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ORIGINAL ARTICLE

Demographic features and hematological profile in patients of chronic lymphocytic leukemia in southern Punjab Pakistan.

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ABSTRACT… Objective: To generate data regarding clinicohematological findings of CLL in patients of Southern Punjab Pakistan. **Study Design:** Descriptive Cross-sectional study. **Setting:** Hematology Section Pathology Department, Nishtar Medical University, Multan. **Period:** January 2016 to September 2019. **Material & Methods:** A total of 44 patients of all age groups diagnosed as CLL were enrolled. Diagnosis was made on morphology and immunohistochemistry of bone marrow trephine biopsies and cases without immunohistochemical panel were excluded from the study. Clinical features and baseline tests were evaluated in all cases. The data was analyzed using SPSS Version 23.0. **Results:** Out of 44 patients, majority were males (70.5%). Mean age was 51±12.6 years. B symptoms were present in 71% patients. Lymph nodes were enlarged in 44%. Splenic and hepatic enlargement was seen in 32% and 15.9% respectively. Anemia was seen in 45.5% and thrombocytopenia in 34.1%. Bone marrow was infiltrated in 100% patients and the most common pattern of infiltration was diffuse (65%). CD20 and CD5 were positive in all of the cases (100%) and CD23 in 96%. Seropositivity for both anti HCV and HBsAg was present in 2.3%. **Conclusion:** The clinicohematological features of CLL in our patients show some differences to the cited literature with a greater majority presenting at younger age with diffuse bone marrow involvement having lower positivity for HBsAg, anti HCV and less hepatosplenomegaly.

Key words: Chronic Lymphocytic Leukemia, Immunohistochemistry, Rai and Binet Stage.

INTRODUCTION

CLL is a clonal lymphoid neoplasm of morphologically mature but functionally incompetent lymphoid cells which accumulate in peripheral blood, bone marrow, spleen, liver, lymph nodes and other lymphoid organs.[1] The diagnosis is made when absolute lymphocyte count is more than 5000/uL with clonality demonstrated by Flow Cytometry according to International Workshop on Chronic Lymphocytic Leukemia (IWCLL) criteria. CLL cells express CD19, CD5, and CD23 with weak or no expression of surface immunoglobulin (Ig), CD20, CD45, CD79b, and FMC7.[2] In addition to complete blood count and flow cytometry, immunohistochemistry, genetic and molecular testing is used to make diagnosis of CLL.

CLL primarily affects elderly individuals. The symptoms include fever, night chills, weight loss, recurrent infections, localized or generalized lymphadenopathy, hepatosplenomegaly and cytopenias.

Many risk factors have been proposed including family history, age, male gender, ethnicity, radiations and benzene exposure.[3,4,5] The clinical course of CLL can be heterogenous with rapid disease progression in some patients to being clinically silent for years in others.[6]

In our country, data regarding cancer incidence and prevalence is not organized yet, there is no cancer registry so far.[7,8,9] Also the data in Southern Punjab is rudimentary regarding clinicohematological parameters of hematological

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malignancies. Due to unequal distribution of healthcare services across country, the statistics of one area might not be generalized to whole country. Therefore we conducted a study to find out the clinical presentation and hematological profile in our patients of CLL in the biggest referral setup of South Punjab to find out if there are similarities or differences with other local and international studies.

MATERIAL & METHODS

A retrospective cross-sectional study was conducted in Pathology department Nishtar Medical University, Multan. A total of 44 patients diagnosed as Chronic Lymphocytic Leukemia on the basis of morphology and immunohistochemistry were recruited during January 2016 to September 2019. Patients with relapsed/refractory CLL and those without immunohistochemical workup were excluded. Anonymity of data was ensured and approval for evaluation of retrospective records was taken from the institutional review board. Records were evaluated for the patient's age, gender and clinical presentation. The diagnosis was established on CBC and peripheral film findings, bone marrow examination and immunohistochemistry for CD5, CD20 and CD23 in all patients. Samples were considered positive if >20% of the lymphoma cells were positive for that specific antigen. Moreover baseline laboratory tests such as hepatitis B and C profile, liver and renal function tests, LDH along with radiological imaging was also performed. The data was analysed on SPSS Version 23.0. The quantitative variables were expressed as mean and standard deviation (SD) while frequencies and percentages were used for all qualitative variables. Chi-square test was applied for categorical variables where P value <0.05 was taken to be significant.

RESULTS

Out of 44 patients, majority were males (70.5%) with M:F ratio of 2.3:1. Mean age of patients was 51±12.6 years with age range of 22-72 years. B symptoms were present in 71% patients. Lymph nodes were enlarged in 44% out of which cervical lymphadenopathy was the commonest site of involvement (39%) and mediastinal nodes in 5%. Splenic and hepatic enlargement was seen in 32% and 15.9% respectively. According to Rai staging, 18.2% patients were in stage 0, 13.6% in stage I, 11.4% in stage II, 27.3% in stage III and 29.5% in stage IV. Applying Binet staging revealed that stage C was the most frequent stage in our patients (56.8%) followed by stage B (25%) and stage A (18.2%). Table-I shows distribution of CLL patients according to age, gender, Rai and Binet Stage.

Mean Hb was 10.7g/dL, mean TLC was 82.6x10^9/L and Mean platelet count 197.9x10^9/L. Anemia was seen in 45.5% and thrombocytopenia in 34.1%.

Bone marrow was infiltrated in 100% patients. The commonest pattern of infiltration was diffuse seen in 65% patients. In immunohistochemistry profile, CD20 and CD5 were positive in all of the cases (100%) while CD23 in 96%. Seropositivity was present in 2.3% for both Anti HCV and HBsAg. LDH was elevated in 12% of our patients.

Table-II shows clinicohematological features of our patients.

Characteristic	Rai						Binet			
	0	I	II	III	IV	P-Value	A	B	C	P-Value
Age group										
<55 years	3	6	4	6	7	0.128	3	10	3	0.036
≥55 years	5	0	1	6	6		5	1	12	
Gender										
Male	4	5	3	9	10	0.604	4	8	19	0.367
Female	4	1	2	3	3		4	3	6	

Table-I. Distribution (n=44) of CLL patients according to age, gender, Rai and Binet stage

Characteristic	<55 Years	≥55 Years	P-Value	Male	Female	P-Value
Mean age	43 years	62 years	**0.000**	51 years	50.6 years	0.924
Mean Hb	11.0g/dL	10.3g/dL	0.274	10.6g/dL	10.9g/dL	0.765
Mean TLC	$104.6x10^9$/L	$50.7x10^9$/L	0.414	$99.9x10^9$/L	$41.3x10^9$/L	0.411
Mean platelet count	$197x10^9$/L	$198x10^9$/L	0.969	$195x10^9$/L	$204x10^9$/L	0.836
Hepatomegaly	03	04	0.419	06	01	0.654
Splenomegaly	07	07	0.211	10	04	0.769
Lymphadenopathy	12	07	0.760	16	09	0.335
B symptoms	18	13	1.000			
Anemia	11	09	0.760	17	03	0.096
Thrombocytopenia	09	06	1.000	12	03	0.488

Table-II. Clinicohematological parameters of CLL patients

DISCUSSION

The study results indicate that CLL is present in 70.5 % of males and 29.5 % of females with M:F ratio of 2.3:1. This is consistent with local[10] and western data (3.3:1) but different from a Nigerian study where M:F ratio was 1:3.[11]

The mean age of diagnosis in our patients was 51±12.6 years which corroborates with results of Bernard et al who reported it to be 58.5 years.[12] However mean age in another local study of Lahore and a Turkish study was higher than ours (62.8 years[13] and 71 years respectively).[14]

B symptoms were seen in 71 % of our patients consistent with a local study of Peshawar where they were seen in 70.6%.[4] Lymphadenopathy was present in 43.2 % in our study which is similar to 51.4% according to Demir C et al.[15] The frequency of splenic enlargement in our study was lower (32%) as compared to an Indian study by Lal Chand et al who has quoted it to be 40.8%.[16] Our study results showed evidence of hepatic enlargement in 15.9% of patients which is lower than 29.1% in Nigerian population.[17]

Bone marrow was infiltrated in 100% of our patients which is higher than 53-60% as reported by Moreno C et al.[18] The most common pattern of bone marrow infiltration was diffuse seen in 65% patients. Our findings are in contrast to an Italian study where non diffuse pattern was the most common pattern of bone marrow infiltration.[19] However our results are in accordance to local and Chinese data.[10]

Anti HCV and HBsAg positivity was seen in 2.3% of our patients as compared to 4.3% for anti HCV reported by Gharagozloo S et al[20] and 10% for HBsAg by Rossi D et al.[21]

Mean Hb was10.7g/dL, mean TLC was $82.6x10^9$/L and Mean platelet count $197.9x10^9$/L in our study which is consistent with a local study conducted in Karachi.[10] Whereas our values of Hb and platelet count are lower and TLC higher than a Turkish study where Hb was 12.7g/dL, TLC was $19.8x10^9$/L and platelet count was $202x10^9$/L.[22]

Out of 44 patients enrolled, 45.5% were anemic while 34.1% had thrombocytopenia. Our data is comparable to results of Sudanese study by Basabaeen et al where 34.5% were anemic and 39.1% were thrombocytopenic.[23]

Most of our patients (56.8%) presented with advanced stage disease i-e Binet stage C. This is similar to 60.5% according to Bernard et al but higher than reported by KG Koffi (28.5%) and Boukhari S (29.3%)[12] where most of patients presented with early stage disease. Patients from other developing countries such as India and Nigeria also presented with advanced stage.[24,25]

CD20 was positive in all of our patients which is similar to 94.5% according to Delgado J et al.[26] Similarly CD23 positivity (96%) and CD5 positivity in 100% patients is also consistent with reported literature.[27]

CONCLUSION

Our study results indicate few notable differences to other local and international studies such as younger age, advanced stage disease

at presentation, diffuse pattern of marrow involvement, less frequent hepatosplenomegaly and hepatitis B and C seropositivity.

REFERENCES

1. Rashid U, Rashid A, Virk S, Rafiq H, Zia R. **Auto Immune Haemolytic in Chronic Lymphocytic Leukaemia (CLL).** Pakistan journal of medical & health sciences. 2018; 12(1):349-51.

2. Salem DA, Stetler-Stevenson M. **Clinical Flow-Cytometric Testing in Chronic Lymphocytic Leukemia.** In Immunophenotyping 2019 pp. 311-321.

3. Khan AR, Ahmad M, Khan SA. **Analysis of clinicoepidemiological features of leukemia at a tertiary care facility in Peshawar.** Journal of Medical Sciences. 2018; 26(1):41-5.

4. Marti G, Abbasi F, Raveche E, Rawstron AC, Ghia P, Aurran T, Caporaso N, Shim YK, Vogt RF. **Overview of monoclonal B□cell lymphocytosis.** British journal of haematology. 2007; 139(5):701-8.

5. Shim YK, Rachel JM, Ghia P, Boren J, Abbasi F, Dagklis A, Venable G, Kang J, Degheidy H, Plapp FV, Vogt RF. **Monoclonal B-cell lymphocytosis in healthy blood donors: An unexpectedly common finding.** Blood, The Journal of the American Society of Hematology. 2014; 123(9):1319-26.

6. Hallek M. **Chronic lymphocytic leukemia: 2017 update on diagnosis, risk stratification, and treatment.** American journal of hematology. 2017; 92(9):946-65.

7. Ahmad Z, Idress R, Fatima S, Uddin N, Ahmed A, Minhas K, Memon A, Fatima SS, Arif M, Hasan SH, Ahmed R. **Commonest cancers in Pakistan-findings and histopathological perspective from a premier surgical pathology center in Pakistan.** Asian Pac J Cancer Prev. 2016; 17(3):1061.

8. Shabir S, Ahmed KN, Marri M, Mengal M, Jan MH, Jamali MS, Anwar N, Khanum S, Ahmed S. **Epidemiological features of Lymphoma in Pakistan.** Pure Appl. Biol. 2019; 8(1): 977-994.

9. Abid MB, Nasim F, Anwar K, Pervez S. **Diffuse large B cell lymphoma (DLBCL) in Pakistan: An emerging epidemic?** Asian Pac J Cancer Prev. 2005; 6(4):531-534.

10. Zeeshan R, Sultan S, Irfan SM, Kakar J, Hameed MA. **Clinico-hematological profile of patients with B-chronic lymphoid leukemia in Pakistan.** Asian Pac J Cancer Prev. 2015; 16(2):793-6.

11. Hallek M. **Chronic lymphocytic leukemia: 2020 update on diagnosis, risk stratification and treatment.** American journal of hematology. 2019; 94(11):1266-87.

12. Bernard CC, Sack FN, Sango A, Lontsi E, Njedock N. **Demographic and clinical enumeration of patients of CLL: Experience of the Hematology-oncology department of the Central Hospital of Yaounde.** Asian Hematology Research Journal. 2020:24-9.

13. Ehsan AY, Lone A, Khan MA. **Autoimmune complications in chronic lymphocytic leukemia: A single center experience.** Biomedica. 2013; 29:37-41.

14. Umit EG. **CD8 expression on clonal b-cll cells and CD8+ lymphocytes in the microenvironment, relations with prognosis and survival.** Eastern Journal of Medicine. 2018; 23(4):237.

15. Demir C, Kara E, Ekinci Ö, Ebinç S. **Clinical and laboratory features of CD5-negative chronic lymphocytic leukemia. Medical Science Monitor:** International Medical Journal of Experimental and Clinical Research. 2017; 23:2137.

16. Lalchandjain JP. **Clinical and biological features of chronic lymphocytic leukemia a single tertiary centre experience from India.** University Journal of Medicine and Medical Specialities. 2017; 2(7).

17. Salawu L, Bolarinwa R, Durosinmi M. **Chronic lymphocytic leukaemia: A-twenty-years experience and problems in Ile-Ife, South-Western Nigeria.** Afr Health Sci. 2010 Jun; 10(2):187-92.

18. Moreno C, Hodgson K, Ferrer G, Elena M, Filella X, Pereira A, Baumann T, Montserrat E. **Autoimmune cytopenia in chronic lymphocytic leukemia: Prevalence, clinical associations, and prognostic significance.** Blood, The Journal of the American Society of Hematology. 2010; 116(23):4771-6.

19. Zanotti R, Ambrosetti A, Lestani M, Ghia P, Pattaro C, Remo A, Zanetti F, Stella S, Perbellini O, Prato G, Guida G. **ZAP-70 expression, as detected by immunohistochemistry on bone marrow biopsies from early-phase CLL patients, is a strong adverse prognostic factor.** Leukemia. 2007; 21(1):102-9.

20. Gharagozloo S, Khoshnoodi J, Shokri F. **Hepatitis C virus infection in patients with essential mixed cryoglobulinemia, multiple myeloma and chronic lymphocytic leukemia.** Pathology Oncology Research. 2001; 7(2):135-9.

21. Rossi D, Sala L, Minisini R, Fabris C, Falleti E, Cerri M, Burlone ME, Toniutto P, Gaidano G, Pirisi M. **Occult hepatitis B virus infection of peripheral blood mononuclear cells among treatment-naive patients with chronic lymphocytic leukemia.** Leukemia & lymphoma. 2009; 50(4):604-11.

22. Falay M, Özet G. **Immunophenotyping of chronic lymphocytic leukemia.** Clin Lab. 2017; 63(10):1621-6.

23. Basabaeen AA, Abdelgader EA, Babekir EA, Eltayeb NH, Altayeb OA, Fadul EA, Bahashwan OS, Ibrahim IK. **Clinical presentation and hematological profile among young and old chronic lymphocytic leukemia patients in Sudan.** BMC research notes. 2019; 12(1):202.

24. Gogia, A. Sharma, V. Raina, et al. **Clinico-hematological characteristics and outcome assessment of patients with chronic lymphocytic leukemia.** J Clin Oncol. 2011; 29(15_suppl):6584-6584.

25. Omoti CE, Awodu OA, Bazuaye GN. **Chronic lymphoid leukaemia: Clinico-haematological correlation and outcome in a single institution in Niger Delta region of Nigeria.** Int J Lab Hematol. 2007; 29:426-32.

26. Delgado J, Matutes E, Morilla AM, Morilla RM, Owusu-Ankomah KA, Rafiq-Mohammed F, Giudice ID, Catovsky D. **Diagnostic significance of CD20 and FMC7 expression in B-cell disorders.** American journal of clinical pathology. 2003; 120(5):754-9.

27. Finn WG, Thangavelu M, Yelavarthi KK, Goolsby CL, Tallman MS, Traynor A, Peterson LC. **Karyotype correlates with peripheral blood morphology and immunophenotype in chronic lymphocytic leukemia.** American journal of clinical pathology. 1996; 105(4):458-67.

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2	Hajrah Syndeed	Data acqusition, Data entry, final approval of manuscript.	
3	Khadija Naeem	Data acquisition, data entry final approval of manuscript.	
4	Maria Batool	Data acquisition, data entry final approval of manuscript.	
5	Muhammad Asif Naveed	Critical review of manuscript, final approval of manuscript.	
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