍመጀመሪያማወቅየምገባዎትንመረጃእንደምከተለዉእናቀር ብልዎታለን፡፡

1. የጥናቱስላማ፡ስርበለደደየኩላሊትሕመምተኞትሳይበተጓደኛሊመጡከሚችሉችግሮችውስጥየደምማነስናየሰውነትንጥረነገር ችመጠንመዛባትንለማሳወቅነው፡፡

2. በጥናቱየሚካተቱተሳታፊዎች፡ማንኛዉምከለድስትወርበሳይስርበለደደየኩላሊትሕመምክትተልየሚያደርግግለሰብእናደረጃ ውምሦስተኛናከዚያበሳይየሆነለክትትልየመጣ/ችእናለመረጃዉቆቃደኛየሆነ/ች፡፡

3. በጥናቱየሚካሄዱነገሮች፡-
   ጥናቱየሚካሄደዉለዚህጥናትየተዘጋጀውንቃለመጠይቅማድረግ፣ስካሳዊምርመራዉእናየደምናሙናመዉሰድናቸው፡፡

4. ከጥናቱጋርየተያያዘጉዳት፡ጥናቱበተሳታፊዎች/ሕመምተኞችስካልሳይምሆነለእምርሳይፈልሞየሚያደርሰውጉዳትየለም፤የ ሚያደርሰውነገርቢኖርየእርስዎንግዜመሻማትናየደምናሙናሲወሰድየሚሰማሕመምብቻነው፤ያልገባዎትንመረጃለመጠየ ስለደገደዱም፡፡

5. ጥቅም፡በጥናቱበመሳተፍዎየሚለፈልዎትክፍያወደምየተለየጥቅምየለዉም፡፡በሌላበኩልበጥናቱሳይበመሳተፍዎለሚጠየቁ ትጥያቁዎችተገቢዉንመረጃመስጠትዎናየደምናሙናውጤትዎለርበለደደየኩላሊትሕመምተኞችክትትልለገልሎትይደክፍ ተኛለገዛደኖረዋል፡፡

6. ሚስጥርየመጠበቅሁኔታ፡በጥናቱሳይየእርስዎለምናካርድቁጥርለደጠቀለም፤የሚሰጡተመረጃምበሚስጥርደጠበቃል፤ለሶስ ተኛለዉተሳልፎለደሰጥም፡፡

ማንኛዉምየጥናቱተሳታፊበማንኛዉምሰዓትጥናቱንየማቋረጥመብትለለው፡፡

የጥናትአድራጊውመግለጫ

እኔስሜ ----------የምባለውበጥናትአድራጊውድንውስጥአንዱአባልነኝ::

ይህጥናትበሰደደየኩላሊትሕመምተኞትላይበተጓዳኝሊመጡከሚችሉችግሮችውስጥየደምማነስናየሰውነትንጥረነገሮችመጠንመዛባትን ለማሳየትነዉ::

በጥናቱላይመሳተፍምሙሉበሙሉየሚመሰረተዉበፈለምጭባጎትናፍቃደኝነትላይነዉ::ከመጀመሪያዉበጥናቱላይመሳተፍምሆነሳለመሳተፍ ይችላሉ::ያልገባዎትንመረጃለመመለስእደገደዱም::ስምዎትከመረጃዉጋርአይዳካተትም:የሰጡትመረጃሁሉበሚስጥርእንደሚጠበቅልዎቃ ልእንገባለን::

ጥናቱየሚወስደዉ ግዜበአማካይ 30
ደቂቃብቻነዉ::ይህጊዜዎትንየሚይዝቢሆንምበጥናቱላይበመሳተፍዎለሚጠየቁትጥያቄዎችተገቢዉንመረጃመስጠትዎናየደምናሙናው ጤትዎስርበሰደደየኩላሊትሕመምተኞችክትትልእንዲደረግሎትእደከፍተኛሚናያለዉመሆኑእንድተባበረንእንጠይቅዎታለን::

የተወሰኑደቂቃዎችባነጋገርዎፈቃደኛነዎት፤በመጨረሻምስላዳመጡኝከልብአመሰግናለሁ::

የጥናትአድራጊሙሌርማ ---------- ቀን: ----------

የጥናትአድራጊዎችአድራሻ:

1. ዶ/ር ሰሚር ኣብዱ:- የሞባይልስ/ቁ 936115271፣ኢሜይል semirabdi61@gmail.com

ኣዲስኣበባዩኒቨርሲቲ

ጤናሳይንስኮሌጅ

በሕክምናትምህርት

የሙስጥደዌትምህርትክፍል (8ኛፎቅ)