

Haematologic Complications in Chronic Lymphocytic Leukemia

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ABSTRACT

Aim: To determine the frequency of haematological complications in patients of CLL.

Study Design: Cross-sectional

Study Setting and duration: Pathology Department KEMU 20th January to 20th June 2016

Results: In this study 150 patients of CLL showed mean age of 65.8±1.5 years and male predominance. Splenomegaly and lymphadenopathy was present in more than 80% and 60% respectively. Maximum patients belonged to stage 2. The mean haemoglobin was 9.8 g/dl±2.6 With 26.67% +DAT. Thrombocytopenia was present in 71% and maximum patient presented in the TLC range of 50000-100000 x 10⁹/L

Conclusions: CLL presents in older age group with male preponderance. Splenomegaly and lymphadenopathy are frequently present

Key words: Chronic lymphocytic leukaemia (CLL), Complications, Cytopenias

INTRODUCTION

Chronic lymphocytic leukemia/ (CLL) is the most prevalent lymphoid malignancy in the western countries with a estimated incidence of approximately 15,000 new diagnoses per year¹. In Pakistan cases of Chronic lymphocytic leukemia (CLL) account for 5% of all the haematological malignancies².

The diagnosis of chronic lymphocytic leukaemia (CLL) is based on clinical and laboratory features. Morphology and immunophenotype are the key tests. Lab diagnostic criteria as follow .1) An absolute lymphocyte count greater than 5x10⁹/l (5000'u/l) with most of the cells being mature lymphocytes.2) Bone marrows aspirate showing greater than 30% lymphocytes among all nucleated cells. 3) Peripheral blood lymphocytes identified as monoclonal B-cells. Any of the above two should be present³.

Patients may present with localized or generalized lymphadenopathy, hepatosplenomegaly, cytopenias or constitutional symptoms. However a number of patients are asymptomatic at the time of diagnosis and are only identified by the incidental finding of lymphocytosis on routine investigation .Patients may present with localized or generalized lymphadenopathy, hepatosplenomegaly, cytopenias or constitutional symptoms.⁴ However a number of patients are asymptomatic at the time of diagnosis and are only identified by the incidental finding of lymphocytosis on routine investigation.

The clinical and haematological course of

patients with B-cell CLL is often made complicated by autoimmune phenomena which mainly target the blood cells. The complications can occur in up to a quarter of all patients during the course of the illness. nonhematologic autoimmunity is very rare but⁵ paraneoplastic pemphigus and acquired angioedema can also occur in CLL. Most cases of AIHA and ITP are caused by high-affinity polyclonal IgG directed against red blood cells (RBCs) or platelet antigens⁶.

There are multiple causes of cytopenia in CLL e.g., bone marrow failure, hypersplenism, chemotherapy, sepsis, autoimmunity, a high degree of suspicion is required to diagnose these patients⁷.

This study was conducted to see the clinical picture of CLL at presentation, frequency and spectrum of haematological complication seen in CLL patients at the time of initial diagnosis and to correlate with stage of disease.

MATERIAL & METHODS

This study was conducted in Pathology Department, King Edward Medical University, Lahore. It was a cross sectional study conducted. The duration of study was from 20th January 2016 to June 2016. Sample size of 150 patients of newly diagnosed and old cases of CLL not on treatment were taken. Non probability conservative sampling technique was used.

Data collection procedure: Patients' history was taken and physical examination was carried out. A complete blood count was carried out using Automated Haematology Analyzer (Sysmex KX-21) and hemoglobin, WBC count, platelets and absolute lymphocytic count were determined. Reticulocyte count was done and direct antiglobulin test using coomb's reagent was done. Immunophenotyping was

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done by immunohistochemistry .Serum creatinine, lactate dehydrogenase (LDH) were detected. Bone marrow aspirate and trephine biopsy specimen were taken through Jamshidi needle.

Data analysis procedure: Data of the patients was compiled and analyzed using SPSS version 21. These results were shown as mean±SD for quantitative variables and qualitative variables were presented as frequency & percentages.

RESULTS

In our study, 150 patients of CLL age ranged from 40-85 years with mean age of 65.8 ±1.5 years with maximum number of 45 (30%) patients falling in the group of 71-80 years while 29 (19.3%) were between 40-50 years, 25 patients (16.67%) were in the range of 51-60 years, 31 patients (20.67%) were of 61-70 years and 31 patients (13.33%) fell between 81-90 years of age. Of all CLL patients 122 (81.33%) were males and 28 (18.67%) were females. - Splenomegaly was found in 87.3 % of all CLL patients whereas lymphadenopathy was found out in 62.7% of people. Maximum number of patients 50(33.3%) fell in stage II (according to Rai classification) followed by 45(30%) in stage III, 42 patients (28%) in stage IV, 12(8%) in stage I and only 1 patient (0.675) in stage 0 .

The mean haemoglobin of all CLL patients was 9.8 g/dl±2.62 and further stratification showed that most number of patients fell in the group of 11.1 -14 g/dl.

The Total leucocyte Count of all the CLL patients was further divided in groups which showed that maximum number of 54 patients fell in the range of 50001- 100000 x 10⁹ /L with other groups to follow. Platelet count in all CLL was more than 100 x 10⁹/L in 107(71.3%) patients whereas 43 (28.7%) had less than 100 x 10⁹/L count.

Among the total of 150 patients, 110(73.33%) had Coomb’s Test negative and 40 patients (26.67%) had a positive result

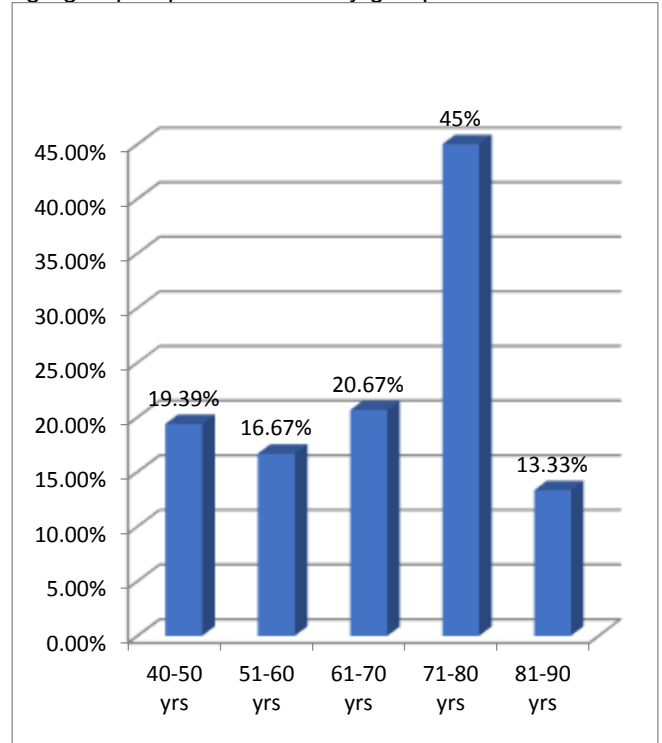
Table 1: Frequencies and percentages of TLC in CLL patients (n=150)

Total Leucocyte Count	Frequency	%age
0-50000µ/L	53	35.3
50001-100000 µ/L	54	36
100001-150000 µ/L	7	4.7
150001-200000 µ/L	28	18.3
200001-250000 µ/L	8	5.3

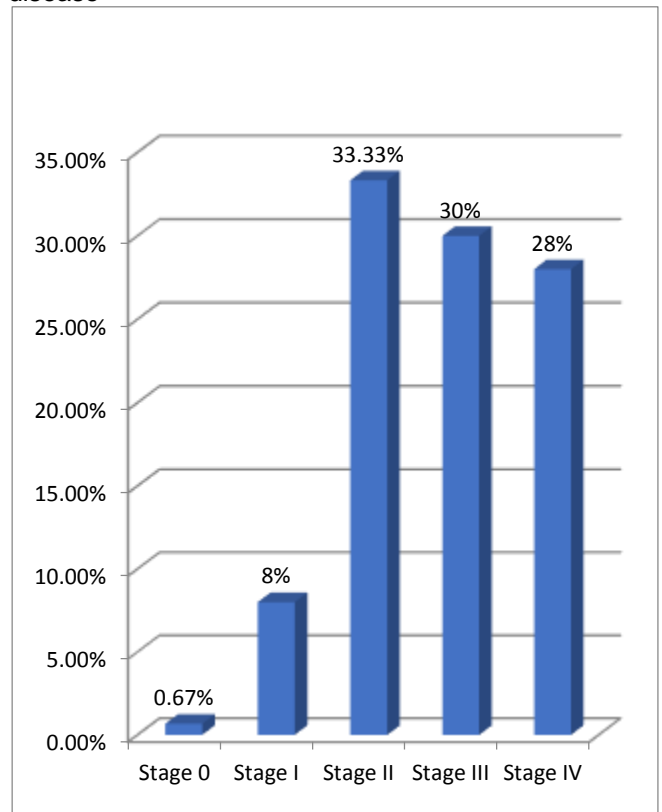
Table 2: Platelet distribution in CLL Patient

Platelet Count x 10 ⁹ /L	%age
0-100	6
101-200	31
201-300	30
301-400	33

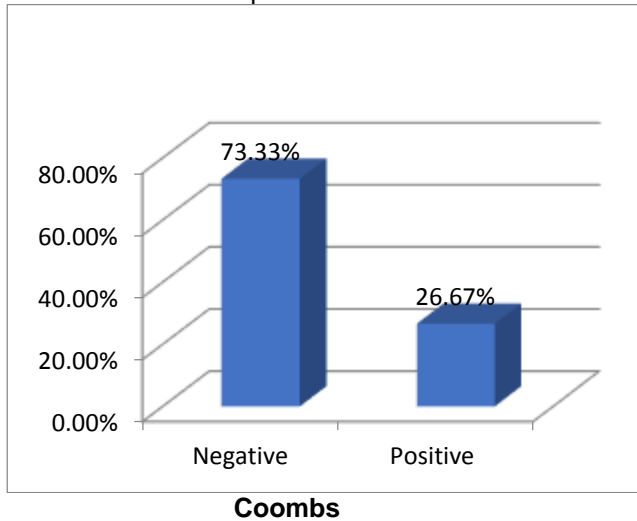
Age group of patients of study group



CLL patients presenting with different stages of disease



Coomb's test in CLL patients



DISCUSSION

In this study, we included 150 patients with diagnosis of CLL. The mean age of the patients was 65.8 ± 1.5 years with maximum patients falling in the group of 71-80 years. In another local study by Ehsan AY et al⁸ the mean age of was 62.84 years and the maximum number of patients presented in the 7th decade (45.2%). This reflects that age distribution of CLL patients is more or less same among different populations and is definitely a disease of later age.

The majority of the patients in our study were male i.e. 81.33% with a male to female ratio of 4.3:1. The study by Ehsan AY (mentioned before), showed similar results of gender distribution with a male to female ratio of 4.6:1.

Splenomegaly was found in 87.3% of all CLL patients whereas lymphadenopathy was found out in 62.7% of people. A study from India 2007 showed similar distribution of splenomegaly and lymphadenopathy⁹.

Maximum number of patients 50 (33.3%) fell in stage II (according to Rai classification) followed by 45 (30%) in stage III, 42 patients (28%) in stage IV, 12(8%) in stage I and only 1 patient (0.675) in stage 0. A study by Agarawal N showed following distribution according to Rai staging 11.6% were in stage 0, 13.3% stage 1, 26.7% each for stage II and stage III while 21.7% patients were in stage IV. Both studies showed maximum no of patients in stage II and III⁹.

Anemia is a serious manifestation associated with poorer prognosis and increased morbidity. The mean haemoglobin of our patients was $9.8 \text{ g/dl} \pm 2.62$, The Total leucocyte Count of all the CLL patients was further divided in groups which showed that maximum number of 54 patients fell in the range of $50001 - 100000 \times 10^9/\text{L}$, Platelet count in all CLL

was more than $100 \times 10^9/\text{L}$ in 107(71.3%) patients whereas 43 (28.7%) had less than $100 \times 10^9/\text{L}$ count. Our findings are closer to another study in Pakistan (Karachi) in which the mean hemoglobin was $10.8 \pm 2.4 \text{ g/dl}$ with a total leukocyte count of $91.5 \pm 87.8 \times 10^9/\text{l}$ and platelets $197.8 \pm 103.2 \times 10^9/\text{l}$. The other study had Anemia and thrombocytopenia in 26.7% and 21.7% of cases¹⁰.

Among the total of 150 patients, 110 (73.33%) had Coomb's Test negative and 40 patients (26.67%) had a positive result. A local study by Ehsan A et al⁸ showed a frequency of AHA to be 19.4% in CLL patients. A study conducted in Iran by Payandeh M¹¹ included 109 patients out of which 15.1% had AIHA highlighting the significance of AIHA in CLL.

CONCLUSION

Chronic lymphocytic leukemia (CLL) presents in older age group with male preponderance. Splenomegaly and lymphadenopathy are frequently present. Autoimmune haemolytic anemia is a significant finding in about quarter of patients.

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