

# A short report on chronic myeloid leukemia from Post Graduate Institute of Medical Education and Research, Chandigarh

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## ABSTRACT

Post Graduate Institute (PGI) Chandigarh is a premier institute of North India. There are approximately 70,000 admissions per year. The adult clinical hematology department sees more than 2000 new patients per year. A preliminary analysis of 299 chronic myeloid leukemia patients registered from January 2001 until December 2007 was done. Out of these, 256 (86%) patients were in chronic phase (CP). The median age at presentation was 40 years. At 6 months of follow-up 95% of patients who were started on Imatinib mesylate based therapy remained in CP. Partial cytogenetic remission was seen in 69% of patients while complete cytogenetic response was seen in only 20% of patients at 6 months on Imatinib mesylate.

**Key words:** *Chronic myeloid leukemia, chronic phase, Post Graduate Institute*

## INTRODUCTION

Chronic myeloid leukemia (CML) is the most common adult leukemia in India and the annual incidence ranges from 0.8 to 2.2/100,000 population in males and 0.6-1.6/100,000 population in females in India.<sup>[1-3]</sup>

Imatinib mesylate, a tyrosine kinase inhibitor, has proved to be the magic bullet for CML patients. Ninety-five percent of CML population achieves complete hematological response with its treatment and continues to remain in chronic phase (CP) for long periods.<sup>[4,5]</sup>

### Adult Hematology Department

The adult hematology clinic is a part of Department of Internal Medicine, Post Graduate Institute (PGI), Chandigarh. The clinic was started in 1982 and currently seeing more than 2000 new hematology patients annually. Department of Pediatrics, PGI runs a separate hematology clinic for children less than 12 years of age.

Since 1999, 1232 patients (more than 12 years of age) of CML in different phases were registered in the adult

hematology clinic. This constitutes approximately 15% of the total hematology patients' registration. Imatinib mesylate (IM) was used in CML for the first time in September 2001. PGI is one of the Glivec International Patient Assistance Program (now NOAP) center in India.

An interim analysis of 299 patients of CML in different phases on IM was performed in 2007 and the results were presented at different forums including the recently concluded CML conference at Mumbai (Milestone July 2010). The present paper summarizes the findings of the presentation.

## PATIENTS AND METHODS

All newly diagnosed patients with suspected CML undergoes following work up – complete blood count (CBC), liver and renal function tests, chest X-ray, electrocardiogram, ultrasound abdomen, bone marrow aspiration and trephine biopsy, conventional cytogenetics on bone marrow or peripheral blood lymphocyte cultures. All patients usually are started on hydroxyurea until cytogenetics is available and then switch to IM once cytogenetic report show Philadelphia chromosome is positive. CP CML patients are started on 400 mg/day and all patients in advance phase (accelerated/blast) are started on 600-800 mg/day. Patients are asked to get weekly CBC until it normalizes. After that they are asked to report to the clinic once in 2-3 months depending upon the distance they have to travel to PGI. A repeat bone marrow with cytogenetics is performed usually at 6 months and thereafter yearly depending upon various

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parameters. Once patients are in complete cytogenetic remission, they are followed-up by real-time quantitative polymerase chain reaction. fluorescence *in situ* hybridization for BCR ABL is generally not performed as a routine.

## RESULTS

### Basic clinical characteristics

As stated earlier, a preliminary analysis of 299 patients in different phases of CML was performed. Out of these, 256 patients belonged to CP, 23 in accelerated phase (AP) and 20 in blast crisis (BC). The median age of CP CML was 40 years (range 13-73 years) with 63% male patients. The median age of AP and BC CML was 39 years with a range of 17-60 years and 21-65 years respectively. Similar to CP CML patients, the male patients predominated as compared with female CML patients. Patients above 60 years of age constituted 6%, 4% and 5% in CP, AP and BC respectively.

### Treatment and response of CML patients in various phases of disease

#### Analysis of CML patients in CP

The presenting complaint in the majority of patients was abdominal mass (58%) followed by low-grade fever (40%). Splenomegaly was present in 89% of patients. In 47% of patients, the size of the spleen was more than 10 cm. Palpable liver was present in 61% of patients. The median hemoglobin at presentation was 10.2 g/dl (range 3.7-16.9), white blood cell count 125000/ul (range 1800-600,000) and platelets 350,000/ul (34000-1800000). Bone marrow aspiration and trephine biopsy was performed in all patients and all were Ph positive. Reticulin stain was performed on trephine biopsy section. Approximately, 10% patients had 1+, 30% had 2+, 56% had 3+ and 5% had 4+ reticulin fibrosis in CP CML.

IM was instituted for the first time in these patients since October 2001 onward. Some of the patients had a diagnosis of CML since September 1992. Nearly, 58% of these patients were on original IM (Glivec) and 48% patients received generic IM (mostly Veenat). Seventy six percent of patient had received hydroxyurea previously for a median of 8 months (range 1-108 months) and 8% patients had received busulfan in the past (some of these patients were referred from other hospitals). At 6-months of follow-up, 95% patient remained in CP after starting of IM while 1.3% patients develop AP and 3.9% patients develop BC. Nearly 20 % of patients achieved complete cytogenetic remission (no Ph chromosome on at least 20 metaphases) at 6 months.

#### Analysis of CML patients in AP

Most of the patients presented with complaints of

abdominal mass (67%) and fever (52%). Ninety six percent patients had a presence of splenomegaly and in 70% of patients; the size of the spleen was more than 10 cm below the left coastal margin. Liver enlargement was present in 61% of patients. The median hemoglobin at presentation was 10.4 g/dL (range 7-13.9), WBC 140000/ul (range 7900-294,800) and platelets 357,000/ul (64,000-1000,000). Reticulin fibrosis of 1+ was present in 14%, 2+ in 29% and 3+ in 57% of patients. IM was used from September 2001 onward. Some patients were diagnosed with CML as far back as since January 1994. The original IM (Glivec) was used in 52% of patients.

#### Analysis of CML patients in BC

The presenting complaints were fever (67%) and lymphadenopathy (53%). Ninety five percent patients had a presence of splenomegaly and in 60% of patients; the size of the spleen was more than 10 cm below the left coastal margin. Liver enlargement was present in 45% of patients. The median hemoglobin at presentation was 8.9 g/dl (range 4.6-12.9), WBC 52,500/ul (range 10200-332000) and platelets 215,000/ul (21,000-1600,000). The reticulin fibrosis of 3+ was present in 87% and 4+ in 17% of patients. IM was used from August 2002 onward. Some patients were diagnosed as far back as since January 1997. The original IM (Glivec) was used in 65% of patients.

## DISCUSSION

CML is the most common adult leukemia seen in the adult hematology clinic. The median age is almost a decade earlier what is usually seen in the west. These finding has led to discussion at various forums whether epidemiology of CML is different in India.<sup>[1-2]</sup> The alternate explanation for these findings could be that CML is a chronic disease and hence seen more frequently in the hospitals. Patients having symptoms and disease present even for 2-3 years without treatment are routinely seen in the hospital whereas acute leukemia patients without treatment are not likely to survive for this much period of time.

The lower median age of CML patients also could be explained by the fact that the majority population in India consists of the younger generation. As the percentage of elderly population will increase, the median age would probably also increase in future. The male female ratio of CML patients in our cohort was 3:2 that points toward the gender bias as is seen in various other malignancies also rather than the disease predilection for the male population. The presenting symptoms of most patients were due to enlargement of spleen. This is also not an uncommon finding. Patients in general especially patients with malignancies present late to the physicians. This is as

opposed to the west where most patients are diagnosed on a routine health check-up. Low hemoglobin and high WBC and platelet counts also point toward the late presentation of patients. Patients in BC present with fever and lymphadenopathy as opposed to CP CML patients who generally present with pain in the left hypochondrium and low-grade fever. Presence of bone marrow fibrosis is a significant finding in CML patients and is possibly related to the advance stage of the disease and late presentation of patients. The late presentation of the patients and presence of bone marrow fibrosis might be the factors for low-rates of complete cytogenetic remission seen in our patients. From this data, we can thus reasonably say that patients in India present in late CP as opposed to the west where they may present in early CP and have better response.

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## CONCLUSION

A general awareness needs to be created among primary care physicians about the curable nature of CML with IM so that they can refer or treat patients with IM early. Early diagnosis and early institution of therapy always lead to

gratifying results as is seen in many other malignancies.

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