# ADDIS ABABA UNIVERSITY

# COLLEGE OF HEALTH SCIENCES

# DEPARTMENT OF MEDICAL LABORATORY SCIENCES

Hematological and Clinical Profile of BCR-ABL Confirmed Chronic Myeloid Leukemia Patients at Presentation in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

By: Boki Lengiso

Advisors: Fekadu Urgessa (Assistant Professor, PhD Candidate)
Aster Tsegaye (PhD, Professor)
Amha Gebremedhin (MD, Associate Professor)
Fozia Abdella (MD, Assistant Professor)

A research Thesis Submitted to the Department of Medical Laboratory Sciences, College of Health Sciences, Addis Ababa University, in Partial Fulfillment of the requirements for Masters of Science Degree in Clinical Laboratory Sciences (Hematology and Immunohematology track).

December, 2023

Addis Ababa, Ethiopia

Addis Ababa University

School of Graduate Studies

This is to certify that the thesis prepared by Boki Lengiso entitled:

**Hematological and Clinical profile of BCR-ABL confirmed Chronic Myeloid Leukemia patients at presentation in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia** and submitted in partial fulfillment of the requirements for Master of Science degree in Clinical Laboratory Sciences (Hematology and Immunohematology) complies with the regulations of the University and meets the accepted standards with respect to originality and quality.

Signed by the Examining Committee:

Examiner_____ Signature _____Date _____

Examiner_____ Signature _____Date _____

Advisor_____ Signature _____Date _____

Advisor_____ Signature _____Date _____

Advisor_____ Signature _____Date _____

_____

Chairman of the Department or Graduate Program Coordinator

## Acknowledgments

First and foremost, I would like to express my gratitude to the Ethiopian Public Health Institute (EPHI) for their sponsorship during my graduate studies. Additionally, I extend my acknowledgment to the Department of Medical Laboratory Sciences, Addis Ababa University for their sponsorship of this research.

Secondly, I would like to sincerely thank my advisors: Mr. Fekadu Urgessa, Prof. Aster Tsegaye, Dr. Fozia Abdella, and Dr. Amha Gebremedhin for their continuous support throughout the study.

Lastly, I would also like to extend my thanks to Mr. Gadissa Gutama, Mr. Dereje Leta, Mr. Kumera Tarfa, Mr. Chala Basha, Mr. Yohannes Belay, and all my friends for their support. I am immensely grateful to the study participants, as well as the staff at Tikur Anbessa Specialized Hospital's hematology clinic, who facilitated the data collection process and made this study possible. My deepest and sincerest gratitude also goes to my wife and all my family members.

Table of Contents

Acknowledgments ..... ii
List of Table ..... v
List Figure ..... vi
Abstract ..... viii
1. Introduction ..... 1
1.1 Background ..... 1
Hematological Profile of Chronic Myeloid Leukemia patients ..... 1
Clinical Profile of Chronic Myeloid Leukemia patients ..... 2
1.2 Statement of the Problem ..... 5
1.3. Significance of the study ..... 7
2. Literature review ..... 8
Hematological profile of Chronic Myeloid Leukemia ..... 8
Clinical Profile of Chronic Myeloid Leukemia patients ..... 9
3. Objectives ..... 11
3.1 General Objective ..... 11
3.2 Specific objectives ..... 11
4. Materials and methods ..... 12
4.1 Study Area ..... 12
4.2 Study design and period ..... 12
4.3 Population ..... 13
4.3.1 Source of population ..... 13
4.3.2 Study of Population ..... 13
4.4 Eligibility criteria ..... 13
4.4.1 Inclusion criteria ..... 13
4.4.2 Exclusion criteria ..... 13
4.5. Study variables ..... 14
4.5.1 Dependent variable: ..... 14
4.5.2 Independent variables ..... 14
4.6 Sampling technique and Sample size determination ..... 14
4.7 Data collection ..... 15
4.7.1 Demographic and clinical data ..... 15
Workflow of the study ..... 16

4.7.2 Sample collection and laboratory analysis ..... 17
4.7.3 Laboratory testing principles and analysis ..... 17
4.8. Data Quality Assurance ..... 18
4.9 Data analysis ..... 19
4.10. Operational definitions. ..... 20
4.11 Ethical considerations ..... 21
4.12 Dissemination of the result ..... 21
5. Results ..... 22
5.1 Socio-demographic characteristics of the study participants ..... 22
5.2 BCR-ABL confirmation method ..... 24
5.3 Hematological profile of the study participants ..... 24
5.4 Clinical profile of the study participants ..... 29
6. Discussion ..... 32
7. Strength and limitation ..... 36
8. Conclusion ..... 37
9. 9. Recommendations ..... 38
10. References ..... 39
Annex I. ..... 43
Annex II ..... 49
Annex III ..... 50
Informed consent form ..... 50
Annex IV ..... 51
Annex V ..... 52
ለጥናቱ ተሳታፊዎች የመረጃና ስምምነት ቅፅ (Amharic Version) ..... 52
Declaration ..... 60

**List of Table**

Table 1: Overall, Socio-demographic characteristics of BCR-ABL confirmed CML patients during presentation at TASH, Addis Ababa, Ethiopia,2022. ..... 22
Table 2: Hematological profile of BCR-ABL confirmed CML patients during presentation at TASH, Addis Ababa, Ethiopia, 2022. ..... 25
Table 3: Distribution of hematological parameters and CML phase of BCR-ABL confirmed CML patients during presentation at TASH, Addis Ababa, Ethiopia 2022..... 26

**List Figure**

Figure 1: Data collection procedure ..... 15
Figure 2:Workflow ..... 16
Figure 3: Anemia of BCR-ABL confirmed CML patients during presentation at TASH, Addis Ababa, Ethiopia,2022. ..... 28
Figure 4: Clinical profile of BCR-ABL confirmed CML patients during presentation at TASH, Addis Ababa, Ethiopia,2022 ..... 30
Figure 5: Previous infection and other chronic disease history of BCR-ABL confirmed CML patients during presentation at TASH, Addis Ababa, Ethiopia,2022 ..... 31

## Abbreviation

| | |
|---|---|
| ALL | Acute lymphocytic leukemia |
| AML | Acute myeloid leukemia |
| ATP | Adenosine triphosphate |
| BCR-ABL | Breakpoint cluster region on chromosome 22 with the Abelson murine leukemia of chromosome 9 |
| CBC | Complete blood count |
| CLL | Chronic lymphocytic leukemia |
| CML | Chronic myeloid leukemia |
| EDTA | Ethylene Diamine Tetra Acetic Acid |
| EPHI | Ethiopian Public Health Institute |
| FAB | French-American-British |
| Hbg | Hemoglobin |
| HSC | hematopoietic stem cell |
| MPDs | Myeloproliferative Disorders |
| Ph | Philadelphia chromosome |
| RT | Reverse transcriptase |
| RT-PCR | Reverse transcriptase polymerase chain reaction |
| SCT | Stem cell transplantation |
| SOP | Standard operational procedure |
| TASH | Tikur Anbessa Specialized Hospital |
| TKI | Thyrosine kinase inhibitors |
| VSC | Volume, scatter and conductivity |
| WBC | White blood cell |
| WHO | World Health Organization |

## Abstract

**Background:** Chronic Myeloid Leukemia (CML) is a risk of morbidity and death across the world particularly in low-income countries, due to late detection, poor adherence and its impact on youth population. However, there is scarcity of evidence in hematological and clinical profile in newly confirmed CML patients in Ethiopia. Thus, we aimed to investigate the hematological and clinical profile of BCR-ABL confirmed Chronic Myeloid Leukemia patients during presentation at Tikur Anbesa Specialized Hospital.

**Objective:** To determine the Hematological and clinical profile of BCR-ABL confirmed Chronic Myeloid Leukemia patients during presentation at Tikur Anbesa Specialized Hospital.

**Methods**: A facility-based cross-sectional study was conducted to address hematological and Clinical Profile among new BCR-ABL confirmed patients at Tikur Anbesa Specialized Hospital (TASH) from August 2021 to December 2022. Convenient sampling technique was used and 256 patients were included. Structured questionnaire was used to collect the patients' socio-demographic, medical history and physical examination. About 5ml of blood sample was collected for hematological profile test. The laboratory analysis was conducted by using Unicel DxH800 analyzer at TASH. Data was entered to Microsoft excel database and analyzed by statistical software for social science version 26. Descriptive statistics was used to explain socio-demographic, Hematological and clinical profile of study participants. A P-value of <0.05 were considered as statistically significant.

**Result:** A total of 256 patients diagnosed with CML were identified. The majority (59.8 %) were male and the median age was 36 years. The distribution of CML phase among the participants was, 217 (84.78%) were in chronic phase, 31 (12.1 %) were in accelerated phase and 8 (3.1 %) patients were in Blast Crisis. Among the participants who were naïve to the Pre-chemo treatments, the median and IQR values for WBC, RBC, HGB and PLT counts were 262.7(190.5-352.1) $x10^3/\mu L$, 3.0(2.6-3.6) $x10^6/\mu L$, 8.8(7.9-10.1) g/dl and 320(209.5-449.8) $x10^3/\mu L$, respectively. All patients exhibited Leukocytosis, with about 93.3% of them experiencing hyperleukocytosis. Additionally, among the study participants, 91.8% of patients developed anemia, with 138 (53.9%) experiencing moderate anemia and 19 (7.4%) encountering severe anemia. Furthermore, about 75 (29.3%) patients had thrombocytosis, while 34 (13.3%) had thrombocytopenia. The most common sign and symptoms developed were Fatigue, abdominal pain, splenomegaly, and weight loss.

**Conclusion:** This study revealed a significant prevalence of hyperleukocytosis and anemia among CML patients during their initial presentation. Fatigue, abdominal pain, splenomegaly, and weight loss emerged as the most commonly observed signs and symptoms in CML patients.

**Keywords:** BCR-ABL newly confirmed chronic myeloid leukemia, hematological profile, Clinical Profile, TASH

# 1. Introduction

## 1.1 Background

Leukemia is a varied collection of hematological cancers that includes multiple biologically different subgroups. It is a clonal neoplasm of hematopoietic cells caused by a variety of causes that cause somatic mutations in pluripotent stem and progenitor cells. It is also a group of clonal diseases caused by a single cell with a genetic alteration in bone marrow or peripheral lymphoid tissue, and the specificity of the source cell determines the type [1,2].

The current classification system for leukemia is based on the World Health Organization (WHO) 2016 classification. It is based on clinical, morphologic, immunophenotypic, and genetic characteristics. Another classification is the French-American-British (FAB) system, which is based on the morphology of abnormal leukocytes. Leukemia is classified in to four broad subtypes; acute lymphoblastic, acute myelogenous, chronic lymphocytic, and chronic myelogenous [3,4,5,6].

Chronic myeloid leukemia (CML) is a hematopoietic stem cell (HSC)-derived myeloproliferative disorder caused by the chromosomal translocation t (9; 22). The formation of the Philadelphia (Ph) chromosome and expression of the Breakpoint Cluster Region (BCR)- Abelson Murine Leukemia viral oncogene homolog 1 (ABL) fusion gene results from the fusion of a portion of the BCR on chromosome 22 with the ABL tyrosine kinase on chromosome-9 [7,8].

More than 95% of CML patients have cytogenetic evidence of the Philadelphia (Ph) chromosome, a reciprocal translocation between the long arms of chromosome 22 at the BCR gene and chromosome -9 at the ABL gene. As a results, a BCR-ABL fusion gene is generated, which results in the synthesis of a chimeric protein with constitutively active tyrosine kinase activity [7,9,10-15].

**Hematological Profile of Chronic Myeloid Leukemia patients**

Leukemia is a hematological disorder caused by clonal proliferation of hematopoietic progenitor stem cell in the bone marrow leading to marked increase in granulocyte series of cells in the peripheral blood and bone marrow [16]. From the classifications of leukemia CML is one; which is characterized by Anemia, thrombocytosis, and leukocytosis with a shift to the left, decreased

neutrophil alkaline phosphatase, hyperuricemia, and elevated serum B12 levels in peripheral blood. In several cases of CML, an examination of the bone marrow will indicate hypercellularity and stroma fibrosis [17].

Most cases of CML can be diagnosed using peripheral blood findings combined with molecular genetic techniques that detect t (9; 22) (q34.1; q11.2) or, more specifically, BCR-ABL1. A bone marrow aspirate, on the other hand, is required to ensure sufficient material for a complete karyotype and for morphologic evaluation to confirm the disease phase [16].

**Clinical Profile of Chronic Myeloid Leukemia patients**

Many CML patients exhibit no sign and symptoms and are frequently detected during routine check-ups. Patients in the chronic phase of CML have less than 10% blasts in their bone marrow samples, and symptoms such as fatigue, weight loss, malaise, and feeling full or pain in the left upper quadrant of the abdomen are usually caused by anemia and splenomegaly [18].

Accelerated Phase of CML is distinguished by bone marrow samples containing 10- 20% blasts. New chromosome changes in leukemia cells with the Philadelphia chromosome cause worsening anemia, splenomegaly, and occasionally other organ infiltration, whereas the CML blast crisis phase has the same picture as acute leukemia. Bone marrow samples from a patient in this stage contain more than 20% blasts, large clusters of blasts are seen in the bone marrow, also spread to tissues and organs other than the bone marrow. These were characterized by frequently having a fever, a loss of appetite, and weight loss [2,18].

In the developed countries, the majority of CML cases are diagnosed in the chronic phase, and the average age is around 65 years. However, in developing word, CML is more commonly diagnosed in the advanced stage and at the age of 39 years. According to the European treatment and outcome study and the sokal prognostic scoring system, the median age in Ethiopia is 36 years, with more than one-third (37%) in the age group of adolescents and young adults (15 to 29year old), and the majority were high risk. Little is known about the cause of these differences in the disease's natural history, whether they are due to the African people's pyramid of ages or unknown environmental and/or genetic factors [9].

CML's etiology has remained unknown until now. Exposure to ionizing radiation and survivors of the atomic disasters at Nagasaki and Hiroshima is the only risk factor known to influence the

occurrence of the CML. The chronic phase, the acceleration phase, and the blast crisis phase are the three stages of CML. A small number of patients in the chronic phase will progress to the accelerated and blast crisis phases [17].
With the emergence of tyrosine kinase inhibitors (TKI), the treatment of chronic myeloid leukemia (CML) has evolved dramatically in previous 20 years. Most patient with chronic phase CML now has life expectancies comparable to their age peers. Understanding the practical aspects of selecting the right TKI, monitoring response, and side effects is critical to long-term success. [19,20].

The diagnosis of CML starts with suspecting cases by their CBC results and blood smear, when there is leukocytosis with left shift and basophilia [8]. Confirmation of the diagnosis requires a demonstration of BCR-ABL by polymerase chain reaction and Fluorescence in-situ hybridization (FISH) for t (9;22) (q34; q11.2). In addition, bone marrow aspirate and unilateral biopsy with conventional cytogenetics and flow cytometry are essential to exclude un-recognized advanced-disease stage, and to detect rare cases with an alternative to BCR-ABL transcript. Flow cytometry will identify cases with unrecognized progression to blast crisis by their phenotypic features, while conventional karyotyping may identify additional cytogenetic abnormalities (cytogenetic clonal evolution) [21,22].

The goals of treatment in chronic phase CML are to keep patients from progressing to the accelerated phase or blast crisis, so that they have a life expectancy comparable to the general population; to avoid adverse events (AEs); and to restore and maintain quality of life [23]. Tyrosine kinase inhibitors (TKIs) are powerful medications that have significantly improved long-term prognosis for CML patients. Second- and third -generation TKIs were created after imatinib (a first -generation TKI). With the approval of five TKIs (imatinib, dasatinib, bosutinib, nilotinib and ponatinib) targeting BCR-ABL in most countries, and the recent approval of asciminib in the United States [24].

Hydroxyurea is an S phase acting agent and acts by inhibiting DNA synthesis. This drug is acting, as an inhibitor of ribonucleotide reductase, can lower blood counts within 1 to 2 days, especially if higher than-standard doses are used. The advantages of hydroxyurea are the rapid onset, the lack of serious side effects and the rapid recovery of counts if excessive lowering of the WBC occurs [24], While Imatinib mesylate is a selective inhibitor of the protein tyrosine kinase has shown promising results in CML in all phases. Its efficacy, specificity and the safety profile makes it a

strong contender for the first line therapy in CML [25]. Because the current medication demonstrated a certain level of efficacy, therapy discontinuation is also a possibility in patient attaining persistent deep molecular response [23].

Treatment decisions are generally complex and necessitate an examination of patient-specific circumstances. Treatment option for CML are evolving, with a greater emphasis on establishing deep molecular responses [26]. Novel medications are required, particularly in patients who have not responded to TKIs and in those with severe disease [23].

## 1.2 Statement of the Problem

Leukemia is a cancer of major public health problem worldwide [12]. In 2018, the global prevalence of CML was estimated to be 503,000, with 53 percent of cases occurring in resource-limited settings. The vast majority of CML instance occur in specific regions of the world, where diagnostic and monitoring technology is unavailable [13]. The estimated number of new cases of CML was 9,110, with 1,220 deaths in 2021 in the USA [12].

The global incidence rate of CML is estimated to be 0.6-2.0 cases per 100,000 people per year. There is a scarcity of epidemiological data on myeloproliferative disease (MPDs), particularly Philadelphia BCR-ABL-positive CML. Incidence rates vary by age and gender; it rises with age and are higher in men than in women [14]. The incidence rate of CML in Africa, including Ethiopia, is little known, with a 2017 report predicting a yearly incidence rate of 0.4 cases per 100,000 individuals. The disparity in incidence rates could be due to geographic and/or ethnic differences [15].

Leukemia claimed the lives of approximately 265,471 people worldwide, with 24,400 dying in Europe, 1,840 in Australia, 21,121 in Africa, and 3,230 in Ethiopia by 2014 [27]. Study done by Kassahun W *et al*.,2020 in Ethiopia, From a total of 332 study patients with abnormal hematological parameters, 3.6 percent had AML, 2.7 percent had ALL, and 1.8 percent had CML, while CLL, Myelodysplastic syndromes, and undifferentiated leukemia had prevalence rates of 0.6 percent, 0.3 percent, and 0.3 percent, respectively [27].

In developed countries, the incidence rate of CML has remained relatively stable over the last decade, at 1-2:100,000, with a slight male predominance, the disease is most commonly diagnosed in the fifth and sixth decades of life, but in low income countries, presentations in the third and fourth decades are more common, possibly reflecting younger population demographics [28]. In the pediatric population, CML is rarely diagnosed. Because of a lack of robust clinical research evidence, CML management in children is not standardized and follows adult-specific protocols. The prognostic ratings for adult CML do not apply to youngsters. CML in children was thought to have the same biology as in adults, however new findings show that there are some genetic distinction between pediatric and adult CML [29].

There is less research available for a though understanding of the distribution and pattern of leukemia in the population, as well as up-to-date better diagnosis, subtype categorization and treatment management of leukemia [27].

Early diagnosis and treatment of CML has paramount significance to prevent and control CML. As the diagnosis and treatment delays the CML condition worsens because its stage may be aggravated to clonal mutation and development of resistant to TKI therapy [24].

CML has a huge impact in low-income countries because of the loss of parents, the loss of output owing to disability, and the high medical costs that influence the population's socioeconomic and health welfare [24].

Furthermore, evidence from Ethiopia in 2021 indicates that 1,800 patients were diagnosed and treated at Tikur Anbessa Specialized Hospital (TASH). CML will become a common oncological condition in the future, despite its current low frequency. In addition, treatment failure may occur as a result of altered existence of thyrosine kinase inhibitor (TKI) therapy [9].

Ethiopia is among low income and resource constraint country where there is limited evidence on Hematological and Clinical profile of BCR-ABL confirmed CML patients during first presentation. Thus, the aim of this study was to determine Hematological and Clinical profile BCR-ABL confirmed CML patients during first presentation at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

### 1.3. Significance of the study

The majority of CML cases occur in area of the world where CML diagnostic and monitoring technology is unavailable. There is less information available based on the hematological and clinical profiles of BCR-ABL confirmed CML patients during their first presentations, depending on geographical region, duration of signs and symptoms, age, and gender in Ethiopia. As a result, this research is critical for a thorough understanding of the distribution or level of hematological and clinical profiles of CML in the population. It contributes evidence for the development of guidelines and policy document for the early detection and diagnosis of CML, as well as a better knowledge of patient therapy and management. Furthermore, it will serve as a starting point for future research in the field.

## 2. Literature review

### Hematological profile of Chronic Myeloid Leukemia

Chang *et al.,* 2015 in Pakistan, investigated Clinico-Hematological Profile and Phase Distribution of CML. Complete Blood Count analysis revealed low hemoglobin, total WBC count between 287 x $10^9$ /L and 535.7x$10^9$ /L, thrombocytopenia or normal platelet count, or thrombocytosis with increased number of granulocytes [30].

In India, a study conducted by Kumar *et al.,* 2019 to determine the clinical and hematological profile in CML patients found that the majority of patients (58.8%) had hemoglobin levels in the 7–10 g/dL range, with severe anemia seen in 13% of patients. Total leucocytes were found to be in the (100–250) x$10^3$/µL range (52.2 %). Approximately 68.9% of patients had platelet counts in the (100–450) x$10^3$/µL range. Thrombocytosis (>450x $10^3$ /µL) was present in approximately 24.4 % of the patients [31].

Wiyono *et al*. (2017) did a study in Indonesia to assess the characteristics and clinical aspect of CML patients. The average leukocyte, platelet, and hemoglobin counts were 254.58x$10^3$ /L ,557x$10^3$/L and 9.55g/dl, respectively. Based on the results of a peripheral blood smear, 57.6% had normochromic normocytic anisopoikilocytosis erythrocyte, increased leukocytes with blast presence in 97% of the patients, and 51.5% had a profile of increased platelets with the discovery of giant platelets in 33.3% of the patients [17].

According to the Hematobiological profile of patients with Chronic Myeloid Leukemia study conducted by Ngono AP *et al.,* 2020 in Cameroon, 66 % of the patients were in the chronic phase, 11.3 % were in the accelerated phase, and 22.7% were in blast crisis. All patients had hyperleukocytosis, with a mean white blood cell count of 128,362/mm3. Anemia was prevalent (77.3 %) and it was typically regarded as moderate (61.4 %). Thrombocytopenia was uncommon (8.3 %), as was basophilia (1.2 %) [7].

In Ethiopia, hematological parameters with respect to chronic leukemia had neutrophilia (71.4%), basophil leukocytosis (100.0%) and eosinophilia (85.7%). All types of leukemia were found to have leukocytosis [27].

Imatinib therapy may be introduced as soon as the diagnosis of Ph-positive CML has been established, even if the WBC is dramatically elevated. For patients with a WBC over 20,000/mm3, attendant therapy with allopurinol is recommended until the WBC is consistently less than 20,000/mm3. Even in patients with advanced-phase disease with maintaining adequate hydration for this complication. After initiating therapy with imatinib, the WBC should begin to normalize within 4 to 6 weeks (32). In patients receiving therapy with hydroxyurea and who have normal blood counts, the hydroxyurea should be tapered and discontinued within the first week of imatinib therapy. For patients with elevated WBCs and platelet counts who begin imatinib while on hydroxyurea, the hydroxyurea may need to be continued for 1 to 3 weeks while closely monitoring the patient's CBC and clinical situation [32,33].

**Clinical Profile of Chronic Myeloid Leukemia patients**

In 2020, Jabbour has conducted study in the United States, Anemia and splenomegaly are the most common signs and symptoms of CML-CP, including fatigue, weight loss, malaise, easy satiety, and left upper quadrant fullness or pain. Rare manifestations include bleeding (associated with a low platelet count and/or platelet dysfunction), thrombosis (associated with thrombocytosis and/or marked leukocytosis), gouty arthritis (from elevated uric acid levels), priapism (usually associated with marked leukocytosis or thrombocytosis), and upper gastrointestinal ulceration and bleeding (from elevated histamine levels due to basophilia) [34].

In the study conducted in Iraq by Al-abady I *et al*., 2021, the most common complain among CML males was fatigue, followed by fullness in the abdomen and constitutional symptoms, while in females the more common complaint was bone pain. Among the enrolled CML patients: 67 patients (95.7%) had splenomegaly at the time of presentation while hepatomegaly found in 15 patients (21.4%). Clinically, 50% of CML patients are asymptomatic, with the remainder exhibiting anemia, splenomegaly, fever, bleeding tendency, hepatomegaly, lymphadenopathy, and complications such as renal failure, hearing loss, and priapism [35].

According to a study conducted in India by Srinivas KG, 60 % of patients presented with fatigue/weakness. Fever was present in 48% of the patients, and weight loss was present in 37% of the patients. About 20% of them were experiencing abdominal pain. In addition, 30% were asymptomatic at the time of presentation. Approximately 70% of the patients had splenomegaly, 20% had hepatomegaly, and 38% had pallor. Bleeding (4%) and lymphadenopathy (3%) were both

uncommon. Diabetes affected 35 (10%) of the total CML patients, while hypertension affected 27 (7.7%) of patients [36].

In the study from India by Kumar *et al*., 2019, all patient were symptomatic at the time of diagnosis. The common symptoms of the patients were fullness of the abdomen (66.6%) followed by weakness (63%), fever (59%), and fatigue (55.5%), splenomegaly and anemia were the most common sign. About 13(17.3%) cases had mild splenomegaly, 20(26.6%) cases had moderate splenomegaly, and 42(56%) cases had massive splenomegaly. In AP, 1(10%) cases had mild splenomegaly and 10(100%) cases had massive splenomegaly whereas in blast crisis phase,100% [31].

In a study done by Tadese F *et al*., in 2021, from patient registry for CML at TASH (which is the only testing and treating center of CML in Ethiopia), more than 1800 patients with CML have been diagnosed so far. The median age at the time of CML diagnosis was 33 years. All patients had splenomegaly with the overall range: 3-26 cm. The authors suggested CML will become a highly prevalent oncologic diagnosis in the future, despite its low prevalence, as TKI therapy improves survival. As a result, it is reasonable to expect that new resistance or progression will emerge [9].

# 3. Objectives

## 3.1 General Objective

To determine Hematological and Assess Clinical profile of BCR-ABL confirmed Chronic Myeloid Leukemia patients during presentation at TASH from August 2021 to December 2022.

## 3.2 Specific objectives

- To determine Hematological Profile among BCR-ABL confirmed Chronic Myeloid Leukemia patients during presentation
- To Clinical Profile among BCR-ABL confirmed Chronic Myeloid Leukemia patients during presentation

# 4. Materials and methods

## 4.1 Study Area

The study was conducted at TASH hematology clinics, a tertiary care center affiliated with College of Health Sciences, Addis Ababa University. Tikur Anbessa (black lion) specialized hospital is the largest referral hospital in Ethiopia. It was established in 1964 E.C and now the main teaching center for both clinical and pre-clinical training of most disciplines. It is also an institution where specialized clinical services that are not available in other public or private institutions are rendered to the whole nations. The various departments, faculties and residents under specialty training in the school of medicine provide patients care in the hospital. In addition, the hospital provides different services and offers diagnosis and treatment patients. This hospital is known for treating cancer patients.

Patients with CML from all around the country sent to this institution to be enrolled in the Glivec International Patient Assistance Program (GIPAP) and get treatment.

## 4.2 Study design and period

A Cross-sectional study design was conducted on hematological and clinical profile among BCR-ABL confirmed chronic myeloid leukemia patients during first presentation at TASH from August 2021 to December 2022.

## 4.3 Population

### 4.3.1 Source of population

The source of population was all CML suspected patients at TASH hematology clinics.

### 4.3.2 Study of Population

The study population was CML patients that have been newly diagnosed and confirmed by BCR-ABL at TASH hematology clinics.

## 4.4 Eligibility criteria

### 4.4.1 Inclusion criteria

- Volunteering CML patients newly diagnosed and confirmed by BCR-ABL oncogene at the time of diagnosis and not yet started first-line therapy.

### 4.4.2 Exclusion criteria

- CML patient who were BCR-ABL negative, and Clients extremely ill and unable to provide consent and sample.

## 4.5. Study variables

### 4.5.1 Dependent variable:

- Hematological profile
- Clinical Profile

### 4.5.2 Independent variables

- Age
- Sex
- Duration of sign and symptoms
- Geographical Location
- Residence
- Educational background
- Occupation
- Marital Status
- Monthly Income level
- BCR_ABL percentage
- Stage of CML
- Pre-chemo treatment

## 4.6 Sampling technique and Sample size determination

## Sampling technique

Convenient sampling technique was used to enroll all newly diagnosed BCR-ABL patients during the study period.

## Sample size determination

This study is part of an ongoing PhD project, all clients who were diagnosed since August 2021 up to December 2022 were included consecutively to determine hematological and clinical profile in CML patients attending TASH.

## 4.7 Data collection

### 4.7.1 Demographic and clinical data

Questionnaires was used to extracted socio-demographic characteristics and medical history from medical record number (MRN by nurse and medical professionals.

**Data collection work flow**

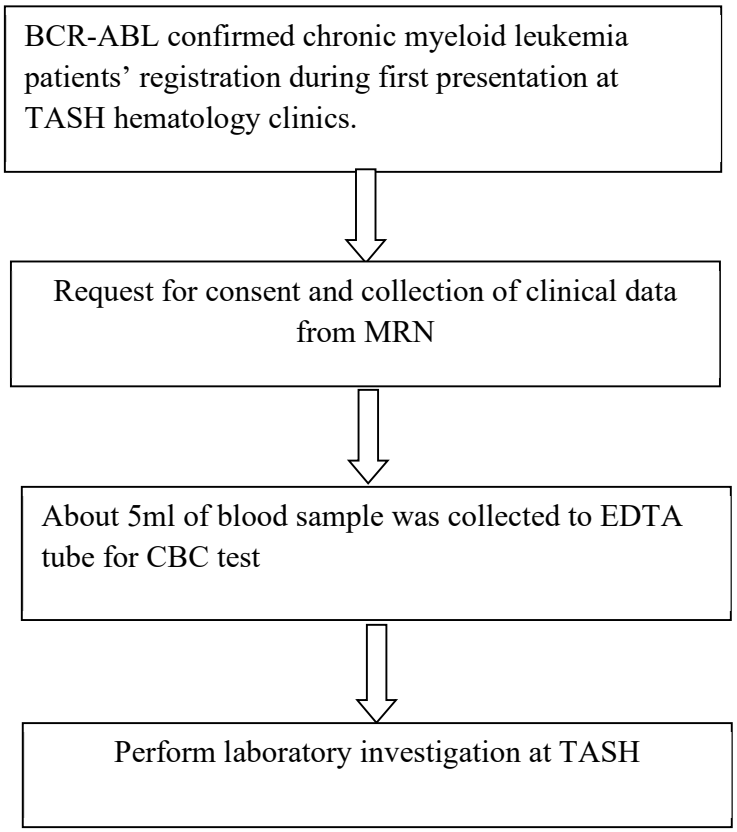



Figure 1: Data collection procedure

**Workflow of the study**

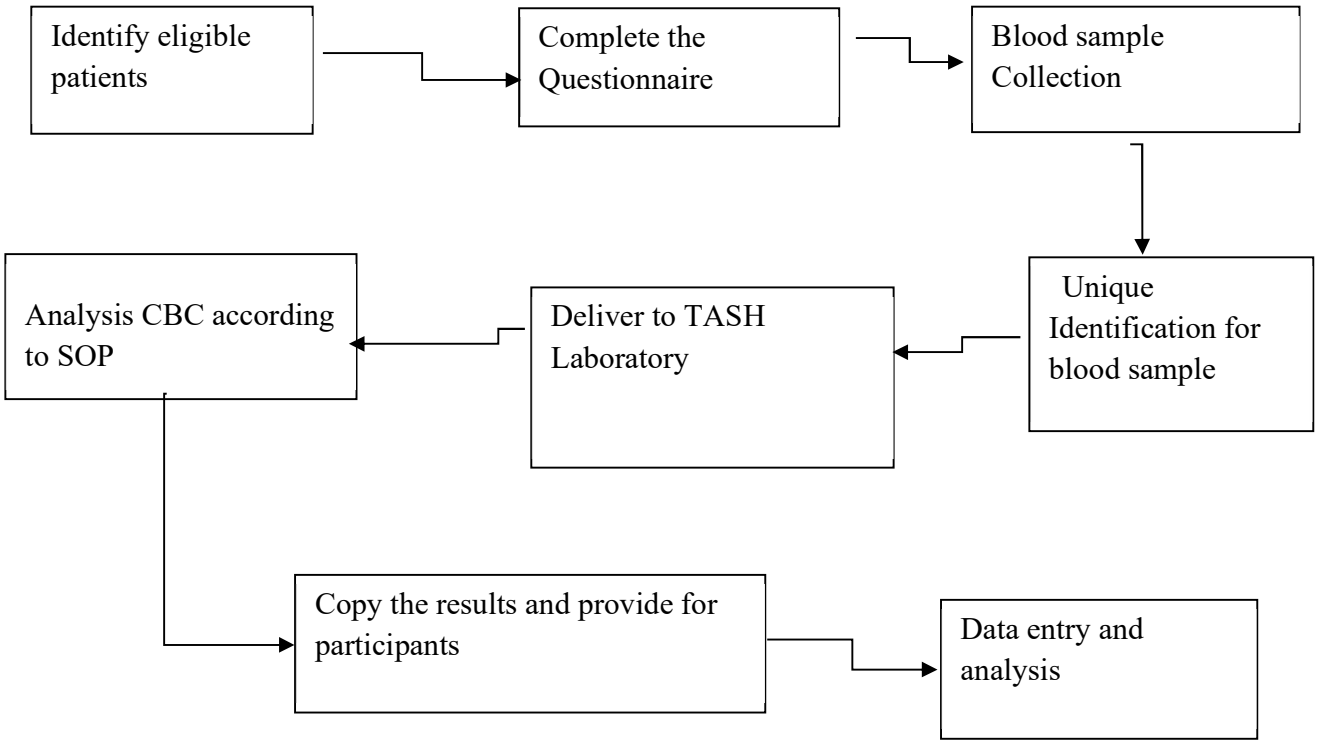



Figure 2:Workflow

### 4.7.2 Sample collection and laboratory analysis

Blood samples with a volume of about 5mL were collected in EDTA test tube from all study participants by a certified laboratory expert. A coded unique identifying number was assigned to each sample. Hematological analysis was performed using Unicel DxH800 at TASH according to SOPs within a maximum of 8 hours following collection.

### 4.7.3 Laboratory testing principles and analysis

A CBC test was analyzed by Beckman coulter DxH 800 automated hematology analyzer based on manufactures recommendation. The DxH 800 Beckman coulter hematology analyzer utilizes electrical impedance and VSC technology (volume, scatter and conductivity) for total cell counting and WBC differential respectively.

**Coulter Method(impedance)**

accurately counts and sizes cells by detecting and measuring changes in electrical resistance when a particle (such as a cell) in a conductive liquid pass through a small aperture. Each cell suspended in a conductive liquid (diluents) act as an insulator. As each cell goes through the aperture, it momentarily increases the resistance of the electrical path between the sub merged electrodes on either side of the aperture. This causes a measurable electronic pulse. For counting, the vacuum used to pull the diluted suspension of cells through the aperture must be at a regulated volume. While the number of pulses indicates particle count, the size of the electrical pulse is proportional to the cell volume.

**VCS Technology**

The COULTER VCS established WBC differential technology using three measurements: individual cell volume, high-frequency conductivity, and laser-light scatter. The combination of low-frequency current, high-frequency current and light-scattering technology provided abundant cell-by-cell information that is translated by the SPM into data plots.

**Volume Analysis**

Electronic Leukocyte Volume Analysis using low-frequency current has been used since 1967.Ithas been evaluated as a possible adjunct to the differential white cell count.

**Conductivity Analysis**

Cell walls act as conductors to high-frequency current. The current, while passing through the cell walls and through each cell interior, detects differences in the insulating properties of the cell

components. The current characterizes the nuclear and granular constituents and the chemical composition of the cell interior.

**Light Scatter Analysis**

Coulter's experience in flow cytometry dates back decades to Fulwyler's pioneering use of light scatter for cell analysis. Loken et al. and Jovin et al. discuss the relationship of particle size and refractivity to the angle of light scattered from a laser beam.

A complete blood count (CBC) gives important information about the kinds and numbers of cells in the blood, especially red blood cells, white blood cells, and platelets. A CBC helps to check any symptoms, such as weakness, fatigue, or bruising. It also helps to diagnose conditions, such as anemia, infection, and many other disorders [37].

## 4.8. Data Quality Assurance

The primary data source was obtained by qualified and experienced health professionals after obtaining training on the objectives and methods of the study.

**Pre-analytic**

The overall activities of data collection were monitored by the principal investigator to maintain the validity of the data during data collection. The data was collected under careful supervision, and the collected data was reviewed for completeness, accuracy, clarity, and consistency on a daily basis by the supervisors and principal investigator. Data and sample collectors were trained on the data collection instrument, the study's objectives, sample collection and transportation.

The samples were verified for hemolysis, clotting, volume, collection time, and proper labeling before proceeding to the analytical procedure. The manufacturer's procedures, as well as the safety precautions and specimen handling procedures were strictly followed.

**Analytical**

The laboratory analysis was done by a senior laboratory technologist and to ensure a high-quality investigation, standard operating procedures were employed for specimen processing. The automated hematology analyzer's performance was evaluated by performing three levels of hematology cell controls (Normal, Low, and High Values).

**Post analytical**

The results of complete blood counts will be registered as the exact number (value) on standardized recording format.

All laboratory assays were performed by skilled and experienced medical laboratory technologists in accordance with standard operating procedures (Annex I).

## 4.9 Data analysis

The data collected was cleaned, checked for its completeness and entered in to Microsoft excel. Then exported to Statistical package for Social Sciences (SPSS) version 26. The data was analyzed using SPSS. Before the main data analysis, the statistical assumption normality test was done by graph and Kolmogorov-Smirnov and Shapiro-Wilk tests. The graphic and statistical test outcomes variables of hematological profile of BCR-ABL confirmed were not normally distributed. Median with interquartile range was used to describe continuous data and frequency and proportion to summarize categorical data.

Descriptive statistics was used to explain socio-demographic, Hematological and clinical profile of BCR-ABL among study participants. Distribution of data was checked and non-parametric test analysis was used for data not distributed normally. A *P*-value of $<0.05$ were considered as a statistically significant difference. Finally, the results of the study were presented on words, charts, graphs and tables.

## 4.10. Operational definitions.

**Haematological Profile**:- All CBC parameters includes:- White Blood Cell count (WBC), Red Blood Cell count (RBC), Hemoglobin (HGB), Hematocrit (HCT), Mean Corpuscular Volume(MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), Red Cell Distribution Width (RDW), Platelet count (PLT), Mean Platelet Volume (MPV), Neutrophil percent (NE), Lymphocyte percent (LY), Monocyte percent (MO), Eosinophil percent (EO), Basophil percent (BA), Neutrophil absolute number (NE#), Lymphocyte absolute number (LY#), Monocyte absolute number (MO#), Eosinophil absolute number (EO#), and Basophil absolute number (BA#).

**Clinical Profile:** - Signs and Symptoms of CML patients during presentation.

**Newly Diagnosed Patients: -** a patient which is newly diagnosed of CML and confirmed by BCR-ABL for the first time

**Pre-chemo treatment: -** A person who have received hydroxyurea or Allopurinol treatment.

**Pre-chemo treatment-naive:** - A person who have never received hydroxyurea or Allopurinol treatment.

**Anemia: -**Patients with anemia are classified as follows: - Severe anemia ≤7g/dl of Hgb count, Moderate anemia 7.01 -10g/dl of Hgb count, Mild anemia 10.01-12g/dl of Hgb count for female, 10.01-13g/dl of Hgb count for male and normal > 12g/dl of Hgb count for female, > 13g/dl of Hgb count for male.

**Leukocytosis: -** is elevation of white cell count above 11.2 $x10^3/\mu L$.

**Hyper leukocytosis: -** is defined as a white blood cell count greater than 100,000 cell/μL.

**Thrombocytopenia: -** when the platelet count in blood is lower than 150 $x10^3/\mu L$.

**Thrombocytosis: -** occurs when platelet count found in blood higher than 450 $x10^3/\mu L$.

**Neutrophilia: -** absolute neutrophil count in the blood higher than 7.9 $x10^3/\mu L$.

**Eosinophilia**: - the absolute eosinophil count in the peripheral blood exceeds $0.5x10^3/\mu L$,

**Basophilia: -** is an elevated absolute basophil count greater than 0.3 $x10^3/\mu L$.

## 4.11 Ethical considerations

Ethical approval was obtained from the department of Medical Laboratory Sciences, College of Health Science, Addis Ababa University and Tikur Anbessa Specialized Hospital department of internal medicine for permission. The objective of the study was explained to the study participants and written informed consent was obtained from patients, care givers or parents and also assent was also obtained from those aged less than 18 years. The confidentiality of participant data was linked to a study code number. Any abnormal test results of study participants were communicated to their attending physician.

## 4.12 Dissemination of the result

The result of the study is reported in a formal document and presented to the school of medical Laboratory Sciences, Addis Ababa University. Besides this the finding of the research will be presented and communicated to the international community through conferences and publication in a peer reviewed journal.

# 5. Results

## 5.1 Socio-demographic characteristics of the study participants

A total of 256 CML diagnosed patients were included in the study. More than half 59.8 % (153) of them were males with male to female ratio of 1.5:1. The median age was 36 (IQR = 28.25 - 47.75) years. Of the total participants 39.5% (101) were in the age between 31-45 years. Majority of the participants 51.6 % (132) were from Rural area, (28.5%) cannot read and write. Furthermore, a total of 83 participants (32.4%) were from the Oromia region, and 85 individuals (33.2%) travelled a distance spanning 300–600 kilometres from their homes to TASH. The median duration of symptoms reported by the participants was 5 months (IQR = 2.25–12.00). Among the participants, 110 individuals (43%) had not received any Pre-chemo treatment (Naïve) prior to the study, while the remaining 146 individuals (57%) had Pre-chemo treatment Treated [Table.1].

Table 1: Overall, Socio-demographic characteristics of BCR-ABL confirmed CML patients during presentation at TASH, Addis Ababa, Ethiopia,2022.

| **Variables** | Category | n (%) |
|---|---|---|
| Age | 15-30 | 83(32.4) |
| | 31-45 | 101(39.5) |
| | 46-60 | 48(18.8) |
| | ≥61 | 24(9.4) |
| Sex | Male | 153(59.8) |
| | Female | 103(40.2) |
| Residence | Urban | 124(48.4) |
| | Rural | 132(51.6) |
| Live in birth place | Yes | 247(96.5) |
| | No | 9(3.5) |
| Region | Addis Ababa | 44(17.2) |
| | Dire Dawa | 1(0.4) |
| | Oromia | 83(32.4) |
| | Amhara | 62(24.2) |
| | SNNPR | 44(17.2) |
| | Tigray | 3(1.2) |
| | Afar | 3(1.2) |
| | Harari | 1(0.4) |

| | | |
|---|---|---|
| | Somali | 12(4.7) |
| | B/ Gumuz | 2(0.8) |
| | Gambela | 1(0.4) |
| Average distance between patient's home and TASH | Less than 100km | 67(26.2) |
| | 100-300km | 73(28.5) |
| | 300-600 km | 85(33.2) |
| | 600 km and above | 31(12.1) |
| Marital Status | Single | 59(23.0) |
| | Married | 188(73.4) |
| | Divorced | 6(2.3) |
| | Widowed | 3(1.2) |
| Educational background | Can't read and write | 73(28.5) |
| | Read and write only | 19(7.4) |
| | Primary Education | 76(29.7) |
| | Secondary Education | 44(17.2) |
| | Higher Education | 44(17.2) |
| Occupation | Farmer | 93(36.3) |
| | House Wife | 28(10.9) |
| | Gov't employee | 18(7.0) |
| | Private company employee | 6(2.3) |
| | Student | 20(7.8) |
| | Merchant | 20(7.8) |
| | Self-employee | 12(4.7) |
| | Driver | 10(3.9) |
| | Construction Related | 9(3.5) |
| | Military | 4(1.6) |
| | Other | 36(14.1) |
| Monthly Income level | Less than 1500 Birr | 24(9.4) |
| | 1501–5000 Birr | 35(13.7) |
| | 5001-10,000 Birr | 19(7.4) |
| | 10,001 Birr and above | 1(0.4) |
| Duration of symptoms in Month | Median (IQR) | 5.00(2.25-12.00) |
| Pre-chemo treatment (Hydroxyurea and Allopurinol) | Pre-chemo treatment Naïve | 110(43%) |
| | Pre-chemo treatment Treated | 146(57%) |

### 5.2 BCR-ABL confirmation method

Out of the 256 confirmed CML patients, 79.7% were diagnosed using FISH. The remaining patients, 5.5% and 14.8%, were diagnosed by GeneXpert and PCR tests, respectively. The median BCR-ABL percentage for the study participants was 95 (IQR = 80–100). About 177 patients (69.1%) had a BCR-ABL percentage of ≥76%, while 26 patients (10.2%) had a BCR-ABL percentage ranging from 51% to 75%. Additionally, 19 patients (7.4%) had a BCR-ABL percentage between 26% and 50%, and 3 patients (1.2%) had a BCR-ABL percentage of ≤25%. Among the confirmed BCR-ABL patients 31(12.2%) (FISH=9, PCR= 19 and GeneXpert =3) were diagnosed qualitatively but not had BCR-ABL percentage.

### 5.3 Hematological profile of the study participants

The overall median value of WBC count was 218.3 $x10^3/\mu L$, with the Minimum to Maximum (54.90- 731.90 $x10^3/\mu L$), The median value of WBC count for patients naïve to pre-chemo treatment was 262.7 $x10^3/\mu L$ while for patients treated with pre-chemo it was 189 $x10^3/\mu L$.
The overall median value for RBC count was 3.21 $x10^6/\mu L$, with Minimum to Maximum range of (0.91- 5.18$x10^6/\mu L$. The median value of RBC for patients naïve to pre-chemo treatment was 3.0 $x10^6/\mu L$ and 3.3 $x10^6/\mu L$ for patients treated with pre-chemo. Again, the overall median value for HGB was 9.3 g/dl, with the Minimum to Maximum (3.00- 15.60g/dl). The respective median values for patients naive to pre-chemo treatment and those treated with pre chemo were 8.8 9.5g/dl, respectively. The overall median value for PLT count was 324 $x10^3/\mu L$, with the Minimum to Maximum (44.00- 3300.00$x10^3/\mu L$). Whereas, the respective median values of PLT for patients naïve to pre-chemo treatment 320and those treated with pre-chemo were 320 and 325 $x10^3/\mu L$.
The overall median value for absolute nneutrophil count of the study participants was174 x103/µL with the Minimum to Maximum (6.30-656.38 x103/µL). The overall median value for absolute eosinophil count of the study participants was 5.1(2.7-8.8 x103/µL) with the Minimum to Maximum (0.10-304.00 x103/µL). The overall median value for aabsolute basophil counts of the study participants was 2.3(0.6-6.3x103/µL) with the Minimum to Maximum (0.00-45.50 x103/µL). Pre-chemo treatment had significant difference in the WBC count *(P=<0.0001)*, HGB *(P=0.024),* and HCT (P=0.024) [Table 2].

Table 2: Hematological profile of BCR-ABL confirmed CML patients during presentation at TASH, Addis Ababa, Ethiopia, 2022.

| Hematological parameters | Total (Median, IQR) | Pre-chemo treatment (Hydroxyurea and Allopurinol) | | *P*-Value |
|---|---|---|---|---|
| | | Naïve (Median, IQR) | Treated (Median, IQR) | |
| WBC (x103/µL) | 218.3(155.61-307.3) | 262.7(190.5-352.1) | 189(138.8-289.9) | <0.0001 |
| RBC (x106/µL) | 3.21(2.7-3.7) | 3(2.6-3.6) | 3.3(2.7-3.7) | 0.153 |
| HGB (g/dl) | 9.3(8.2-11) | 8.8(7.9-10.1) | 9.5(8.2-11.1) | 0.024 |
| HCT (%) | 29.1(25.7-33.5) | 28.1(24.3-32.2) | 29.6(26.9-34.4) | 0.024 |
| MCV (fL) | 92.8(87.3-97.15) | 92.6(87.1-96.4) | 93.1(88.7-99) | 0.217 |
| MCH (pg) | 29.5(27.8-31.4) | 29.1(27.5-30.63) | 29.7(27.8-31.4) | 0.061 |
| MCHC (g/dl) | 31.6(30.8-32.63) | 31.6(30.6-32.6) | 31.6(30.9-32.4) | 0.538 |
| RDW (%) | 20.7(19.5-23.23) | 20.6(19.4-22.2) | 21.2(19.5-23.4) | 0.304 |
| PLT (x103/µL) | 324 (211-499) | 320(209.5-449.8) | 325 (210-499) | 0.592 |
| MPV (fL) | 8.9 (8.1-9.8) | 8.85 (8.1-9.8) | 9 (8.2-9.8) | 0.628 |
| NE % | 86 (78.1-89.8) | 87.5 (81.5-90.5) | 84.6 (78-88.6) | 0.001 |
| LY % | 4.5 (2.6-7.2) | 3.7 (2.2-5.8) | 5.2 (2.9-7.6) | 0.008 |
| MO % | 4.3 (2.75-6.3) | 3.5 (2.4-5.1) | 4.7 (3-6.7) | 0.005 |
| EO % | 2.3 (1.4-3.7) | 2.4 (1.5-3.6) | 2.2 (1.2-4) | 0.557 |
| BA % | 1.1 (0.3-3.1) | 0.8 (0.3-2) | 1.3 (0.4-4.7) | 0.002 |
| NE # x103/µL | 174(109.7-263.2) | 203.8(145.3-295.6) | 146.7(99.3-244.5) | <0.0001 |
| LY # x103/µL | 7.9(5.1-14.9) | 7.5(5.1-14.03) | 8.1(4.7-15.3) | 0.975 |
| MO # x103/µL | 9.2(4.9-14.2) | 9.1(4.8-13.13) | 8.9(4.9-14.4) | 0.926 |
| EO # x103/µL | 5.1(2.7-8.8) | 5.95(3.0-10.08) | 4.1(2.1-13.3) | 0.004 |
| BA # x103/µL | 2.3(0.6-6.3) | 2.1(0.5-5.7) | 2.8(0.7-7.5) | 0.083 |

NB:- HGB= Hemoglobin, HCT= Hematocrit, RBC=Red blood cell, MCV=Mean corpuscular volume, MCH= Mean corpuscular hemoglobin, MCHC= Mean corpuscular hemoglobin concentration, WBC=White blood cell, PLT= Platelets, MPV=Mean platelets volume, RDW=Red blood cell distribution width, NE% =Neutrophil Percent, LY% =Lymphocyte Percent, MO% =Monocyte Percent, EO % =Eosinophil Percent, BA% =Basophil Percent, NE # = Neutrophil Absolute Number, LY# = Lymphocyte Absolute Number, MO# = Monocyte Absolute Number, EO# =Eosinophil Absolute Number, BA# =Basophil Absolute Number.

### 5.3.1 Distribution of hematological parameters and CML phase

Out of a total of 217 CP CML patients, 114 (44.53%) exhibited a WBC count ranging from 101 to 250 x $10^3$/µL. Among 205 CP CML patients, 155(64.05%) had an RBC count below or equal to 3.72 x $10^6$/µL. Also, among the HGB count, out of the total 217 CP CML patients, 115(44.92%) had a Hgb count ranging from 7.01 to 10 g/dL. Likewise, among the 217 CP CML patients, 126(49.22%), had a PLT count between 151 and 450 x 103/µL[Table 3].

Table 3: Distribution of hematological parameters and CML phase of BCR-ABL confirmed CML patients during presentation at TASH, Addis Ababa, Ethiopia 2022.

| Hematological parameters | | Chronic Myeloid Leukemia phase | | | |
|---|---|---|---|---|---|
| WBC ($x10^3$/µL) | Categories | CP n (%) | AP n (%) | BC n (%) | Total n (%) |
| | ≤100 | 10 (3.9) | 1(0.39) | 0(0) | 11(4.29) |
| | 101-250 | 114 (44.53) | 14 (5.46) | 5(1.95) | 133(51.96) |
| | 251-350 | 59 (23.04) | 6 (2.34) | 3(1.17) | 68(26.57) |
| | ≥ 351 | 34 (13.28) | 10 (3.9) | 0 (0) | 44(17.18) |
| | Total n(%) | 217(84.76) | 31(12.11) | 8(3.13) | 256(100) |
| RBC ($x10^6$/µL | ≤3.72 | 155(64.05) | 27(11.16) | 5(2.16) | 187(77.27) |
| | 3.73-5.5 | 50(20.66) | 2 (0.83) | 3(1.24) | 55(22.73) |
| | Total n(%) | 205(84.71) | 29(11.98) | 8(3.3) | 242(100) |
| HGB (g/dl) | ≤7 | 12(4.69) | 5(1.95) | 2(0.78) | 19(7.42) |
| | 7.01-10 | 115(44.92) | 20(7.81) | 3(1.17) | 138(53.9) |
| | 10.01-12 | 67(26.17) | 3(1.17) | 2(0.78) | 72(28.12) |
| | >12 | 23(8.98) | 3(1.17) | 1(0.39) | 27(10.55) |
| | Total n(%) | 217(84.76) | 31(12.11) | 8(3.13) | 256(100) |
| HCT (%) | ≤33.2 | 148(60.9) | 26(10.7) | 6(2.47) | 180(74.07) |
| | 33.3-45.7 | 58(23.87) | 3(1.23) | 2(0.82) | 63(25.92) |
| | Total n(%) | 206(84.77) | 29(11.93) | 8(3.29) | 243(100) |
| MCV (fL) | ≤73.6 | 2(0.82) | 1(0.41) | 0(0.0) | 3(1.22) |
| | 73.7-95.5 | 136(55.51) | 18(7.35) | 6(2.45) | 160(65.31) |
| | ≥95.6 | 70(28.57) | 10(4.08) | 2(0.81) | 82(33.47) |
| | Total n(%) | 208(84.9) | 29(11.84) | 8(3.26) | 245(100) |
| MCH (pg) | ≤24.2 | 4(1.65) | 2(0.82) | 0(0.0) | 6(2.47) |
| | 24.3-33.2 | 179(73.66) | 22(9.1) | 8(3.29) | 209(86) |
| | ≥33.3 | 23(9.5) | 5(2.1) | 0(0.0) | 28(11.52) |
| | Total n(%) | 206(84.77) | 29(11.93) | 8(3.3) | 243(100) |
| MCHC (g/dl) | ≤32.4 | 145(59.9) | 19(7.85) | 6(2.5) | 170(70.24) |
| | 32.5-35.8 | 54(22.31) | 6(2.5) | 1(0.41) | 61(25.21) |
| | ≥35.9 | 6(2.5) | 4(1.65) | 1(0.41) | 11(4.54) |
| | Total n(%) | 205(84.71) | 29(11.98) | 8(3.3) | 242(100) |
| RDW (%) | 12.3-17 | 6(2.5) | 0(0. 0) | 0(0.0) | 6(2.5) |
| | ≥17.1 | 199(82.22) | 29(11.98) | 8(3.3) | 236(97.52) |
| | Total n(%) | 205(84.71) | 29(11.98) | 8(3.3) | 242(100) |

| | | | | | |
|---|---|---|---|---|---|
| PLT (x103/µL) | ≤150 | 27(10.55) | 3(1.17) | 4(1.56) | 34(13.3) |
| | 151-450 | 126(49.22) | 18(7.03) | 3(1.17) | 147(57.42) |
| | >451 | 64(25) | 10(3.9) | 1(0.39) | 75(29.29) |
| | Total n(%) | 217(84.77) | 31(12.11) | 8(3.12) | 256(100) |
| MPV (fL) | ≤7.4 | 17(7.02) | 3(1.24) | 2(0.83) | 22(9.1) |
| | 7.5-11.2 | 175(72.31) | 22(9.1) | 6(2.48) | 203(83.88) |
| | ≥11.3 | 13(5.37) | 4(1.65) | 0(0.0) | 17(7.02) |
| | Total n(%) | 205(84.71) | 29(11.98) | 8(3.3) | 242(100) |
| NE# x103/µL | ≤1.7 | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) |
| | 1.8-7.8 | 1(0.41) | 0(0.0) | 0(0.0) | 1(0.41) |
| | ≥7.9 | 203(84.23) | 29(12.03) | 8(3.32) | 240(99.59) |
| | Total n(%) | 204(84.65) | 29(12.03) | 8(3.32) | 241(100) |
| LY# x103/µL | ≤0.9 | 3(1.24) | 1(0.41) | 0(0.0) | 4(1.7) |
| | 1-3.0 | 13(5.4) | 0(0.0) | 0(0.0) | 13(5.4) |
| | ≥3.1 | 188(78) | 28(11.61) | 8(3.32) | 224(92.95) |
| | Total n(%) | 204(84.65) | 29(12.03) | 8(3.32) | 241(100) |
| MO# x103/µL | ≤0.2 | 7(2.9) | 0(0.0) | 0(0.0) | 7(2.9) |
| | 0.3-1 | 4(1.66) | 0(0.0) | 0(0.0) | 4(1.66) |
| | ≥1.1 | 192(80) | 29(12.03) | 8(3.3) | 229(95.42) |
| | Total n(%) | 203(84.6) | 29(12.1) | 8(3.3) | 240(100) |
| EO# x103/µL | ≤0.0 | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) |
| | 0.5 | 7(3) | 1(0.43) | 0(0.0) | 8(3.42) |
| | ≥0.51 | 193(82.48) | 26(11.11) | 7(3) | 226(96.6) |
| | Total n(%) | 200(85.47) | 27(11.54) | 7(3) | 234(100) |
| BA# x103/µL | ≤0.0 | 20(8.6) | 1(0.43) | 0(0.0) | 21(9.01) |
| | 0.1-0.2 | 17(7.3) | 3(1.3) | 0(0.0) | 20(8.6) |
| | ≥0.3 | 162(69.52) | 23(9.87) | 7(3) | 192(82.4) |
| | Total n(%) | 199(85.4) | 27(11.6) | 7(3) | 233(100) |

NB:- HGB=Hemoglobin, HCT=Hematocrit, RBC=Red blood cell, MCV= Mean corpuscular volume, CH= Mean corpuscular hemoglobin, MCHC= Mean corpuscular hemoglobin concentration, WBC= White blood cell, PLT=Platelets, MPV=Mean platelets volume, RDW= Red blood cell distribution width, NE% =Neutrophil Percent, LY% =Lymphocyte Percent, MO% = Monocyte Percent, EO% =Eosinophil Percent, BA% =Basophil Percent, NE# =Neutrophil Absolute Number, LY# = Lymphocyte Absolute Number, MO# = Monocyte Absolute Number, EO# =Eosinophil Absolute Number, BA# =Basophil Absolute Number, CP = Chronic phase, AP= Accelerated phase, BC=Blast crisis phase, % is calculated from the column total

### 5.3.2 Hematological Parameter Abnormality

All patients have Leukocytosis, while greater than 95.7% of the patients had hyper leukocytosis and 91.8% of patients were developed anemia. The anemia was moderate for 138(53.9 %) and severe for 19(7.4%) of the study participants [Figure 3]. About 75 (29.3%) patients had thrombocytosis and 34 (13.3%) had thrombocytopenia. Out of CML patients, 240(99.59%) showed neutrophilia, eosinophilia was shown in 226(96.6%) patients. Additionally, basophilia was seen 192(82.4%) patients.

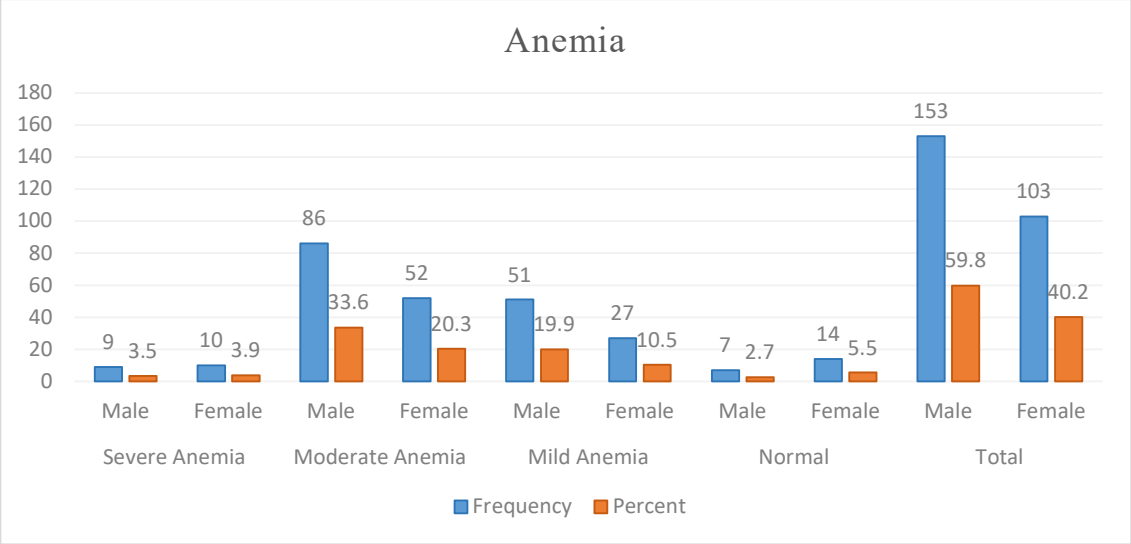



Figure 3: Anemia of BCR-ABL confirmed CML patients during presentation at TASH, Addis Ababa, Ethiopia,2022.

### 5.4 Clinical profile of the study participants

The 256 patients had different stage of CML at presentation; 217 (84.8%) were at CP stage, 31 (12.1%) were at AP stage, and 8(3.1%) patients were at BC stage [Table 3]. The majority of CML patients were symptomatic at the time of diagnosis. The most common sign and symptoms were Fatigue 247(96.5 %), abdominal pain 236(92.2%), splenomegaly 229(89.5%) and weight loss 226(88.3 %) [Fig:4]. From total 229 of study participants, 60.3%, were developed massive Splenomegaly with spleen Size of > 10 cm, (36.7%) moderate Splenomegaly with spleen Size of 4-9cm and (3.1%) mild Splenomegaly with spleen Size of 1-3cm.

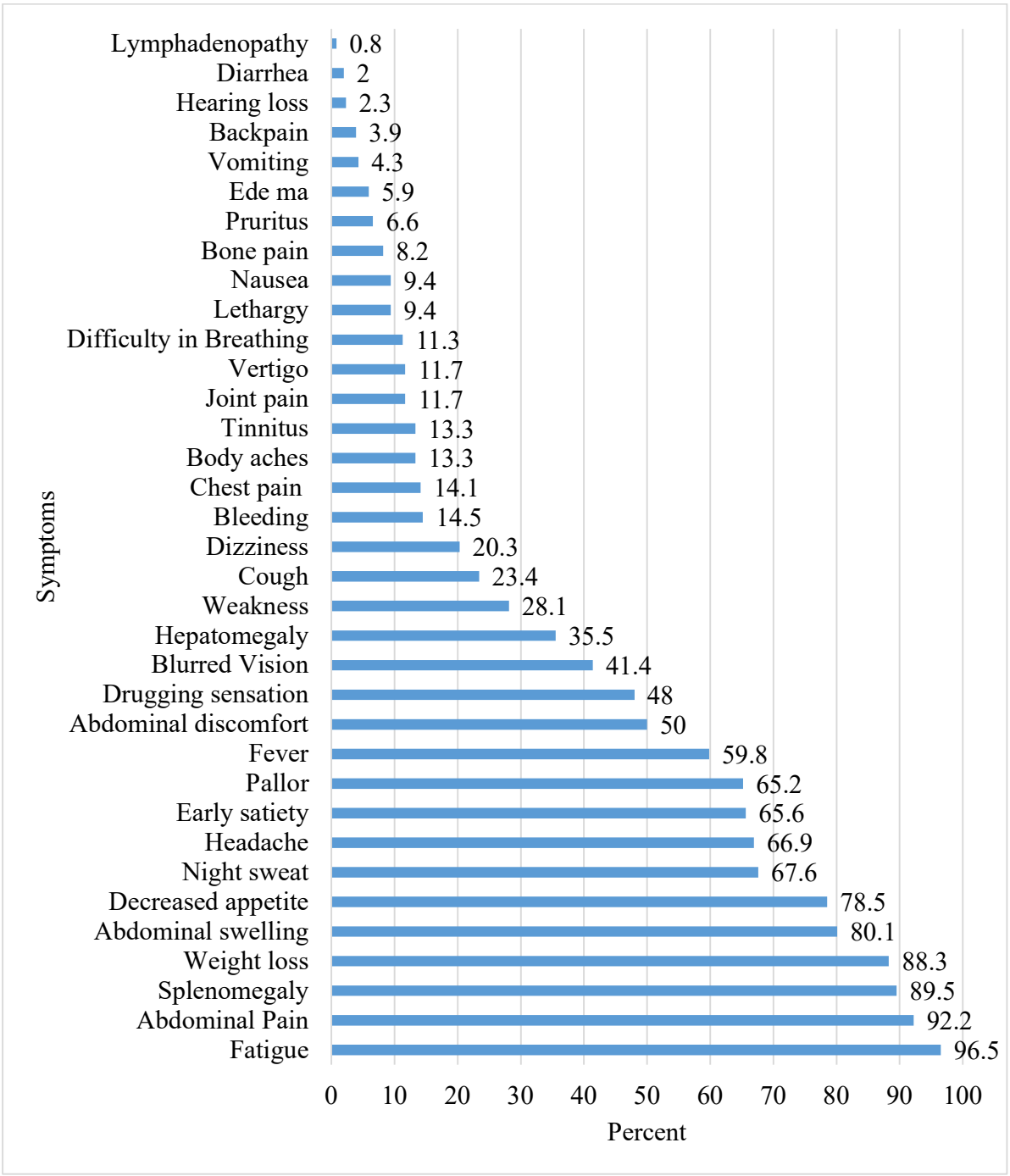
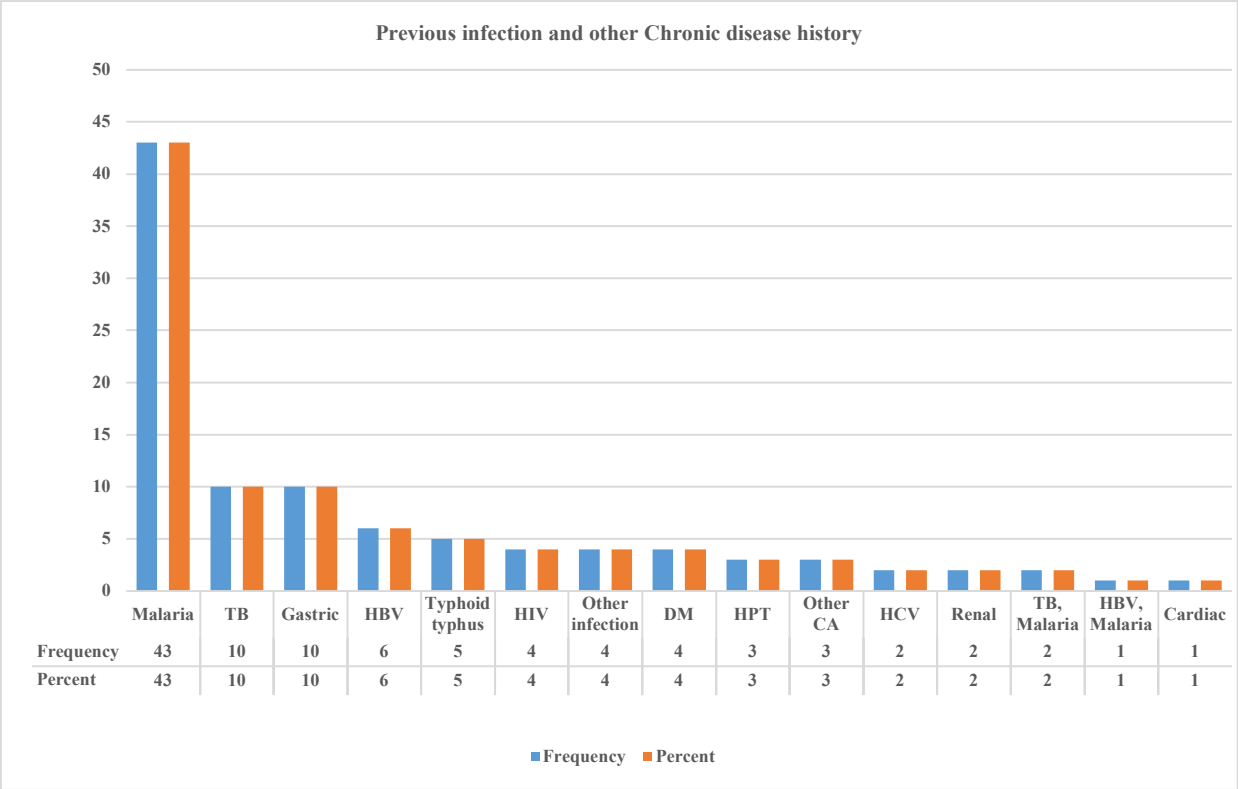



Figure 4: Clinical profile of BCR-ABL confirmed CML patients during presentation at TASH, Addis Ababa, Ethiopia,2022

### 5.4.1 Previous infection and chronic disease history of the participant

From total 256 CML patients, about 100 (39 %) of patients had previous infection history. Among the 100 patients, malaria was the most prevalent with 43 (43%), Tuberculosis10(10%), hepatitis B 6(6%), HIV and other infection have the same prevalence 4(4%). Some of the patients had Chronic disease history like DM 4(4%), HPT and other CA had 3(3%) each. While, Renal and cardiac problem was the least prevalent 2(2%) and 1(1%), respectively [Figure 5]. 0




NB: - TB=Tuberculosis, HBV=Hepatitis B virus, HIV=human immune acquired deficiency virus, DM=Diabetic Meletus, HPT=hypertension, CA=Cancer, HCV= Hepatitis C virus, TB-Malaria =Co-infection, HBV-Malaria=Co-infection, Other infection=Soft tissue infection.

Figure 5: Previous infection and other chronic disease history of BCR-ABL confirmed CML patients during presentation at TASH, Addis Ababa, Ethiopia,2022

## 6. Discussion

This study aimed to describe hematological and clinical profile of BCR ABL confirmed CML patients during presentation at TASH, Addis Ababa, Ethiopia. A total of 256 patients diagnosed with CML. According to this finding WBC count, Hgb, absolute neutrophil and absolute eosinophil counts have significant variation among pre-treated and naïve to treatment group of CML patients while basophil count having a marginally significant variation (p=0.08). All case of CML patients were at some clinical stage with the majority of them on CP followed by AP with minority on BC. In addition to the above stage's fatigue, abdominal pain, splenomegaly, and weight loss were the major sign and symptoms of the participants.

The median age of participant was 36 years and the most common age group (101 (39.5%)), of CML was between 31-45 years. This is similar with the study conducted by *Mulu A et al*.; 2019, 31–40 years 27.2% [38]. And this is relatively comparable with the study conducted in Ethiopia by Tadese F *et al*., in 2021, the median age is 33 years [9] and comparable with study conducted by Ngono AP *et al.,* 2020, with a mean age of 39.2 years and with 54 (40.9%) patients, the most common age group was 31 to 45 years [7].

In this study male (59.8 %) were relatively more affected by CML than female, with ratio of 1.5:1 male to female. This finding is similar to study conducted in Pakistan male to female ratio 1.6:1 [30, 39]. In Cameroon (57.6%) by Ngono AP *et al.,* 2020 [7]. It is also almost similar with the study conducted in Iraq, males were (57.1%) by Al-abady I *et al*., 2021 [35]. This finding could be attributed to males being more exposed to environmental or occupational hazards.

Out of the 256 confirmed CML patients 79.7% were confirmed by FISH molecular test. About 5.5% and 14.8% of the patients were confirmed by GeneXpert and PCR respectively. These molecular testing methods are also used by other studies, for example *Ngono AP et al*., 2020, from Cameroon used (22.7%) by FISH and (4.5%) by RT-PCR and shows the presence of the t (9; 22) or BCR-ABL transcript in all patients [7]. Detection of the BCR-ABL transcript by RT-PCR, or of the Ph chromosome by FISH [11, 36, 40] is possible. The difference may be the affordability or availability of the testing method.

In this study the overall median (IQR) value of WBC count was 218.3(155.61-307.3) $x10^3/\mu L$ and all patients have Leukocytosis. The median (IQR) value for HGB was 9.3(8.2-11) g/dl and majority of them 91.8% have anemia. About 75 (29.3%) of patients had thrombocytosis and 34 (13.3%) had thrombocytopenia. About 19(7.4%) had severe anemia,138(53.9 %) had moderate anemia,

78(30.4%) had mild anemia and 21(8.2%) had no anemia. This is similar with the study conducted in Ethiopia by Tadese F *et al*., in 2021, All the patients had leukocytosis with mean WBC count of 380,618/mL (range: 75,000- 723,730/mL), almost all patients (96.7%) had anemia [9], other study conducted in Pakistan, by Chang *et al.,* 2015, that revealed low hemoglobin, total WBC count between 287 x $10^9$ /L and 535.7x$10^9$ /L, thrombocytopenia or normal platelet count, or thrombocytosis [30].

In addition, the study conducted in Iraq, by Al-abady I *et al.,* 2021, the mean WBC were 153.7x$10^9$ /L ranged from 29- 436 x $10^9$ /L, (34.3 %) had neutrophilia and (72.9 %) had basophilia [35]. Another study done in Tanzania, by Henke O *et al*., 2020, the median WBC was 300.5 × $10^9$/L (78–499 × $10^9$/L) and 327.5 × $10^3$/μL (115–1004 × $10^3$/μL) for thrombocytes, [41]. This finding is also similar to the study which reported 13% severe anemia, 58.8% had moderate anemia, 28.2% mild anemia conducted by Kumar S, et al., 2019 in India [31], in Cameroon by Ngono AP et al., 2020, anemia was 86.4%, moderate for 61.4% and severe for 5.3% [7] and in Pakistan by Chang F et al.,2015, 95.1% developed anemia and Mild (22.8%), Moderate (46.9%), but different for Severe anemia (30.1%) [30], the difference may be due to sample size and geographical location. Another finding conducted in Iraq by Al-abady I et al., 2021 (85.7%) was almost similar with this study and by Sinha R, et al., 2019 in India, 87.5% [35, 40].

Among the participants, naïve to the Pre-chemo treatment, the median and IQR of the WBC, RBC, HGB and PLT count was 262.7(190.5-352.1) x103/μL, 3.0(2.6-3.6) x106/μL, 8.8(7.9-10.1) g/dl and 320(209.5-449.8) x103/μL, respectively. While the participants treated with Pre-chemo treatment median and IQR of the WBC, RBC, HGB and PLT count was 189(138.8-289.9) x103/μL, 3.3(2.7-3.7) x106/μL, 9.5(8.2-11.1) g/dl and 325 (210-499) x103/μL respectively. These results suggest that, there is a significant difference in the WBC, HGB and HCT count between naïve to the Pre-chemo treatment and treated with Pre-chemo treatment. Patients naïve for Pre-chemo treatment had increased WBC count than treated with Pre-chemo treatment. The difference could be due to the fact that medication reduce the proliferation of the cells [32,33]. Even tough, the hematological parameters result is less for pre-treated compared with naïve it is still within the hyper leukocytosis range. This might be due to the fact that they were received the medication for short period of time or they have been provided low dose of hydroxyurea and allopurinol during the presentation. Hydroxyurea was utilized as cytoreduction therapy before imatinib until CML was confirmed or imatinib was available. Allopurinol was used as preventive of Tumor/cell lysis syndrome [33,42].

From total 217 CP CML patients 114 (44.53) with WBC count (101-250) x$10^3$/µL. This is comparable to a study conducted in India by Kumer et al., 2019, in which the majority of CP CML patients (56%) had a leukocyte count in the range (100-250x $10^3$/µL) [31].

Among the study participants, absolute neutrophil number of overall median (IQR) 174(109.7-263.2) x$10^3$/µL. The median (IQR) of neutrophil for naïve and pre-chemo treated participants were 203.8(145.3-295.6) x$10^3$/µL and 146.7(99.3-244.5) x$10^3$/µL respectively. This result shows all participant had neutrophilia and in line with the results reported from Tanzania by Tebuka E, *et al*.,2016, Mean (±SD) of total white blood count before treatment was 224 (±139) K/µL and absolute neutrophil number 179(±123) K/µL [43].

From total 217 CP CML patients 126(49.22%) have normal PLT Count (151-450) x$10^3$/µL, 64(25%) have thrombocytosis (>451) x103/µL and 27(10.55%) have thrombocytopenia (≤150) x$10^3$/µL. This is in line to the study reported from India by Kumar *et al*.,2019, where 68% of CP patients had normal platelet count (100-450x$10^3$/µL), 24.4% had, Increased platelet count (>450 × $10^3$/µL) and 6.7% had Thrombocytopenia [31].

In this study the results of bone marrow aspiration and Peripheral morphology examination of 256 CML patients, shows the stage of the CML, 217 (84.78%) of them were in CP, 31 (12.1 %) in AP and 8 (3.1 %) in BC. This study is comparable to one conducted Tadese F *et al*., in 2021, 90% presented in CP-CML and 9.7% presented in AP [9] while 83% CML-CP, 12% AP, and 5% BC phase was reported by Kumar S, *et al*., 2019 in India [31] and from India. Srinivas KG*, et al*., 2013, found CP (90.1%), AP (4.5%) and with BC (5.4%) [36]. This study results are higher than the study conducted by Ngono AP *et al*., 2020 in Cameroon, 66 % and 64% by Sinha R, *et al*., 2019 in India [7,40]. This difference could be due to sample size difference the sample size for the above study is 132, 64, while in this study it is 256. The finding in the AP is similar with the study conducted by Ngono AP e *et al.,* 2020 in Cameroon, 11.3 %. While the finding in BC, was less than the finding reported from Cameron, 22.7% by Ngono AP *et al.,* 2020 and 7.8% by Sinha R, *et al*., 2019 in India, but for AP it was 28.1% [7,40]. This difference could be due to sample size difference.

The duration of symptoms in a month for participant was Median (IQR) 5.00(2.25-12.00). This result was consistent with the study done in Ethiopian by Tadese F *et al*., in 2021, the median length sickness before to CML diagnosis was 5.0 month (IQR, 4.3 months) [9]. This results relatively

much higher than the results reported from Tanzania by Tebuka E, *et al*.,2016, duration of symptoms was found to be 15 (±9) months ranging from 0 to 48 months [43].

All CML patients in the current study were symptomatic at the time of presentation and the most common complaint was fatigue (96.5%) followed by the abdomen pain (92.2%), Splenomegaly (89.5%), Abdominal swelling (80.1%), weight loss (88.3%), Decreased appetite (78.5%), and night sweat (67.6%)). This finding is in line with the study conducted by Al-abady I *et al*., 2021: Sultan S *et al*.,2021 [35, 39, 40]. This was higher than the Indian study, which found that the most prevalent symptom was fatigue (60%), fever (48%), weight loss (37%) and 70% of the patients had splenomegaly [36]. Another Indian study found that fullness in the abdomen was 66.6%, fever was 59%,and fatigue 55.5%, which can be attributable to differences in sample size between studies and the duration symptoms[ 2,18,31,42].

In This study, Splenomegaly was (89.5%), and the spleen size was presented in different categorical sizes in this study, about 138 (60.3%) cases had massive splenomegaly (>10 cm), 84 (36.7%) developed moderate size (4-9 cm) and 7 (3.1%) case had mild splenomegaly with size of 1-3 cm. This finding was consistent with the study done in Ethiopia by Tadese F *et al*., in 2021, All patients had splenomegaly with the overall range: 3-26 cm [9] The study reported from India, massive splenomegaly 62.2%, moderate size 22.2%, and mild 15.6% by Kumar *et al*., 2019 that is comparable with this study [31]. However, this finding is in contrast with study done in Pakistan that report 32.5% of massive splenomegaly [39]. This difference may be due to sample size difference among study participant.

## 7. Strength and limitation

This study has relatively large participants and though the study place were in Addis Ababa, the participants regions were representative across Ethiopia. Since this study was the first conducted with detailed analysis, it gives information on hematological and clinical profile for newly diagnosed CML patients. Furthermore, a lot of variables were mentioned, that might indicate CML.

As a limitation further testing was not done like clinical chemistry, cytogenetic or molecular study due to unavailability and affordability of such tests.

## 8. Conclusion

This study revealed a significant prevalence of hyperleukocytosis and anemia among CML patients during their initial presentation. Fatigue, abdominal pain, splenomegaly, and weight loss emerged as the most commonly observed signs and symptoms in CML patients. Males were more affected than females. The most common CML phase was CP. Most of CML patients were among 31-45 younger population.

## 9. Recommendations

Early detection, affordable BCR-ABL test, treatment and management of CML patients is important. Most of the patient come from distant area as a result they develop these sign and symptoms, so better to decentralization of the service is very critical.

There may be need to identify markers for hematological and clinical profile to considering the early detection of CML. These markers and type of clinical profile might be also considering age, sex, geography and other portions. Further, prospective studies with more laboratory exams are needed as well as an improvement of the technical platform of Ethiopian laboratories in order to locally perform diagnosis and tests (standard karyotype and PCR).

## 10.References


1. Ponte ESD, Wagner SC, Linden R, Schirmer H. Study of correlation between imatinib mesylate plasma levels and hematological profile of patients undergoing treatment for chronic myeloid leukemia. *JBPML*. 2017;(June):159–64.

2. Radich JP, Deininger M, Abboud CN, Altman JK, Berman E, Bhatia R, et al. Chronic myeloid leukemia, version 1.2019. JNCCN J Natl Compr Cancer Netw. 2018;16(9):1108–35.

3. Barbui T, Thiele J, Gisslinger H, Kvasnicka HM, Vannucchi AM, Guglielmelli P, et al. The 2016 WHO classification and diagnostic criteria for myeloproliferative neoplasms: document summary and in-depth discussion. *Blood Cancer J*. 2018;8(2):15.

4. Terwilliger T, Abdul-Hay M. Acute lymphoblastic leukemia: a comprehensive review and 2017 update. *Blood Cancer J*. 2017;7(6): e577.

5. Zhang S, Kipps TJ. The pathogenesis of chronic lymphocytic leukemia. Annu Rev Pathol Mech Dis. 2014; 9:103–18.

6. Hwang SM. Classification of acute myeloid leukemia. *Blood Res*. 2020;55(S1):1–4.

7. Ngono AP, Tipane PA, Raoul S, Njonnou S, Timnou AT, et al. Hematobiological Profile of Patients with Chronic Myeloid Leukemia at the Diagnosis in Yaoundé: A Cross-Sectional Study. *Open J. Blood Dis*. 2020;110–23.

8. Ogunleye F, Ibrahim M, Allen E, Brennan N, Huang J, Yu Z, Huben M, Jaiyesimi I. BCR-ABL testing by polymerase chain reaction in patients with neutrophilia: The William Beaumont Hospital experience and the case for rational laboratory test requests. *J. Oncol. Pract.* 2016 Dec;12(12):e1001-5.

9. Tadesse F, Asres G, Abubeker A, Gebremedhin A, Radich J. Spectrum of BCR-ABL Mutations and Treatment Outcomes in Ethiopian Imatinib-Resistant Patients with Chronic Myeloid Leukemia original reports abstract. *JCO Glob Oncol*. 2021;1187–93.

10. Smith G, Apperley J, Milojkovic D, Cross NCP, Foroni L, Byrne J, et al. A British Society for Haematology Guideline on the diagnosis and management of chronic myeloid leukaemia. Br. *J. Haematol*. 2020;(July):171–93.

11. Minciacchi VR, Kumar R, Krause DS. Chronic myeloid leukemia: A model disease of the past, present and future. *Cells*. 2021;10(1):1–23.

12. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2021. *Ca Cancer J Clin*. 2021 Jan 12;71(1):7-33.

13. Tadwalkar S HM. Global impact of tyrosine kinase inhibitors on chronic myeloid leukemia epidemiology over the next ten years. *JCO Glob Oncol*. 2018;8(107s, 2018 (suppl 2)).

14. Rohrbacher M HJ. Epidemiology of chronic myeloid leukaemia (CML). Best Pr *Res Clin Haematol.* 2009; 22:295–302.

15. Tadwalkar S. The global incidence and prevalence of chronic myeloid leukemia over the next ten years (2017-2027). *J Blood Disord Transfus*. 2017; 8:2155–64.

16. Arber DA, Orazi A, Hasserjian R, Thiele J, Borowitz MJ, Le Beau MM, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood*. 2016;127(20):2391–405.

17. Wiyono MR, Ugroseno S, Bintoro Y, Hernaningsih Y. Characteristic of chronic myelogenous leukemia patients at the Polyclinic of Oncology, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia in 2017. *MBIOMJ*. 2020;30(1):27–33.

18. Jabbour E, Kantarjian H. Chronic C, Leukemia M, Found B, To Q, About A, Myeloid C. Chronic Myeloid Leukemia Early Detection, Diagnosis, and Staging Can Chronic Myeloid Leukemia Be Found Early? Signs and Symptoms of Chronic Myeloid Leukemia. *Cancer* 2018 :1–13.

19. Murthy GS. How I Manage Patients with Chronic Myeloid Leukemia (CML): Perspectives from Clinical Practice. Blood and Lymphatic Cancer: Targets and Therapy. 2022; 12:1.

20. Cortes J. How to manage CML patients with comorbidities. Hematology 2020, the American Society of Hematology Education Program Book. 2020 Dec 4;2020(1):237-42.

21. Thompson PA, Kantarjian HM, Cortes JE. Diagnosis and treatment of chronic myeloid leukemia in 2015. InMayo Clinic Proceedings 2015 Oct 1 (Vol. 90, No. 10, pp. 1440-1454). Elsevier

22. Bonifacio M, Stagno F, Scaffidi L, Krampera M, Di Raimondo F. Management of chronic

myeloid leukemia in advanced phase. Frontiers in Oncology. 2019 Oct 25; 9:1132.

23. Hochhaus A, Breccia M, Saglio G, García-Gutiérrez V, Réa D, Janssen J, Apperley J. Expert opinion—management of chronic myeloid leukemia after resistance to second-generation tyrosine kinase inhibitors. Leukemia. 2020 Jun;34(6):1495-502.

24. García-Gutiérrez V, Breccia M, Jabbour E, Mauro M, Cortes JE. A clinician perspective on the treatment of chronic myeloid leukemia in the chronic phase. *Journal of Hematology & Oncology*. 2022 Dec;15(1):1-5.

25. Singhal MK, Sengar M, Nair R. Summary of the published Indian data on chronic myeloid leukemia. South Asian *J Cancer*. 2016;05(03):162–5.

26. Singh A, Kulshrestha AR, Singh SK, Kulshrestha MR. To Study the Clinical and Haematological Profile of CML Patients and To Compare the Haematological Response of Imatinib and Hydroxyurea in Different Subsets of CML Patients. *Saudi J Pathol Microbiol*. 2019; 3362:127–33.

27. Kassahun W, Tesfaye G, Bimerew LG, Fufa D, Adissu W, Yemane T. Prevalence of Leukemia and Associated Factors among Patients with Abnormal Hematological Parameters in Jimma Medical Center , Southwest Ethiopia : A Cross-Sectional Study. *Adv Hematol.* 2020; 2020:3–9.

28. John Wiley & Sons. Postgraduate haematology. Seven edit. Hoffbrand A.V, Higgs D.R, Keeling D.M MA., editor. UK: John Wiley & Sons Ltd; 2016. p. 419-437

29. Hijiya N, Schultz KR, Metzler M, Millot F, Suttorp M. Pediatric chronic myeloid leukemia is a unique disease that requires a different approach. *Blood*. 2016;127(4):392–9.

30. Chang F, Qazi RA, Khan M, Baloch S, Sahito MM, Mir A. Clinico hematological profile and phase distribution of chronic myeloid leukemia. *Biol Med*. 2015;7(5):5–8.

31. Kumar S, Gupta VK, Bharti A, Meena LP, Gupta V, Shukla J. A study to determine the clinical, hematological, cytogenetic, and molecular profile in CML patient in and around Eastern UP, India. *J Family Med Prim Care*. 2019; 8:2450-5.

32. Mcligeyo A, Rajab J, Ezzi M, Oyiro P, Bett Y, Odhiambo A, et al. Cytopenia among CML Patients on Imatinib in Kenya: Types, Grades, and Time Course. *Adv Hematol*.2020;2020.

33. Deininger BMWN, Brien SGO, Ford JM, Druker BJ. Practical Management of Patients with

Chronic Myeloid Leukemia Receiving Imatinib. *J. Clin. Oncol*. 2022;21(8):1637–47.

34. Jabbour E, Kantarjian H. Chronic myeloid leukemia: 2018 update on diagnosis, therapy and monitoring. *Am. J. Hematol*. 2018 Mar;93(3):442-59.

35. Al-abady I. Clinico-Hematological Profile in Patients with Chronic Myeloid Leukemia. Annals of the College of Medicine, *Mosul.* 2021 Jun 1;43(1):1-9.

36. Srinivas KG, Patil S, Shashidhara S. Epidemiological and clinical profile of patients with chronic myeloid leukemia at health-care global, Bangalore institute of oncology. *Indian J Med Paediatr Oncol.* 2013;34(3):211–2.

37. Beckman Coulter. Instructions for Use System Hematology Specimen Processing Module with System Manager. 2009;(March 2009).

38. Mulu Fentie A, Tadesse F, Engidawork E, Gebremedhin A. Prevalence and determinants of non-adherence to Imatinib in the first 3-months treatment among newly diagnosed Ethiopians with chronic myeloid leukemia. *PloS one*. 2019 Mar 7;14(3): e0213557.

39. Sultan S, Jaffri SA, Zeeshan R, Irfan SM. Chronic Myeloid Leukemia: Clinico-Hematological Profile from Southern Pakistan.;30(46):34-8.2021 DOI: https://doi.org/10.53350/pjmhs2115113047

40. Sinha R, Jamal I, Priyamvada PP. Clinico-haematological Profile of Chronic Myeloid Leukaemia: An Institutional Based Study from Bihar. Age. *NJLM* .2019;28(7):43-6.

41. Henke O, Mapendo PJ, Mkwizu EW, le Coutre P. Early molecular response in East African Philadelphia chromosome-positive chronic myeloid leukaemia patients treated with Imatinib and barriers to access treatment. *ecancermedicalscience.* 2020;14.

42. Nasser A, Hussein A, Chamba C, Yonazi M, Mushi R, Schuh A, Luzzatto L. Molecular response to imatinib in patients with chronic myeloid leukemia in Tanzania. Blood advances. 2021 Mar 9;5(5):1403-11.

43. Tebuka E, Makubi A, Maunda K. Complete haematological response to imatinib in chronic myeloid leukaemia patients attending the Ocean Road Cancer Institute in Tanzania. Tanzan J Health Res. 2016 Oct 26;18(4).

**Annex I.**

**Procedure for examination on UniCel® DxH 800 Beckman- Coulter automated hematology Analyzer**

**Purpose**:

The UniCel® DxH 800 Analyzer is a quantitative, automated hematology analyzer for in vitro diagnostic use in screening patient populations found in clinical laboratories. The UniCel® DxH 800Analyzer provides a:

- ❖ Complete Blood Count (CBC),
- ❖ Leukocyte 5 Part Differential (Diff),

**Scope:** This is applicable in all examination procedures applied using UniCel® DxH 800 instrument in Hematology laboratory.

**Abbreviations**:

| | | | |
|---|---|---|---|
| CBC | complete blood count | MPV | Mean Platelet Volume |
| fl | femtoliters | NE | Neutrophil percent |
| pg | picogram | LY | Lymphocyte percent |
| µl | Microliter | MO | Monocyte percent |
| WBC | White Blood Cell count | EO | Eosinophil percent |
| RBC | Red Blood Cell count | BA | Basophil percent |
| Hgb | Hemoglobin | NE# | Neutrophil absolute number |
| Hct | Hematocrit | LY# | Lymphocyte absolute number |
| MCV | Mean Corpuscular Volume | MO# | Monocyte absolute number |
| MCH | Mean Corpuscular Hemoglobin | EO# | Eosinophil absolute number |
| MCHC | Mean Corpuscular Hemoglobin Concentration | BA# | Basophil absolute number |
| RDW | Red Cell Distribution Width | QC | Quality Control |

**Principle**

**Coulter Method (impedance)**

Accurately counts and sizes cells by detecting and measuring changes in electrical resistance when a particle (such as a cell) in a conductive liquid pass through a small aperture. Each cell suspended in a conductive liquid (diluents) act as an insulator. As each cell goes through the aperture, it momentarily increases the resistance of the electrical path between the sub merged electrodes on either side of the aperture. This causes a measurable electronic pulse. For counting, the vacuum used to pull the diluted suspension of cells through the aperture must be at a regulated volume. While the number of pulses indicates particle count, the size of the electrical pulse is proportional to the cell volume.

**VCS Technology**

The COULTER VCS established WBC differential technology using three measurements: individual cell volume, high-frequency conductivity, and laser-light scatter. The combination of low-frequency current, high-frequency current and light-scattering technology provided abundant cell-by-cell information that is translated by the SPM into data plots.

**Volume Analysis**

Electronic Leukocyte Volume Analysis using low-frequency current has been used since 1967.Ithas been evaluated as a possible adjunct to the differential white cell count.

**Conductivity Analysis**

Cell walls act as conductors to high-frequency current. The current, while passing through the cell walls and each cell interior, detects differences in the insulating properties of the cell components. The current characterizes the nuclear and granular constituents and the chemical composition of the cell interior.

**Light Scatter Analysis**

Coulter's experience in flow cytometer dates back decades to Fulwyler's pioneering use of light scatter for cell analysis. Loken et al. and Jovin et al. discuss the relationship of particle size and refractivity to the angle of light scattered from a laser beam.

**Clinical utility**:

A complete blood count (CBC) gives important information about the kinds and numbers of cells in the blood, especially red blood cells, white blood cells, and platelets. A CBC helps to check any symptoms, such as weakness, fatigue, or bruising. It also helps to diagnose conditions, such

as anemia, infection, and many other disorders. In general, the complete blood count can be done as part of routine health examination and general screening.

**Reagents**

**COULTER® DxH Diluent**

COULTER DxH Diluent is a cyanide-free, isotonic buffered saline solution. COULTER DxH Diluent dilutes the specimen, is used for rinsing SPM components between sample analyses, and provides a sheath stream to transport the sample through the flow cell.

**COULTER® DxH Cell Lyse**

COULTER DxH Cell Lyse is a cyanide-free CBC lytic reagent that lyses red blood cells for the white blood cell count, and works in conjunction with COULTER DxH Diluent to generate a stable hemoglobin measurement. Also used to lyse the red blood cells and discriminates nucleated red blood cells from white blood cells.

**COULTER® DxH Diff Pack**

The COULTER DxH Diff Pack consists of the Erythrolyse™ Lytic Reagent and StabiLyse™

Preservative reagent. The Erythrolyse Lytic Reagent is a cyanide-free lytic reagent that dilutes the blood sample, and lyses red blood cells in preparation for white blood cell measurement in the flow cell. The StabiLyse Preservative Reagent neutralizes the Diff lytic reagent and preserves the white blood cells for measurement in the flow cell. Together, Erythrolyse and StabiLyse provide the five-part differential.

**COULTER® DxH Retic Pack**

The DxH Retic Pack consists of a reticulocyte stain reagent and a reticulocyte-clearing reagent. The reticulocyte stain reagent is a cyanide-free reagent that uses a dye to stain reticulocytes. The reticulocyte-clearing reagent is a cyanide-free reagent that stabilizes the dye-reticulum complex to enhance discrimination of reticulocytes from mature red blood cells utilizing the VCSn technology.

**COULTER® DxH Cleaner**

DxH Cleaner is a cyanide-free, aldehyde-free cleaning agent that degrades residual materials so that they may be flushed from the system with the diluent.

| **Consumable supplies** | |
|---|---|
| Distilled water | Container for a bleach solution |
| Ethanol (70%) | Container for DI water |
| Alcohol resistant marker | 5 to 6% solution of sodium hypochlorite |
| Plastic dispensing bottles | Soft cloth or tissue, lint-free swab or tissue |
| Gauze | |

**Reagent stability and storage:**

- ✓ Stable up to expiry date and, up to 60 days after opening and store at room temperature except for cleaner it's stable up to 90 days after opening.

**Equipment:**

- ✓ UniCel® DxH 800 hematologyAnalyzer
- ✓ Printer
- ✓ Test tube cassette
- ✓ LIS computer
- ✓ Barcode reader

**Sample and container type**

Collect whole blood in EDTA according to tube manufacturer's instructions and procedures in:

• CLSI publication H4-A5 (for capillary)

• CLSI publication H3-A6 (for venipuncture)

Beckman Coulter recommends using K2 or K3 EDTA.

**Sample collection materials**

- ➢ Vacutainer needle Glove
- ➢ Vacutainer test tube Alcohol
- ➢ Cotton

**Safety precautions**

Read all product safety data sheets and don't attempt to perform any procedure before carefully reading all instructions. Always follow product labeling and manufacturer's recommendations. If in doubt as to how to proceed in any situation, contact your Beckman Coulter representative.

**Controls**

The COULTER 6C Cell Control is an integrated control (3level), that enables monitoring of system Performance and calibration status for all directly measured and calculated CBC and Diff parameters.

**Background - Daily Checks**

| **Parameter** | **Limit** |
|---|---|
| WBC | ≤0.05 x 103/µL |
| RBC | ≤0.005 x 106/µL |
| HGB | ≤0.1 g/dL |
| PLT | ≤3 x 103/µL |
| DIFF | ≤100 events |

**Result interpretation**:

A low hemoglobin level indicates anaemia. However, hemoglobin findings are even more dependent upon the total number of RBC's. In other words, for the diagnosis of anemia, the number of RBC's is as important as the hemoglobin level. In response to an acute infection, trauma, or inflammation, white blood cells release a substance called colony-stimulating factor (CSF). CSF stimulates the bone marrow to increase white blood cell production.

**Whole Blood Reference Ranges Overall**

| Parameter | Units | Overall | | |
|---|---|---|---|---|
| | | Mean | 95% Confidence Low Limit | 95%Confidence High Limit |
| WBC | x103/µl | 6.3 | 3.6 | 11.2 |
| RBC | x106/µl | 4.52 | 3.73 | 5.5 |
| HGB | g/dl | 13.4 | 11.4 | 15.9 |
| HCT | % | 39 | 33.3 | 45.7 |
| MCV | fL | 86.4 | 73.7 | 95.5 |
| MCH | pg | 29.6 | 24.3 | 33.2 |
| MCHC | g/dl | 34.2 | 32.5 | 35.8 |
| RDW | % | 13.8 | 12.3 | 17 |
| RDW-SD | fL | 41.4 | 37.1 | 47.8 |
| PLT | x103/µl | 257 | 159 | 386 |
| MPV | fL | 9.2 | 7.5 | 11.2 |
| NE | % | 58.5 | 43.3 | 76.6 |
| LY | % | 29.6 | 16 | 43.5 |
| MO | % | 8.3 | 4.5 | 12.5 |
| EO | % | 2.8 | 0.6 | 7.9 |
| BA | % | 0.7 | 0.2 | 1.4 |
| NE# | x103/µl | 3.7 | 1.8 | 7.8 |
| LY# | x103/µl | 1.8 | 1 | 3.0 |
| MO# | x103/µl | 0.5 | 0.3 | 1.0 |
| EO# | x103/µl | 0.2 | 0.0 | 0.5 |
| BA# | x103/µl | 0 | 0.0 | 0.1 |
| MRV | fL | 108.8 | 97.4 | 120.2 |

**Limitations**

All Specimens Misleading results can occur if the specimen is: -

- If the specimen is not properly collected
- If the specimen is not Stored or transported
- If the specimen is Contain clots.
- If the specimen is not properly mixed.

**Annex II**

**Participant information sheet**

My name is Boki Lengiso, a master's student at the Department of Medical Laboratory Sciences of Addis Ababa University. I invite you to participate in a study to Hematological and Clinical profile of BCR-ABL confirmed Chronic Myeloid Leukemia patients during presentation in Tikur Anbessa specialized hospital, Addis Ababa, Ethiopia. This study and consent form will be approved by Ethical review committee of Medical Laboratory Sciences, College of Health Science, Addis Ababa University and Tikur Anbessa specialized hospital, department of internal medicine ethical review committee to make sure that your rights are protected. The objective of this study is to determine Hematological and Clinical profile of BCR-ABL confirmed Chronic Myeloid Leukemia patients during presentation. You will be selected as a candidate for this study because you met the criteria for inclusion as a participant. For the purpose of this study, you will be asked to receive punctures for the purpose of drawing a sample of approximately 5ml of whole blood from the vein. The samples taken for the purposes of the study will not be identified with your name and no information regarding your sample will be used for any purpose other than the objective of the study. During the process of drawing blood for performing the laboratory tests, you will feel a small amount of temporary discomfort. You will not receive any extra money by participating in this study. However, you have the right to receive the laboratory test results for routine medical care.

Any information that is obtained in this study regarding you will be kept completely confidential. By agreeing to participate in this study, you agree to allow the investigators to use any results obtained through the use of your blood sample and clinical findings for publication or discussion in any national or international conference. In any publication where the results of the study appear, the information will be disseminated in such a way that your name is not identified. In agreeing to participate you are free to terminate your participation at any time and without any consequence in your routine medical service in the hospital. You are encouraged to ask any questions regarding the study at this time. If you have any further questions in the future, the investigator will be available to respond to you. Any individual who has questions regarding to the study can contact Mr. Boki Lengiso at the Addis Ababa University (**mobile**: -+251 921 599 989, **e-mail**: - bokilenjiso@gmail.com ).

The participant will be given a copy of this form to retain for his/her records if applicable.

Thank you for your Patience!!

**Annex III**

**Informed consent form**

I, hereby agree to participate in the study of Hematological and Clinical profile of BCR-ABL confirmed Chronic Myeloid Leukemia patients during presentation in TASH, Addis Ababa, Ethiopia. I have read and fully understand the participant information sheet and have the opportunity to ask questions related to this study. To participate in this study, I agree to receive punctures for the purpose of drawing blood for laboratory testing. This is the same procedure that I would undergo under normal testing circumstances. I understand that these punctures will cause a small amount of temporary discomfort at the puncture site.

I understand that the sample will not be used for any other purpose. All information regarding my sample will remain completely confidential and will not be used for any other purpose than the objective of this study.

I understand that I am not obligated to participate in this study, and I can decide not to participate at any time. I understand that this study does not place me at any greater medical risk than is customary with the test that I am receiving, nor does it interfere with the medical care that I am entitled to. I have read the above document and I understand that I have agreed to participate in this study.

Name of participant: _____ Signature of participant (or parent/legal guardian): _____

Signature of person obtaining consent_____ Date: ___/___/_____

Signature of witness: _____ Date: ____/____/____

**Annex IV**

**Assent form**

I agree to participate in the study of Hematological and Clinical profile of BCR-ABL confirmed Chronic Myeloid Leukemia patients during presentation in TASH, Addis Ababa, Ethiopia. My parents /care givers are informed and they are volunteer and allowed me to participate in this study. I also understand that even if my parents/care givers are volunteer being part of this study is up to me. This study does not place me at any greater medical risk and does not interfere with the medical care provided to me.

Name of participant: _____ Signature of participant _____

Signature of person obtaining assent_____ Date: ___/___/_____

Signature of witness: _____ Date: ____/____/____

**Annex V**

**ለጥናቱ ተሳታፊዎች የመረጃና ስምምነት ቅፅ** (Amharic Version)

**ለጥናቱ ተሳታፊዎች የመረጃ ቅፅ**

ጥናቱ የሚካሄድበት ቦታ _____

**የጥናቱ ርዕስ፡** ስር የሰደደ የደም ካንሰር ታካሚዎች ላይ ያለውን የሄማቶሎጂ እና ክሊንካል መረጃ ዝርዝር ሁኔታ **(**Hematological and Clinical profile of BCR-ABL confirmed Chronic Myeloid Leukemia patients during presentation**) ላይ ማጥናት**

**የተከበሩ የጥናቱ ተሳታፊ**

ስር የሰደደ የደም ካንሰር ታካሚዎች ላይ ያለው የሄማቶሎጂ እና ክሊንካል መረጃ ዝርዝር ሁኔታ (Hematological and Clinical profile of BCR-ABL confirmed Chronic Myeloid Leukemia patients) በሚዳስስ ጥናት ውስጥ እንዲሳተፉ ልንጠይቅዎት እንወዳልን፡፡የጥናቱን ሁኔታ በተመለከተ ማብራሪያ እንሰጥዎታለን፡፡እናም ጥያቄ ካለዎት ግልፅ ማድረግ እንችላለን፡፡ በዚህ ጥናት ለመሳተፍ ግዴታ የሌለበዎት ሲሆን ለመሳተፍ ፍቃደኛ ከሆኑ ግን ይህን ቅፅ አንብበዉ በቅፁ መጨረሻ ላይ ይፈርማሉ፡፡ ይህ ጥናትና የስምምነት ቅፅ በአዲስ አበባ ዩኒቨርሲቲ ሜዲካል ላቦራቶሪ ሳይንስ እንዲሁም በአዲስ አበባ ዩኒቨርሲቲ የዉስጥ ደዌ ህክምና ክፍል የጥናትና ምርምር ስነምግባር ገምጋሚ ኮሚቲዎች የእርስዎን መብት እንደሚያስጠብቅ በማረጋገጥ ፈቃድ ተሰጥቶታል፡፡

**የጥናቱ ዓላማ**

የጥናቱ ዋና ዓላማ ስር የሰደደ የደም ካንሰር ታካሚዎች ያለው የሄማቶሎጂ እና ክሊንካል መረጃ ዝርዝር ሁኔታ (Hematological and Clinical profile of BCR-ABL confirmed Chronic Myeloid Leukemia patients)) ማጥናት ነዉ፡፡

**በዚህ ጥናት የሚሳተፉት ሰዎች**

የደም ካንሰር ያለባቸዉና ለመሳተፍ ፍቃደኛ የሆኑ

**የሚወሰደዉ ናሙና**

ለዚህ ጥናት ከእርስዎ የሚፈለገዉን 5 ሚሊ ሊትር የደም ናሙና ከክንድዎት በመስጠትዎ የማያሰጋ በሳይንስ በተረጋገጠና ለምንም በማያጋልጥ መልኩ ይወሰዳል፡፡ነገር ግን ከዚህ ጥናት ዉጭ ለሌላ የተለየ ዓላማ አይዉልም፡፡ በፈለጉት ጊዜ ይህን ስምምነት ሊያቃርጡ ይችላሉ፡፡ ባቋረጡ ጊዜም እርስዎን የሚመለከቱ ነገሮች ሁሉ ከላብራቶሪ የመረጃ መረብ እናስወግዳለን፡፡

**ተያያዥነት አላቸዉ ተብለዉ የሚታሰቡ ጉዳቶች**

እርስዎ እዚህ ጥናት ላይ በመሳተፍዎ እና ከላይ የተጠቀሰዉን የደም ናሙና በመስጠትዎ በጤናዎ ላይ የከፋ ችግር አያመጣም፡፡ ነገር ግን መርፌ በሚወጋበት አካባቢ ትንሽ የህመም ስሜት ሊኖር ይችላል፡፡ይሁን እንጅ ይህም በጤና ባለሙያዎቹ እይታ ስር ስለሆነ ለከፋ ጉዳት አይዳርግም፡፡

**ጥቅማጥቅምና ክፍያ**

እርስዎ በዚህ ጥናት በመሳተፍዎ ብቻ የሚከፈለወት ተጨማሪ ገንዘብ ክፍያ የለዉም፡፡ነገር ግን ከሚሰጡት የደም ናሙና የሚሰራዉን የላቦራቶሪ ዉጤት የማግኘት መብት አለዎት፡፡

**የመረጃዉ ምስጢራዊነትና የተሳታፊዉ መብት**

በጥናቱ የሚሳተፉት የፍቃደኝነት ማረጋገጫ ሲሰጡን ብቻ ሲሆን በፈለጉት ጊዜ ስምምነቱን ሊያቋርጡ ይችላሉ፡፡ እርስዎን የሚመለከት ሁሉም ነገር በምስጢር ይቀመጣል፡፡የእርስዎ ስምም ከእርስዎ ከምንወስደዉ ናሙና ጋር አይገናኝም፡፡ከእርስዎ የምንወስዉ መረጃ ለተጠቀሰዉ ዓላማ የሚዉል ሲሆን ምስጢራዊነቱን በጠበቀ ሁኔታ ለህትመት ይላካል፡፡ በጥናቱ ሲሳተፉ ግልፅ ያልሆኑ ጉዳዮች የመጠየቅ ሙሉ መብት አለዎት፡፡እኛም የተነሱትን ጥያቄዎች ግልፅ እናደርግልዎታለን፡፡ ጥናቱን በተመለከተ ማነጋገር ቢያስፈልግዎ የጥናቱን አስተባባሪ ስምና አድራሻ እንደሚከተለዉ ነዉ፡፡

**ስም፡ አቶ** ቦኪ ሌንጅሶ **ሞባይል**:0921 599 989 Email: bokilenjiso@gmail.com

በጥናቱ ለመሳተፍ ፍቃደኛ በመሆንዎ እናመሰግናለን!!!

ቃለ መጠይቁን ያካሄደዉ ሰዉ

ስም፡_____

ፊርማ:_____

ቀን: _____/_____/_____

## የስምምነት ቅፅ

በሚቀጥለዉ ርዕስ ላይ የተመለከተ ጥናትን ለማካሄድ ስለመሳተፍ የሚያመለክት የስምምነት ቅፅ

**የጥናቱ ርዕስ**: ስር የሰደደ የደም ካንሰር ታካሚዎች ላይ ያለው የሄማቶሎጂ እና ክሊንካል መረጃ ዝርዝር ሁኔታ (Hematological and Clinical profile of BCR-ABL confirmed Chronic Myeloid Leukemia patients) ማጥናት ነዉ፡፡

በዚህ ጥናት ዉስጥ ለመሳተፍ እባክዎን የሚከተለዉን ቅፅ አንብበዉ በሚተሉት ባዶ ቦታዎች ወይም ሳጥኖች ዉስጥ ምልክት ያድርጉ፡፡

1. የጥናቱን ዓላማ ተገንዝቤአለሁ ጥናቱን የሚያካሂደዉን ሰዉ ስፈልገዉ ማግኘት እንደምችል ተረድቻለሁ፡፡ ☐
2. የእኔ የደም ናሙና ተወስዶ ለጥናቱ ዓላማ እንደሚዉል ተረድቻለሁ፡፡ ☐
3. ለጥናቱ የሚሰጡ መረጃዎች እና ከጥናቱ የሚገኙ ዉጤቶች በሚስጢር እንደሚቀመጡ ተረድቻለሁ፡፡ ☐
4. ከዚህ ጥናት ገንዘብ በተለየ መልኩ አንደማላገኝ ተረድቻለሁ ፡፡ ☐
5. ከዚህ ጥናት በፈለግሁ ጊዜ አቋርጬ መዉጣት እንደምችልም ተረድቻለሁ፡፡ ☐
6. በጥናቱ ባለመሳተፌ ምክንያት በተለመደዉ ሁኔታ የሚደረግልኝ አገልግሎት እንደማይቋረጥ ተረድቻለሁ፡፡ ☐

የጥናቱ ተሳታፊ ስም፡_____ ፊርማ፡ _____

ስምምነቱ የተሰጠበት ሁኔታ (በራሱ/ህጋዊ ተወካይ)

ስምምነቱን የወሰደዉ ስም፡ _____ ፊርማ :_____ ቀን : __/____/__

የምስክር ስም:_____ ፊርማ :_____ ቀን : __/____/____

**የልጆች ስምምነት ቅፅ**

ስር የሰደደ የደም ካንሰር ታካሚዎች ያለው የሂማቶሎጂ እና ክሊንካል ሁኔታ Hematological and Clinical profile of BCR-ABL confirmed Chronic Myeloid Leukemia patients) ላይ በሚጠና ጥናት ላይ ለመሳተፍ ፍቃደኛ ስሆን ቤተሰቦቼም እንድሳተፍ ሙሉ ፈቃደኞች ናቸዉ፡፡ ነገር ግን ቤተሰቦቼ በዚህ ጥናት እንድሳተፍ ፍቃደኛ ቢሆኑም በዚህ ጥናት መሳተፍ የእኔ ዉሳኔ መሆኑን ተረድቻለሁ፡፡በጥናቱ በመሳተፌ በጤንነቴ እንዲሁም በሚሰጠኝ ህክምና ላይ ችግር እንደማይፈጥርም ተገንዝቢያለሁ፡፡

የጥናቱ ተሳታፊ ስም፡_____ ፊርማ፡ _____

ስምምነቱን የወሰደዉ ስም፡ _____ ፊርማ :_____ ቀን : __/____/__

የምስክር ስም:_____ ፊርማ :_____ ቀን : __/____/____

**Annex VI**

Questionnaires to be filled by health professionals

**Part I. General information**

Code Number_____ Region _____ Zone _____

Woreda_____ / city /_sub city _____ Kebele _____

**Part II. Personal information**

1. Place of Birth_____
2. For how long (years) did you live in the birth place? _____

How long do you live in this specific area? (If different from the birth place) _____years

| s/r | Variables | Alternative | Response | Comment |
|---|---|---|---|---|
| 3 | Age (in years) | | | |
| 4 | Sex | Male | | |
| | | Female | | |
| 5 | Marital Status | Single | | |
| | | divorced | | |
| | | widowed | | |
| | | Married | | |
| 6 | Educational background | Can't read and write | | |
| | | Read and write only | | |
| | | Primary Education | | |
| | | Secondary Education | | |
| | | Higher Education | | |
| 7 | Residence | Rural | | |
| | | Urban | | |
| 8 | Occupation | Farmer | | |
| | | House Wife | | |
| | | Gov't employee | | |
| | | Private company employee | | |
| | | Student | | |
| | | Merchant | | |
| | | Self-employee | | |

| | | | | |
|---|---|---|---|---|
| | | If other specify _____ | | |
| 9 | Average distance between patients' home & TASH | < 100km | | |
| | | 100-300km | | |
| | | 300-600 km | | |
| | | >600 km | | |
| 10 | Monthly Family Income level | <1500 | | |
| | | 1501–5000 | | |
| | | 5001-10,000 | | |
| | | > 10,001 | | |
| | | | | |
| | **Symptoms / clinical history** | **Yes** | **No** | **Comment** |
| 11 | Symptomatic | | | <u>If yes</u>, specify duration of symptoms |
| 12 | Asymptomatic | | | |
| 13 | Abdominal pain | | | |
| 14 | Weakness | | | |
| 15 | Decreased appetite | | | |
| 16 | Weight loss | | | |
| 17 | Cough | | | |
| 18 | Chest pain | | | |
| 19 | Joint pain | | | |
| 20 | Fever | | | |
| 21 | Splenomegaly | | | <u>If yes,</u><br>Massive (≥ 10cm)<br>Moderate (4-9 cm)<br>Mild (1-3 cm) |
| 22 | Hepatomegaly | | | |
| 23 | Lymphadenopathy | | | |
| 24 | Pallor | | | |
| 25 | Lethargy | | | |

| | | | | |
|---|---|---|---|---|
| 26 | Fatigue | | | |
| 27 | Body aches | | | |
| 28 | Headache | | | |
| 29 | Pruritus | | | |
| 30 | Dizziness | | | |
| 31 | Nausea | | | |
| 32 | Vomiting | | | |
| 33 | Difficulty in breathing | | | |
| 34 | Bleeding | | | |
| 35 | Night sweat | | | |
| 36 | Bone pain | | | |
| 37 | Blurred vision | | | |
| 38 | Previous Infection History | | | If yes, specify |
| 39 | BCR-ABL percentage | | | |
| 40 | Pre-treatment | | | If yes, specify Allopurinol or/ and Hydroxyurea |

| | Hematological Parameter | Mean ± SD | Median | Inter quartile range |
|---|---|---|---|---|
| | WBC - White Blood Cell Count | | | |
| | RBC - Red Blood Cell Count | | | |
| | HBG - Hemoglobin | | | |
| | HCT - Hematocrit | | | |
| | MCV - Mean Corpuscular Volume | | | |
| | MCH - Mean Corpuscular Hemoglobin | | | |

| | | | | |
|---|---|---|---|---|
| | MCHC - Mean Corpuscular Hemoglobin Concentration | | | |
| | RDW - Red Cell Distribution Width | | | |
| | RDW-SD- Red Cell Distribution Width Standard Derivation | | | |
| | PLT - Platelet Count | | | |
| | MPV - Mean Platelet Volume | | | |
| | NE % - Neutrophil Percent | | | |
| | LY % - Lymphocyte Percent | | | |
| | MO % - Monocyte Percent | | | |
| | EO % - Eosinophil Percent | | | |
| | BA % - Basophil Percent | | | |
| | NE # - Neutrophil Absolute Number | | | |
| | LY # - Lymphocyte Absolute Number | | | |
| | MO # - Monocyte Absolute Number | | | |
| | EO # - Eosinophil Absolute Number | | | |
| | BA # - Basophil Absolute Number | | | |

## Declaration

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

Boki Lengiso (BSc, MSc. Candidate)

Signature: _____

Date of submission: _____

This thesis has been submitted with This approval as advisors.

Advisor: Fekadu Urgessa (Assistant Professor, PhD Candidate)

Signature: _____

Date: _____

Place: Addis Ababa, Ethiopia.

Advisor: Aster Tsegaye (PhD, Professor)

Signature: _____

Date: _____

Place: Addis Ababa, Ethiopia.