Clinico Hematological Profile and Phase Distribution of Chronic Myeloid Leukemia

Farzana Chang1, Riaz Ahmad Qazi1, Mehrab Khan1, Sarmad Baloch1, Mir Muhammad Sahito2 and Amber Mir1

1Department of Pathology, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan
2Department of Pathology, Peoples University of Medical and Health Sciences for Women, Shaheed Benazir Abad, Sindh, Pakistan

Summary

Objectives: To evaluate the Clinico hematological profile based on the age, sex and Clinico hematological presentations and frequencies of three phases of chronic myeloid leukemia (CML). This study highlight the Ph positively by real time polymerase chain reaction (RT-PCR) technique contribute towards understanding the disease biology, and have important implications for diagnosis and management of CML patients.

Study design: This is an experimental and observational study.

Place and duration: This study was conducted in medical ward and pathology department of Peoples University of Medical and Health Sciences for women (PUMHS-W) Nawabshah from June 2013 to June 2014.

Materials and methods: Total 83 patients including 52 male, 31 female at their age ranges between 23 and 57 years admitted in medical ward of PUMHS hospital were selected for study. The clinical history and physical examination of these patients were noted. All the blood samples and bone marrow biopsy sent to the pathology department of PUMHS for the analysis of complete blood count, peripheral blood and bone marrow examination for the diagnosis of three phases of chronic myeloid leukemia.

Results: Out of 83 patients, 52 were male and 31 were female with male to female ratio of 1.6:1, the mean age of these subjects was 39.5 ± 16.5 years. The mean total leukocyte counts, platelet counts, hemoglobin levels and marrow blast frequencies were 121,000 ± 35,000/cmm, 285,000 ± 122,000/cmm, 7.5 ± 4.9 and 15 ± 9 respectively. The majority of patients 62 (74.6%) were classified in the chronic phase (CP), 17 (20.4%) in the accelerated phase (AP) and 3 (5.0%) in blast crisis (BC). The most frequent patient age ranges were 21-30 years for CP, 41-50 years for AP and 41-50 years for BC.

Conclusion: This study concluded that most CML patients are from a younger age group (33-47 years). Males were more commonly affected than the females. The detection of Ph chromosome positively by resent and advanced RT-PCR technique is mandatory for the diagnosis and treatment of CML patients.

Keywords: Chronic myeloid leukemia; Phase distribution; Response to therapy; RT-PCR; Philadelphia chromosome

Introduction

Chronic myeloid leukemia (CML) is a clonal malignant neoplasms of pluripotent hematopoietic stem cell characterized by the excessive proliferation of mature granulocytes and their precursors in the bone marrow and peripheral blood caused by in 90% of cases due to the presence of Philadelphia chromosome and rarely by Hyperdiploidy of >50 chromosomes [1]. The translocation between chromosome 9 and 22 t (9;22) (q34;q11) leads to the formation of break point cluster region and Abelson’s (BCR-ABL) a new hybrid fusion genes that encodes for an oncoprotein (P210) located in the cytoplasm that has a strong, capacity to activate tyrosine kinases resulting in the activation of several downstream signals that transform hematopoietic stem cells in to the leukemic cells, thus increased tyrosine kinases activity is currently thought to play a central role in the pathogenesis of CML [2]. In spite of leukemia induced factors, there are risk factors that enhance the CML and these factors include lower socio-economic status, occupational exposure to benzene, formaldehyde, high doses of ionizing radiation among the atomic bomb survivors, other risk factor such as alcohol abuse, obesity, weight gain during adulthood and effects of preservatives or pesticides used in the food industry causes CML [3,4].

Clinically in 50% of cases patients with CML are asymptomatic and remaining were present with anemia, splenomegaly, fever, bleeding tendency, hepatomegally, lymphadenopathy and complications such as renal failure, hearing loss and priapism, and laboratory findings include complete blood count, peripheral blood and bone marrow examinations showing low hemoglobin, total WBC count between 287×109/L and 535.7×109/L, thrombocytopenia or normal platelet count or thrombosytosis and peripheral blood smear showing increase number of mature and immature granulocytes including predominantly [5,6]. The Bone marrow pictures in CML without treatment showing hypercellularity due to excessive proliferation of the granulocytes with myelocytes predominantly and presence of blast cells from <10% to >20% in the bone marrow and peripheral blood according to the world health organization criteria that divide the CML in to chronic, accelerated phases and blast crisis, there is decreased or normal or increased megekayriopiosis as well as moderate to marked reticulin fibrosis with presence of small megakaryocyte containing hypolobulated nuclei, sea-blue histiocytes and gaucher cell and...

*Corresponding author: Dr. Farzana Chang, Associate Professor, Department of Pathology, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan, Tel: +92-92133515; E-mail: changfarzana@gmail.com

Received September 12, 2015; Accepted October 31, 2015; Published November 07, 2015


Copyright: © 2015 Chang F, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.
these changes are return to the normal state after treatment and the immunohisto-chemistry is used for differentiating the myeloblastic and lymphoblastic crisis of CML [7,8]. The recent developments in the confirmation of diagnosis of CML by sensitive tests such as qualitative real time-polymerase chain reaction (RT-PCR) to identify transcript variants of BCR-ABL fusion genes and quantitative droplet digital PCR as well as RT-PCR tests are used for ratio of BCR-ABL transcripts levels with normal genes on the international scale (>1016 and monitoring the response to therapy of patients with chronic myeloid leukemia [7,8]. The Cyto genetic must be performed by chromosome banding analysis (CBA) of marrow cell metaphases for the detection of BCR-ABL+ nuclei and additional chromosome abnormalities among patient with CML, if marrow cell cannot be obtained, CBA can be substituted by inter-phase fluorescence in site hybridization (I-FISH) of blood cell using dual color dual fusion probes [9]. The marked improvements in the management of CML with first line gold slandered therapy of imatinib mesylate (IM), the first tyrosine kinase inhibitor (TKI) targeting the management of CML with first line gold slandered therapy of imatinib dual color dual fusion probes [9]. The marked improvements in the management of CML with first line gold slandered therapy of imatinib mesylate (IM), the first tyrosine kinase inhibitor (TKI) targeting the phase fluorescence in site hybridization (I-FISH) of blood cell using dual color dual fusion probes [9]. The marked improvements in the management of CML with first line gold slandered therapy of imatinib mesylate (IM), the first tyrosine kinase inhibitor (TKI) targeting the phase fluorescence in site hybridization (I-FISH) of blood cell using dual color dual fusion probes [9]. The marked improvements in the management of CML with first line gold slandered therapy of imatinib mesylate (IM), the first tyrosine kinase inhibitor (TKI) targeting the phase fluorescence in site hybridization (I-FISH) of blood cell using dual color dual fusion probes [9]. The marked improvements in the management of CML with first line gold slandered therapy of imatinib mesylate (IM), the first tyrosine kinase inhibitor (TKI) targeting the phase fluorescence in site hybridization (I-FISH) of blood cell using dual color dual fusion probes [9]. The marked improvements in the management of CML with first line gold slandered therapy of imatinib mesylate (IM), the first tyrosine kinase inhibitor (TKI) targeting the phase fluorescence in site hybridization (I-FISH) of blood cell using dual color dual fusion probes [9].
Mean age in years | Sex | Socioeconomic status
--- | --- | ---
40 ± 17 years | Male 52 (63.8%) Female 31(37.4%) Male to female ratio 1.6:1.0 | Poor 83 (75.9%) Lower middle class 15 (18.0%) Upper middle class 4 (4.8%)

Symptoms / clinical history
- Asymptomatic; 10(12.03%)
- Symptoms due to Anemia 79 (95.1%) Pallor Fatigue, lethargy, Body aches, dizziness, nausea & vomiting
- Symptoms due to splenomegally 70 (84.3%) Abdominal distension Abdominal discomfort Pain left side of abdomen History of bleeding 12 (14.4)
- Symptoms due to infection; fever with cough 18(21.6%) Hypermetabolic state, loss of weight night sweat 10(12.0%)

Symptoms / clinical history
- Physical examination
  - Anemia
    - Mild 19 (22.8)
    - Moderate 39 (46.9)
    - Severe 25 (30.1)
  - Splenomegally
    - Massive (≥ 10cm) 60 (70.2%)
    - Moderate(4-9 cm) 55(66.2%)
    - Mild (1-3 cm) 14 (16.8%)
    - Hepatomegally 15(18.0%)
    - Lymphadenopathy 8 (9.6%)

Hematological parameters
- Hemoglobin g/dl, Total leucocyte count /cumm
  - 9.5 ± 2.9 g/dl
  - 121000 ± 35000 /cumm
- Differential leucocyte count, The % of mature and immature cells calculated out of 100 leucocytes / HPF
  - Mature cells 43%
    - (neutrophils 21±7, lymphocyte 8± 2, eosinophils 9± 2, monocytes 5±3 )
  - Immature cells57%
    - (Blast 18±12, promylocytes 4± 1, Myelocytes 25± 5, Metamyelocytes 9±2, band cells 13±3 )
  - 285000 ± 220000 / cumm
- Examination of PBS
  - Examination of bone marrow
    - The red blood cells are nomocytic normochronic with variable in size and shapes. Plenty nucleated red blood cells are seen and many mature and immature leucocytes are seen, the majority of cells are myelocytes.
    - The bone marrow is hypercelular due to excessive proliferation of myeloid cell line predominantly of myelocytes with few blue histocytes and pseudogaucher cell. The megakaryocytes or hypolobated.

Table 1: The evaluation of chronic myeloid leukemia based on age in year, sex, socioeconomic status and Clinico laboratory findings. (N=83)

<table>
<thead>
<tr>
<th>Phases of CML</th>
<th>Chronic Phase</th>
<th>Accelerated Phases</th>
<th>Myeloid Blast Crisis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>62 (74.6%)</td>
<td>17 (20.4%)</td>
<td>3 (5.0%)</td>
</tr>
<tr>
<td>Age</td>
<td>30 ± 7</td>
<td>45 ± 6</td>
<td>45.5 ± 9.5</td>
</tr>
<tr>
<td>Sex</td>
<td>Male 42</td>
<td>Male 11</td>
<td>Male 2</td>
</tr>
<tr>
<td>Female 20</td>
<td>Female 6</td>
<td>Female 1</td>
<td></td>
</tr>
<tr>
<td>Ratio 2.1.1</td>
<td>Ratio 1.8.1</td>
<td>Ratio 2.0;1.0</td>
<td></td>
</tr>
<tr>
<td>Spleenic Size</td>
<td>&lt; 10 / cm</td>
<td>&gt;10 / cm</td>
<td>&gt; 15 / cm</td>
</tr>
<tr>
<td>Number of blast cells in peripheral blood and bone marrow smears</td>
<td>6 ± 2</td>
<td>16 ± 4</td>
<td>26 ± 5</td>
</tr>
</tbody>
</table>

Table 2: The frequency of three phases of CML based on age, sex, spleenic size and number of blast cells in peripheral blood and bone marrow smears N=83

Formalin applied on fish for preservation, calcium carbide on fruits to ripen, brick dust in chili powder, urea to whiten rice and puffed rice, sawdust in loose tea, soap in Ghee, artificial sweetener, coal tar, textile dyes in sweetmeats and occupationally exposure of benzene, ionizing radiation in x-ray department, any form of formaldehyde used in industries including formalin. Studies detected Abelsons and break point cluster region (ABL-BCR) positive cases of CML in 40 patients, out of 48 patients by RT-PCR test with the mean age of 37.6 ± 14.1 years, male to female ratio 1.8:1 spleenic size 9.8 ± 5.8 cm, TLC 284.5 ×109± 267.5×109. That indicated 92% specificity sensitivity and reliability of this test. Yaghmaie et al. [14] detected expression of one of the P120BCR-ABL transcripts including b3a2 (62%) and b2a2 (21%) among the 83% out of 75 Iranian patients, while the remaining showed one of the transcript of b3a3 and b2a2 while the similar two types of transcripts and additional cytogenetic abnormalities such as double PH chromosome, +8, +19 among the Indian 208 patients with CML ph chromosome positive had male to female ratio of 1.8:1 and mean age of 38 years of all the three phases of CML were observed by Anand et al. [15].

Conclusion
From the above discussions, following conclusion and recommendation were made. In our study, total 83 patients including 52 male and 31 female with male to female ratio of 1.6:1 and their mean ages was 39.5 ± 16.5 years and frequency of three phase of CML was 62. (76.4%) were in the chronic phase (CP), 17 (14.58%) respectively. The male are affected more than the female and chronic phase of CML was common in younger age group. The Philadelphia chromosome detection by RT-PCR in CML patients due to the limited sources, we can't perform this advanced test for the molecular analysis of CML.
References


