Changes in the Basic Haematological Parameters in Chronic Leukemia Patient (Myeloid and Lymphoid)

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ABSTRACTS

Background: Chronic myeloid leukaemia (CML) is a clonal disorder of hematopoietic stem cells. The disease arises as a consequence of a rare gene abnormality. Chronic lymphocytic leukaemia is a neoplastic disease characterized by the accumulation of small mature-appearing lymphocytes in the blood, marrow, and lymphoid tissues. Aim of the study: To determine the pattern of alteration in the basic hematological parameters in patients with chronic leukemia. And who have laboratory evidence of hyperleucocytosis.

Methods: In this study 104 patients were enrolled with chronic Leukemia patient (Myeloid and Lymphoid) at Al-Gumhouri Teaching Hospital Sana’a and National oncology center Sana’a in the period of the study (from 18 August to 30 November 2013) and studied, (CBC) were done using automated blood cell analyzer, Blood film examination and Bone marrow examination.

Results: About (76.9%) of patients were affected with CML, whereas (57.5%) of patients were male and (42.5%) were female in CML. While (23.1%) were suffering from the CLL in which (83.3%) were male and 16.7% were female. Moreover, Thrombocytosis found in (35.6%) of patients in whom (94.6%) of CML patient type & (5.4%) were CLL type. Thrombocytopenia was also found in 25% of patients in whom (42.3 %) of patients were CML type & 57.7% were CLL type. Hyperleucocytosis (white counts over 300x10⁹/liter) was detected in (6.25%) CML patients & in (8.3%) CLL patient.

Conclusion: The main type of anaemia in chronic leukaemia is the mild to moderate normochromic normocytic anaemia and Hyperleucocytosis occur more in CML than in CLL type of chronic leukaemia.

Key Words: CML, CLL, (CBC), Blood film examination and Bone marrow examination.

1. Introduction

CHRONIC MYELOGENOUS LEUKEMIA

Chronic myeloid leukemia (CML) is a clonal disorder of hematopoietic stem cells (1). The disease arises as a consequence of a rare gene abnormality. The course of the disease is characteristically triphasic: a chronic phase (CP) lasting three to six years is followed by transformation to an accelerated phase (AP) and then a terminal blast phase of short duration (2). Initially described in 1845 (3, 4), CML is one of the best understood diseases from the aspect of its cytogenetic abnormalities and the molecular mechanisms involved. CML was the first human disease in which a specific abnormality of the karyotype, the Philadelphia (Ph) chromosome, could be linked to a malignant disease (4). Clinical characteristics of CML

CML has an incidence of 1 case per 100,000 people per year and accounts for 15 percent of leukaemia’s in adults (5). The median age of patients at presentation is 45 to 55 years. Up to one third of the patients are over 60 years old, which is an important consideration for therapeutic strategies such as stem cell transplantation and INF-α treatment. In general, the cause of CML is unclear but high doses of ionizing radiation may be an etiologic factor (6). Most cases (85 percent) of CML are diagnosed in CP. The typical symptoms at presentation are fatigue, anorexia, and weight loss. The most common abnormality on physical examination is splenomegaly, which is present in up to half of the patients. About 40 percent of patients are asymptomatic, and in these patients, the diagnosis is suspected because of accidental detection of
abnormal blood counts\(^{(7)}\). The main laboratory findings are peripheral blood neutrophilia with a left shift of the differential count, and basophilia. Bone marrow examination shows myeloid predominance, left shift and abnormalities. Without curative intervention, CP CML will invariably transform through an AP, often heralded by the appearance of increased number of immature myeloid cells in the bone marrow and peripheral blood, as well as new cytogenetic changes in addition to the Ph chromosome.

After a short period of 3-18 months, progression then proceeds to blast crisis (BC), which is defined by the presence of 30 percent or more blast cells in peripheral blood or bone marrow, or the presence of extra medullary infiltrates of blast cells\(^{(8, 9)}\). **Chronic lymphocytic leukemia**

Chronic lymphocytic leukemia is a neoplastic disease characterized by the accumulation of small mature-appearing lymphocytes in the blood, marrow, and lymphoid tissues.\(^{(10)}\) CLL has an average incidence of 2.7 persons per 100,000 in the United States. The risk of developing CLL increases progressively with age and is 2.8 times higher for older men than for older women.\(^{(11)}\) Because of its relative indolence, this disease accounts for approximately 0.8 percent of all cancers and nearly 30 percent of all leukemia’s at any point in time.

It is the most common adult leukemia in Western societies. Generally, the neoplastic lymphocytes are of the B-cell lineage. In less than 2 percent of cases, however, the neoplastic cells are of T-cell origin and are considered under the heading T-cell prolymphocytic leukaemia\(^{(12)}\).

The first descriptions of patients with CLL were published in the early nineteenth century. In the 1840s, Virchow described two forms of chronic leukemia, these probably corresponding to CLL and chronic myelogenous leukemia. Patients with the former were noted to have mild-to-moderate splenic enlargement, lymphadenopathy, and large numbers of small a granular cells in the blood that resembled those found in enlarged lymph nodes. Virchow considered this type of leukemia to be principally related to disease of the lymph nodes rather than of the spleen.

A clinical staging system for patients with CLL was introduced in 1975 by Rai and colleagues, delineating the adverse implication of anemia or thrombocytopenia on patient survival\(^{(13)}\).

2. Material and Methods:

The study included all patients with Chronic Leukemia (Myeloid and Lymphoid) attended to AI-Gumhouri Teaching Hospital Sana'a and National oncology center Sana'a Yemen. In the period of the study (from 18 August to 30 November 2013). Basic Hematological Parameters:

All the basic hematological tests (CBC) were done using automated blood cell analyzer with morphological study.

Blood film examination (peripheral blood smear).

Bone marrow examination.

**Study design:** cross-sectional study.

**Sample size:** 104 participants.

**Ethics issues:**

The study was approved by the Human Research Ethics Committee (HREC) in Al-Gumhouri Teaching Hospital Sana'a and National oncology center Sana'a Yemen and from SHREE P.M. PATEL COLLEGE OF PARAMEDICAL SCIENCE & TECHNOLOGY, ANAND, SARDAR PATEL UNIVERSITY.

**Statistical Analysis :**

Descriptive statistics were computed with percentages and proportion. Group comparisons were done by Chi-square test. P.

The mean plus or minus standard deviation (±SD) and “t” tests were employed for statistical evaluation of the results using standard methods by computer programs:

A: Excel program under windows 7. B: Word program under Windows 7 & SPSS statistical computerized program and EndnoteX7 for management references.

3. RESULTS:

**Laboratory data are depicted as follow:**

It shows chronic leukemia distribution. Out of the total 104 patients studied, 80/104 (76.9%) were chronic myeloid leukemia and 24/104 (23.1%) were chronic lymphocytic leukemia. 81/104 (77.9%) were more than 30 years old and 23/104 (22.1%) were less than 30 years old. In CLL: 46/80 (57.5%) were males and 34/80 (42.5%) were females, with male: female (M: F ratio) of 1.4:1. In CLL: 20 (83.3%) were males and 4 (16.7%) were females, with male: female (M: F ratio) of 5:1.

It shows that 100/80 (92.6%) CML patients were anaemic at diagnosis with a hemoglobin level ranging between4.1 and 15 g/dl. Mild to Moderate anaemia found in the majority of the CML patients studied 72/80 (90%). 6/80 (7.5%) patient had normal hemoglobin level (13-15 g/dl). Anaemia present in 95/104 (91.3%) patients with 74/80 (92.5%) CML type & 21/24(87.5%) CLL type. 9/104(8.65%) patient shows normal hemoglobin concentration. Thrombocytopenia found in 26/104 (25%) patient with 11/80 (13.8 %) CML type & 15/24(62.5%) CLL type. Thrombocytosis with platelet count more than 1000 found in 3/80 (3.8) CML patient only.
Distribution of Chronic Lymphocytic Leukemia According to Severity of Anaemia with a haemoglobin level ranging between 4.1 and 14.2 g/dl, the majority 19/24 (79.16%) were with mild-moderate anaemia. 3/24 (12.5%) patient had normal haemoglobin level (up to 13.8 g/dl).

It shows that leukocytosis was present in all (100%) patients, of which 9/104 (8.7%) patients had WBC count ranging from $12 \times 10^9$ to $50 \times 10^9$/L. 26 (25%) out of 104 patients had leukocytosis (more than $50 \times 10^9$/L). hyperleucocytosis with WBC count more than $100 \times 10^9$/L found in 62/104 patient (59.6%) & those with hyperleucocytosis (WBC count more than $300 \times 10^9$/L) found in 7/104 (6.7%). The total WBC count in the majority of CL patients studied (73/80 (91.2%) CML cases / 22/24 CLL (91.7%) cases) were more than 50 to $653 \times 10^9$/L.

Figure (1) Distribution of Chronic Myeloid Leukaemia According to Severity of Anaemia.

Figure (2) Distribution of Chronic Lymphocytic Leukemia According to Severity of Anemia
Table (1): Distribution of Chronic Leukemia Patients studied According to the Type, Age and Gender.

<table>
<thead>
<tr>
<th>Types Leukemia</th>
<th>Gender</th>
<th>Total</th>
<th>M: F ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td></td>
</tr>
<tr>
<td>CML</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &lt;30</td>
<td>count</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>17</td>
<td>6</td>
<td>23</td>
</tr>
<tr>
<td>% of total</td>
<td>21.3%</td>
<td>7.5%</td>
<td>28.8%</td>
</tr>
<tr>
<td>Age &gt;30</td>
<td>count</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>29</td>
<td>28</td>
<td>57</td>
</tr>
<tr>
<td>% of total</td>
<td>36.3%</td>
<td>35.0%</td>
<td>71.3%</td>
</tr>
<tr>
<td>Total</td>
<td>Count</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>46</td>
<td>34</td>
<td>80</td>
</tr>
<tr>
<td>% of total</td>
<td>57.5%</td>
<td>42.5%</td>
<td>100%</td>
</tr>
<tr>
<td>CML</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &gt;30</td>
<td>count</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>4</td>
<td>24</td>
</tr>
<tr>
<td>% of total</td>
<td>83.3%</td>
<td>16.7%</td>
<td>100%</td>
</tr>
<tr>
<td>Total</td>
<td>count</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>20</td>
<td>4</td>
<td>24</td>
</tr>
<tr>
<td>% of total</td>
<td>83.3%</td>
<td>16.7%</td>
<td>100%</td>
</tr>
<tr>
<td>Total</td>
<td>Age &lt;30</td>
<td>count</td>
<td></td>
</tr>
<tr>
<td></td>
<td>17</td>
<td>6</td>
<td>23</td>
</tr>
<tr>
<td>% of total</td>
<td>16.3%</td>
<td>5.8%</td>
<td>22.1%</td>
</tr>
<tr>
<td>Age &gt;30</td>
<td>count</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>49</td>
<td>32</td>
<td>81</td>
</tr>
<tr>
<td>% of total</td>
<td>47.1%</td>
<td>30.8%</td>
<td>77.9%</td>
</tr>
</tbody>
</table>

Table (2): Blood Cells Parameters of Chronic Leukaemia.

<table>
<thead>
<tr>
<th>Types. Leukemia</th>
<th>Hb</th>
<th>WBC.c</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>12-50</td>
<td>51-100</td>
</tr>
<tr>
<td>Hb &lt;6</td>
<td></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>% of Total</td>
<td></td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Hb 6-9</td>
<td></td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>% of Total</td>
<td></td>
<td>2.5%</td>
<td>8.8%</td>
</tr>
<tr>
<td>Hb 9.1-13</td>
<td></td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>% of Total</td>
<td></td>
<td>5.0%</td>
<td>10.0%</td>
</tr>
<tr>
<td>Hb &gt;13</td>
<td></td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>% of Total</td>
<td></td>
<td>1.3%</td>
<td>3.8%</td>
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</table>
4. DISCUSSION
Chronic myeloid leukemia (CML) is a potentially fatal stem cell neoplasia that constitutes nearly 14% of all leukaemia. CML is caused by translocation of chromosome 9 and 22 to create what is called Philadelphia chromosome.

In the present study, Chronic leukaemia (CL) distribution shows CML type predominance compared to CLL, with CML to CLL ratio of 3.3:1 (Table: 1), which agrees with the results of most workers\(^{14,15}\).

CML was the predominant type of CL in adults included in this study (Table: 2) 80/104 (76.9%), this agrees with the universal observation about the predominance of CML in adults\(^{1,2,3,4,5}\).

The majority of our CML patients 57/80 (71.25%) were adults (with>30 yrs.), (Table: 1) which agree with the universal concept about the predominance of CML in adults\(^2\).

Table(3): Relationship between hyperleucocytosis and Hematological Parameters of Chronic Myeloid Leukaemia.

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>HYPERLEUCOCYTOSIS in CML (total WBC count: more than 300 ((\times 10^9/L)))</th>
<th>Present</th>
<th>Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO. (%)</td>
<td>6(7.5%)</td>
<td>74(92.5%)</td>
<td></td>
</tr>
<tr>
<td>6-9</td>
<td>3(9)</td>
<td>9(31)</td>
<td></td>
</tr>
<tr>
<td>9.1-13</td>
<td>5(12)</td>
<td>4(24)</td>
<td></td>
</tr>
<tr>
<td>&gt;13</td>
<td>1(5)</td>
<td>3(0)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>9(26)</td>
<td>26(62)</td>
<td></td>
</tr>
</tbody>
</table>

* p<0.0001 (Independent Samples Test)
# p<0.001 (Independent Samples Test)
Gender distribution of our CL patients shows male to female ratio of 1.7:1, also our CML patients shows male: female ratio of 1.4:1 (Table: 1) these results agrees with that found in other studies & CLL male to female ratio was 5:1, (Table: 1)

Mild to Moderate anaemia found in the majority of the CML patients studied 95/108 (87.9%) (Fig. 1), severe anaemia found in 5/108(4.6%).

Mild to Moderate anaemia found in the majority of the CLL patients studied 19/24 (79.2%) (Fig. 2), severe anaemia found in 2/24(8.3%).

In the present study , The total leukocyte count in CML is always elevated at the time of diagnosis and is nearly always over 25 × 10^9/L; over two third of the CML patients have total white counts over 100 × 10^9/litter (55/80 (60.88%). Hyperleucocytosis (white counts over 300 × 10^9/litter) was detected in 5/80 (6.25%) CML patients & in 2/24 (8.3%) CLL patient. This agrees with almost all standard works in this field of study.

The total WBC count in the majority of CL patients studied (73/80/91.25%) CML cases / 22/24 CLL (91.7%) cases were more than 50 to 653×10^9/L, this range agree with the finding of another worker (16).

The platelet count is elevated in about 35/80 (43.75% ) percent of CML patients at the time of diagnosis and is normal in most of the rest 34/80 (42.5%) (Table: 2). The diagnosis of CLL requires a sustained monoclonal lymphocytosis greater than 5 × 10^9/litter, all the included cases in this study shows this fact and in the present study the mean absolute lymphocyte count generally is 90.9 × 10^9/litter.

Mild anemia (10/24 (41.7%) (Table: 10). And/or thrombocytopenia (14/24(58.3%) (Table: 2). are common at diagnosis in this study, but significant decreases (haemoglobin <6 g/dl found in 2/24 (8.3%)) (figure: 2).

Thrombocytopenia detected in 14/24 (58.3%) CLL cases studied, this thrombocytopenia might attributes to marrow replacement/infiltration and / or hypersplenism.

About 15 percent of patients present with symptoms or signs referable to leukostasis as a result of the intravascular flow-impeding effects of white cell counts over 300 × 10^9/liter (in the present study hyperleucocytosis in CML found in 7/104 (6.7%). In CLL: Leukemic leukocytosis in excess of 800 × 10^9/litter may produce blood hyperviscosity (in the present study hyperleucocytosis in CLL found in 1/24 (4.17%)) (16.20).

5. Conclusion
CML & CLL are an adulthood leukaemia mainly with male being more affected.

The main type of anaemia in chronic leukaemia is the mild to moderate normochromic normocytic anaemia.

The frequency of occurrence of chronic hyperleucocytic leukaemia (CHL) is not uncommon. Hyperleucocytosis occur more in CML than in CLL type of chronic leukaemia. Laboratory evidence of hyperleucocytosis in chronic leukaemia requires particular attention with special care in the diagnosis and treatment. Hyperleucocytosis in chronic leukaemia is associated with lower Hemoglobin concentration compared to patients without hyperleucocytosis.

Hyperleucocytosis in chronic leukaemia affects older age group more than young patients with chronic leukaemia. The frequency of hyperleucocytosis in chronic leukaemia is more in the myeloid than the lymphocytic chronic leukaemia type. The distribution pattern of the differential white blood cells count aid in the differentiation of the typical CML from other variant of CML.

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