ADDIS ABABA UNIVERSITY

SCHOOL OF GRADUATE STUDIES

PREVALENCE OF ANEMIA AND ASSOCIATED FACTORS AMONG NEWLY DIAGNOSED PATIENTS WITH SOLID MALIGNANCY AT TIKUR ANBESSA SPECIALIZED HOSPITAL, RADIOTHERAPY CENTER, ADDIS ABABA, ETHIOPIA

BY

EDOSA KIFLE (BSC)

DEPARTMENT OF MEDICAL LABORATORY SCIENCE, COLLEGE OF HEALTH SCIENCE, ADDIS ABABA UNIVERSITY

APPROVED BY THE EXAMINING BOARD

_____	_____
CHAIRMAN, DEP. GRADUATE COMMITTEE	*SIGNATURE*
_____	_____
ADVISOR	*SIGNATURE*
_____	_____
EXAMINER	*SIGNATURE*

ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

DEPARTMENT OF MEDICAL LABORATORY SCIENCE

PREVALENCE OF ANEMIA AND ASSOCIATED FACTORS AMONG NEWLY DIAGNOSED PATIENTS WITH SOLID MALIGNANCY AT TIKUR ANBESSA SPECIALIZED HOSPITAL, RADIOTHERAPY CENTER, ADDIS ABABA, ETHIOPIA

INVESTIGATOR: EDOSA KIFLE (BSc)

ADVISORS: - Ms. MINTEWAB HUSSEIN (BSc, MSc)

Mr. JEMAL`ALEMU (BSc, MSc)

Dr. WONDEMAGEGNHU TIGENEH (MD, Oncologist)

Dr. BEKURE TSEGAYE (MD, Pathologist)

A THESIS SUBMITED TO ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCES, DEPARTMENT OF MEDICAL LABORATORY SCIENCE IN PARTIAL FULLLFILMENT OF THE REQUIRMENT FOR THE DEGREE OF MASTERS INHAEMATOLOGY AND IMMUNOHAEMATOLOGY.

JUNE, 2014

ADDIS ABABA, ETHIOPIA

Acknowledgements

First and for most, I would like to say thank you to the almighty God for his endless help throughout my life. Next, my special thanks goes to my advisors, Ms. Mintewab, Mr. Jemal, Dr. Wondemagegnhu and Dr. Bekure for devoting their precious time in providing constructive comments and advice which finally helped me to prepare this thesis draft. All my classmates and my best friends particularly Mr. Hika Mijena, Mrs. Lalise Wakjira and Mr. Bikila Tesfa deserve a lot of thanks for their indispensable support during the process of conducting research paper.

Nursing staff of Radiotherapy center also deserve a lot of thanks for their cooperation in filling the questionnaires and card room staff of that unit in providing patient medical charts. I also acknowledge patients that participated in our study.

My special gratitude goes to Mr. Tolesa Fanta and Mr. Yoseph Endris for their crucial guidance on SPPS software analysis. My heartfelt thanks also go to Dr. Aster Tsegaye and Mr. Melaku Temene for reviewing my draft proposal.

Last but not least, I would like to appreciate the department of Medical Laboratory Science and Radiotherapy center of TASH for allowing me to do this interesting and very vital clinical research.

Table of contents

List of Tables

List of Figures **Page**

Acronyms

ACAS----------Australian cancer anemia survey

CBC----------Complete blood count

CI----------Confidence of interval

$CTCAEV_3$----------Common Toxicity Criteria for adverse events version 3

DRERC----------Departmental research and ethics review committee

ECAS----------European anemia cancer survey

ECOG---------- Eastern Cooperative Oncology Group

EORTC---------- European Organization for Research and Treatment of Cancer

EPO---------- Erythropoietin

ESA---------- Erythropiesis-stimulating agents

Hb---------- Haemoglobin

Hct---------- Hematocrit

HIV---------- Human immuno-deficiency virus

IFN---------- Interferon

IL----------Interleukin

NCCN----------National comprehensive cancer network

NCI----------National Cancer Institute

PRBC----------Packed red blood cell

QOL----------Quality of life

RES----------Reticuloendothelial system

TASH---------- Tikur Anbessa Specialized Hospital

TB----------Tuberculosis bacteria

TGF----------Transforming growth factor

TNF----------Tumor necrosis factor

Abstract

Background: Anemia is a common finding in cancer, which is caused by many factors. It is a major cause of morbidity in cancer patients resulting in impaired organ function, reduced health-related quality of life, aggressive tumor behavior, lower sensitivity to chemotherapy and radiotherapy, even shorter survival; however, little is known about the prevalence of anemia and associated factors among cancer patients during diagnosis in developing countries like Ethiopia.

Objective: To assess the prevalence of anemia and associated factors among newly diagnosed patients with solid malignancy at Tikur Anbessa Specialized Hospital, Radiotherapy center, Addis Ababa, Ethiopia.

Methods: Descriptive cross-sectional study was conducted from April - May, 2014 G.C. A total of 422 newly diagnosed patients with solid malignancy attending Radiotherapy center, TASH were enrolled to assess anemia prevalence and associated factors. Data was coded, entered and analyzed using SPSS version 16. Univariate analysis was applied to compute descriptive statistics for many variables. Bivariate and multivariate logistic regressions were also used to examine the effect of selected variables on prevalence of anemia and severity of anemia by the help of Odds ratio (OR) with 95% Confidence Interval (CI). P-Value < 0.05 was taken as statistically significant. Variables that showed statistically significant association ($p<0.05$) in Bivariate analysis, were entered and analyzed by multivariate analysis.

Result: Out of 422 respondents, 285(68%) were females and 153(36%) of respondents fell into 35-49 age group with age range between 18-80 years and median age of 45. The overall prevalence of anemia across different tumor was 23% and higher anemia prevalence was noted in gynecology (37.7%) and colorectal carcinomas (26.7%). Majority of the anemic patients (68%) remained untreated for anemia. The mean trigger hemoglobin for transfusion was 7.7 g/dl. About 83.5% of anemia was mild to moderate type. Performance status (AOR = 3.344; 95% CI 1.410 – 7.927) and bleeding history (AOR = 3.628; 95% CI 1.800 – 7.314) showed statistically significant association with occurrence of anemia with p-value < 0.05.

Conclusion: The overall prevalence of anemia across different tumor was 23 %, in which gynecology and colorectal showed relatively higher anemia prevalence, 37.7 % and 26.7 % respectively.

1. Introduction

1.1 Anemia associated with cancer

Anemia is a condition that develops when whole blood lacks sufficient healthy red blood cells, which is characterized either by reduction in Hb concentration, red blood cell count or packed cell volume below normal levels [1-4]. As per National Comprehensive Cancer Network (NCCN) guideline, anemia is defined as Hb $\leq$ 11 g/dl or $\geq$ 2 g/dl below baseline. Cancer is one of the most frequent conditions associated with anemia of chronic disease; meantime, anemia is a common complication of cancer [5]. The estimated prevalence of anemia varies ranging from 30% to 90% of cancer patients during the course of their diseases [2, 5, 6].

The pathophysiological origins of anemia can be grouped into different categories: blood loss, increased destruction of red blood cells and decreased production of functional red blood cells [2, 6].The origin of anemia in cancer patients is often multifactorial. A number of underlying mechanisms may contribute to anemia of cancer, for instance the underlying co-morbidities such as coagulation disorders, bleeding, hemolysis, hereditary diseases (e.g. thalassemia, hemoglobinopathies, etc), renal insufficiency, nutritional deficiencies (e.g. due to cancer-induced anorexia or resection of gastrointestinal malignancies), inflammatory disease, or a combination of these mechanisms [2, 7].

Cancer-related anemia may occur as a direct effect of neoplasm (by direct invasion of bone marrow, by releasing proteins or substances), by the sensitization of the immune system, or as a result of the cancer treatment whether surgery, radiotherapy or chemotherapy. For examples, procoagulants released from some cancers like gastrointestinal and prostate, development of antibodies in cancer like adenocarcinoma, deposit of amyloid leading to bone marrow replacement in cancer like plasma cell dyscrasia, which all may lead to some type of anemia [8, 9].

Cancer itself can directly cause or exacerbate anemia either by suppressing hematopoiesis through bone marrow infiltration (e.g. breast and prostate cancer) or production of cytokines that lead to iron sequestration, inhibit release and synthesis of endogenous erythropoietin, reduce the

response of erythroid progenitor cells to erythropoietin, which ultimately impair erythropoiesis [7,10]. Cancer-related anemia is a cytokine-mediated disorder resulting from complex interactions between tumor cells and the immune system. Overexpression of certain inflammatory cytokines results in shortened survival of red blood cells, suppression of erythroid progenitor cells, impaired iron utilization, and inadequate erythropoietin production [11].

Tumor cells are known to produce and secrete several soluble cytokines such as IL-1, interferon-γ, Il-6 and TNF that may be able to decrease Hb levels by hemolysis, suppression of erythropoiesis, and impairment of erythropoietin response of erythroid medullary precursors [12]. TNF-α and IL-1 inhibit EPO mRNA synthesis leading to inhibition of EPO synthesis by the kidney and possibly EPO responsiveness of the marrow erythroid progenitors, and induce lymphocytes to release Interferon γ and β that in turn inhibit the proliferation and differentiation of erythroid progenitor cells. TNF-α also reduces red blood cell survival. Others such as IL-6 worsen anemia through expansion of plasma volume and also increases hepcidin secretion by the liver. This increased level of hepcidin, the key regulator of iron homeostasis, impairs iron metabolism by blocking ferroportin-mediated release of iron from the macrophage and enterocytes of RES [13]. IL-6 and TGF-β also suppress erythropoiesis and iron metabolism, although the role of specific cytokine to specific neoplasm is not known [8].

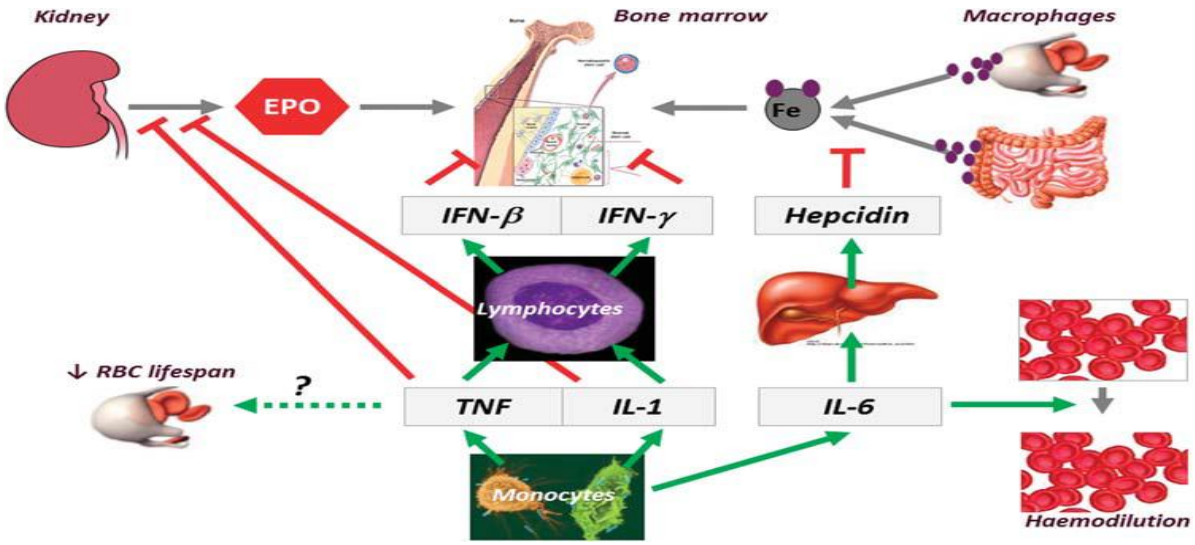

Figure 1: Hepcidin-mediated blockade of iron homeostasis due to inflammation in anemia of chronic disease [13].

Blood loss can result from hemorrhage of the tumor itself (e.g., hepatoma, gastrointestinal, bladder, gynecologic) [10, 15] and organ damage can further exacerbate anemia from cancer. Additional indirect effects may include nutritional deficiencies caused by loss of appetite in patients with cancer, hemolysis by immune-mediated antibodies, or changes in coagulation capability. For these myriad reasons, anemia is prevalent among patients with cancer at initial presentation [2].

In addition, studies have identified patients with lung cancer and gynecologic malignancies as having a very high incidence of chemotherapy-induced anemia [7]. Platinum-based regimens, commonly used in lung, cervical, and head and neck cancers, are well known to induce anemia caused by combined bone marrow and kidney toxicity, leading to decreased renal production of erythropoietin thereby impairing erythropoiesis [2, 5, 7].

1.2 Statement of the problem

Anemia can compromise the delivery of sufficient amounts of oxygen to all cells, including tumor cells. This hypoxic condition can worsen the results of radiotherapy and chemotherapy, because low tissue oxygenation is associated with a reduced sensitivity of tumors to radiation and some forms of chemotherapy, contributing to the progression of cancer and reduction in survival. Furthermore, there is abundant evidence suggesting that hemoglobin levels of less than 12 g/dl result in worse QoL and functional status for cancer patients when compared with higher levels [16].

Anemia is a major contributing factor to tumor hypoxia, which occurs when the tumor growth exceeds the ability of the local microvasculature to supply oxygen to the tumor cells [12].These hypoxic tissues mediate resistances to therapy, leading to increased rate of local failures in advanced tumor stage which then prolongs the duration of the treatment time and lessens the survival rate i.e. induce increased morbidity and mortality [18].

Anemia, in turn, leads to a wide array of symptoms that can negatively affect patients' physical status and functional capacity, and subsequently impair their QOL. Notable among these symptoms are fatigue, dyspnea, palpitations and other cardiovascular complications, cognitive dysfunction, depression, nausea, sexual/reproductive dysfunction, and impaired immune function [20]. A common consequence of anemia in cancer patients is fatigue, which is seen in 78% of anemic patients. Fatigue due to anemia can be even more debilitating than pain but is largely ignored during treatment [17].Anemia and fatigue might precipitate functional dependence in the elderly considering that higher mobility difficulties have been reported in women aged >70 years with lower Hb level. Furthermore, anemia causes energy imbalance and emotional distress (fatigue) [21]

Accumulating data has indicated that anemia has the negative impact on the cancer patients such as impaired organ function, reduced quality of life, and aggressive tumor behavior, lower sensitivity to chemotherapy and radiotherapy, even shorter survival. Thus, the treatment for cancer-related anemia attracted attention of oncologists [19].

2. Rationale of the Study

The prevalence of anemia in solid cancer among treatment-naïve patients is high. The consequence of anemia in making the disease status worsen and impairing the treatment outcome necessitates emphasis of anemia management, which is underestimated in most cases. There was no study done in our country regarding prevalence of anemia and associated factors in newly diagnosed cancer patients with solid malignancy.

In response to this, we planned to conduct a research with the aim of assessing the prevalence of anemia and associated factors in newly diagnosed cancer patients with solid malignancy attending TASH, Radiotherapy center during our study period. In doing so, we provided updated and estimated magnitude of anemia in solid cancer patients during diagnosis prior to radiotherapy or chemotherapy and to identify those factors associated with cancer-related anemia during the enrollment study period.

Finally, we disseminated our study findings to the respective departments, especially to radiotherapy center of the TASH so as to create attention regarding the high anemia prevalence requiring optimal and ongoing anemia management in routine oncology practice. Copy of the study findings is also submitted to the Department of Medical Laboratory Science.

Furthermore, the research findings is sent for possible publication in national and /or international medical journals and also presented at different seminars and conferences to share our finding and suggestion to our colleagues.

3. Literature Review

3.1 Magnitude of anemia in cancers

From the European Cancer Anemia Survey (ECAS) study conducted by Ludwig H et al, 2004 revealing the prevalence of anemia with hemoglobin level < 12 g/dl at enrollment was 39.3% [22]. The Australian Cancer Anemia Survey (ACAS) study similarly concluded that prevalence of anemia at their enrollment was 35%, with 78% of the anemic patients having mild anemia (hemoglobin (Hb) 10.0–11.9 g/L) [11]. Retrospective Study conducted by Harrison L et al, 2001 in USA showed the magnitude of anemia among 574 study subjects to be 41% at presentation [24]. From the tumor types, anemia is most prevalent in patients with uterine-cervical cancer which accounts 75% [24]. For the nearly all tumors, the majority of patients had or developed mild to moderate anemia (10 to 11.9g/dl) [24].

Study done by Gao F et al, 2011 in China revealed that the prevalence of anemia at diagnosis of cancers was 18.98% in unclassified cancers [19].Majority of anemia (68.64%) was normocytic anemia, and others were microcytic anemia (13.02%), microcytic hypochromic anemia (11.63%), normocytic hypochromic anemia (4.65%) and macrocytic anemia (1.86%)[19].Anemia was treated in 41% of patients with anemia at enrolment--by transfusion (36%), iron (5%) and erythropoietic agents (2%). The mean "trigger Hb" for initiating transfusion was 9.5 g/dl [23].

As study of Mahasittiwat P et al, 2008 in Thailand revealed, the prevalence of anemia before commencing radiotherapy is 54.4%. Only 25/112 (22.3%) of anemic patients at initial evaluation received treatment for anemia; most of the patients were treated with a blood transfusion and none was treated with erythropoietin. The mean trigger hemoglobin level for treatment of anemia was 9.3 g/dl [25]. In another study done by Achariyapota V et al, 2010 in Thailand showed high prevalence of anemia in gynaecologic cancer (66.1 %) at enrollment [12]. Bahl A et al, 2008 in India have reported 54.7% of cancer patients as having anemia before starting any treatment [17]. A study done by VerbekeN et al, 2012 in Belgium showed the prevalence of anemia (Hb < 12 g/dl) was 55.7% (95% CI, 53.1–58.3%), in which 35.9% mild, 17.8% moderate and 2.1% severe anemia [26].

3.2 Factors associated with cancer-related anemia

The prevalence of anemia varies according to the type of neoplasia [6]. A report from the study of Barrett-Lee P et al, 2005 in Europe revealed 30.4% and 49.1% of breast cancer and gynecologic cancer patients were anemic at enrollment respectively [20]. In a survey containing 15367 cancer cases in Europe, gastrointestinal/colorectal cancers (43%) were the first among other cancers occurred [22].Prevalence also varied by disease stage: 40% of patients with early-stage colon tumors and nearly 80% of patients with advanced disease had anemia in accordance with report of Knight K et al, 2004 in USA [6].According to report by the Ministry of Health and Welfare of South Korea, the most common cancer in the whole population was stomach cancer (16.0%), followed by thyroid cancer (13.1%), colorectal cancer (12.7%), lung cancer (11.0%), hepatocellular carcinoma (HCC; 9.2%), breast cancer (7.2%), and prostate cancer (3.3%) [12]. In a survey of gynecologic malignancy comprising of 186 patients conducted in Thailand, high prevalence of anemia was seen among patients with endometrial cancer (72.2 %) and ovarian cancer (72%) [12]. In study done at southwest china of 1133 treatment-naïve solid cancer patients, gastric (38.02%), colorectal (23.13%) and hepatopancreatobliliary (22.06%) cancers occupied the first three ranks [19].

As various reports revealed, age, food intake, bleeding, etc were considered as associated factors for the occurrence of anemia in cancer patients. A study conducted by Gao F et al, 2011 in China showed three variables significantly related to the occurrence of anemia, namely age, food intake and bleeding. Elder patients of beyond 65 years have a higher risk of developing anemia compared with those below 65 years old [19]. Cancer may lead to decreased food intake by varieties of mechanisms, such as anorexia, maldigestion, nausea, fatigue, pain, obstruction in the digestive tract, diarrhea or constipation, and so on, which eventually lead to poor nutrition absorption and malnutrition [19]. Study done by Bahl et al, 2008 in India indicates poor pre-treatment nutritional status and bleeding from tumors were major contributing factors for the occurrence of anemia in patients with solid malignancies [17].Anemia was more frequent in females than in males [26]. Anemia prevalence increases after 65 years[21].

4. Study Objectives

4.1 General objective

- To assess prevalence of anemia and associated factors in patients with solid tumors during diagnosis in TASH , Radiotherapy center, Addis Ababa, Ethiopia

4.2 Specific Objectives

- To determine the magnitude of anemia in patients with solid tumorduring diagnosis in TASH, Radiotherapy center, Addis Ababa, Ethiopia
- To describe factors associated with anemia among patients with solid tumor during diagnosis in TASH, Radiotherapy center, Addis Ababa, Ethiopia
- To describe the mean trigger Hb level for anemia supportive therapy among patients with solid malignancy attending Radiotherapy center, TASH, Addis Ababa, Ethiopia

5. Materials and Methods

5.1 Study design

A descriptive cross-sectional type was used.

5.2 Study area and Period

The study was undertaken at Tikur Anbessa specialized Hospital from April - May , 2014 G.C. TASH , the only national hospital enrolled in cancer diagnosis work-up, is located in Lideta Sub-city, Addis Ababa, Ethiopia.

5.3 Population

5.3.1 Source population

All patients confirmed with solid cancers attending Radiotherapy center, TASH, Addis Ababa, Ethiopia.

5.3.2 Study population

Newly diagnosed patients with solid cancers attending Radiotherapy center TASH during the study period.

5.4 Inclusion and Exclusion criteria

5.4.1 Inclusion criteria

- → Patient with ≥ 18 years
- → Patients who had pathology or cytology which confirmed solid malignancy
- → Patients who were scheduled to receive treatments
- → Patients who had complete date of medical history and physical examination
- → Patients who had CBC ordered on the date of visit.

5.4.2 Exclusion criteria

- → Patients who had hematological malignancy
- → Patients who had TB, HIV, cardiovascular problems and renal insufficiency
- → Patients with prior anti-tumor therapy

- → Patients who had received anemia correction treatments (either transfusion, iron, ESA, etc) within the past three months prior to diagnosis
- → Patients having parasitic infection and nutritional deficiency

5.5 Sample size determination and Sampling Procedure

5.5.1 Sample size determination

The maximum number of sample required for this study is determined by using single population proportion formula considering the following assumptions:

$$n_i = \frac{(Z\alpha/2)^2 p\,(1-p)}{d^2}$$

Where

n*i*= minimum sample size required for the study.

Z= standard normal distribution (Z=1.96) with confidence interval of 95% andα=0.05

P= since similar study was not done in Ethiopia, p value of 0.5 will be used.

d= Absolute precision or tolerable margin of error (d) =5%=0.05

ni = $\frac{(Z\alpha/2)2\ p\ (1-p)}{d2\ (0.05)2} = \frac{(1.96)2 \times .5(1-.5)}{} = 384$

The overall sample size was found to be 384 + 38 (10% non-response rate) = 422.

5.5.2 Sampling Procedure

Convenient sampling technique was utilized to obtain the required sample size from the study population.

5.6 Data Collection Method

The study subjects were interviewed using structured questionnaire, which was developed by reviewing relevant literatures. The contents of questionnaire include socio demographic characteristics of patients, Clinical factors and CBC results. Socio-demographics characteristics were collected using an interview guide whereas clinical factors and CBC results were captured by reviewing medical records of the patient when patients visited their physician with their

result. Primarily the questionnaire was an English version and then translated to Amharic Language. This helps data collectors to communicate easily with respondents.

5.7 Study variables

5.7.1 Dependent variables

- → Prevalence of anemia
- → Severity of anemia

5.7.2 Independent variables

- → Age
- → Sex
- → Residence
- → Marital status
- → Occupational status
- → Educational status
- → Type and Stage of tumor
- → ECOG performance score

5.8 Data Processing and Analysis

Data was coded, entered and analyzed using Statistical Package for the Social Sciences (SPSS) version 16. Descriptive statistics were computed for many of the variables. Tables and graphs were used to depict frequencies and main findings. Chi-square statistics was also used to examine differences in anemia occurrence between dichotomous variables. Variables found to have association with dependent variable in Bivariate logistic analysis were entered and analyzed by multiple logistic regression analysis. The association between dependent and independent variables were measured and tested using Odds Ratio (OR) with 95% CI. P-value less than 0.05 was taken as statistically significant.

5.9 Data quality assurance

Following Pilot study, some corrections were done to the questionnaire prior to actual data collection. The questionnaire was prepared in local language and then translated back to English language. Training was given for data collectors and they were instructed to check the completeness of each questionnaire at the end of each interview. The principal investigator also checked for completeness of the questionnaire during submission.

5.10 Operational Definitions

Anemia: Anemia is defined as Hb ≤11g/dl or ≥ 2 g/dl below baseline [5]

Mild/**Grade 1**anemia: Hb value of 10-Lower Limit of Normal (LLN) g/dl [27]

Moderate/**Grade 2** anemia: Hb value of 8-10 g/dl [27]

Severe/**Grade 3** anemia: Hb value of 6.5-8 g/dl [27]

Life threatening or unstable/**Grade 4** anemia: Hb value of 6.5 g/dl [27]

5.11 Ethical consideration

Ethical clearance and approval was obtained from Departmental Research and Ethical Review Committee of Addis Ababa University, Department of Medical Laboratory science. Official letter of co-operation was written to TASH by the Department of Medical Laboratory science, and then the Medical director of the hospital wrote letter of co-operation to Radiotherapy center. Data was collected after obtaining verbal consent from each participant. The right was given to the study participants to refuse or discontinue participation at any time they want. We used patient card number as patient unique ID number.

6. Result

6.1 Distribution of socio-demographic factors

Out of 422 respondents, 278 (66%) were females and the rest 144 (34%) were males. From the age category, majority of respondents, 153(36%) fell into 35-49 age group with age range between 18-80 years and median age of 45. Two hundred twenty seven (53.8%) and three hundred twenty one (76.1%) respondents were urban dwellers and married respectively. More than half of the respondents were illiterate and 156 (37.0%) patients were house wife (Table 1 shows socio-demographic distribution of the respondents)

Table 1: Distribution of socio-demographic factors of the respondents at Radiotherapy center, TASH, Addis Ababa, 2014 G.C (n= 422)

Variables	Frequency, №	Percentage,%
Age, in years		
18-34	78	18.5
35-49	153	36.3
50-64	135	32.0
>65	56	13.3
Sex		
Male	144	34.1
Female	278	65.9
Residence		
Rural	195	46.2
Urban	227	53.8
Marital status		
Single	51	12.1
Married	321	76.1
Divorced	15	3.6
Widowed	35	8.3
Level of education		
Literate	186	44.1
Illiterate	236	55.9
Occupation status		
Employed	85	20.1
Merchant	48	11.4
Farmer	94	22.3
Student	17	4.0
Day laborer	22	5.2
House wife	156	37.0

6.2 Prevalence of anemia

A total number of 422 cancer patients, who were first diagnosed at TASH, Radiotherapy center of Addis Ababa University during April - May, 2014 G.C were searched and enrolled for analysis. The types of cancer included gynecology (122 cases), Breast (96 cases), Nasopharyngeal (32 cases), colorectal (30 cases), Soft tissue sarcoma (29 cases), head and neck cancers (19 cases), thyroid (14 cases), hepatoma (8 cases) and other cancers (72 cases) as shown in Table 2.

The hemoglobin level for the whole patients ranged from 4.6 g/dl to 18.9 g/dl with a mean of 12.6 ± 2.3 (mean ± SD). The mean hemoglobin for male patients was 13.3 ± 2.5 and for female patients, 12.2 ± 2.1g/dl. More than 1/3 of the anemic patients (68%) remained untreated for anemia. Only 25.8% and 6.2 % of anemic patients were treated with transfusion and iron respectively. The mean trigger hemoglobin for transfusion was 7.7 ± 1.7(mean, SD) g/dl.

Anemia was diagnosed in 97 of the 422 patients (23%) and mean concentration (± SD) of Hb was 13.5 ± 1.5 g/dl in 325 non anemic patients while that was 9.4g/L ± 1.6 g/dl in 97 anemic patients..Overall, prevalence of anemia at diagnosis of cancers was 23.0% in unclassified cancers, and higher anemia prevalence was noted in gynecology (37.7%) and colorectal cancers (26.7%) (see Table 2) Majority of the anemia (83.5%) was mild-moderate type whereas 11.3 % and 5.2 % were severe and life threatening type (see Figure 3)

Among the anemic solid cancer patients, anemia was morphologically categorized based on MCV and MCHC values using the following cut off values:

<80	microcytic	<32	hypochromic
80-100	normocytic	32-36	normochromic
>100	macrocytic	>36	Polychromic

(Taken from Wintrobe`s Clinical hematology, 12 th edition and McGraw-Hill`s Manual of laboratory and diagnostic tests, 2008)

From the total of 97 patients, half of anemia (50.5%) was normocytic anemia, in which normocytic normochromic is 22.7% and normocytic hypochromic is 26.8%, and others were

(47.4%) microcytic anemia, in which microcytic hypochromic is 30.9% and microcytic normochromic is 16.5%), and macrocytic anemia (2.1%) (as shown in Figure 2)

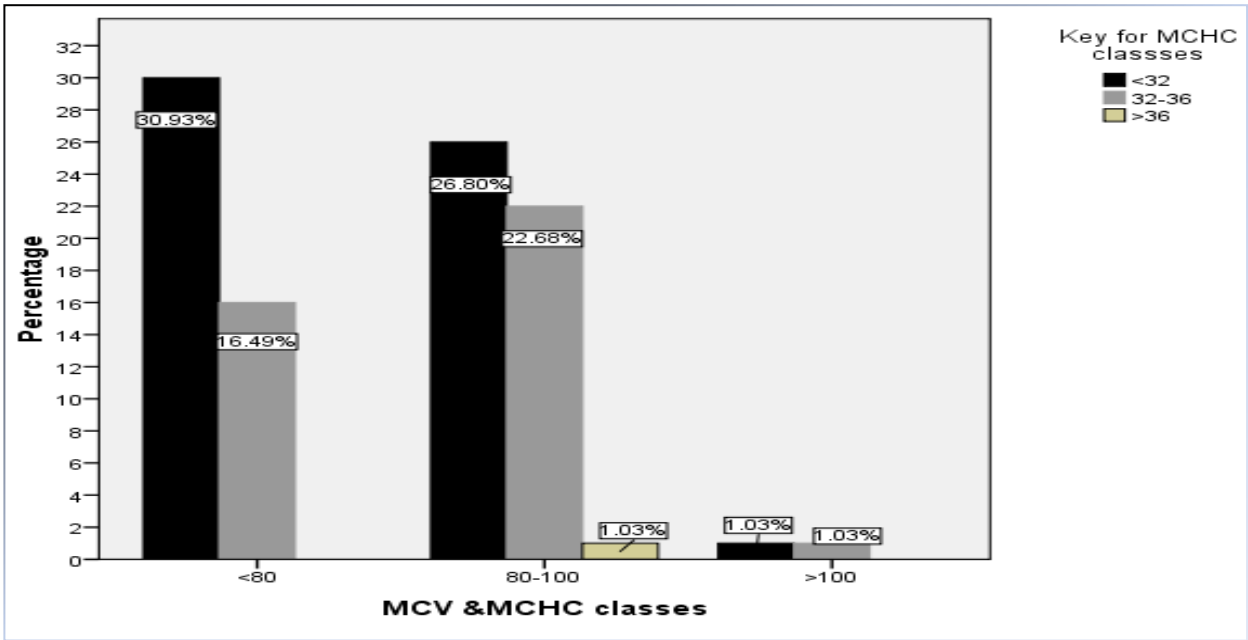

Figure 2: Morphological classification of anemia among anemic patients with solid tumor attending TASH, Radiotherapy center, Addis Ababa, 2014 (n= 97)

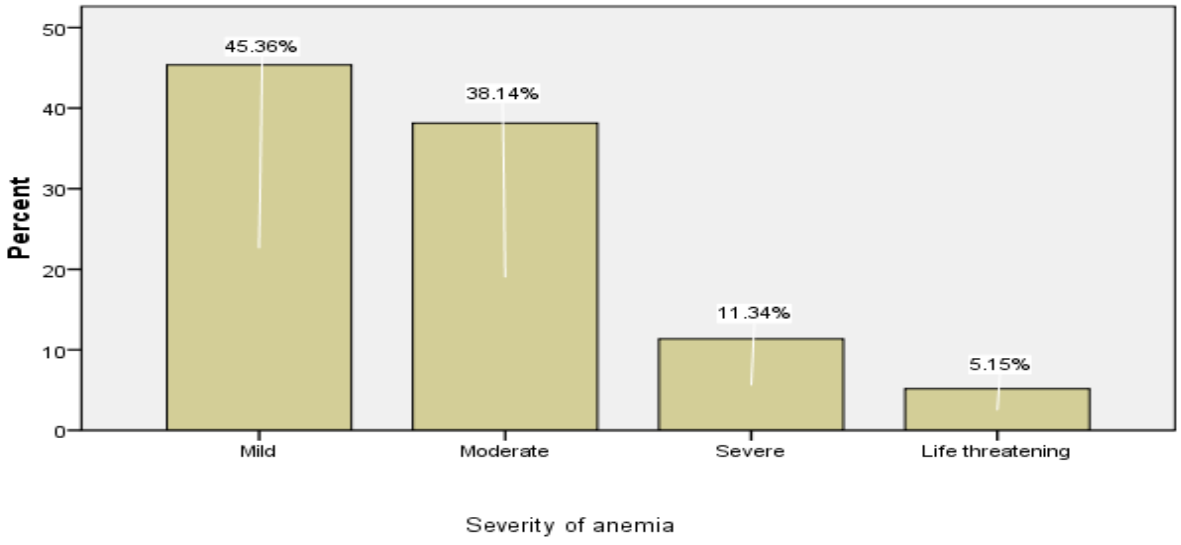

Figure 3: Distribution of severity of anemia among anemic respondents at TASH, Radiotherapy center, Addis Ababa, 2014 G.C (n= 97)
Anemia grading: grade 1 or mild = 10 – Lower Limit of Normal g/dl; grade 2 or moderate = 8 – 10 g/dl; grade 3 or severe = 6.5 – 8 g/dl; grade 4 or life-threatening = <6.5 g/dl

Table 2: Prevalence of anemia among associated factors in newly diagnosed solid cancers at TASH, Addis Ababa, 2014 G.C (n=422)

Factors	№ (%)	Hb range, in g/dl	Mean Hb ± SD, in g/dl	Percentage with Hb≤11 g/dl
Sex				
Male	144(34.1)	4.8-18.9	13.28 ± 2.47	25(17.4)
Female	278(65.9)	4.6-18.7	12.18 ± 2.1	72(25.9)
Age category				
18-34	78(18.5)	7.8-18.4	13.43 ± 2.15	10(12.8)
35-49	153(36.3)	4.6-18.7	12.45 ± 2.4	40(26.1)
50-64	135(32.0)	5.1-18.9	12.45 ± 2.2	30(22.2)
>65	56(13.3)	6.2-14.8	11.89 ± 2.11	17(30.4)
Tumor type				
Gynecology	122(28.9)	4.6-16.2	11.45 ± 2.32	46(37.7)
Breast	96(22.7)	8.2-16.4	12.95 ± 1.52	14(14.6)
Colorectal	30(7.1)	4.8-18.3	12.34 ± 2.83	8(26.7)
NPC	32(7.6)	8.6-16.4	12.49 ± 1.95	8(25.0)
Sarcoma	29(6.9)	7.2-18.4	13.09 ± 2.46	5(17.2)
Head and neck	19(4.5)	7.8-15.9	13.29 ± 2.29	3(15.8)
Thyroid	14(3.3)	10.9-15.7	13.19 ± 1.70	2(14.3)
Hepatoma	8(1.9)	10.5-14.7	13.16 ± 1.19	1(12.5)
Others	72(17.1)	4.8-18.9	13.43 ± 2.46	10(13.9)
Tumor stage				
Stage I	54(12.8)	4.8-18.7	13.35 ± 2.35	7(13.0)
Stage II	129(30.6)	4.8-18.3	12.53 ± 2.30	32(24.8)
Stage III	174(41.2)	4.6-18.9	12.15 ± 2.39	51(29.3)
Stage IV	65(15.4)	8.3-17.7	13.02 ± 1.66	7(10.8)
ECOG PS				
Grade 0	78(18.5)	7.9-18.7	13.04 ± 2.09	12(15.4)
Grade 1	154(36.5)	6.9-18.9	12.77 ± 2.19	33(21.4)
Grade 2	87(20.6)	4.6-17.7	11.95 ± 2.56	26(29.9)
Grade 3	79(18.7)	6.2-18.4	12.17 ± 2.19	24(30.4)
Grade 4	24(5.7)	5.1-15.9	13.07 ± 2.32	2(8.3)

ECOG performance score: 0 = fully active; 1 = restricted in physically strenuous activity but able to carry out light work or activities; 2 = ambulatory and capable of self-care but unable to work; 3 = capable of only limited self-care, confined to bed or chair> 50% of time; 4 = completely disabled, totally confined to bed or chair; NPC= Nasopharyngeal carcinoma, ECOG PS= Eastern cooperative oncology group performance status

6.3 Risk factors associated with the severity of anemia

Patients with bleeding history suffered more severe anemia as compared to patient without bleeding history with p-value < 0.05.However, there were no statistically significant difference found in gender and age group among severity of anemia (see Table 3).

Table 3: Relationships between severity of anemia and factors among newly diagnosed solid cancer patients at TASH, Addis Ababa, 2014 G.C (n=97)

Factors	Severity of anemia				X^2	P-value
	Grade 1	Grade 2	Grade 3	Grade 4		
Sex						
Male	14(56.0%)	7(8.0%)	2(8.0%)	2(8.0%)		
Female	30(41.7%)	30(41.7%)	9(12.5%)	3(4.2%)	2.609	0.498
Age (yrs)						
18-64	37(46.2%)	29(36.2%)	10(12.5%)	4(5.0%)		
>=65	7(41.2%)	8(47.1%)	1(5.9%)	1(5.9%)	1.072	0.829
Bleeding history						
NO	31(59.6%)	14(26.9%)	5(9.6%)	2(3.8%)		
YES	13(28.9%)	23(51.1%)	6(13.3%)	3(6.7%)	9.387	0.024

Grading of anemia: grade 1 or mild = 10 – Lower Limit of Normal g/dl; grade 2 or moderate = 8 – 10 g/dl; grade 3 or severe = 6.5 – 8 g/dl; grade 4 or life-threatening = <6.5 g/dl

6.4 Risk factors for the occurrence of anemia

In Bivariate analysis, occurrence of anemia showed statistically significant association with gender, age group, bleeding history, tumor type, tumor stage and ECOG performance status with p-value <0.05.

When multivariate analysis was computed for these variables, statistically significant association was noted only between the occurrence of anemia with bleeding history and ECOG performance status while considering other variables as confounders.

Patients complained of bleeding history were 4 times more likely to develop anemia than those lacking bleeding history (AOR = 3.628; 95% CI 1.800 – 7.314)

Patients with ECOG performance status of 3 were 3 times more prone to develop anemia than patients of 0 ECOG performance score (AOR = 3.344; 95% CI 1.410 – 7.927) (Table 4 demonstrates determinants of anemia occurrence)

Table 4: Relationships between prevalence of anemia and factors among newly diagnosed solid cancer patients at TASH, Addis Ababa, 2014 G.C (n= 422)

Variables	Anemia		COR(95% CI)	P-value	AOR(95% CI)	P-value
	absent	present				
Gender						
Male	119(82.6%)	25(17.4%)	1		1	
Female	206(74.1%)	72(25.9%)	1.664(1.001-2.765)*	0.049	1.094(0.504-2.374)	0.819
Age (yrs)						
18-34	68(87.2%)	10(12.8%)	1		1	
35-49	113(73.9%)	40(26.1%)	2.407(1.131-5.124)*	0.023	1.956(0.845-4.526)	0.117
50-64	105(77.8%)	30(22.2%)	1.943(0.892-4.230)	0.094	1.237(0.516-2.961)	0.634
≥ 65	39(69.6%)	17(30.4%)	2.964(1.236-7.108)*	0.015	2.422(0.925-6.342)	0.072
Bleeding						
No	278(86.1%)	45(13.9%)	1		1	
Yes	58(58.6%)	41(41.4%)	4.343(2.649-7.121)*	0.000	3.628(1.800-7.314)*	0.000
Tumor type						
Gynecology	76(62.3%)	46(37.7%)	3.753(1.752-8.038)*	0.001	1.444(0.480-4.346)	0.514
Breast	82(85.4%)	14(14.6%)	1.059(0.441-2.542)	0.899	1.005(0.355-2.850)	0.992
Colorectal	22(73.3%)	8(26.7%)	2.255(0.790-6.438)	0.129	1.688(0.544-5.231)	0.365
NPC	24(74.9%)	8(25.0%)	2.067(0.729-5.860)	0.172	2.027(0.661-6.218)	0.217
Sarcoma	24(82.8%)	5(17.2%)	1.292(0.400-4.172)	0.669	1.470(0.422-5.124)	0.545
Head and neck	16(84.1%)	3(15.9%)	1.162(0.286-4.725)	0.833	0.849(0.183-3.936)	0.835
Thyroid	12(85.7%)	2(14.3%)	1.033(0.201-5.323)	0.969	1.234(0.206-7.408)	0.818
hepatoma	7(87.5%)	1(12.5%)	0.886(0.098-7.987)	0.914	0.874(0.086-8.842)	0.909
Others	62(86.1%)	10(13.9%)	1		1	
Tumor stage						
Stage I	47(87.0%)	7(13.0%)	1		1	
Stage II	97(75.2%)	32(24.8%)	2.215(0.911-5.388)	0.08	1.487(0.564-3.920)	0.423
Stage III	123(70.7%)	51(29.3%)	2.784(1.180-6.569)*	0.019	1.503(0.565-3.994)	0.414
Stage IV	58(89.2%)	7(10.8%)	0.810(0.265-2.474)	0.712	0.827(0.240-2.858)	0.764
ECOG PS						
Grade 0	67(19.9%)	11(12.8%)	1		1	
Grade 1	127(37.8%)	27(31.4%)	1.500(0.726-3.099)	0.273	2.013(0.918-4.415)	0.081
Grade 2	61(18.2%)	26(30.2%)	2.344(1.088-5.050)*	0.030	3.102(1.345-7.152)*	0.008
Grade 3	59(17.6%)	20(23.3%)	2.400(1.100-5.235)*	0.028	3.344(1.410-7.927)*	0.006
Grade 4	22(6.5%)	2(2.3%)	0.500(0.104-2.410)	0.388	0.952(0.168-5.384)	0.955

Constants are indicated by 1; whereas * indicates statistical significant association

7. Discussion

Anemia in cancer patients observed as a result of the malignancy itself, anti-cancer treatment, blood losses, nutritional deficiencies, hemolysis, endocrine disorders, or an inflammatory cytokines associated with chronic diseases. In our data, 422 treatment-naïve, newly diagnosed solid cancer patients in TASH, radiotherapy center were included for this analysis. According to this study, the overall prevalence of anemia across different tumor was 23%, which is higher than the study conducted in China, 18.98% [19]. However, our finding is lower than the reports made by other researchers that showed 39.3%, 35%, 41%, 54.4%, 54.7%, and 55.7% in Europe, Australia, USA, Thailand, India and Belgium respectively [22, 11, 24, 25, 17, 26]. The low prevalence in our study is because of difference in definition of anemia, study population and survey period.

As our report revealed, the most common cases noted were gynecology (28.9%) followed by Breast carcinoma (22.7%), which is similar with result conducted in Thailand, where Gynecology (30.6%) and Breast cancers (26.2%) scored the first two ranks among observed tumor types [25].

The prevalence of anemia was varied by tumor type. Our study demonstrated that 37.7% and 26.7 % of gynecologic and colorectal cancer patients were anemic respectively. This finding is lower with the report in Europe and Australia which revealed 49.1% and 65% of gynecologic cancer patients were anemic at enrollment respectively [20, 23]. This may be attributed to the difference in definition of anemia and study design used.

Females and elderly patients with ≥ 65 years ranked higher anemia prevalence rates. We found similar result in China, Sudan, Belgium [19, 21, 26]. In our survey, females are more anemic than males because of the fact that majority of the cancer cases noted are gynecology and majority of gynecologic patients (53.7%) were complained of bleeding history. The primary possible reason for the higher anemia proportion in elder than younger patients is due to the fact that as one gets older, there is a physiological change. As a result of this, for example there is a decline in hematopoietic stem cell reserves and proliferation capacity, which leads to suppression of erythropoiesis.

Our study showed two factors were significantly associated with the occurrence of anemia; those were ECOG Performance score and bleeding history. Patients with ECOG Performance status 3 were 3.344 times higher risk to develop anemia than patients of 0 ECOG performance score, which is in agreement with study done in USA[6].

Our study also indicated that patients with bleeding history were 4 times at a higher risk to develop anemia than those patients lacking bleeding history. This finding is similar with reports made in India and China [17, 19] which revealed that bleeding from tumor were major contributing factors for the occurrence of anemia in patients with solid malignancies. In our study, majority of the anemic gynecologic patients were complaining of bleeding history 34/97 (35%), which is a contributing factor for the higher (37.7%) anemia prevalence of gynecologic among observed tumor types.

In our data, majority of the anemia (83.5%) was mild to moderate type. The mean trigger hemoglobin level for initiating transfusion in our data was 7.7 g/dl, which is lower as compared to reports made in ACAS (9.5 g/dl), Thailand (8.6 g/dl),Thailand (9.3 g/dl) and ECAS (9.7 g/dl)[12,22, 23, 25]. The possible justifications for the low mean trigger hemoglobin level in our study are due to variation among Doctors` decision in initiating anemia supportive treatment and also as a result of high frequency of Grade 3 anemia when compared to other findings.

Regarding the anemia treatment patterns, our data showed that anemia was treated in 32 % of patients with anemia. Our result was similar with the reports made in ECAS [22] and ACAS [23] in which 38.9% and 41% of patients with anemia were treated for their anemia before commencing anti-tumor agents respectively, whereas relatively higher as compared to that of Thailand [25], in which 22.3%of patients with anemia got anemia correction treatment prior to commencing ant-cancer treatment. The most commonly used supportive treatment for anemia correction was transfusion (25.8%), which is in agreement with that of Thailand and ACAS (36%) [22, 23].

Anemia prevalence was also varied by tumor types. Higher anemia prevalence was noted in gynecologic and colorectal carcinomas, 37.7 % and 26.7 % respectively. The possible underlying justifications for this finding are because of the disorder of digestive function, unperceived and

long term bleeding occurred in colorectal tumor [19]. The other possible reason for gynecologic patients is all of them are females in gender and several of them also complained of vaginal bleeding history. This is in agreement with the reports made in China , Colorectal (23.13%) scoring 2nd rank following Gastric (38.02%) and in Australia, where Gynecology (65%) followed by Urogenital (50%) [19, 23].

Our data also showed that bleeding history was found to be a risk factor for severity of anemia with p-value > 0.05. This is similar with study done in china showing that patients with bleeding were more likely to have more severe anemia as compared to patients without bleeding [19]. Gender and age category did not show any evidence of association with severity of anemia.

The majority of the anemia in our study was hypochromic (59%), which was different from the study done in China [19], in which 68.6% were normocytic. The underlying possible justification for the this variation may be due to the difference in study population and study period whereas, the proportion of macrocytic anemia (1.9%) was similar with our result (2.1%)

Our study demonstrated that ECOG performance status and bleeding history showed statistically significant association with prevalence of anemia. This finding is similar with the result reported in China [19] (OR = 1.78, 95%CI; 1.29-2.45) and India [17], in which bleeding from tumor showed statistically significant association with the occurrence of anemia.

Strengths and Limitations of the study

Strengths

- The research finding and clinical significance is highly correlated.
- The study finding may be served as a base line data since no other related study was done within the country.

Limitations

- Minor variation of Hb value may be noted since various types of CBC machines were used in the analysis.
- Stool examination was not performed to exclude cancer patients suffer from parasitic infection
- Nutritional screening test was also not done

8. Conclusion and Recommendation

8.1 Conclusion

Based on the findings of the study, the following conclusions can be drawn:

- → The overall prevalence of anemia across different tumor is 23%.
- → From the tumor types, gynecology and colorectal scored higher anemia prevalence compared to others, which is 37.7% and 26.7% respectively.
- → Female and ≥ 65 aged patients showed higher frequency of anemia when compared with male and < 65 aged patients respectively.
- → Our study also revealed that ECOG PS and bleeding history indicated statistical significant association with the occurrence of anemia.
- → Bleeding history also showed statistical significant association with severity of anemia.
- → The mean hemoglobin for initiating transfusion was 7.7 g/dl
- → 68% of anemic patients remained untreated for anemia

8.2 Recommendation

- → The prevalence of anemia among patients on different cycles of therapy need the attention of other researchers since prevalence of chemotherapy-induced anemia is about 2 fold as high as prevalence of cancer-related anemia.
- → The oncology unit of TASH should pay attention regarding anemia management as a routine practice.
- → Stool examination and nutritional deficiency screening test should be performed for the exclusion of cancer patients suffer from parasitic infection and having nutritional deficiency from the study participants

9. References

1. Cheng K, Zhao F, Gao F, Dong H, Men H-T, Chen Y, et al. Factors Potentially Associated with Chemotherapy-induced Anemia in Patients with Solid Cancers. *Asian Pacific J Cancer Prev 2012;* 13 (10):5057-5061
2. Steegmann JL, Torres JMS , Colomer R, Vaz A , Lo´pez J , Jalo´n I, et al. Prevalence and management of anaemia in patients with non-myeloid cancer undergoing systemic therapy: a Spanish survey. *ClinTranslOncol* 2013; 15:477–483
3. Schrijvers D , De Samblanx H and Roila F. Erythropoiesis-stimulating agents in the treatment of anaemia in cancer patients: ESMO Clinical Practice Guidelines for use *Annals of Oncology* 2010; 21: 244–247
4. Wan S, Lai Y, Myers RE, Li B, Palazzo JP, Burkart AL, et al. Post-diagnosis hemoglobin change associates with overall survival of multiple malignancies – results from a 14-year hospital-based cohort of lung, breast, colorectal, and liver cancers. *BMC Cancer* 2013;13:341-351
5. Rodgers III GM, Becker PS, Blinder M, Cella D, Chanan-Khan A , Cleeland C, et al . Cancer- and Chemotherapy-Induced Anemia. *J NatlComprCancNetw* 2012; 10(5):628-653
6. Knight K, Wade S, Balducci L: Prevalence and outcomes of anemia in cancer: a systematic review of the literature. *Am J Med* 2004,116:11–26
7. Dicato M, Plawny L, Diederich M. Anemia in cancer .*Annals of Oncology* 2010;21: 167–172
8. Jamil K, Kalyani P, Perimi R, Kameshwari SV. Assessment of severity of anemia and its effect on the quality of life (QOL) of patients suffering with various types of neoplasia. *Biology and Medicine* 2009;1 (3): 63-72
9. Saba HI. Anemia in Cancer Patients: An Introduction and Overview. *Journal of the Moffitt Cancer Center* 1998;5(2)
10. Schwartz RN. Anemia in patients with cancer: incidence, causes, impact, management, and use of treatment guidelines and protocols. *Am J Health Syst Pharm* 2007; 64 (3):5-13.
11. Birgegård G, Aapro MS, Bokemeyer C, Dicato M, Drings P, HornedoJ,et al. Cancer-related anemia: pathogenesis, prevalence and treatment. *Oncology*2005;68:3-11

12. Achariyapota V, Benjapibal M, Chaopotong P .Prevalence and Incidence of Anemia in Thai Patients with Gynecologic Cancer. *Asian Pacific J Cancer Prev*2010;11:1229-1233
13. Aapro M, Österborg A, Gascón P, Ludwig H, BeguinY. Prevalence and management of cancer-related anaemia, iron deficiency and the specific role of i.v. iron. *Annals of Oncology* 2012; 23(8): 1954–1962
14. Zarychanski R, Houston DS**.** Anemia of chronic disease: A harmful disorder or an adaptive, beneficial response? *CMAJ* 2008; 179(4):333-337
15. Grotto HZ. Anaemia of cancer: an overview of mechanisms involved in its pathogenesis. *Med Oncol* 2008; 25:12-21.
16. MarchalC, Rangeard L, Brunaud C. Anaemia impact on treatments of cervical carcinomas. *Cancer Radiother* 2005; 9: 87-95
17. Bahl A, Sharma DN, Basu J, RathGk, Julka Pk. Pre-Treatment Anemia Evaluation In Cancer Patients Attending Radiotherapy Clinic: Results From A Single Indian Center. *Indian J Med Sci* 2008;62(10) :417-20
18. Abuzallouf S, Vasishta S, Rageb A , Varghese A , El-Hattab O. Prognostic Value of Hemoglobin Levels Prior to Radiotherapy for Cervical cancer – Kuwait Experience. *Austral - Asian Journal of Cancer* 2007; 6(3): 169-173
19. Gao F, Cheng K, Zhao F, ChenY , Li LH, Dong H, et al. Prevalence and Characteristics of Anemia in Patients with Solid Cancers at Diagnosis in Southwest China**.** *Asian Pacific J Cancer Prev 2011;* 12: 2825-2828
20. Barrett-Lee P, Bokemeyer C, Gascon P, Nortier JWR, Schneider M, Schrijvers D, et al. Management of Cancer-Related Anemia in Patients with Breast or Gynecologic Cancer: New Insights Based on Results from the European Cancer Anemia Survey. *The Oncologist* 2005; 10: 743–757
21. Hassan FM, Weeda EA. Anemia in Elderly Sudanese Lung Cancer Patients Treated with Chemotherapy**.** *The Open Lung Cancer Journal* 2010; *3:*34-37
22. Ludwig H, Van BS, Barrett-Lee P, Birgegård G, Bokemeyer C, Gascón P, et al. The European Cancer Anemia Survey (ECAS): a large, multinational, prospective survey defining the prevalence, incidence, and treatment of anaemia in cancer patients. *Eur J Cancer* 2004; 40 (15):2293-2306

23. Seshadri T, Prince HM, Bell DR, Coughlin PB, James PP, Richardson GE, et al. The Australian Cancer Anemia Survey: a snapshot of anemia in adult patients with cancer. *Med J* 2005;182(9):453-7
24. Harrison L, Shasha D , Shiaova L, White C, Ramdeen B, Portenoy R. Prevalence of anemia in cancer patients undergoing radiation therapy. *SeminOncol* 2001;28: 54-9
25. Mahasittiwat P, Pataranutraporn P, Ieumwananonthachai N, Dankulchai P, Chansilpa Y, Sangruchi S, et al. Prevalence, Incidence and Management of Anemia in Cancer Patients Treated in the Radiation Oncology Division, Siriraj Hospital,*Siriraj Med J 2008;60(5):*235-239
26. Verbeke N, Beguin Y, Wildiers H, Canon JL, Bries G, Bosly A, et al. High prevalence of anemia and limited use of therapy in cancer patients: a Belgian survey (Anaemia Day 2008).*Supportive Care in Cancer*2012; 20: 23-28
27. Cancer Therapy Evaluation Program, Common Terminology Criteria for Adverse Events, Version 3.0, DCTD, NCI, NIH, DHHS. August 9, 2006

10. ANNEXES

Annex I: Participant Information sheet and Consent form

Participant Information Sheet Code No: _____

Dear Participants

My name is Edosa Kifle. I am a student at Addis Ababa University, school of Medical laboratory Sciences, undertaking a Masters degree in Clinical Laboratory Science, Hematology and Immuno-hematology Specialty track. One of the requirements for the degree is to conduct a research project. This letter serves to ask consent from you to take part in this research. The purpose of this research is to assess prevalence of anemia and associated factors among newly diagnosed solid cancer patients. The study will be helpful to know the current prevalence of anemia in specific and general cancers and to create awareness about the consequences of anemia up on patients those coping up with cancer. It will also serve as provide some information to researchers who are voluntary to conduct further research in similar areas in the country.

Your participation in this research is voluntary. If you decide not to participate there will be no negative consequences for you. If you decide to participate there will be no benefits for you. However your participation on this study is very important for achievement of the study. There will not any risk occurring to you because of your participation in this study. All the responses given by you and results obtained will be kept confidential using coding system whereby no one will have access to your response. You are not expected to give your name or phone number. Without permission from you and legal body, any part of this study will not be disclosed to third person. You have full right to refuse and withdraw from the participation at any time if you don't wish to continue. We hope you will participate in the study for the sake of the benefit of the research result. If you are willing to participate in this study, please sign the agreement form.

Are you voluntary to participate in the interview? Yes ☐ No ☐

Informed consent form

I hereby confirm that I understand the consents of this document and the nature of the research project, and I consent to participating voluntarily in the research project. I understand that I am at autonomy to withdraw from the project at any time.

Are you voluntary to participate in the interview? (Tick one)

1. Yes ☐ 2. No ☐

Name and signature of supervisor_____ Date_____

Name and signature of data collector_____ Date_____

Annex II: Questionnaire (English version)

INTRODUCTION: Thank you for agreeing to take part in this brief interview. This study is intended to assess the prevalence of anemia and associated factors among newly diagnosed solid cancers patients at TASH, Radiotherapy center, Addis Ababa, Ethiopia. Every data obtained from you will be kept confidential. Without permission from you and legal body, any part of this study will be disclosed to third person. The questionnaire has 3 parts, out of which you belong to one part. It took about 10 minutes to complete the interview. Please try to respond all questions. Thank you very much for your patience.

Part I: Socio-demographic factors questionnaires

S.N	Questionnaires	Alternative response
Q-1	How old are you?	In years, _____
Q-2	Sex	1. Male 2. Female
Q-3	Where is your residence?	1. Rural 2. Urban
Q-4	What is your marital status?	1. Single 2. Married 1. Divorced 4. Widowed
Q-5	What is level of your education?	1. Illiterate 2. Literate
Q-6	What is your job?	1. Employed 2. Merchant 3. Farmer 4. Student 2. Day laborer 6. House wife

Thank you for your participation!

Part II: Questionnaires for disease and anemia-related factors to be reviewed from medical records

S.N	Questions	Alternative response	
1	Type of tumor	1. Gynecology 2. Breast 3. Colonic 4. Urogenital 5. Lung 6. Thyroid 7. sarcoma	8. anorectal 9. Gastric 10. NPC 11. Head and neck 12. Tongue 13. Others
2	Stage of cancer	1. Stage I 2. Stage II	3. Stage III 4. Stage IV
4	Performance status (ECOG)	1. 0 2. 1	3. 2 4. 3 5. 4
5	Is anemia supportive agents ordered for you?	1. YES 2. NO If yes, which one?	1.1 iron supplement 1.2 transfusion 1.3 ESA 1.4 Others _____
6	Do you have bleeding history?	1. YES 2. NO If YES, which one?	1. Hemoptysis 2. Haematemesis 3.Epistaxis 4. Hematuria 5. Vaginal Bleeding 6. Other

ECOG performance score: 0 = fully active; 1 = restricted in physically strenuous activity but able to carry out light work or activities; 2 = ambulatory and capable of self-care but unable to work; 3 = capable of only limited self-care, confined to bed or chair> 50% of time; 4 = completely disabled, totally confined to bed or chair

Part III: Laboratory results captured

Specimen ID code :		
CBC parameters	Measured value	Reference ranges
RBC count		
Hb		
Hct		
MCV		
MCH		
MCHC		

Annex III: Questionnaires (Amharic version)

የታካሚዉመረጃቅጽእናየተሳትፎማረጋገጫ

ኮድቁጥር_____

ዉድተሳታፊዎች

ሥሜኢዶሳከፈሌይባላል

በአዲስአባባዩኒቨርሲቲበህክመናላበራቶሪሳይንሰማስተርስተማሪስሆንለመመረቅዋናዉመደረግያለበትተግባርየምርምርጥናትማከ ናወንነዉ::ይህደብዳቤበዚህምርምርላይተሳታፊእንድሆኑለመጋበዝነዉ::የምርምሩአላማካንሰርያለባቸዉታካሚዎችስንቶቻቸ ዉበደምማይነስእንደተጠቁእናእንድሁምተዛማጅየሆኑምክንያቶችለማጥናትየተዘጋጀመጠይቅነዉ::በዚህዙሪያምርምርለማድረ ግለሚፈልጉተመራማሪዎችምየተወሰነመረጃበመስጠትይጠቅማል::የእርስዎተሳታፊነትበፍቃደኝነትላይየተመሰረተሲሆንበፈለጉ በትስአትያለምንምስጋትማቋረጥይችላሉ::የእርስዎተሳትፎግንለምርምሩበጣምጠቃሚነዉ::በዚህምርምርላይበመሳተፍዎየሚያ ገኙትጥቅምምሆነየሚደርስብዎትጉዳትየለም::ጥያቄዉለ10ደቂቃያህልየሚቆይስሆንየጥናቱዉጤትጥቅምበማሰብጥያቄዉንበ መመለስእንደሚተባበሩኝተስፋአደርጋለሁ::በጥናቱላይለመሳተፍፍቃደኛከሆኑየስምምነትፎርሙላይምልክትያድርጉ::

በቃለመጠየቁላይለመሳተፍፍቃደኛነዎት?

ኣዎ ☐ ኣይደለም ☐

የሱፐርቫይዘርስምእናፍርማ _____ቀን_____

የዳታሰብሳቢስምእናፍርማ _____ቀን_____

መጠየቅ

መግቢያ

በዚህቃለመጠየቅላይለመሳተፍፍቃደኛበመሆንዎአመሰግናለሁ፡፡ይህጥናትካንሰርያለባቸዉታካሚዎችስንቶቻቸዉበደምማይነስ እንደተጠቁእናእንድሁምተዛማጅየሆኑምክንያቶችለማጥናትመጠይቅነዉ፡፡በእርስዎየሚሰጥማንኛዉምመረጃበሚስጥራዊነትየ ሚቀመጥይሆናል፡፡ካለእርስዎፍቃድወይምየሕግአካልበስተቀርይህመረጃለሦስተኛወገንአይሰጥም፡፡መጠይቁአራትክፍልይኖረዋ ል፡፡ቃለመጠየቁንለማጠናቀቅ 10 ደቂቃየሚፈጅስሆንሁሉንምጥያቄዎችለመመለስይሞክሩ፡፡ለትዕግስትዎአመሰግናሌሁ፡፡

የማህበራዊናአኗኗርመረጃዎች

ተ.ቁ	ጥያቄዎች	የጥያቄዎችምርጫ
1	ዕድሜዎስንትነዉ?	ዕድሜበዓመት_____
2	ፆታ	1. ወንድ 2. ሴት
3	መኖሪያዎየትነዉ?	1. ገጠር 2. ከተማ
4	የጋብቻሁኔታዎች	1.ያላገባ/ች 2.ያገባ/ች 3.ተለያይቶየምኖሩ/የፈታ/ች 4. የሞተባት/በት
5	የትምህርትደረጃ	1. ያልተማረ/ች 2. የተማረ/ች
6	ስራዎምንድንነዉ?	1.ሠራተኛ 2. የንግድሥራ 3.የግብርናሥራ 4. ተማሪ 5.የቀንሠራተና 6.የቤትእመቤት

መልስዎንበመስጠትስለተባበሩኝአመሰግናለሁ፡፡

Annex IV: Declaration

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

Name: Edosa Kifle

Signature _____

Place _____

Date of submission _____

This thesis has been submitted with my approval as University advisor.

Name _____

Signature _____

Place _____

Date of submission _____