

Auto Immune Haemolytic in Chronic Lymphocytic Leukaemia (CLL)

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ABSTRACT

Aim: Detection of frequency of autoimmune haemolytic anaemia in chronic lymphocytic leukaemia

Study design: Descriptive Cross-Sectional

Study Setting and duration: A 3 year study (Jan 2013- Dec 2016) conducted in THE Department of Pathology and Oncology of KEMU.

Results: AIHA was present in 26.67% of patients of CLL.

Conclusions: Frequency of Autoimmune haemolytic anaemia in patients of CLL is ABOUT 27% and is related with disease stage.

Keywords: chronic lymphocytic leukaemia, AIHA, Direct antiglobin test.

INTRODUCTION

Anaemia is a condition in which the number of red blood cells (and consequently their oxygen-carrying capacity) is insufficient to meet the body's physiologic needs. ¹Auto immune mediated haemolytic anaemia is the result of auto antibodies against patient's own red cell antigens mostly present in the plasma of the patient. Autoimmune haemolytic anaemias may be idiopathic or secondary associated mainly with lymphoproliferative disorders and autoimmune disorders.

CLL is characterized by proliferation, accumulation and sustained increase of morphologically mature but functionally incompetent lymphocytes. Peripheral lymphocytosis is accompanied by an accumulation of similar cells in the bone marrow, spleen, liver, lymph nodes and other lymphoid organs². Lab diagnostic criteria for CLL is as follow

1. An absolute lymphocyte count greater than $5 \times 10^9/l$ ($5000/\mu l$) 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.

The overall incidence of lymphoma is higher in men than in women. Chronic lymphocytic leukemia (CLL) is the most common leukemia in the Western world with an incidence of 4.2/100 000/year. In East

Europe and USA the disease incidence is high while in Asia and Africa CLL is rare⁵.

The staging methods of chronic lymphocytic leukaemia that are currently in use throughout the world are the Rai and the Binet systems. In the three-stage Rai system low risk encompasses Rai stage 0, with the clinical features of lymphocytosis in blood and bone marrow only. Intermediate risk encompasses stage I, with lymphocytosis and enlarged nodes, and stage II, with lymphocytosis plus splenomegaly and or hepatomegaly (nodes positive or negative). High risk encompasses stage III, with lymphocytosis plus anemia, and stage IV, with lymphocytosis and thrombocytopenia. Binet staging is based on the number of involved areas, and the level of haemoglobin (Hb) and platelet count. Whether significant adenopathy (> 1 cm in diameter) is bilateral or unilateral is recorded⁶.

Autoimmune phenomena are a well-known complication of lymphoproliferative diseases. In a study conducted by Ehsan A, autoimmune haemolytic anemia was found in 19.4%, immune thrombocytopenic purpura in 3.2% and no case of pure red cell aplasia in chronic lymphocytic leukemia patients⁸. In another study by Kate Hodgson done at university of Barcelona autoimmune hemolytic anaemia appears in 7% of chronic lymphocytic leukemia patients⁹.

Establishing a relationship between autoimmune haemolytic anaemias and chronic lymphocytic leukaemia will help the clinicians in modifying the treatment and decreasing the misery of the patients. Guidelines can be established to screen all CLL patients for autoimmune haemolytic anaemia to alter timely management.

The objective of the study was detection of frequency of autoimmune haemolytic anaemia in chronic lymphocytic leukaemia

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METHODS AND MATERIALS

This descriptive cross sectional study was conducted in the Department of Pathology & Oncology, King Edward Medical University, Lahore during a period of 3 year i.e., Jan 2013- Dec 2016. Sample size was 99 patients of chronic lymphoid leukaemia. A total of 99 untreated and newly diagnosed patients with chronic lymphocytic leukaemia were included

Inclusion Criteria: Newly diagnosed cases and old cases of chronic lymphocytic leukaemia. Both males and females with age between 18 years to 85 years.

Data collection procedure: For every patient a fresh 3 ml blood sample will be collected by a syringe using aseptic technique in a vacutainer containing EDTA. A complete blood count will be carried out using Automated Haematology Analyzer (*Sysmex KX-21*) and peripheral blood smear will be prepared using wright giemsa stain to establish whether anaemia is present or not. Reticulocyte count done by supravital staining will depict the burden of anaemia. Direct antiglobulin test using antihuman globulin (coomb's reagent) will determine the immune cause of anaemia.

Data analysis: Data will be entered and analysed on SPSS version 10, computer software and program for data analysis. Quantitative variables including age of the patient, reticulocyte count will be presented as mean ± standard deviation. Qualitative variable i.e., results of direct antiglobulin test (coomb's test) will be stratified to reduce bias and will be presented in the form of frequency and percentages

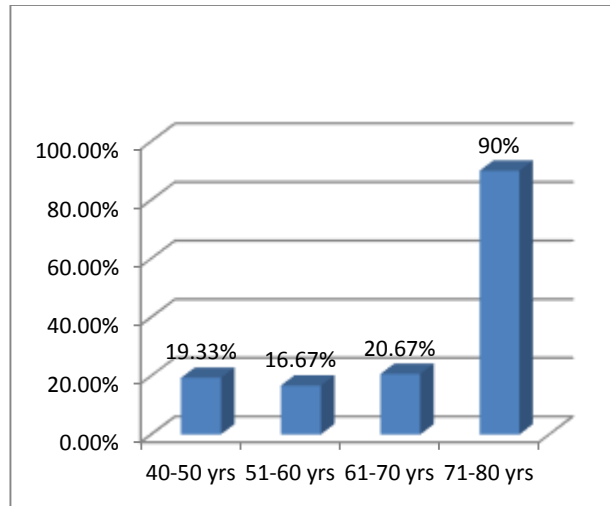
RESULTS

Out of 99 patients of CLL females were 19 and males were 81 with a M:F ratio of 4:1. Mean age of the CLL patients was 65.8±1.5 years. Out of 99 patients 26(26.67 %) showed positive DAT test whereas 73(73.33%) were negative. However those who had Coomb's positive had a lower level of haemoglobin with a mean of 7.69 g/dl ± 2.3 and with maximum number of patients were in range of 8.1 -11 g/dl. Among those patients who had DAT positive , 85% patients had haemoglobin less than 11g/dl depicting a real frequency of autoimmune haemolytic anemia in 22.66 % patients out of the total patients.

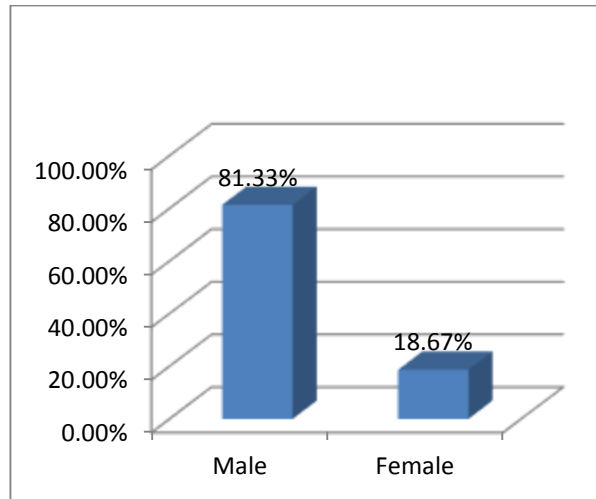
Retic percentage in dat positive cases: Only 1% of cases showed normal retic count whereas rest 99% had high retic with a percentage 15 showing 2-4 retic %age 47.5 4-6 percentage and about 27 showing 6-8 retic. So generally the retic count is raised.

Disease stage: Further analysis showed that patients who had autoimmune haemolytic anaemia presented with advanced disease stage of 3 (10%) and 4 (18.67%) whereas others had mostly stage 2.

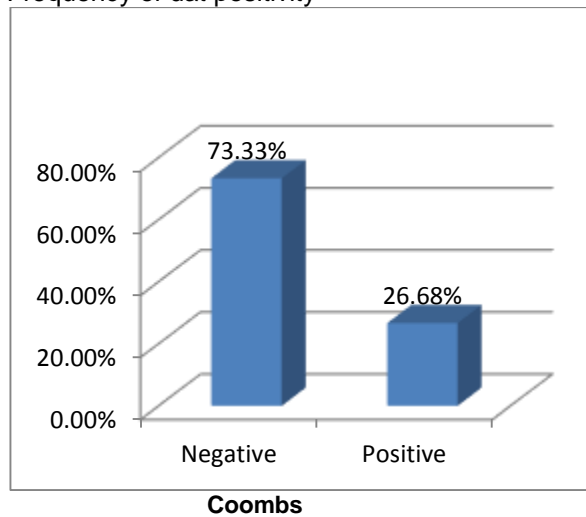
Age distribution



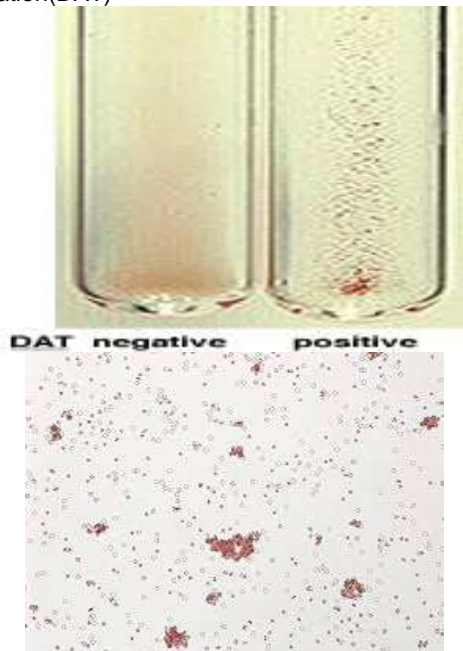
Gender distribution



Frequency of dat positivity



Naked and microscopic examination of Direct Antiglobulin Examination(DAT)



DISCUSSION

The mean age of the patients in our study was 65.8 ± 1.5 years with maximum most of patients falling in the group of 71-80 years. While in another local study by Ehsan AY et al¹⁰ the mean age of cohort was 62.84 years. The maximum number of patients presented in the 7th decade (45.2%). In another study by Diehl¹¹ the average age was 69.6 years with a peak incidence in the age bracket of 70–79 years.

The majority of the patients in our study were male i.e. 81.33% with a male to female ratio of 4;1. Oppezo P et al¹² conducted a study showed that 63% of the population under study was male. In another study conducted by Catovsky D et al¹³, on a large number of 660 cohorts showed that male population suffered from CLL twice as more.

A local study by Ehsan A et al¹⁰ showed a frequency of AHA to be 19.4% in CLL patients. A study conducted in Iran by Payandeh M¹⁴ included 109 patients out of which 15.1% had AIHA. Another study by Borthakur G¹⁵ stated that in CLL patients the frequency of AHA varies from 4-5–11%. The results of our study are close to that of local studies but international data is different. It may be the patients in our setup and society have less awareness and lack of health facilities¹⁶.

Our study showed that patients with coomb's positive presented with advanced stage of 3 and 4. This is in concordance to the study by Kyasa MJ et al¹⁷ which establishes that DAT positive is a poor prognostic factor.

In this study the mean level of haemoglobin of patients having coomb's positive was 7.69 ± 2.3 g/dl.

The study by Ehsan A¹⁰ showed close values of haemoglobin levels of 8.3 ± 2.1 g/dl in patients with AHA.

CONCLUSION

Frequency of Autoimmune haemolytic anaemia in patients of CLL is ABOUT 27% and is related with disease stage.

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