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Original Article

Frequency of Autoimmune Hemolytic Anemia in Chronic Lymphocytic Leukemia

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ABSTRACT

Introduction: Patients suffering from chronic lymphocytic leukemia (CLL) develop autoimmune complications between 5–10%, which primarily cause cytopenias. These autoimmune cytopenias can occur at various stages of CLL and do not have independent prognostic significance.

Objective: To determine the frequency of autoimmune hemolytic anemia in patients having chronic lymphocytic leukemia

Setting: Department of Hematology, Hayatabad Medical Complex, Peshawar.

Study Design: Descriptive Cross sectional study

Duration: 6 months

Material & Method: In this study, 253 patients were investigated and observed. Blood counts were performed on automated hematology analyser. Examination of Bone marrow included both bone marrow aspiration as well as trephine biopsy. Both peripheral blood smears as well as bone marrow smears was stained with Geimsa. Haematoxylin and eosin stains were used for trephine biopsies. Coomb's test was performed on blood samples of CLL patients

Results: Mean age was 58 years in this study with SD ± 11.341. Male patients were 72% and 28% patients were female. The frequency of autoimmune hemolytic anemia was found to be 8%only.

Conclusion: Our study concludes that the frequency of autoimmune hemolytic anemia was 8% in patients suffering from chronic lymphocytic leukemia

Key Words: Autoimmune Hemolytic Anemia, Chronic Lymphocytic Leukemia

Introduction

Patients suffering with chronic lymphocytic leukemia (CLL) develop autoimmune complications between 5–10%, which mainly causes cytopenias. These autoimmune cytopenias can be observed at various stages of CLL throughout the disease course and do not have independent prognostic significance. The commonest complication is autoimmune hemolytic anemia followed by immune thrombocytopenia and pure red blood cell aplasia while rarely with autoimmune granulocytopenia.

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Patients suffering from CLL who present with cytopenias, autoimmune cause should always be considered in differential diagnosis. Patients with CLL can sometimes presents with different types of autoimmune cytopenia which can be seen together with bone marrow failure too. Management is rarely curative but usually effective with long term treatment for autoimmune cytopenia in patients with CLL.[1]

In series of1203 patients (4.3%) suffering from CLL during treatment, Fifty-two cases were diagnosed having autoimmune hemolytic anemia (AHA) were observed and treated at a single hospital. Nineteen patients were diagnosed at the time of CLL diagnosis and 33 during the clinical follow-up. 90% of these patients who have CLL/AHA showed active CLL manifestations while 25% received treatment previously.[2] after treatment with steriod in CLL, antibody disappeared in 70% of patients and remission was induced. There was no relapse of AHA manifestations in 54% patients at 5 years and 41 months was median survival probability. Infections

were the main cause of morbidity and mortality during follow-up. Those independent factors that are associated with better survival in AHA/CLL patients are IgG AHA as well as the occurrence of AHA and CLL diagnosis at the same time.[2] Autoimmune hemolytic anemia is a rear disease caused by autoantibodies that attacks on his own body red blood cells with an incidence rate of 0.8–3 per 10^5/year in adults while a prevalence of 17:100,000 and 11% is mortality rate.[3,4] 50% cases can be idiopathic while 20% can be due to lymphoproliferative syndromes. While 20% can be due to other autoimmune diseases, infections and tumors.[5]AIHA is rare in infants and children (0.2 per 10^5/year), [6] where 37% occurs in primary diseases while 53% occurs with other immune disorders. Mortality is not that common in children (4%), but when associated with immune thrombocytopenia (Evans syndrome), mortality rises to 10%. [7]

The rationale of the current study is to determine the frequency of autoimmune hemolytic anemia in patients having chronic lymphocytic leukemia. We will briefly consider the main therapeutic tools for this disease, with a focus on patients with idiopathic AIHA refractory to the traditional therapy.

Medical Complex, Peshawar.

Material and Method

Setting: Department of Hematology, Hayatabad

Study Design: Descriptive Cross sectional study

Duration: 6 months 1/4/2017 to 1/10/2017

Sample Size: Sample size was 253. Using 4.3% proportion of autoimmune hemolytic anemia, 95% confidence interval and 2.5% margin of error under W.H.O software for sample size determination (Reference #2).

Sampling Technique: Consecutive (Non-Probability) sampling.

Inclusion Criteria: Following were included in the study:

1. All patients who was diagnosed as chronic lymphocytic leukemia by bone marrow examination
2. Age 40-80 years.
3. Both genders.
4. CLL patients having positive Coomb's test.

Exclusion Criteria

Following were excluded from the study:

1.All patients who have been diagnosed as acute leukemia or chronic myelocytic leukemia in which bone marrow examination was performed for remission status; and those with diagnosis other than leukemia (e.g. anemia, myelodysplastic syndrome, multiple myeloma, etc).

The conditions mentioned in exclusion criteria act as confounders and if included had introduce biases in our study outcome.

Data Collection Procedure

After approval of the study from hospital ethical committee informed consent was taken from all the included cases. All the patients fulfilling the inclusion criteria were subjected to bone marrow examination for evaluation of the underlying cause. Bone marrow examination had included both aspiration and also trephine biopsy if needed. Detailed relevant history was taken and clinical examination was carried out. All the hematological parameters were recorded. Blood counts were performed on automated hematology analyser. Bone marrow examination included bone marrow aspiration and trephine biopsy. The peripheral blood smears and bone marrow smears was stained with Geimsa. Haematoxylin and eosin stains were used in trephine. Coomb's test was performed on blood samples of CLL patients. Confounding variable and bias was controlled with the help of exclusion criteria. The bone marrow report of the Department of Hematology, and other information, was collected and incorporated to the proforma (given at the end of this protocol) for further analysis.

Data Analysis

The data was analyzed using SPSS version 20 software computer programme. Mean ± standard deviation calculation was done for variables like age and duration of disease. Frequencies and percentages calculations were done for categorical variables like gender, autoimmune hemolytic anemia. Autoimmune hemolytic anemia was stratified among age, gender, duration of disease to see the effect modifiers. Post stratification application of chi square test was done keeping p value ≤ 0.05 as statistically significant. All the interpretations and results were presented in the form of graphs and tables.

Results

In our study distribution of age among 253 patients with CLL was analyzed as 20(8%) were having age range of 40-50 years, 89(35%) having age range 51-60 years, 106(42%) patients were in age group of 61-70 years, 38(15%) patients were in age group of 71-80. 58 years was mean age having SD ± 11.341 (table no 1)

TABLE NO 1. Age Distribution (n=253)

AGE	FREQUENCY	PERCENTAGE
40-50 years	20	8%
51-60 years	89	35%
61-70 years	106	42%
71-80 years	38	15%
Total	**253**	**100%**

Mean age was 58 years with SD ± 11.341

Gender distribution among 253 patients was analyzed as 182(72%) were male patients and 71(28%) were female patients. (Table no 2)

TABLE NO 2. Gender Distribution (n=253)

GENDER	FREQUENCY	PERCENTAGE
Male	182	72%
Female	71	28%
Total	**253**	**100%**

Duration of disease among 253 patients was analyzed as 177(70%) patients had duration of disease ≤1 year while 76(30%) patients had duration of duration of disease 1> year. Mean duration was 8 months with SD ± 5.336 (table no 3)

TABLE NO 3. Duration of Disease (n=253)

DURATION	FREQUENCY	PERCENTAGE
≤1 year	177	70%
>1 year	76	30%
Total	**253**	**100%**

Frequency of Autoimmune hemolytic anemia among 253 patients was analyzed as 20(8%) patients had autoimmune hemolytic anemia while 233(92%) patients didn't had autoimmune hemolytic anemia. (Table no 4)

TABLE NO 4. Autoimmune Hemolytic Anemia (n=253)

Autoimmune Hemolytic Anemia	Frequency	Percentage
Yes	20	8%
No	233	92%
Total	**253**	**100%**

Stratification of autoimmune hemolytic anemia with age, gender, duration of disease is given in table no 5, 6, 7

TABLE NO 5. Stratification of Autoimmune Hemolytic Anemia W.R.T Age Distribution (n=253)

Autoimmune Hemolytic Anemia	40-50 years	51-60 years	61-70 years	71-80 years	Total
Yes	2	7	8	3	20
No	18	82	98	35	233
Total	**20**	**89**	**106**	**38**	**253**

Chi square test applied, P value was 0.9867

TABLE NO 6. Stratification Of Autoimmune Hemolytic Anemia W.R.T Gender Distribution (n=253)

Autoimmune Hemolytic Anemia	Male	Female	Total
Yes	14	6	20
No	168	65	233
Total	**182**	**71**	**253**

TABLE NO 7. Stratification of Autoimmune Hemolytic Anemia W.R.T Duration of Disease (n=253)

Autoimmune Hemolytic Anemia	≤1 year	>1 year	Total
Yes	14	6	20
No	163	70	233
Total	**177**	**76**	**253**

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A. Conception/Study/Designing/Planning
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