DOI: https://doi.org/10.53350/pjmhs2115113047

ORIGINAL ARTICLE

Chronic Myeloid Leukemia: Clinico-Hematological Profile from Southern Pakistan

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ABSTRACT

Background: Chronic myeloid leukemia is a form of chronic myeloproliferative disorder described by the presence of specific haematological and cytogenetic markers. It is a very common blood neoplasm that usually requires a basic clinical history, review, and regular blood examination to diagnose. If detected early, it has a high cure rate.
Objective: To assess the clinical and laboratory features of chronic phase chronic myeloid leukemia patients.
Study Design: Cross-sectional study
Place and Duration of Study: Department of Haematology, Liaquat National Hospital and Medical College, Karachi 1st January 2012 to 31st December 2016
Methodology: One hundred and forty four chronic myeloid leukemia patients visited the study site during this period, of which 132 were in the chronic phase and met the eligibility criteria. The patient's data, including age, gender, clinical and laboratory parameters were obtained.
Results: One hundred and fifteen (87.1%) had constitutional symptoms, predominantly fatigue and abdominal discomfort. The clinical presentation displayed splenomegaly among 89.3% of patients with a mean spleen span of 18.9±3.7 cm and massive splenomegaly in 32.5% of patients. Haematological presentation at baseline showed that the mean haemoglobin level of the enrolled patients was 9.6±2.0g/dl, TLC was 167.6±123.3x10^9/l, and platelet count was 398.7±281.9x10^9/l. Furthermore, 19.4%of patients were anaemic, and hyperleukocytosis was detected in 24.2%. High LDH, hyperuricemia and elevated serum creatinine were present in 38.6%, 40.9%, and 14.3%, respectively.
Conclusion: Unlike the western countries, chronic myeloid leukemiais more prevalent in a very young age group in Pakistan. The chronic myeloid leukemia patients displayed variable clinical and haematological presentation. Constitutional symptoms and splenomegaly were consistent features among the majority of patients.
Keywords: Chronic myeloid leukemia, Clinico-hematological, Pakistan

INTRODUCTION

Chronic myeloid leukemia (CML) was placed under chronic myeloproliferative diseases (CMPD) by the World Health Organization.[1,2] Chronic myeloid leukemiais a myeloproliferative neoplasm associated with a balanced chromosomal translocation between chromosome 9 and 22, resulting in a fusion gene BCR-ABL1, which encodes for BCR-ABL fusion protein, i.e. 210 kDa.[3,4] The specific tyrosine kinase activity of this fusion protein triggers multiple transduction pathways, which leads to malignant proliferation.[5,6]

With the targeted therapies, the disease incidence has been steady, resulting in substantial prolongation of survival.[7,8] Geographically, the diversity can be seen; the disease incidence in Africa is 0.4 cases per 100,000/year, Latin America (0.7), Asia Pacific countries (1.2), Europe (1.4), and North America (2).[9] Furthermore, the diagnostic age also varies worldwide, i.e. the disease prevalence is highest among the individuals in 50's among developing countries and in 60's among developed countries.[10,11]

The clinical features of the disease are usually vague include abdominal discomfort, early satiety, constitutional symptoms, fatigue, night sweats and bleeding. Nevertheless, about 15% of patients might present with symptoms of leukostasis, attributed to very high presenting total leukocytic count.In Pakistan, patients often present in the late stages of the disease to seek medical attention[12]. This may be due to the delayed referrals, limited haematological consultation, cost and ignorance about healthcare practices resulting in a high disease burden.

The life expectancy of CML patients in the west is now somehow equal to that of the general population. Still, herein no prospective randomized studies are available to determine the life expectancy in our population. Furthermore, financial constraints of expensive treatment constitute a significant limitation of the adequacy of treatment in Pakistan. Studies on CML are less commonly reported from this part of the world. To date, neither incidence statistics nor tumour registries exist in Pakistan. Therefore, through this study, we aimed to investigate the clinical and laboratory features of chronic phase CML patients.

MATERIALS AND METHODS

This cross-sectional study was conducted at Liaquat National Hospital and Medical College in Karachi, from 1st January 2012 to 31st December 2016. A total of 144 patients with established CML visited the haematology clinic during the study period. The ethical approval for the study was obtained from the Institutional Review Committee. The patients were well-informed regarding the study objective, and informed consent was obtained before inclusion.

According to World Health Organization (WHO) criteria, conventional G-band karyotype analysis (cytogenetic) was performed on bone marrow aspirate specimens to detect the Philadelphia chromosome or any other additional concomitant cytogenetic aberrations.[13] The cells were cultured and processed by conventional methodology. Following Trypsin-Giemsa banding, 20 metaphases were analyzed and interpreted according to the International System for Human Cytogenetic Nomenclature.[14]Bone marrows trephine biopsy samples were taken with a Jamshidi needle.

Patients who refused for bone marrow procedure and those who were having technical difficulties in the procedure underwent Fluorescence in situ hybridization (FISH) analysis for BCR-ABL translocation on peripheral blood. Patients who had Philadelphia chromosome or BCR-ABL translocation positivity were included. Patients having other myeloid neoplasms such as myelodysplastic syndrome, BCR-ABL negative myeloproliferative neoplasms and MDS/MPN diseases were excluded.

Complete blood counts (CBC) were determined by Cell Dyne Ruby (Abbott, Diagnostics). Biochemical tests, including serum creatinine, lactate dehydrogenase (LDH) and serum uric acid, were detected by Hitachi 912 (Japan) through photometric assay.

Data were analyzed using SPSS-22. Mean and standard deviation was used to express quantitative variables, while

qualitative variables were presented as frequencies and percentages.

RESULTS

One hundred and thirty two(91.6%) were in the chronic phase and included in the final analysis, while 8(5.5%) and 4(2.7%) patients were in accelerated and blastic disease phases, respectively (Table 1).

There were 115 (87.1%) patients had constitutional symptoms. The most common symptom was fatigue (75.0%), followed by abdominal fullness or discomfort (73.4%). Overall, 89.3% of patients had splenomegaly, with the mean spleen span of 18.9±3.7 cm (Table 2).

The mean haemoglobin was 9.6±2.0 g/dl, and around 19.4% of patients were anaemic (Hb<10 gm/dl). Furthermore, 24.2% had hyperleukocytosis, while the sign of leukostasiswas seen in only 3.0% of patients (Table 3).

Table 1: Baseline characteristics of the study participants (n=132)

Variable	No.	%
Age (years)		
<30	46	34.8
30-60	76	57.5
>60	10	7.5
Gender		
Male	86	65.1
Female	46	34.9
Duration of practice (years)		
≤ 10	190	65.1
> 10	102	34.9

Table 2: Clinical presentation of CML patients (n=132)

Variable	No.	%
Constitutional symptoms	115	87.1
Duration of disease symptoms (11-34 months)	14.3±12.04	
Fatigue	99	75.0
Abdominal fullness/ Discomfort	97	73.4
Night sweat	48	36.3
Weight loss	43	32.5
Splenomegaly	118	89.3
Massive splenomegaly	43	32.5
Mean spleen span (13-34cm)	18.9±3.7	

Table 3: Haematological parameters of CML patients

Variable	Mean±SD	
Hemoglobin (g/dl)	9.6±2.0	
Total leukocyte count (x10^9/l)	167.6±123.3	
Platelets (x10^9/l)	398.7±281.9	
	No.	%
Anaemia	28	19.4
Hyperleukocytosis (TLC ≥300x10^9/l)	32	24.2
Leukostasis	4	3.0
High LDH	51	38.6
Hyperuricemia	54	40.9
Elevated serum creatinine	19	14.3

DISCUSSION

Chronic myeloid leukemia is a common malignancy of myeloid lineage; the clinical course is variable, increasing the risk for acute transformation and shortening overall life expectancy. Effective management of CML is essential, owing to the high risk for morbidity and mortality. Such haematological malignancies are more frequent amongAsians than Europeans; the reason may be inadequate diagnostic services and financial restrictions. However, the delayed diagnosis can lead to decreased survival chances and affects the overall quality of life, especially in advanced stages. We studied the clinical and haematological profiles to gain disease insight.

Although CML affects individuals of all age groups, the disease occurrence is more significant among older adults in the western world[15]. Surprisingly in the present study, the disease incidence was higher in the younger population (39.4±13.8 years). Existing local literature also supports this finding.[16,17] The factors responsible for this age presentation might be genetic predisposition, environmental risk exposure, and shorter life expectancy. Furthermore, the definite male dominance reported in the present study was similar to that reported in international and regional studies.[18,19] Similarly, a large Indian case series also reported higher disease incidence among males.[20]

Patients with CML often present with constitutional symptoms (B symptoms), including weight loss, fever, night sweat and fatigue due to the catabolic state, observed in 87.1% of patients in the present study. The frequency of constitutional symptoms reported in other studies varies greatly.[21,22] A remarkably low disease incidence and minimum B symptoms have been reported in an Iranian study; given that there was comparatively high disease awareness hence, the patients from this particular geographical region acquire consultancy before the disease symptoms exacerbate.[23] The high disease burden in our region is basically due to the delayed presentation as the patients avoid timely medical consultations, which is also reflected by the observed mean symptoms duration (14.3±22.04 months).The majority of the patients in the present study were symptomatic and presented with fatigue (75%) and abdominal discomfort (73.4%) secondary to splenomegaly (89.3%).Following our findings, a prior study from Egypt reported a similar prevalence of splenomegaly 91%.[24] Similarly, an Indian study also detected splenomegaly in 85.9% of study subjects.[25]

Anaemia at presentation has usually been found to be an indicator of advanced-stage disease. In our series, around 19.4% of patients were found to be anaemic. Hyperleukocytosis leads to leukostasis that may be complicated by hearing loss, papilledema, impairment of memory function, intracranial haemorrhage, respiratory depression, acute renal failure and priapism. In the present study, hyperleukocytosis was detected in 24.2% of patients, while luckily only 3.0% had the signs of leukostasis. In concordance to this, Khaled et al[24] also determined raised TLC count in 53.9%.

CONCLUSION

Predominantly CML affected males and individuals of the younger age group. Their clinical and haematological parameters were similar, as reported in the literature. Most of the patients presented with a high disease burden with a significant delay in diagnosis. More than 80% of the patients had splenomegaly.

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