UNIVERSITY OF RWANDA
COLLEGE OF MEDICINE AND HEALTH SCIENCES
SCHOOL OF MEDICINE AND PHARMACY
INTERNAL MEDICINE DEPARTMENT

PREVALENCE OF ANEMIA AND SHORT-TERM OUTCOME AMONG INTERNAL MEDICINE PATIENTS AT UNIVERSITY TEACHING HOSPITAL OF KIGALI ''PROSPECTIVE OBSERVATIONAL ANALYTICAL STUDY''

A Dissertation submitted in partial fulfillment of the requirements for the degree of MASTER OF MEDICINE IN INTERNAL MEDICINE In the college of Medicine and Health Sciences

BY
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Master of Medicine in Internal Medicine

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Declaration

I, **Dr. HAVUGIMANA Phocas**, to the best of my knowledge hereby declare and certify that the work presented in this dissertation ***entitled "Prevalence of Anemia and short-term Outcome among Internal Medicine Patients at University Teaching Hospital of Kigali"*** is entirely my own and original work except where specifically acknowledged and it has never been presented or submitted in whole or in part to the University of Rwanda or any other Institution.

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Signature

I, hereby Declare that this dissertation has been submitted with my approval as the supervisor
Prof. MASAISA Florence

Date: 31st August ,2021

Signature

DEDICATION

To my beloved Wife MUSHIMIYIMANA Diane

To my Daughter HAVUGIMANA Eza Unique Gianna

To all members of my Family

This work is dedicated with great pleasure

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To God the Almighty, source of life, knowledge, and wisdom.

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May all receive the expression of my sincere gratitude!

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ABSTRACT

Background: Anemia is defined by World Health Organization as hemoglobin level of <13.0g/dl in men and <12g/dl in women. Anemia is a big concern worldwide with around 2 billion people affected. It has numerous predisposing factors including Nutritional deficiencies, Infections, Malignancies, Chronic inflammations, chronic kidney disease, etc. Admitted patients with concurrent anemia are at increased morbidity and mortality risk and there is evidence that it prolongs hospital stay and increases re-admission rates. In Rwanda, we know from Rwanda demography and health survey 2015 that the prevalence of anemia is around 36.5% in children and 19.2% in females. Data in high-risk patients like those in hospital with different comorbidities are lacking. Our aim was determining the prevalence of anemia in admitted patients but also their length of hospital stay and mortality risk according to their hemoglobin level.

Method: A Prospective Observational Analytical Study at University Teaching Hospital of Kigali was done and recruited 166 Patients admitted in March and April of 2021; among whom 143 were eligible for the study and followed up until discharge.

Results: The Prevalence of anemia was 52.4% among 143 enrolled patients. The majority had Normocytic anemia with 41.9% and macrocytic anemia was the least common with 2.8% of participants. Hypertension and Diabetes were the most common comorbidities found in 50 (35%) and 37 (25.9%) of respondents respectively. CKD (OR 12.108, p0.001), Cancer (OR 10.488; p 0.027) and HIV/AIDS had higher odds of developing anemia. Mortality rate was 13.3 % in all participants but the mean Hemoglobin of patients who died was lower compared to the mean hemoglobin of patients who were discharged alive with 11.4±4.1g/dL and 12±3.3 g/dL respectively (P-value 0.551). Patients with severe anemia were 4 times more likely to die while mild and moderate anemia did not significantly impact the likelihood of death compared to patients with normal Hemoglobin. Hemoglobin level correlates with the length of hospital stay as the lower the hemoglobin level, the longer the hospital stay was (P-value 0.010).

Conclusion: Anemia is prevalent among in-patients at CHUK patients with CKD, cancers, and HIV/AIDS as leading predisposing factors. Patients with anemia are at increased risk of mortality and longer length of hospital stay compared to those with normal hemoglobin level.

Key Words: Anemia, Outcome, CHUK, Internal Medicine and In-patients.

Abbreviation

AIDS: Acquired immunodeficiency syndrome

BM: Bonne marrow

CHUK: University Teaching Hospital

CI: Confidence interval

CKD: Chronic Kidney disease

CMHS: College of Medicine and Health Sciences

DM: Diabetes

FBC: Full Blood Count

GFR: Glomerular Filtration rate

GI: Gastrointestinal

HAART: Highly Active Anti-Retroviral therapy

Hb: Hemoglobin

HCT: Hematocrit

HF: Heart Failure

HIV: Human immunodeficiency virus

HR: Hazard Ratio

HR: Hazard ratio

HTN: Hypertension

IDA: Iron deficiency anemia

IRB: Institutional Review Board

LOS: Length of hospital stay

MCHC: Mean corpuscular hemoglobin concentration

MCV: Mean Corpuscular Volume

Mmed: Master of Medicine

NSAIDS: Non-steroidal anti-inflammatory drugs

OR: Odd ratio

PBF: Peripheral blood film

PUD: Peptic ulcer disease

RA: Rheumatoid Arthritis

RBC: Red blood cell

SD: Standard deviation

UR: University of Rwanda

USA: United States of America

VTE: Venous Thrombo-embolic Event

WBC: White blood cell

WHO: World health organization

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CHAPTER I. INTRODUCTION

1.1. General Introduction and Justification of the Study

Anemia is defined as decreased level of hemoglobin below the normal limit of less than 13g/dl and 12g/dl in men and women respectively (1,2). According to WHO, Anemia is any hemoglobin level less than 13g/dl and 12g/dl in men and women respectively. WHO categorizes anemia as mild when hemoglobin is from 10 to 11.9g/dl and 10 to 12.9 g/dl in women and men respectively; moderate when hemoglobin level is from 7 to 9.9g/dl in both genders and severe when hemoglobin is less than 7g/dl in both men and women (3–5). Anemia remains a big concern worldwide, affecting all genders and all age categories across all countries but lower and middle income countries with less resources , deficiency in diet and many comorbidities are more affected(2,6–8). Anemia tops all known blood abnormalities worldwide with around 28.4% of the world's population affected around the globe(6,9). The most affected population worldwide include women, young children, and people with chronic diseases. Anemia was highest prevalent among pre-school children with 47.4% and less prevalent among men with 12.7%(6,7). Anemia affects more than 2 billion people worldwide and is causing significant morbidity and mortality among anemic subjects (10–12). The etiologies of anemia is multifactorial in most cases with many predisposing factors including nutritional deficiencies, infections, Malignancies, chronic inflammations and other chronic diseases like RA, chronic liver disease, Chronic kidney disease etc. (2,10,13).

Admitted patients with concurrent anemia are at increased morbidity and mortality risk and there is evidence that co-existing anemia prolongs hospital stay and increases re-admission rates and the outcomes in hospitalized patients can be improved by managing anemia along with the primary cause of admission (2,9,14). From the WHO data, most cases of anemia are in Africa. In Ghana , it was found that anemia was the leading cause of admission and second most common contributing factor for death (6).

The Prevalence of anemia in Africa is diverse. There is a reported study in Uganda with a prevalence of 16.8 to 33.8% among adults with all genders. Another study reported a prevalence of 12.5 % and 13.2% in older men and women respectively in South Africa and 23 % prevalence in Zimbabwe for general population. In Ghana a study reported as much as 53.2% prevalence in pregnant women. In Ethiopia , studies have reported the prevalence of anemia ranging from 17 to 52.3% and WHO data indicates that the prevalence of anemia among non-pregnant women in Ethiopia is around 23.3% as of 2016 (10).

In Rwanda, we don't have much data regarding anemia in general population but we know from Rwanda demography and health survey 2015 that the prevalence of anemia is around 36.5% in children and 19.2% in females but the data in high risk population like those who are admitted in hospitals with different comorbidities are lacking(15).

In 2018, Nkeshimana M.et al, have conducted a study in different hospitals including CHUB in southern province, Bushenge Provincial hospital in western province, Nemba and Kinihira Hospitals in Northern Province, Masaka hospital in Kigali city and Rwamagana hospital in Eastern province. In this study, they enrolled 191 healthy subjects who were caretakers in different hospital. The prevalence of anemia was 6%. However, the prevalence of vitamin B12 deficiency was recorded in 9.9% of the participants, Iron deficiency was recorded in 3.6% and none of them had folic acid deficiency(29).

1.2. Problem statement

Anemia remains a big concern worldwide, affecting all genders and all age categories in both developed and developing countries but lower- and middle-income countries with less resources and deficiency in diet and many comorbidities. Admitted patients with concurrent anemia are at increased morbidity and mortality risk and there is evidence that co- existing anemia prolongs hospital stay and increases re-admission rates and the outcomes in hospitalized patients can be improved by managing anemia along with the primary cause of admission.

Few available data have shown that anemia is prevalent in the general population, however, we don't have the extent of its burden on admitted patients and they are the ones at high risk of developing anemia and its complications.

The current study evaluated the prevalence of anemia but also its impact on admitted patients during their hospital stay which will increase the awareness among clinicians so that anemia can be timely detected and treated effectively to limit its impact on admitted patients.

1.3. Hypothesis

Anemia is prevalent among patients admitted at University Teaching Hospital of Kigali (CHUK)
Anemia severity among Internal Medicine patients admitted in University Teaching hospital of Kigali correlate with length of hospital stay and mortality risk.

1.4. General objective

To document the profile and short-term outcomes of anemia among Internal Medicine patients admitted at University Teaching Hospital of Kigali (CHUK).

1.4.1. Specific objectives

To determine the prevalence and types of anemia among Internal Medicine patients admitted at University Teaching Hospital of Kigali
To determine the risk factors of anemia among Internal Medicine patients admitted at University Teaching Hospital of Kigali
To assess the correlation between anemia severity with both length of hospital stay and mortality rate among Internal Medicine patients admitted at University Teaching Hospital of Kigali

CHAPTER II. LITERATURE REVIEW

2.1. Overview of Anemia

2.1.1. Definition

Anemia is a condition in which hemoglobin concentration is lower than normal and no longer meeting individual's physiological demand (6). According to WHO, Anemia is any hemoglobin level less than 13g/dl and 12g/dl in men and women respectively. WHO categorizes anemia as mild (Hb 10-11.9 g/dl for females and 10-12.9 g/ dl for males), moderate (Hb 7-9.9 g/dl for both genders) or severe (Hb <7 g/ dl for both genders(3)(4)(5).Admitted patients with concurrent anemia are at increased risk for both mortality and morbidity but also prolonged length of hospital stay. Anemia was found to increase re-admission rates and the outcomes in hospitalized patients can be improved by managing anemia along with the primary cause of admission (2,9,14)

2.1.2. Etiologies of Anemia

Generally, the imbalance in red blood cells production and loss results in anemia. This can results from the reduced erythropoiesis by the bonne marrow as a results of numerous factors including Nutritional deficiencies, Bonne marrow infiltration, Inflammation, genetic hemoglobin disorders or excessive RBC loss either from hemolysis , blood loss or both) (2,16,17).

2.1.3. Classification of Anemia

Anemia is basically classified based on red blood cell morphology or by etiology of anemia.

2.1.3.1. Classification of anemia based on morphology

Normocytic normochromic anemia: anemia with normal MCV and normal MCHC. Normocytic normochromic anemia is most of the time seen in acute blood loss, chronic liver diseases, infections , endocrine disorders and aplastic anemia etc. (16,18,19)

Microcytic Hypochromic anemia: In this type of anemia, Red blood cell indices are characterized by reduced MCV and low MCHC and mainly seen in IDA which is the world's commonest cause of anemia, Thalassemia, Sideroblastic anemia, Pyridoxine deficiency, etc.(16,18,19).

Macrocytic normochromic anemia: This is when red blood cell indices are mainly characterized by increased MCV and normal MCHC. Macrocytic anemia is mainly caused by B12 deficiency and Folic acid deficiency among others (17–19).

2.1.3.2. Classification of anemia based on etiology

Blood loss related anemia: it can be due to acute blood loss or chronic blood loss. Anemia from acute blood loss can be from trauma , obstetrical hemorrhage , GI bleeding , ruptured spleen etc. whereas chronic blood loss can be due to worm infection, Menses , chronic GI loss etc. (17,18,20)

Impaired Red blood cell production: this can be due to anything causing defective proliferation and differentiation of stem cells(17,18,20)

Other causes of Anemia include Aplastic anemia, CKD, Hemolytic anemia, myeloproliferative disorders and Nutritional deficiencies(17,18,20)

2.1.4. Diagnosis and Investigations

The diagnosis of anemia requires various investigations including(17,18)

Routine Investigation: Routine investigation for anemia include FBC with WBC, Platelet count and RBC count with red blood cells indices but also reticulocyte count.

Peripheral Smear: Anemia diagnosis using the red blood cell morphology.

Peripheral smear in IDA: It shows microcytic and hypochromic picture. On PBF, red blood cells look pale and small with central vacuoles (hypochromic RBCs)

Peripheral smear in Megaloblastic anemia: With megaloblastic anemia, main features on peripheral smear are presence of Macrocytes and Megaloblasts but also hyper-segmented neutrophils and fully hemoglobinized red blood cells.

Peripheral Smear in Hemolytic Anemia: with hemolytic anemia, platelets are increased in size with the presence of polychromatic, stippled and target cells.

Peripheral Smear in Combined Folate and Iron Deficiency: In mixed Folate and iron deficiency, the PBF shows a population of mixed macrocytes and microcytic hypochromic cells which can end up by MCV normalization.

Bone Marrow Examination: Bonne marrow examination is performed in selected anemia cases mainly in cases of unexplained anemia, splenomegaly, pancytopenia, and anemia with constitutional symptoms. It can show primary BM diseases like aplastic anemia and myelodysplastic anemia), BM involvement from diseases like Infections, Lymphoma, or other Malignancies. BM is also used to accurately estimate iron stores and non-malignancy processes involving BM like Hemophagocytic syndromes and Gaucher disease).

2.1.5. Management of Anemia

Anemia management is based on specific cause of anemia.

Iron Deficiency anemia: IDA is mainly treated using oral preparations, but parenteral preparations are also used (Ferrous sulfate, Ferrous Fumarate and Ferrous gluconate) based on clinical status of the patients. Oral preparations of iron are adequate in asymptomatic patients and 300mg elemental iron per day can be adequate for up to 6months. For those who can't tolerate oral iron, Poor absorption, Ongoing GI blood loss and those in relatively acute need, Intravenous iron is required (17,18).

Megaloblastic Anemia: Oral and Intravenous B12 and folic acid preparations are used for megaloblastic anemia management by correcting their deficits and restore body stores. The available B12 preparations are hydroxyl and cyanocobalamin and are given at 100-1000mcg daily for 2 weeks, then weekly until normalization of hematocrit, the monthly for life. Folic acid is given at 3 to 5mg orally daily (17,18) .

Anemia in Chronic Kidney Disease : Anemia management in CKD is indicated when hemoglobin level drops below 10g/ dl and is done by administration of Erythropoietin stimulating agents like Darbepoetin and Erythropoietin but also iron supplementation accordingly(17,18)

Aplastic Anemia: Bonne marrow transplant is the treatment of choice in young adults and can be done using Immunosuppressant with anti-thymocyte globulin and cyclosporine in elderly population(17,18)

Anemia of Chronic Diseases: Erythropoietin is the treatment of choice in the management of anemia of chronic diseases and can be given at 50 to 150 units/ kg three times per week but can also be increased especially in cancer patients (17,18).

CHAPTER III.METHODOLOGY

3.1. Study Setting

The Study was conducted in In-patients admitted in Internal Medicine wards or medical patients at Emergency department waiting for beds in medical wards at University Teaching Hospital of Kigali (CHUK) after obtaining the approval from University of Rwanda ethical and research committee (CMHS IRB) and research committee from CHUK.

CHUK was selected based on its large number of population and large catchment area, and it is in the center and serving as a reference center for the eastern, north, and western regions in Rwanda, with around 519 bed capacity.

3.2. Study Population

The study population was all patients aged 15 years and above, who were admitted in University Teaching Hospital of Kigali in Internal medicine, being in medical wards or at emergency department waiting for beds in medical wards during 2months period for data collection. We have enrolled patients admitted at CHUK in March and April 2021.

3.3. Study design

This was a Prospective observational analytical study which was conducted in University Teaching Hospital of Kigali (CHUK) among Internal medicine in- patients.

3.4. Sampling strategy and Sample size

As we don't know the prevalence of anemia among admitted patients in Rwanda nor in neighborhood countries, we have calculated our sample size using the prevalence found in a similar study as ours done by Rachoin et al published in 2012 where the prevalence of anemia in hospitalized patients was 10.4%.(24) . We used the following Formula to calculate our Sample Size: $N = \frac{Z^2\ P(1-P)}{d^2}$

Where:

N=Sample size

Z=Z statistic for a level of confidence, 1.96 at confidence interval 95% P= Prevalence of anemia in a similar study was 10.4%

d=Precision (In proportion of one), 0.05

Therefore, $N = \frac{Z^2\ P\ (1-P)}{d^2}$

$$\mathbf{N= \frac{1.96^2\ 0.104(1-0.104)}{0.05^2} = \frac{3.8416*0.104*0.896}{0.0025} = \frac{0.357975}{0.0025} = 143.19 = 144}$$

To ensure that the 95% confidence interval estimate the prevalence of anemia among patients admitted in internal medicine, CHUK, is within 5% of the true proportion, a sample size of 144 patients is needed.

3.5. Patients Selection

3.5.1. Inclusion Criteria

All patients who were admitted in medical ward during the period of data collection who willingly gave their consent for study participation.

3.5.2. Exclusion criteria

Patients below 15 years of age were excluded from the study
Patients who did not willingly provided their consent were excluded
Patients who or whose surrogates were unable to provide enough information were excluded
Patients who were ineligible to give consent (i.e., Under 18 years and those with decreased level of consciousness) whom surrogates did not provide their consent for the study were not enrolled.
Internal Medicine patients with Active Gastrointestinal tract bleeding were excluded.

3.5.3. Patients' enrollment

Entry points were Internal medicine wards and Emergency department. Therefore, patients admitted in medical wards and those admitted at Emergency department waiting for beds in medical wards who met the inclusion criteria were enrolled. Their full blood count and admission outcome were followed up. In total, 166 patients were enrolled but 23 of them were not considered for analysis as they were not meeting inclusion Criteria.

3.6. Data Analysis and Statistics

SPSS version 25 was used for data analysis. Demographic characteristics, main diagnosis at admission, comorbidities, Anemia record, Anemia classification, length of hospital stay, and admission outcome were assessed. Descriptive analysis included frequencies, mean and standard deviation. The associations were tested using chi-square tests. The outcome variable (anemia) was cross tabulated with all factors associated with anemia. We considered p-values <0.05 to be statistically significant. We used the bivariate and multivariate logistic regression analyses to calculate odds ratios, with 95% confidence intervals for the outcome measure: anemia. Analyses were performed stepwise, including all factors associated with anemia. Model 1 included each of the explanatory variables (Factors associated with anemia) where significance was found in bivariate analysis. Model 2 included only the variables found significant in model 1.

3.7. Ethical Consideration

The Study was initially presented to and approved by Internal medicine academic department and was presented to the University of Rwanda ethical and research committee (CMHS IRB) for approval after which permission from ethic committee from CHUK was sought and Data collection was initiated. Written and signed consents were given by the patients or their surrogates in case of patients who were ineligible to consent (i.e., Under 18 years and those with decreased level of consciousness) before enrollment. Patients' freedom and rights was respected, and patients were not needed to pay any fees for the study as we used FBC results which were requested by their treating Physician at ad
mission.

3.8. Data Retention

Following closure of the study, the investigator maintained all study records in a safe and secure location.

CHAPTER IV. DATA PRESENTATION AND ANALYSIS

4.1. Patients' enrollment

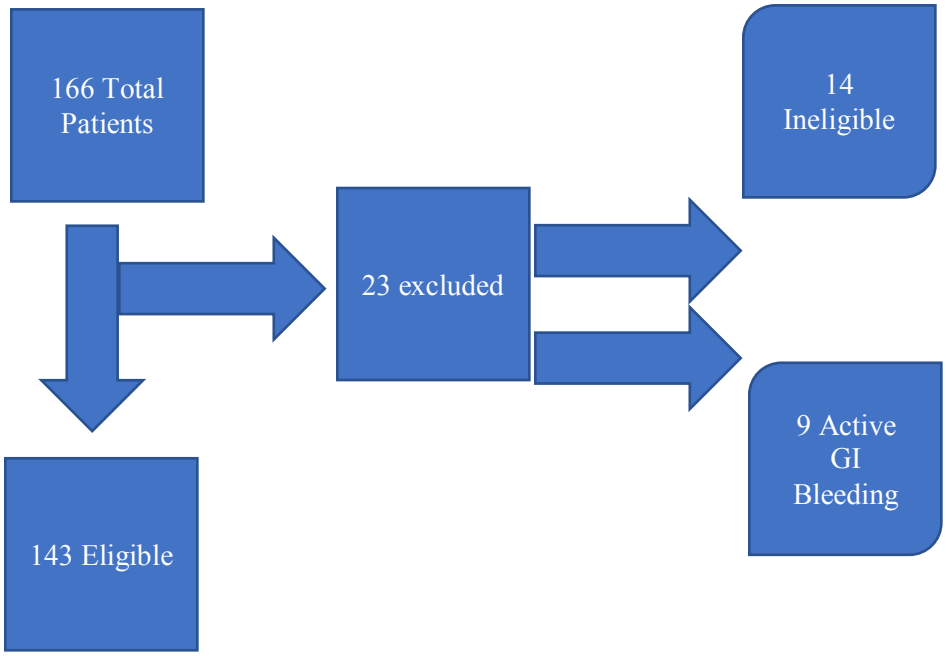

Figure 1.Patients' Enrollment

Entry points were Internal medicine wards and emergency department. Therefore, patients admitted in medical wards and those admitted at Emergency department waiting for beds in medical wards who met the inclusion criteria were enrolled and we followed up their Full blood count and their admission outcome. In total, 166 patients were enrolled but 23 of them were ineligible for analysis.

Table 1.Baseline characteristics

Characteristics	N	%
Age (Mean+/-SD) 51.6±19.6		
Gender		
Men	76	53.1
Women	67	46.9
Residence		
Urban	76	53.1
Rural	67	46.9
Education Level		
No school attendance	34	23.8
Primary level	62	43.4
Secondary level	34	23.8
University	13	9.1
Food Security		
2 or less meals per day	52	36.4
3 or more meals per day	91	63.6
Animal Products	137	95.8
Nutritional Consultation	34	23.8
Comorbidities		
Hypertension	50	35.0
Diabetes Mellitus	37	25.9
Chronic Kidney Disease	18	12.6
Cancers	16	11.2
Chronic Liver disease	14	9.8
HIV/AIDS	13	9.1
Heart Failure	11	7.7
Chronic Lung disease	7	4.9
Peptic Ulcer disease	6	4.2

Among 143 participants, 76 (53.1 %) of them were males and 67(46.9 %) were females with mean age of 51.9±19.6 years.

The above table also shows that 76(53.1 %) of respondents were from urban areas whereas 67(46.9 %) of them were from rural areas.

On education status, the majority had primary education level with 62 (43.4%) of respondent.

Most of them 91 (63.6) were having three meals a day.

Most of the participants 137 (95.8%) Consume animal products and majority of them 109 (76.2%) never got any consultation from nutritionist

Hypertension, Diabetes and Chronic Kidney disease were the most common comorbidities found in 50 (35%), 37 (25.9%) and 18 (12.6%) of respondents, respectively.

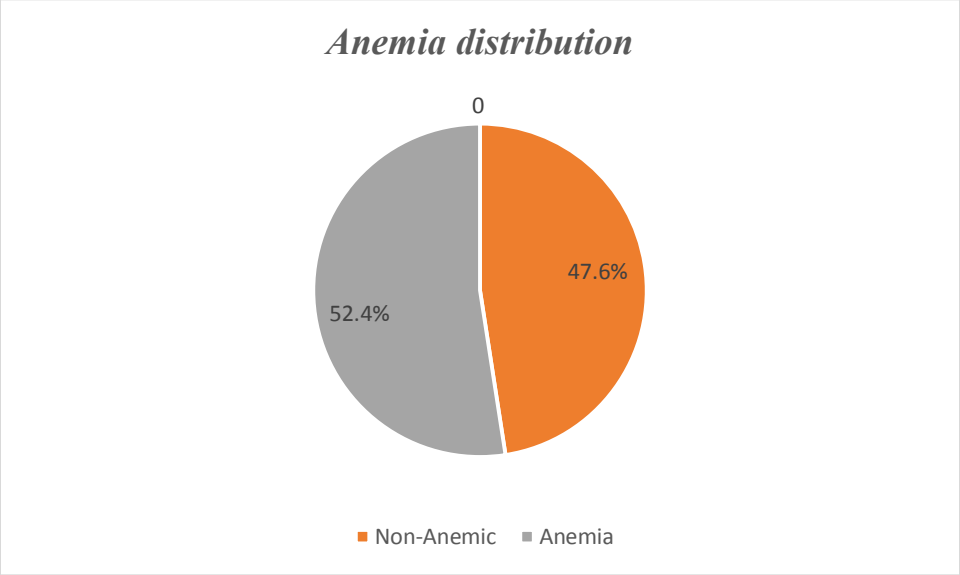

Figure 2. Anemia distribution

The above diagram shows that the prevalence of anemia was 52.4% among 143 participants and further analysis have shown that Female's participants had lower hemoglobin mean compared to male participants with a mean difference of 1.052g/dL.

Table 2.Types of anemia and their prevalence

		Severity of anemia					
		Mild		Moderate		Severe	
		N	%	N	%	N	%
Type of anemia	Microcytic	3	2.1	5	3.5	3	2.1
	Normocytic	21	14.7	31	21.6	8	5.6
	Macrocytic	2	1.4	0	0	2	1.4

Anemia was found in 75 (52.4%) of the participants with many of them (48%) had moderate anemia, (34.7%) of them had mild anemia and (17.3%) of them had severe anemia. Normocytic was the most common type found in 41.9% of the participants and macrocytic type was the least common with 2.8% of the participants.

Table 3.Effect of severity of anemia on death relative to patients with normal hemoglobin

Severity of anemia	**Admission Outcome, N (%)**		**Logistic regression**			
	Survived	Died	OR	95% CI		p-value
Mild	22 (84.6)	4 (15.4)	1.192	0.333	4.268	0.787
Moderate	35 (97.2)	1 (2.8)	0.187	0.023	1.542	0.119
Severe	**8 (61.5)**	**5 (38.5)**	**4.097**	**1.095**	**15.326**	**0.036**
No anemia	59 (86.8)	9 (13.2)	Ref.			

Relative to patients with normal hemoglobin, patients with severe anemia were 4 times more likely to die while mild and moderate anemia did not significantly impact the likelihood of death compared to patients with normal Hemoglobin.

Table 4.Bivariate analysis of factors associated with anemia.

Variables	**Overall, N (%)**	**Anemia, N (%)**			
		Yes	No	OR (95%CI)	p-value
Age					
<65 years	96 (67.1)	51 (53.1)	45 (46.9)	0.921(0.458-1.851)	0.817
>=65	47 (32.9)	24 (51.1)	23 (48.9)	1	
Gender					
Male	76 (53.1)	40 (52.6)	36 (47.4)	0.984 (0.51-1.9)	0.963
Female	67 (46.9)	35 (52.2)	32 (47.8)	1	
Residence					
Rural	67 (46.9)	37 (55.2)	30 (44.8)	1.233(0.638-2.383)	0.532
Urban	76 (53.1)	38 (50.0)	38 (50.0)	1	
Food Security					
≤2 meals per day	52 (36.4)	31 (59.6)	21 (40.4)	1.577 (0.791-3.143)	0.194
≥ 3 meals per day	91 (63.6)	44 (48.4)	47 (51.6)	1	
Consumes animal products	137(95.80	70(51.1)	67(48.9)	0.209 (0.024-1.836)	0.122
Nutritional consult	34 (23.8)	16 (47.1)	18 (52.9)	0.753 (0.348-1.63)	0.471
CKD	**18 (12.6)**	**14 (77.8)**	**4 (22.2)**	**3.672 (1.145-11.775)**	**0.021**
Heart failure	11 (7.7)	8 (72.7)	3 (27.3)	2.587 (0.657-10.182)	0.161
Hypertension	**50 (35.0)**	**20 (40.0)**	**30 (60.0)**	**0.461 (0.229-0.928)**	**0.029**
Cancer	**16 (11.2)**	**15 (93.8)**	**1 (6.3)**	**16.75(2.148-130.634)**	**<0.001**
HIV	**13 (9.1)**	**11 (84.6)**	**2 (15.4)**	**5.672 (1.209-26.6)**	**0.015**
Diabetes Mellitus	**37 (25.9)**	**10 (27.0)**	**27 (73.0)**	**0.234 (0.102-0.533)**	**<0.001**
Chronic Dyspepsia	86 (60.1)	48 (55.8)	38 (44.2)	1.404 (0.717-2.748)	0.322
Anticoagulants	5 (3.5)	1 (20.0)	4 (80.0)	0.216 (0.024-1.984)	0.139
Menstruation	22 (15.4)	14 (63.6)	8 (36.4)	1.721 (0.673-4.402)	0.253

Stepwise Logistic regression model with variables significant from the bivariate analysis.

Outcome variable: Anemia

Table 5. Step 2 of bivariate analysis of factors associated with anemia

		OR	95% C.I.		p-value
Step 1	CKD	11.796	2.743	50.731	0.001
	Hypertension	0.374	0.153	0.913	0.031
	Cancer	10.827	1.325	88.468	0.026
	Diabetes Mellitus	0.214	0.079	0.583	0.003
Step 2	CKD	12.108	2.798	52.396	0.001
	Hypertension	0.383	0.157	0.931	0.034
	Cancer	10.488	1.301	84.512	0.027
	Diabetes Mellitus	0.223	0.083	0.602	0.003

The above table had shown numerous factors associated with anemia. CKD (OR 12.108, p0.001), Cancer (OR 10.488; p 0.027), Hypertension (OR 0.383; p 0.034), Diabetes mellitus (OR 0.223; p 0.003) and HIV/AIDS (OR 5.672, p 0.015) were significant factors associated with anemia.

Table 6.Hemoglobin mean comparison between survivors and non-survivors

		Hemoglobin level				p-value
		Mean	SD	Minimum	Maximum	
Admission Outcome	Died	11.4	4.1	4.2	17.0	0.551
	Discharge	12.0	3.3	5.6	20.0	

On the above table, the mean Hemoglobin of 19 patients who died was low compared to the mean hemoglobin of patients who were discharged alive with 11.4±4.1g/dL and 12±3.3 g/dL respectively (P-value 0.551).

Among 19 died patients 10 (6.9%) of them were anemic including 2 with end stage renal disease, 2 with end stage cancers, 3 with advanced HIV/AIDS and 3 of them had no known comorbidities.

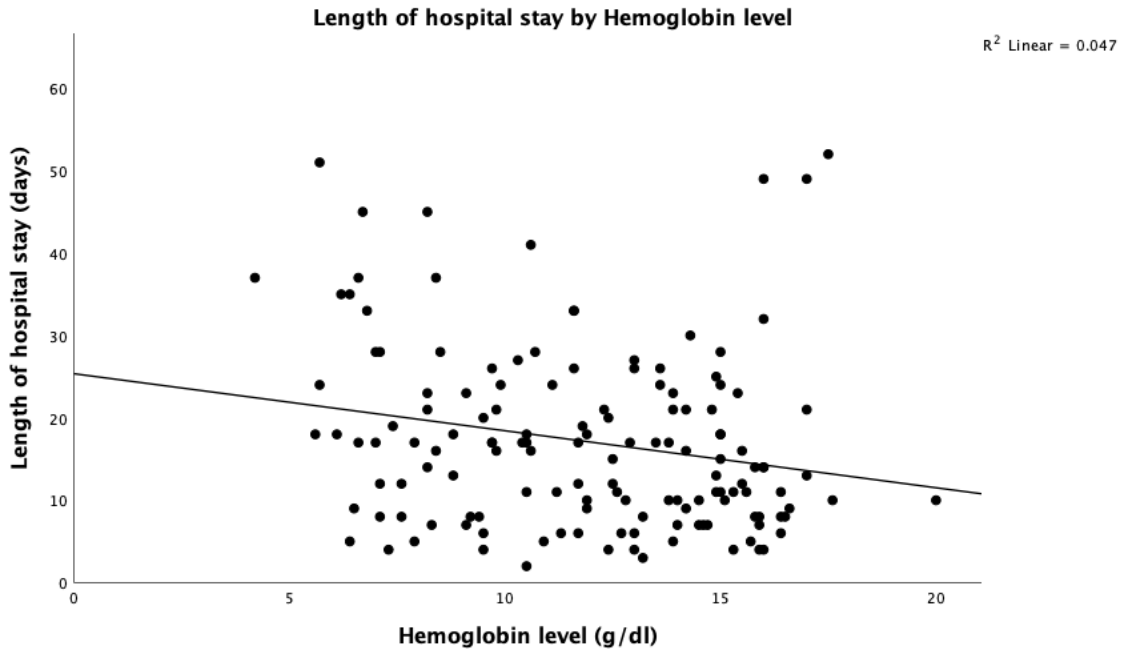

Figure 3. Length of Hospital stay by Hemoglobin level at admission.

On the above dotted diagram, the severity of anemia of admitted patients correlates with the length of hospital stay as the lower the hemoglobin level, the longer the hospital stay was (P-value 0.010)

CHAPTER V. Discussion, Conclusion and Recommendations

5.1. Discussion

5.1.1. Anemia Prevalence

In our study, the prevalence of anemia was 52.4 % and there are mixed results among consulted studies with common tendency of high anemia prevalence with female gender predominance. In a study done in Pakistan, in 2016, the prevalence of anemia was 71% including 72.5% of female population and 67% of male population(2). In a study done in university medical center, Bronx-NY, 590 participants were enrolled and the prevalence of anemia was 62%(27). In the study done in Italy , they enrolled 856 participants with male predominance at 51.3% and anemia prevalence was 58.4 % (23). In the study done in Ethiopia, 2019, where 400 patients were anemic. The prevalence of anemia was 13 % and amongst participants 58% were male and 42% were female(6). We realized that the anemia was prevalent in our population. This can be attributed to the fact that most of our participants had other comorbidities but also most of them were admitted due to infectious or inflammatory causes which are well known to be anemia triggers.

5.1.2. Morphologic types of anemia

In our study, the prevalence of anemia was 52.4%. Most of our participants (80%) had Normocytic anemia, followed by 14.7 % of participants who had Microcytic anemia and few of them 5.3% had Macrocytic anemia. This has a similar distribution with a study done in King Abdul-Aziz Medical City-Riyadh, 2015. Among 150 participants, normocytic anemia was more prominent with 75.3% participants while 24% and 0.7% participants had Normocytic and macrocytic anemia respectively(20). Our findings were not in accordance with the study done India, 2020. Among 500 patients enrolled, many of them 55% had Microcytic anemia , with 29% and 16 % who had Normocytic and Macrocytic respectively (19). Our findings were also different from those found in the study done in 2019 in a tertiary care center. Among 1477 patients enrolled, many of them had microcytic and normocytic anemia with 47.8% and 45.7% respectively (21).

Our findings were also in discordance with those found in the study done in Sri Manakula medical college and Hospital, India, done in 2016. They enrolled 200 and the majority 46% had microcytic anemia followed by 22.5% who had normocytic and 13% with macrocytic anemia(22). This may be explained by the fact that our participants were mainly males (who are not at high risk of IDA and chronic blood loss as menstruating or pregnant females do) but also the distribution of our patients who most of them had Chronic diseases predisposing them to have normocytic anemia.

5.1.3. Risk factors associated with anemia

In our study, the most common significant factors associated with anemia were CKD (OR 12.108, p0.001), Cancer (OR 10.488; p 0.027), Hypertension (OR 0.383; p 0.034), Diabetes mellitus (OR 0.223; p 0.003) and HIV/AIDS (OR 5.672, p 0.015). This was like those found in the study done in 2017, Italy. They have enrolled 856 patients and CKD; $p < 0.001$, Chronic liver diseases; $p = 0.004$), Hematological malignancies; $p < 0.001$, and solid tumors; $p = 0.005$ were the most significant risk factors associated with anemia. In their study, Diabetes and Hypertension were significantly associated with mild form of anemia which is supported by numerous studies (23). From our findings, relevant risk factors associated with anemia were the usual known risk factors worldwide.

5.1.4. Severity of anemia

In our study of 143 participants, 75 (52.4%) of them were anemic and many of them 48% had moderate anemia, 34.7% of them had mild anemia and 17.3% of them had severe anemia. Our findings have the same distribution as those of most consulted studies. This is in accordance with the findings of the study done in India, 2016. Among 200 participants ,the majority of participants 129 (64.5%) had moderate anemia with 36 (18%) and 35 (17.5%) of them had mild and severe anemia respectively (22). Our findings are also like those found in the study done in Italy, 2020. Among 435 patients, there were 191 (43.9%) anemic participants, of whom 133 (49%) had moderate anemia while 97 (35.8) and 40 (14.7%) had mild and severe anemia respectively(30). They are also almost similar to those found in the study done in Italy. They enrolled 856 patients with 500(58.6%) anemic participants. Of anemic patients, 57.2% had Moderate anemia with 28.4 and 14.4 % had Mild and severe anemia respectively(23).

Our findings were also in accordance with a study done in Qatar, 2017. Among 522 anemic patients ,most of them 60.3% had moderate anemia followed by 21.8% and 17.4% who had mild and severe respectively(3). The distribution of our findings maybe explained that we excluded patients who had active bleeding, and most of our participants were admitted due to infectious causes which can explain why severe anemia cases where not prevalent in our study.

5.1.5. Relationship between anemia severity and Mortality risk

In Our study, there is a correlation between anemia severity and mortality risk. Patients with severe anemia had risk of death four times higher than those with normal hemoglobin. Mild and moderate anemia did not significantly impact the likelihood of death in comparison to those with normal Hb level (P-value=0.036). The mean Hemoglobin of patients who died was low compared to the mean hemoglobin of patients who were discharged alive with 11.4±4.1g/dL and 12±3.3 g/dL respectively (P-value 0.551).

This was similar to the findings of the study done in Cooper University Hospital, USA. They realized that anemic patients had overall increased mortality risk (6.5% vs. 2.5%; OR 2.68 [2.51-2.86]) than patients without anemia and anemia had an overall significant unique association with mortality (OR 4.5[3.4-6]) after adjustment for demographic factors and comorbidities (24).

Our findings are also similar to those found in the study done 2006 Among 17,030 enrolled participants. In their study, there was a 5-fold increase in all-cause mortality risk at Hb less than 11g/dl in unadjusted analysis (HR 5.01; 95% CI, 4.43-5.66). Among patients with normal GFR, anemia was associated with a 4 fold mortality risk in the fully adjusted model (HR 4.29, 95% CI, 3.55-5.12)(28) , as there was a significant interaction between the mean GFR and anemia; p =0.001.

High mortality associated with severe anemia may be explained by the fact that most patient with severe anemia had advanced HIV/AIDS and End stage renal disease which are associated with high mortality risk.

5.1.6. Relationship between anemia severity and Length of Hospital stay

In our study, we found that anemia severity correlates with the length of hospital stay as the lower the hemoglobin level, the longer the hospital stay was (p-value <0.01).

This was in accordance with those found in the study done in Italy, 2017. In total, they had 856 participants. Patients with anemia had a median LOS of 11 days which was significantly longer than that of those without anemia who had a median LOS of 10 days (P-Value=0.001). Interestingly, participants with severe and moderate anemia had a median LOS of 12 days and the degree of anemia was an independent predictor of a long term hospital stay (P-value 0.015)(23).

Our findings were similar to those found in a retrospective study done in USA, 2012.Anemic patients had a longer LOS than non-anemic patients (9.8 ± 14.1 days vs. 5.35 ± 8.7 days; P< 0.001) and there was Overall unique significant association between anemia and long LOS; OR 2.6 (2.4-3) after adjustment for demographic factors and comorbidities(24).

Our findings were also in accordance with those found in the study done in New York, 2013. They enrolled 314 patients where anemic patients had significantly longer mean and median LOS compared with non-anemic patients with 8.29 vs. 5 days (P-value =0.0093) for mean and 5 vs. 2 days (p-value <0.001) for median respectively(31).

It is also similar to the findings from a study done in Italy, 2020. They enrolled 435 patients and the LOS was significantly longer in anemic patients comparing to non-anemic, regardless of the cause of admission. Patients with anemia had LOS of 10 days ranging from 1 to 84 days compared to 7 days ranging from 1 to 21 days for patients with normal hemoglobin (P-value <0.001). the LOS was inversely correlating with Hb level in each patient and all levels of anemia were an independent risk factor for a longer hospitalization (P=0.003, RR=1.88, CI 95% =1.3-2.85)(30). Patients with anemia were having associated comorbidities which can explain why anemia was associated with longer length of hospital stay.

5.2. Limitation of the study

Different causes of anemia like Iron deficiency, B12 deficiency, Bonne Marrow failure etc. were not determined due to financial limitation.

Participants might not have had the same baseline characteristic as it wasn't a randomized study which can be the source of false assumptions

5.3. Conclusion

In our study, anemia is common among patients admitted in Internal Medicine Department at CHUK.

CKD and Malignancies were the leading predisposing factors for developing anemia among participants.

Patients with anemia are at increased risk of mortality and longer length of hospital stay compared to those with normal hemoglobin level.

5.4. Recommendations

5.4.1. To Researchers

To conduct further research and assess whether treating anemia would reverse bad outcomes in in-hospital anemic patients

5.4.2. To all Health Care Providers

Early detection, diagnosis, and treatment of anemia among in-hospital patients.

5.4.3. To the Ministry of Health

To conduct national surveillance assessing the extent of anemia in general population but also promoting capacity building in Prevention, detection, and treatment of anemia within the community.

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CHAPTER VI. ANNEXES

6.1. Informed consent form

Dear Respondents,

My name is Dr HAVUGIMANA Phocas, I am a student in University of Rwanda (UR), pursuing Master of Medicine (Mmed) in Internal medicine. I am conducting research entitled: *Prevalence of Anemia and short-term Outcome among Internal Medicine Patients at Kigali Teaching University Hospital*. Anemia is a decreased level of hemoglobin below the normal limit, and it is a global public health problem affecting both genders and all ages with predominance in lower socioeconomic settings and admitted patients with concurrent anemia are at increased morbidity and mortality risk but also prolongs hospital stay and increases re- admission rates and the outcomes in hospitalized patients can be improved by managing anemia along with the primary cause of admission

Therefore, we are conducting this study to document the burden of anemia among admitted patients in our settings to be recognized and properly treated. We will not perform any painful or harmful procedure and you will get treatment if found anemic. Participation in this study is voluntary and you can choose not to answer any individual question, or all of the questions and you have the right to withdraw from the study at any time. However, we hope that you will participate in this study because of its importance. Whatever information you provide will be kept strictly confidential and no reference to your name or other family members will be made anywhere. We do not anticipate that there would be any harmful event that would occur with this study, for any query you can refer to the Chairperson of the CMHS IRB (0788 490 522) or the Deputy Chairperson (0783 340 040) or research committee (researchcenter@ac.ur.rw Tel +250 788563311).

I ……understand the explanation by ……

about the risks and benefits of this research on, *Prevalence of Anemia and Admission Outcome among Internal Medicine at Kigali University Teaching Hospital* and I accept willingly to participate in this research.

Participant's signature Researcher's signature

Date……../……./2021

6.2. Kwemera kwitabira ubushakashatsi

Nitwa Phocas HAVUGIMANA umunyeshuri muri kaminuza y'Urwanda mwishami ry'ubuzima ndimo gukora ubushakashatsi ku bijyanye n'amaraso makeya ningaruka zabyo kubarwayi bari mubitaro bya KUTH, serivisi y'indwara zo mumubiri.

Kugira amaraso makeya ni ikibazo kiri ku isi yose cyane mubihugu biri munzira yamajyambere kandi kikaba cyongera ibyago byo kuremba ndetse nurupfu kubagifite, ndetse byagaragaye ko abarwayi bari mubitaro bibasirwa cyane niki kibazo, bikabaviramo gutinda mubitaro, kwishyura amafaranga menshi ndetse nurupfu, kdi kuvura iki kibazo hamwe nuburwayi birikumwe bikaba bishobora kugabanya izingaruka zavuzwe haruguru. Turashaka rero gukora ubu bushakashatsi ngo tumenye uko iki kibazo gihagaze iwacu, murwego rwo kwita kubagifite vuba kandi neza.

Kujya muri ubu bushakashatsi ni ubushake kandi ni ubufasha uzaba uhaye umuryango rusange wabanyaRwanda. Igihe usanganywe ubu burwayi uzavurwa. Muri ubu bushakashatsi urasubiza inyandiko iriho ibibazo byerekeye imibereho yawe, noneho turebe ingano yamaraso yawe mubizamini wakorewe ariko twe ntagikorwa nakimwe gitera ububabare tuzagukorera kandi Amakuru n'ibisubizo by'ibipimo byawe biragirwa ibanga mu gihe ndetse na nyuma y'ubu bushakashatsi kandi uzabimenyeshwa igihe cyose ubikeneye,

Kwinjira muri ubu bushakashanzi ni uburenganzira bwawe,igihe uzakenera guhagarika gukorerwaho ubu bushakashatsi uzabyemererwa nta mananiza mu gihe utanyuzwe ,wakwiyambaza ikigo gishinzwe ubushakashatsi(Chairperson of the CMHS IRB (0788 490 522) Deputy Chairperson (0783 340 040),research committee (researchcenter@ac.ur.rw Tel +250 788563311).

Twiringiye ko utwemerera gukorerwaho ubu bushakashatsi kuko ari ingenzi cyane. Njyewe……, maze gusobanurirwa na …….

Ingaruka n'inyungu kuri ubu bushakashatsi, nemeye nta gahato kubujyamo.

Umukono w'uwamusignishije

Itariki……/……../2021

6.3. Questionnaire

4.3.1. Baseline characteristics

1. Hospital ID:
2. Age:
3. Sex:
4. Alcohol use
5. Tobacco use
6. Rural
7. Urban
8. No education
9. Primary
10. Secondary education

4.3.2. Food Security/ Nutritional habit

1. More or equal to 3 meals/ day	Yes	No
2. Equal or less than 2 meals/ day	Yes	No
3. Animal products consumption	Yes	No

4.3.3. Awareness

1. Dietary counselling	Yes	No

4.3.4. Clinical

1. Reason of admission/ Diagnosis:……

2. Comorbidities:

A. Chronic Kidney disease (CKD)	Yes	No
If Yes, KIDGO stage:……..		
B. Hypertension (HTN)	Yes	No
C. Chronic liver disease	Yes	No
If Yes, Child Pugh score:…….....		
D. Heart Failure (HF)	Yes	No
If Yes, Ejection Fraction:…….		
E. Cancer	Yes	No
If Yes, Which Cancer:……		
F. Chronic lung disease	Yes	No

If Yes, Which one:…….

G. Diabetes (DM) Yes No

H. Peptic ulcer disease (PUD) Yes No

If Yes, Active Bleeding?

I. HIV/AIDS Yes No

If Yes, WHO staging:……..

4.3.5. Medications

1. HAART Regimen containing AZT or TDF? Yes No

2. Metformin use Yes No

3. Anticoagulants Yes No

4. Antiplatelet Yes No

5. NSAIDS Yes No

4.3.6. Investigations

1. FBC (HB; HCT: MCV:)

A. Anemic:

B. Non-Anemic:

4.3.7. Anemia interpretation

1. Mild 2. Moderate 3. Severe

4. Microcytic 5. Normocytic 6. Macrocytic

4.3.8. Relevant Medical history

1. Prior Gastric or Intestinal surgery Yes No

2. Chronic Dyspepsia Yes No

3. Menstruating Females Yes No

If Yes, How many days per month……

4.3.9. Short term Outcome

1. Discharged

2. Death

3. Length of Hospital stay in days:

6.4. Budget

Item		Quantity	Unit price (Frws)	Total price (Frws)
1.	Printing of Data collection forms	200X2pages	50	20,000
2.	Transport to research site for the PI		2000/day	100,000
3.	Statistical data analysis by a Consultant Statistician	1	500 000	500 000
4.	Printed copies of the draft / dissertation, 60 pages each	5copies	3 000	15 000
5.	Final printed copies of the dissertation, 60 pages each	5copies	3 000	15 000
6.	Book binding	5copies	5 000	25 000
7.	Communication (Airtime and Internet)	3 months	20 000	60 000
8.	S/Total			735,000
9.	Miscellaneous 15%			111,750
10	Total			846,750

6.5. Time frame for study activities

	Dec2020-Jan 2021	Feb -April 2021	April 2021	May 2020
-Proposal writing -Approval -Fundraising	√			
Data collection		√		
Data analysis			√	
Paper writing				√

6.6. Letter for submission to the ethic committee

HAVUGIMANA Phocas
MMed Candidate in Internal Medicine
University of Rwanda

Kigali, 07th, February 2021

Phone number: 0785091407/0727040195 Email address: rukingah@gmail.com

Re: Request for submission of a research project to the ethic committee.

To: research committee center

I am a student doing a postgraduate program in Internal Medicine, I have a dissertation entitled, *Prevalence of Anemia and short-term Outcome among Internal Medicine Patients at Kigali Teaching University Hospital* a cross sectional prospective observational Descriptive study for a 2months period.

I am writing this letter, requesting for a submission of the protocol of the research project and a review by the ethic committee, so that I may be given a go ahead on data collection, once you find this work qualified ethically and scientifically.

HAVUGIMANAPHOCAS

UNIVERSITY of RWANDA

COLLEGE OF MEDICINE AND HEALTH SCIENCES

DIRECTORATE OF RESEARCH & INNOVATION

CMHS INSTITUTIONAL REVIEW BOARD (IRB)

Kigali, 1st / March /2021

Dr HAVUGIMANA Phocas
School of Medicine and Pharmacy, CMHS, UR

Approval Notice: No 063/CMHS IRB/2021

Your Project Title ***"Prevalence of Anemia and Admission Outcome among Internal Medicine Patients at Kigali University Teaching Hospital "Cross-sectional Study among Internal Medicine Patients Admitted in CHUK"*** has been evaluated by CMHS Institutional Review Board.

		Involved in the decision		
			No (Reason)	
Name of Members	**Institute**	Yes	**Absent**	**Withdrawn from the proceeding**
Prof Kato J. Njunwa	UR-CMHS	X		
Dr Stefan Jansen	UR-CMHS	X		
Dr Brenda Asiimwe-Kateera	UR-CMHS	X		
Prof Ntaganira Joseph	UR-CMHS	X		
Dr Tumusiime K. David	UR-CMHS	X		
Dr Kayonga N. Egide	UR-CMHS	X		
Mr Kanyoni Maurice	UR-CMHS		X	
Prof Munyanshongore Cyprien	UR-CMHS	X		
Mrs Ruzindana Landrine	Kicukiro district	X		
Dr Gishoma Darius	UR-CMHS	X		
Dr Donatilla Mukamana	UR-CMHS	X		
Prof Kyamanywa Patrick	UR-CMHS		X	
Prof Condo Umutesi Jeannine	UR-CMHS		X	
Dr Nyirazinyoye Laetitia	UR-CMHS	X		
Dr Nkeramihigo Emmanuel	UR-CMHS		X	
Sr Maliboli Marie Josee	CHUK	X		
Dr Mudenge Charles	Centre Psycho-Social	X		

After reviewing your protocol during the IRB meeting of where quorum was met and revisions made on the advice of the CMHS IRB submitted on 22nd January 2021, **Approval has been granted to your study.**

Please note that approval of the protocol and consent form is valid for **12 months**.

You are responsible for fulfilling the following requirements:

1. Changes, amendments, and addenda to the protocol or consent form must be submitted to the committee for review and approval, prior to activation of the changes.
2. Only approved consent forms are to be used in the enrolment of participants.
3. All consent forms signed by subjects should be retained on file. The IRB may conduct audits of all study records, and consent documentation may be part of such audits.
4. A continuing review application must be submitted to the IRB in a timely fashion and before expiry of this approval
5. Failure to submit a continuing review application will result in termination of the study
6. Notify the IRB committee once the study is finished

Sincerely,

Date of Approval: The 1st March 2021

Expiration date: The 1st March 2022

Dr Stefan Jansen
Ag. Chairperson Institutional Review Board,
College of Medicine and Health Sciences, UR

Cc:
- Principal College of Medicine and Health Sciences, UR
- University Director of Research and Postgraduate Studies, UR