Evaluation of the approach to chronic lymphocytic leukemia

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Research Article

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Abstract

The aim of the research: to follow up the therapeutic and diagnostic procedures used in Al-Bayrouni University Hospital and Al-Mujtahid Hospital, and to compare these procedures between the two hospitals.

Materials and Methods: This study was a retrospective cross-sectional study, in which a sample of the files of patients attending Al-Bayrouni University Hospital and Damascus Hospital was referred to, and their laboratory analyzes, and the diagnostic and therapeutic procedures that were applied to them, in addition to the methods of following them up for three and six months.

Results: The sample consisted of 69 patients with chronic lymphocytic leukemia, the largest number of whom were from Al-Bayrouni University Hospital, where they constituted 64%, while the remaining 25 patients were from Al-Mujtahid Hospital in Damascus, with a rate of 36%, which was the largest percentage. Among them were males (70%), the blood smear showed an increase in the percentage of lymphocytes in patients, and the diagnostic procedures such as myelopuncture, fish technique, and immunophenotyping were performed in Al-Bayrouni Hospital more than in Al-Mujtahid Hospital.

Conclusion: Chronic lymphocytic leukemia is considered one of the diseases that need to follow up the latest international recommendations in terms of treatment, follow-up and diagnosis, and this was evident among patients attending Al-Bayrouni University Hospital compared to patients at Al-Mujtahid Hospital.

Introduction

leukemia (CLL) is defined as a monoclonal proliferation at the expense of mature lymphocytes. It is the most common form of leukemia in adults in Western countries, accounting for 25% of all leukemias. In the United States, 95% of CLL cases are of the B-cell phenotype, while in Asia, T-cell CLL predominates. It is difficult to assess the true incidence, as it may be in patients with chronic lymphocytic leukemia. Asymptomatic before diagnosis, asymptomatic was estimated to account for 30% of cases, but in the past 20 years the number of CLL cases presenting in asymptomatic stages has doubled from 30–60%, likely due to an increase in the number of blood tests being performed performed for other medical or surgical reasons, Moreover, sensitive techniques for diagnosing and differentiating CLL from other chronic lymphoproliferative disorders have only recently become routinely available.

The current estimated annual incidence in the USA ranges from 7,300 to 12,500 new cases, with an overall incidence of 2.3/100.00.

The Reasons
The cause is unknown, but much evidence points to a genetic component, such as the increased prevalence of CLL among first-degree relatives, the anticipation phenomenon, which shows an increase in severity, an earlier age with each generation, and an increased frequency of autoimmune disorders in relatives of patients with chronic lymphocytic leukemia. 7,9

No relation was shown to environmental factors, such as ionizing radiation, chemicals (gasoline and solvents from the rubber industry) and drugs. 10,11

**Molecular Biology**

Chronic lymphocytic leukemia is a model of failed apoptosis BCL-2 family proteins are expressed (which are key regulators of apoptosis) are overexpressed in 90% of B-CLL cells, although in the vast majority of cases (96–99%) there is no translocation involving BCL-2.

Slow growing B-CLL cells accumulate in the body, mostly in the G0 phase of the cell cycle. One consequence is acquired resistance to agents active in the cell cycle.

Imbalance in the ratio of key inducible and anti-apoptotic proteins, such as BAX and BAK (induction of apoptosis), BCL−2 (anti-apoptotic), and HRK (inhibitors of apoptosis). It seems they play an important role in the behavior and treatment response of CLL, although convincing clinical evidence is not yet available. 12,13

Mutations of the p53 tumor suppressor gene and increased levels of expression of the cyclin-dependent p27 kinase inhibitor have been shown to be associated with disease progression and overall poor prognosis. Impaired response to treatment with p53 mutants. 13,14

Cytokines are produced and released directly by CLL cells, such as tumor necrosis factor (TNF) and interleukin 8 (IL-8), as well as IL-2, which is produced by T lymphocytes and uptaken by CLL cells through specific receptors, involved in autocrine or paracrine loops and affecting CLL cell survival and proliferation. 15,16

IL-4 production is associated with increased expression of CD30. Since there is evidence that most CLL cells express CD30, this interaction may affect the environment of CLL cells and their immune functions. 17

One of the critical steps of the immune response to an antigen is the crosslinking expression of CD40 or CD154, which is produced by activated T cells. An upregulation of this ligand induced by CLL leukemic lymphocytes results in severe immunodeficiencies. 18

**Cytogenetics:**
There is no single identifiable cytogenetic abnormality in CLL, and the development of new techniques, such as fluorescent in situ hybridization (FISH), has increased the detection of chromosomal numerical and structural abnormalities. ¹

The most common cytogenetic alteration is a deletion of 13q14 (51%), followed by a deletion of 11q22q23 (17%-20%) Trisomy 12 (15%), deletion 17p13. ¹⁹,²²

there may be complex abnormalities; For example, CLL patients with trisomy 12 may have 13q 14 deletions. sync. ²²,²⁴

A number of cytogenetic abnormalities, including trisomy 12 and the presence of abnormalities on chromosomes 14q, 11q, and 17p, have been linked to poor treatment outcomes.

Trisomy 12 is associated with atypical lymphocyte morphology and immunophenotype (CD5–), FMC7 and disease progression.

Patients with 11q to be younger, with an advanced clinical stage at diagnosis With peripheral and abdominal lymphadenopathy mean, and a treatment-free period of nine months, as opposed to 43 months for those without deletion.

A chromosome 17 abnormality has been associated with a p53 mutation and fludarabine - resistant treatment and treatment failure in patients with Richter syndrome. and atypical CLL morphology, and it is unclear whether these cytogenetic abnormalities are primary or secondary events. ²⁰,²¹,²⁵,²⁶

IgV gene mutations has been associated with decreased CD38 expression in a cohort of patients with good clinical outcome and improved survival. Therefore, CD38 may be useful as a surrogate for IgV genetic mutations and as a prognostic factor. ²⁷,²⁸

Clinical Manifestations:

About 40%-60% of patients with CLL are diagnosed in the absence of disease-related symptoms, even with very high circulating lymphocyte counts > 100 * 10⁹/L.

Often, the presence of lymphadenopathy or an abnormal CBC during a routine medical exam is the only reason to suspect the diagnosis. ²⁹

fever and may or may not be infected Have an infection or autoimmune disease. ³⁰,³¹

Physical examination generally reveals painless, mobile lymphadenopathy or an enlarged spleen and/or hepatomegaly. ¹
Metabolic disorders (such as hyperuricemia) or mechanical disorders (such as airway obstruction) associated with tumor burden may also be present.

CLL cells can infiltrate any part of the body, including the skin and meninges; However, such findings are uncommon in chronic lymphocytic leukemia. ²⁹

Myeloid insufficiency, particularly significant anemia (hemoglobin < 11 g/dL) or thrombocytopenia (platelet count < 100 x 10⁹/L), was observed at diagnosis in 15% of CLL patients.

A positive direct antiglobulin test (DAT) was noted. It occurs in about 20% of patients at diagnosis but is not usually associated with hemolytic anemia. ³²

**Diagnosis:**

The National Cancer Institute - Sponsored Working Group (NCI-WG) has published guidelines for diagnosis and response criteria for CLL. ³³

1. Having at least 5 x 10⁹ B lymphocytes/L in peripheral blood smear
2. An immunophenotype profile showing:
   - CD5 expression
   - CD23 expression
   - Decreased levels of CD20 and CD79b and surface immunoglobulin expression.

The aspirate should show bone marrow aspiration BM More than 30% of all nucleated cells are lymphoid. ³³

Although BM examination is rarely required to make a diagnosis of CLL in general practice, it may be useful before treatment is initiated in order to identify prognostic factors.

BM examination is primarily indicated to assess response to treatment or to assess normals if unexplained anemia or thrombocytopenia is present. ³³

**Differential Diagnosis:**

CLL can be distinguished from other closely related chronic lymphoproliferative disorders on the basis of morphology and immunophenotype (Table 1), such as (MCL-L) and follicular lymphoma (FL-L), PLL, hairy cell leukemia (HCL), and splenic lymphoma with villous cell lymphoma (SLVL). ³³³⁴

Table 1: Phenotype of B-cell chronic lymphocytic leukemia.
Flow cytometry is very useful in differentiating MCL - L from CLL. The morphology of MCL is cleft small lymphocytes, and the immunophenotype is type B cell neoplasia.

CD5+, CD19+, CD20+), but MCL can be distinguished from CLL based on their expression of cyclin D1 and lack of CD23 expression.

In addition, MCL has more intense surface immunoglobulin J and CD20 expression than CLL.

**Prognostic And Staging Factors:**

Rai and Binet systems (Table 2) are the most common alarm and phase determination systems for CLL. 35,36

Lymphocytosis alone is not classified by the Binet system, and neither system includes splenomegaly alone.

Prognostic factors regardless of the clinical stage are:

- Age over 55 years old.
- Male sex.
- Black race.
- Clinical condition bad.

Older and younger CLL patients in trait presentation, response rates, or response duration.

Prognostic factors that may predict outcome include: 37

- Lymphocyte doubling time is within 6 months, with a break of 12 months.
- Beta 2-microglobulin.
- CD23 Soluble.
- LDH.
<table>
<thead>
<tr>
<th>survival (years)</th>
<th>Clinical manifestations</th>
<th>danger</th>
<th>stage</th>
<th>classification system</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;10</td>
<td>Lymphocytes only (in blood and marrow)</td>
<td>low</td>
<td>0</td>
<td>Rai</td>
</tr>
<tr>
<td>7</td>
<td>Lymphocytosis + lymphadenopathy</td>
<td>Average</td>
<td>I</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Lymphocytosis + splenomegaly and/or hepatomegaly ± lymphadenopathy</td>
<td></td>
<td>II</td>
<td></td>
</tr>
<tr>
<td>1.5</td>
<td>Lymphocytosis + anemia ± lymphadenopathy ± splenomegaly ± hepatomegaly</td>
<td>high</td>
<td>III</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lymphocytosis + thrombocytopenia (thrombocytopenia &lt; / 100 x 109 liters) ± anemia ± lymphadenopathy ± splenomegaly ± hepatomegaly</td>
<td></td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>&gt;10</td>
<td>Less than 3 decades</td>
<td></td>
<td>A</td>
<td>Binet</td>
</tr>
<tr>
<td>5</td>
<td>3 decades or more</td>
<td></td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Anemia and/or thrombocytopenia</td>
<td></td>
<td>C</td>
<td></td>
</tr>
</tbody>
</table>

Table (2): Rai and Binet systems.

**Mixtures:**

There are several typical complications of chronic lymphocytic leukemia, including infections, autoimmune leukopenia, and transformation into high-grade lymphoma.  

Transformation of chronic lymphocytic leukemia into diffuse large B-cell lymphoma or Hodgkin’s lymphoma occurs in approximately 1% of patients with chronic lymphocytic leukemia annually, and thus may affect up to 16% of patients during the course of the disease.

is termed Richter’s transformation and usually has a very poor prognosis when diffuse large B-cell lymphoma is associated with primary chronic lymphocytic leukemia.

NOTCH1 mutations in patients with chronic lymphocytic leukemia increases the risk of Richter’s transformation.

B - cell lymphoma, such as rituximab plus CHOP (cyclophosphamide, vincristine, doxorubicin, prednisolone), or more treatment Offensives such as rituximab plus cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternated with methotrexate and cytarabine, etoposide, prednisolone, vincristine, cyclophosphamide, doxorubicin (cytarabine, rituximab).

The duration of treatment response in Richter transformation is usually short, and allogeneic stem cell transplantation should be considered in all responding patients with an available donor.
allogenic transplantation usually fails to prevent disease progression. 46

Transformation of chronic lymphocytic leukemia into Hodgkin's disease is a separate and rare entity that traditional chemotherapy against lymphoma achieves Hodgkin's lymphoma is often long-term remission Hodgkin. 41

Patients with chronic lymphocytic leukemia are also at increased risk of developing secondary cancers. 47,48

This risk is higher in elderly patients and in patients with comorbidities and increases with each round of treatment. Immuno-chemotherapy increases the risk of developing secondary myelodysplastic syndromes or acute myeloblastic leukemia. 47

The incidence of secondary myelodysplastic syndromes and acute myelogenous leukemia after FCR treatment is 2–5% depending on age and exposure to growth factors. 49

Immunochemotherapy with bendamustine may be associated with a lower risk of secondary myeloid malignancies than fludarabine plus cyclophosphamide. 49

Patients with chronic lymphocytic leukemia are also at risk B immune hemolytic anemia (in 2–4%), immune thrombocytopenic purpura (2–5%), red blood cell aplasia (0 5–1%) and autoimmune granulocytopenia (<1%, Autoimmune leukopenia, particularly hemolytic anemia, can also be triggered by exposure to purine nucleoside analogues. 50

Treatment for autoimmune leukopenia depends on the type of autoimmune leukopenia and whether the patient also requires treatment for primary chronic lymphocytic leukemia. 50

Patients with chronic lymphocytic leukemia often develop septic complications.

Until recently, infection was among the most common causes of death in patients with chronic lymphocytic leukemia, and acute blood infections continue to occur when treated with newer drugs. 50

The type of infection depends on the type of anti-leukemia treatment: immunosuppressive therapies such as purine analogues or alemtuzumab, kinase inhibitors, and BCL-2 inhibitors may reactivate opportunistic infections such as Pneumocystis jirovecii, cytomegalovirus, or Herpesviridae; 51 As for irrigation, toximab may lead to the activation of hepatitis B virus; 52 Myelosuppressive chemotherapy or immunochemotherapy may increase the risk of bacterial infection. Patients on distinct anti-leukemia therapies should therefore receive appropriate prophylaxis such as co-trimoxazole, antiviral therapies, or growth factor support to prevent persistent neutropenia.

**Treatment With Ivig:**
Hypogammaglobulinemia is the most prevalent inherent immune abnormality in CLL, and immunoglobulin replacement therapy (IgRT) is an alternative for patients with hypoglycemia and recurrent bacterial infections. 53

Although administration of immunoglobulin either intravenously (IVIg) or subcutaneously (SCIg) significantly reduces the rate of bacterial infections for CLL patients, it has no effect on the incidence of non-bacterial infections or on the patient's overall survival. 54

Ig preparations currently used in CLL contain more than 95% IgG and as a result, IgA deficiency persists and IgM. Analysis of infection-related factors in CLL patients showed a stronger association between the primary infection and a common antibody deficiency, that is, low levels of IgG. and IgA or IgM, rather than isolated deficient IgG. 55

While IVIg formulations were originally developed for IgRT in antibody-deficient patients, higher doses have been found to be effective as anti-inflammatory therapy in patients with autoimmune or inflammatory conditions. 56

Various mechanisms of action responsible for the immune-modulating ability of high doses of IVIg have been identified, eg: direct and indirect inhibition of T-cell activation and allergy induction, impairment of BCR- and TLR-signaling on B cells, and inhibition of the mononuclear phagocytic system. 57

Interestingly, patients receiving IgRT that increases IgG levels above 9 g/L have been shown to show evidence of disease control, suggesting that higher doses of Ig may have anti-leukemic activity in CLL patients. 58

**Practical Study**

**research importance:**

In view of the recent developments in the field of chromosomal studies and targeted therapies in patients with chronic lymphocytic leukemia, and to determine the extent of commitment of workers in this field in the health approach to patients with chronic lymphocytic leukemia.

**research aims:**

To know the extent of application of the chromosomal approach and immunophenotyping in patients with chronic lymphocytic leukemia, and to determine the treatment plan and its relationship to laboratory and clinical findings.

**research hypothesis:**

To follow up on what is new in the world in chronic lymphocytic leukemia patients and adopt them as a treatment option.
Materials and working methods:

Study type

A retrospective, observational, cross-sectional study.

Place of study

Al-Bayrouni University Hospital and Al-Mujtahid Hospital.

Study time

Data of patients attending Al-Mujtahid Hospital were collected between 2015 and 2022. As for Al-Bayrouni Hospital, data for patients attending were collected between 2018 and 2022.

Sample size

The sample consisted of 69 patients, 44 of whom were from Al-Bayrouni Hospital, and 25 patients from Al-Mujtahid Hospital.

Entry criteria: The entry criteria included the patient's age, gender, place of residence, and whether or not he smoked or consumed alcohol, with regard to the patients' personal variables. The questionnaire also included the patients' symptoms, medical history, and laboratory analyzes, in addition to methods of diagnosing chronic lymphocytic leukemia, medications prescribed to them, and methods of follow-up after their discharge over a period of three and six months.

Statistical analysis

Statistical analysis was performed using SPSS-25 software.

Results

The sample in our study consisted of 69 patients with chronic lymphocytic leukemia, the largest number of whom were from Al-Bayrouni University Hospital, where they constituted 64% of the sample. The ages of the patients ranged between 60 and 70 years, where 19 patients were under the age of 60 with a rate of 28%, and 18 patients were in the age group between 60–65 years with a rate of 26%, while 17 patients were in the age group between 65–70 years. With a rate of 25%, while the lowest number of patients was over 70 years old, with a rate of 22%.

constituted the largest number of patients, as they numbered 48 patients, or 70%, while female patients were 21, or 30%.

When asked about the profession of the patients, the largest percentage of the patients worked as housewives, as their number reached 18 patients at a rate of 26%, 25 patients worked as workers at a rate
of 36%, 7 patients worked in different professions such as the military, the engineer, the farmer, the teacher, the nurse and the employee. 9 patients were retired at a rate of 13%, and finally 11 patients were not working at a rate of 16%.

21 of these patients were smokers with a percentage of 30%, while 19 patients were non-smokers with a percentage of 28%, while the rest of the 29 patients did not mention whether they smoked or not with a percentage of 42% of the patients. Also, there was only one patient who were alcoholics, while the remaining 26 and 42 patients were non-alcoholics or it was not mentioned whether they were alcoholics or not, by 38% and 61%, respectively.

The demographic and personality variables of the patients are indicated in Table 3.
### Table 3
Patients’ demographic and personality variables.

<table>
<thead>
<tr>
<th>N (%)</th>
<th>hospital</th>
<th>sex</th>
<th>Occupation</th>
<th>smoking</th>
<th>Alcohol</th>
</tr>
</thead>
<tbody>
<tr>
<td>44 (64)</td>
<td>Al-Biruni</td>
<td>to mention</td>
<td>House wife</td>
<td>yes</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>25 (36)</td>
<td>hardworking</td>
<td>feminine</td>
<td>Worker</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>1 (1)</td>
<td>Soldier</td>
<td>peasant</td>
<td>retired</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td>1 (1)</td>
<td>Engineer</td>
<td>retired</td>
<td>Teacher</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td>1 (1)</td>
<td>Engineer</td>
<td>retired</td>
<td>Nurse</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td>1 (1)</td>
<td>Officer</td>
<td>retired</td>
<td>Officer</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td>11 (16)</td>
<td>none</td>
<td>smoking</td>
<td>none</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td>21 (30)</td>
<td>yes</td>
<td>Alcohol</td>
<td>none</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td>19 (28)</td>
<td>No</td>
<td>Alcohol</td>
<td>none</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td>29 (42)</td>
<td>Not mentioned</td>
<td>Alcohol</td>
<td>none</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td>N (%)</td>
<td>hospital</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------</td>
<td>----------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (1)</td>
<td>yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>26 (38)</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>42 (61)</td>
<td>Not mentioned</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 (7)</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>64 (93)</td>
<td>Not mentioned</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

By examining the general symptoms reported by the patients, 20 patients suffered from fatigue and weakness by 46%, while 15 patients suffered from a history of weight loss by 34%, and 9 patients from anorexia by 21%, 5 patients suffered from night sweats by 11%. As for the remaining 22 patients, 50% did not suffer from these symptoms.

found in two patients with a rate of 3%, while 32 patients were suffering from splenomegaly at a rate of 46%, and there were also 19 patients suffering from hepatosplenomegaly at a rate of 28%, while the remaining 16 patients did not suffer from any enlargement by 23%.

By examining the lymph nodes, we found enlargement of the cervical lymph nodes in 25 patients with a rate of 66%, 20 patients had enlargement of the axillary lymph nodes with a rate of 53%, 11 patients had enlargement of the groin nodes with a rate of 29%, and 10 patients had enlargement of the thoracic nodes with a rate of 29%. 26%, while the remaining 5 patients had generalized nodular hyperplasia with a rate of only 13%.

By asking about the patients’ medical histories, we found that 8 patients had a history of heart disease with a rate of 10%, and 5 patients had a history of chest diseases with a rate of 7%, and diabetes was found in only one patient, while 23 patients suffered from other medical history with a rate of 33%, while the rest The 33 patients who did not suffer from any medical history accounted for 48%.

The patients' clinical symptoms and medical history are indicated in Table 4.
Table 4
Patients' clinical symptoms and anamnesis.

<table>
<thead>
<tr>
<th>General symptoms</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue and weakness</td>
<td>20 (46)</td>
</tr>
<tr>
<td>Underweight</td>
<td>15 (34)</td>
</tr>
<tr>
<td>Loss of appetite</td>
<td>9 (21)</td>
</tr>
<tr>
<td>Night sweats</td>
<td>5 (11)</td>
</tr>
<tr>
<td>None</td>
<td>22 (50)</td>
</tr>
<tr>
<td>Visceral enlargements</td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Spleen</td>
<td>32 (46)</td>
</tr>
<tr>
<td>Liver/spleen</td>
<td>19 (28)</td>
</tr>
<tr>
<td>None</td>
<td>16 (23)</td>
</tr>
<tr>
<td>Lymph nodes</td>
<td></td>
</tr>
<tr>
<td>Cervical</td>
<td>25 (66)</td>
</tr>
<tr>
<td>Axillary</td>
<td>20 (53)</td>
</tr>
<tr>
<td>Moroccan</td>
<td>11 (29)</td>
</tr>
<tr>
<td>Generalized</td>
<td>5 (13)</td>
</tr>
<tr>
<td>Waistcoat;</td>
<td>10 (26)</td>
</tr>
<tr>
<td>Medical history</td>
<td></td>
</tr>
<tr>
<td>Heart attack</td>
<td>8 (10)</td>
</tr>
<tr>
<td>Drunken</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Chest illness</td>
<td>5 (7)</td>
</tr>
<tr>
<td>Other</td>
<td>23 (33)</td>
</tr>
<tr>
<td>None</td>
<td>33 (48)</td>
</tr>
</tbody>
</table>

And given to me analyzes laboratory galaxy for patients. We found that 48 patients. It was. They have hemoglobin bloody less from 12 g/dl 70%, and it was 21 patients. They have Values pigment bloody Between 12–16 g/dl by 30%.
And at Procedure smear the blood peripheral (neutrophils) we found that All The patients And the adult Their number is 69 patients did not they suffer From Shortage neutrophils; 100%. As for about for a smear Hematologic (lymphocytic) 29 patients were infected They have Percentage normal From lymphocytes; by 42% of The patients, And it was There are 40 patients of whom They have Percentage lymphocytes High by 58% of The patients. As for about for monocytes in a smear the blood peripheral At the disease, So it was less from 2% in 6 patients by 9%, and reached 2–8% in 54 patients 78%, and 9 patients Just So it was They have Percentage monocytes in a smear the blood surround Larger from 8% and so on At What rate of 13% of Total The patients.

reach enumeration thrombocytopenia; less from 150 thousand And that in 46 patients 67%, and reached The population is 150 thousand to 400 thousand at 23 patients by 33%. As for about to enumerate pellets eggs reach census a number Between 5,000–10,000 pellets in 14 patients by 20%, either At the number the biggest From The patients And the adult Their number is 55 patients So it was census Larger from 10,000 pellets And that At What 80% of The patients.

As for about for yeasts hepatitis So it was alt normal At the number the biggest From The patients of 49 patients by 96%, either Remainder The patients And the adult their number Two patients Just She was They have this is yeast High by 4%. As for about AST So it was Value nature At The majority of The patients unless ill one She was he have this is yeast elevated. As for about Of LDH So it was Rate it normal in 19 patients 45%, and it was High at 23 patients by 55%

It was the Pt Wall PTT They are tall at 2, and 5 Patients by 9%, 23% On respectively, And they were They are normal At 20, and 17 ill by 91%, 77% On respectively.

As for about for the job renal At The patients, So it was urine normal in 40 patients 78%, and high at 22 patients by 11%. And she was Values creatinine At the majority From The patients between 0.6–1.3 and so on at 49 patients by 77%. As for acid urine So it was with Values normal in 41 patients by 87%.

These values and laboratory analyzes are indicated in Table 5.
Table 5  
Laboratory values and analyzes in patients.

<table>
<thead>
<tr>
<th><strong>N (%)</strong></th>
<th><strong>pigment the blood</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>48 (70)</td>
<td>&lt; 12</td>
</tr>
<tr>
<td>21 (30)</td>
<td>12–16</td>
</tr>
</tbody>
</table>

**smear the blood peripheral (neutrophils)**

| 0 (0.00)  | Shortage neutrophils; |
| 69 (100)  | natural               |

**smear the blood peripheral (lymphocytes)**

| 29 (42)   | natural               |
| 40 (58)   | High                  |

**smear the blood peripheral (monocytes)**

| 6 (9)     | < 2%                   |
| 54 (78)   | 2–8%                  |
| 9 (13)    | > 8%                   |

**thrombocytopenia;**

| 46 (67)   | < 150 thousand         |
| 23 (33)   | 150–400 thousand       |

**pellets egg Total**

| 14 (20)   | 5000–10000             |
| 55 (80)   | > 10,000               |

**alt**

| 49 (96)   | natural               |
| 2 (4)     | High                  |

**LDH**

| 19 (45)   | natural               |
| 23 (55)   | High                  |

**AST**

<p>| 46 (98)   | natural               |
| 1 (2)     | High                  |</p>
<table>
<thead>
<tr>
<th>N (%)</th>
<th>pigment the blood</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PT</td>
</tr>
<tr>
<td>2 (9)</td>
<td>elongated</td>
</tr>
<tr>
<td>20 (91)</td>
<td>not elongated</td>
</tr>
<tr>
<td></td>
<td>PTT</td>
</tr>
<tr>
<td>5 (23)</td>
<td>elongated</td>
</tr>
<tr>
<td>17 (77)</td>
<td>not elongated</td>
</tr>
<tr>
<td></td>
<td>urine</td>
</tr>
<tr>
<td>40 (78)</td>
<td>natural</td>
</tr>
<tr>
<td>11 (22)</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>creatinine</td>
</tr>
<tr>
<td>7 (11)</td>
<td>&lt; 0.6</td>
</tr>
<tr>
<td>49 (77)</td>
<td>0.6–1.3</td>
</tr>
<tr>
<td>8 (13)</td>
<td>&gt; 1.3</td>
</tr>
<tr>
<td></td>
<td>acid urine</td>
</tr>
<tr>
<td>41 (87)</td>
<td>My nature</td>
</tr>
<tr>
<td>6 (13)</td>
<td>High</td>
</tr>
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</table>

As for the chromosomal study, using the fish technique (del 17, 11,13), it was positive in 10 patients with a rate of 14%, and negative in 11 patients with a rate of 16%, while it was not conducted in 48 patients with a rate of 70%. When Flow Cytometry was performed, the result indicated the presence of CD 20+ / CD19 / CD 5 / CD 23 in 43 patients with a rate of 62%, and this technique was not performed in 26 patients with a rate of 38%.

When performing a marrow biopsy, it was positive in 66 patients, with a rate of 96%, while the rest of the 3 patients did not have a marrow biopsy, with a rate of 4% of the total patients in the sample.

When axial tomography was performed, radiological findings indicative of chronic lymphocytic leukemia were found in 45 patients with a rate of 65%, and these findings were not found in only 6 patients with a rate of 9%, in contrast, this procedure was not performed in 18 patients with a rate of 26%. When conducting the ultrasound for patients, evidence of infection was found in 48 patients, with a rate of 70%, while these findings were found in only 6 patients, with a rate of 9%, while the rest of the 15 patients did not perform this procedure, with a rate of 22%.
The most common drug used in this sample of patients was FCR, which was used in 37 patients with a rate of 71%, and the first line of treatment was used in 15 patients with a rate of 71%, and the second line of treatment was used in 5 patients with a rate of 24%, while the third line of treatment was used in one patient just one.

The vast majority of patients were followed-up during 3 months through clinical examination, in addition to radiography and blood tests, in 22 patients with a rate of 43%. The same applies to follow-up during 6 months, when 7 patients were followed up in this way, with a rate of 47%.

Diagnosis and treatment methods for patients are indicated in Table 6.
<table>
<thead>
<tr>
<th>N (%)</th>
<th>Karyotype del (17,11,13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 (14)</td>
<td>positive</td>
</tr>
<tr>
<td>11 (16)</td>
<td>negative</td>
</tr>
<tr>
<td>48 (70)</td>
<td>did not pull</td>
</tr>
</tbody>
</table>

**Flow cytometry**

| 43 (62) | CD20 - CD19 - CD23 |
| 26 (38) | did not pull |

**biopsy pure**

| 66 (96) | > 30% |
| 3 (4) | negative |

**class pivotal**

| 45 (65) | assets |
| 6 (9) | No |
| 18 (26) | did not pull |

**Echo**

| 48 (70) | assets |
| 6 (9) | No |
| 15 (22) | did not pull |

**treatment**

| 37 (71) | FCR |
| 5 (10) | R, IBRUTINIB |
| 2 (4) | , R. bendamustin |
| 7 (13) | IBRUTINIB |
| 1 (2) | R. bendamustine |

**Follow-up within 3 months**

| 1 (2) | CBC |
| 1 (2) | take photo Radial + CBC |
| 16 (31) | check up Clinical + CBC |
And at Comparison between My healers Al-Biruni And hardworking From Where procedures followed in a Follow-up and diagnosis for patients We found : a hospital Al-Biruni:

1- Done Procedure Technique Fish in 21 patients by 48% of Total The patients accepted in a hospital Al-Biruni .

2- For technique Flow Cytometry Where It was There are 38 patients may be She rose hospital conducting profiling Immune for them by 86%.

3- For biopsy pure, Lost It was completed conduct it in a hospital Al-Biruni for 35 patients by 80% of Total The patients accepted .

4- For photography radial as a caste pivot Lost go run for 36 patients From The patients accepted in a hospital Al-Biruni by 82%.

5- and it was Follows On Bezel three Months and six Months Include All surveys available From Pictures radial, And analyzes laboratory, And puncture pure, addition to examine clinical.

As for in a hospital The hardworking :

1- Why ? drag Technique Fish At any From The patients accepted

2- Done Procedure profiling immune in 5 patients Just

3- as well It was completed Procedure biopsy pure for five Patients Just

4- Finally go run class pivot for 15 patients 60%, and this The ratio Prepare less From Percentage The patients Whose They rose conducting class pivot in a hospital Al-Biruni.

5- Either about for follow-up On Bezel three Months So I was limited procedures followed On analyzes laboratory bloody and examination clinical, In what did not drag Follow ups On orbit the six Months about for patients hospital hardworking.
Done Signal to me the difference in a Procedure techniques Diagnostic that Complete conduct it in a All From hospital Al-Biruni And a hospital hardworking in a Table 5.

schedule 7: divergence in a Percentage The patients From Where techniques galaxy for them during accept them in a hospital.

<table>
<thead>
<tr>
<th>hospital</th>
<th>procedures</th>
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<tbody>
<tr>
<td>Al-Biruni</td>
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<tr>
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<td>Fish</td>
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<td>38 (86)</td>
<td>Flow Cytometry</td>
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<tr>
<td>35 (80)</td>
<td>biopsy pure</td>
</tr>
<tr>
<td>36 (82)</td>
<td>class pivotal</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>hospital</th>
<th>procedures</th>
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<tbody>
<tr>
<td>hardworking</td>
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</tr>
<tr>
<td>0 (0.00)</td>
<td>Fish</td>
</tr>
<tr>
<td>5 (20)</td>
<td>Flow Cytometry</td>
</tr>
<tr>
<td>5 (20)</td>
<td>biopsy pure</td>
</tr>
<tr>
<td>15 (60)</td>
<td>class pivotal</td>
</tr>
</tbody>
</table>

**Discussion**

Chronic lymphocytic leukemia (CLL) is the most common leukemia in the Western world. According to the American Cancer Society, an estimated 15,680 individuals in the United States will be diagnosed with CLL in 2013.  

The largest percentage of ages in our study ranged between 60–70 years, and this is consistent with international studies, where the average age at diagnosis of chronic lymphocytic leukemia ranged between 65–70 years.  

Males constituted the largest percentage of patients compared to females, where they accounted for 70% compared to only 30% for females, and this is consistent with one observational study that consistently reported a lower incidence and superior survival of female patients with chronic lymphocytic leukemia (CLL). These findings have been confirmed by various national cancer database reports and confirmed in recent prospective trials. It is not known whether the improved survival of women is attributable to increased comorbidities in men, improved response and/or tolerance to treatment in women, or a fundamental difference in the molecular biology of the disease (or a combination thereof).
30% of the patients in our study were smokers, which indicates that there is a correlation between smoking and the occurrence of chronic lymphocytic leukemia in these patients. Also, chronic lymphocytic leukemia (OR = 1.6) for both tobacco and cigarette smokers. Also, there was a significantly elevated risk for the longest-term cigarette smokers of all types of leukemia (OR = 1.6), chronic myelogenous leukemia (OR = 3.3), and lymphoblastic leukemia. Thus, the results of this study provide additional support for the association between smoking and the risk of developing several types of leukemia.  

The mechanism by which tobacco products may affect leukemia risk is not known. However, cigarette smoke contains many compounds, some of which have been linked to an increased risk of leukemia. Benzene, radioactive components, and possibly other carcinogens are present in tobacco and tobacco smoke, and may act by producing chromosomal defects. Cigarette smoking has also been linked to immune disorders. Therefore, it is possible that cigarette smoking affected the development of leukemia through possible indirect mechanisms.

The symptoms experienced by the patients in our study varied between fatigue and general weakness, lack of appetite and night sweats, in addition to the occurrence of visceral enlargements such as the liver, spleen, and streptococcus such as the cervical and axillary nodes, leading to generalization of enlargements to all lymph nodes, and this is consistent with studies that indicated that CLL is a tumor A dormant malignancy is characterized by increased production of mature but dysfunctional B lymphocytes. Sites of primary disease include peripheral blood, spleen, lymph node, and bone marrow. Signs and symptoms are absent in many patients, but when present, include B symptoms (fever, night sweats, unintentional weight loss), fatigue, early satiety, enlarged liver, enlarged spleen, and lymphadenopathy.

The diagnosis of chronic lymphocytic leukemia, many diagnostic procedures were performed such as blood analysis, immunophenotyping, marrow biopsy, and Fish technique. The most consistent laboratory abnormality observed is an increase in the absolute number of lymphocytes in the blood above the upper limit of normal for adults of ~ 3500 cells per µL, which is detected by blood counts, as well as by cytological or immunohistochemical analyzes of mononuclear cells in blood. Or the marrow or lymph nodes They can help distinguish CLL from other types of lymphoma.

Also, a lymph node biopsy may be performed in a patient with lymph node enlargement as part of a diagnostic evaluation for suspected chronic lymphocytic leukemia.

Fish technique was applied in Al-Bayrouni Hospital more commonly than in Al-Mujtahid Hospital, which indicates the quality of the procedures followed in the first hospital compared to the second hospital, as the Fish technique and as a result of the low proliferative index, only 50% of chronic lymphocytic leukemia cases are sufficient for genetic analysis. Of these, about half have birth defects. The application of fluorescent in situ hybridization (FISH) to CLL has greatly enhanced our ability to detect
chromosomal aberrations. A number of recurrent malformations have been demonstrated, providing new insights into the pathogenesis of this disease with direct impact on prognosis and treatment option.\textsuperscript{70}

**Recommendations:**

1. Conducting a prospective study aimed at following up patients on the long term in order to know their recovery rate according to the treatment used.
2. Conducting a prospective study with a larger sample size to study the personal and family variables that lead to chronic lymphocytic leukemia in patients.
3. Conducting periodic lectures for medical personnel about global updates on treatment plans and follow-up of patients with chronic lymphocytic leukemia.
4. Ensuring the application of the latest recommendations in the diagnostic procedures for patients in order to detect their disease early.
5. Work on developing the archive department in hospitals to facilitate reference to patient data for further research and future studies.

**Study limitations:**

1. The type of cross-sectional study that does not contribute to giving causation between the variables studied in the research.
2. Relatively small sample size
3. Difficulty dealing with patients’ files in the archive section due to the scarcity of information in them.

**Declarations**

**Competing interests:**

The authors declare that they have no competing interests

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**References**


27. RN Damle, F Fais, T Wasil et al. B-cell patients can be divided into two distinct clinical categories based on CD38 expression and IgV gene mutation status. *Blood* 1998.


Table 1 is available in the supplementary files section.

Figures

Figure 1

Distribution of patients according to the hospital in which the treatment was carried out
Figure 2

Distribution of patients according to age

Figure 3

Distribution of patients by occupation
Figure 4

Smoking among patients in the sample

Figure 5

Alcohol consumption in patients in the sample
Figure 6

Presence of shunting in patients

Figure 7

General symptoms in patients
Figure 8

Visceral enlargements in patients

Figure 9

Lymph nodal enlargement in patients
Figure 10

Patients' anamnesis

Figure 11

Some laboratory analyzes of patients
Figure 12

Patients' peripheral blood smear

Figure 13

Hemoglobin in patients
Figure 14

Methods for diagnosing chronic lymphocytic leukemia in patients

Figure 15

Medications used in the treatment of patients

Supplementary Files
This is a list of supplementary files associated with this preprint. Click to download.

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