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Our Experience with Chronic Myeloid Leukemia: Real World Data

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Abstract:
Background*:*
Chronic myeloid leukemia (CML) is a disorder of the clonal hematopoietic stem cells, characterized by presence of the Philadelphia chromosome t(9;22). It is the most common myeloproliferative neoplasm among adults. With the availability of various Tyrosine Kinase inhibitors, survival probability of CML in early phase is equal to that of general population. In this study we present the demographic, clinical, hematological and treatment pattern among CML patients diagnosed in a tertiary hospital.
Materials and Methods*:*
This is a retrospective, medical record-based, single institutional study done between 2021-22. Data of patients aged >18 years and diagnosed to have CML were collected to analyze the following parameters: demographic, symptoms, hematological, Sokal risk scoring, phase of disease, and therapy utilized. Descriptive statistics were used for demographic parameters.
Results*:*
A total of 26 patients were included in the present study. Males constituted 61% the median age is 44.5 years (range 20-69).Commonest symptom is abdominal discomfort (76%) followed by fever (69%) and weight loss (61%). Anemia is seen in 73% of cases, leucocytosis in 94%, thrombocytosis in 94%, and splenomegaly in 92% of patients. The majority of patients had a high-risk Sokal score (69%) and 81% patients were in chronic phase. Imatinib is the common TKI used. At the time of publication, all the patients were alive (100%).
Conclusion:
CML commonly diagnosed in chronic phase with constitutional symptoms. Majority of them are in high risk and treated with Imaitnib. The survival probabilities are near to that of general population.
Key Word*:*
Chronic myeloid leukemia,hematology,splenomegaly, imatinib,sokal score

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I. Introduction

Chronic myeloid leukemia is a disorder of the clonal hematopoietic stem cells , characterized by a chromosomal translocation between chromosomes 9 and 22. It is the most common myeloproliferative neoplasm among the adults and rare in children. It predominantly affects the peripheral smear and the bone marrow. The resultant active BCR-ABL1 fusion oncoprotein establishes the whole pathogenesis, diagnosis and treatment of CML. CML had been initially treated with conventional chemotherapy with hydroxyurea or busulfan. Four tyrosine kinase inhibitors are approved for treatment of CML. The development of tyrosine kinase inhibitors has revolutionized the management of CML in clinical practice. The survival of CML patients is elevated to that of the general population.

II. Material And Methods

This retrosprospective medical record based study ,was carried out at Department of general Medicine at viswabharathi medical college and Hospital, RT Nagar, penchikalapadu, Andhra Pradesh from february 2021 to may 2022. A total 26 adult subjects (both male and females) of aged ≥ 18, years were for in this study.

Study Design: retrospective medical record based study

Study Location: This was a tertiary care teaching hospital based study done in Department of General Medicine, at viswabharathi medical college and Hospital, RT Nagar, penchikalapdu, Andhra Pradesh.

Study Duration: february 2021 to may 2022.

Sample size: 26 patients.

Subjects & selection method:

A total of 26 patients were selected from medical records and patients who attended our out patient department at viswabharathi medical college and hospital.

Procedure methodology

A total of 26 patients were selected from medical records and patients who attended our out patient department . department of general medicine, viswabharathi medical college and hospital,RT nagar, penchikalapadu, Andhra Pradesh. Data of patients aged >18 years and diagnosed to have Chronic myeloid leukemia were collected to analyze the following parameters: demographic, symptoms, hematological, Sokal risk scoring, phase of disease, and therapy utilized.

Statistical analysis-

Descriptive statistics were used for demographic parameters.

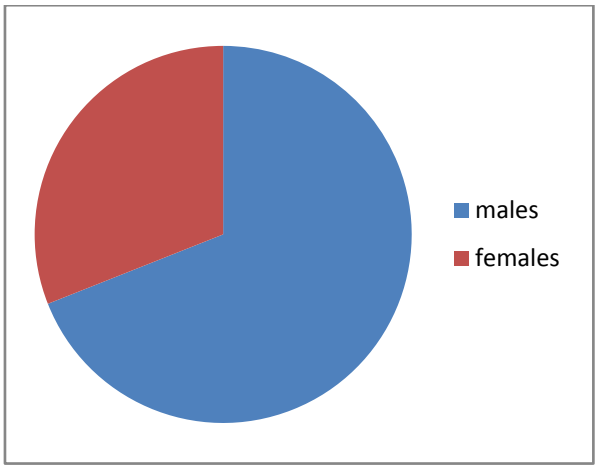
III. Result

A total of 26 patients were included in the present study. Males constituted 61% and the median age is 44.5 years (range 20-69).The commonest symptom is abdominal discomfort (76%) followed by fever (69%) and weight loss (61%). Anemia is seen in 73% of cases, leucocytosis in 94%, thrombocytosis in 94%, and splenomegaly in 92% of patients. The majority of the patients had a high-risk Sokal score 69%.

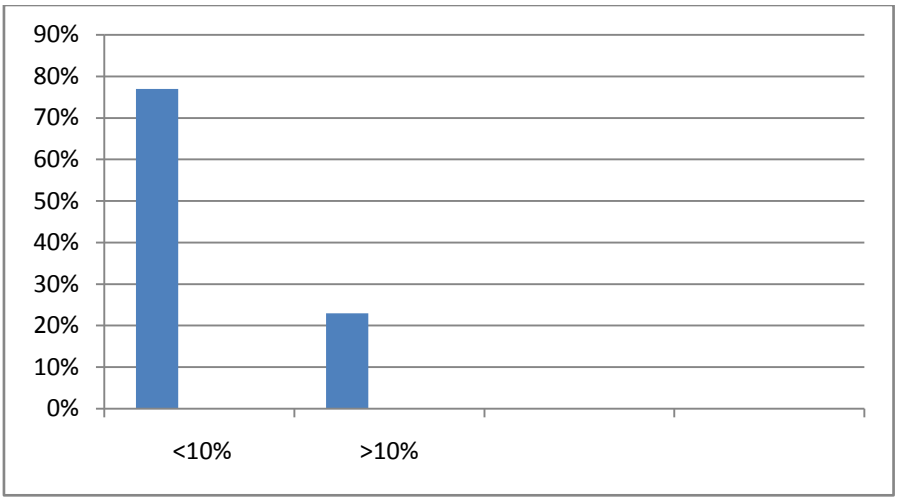
PARAMETER	VALUE%
Median age in years	44.5(range 20-69)
Gender Male female	 16(69%) 10(31%)
abdominal pain	20(76%)
Fever	18(69%)
Weight loss	16(61%)
Median hemoglobin (g/dl) <10 >10	7.6(range- 3.2 – 13.2) 20(77) 6(23%)
Median wbc	120 per cumm (range3.9 - 240)

PARAMETER	VALUE
Median platelet count range	400(50-900)
Splenomegaly	24(92%)
Phase of the disease Cp Ap Bc	 21 1 4
Sokal score Low Intermediate High	 6 2 18
TKI used Imatinib Dasatinib Nilotinib	 19 6 1
Survival of the patients	26 (100)

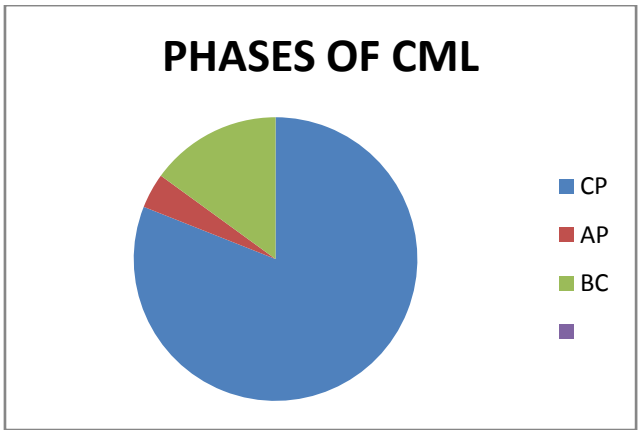
Graph 1 – showing gender (male) preponderance among CML patients



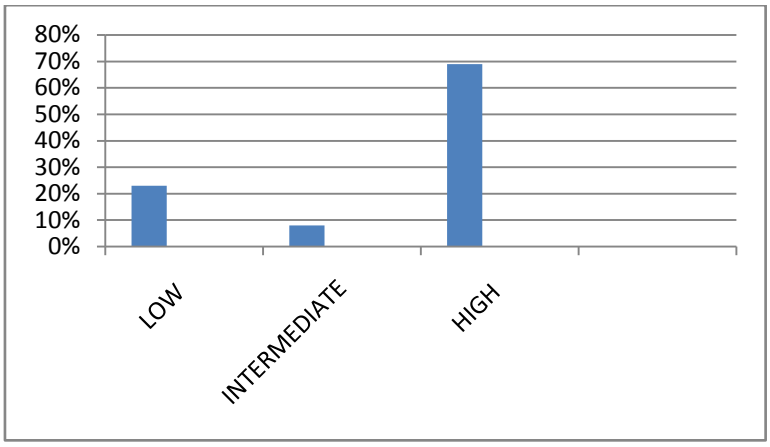
Graph 2- showing hemoglobin in patients with CML.



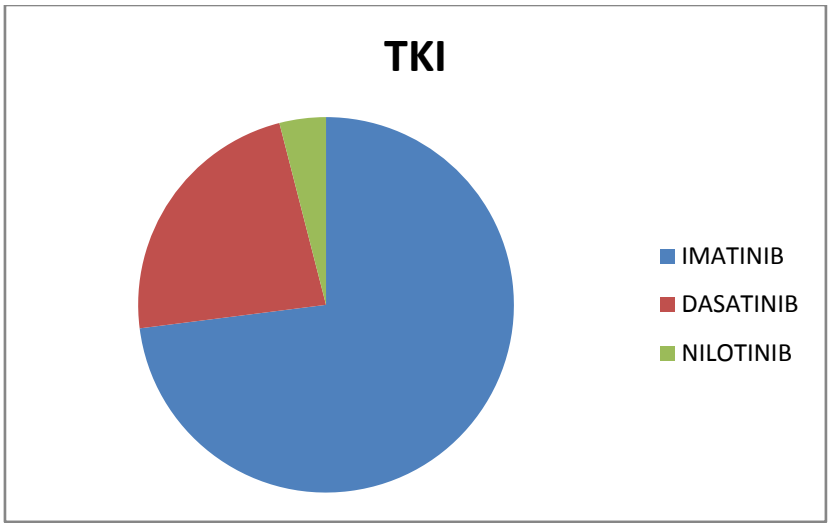
Graph 3- phases of CML



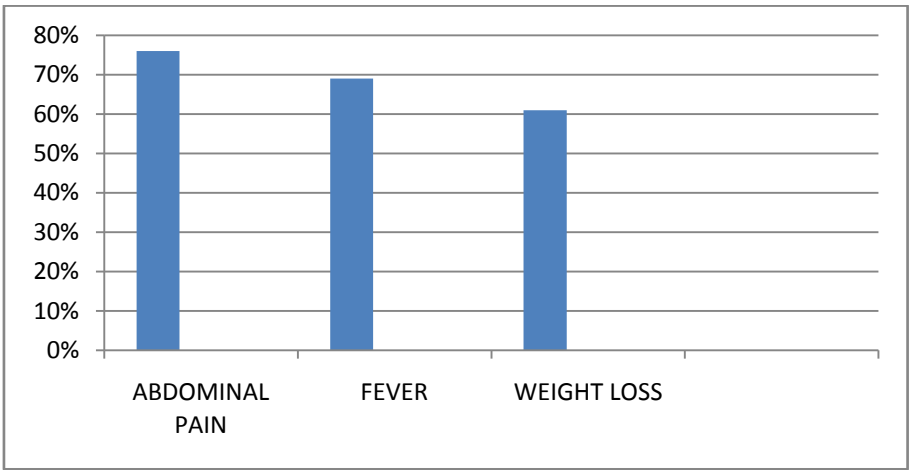
Graph 4 – showing sokal scores in patients of CML



Graph 5 – showing the tyrosine kinase inhibitors used in CML patients



Graph 6 – showing different clinical features of CML patients



IV. Discussion

CML is the first malignant condition in which a specific causative genetic abnormality is detected and the first successful disease treated by targeted therapy by using imatinib mesylate. In this retrospective study, the median age of diagnosis chronic myeloid leukemia is 44.5 years. CML accounts for about 10-15% of total cases of all malignancies and the incidence of chronic myeloid leukemia ranges between 10 and 15 cases/1000000/year without any major geographic or ethnic differences. The median age at diagnosis ranges between 60 and 65 years in Europe, but is considerably lower in countries with a younger population. In another study,the median age of diagnosis is 56 years old.(1) In the United States, the annual incidence rate between 2009 and 2013 was 1.4 and 2.2 per100000 for females and males respectively(2).

There is an inclination towards males(69%) and in this study we included only adult population as chronic myeloid leukemia has lesser incidence in children.CML in children is rare, biology and treatment strategies in paediatric patients reveal specific aspects. CML arises from hematopoietic stem cells with translocation of t(9,22)(q34,q11). It has short chromosome 22, which is known as the Philadelphia chromosome.

This translocation paves a path for juxtaposition of ABL 1 gene from chromosome 9 and BCR gene from chromosome 22, resulting in BCR-ABL fusion gene. This fusion of chromosomes causes myeloid cells to undergo unchecked replication. Te down stream pathways affected include JAK/STAT,PI13K/AKT, and RAS/MEK; they involve cell growth, cell survival inhibition of apoptosis and activation of transcription factors.(3) the remainder of patients has variant or complex translocations involving additional chromosomes detected by routine cytogenetics or a cryptic BCR-ABL1 translocation detected with fluorescent in situ hybridization(FISH) or reverse transcriptase-polymerase chain reaction(PCR)(4).

The diagnosis of CML is always straightforward and well established. The patients have left sided abdominal pain, fever and significant weight loss at the time of presentation. In most cases, the diagnosis begins with a basis of a characteristic blood count and differential count.

The median haemoglobin is 7.6 with a range of 3.2 to 13.2, median platelet count being 400 with a range of 500 – 900. Spleen was enlarged in size by 3-4 times, a characteristic feature of CML. Splenomegaly was found in 92% of patients and sometimes even hepatomegaly was found in patients with CML. There are 3 phases of the disease, chronic phase,acute phase and blast phase. Chronic phase disease is associated with <15% blasts in blood and bone marrow. Headaches, bone pain, arthralgias,pain from splenic infarction and fever are more frequent with CML transformation. SOKAL score is used to determine and decide the therapy for CML patients, scored as low, intermediate and high. There were about 69% of patients with high sokal score. Diagnosis of CML is done using karyotyping. The cytogenetic report contains metaphases counted,analysed and karyotyped, mitotic index, culture type, banding technique and resolution and quality of metaphases.

Tyrosine kinase inhibitors are the drugs used to treat CML patients, there are 4 drugs that are currently approved are imatinib, dasatinib, nilotinib and bosutinib. Imatinib mesylate was the first tyrosine kinase inhibitor got approved for treating patients with CML.imatinib is a competitive inhibitor of adenosine triphosphate, which binds at the site of BCR-ABL-1 gene resulting in inhibition of protein phosphorylation. It also blocks platelet derived growth factor, KIT tyrosine kinases. A recent meta- analysis revealed an advantage of high dose imatinib with regard to achievement of major molecular response(MMR) at 12 months of therapy. When a diagnosis of CML is pending, hyroxyurea can be started. Radotinib has been approved in south korea only(5)

Imatinib is effective in all phases of CML, and therapy has resulted in a normal life expectancy of most patients treated on chronic phase (CP) in clinical trials. No serious toxicity has surfaced after more than 20 years of use. Patients are advised to use same treatment generic brand to exclude side effects which could be potentially be due to change in structure of drug, bioavailability and preparation of drug. In the study all the patients were alive , with a survival rate of 100%.

IV. Conclusion

CML commonly diagnosed in chronic phase with constitutional symptoms. Majority of them are in high risk and treated with Imaitnib. The survival probabilities are near to that of general population.

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