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Laboratory analysis of 182 cases of B-cell lymphoproliferative disorders other than typical chronic lymphocytic leukemia: Single-center study

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Abstract:

BACKGROUND: Chronic mature B-cell lymphoproliferative disorders (B-LPDs) are characterized by the clonal proliferation of mature B-lymphocytes in the peripheral blood (PB), bone marrow, and lymphoid tissues. These disorders are classified based on morphology, flow cytometry (FC), biological features, and genetics.

OBJECTIVES: This study aimed to characterize the demographic and clinical features of patients and to analyze their immunophenotypic profiles.

MATERIALS AND METHODS: This retrospective study examined 182 cases of non-CLL B-LPDs diagnosed over 2 years (April 2022–March 2024) at Baghdad Medical City Complex. Data included patient demographics, clinical features, complete blood count (CBC) parameters, PB absolute lymphocyte count (ALC), and immunophenotypic profiles. FC utilizing the BD FACSCanto™ II System and immunophenotypic markers was assessed to establish diagnostic subtypes. Statistical analysis was performed using SPSS version 25.

RESULTS: The most common subtypes included marginal zone lymphoma (MZL) (30.2%), mantle cell lymphoma (MCL) (24.7%), and splenic MZL (13.7%). Age at diagnosis varied significantly among subtypes, with a median of 61 years. Immunophenotypic analysis revealed distinct patterns, such as CD5 positivity in MCL and atypical CLL, CD200 negativity differentiating MCL from other disorders, and CD10 positivity in follicular lymphoma (FL). CBC parameters exhibited significant variability, with elevated ALC in atypical CLL and distinct anemia and thrombocytopenia profiles in diffuse large B-cell lymphoma subtypes.

CONCLUSION: This study highlights the diagnostic and clinical heterogeneity of non-CLL B-LPDs, emphasizing the critical role of FC and immunophenotypic markers in subtype differentiation. Age and hematological parameters displayed significant variability, reflecting biological diversity. Immunophenotypic analysis revealed distinct patterns, such as CD5 positivity in MCL and atypical CLL, CD200 negativity differentiating MCL from other disorders, and CD10 positivity in FL. These findings provide insights into the diagnostic challenges and underscore the importance of tailored approaches in resource-limited settings.

Keywords:

B lymphocyte, leukemia, lymphoma, lymphoproliferative

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Introduction

Lymphoproliferative disorders (LPDs) encompass a diverse group of diseases affecting B lymphocytes, T lymphocytes, or natural killer cells at various stages of development. Among these, chronic mature B-cell LPDs (B-LPDs) are characterized by the clonal proliferation of mature B-lymphocytes within the peripheral blood (PB), bone marrow (BM), and lymphoid tissues.[1,2]

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The World Health Organization (WHO) classifies LPDs using a comprehensive approach that incorporates morphology, flow cytometry (FC), biological characteristics, and genetic profiling. The latest WHO classification of hematolymphoid neoplasms identifies 12 major subcategories of B-cell malignancies, which include preneoplastic and neoplastic small lymphocytic proliferative B-cell lymphomas and leukemias, lymphoplasmacytic lymphoma (LPL), marginal zone lymphoma (MZL), follicular lymphoma (FL), mantle cell lymphoma (MCL), large B-cell lymphomas (LBCL), and Burkitt lymphoma (BL), among others.[3,4] Chronic lymphocytic leukemia (CLL) is the most common B-LPD in Western populations, although other subtypes present diagnostic challenges.[5]

Common clinical features include lymphadenopathy, splenomegaly (SMG), fatigue, cytopenia, or incidental lymphocytosis detected on routine complete blood counts (CBCs). Diagnosis requires morphological examination and immunophenotyping of PB or BM samples, with additional studies on effusions, cerebrospinal fluid, or disaggregated lymph nodes as needed.[6,7]

Genetic analyses, such as fluorescence *in situ* hybridization or next-generation sequencing, are employed for cases with inconclusive findings or to detect hallmark translocations in specific diseases such as FL and MCL.[8]

The prevalence of LPD was assessed in a study by Al-Saadi and Abdulnabi at the National Center of Hematology and found to be different from the literature.[9]

Despite their clinical significance, limited data is addressing these disorders, particularly in Iraq. By analyzing key hematological parameters, clinical presentations, and immunophenotypic profiles of 182 cases, this study aims to bridge gaps in the understanding of non-CLL LPDs. The findings have the potential to enhance diagnostic accuracy, facilitate early intervention, and support the development of personalized therapeutic approaches, aligning with the principles of precision medicine. We aim to contribute to the existing knowledge database of these diseases, particularly in our region, as the Baghdad Medical City Complex center is a primary center of FC that receives patients nationwide, and to support more refined diagnostic and therapeutic approaches in managing non-CLL B-LPDs.

Subjects and Methods

Study design

This retrospective study aimed to characterize non-CLL B-LPD patient cases as per demographics, clinical features, and cellular markers using data from the FC unit in the Baghdad Medical City Complex. It analyzed the demographic distribution (gender and age) of patients, hemoglobin (Hb) level, and white blood cell (WBC) and platelets counts (collectively referred to as CBC parameters in this article) in both genders, assess the clinical features and absolute lymphocyte count (ALC) in PB, evaluate the expression of CD markers and their implications for diagnosis and prognosis.

Data collection

Newly diagnosed non-CLL LPD cases (April 2022–April 2024) were retrospectively reviewed. Data included demographics (age, gender), clinical features, CBC parameters, ALC in PB, and immunophenotypic markers from PB/BM samples collected in K3-EDTA tubes made in China (13 mm × 75 mm each). CBC was performed using an XN-330™ automated hematology analyzer (Sysmex Corporation, Japan) and a BD FACSCanto II Flow cytometer (Becton, Dickinson and Company, USA), providing the CD marker kits.

Inclusion criteria

Newly diagnosed B-cell non-CLL LPD cases of all ages with complete data.

Exclusion criteria

Secondary LPDs and incomplete data.

Variables

Demographics, hematological parameters (Hb, WBC, platelets, ALC), clinical features, and immunophenotypic markers (e.g. CD5, CD10, CD20, kappa/lambda light chains).

Key flow cytometry criteria: CD5-positive disorders

- Atypical CLL: Matutes score ≤3, weak CD81, strong CD43, or CD200, excluding MCL through genetic testing for translocation t(11;14)(q13;q32), cycling D1 overexpression, and SOX11 expression, according to the availability of testing kits in the genetics unit
- MCL: Matutes score <3, dim CD23, bright CD20/CD22, negative CD200, with positive genetic testing for translocation t(11;14)(q13;q32), cycling D1 overexpression, or SOX11 expression, according to the availability of testing kits in the genetics unit.

CD5-negative disorders

- LPL: Immunoglobulin (Ig) M peak, dim CD22, CD25 positive
- FL: Positive CD10, CD19, CD20, CD22; dim CD19
- Hairy cell leukemia (HCL): Positive CD123, CD103, CD25, CD11c
- MZL: No IgM peak, positive CD19, CD20, CD22, CD24; negative CD5, CD10, CD200
- Splenic MZL (SMZL): Negative CD5, CD10; positive CD24

- BL: Dim CD45, positive CD19, CD10, CD20 (bright), negative CD5
- Diffuse LBCL (DLBCL): Positive CD19, CD20 (dim in some cases), often CD10 on germinal center (GC) type.

Hans algorithm is used to diagnose DLBCL. Activated B cell (ABC) cases are considered (CD10−, BCL6±, MUM1+), and GC cases are (CD10±, BCL6+, MUM1−).

Data analysis

Data analysis was conducted using version 25.0 of the Statistical Package for the Social Sciences (SPSS) (International Business Machines Corporation (IBM Corp.), New York, United States). Results were presented as mean ± standard deviation (SD) for normally distributed data, whereas nonnormally distributed data were expressed as medians (minimum-maximum). Categorical data were summarized using frequencies and percentages. The Chi-square and Fisher's exact tests were applied to assess correlations between categorical variables and the distribution of patients in groups. Differences in clinical notes between gender subgroups were examined using the Mann–Whitney *U*-test. Comparisons of variables across disease subtypes were carried out using the ANOVA *F*-test with *post hoc* least significant difference analysis for normally distributed data and the Kruskal–Wallis *H*-test with *post hoc* Dunn test for nonnormally distributed data. A *P* value was calculated at a 95% confidence interval.

Ethical considerations

The study was approved by the FC Unit's institutional authority. Owing to its retrospective design, strict measures were implemented to ensure patient confidentiality and privacy. All identifiable patient information was removed from the records, and each case was assigned a unique code number. Patients or their legal guardians were informed in advance about the potential inclusion of their cases in this study.

Results

One hundred and eighty-two patient cases of B-LPD were collected.

Patients' demographics

The mean age of diagnosis was around 61 years. Males were more than females [Table 1].

Disease categorization

Most patients were diagnosed with MZL, followed by MCL. A single case of FL was documented [Table 2].

Patient age and gender are related to their diagnosis

The highest age group (around 70 years) was diagnosed with LPL, whereas the youngest group was diagnosed with atypical CLL. The highest percentage of male patients were diagnosed with MCL, followed by MZL, whereas the highest percentage of female patients were diagnosed with MZL, followed by MCL. Age was found to play a significant role in the final diagnosis of patients, whereas gender did not show any significant correlation to the final diagnosis [Table 3].

A significant age difference was noticed in diagnosing patients with atypical CLL versus HCL, atypical CLL versus BL, DLBCL-ABC and HCL, DLBCL-ABC and BL, DLBCL-GC and HCL, DLBCL-GC and BL, MCL and HCL, MCL and BL, SMZL and HCL, and BL [Table 4].

Hematological parameters

Values of Hb level, WBC count, platelet count, and absolute lymphocyte count displayed non-Gaussian distribution among different categories of diagnosis, with *P* values showing significant differences in CBC parameters among disease categories [Table 5].

On the other hand, differences in hematological parameters between diseases were studied. A significant difference was noticed between atypical CLL and SMZL in WBC count, platelet count, and ALC. DLBCL-ABC and SMZL also showed a significant difference in Hb and WBC count. Other details are displayed in Table 6.

Clinical features

Patients presented mainly with Lymphadenopathy (LAP), weight loss, fever, night sweats, fatigue, bleeding,

Table 1: Patient's demographics

Variables	*n*=182, *n* (%)
Age (year), mean±SD	61.20±15.43
Gender	
Male	97 (53.3)
Female	85 (46.7)

SD=Standard deviation

Table 2: Disease categories of the study population

Diagnosis	Subjects, *n* (%)
MZL	55 (30.2)
MCL	45 (24.7)
SMZL	25 (13.7)
HCL	24 (13.2)
DLBCL-ABC	11 (6.0)
DLBCL-GC	6 (3.3)
Atypical CLL	6 (3.3)
LPL	5 (2.7)
BL	4 (2.2)
FL	1 (0.5)
Total	182 (100)

DLBCL-ABC=Diffuse large B-cell lymphoma-activated B cell, DLBCL-GC=Diffuse large B-cell lymphoma-germinal center, FL=Follicular lymphoma, BL=Burkitt lymphoma, LPL=Lymphoplasmacytic lymphoma, CLL=Chronic lymphocytic leukemia, HCL=Hairy cell leukemia, SMZL=Splenic marginal zone lymphoma, MCL=Mantle cell lymphoma, MZL=Marginal zone lymphoma

Table 3: Patient's age and gender in relation to the final diagnosis

Diagnosis	Age (mean±SD)	Gender	
		Male♂, *n* (%)	Female♀, *n* (%)
Atypical CLL	61.5±13.42	1 (0.6)	5 (2.8)
DLBCL-ABC	67.72±9.54	4 (2.2)	7 (3.9)
DLBCL-GC	63.50±22.85	2 (1.1)	4 (2.2)
MCL	65.91±12.42	27 (14.9)	18 (9.9)
SMZL	64.20±11.83	14 (7.7)	11 (6.1)
MZL	62.60±11.82	26 (14.4)	29 (16)
HCL	49.83±11.74	16 (8.8)	8 (4.4)
LPL	70.80±6.76	5 (2.8)	0
BL	7.25±3.30	2 (1.1)	2 (1.1)
ANOVA	*F* test=14.35	χ^2=13.27	
	P=<0.001*	*P*=0.103 (NS)	

A statistically significant difference in disease type was observed across age groups, while no significant difference was found based on gender. *Significant difference. NS=Nonsignificant, CLL=Chronic lymphocytic leukemia, DLBCL GC=Diffuse large B cell lymphoma germinal center, DLBCL ABC=Diffuse large B cell lymphoma activated B cell, HCL=Hairy cell leukemia, SMZL=Splenic marginal zone lymphoma, MCL=Mantle cell lymphoma, MZL=Marginal zone lymphoma, LPL=Lymphoplasmacytic lymphoma, BL=Burkitt lymphoma, SD=Standard deviation

SMG, and hepatosplenomegaly, pallor, bone pain, and backache. These clinical features were compared between diseases using Chi-square testing with a $P = 0.05$. LAP, fever, SMG, and backache have shown significant differences among patients, with higher percentages of presentation in atypical CLL, MZL, SMZL, and LPL, respectively.

The variation of these clinical features at presentation was studied between male and female patients using Chi-square and Fisher's exact tests, showing a nonsignificant difference between the two genders with a $P > 0.05$. Furthermore, patients' age was studied in relation to the presenting clinical features, with the highest age for LAP and the youngest age for fever and bleeding, with a statistically insignificant difference [Table 7].

The variation of clinical presentation between male and female patients was studied using the Mann–Whitney *U*-test, yielding a nonsignificant difference between the two genders with a $P = 0.551$. Moreover, the clinical features mentioned beforehand were assessed among the different disease categories using the Kruskal–Wallis *H*-test, which showed a $P = 0.064$, indicating a nonsignificant difference.

The immunophenotype of the study population

CD5, CD10, CD23, CD200, CD31, CD11c, Kappa light chain restriction, CD38, LAIR, surface IgM, FMC7, CD117, and CD56 have shown statistically significant differences among the disease categories, with highest percentages in MCL, HCL, MZL, MZL, HCL, MZL, MZL, MCL, MZL, MCL, HCL, and HCL, respectively. Other CDs are shown in Table 8.

Table 4: Age comparison among B-cell lymphoproliferative disorder categories *post hoc* ANOVA-least significant difference test

Groups		*P*, age (year)
Atypical CLL	DLBCL-ABC	0.315 (NS)
Atypical CLL	DLBCL-GC	0.776 (NS)
Atypical CLL	MCL	0.406 (NS)
Atypical CLL	SMZL	0.626 (NS)
Atypical CLL	MZL	0.834 (NS)
Atypical CLL	HCL	0.037*
Atypical CLL	LPL	0.209 (NS)
Atypical CLL	BL	<0.001*
DLBCL-ABC	DLBCL-GC	0.495 (NS)
DLBCL-ABC	MCL	0.658 (NS)
DLBCL-ABC	SMZL	0.425 (NS)
DLBCL-ABC	MZL	0.204 (NS)
DLBCL-ABC	HCL	<0.001*
DLBCL-ABC	LPL	0.641 (NS)
DLBCL-ABC	BL	<0.001*
DLBCL-GC	MCL	0.649 (NS)
DLBCL-GC	SMZL	0.900 (NS)
DLBCL-GC	MZL	0.864 (NS)
DLBCL-GC	HCL	0.015*
DLBCL-GC	LPL	0.324 (NS)
DLBCL-GC	BL	<0.001*
MCL	SMZL	0.574 (NS)
MCL	MZL	0.178 (NS)
MCL	HCL	<0.001*
MCL	LPL	0.396 (NS)
MCL	BL	<0.001*
SMZL	MZL	0.587 (NS)
SMZL	HCL	<0.001*
SMZL	LPL	0.270 (NS)
SMZL	BL	<0.001*
MZL	HCL	<0.001*
MZL	LPL	0.151 (NS)
MZL	BL	<0.001*
HCL	LPL	0.001*
HCL	BL	<0.001*
LPL	BL	<0.001*

*Significant difference. NS=Nonsignificant, CLL=Chronic lymphocytic leukemia, DLBCL-GC=Diffuse large B-cell lymphoma-germinal center, DLBCL-ABC=Diffuse large B-cell lymphoma-activated B cell, HCL=Hairy cell leukemia, SMZL=Splenic marginal zone lymphoma, MCL=Mantle cell lymphoma, MZL=Marginal zone lymphoma, LPL=Lymphoplasmacytic lymphoma, BL=Burkitt lymphoma, SD=Standard deviation

Discussion

B-LPDs are heterogeneous disorders ranging from indolent to aggressive forms, often presenting with lymphadenopathy, SMG, fatigue, or abnormal CBC results.[7]

This study analyzed 182 cases, with diagnoses based on absolute lymphocytosis, morphology, clinical findings, FC monoclonality, light chain restriction, and, when available, BM examination and immunohistochemistry. Key FC criteria were followed. They are mentioned in

Table 5: Hematological parameters in the study population

Diagnosis, median (minimum–maximum)	Hb (g/dL)	WBC, (×10⁹/L)	Platelets (×10⁹/L)	ALC, (×10⁹/L)
Atypical CLL	8.75 (7.0–13.4)	27.0 (18.0–30.0)	133.0 (100.0–150.0)	14.0 (9.0–21.0)
DLBCL-ABC	9.0 (5.0–13.0)	21.0 (12.0–142.0)	141.0 (90.0–381.0)	9.0 (4.0–112.0)
DLBCL-GC	8.5 (6.0–10.0)	12.0 (2.0–54.0)	85.5 (15.0–165.0)	7.0 (1.0–20.0)
MCL	9.0 (6.0–14.0)	19.0 (3.0–110)	130.0 (18.0–310.0)	9.0 (0.9–77.0)
SMZL	12.0 (9.0–13.0)	10.0 (6.0–64.0)	187.0 (43.0–446.0)	6.0 (3.0–50.0)
MZL	10.0 (6.0–16.0)	16.0 (2.0–135.0)	170.0 (8.0–314.0)	8.0 (1.6–114.0)
HCL	7.0 (5.0–14.0)	3.6 (1.2–43.0)	90.0 (32.0–200.0)	2.0 (0.8–33.0)
LPL	11.0 (4.0–13.0)	12.0 (11.0–24.0)	161.0 (14.0–188.0)	8.0 (7.6–117.0)
BL	8.75 (8.2–9.0)	20.0 (10.0–28.0)	117.5 (100.0–306.0)	10.0 (6.0–12.0)
Kruskal–Wallis *H*-test value	38.24	46.98	42.31	36.97
P	<0.001*	<0.001*	<0.001*	<0.001*

*Significant difference. NS=Nonsignificant, CLL=Chronic lymphocytic leukemia, DLBCL-GC=Diffuse large B-cell lymphoma-germinal center, DLBCL-ABC=Diffuse large B-cell lymphoma-activated B cell, HCL=Hairy cell leukemia, SMZL=Splenic marginal zone lymphoma, MCL=Mantle cell lymphoma, MZL=Marginal zone lymphoma, LPL=Lymphoplasmacytic lymphoma, BL=Burkitt lymphoma, WBC=White blood cell, ALC=Absolute lymphocyte count, Hb=Hemoglobin

Table 6: Comparing hematological parameters in relation to the final diagnosis-*post hoc* Kruskal–*H* Wallis Dunn test

Groups		*P*			
		Hb (g/dL)	WBC (×10⁹/L)	Platelets (×10⁹/L)	ALC (×10⁹/L)
Atypical CLL	DLBCL-ABC	0.695 (NS)	0.769 (NS)	0.304 (NS)	0.496 (NS)
Atypical CLL	DLBCL-GC	0.238 (NS)	0.060 (NS)	0.437 (NS)	0.032 (NS)
Atypical CLL	MCL	0.522 (NS)	0.245 (NS)	0.706 (NS)	0.103 (NS)
Atypical CLL	SMZL	0.128 (NS)	0.019*	0.047*	0.025*
Atypical CLL	MZL	0.641 (NS)	0.127 (NS)	0.190 (NS)	0.082 (NS)
Atypical CLL	HCL	0.067 (NS)	<0.001*	0.123 (NS)	<0.001*
Atypical CLL	LPL	0.605 (NS)	0.116 (NS)	0.662 (NS)	0.259 (NS)
Atypical CLL	BL	0.500 (NS)	0.422 (NS)	0.773 (NS)	0.357 (NS)
DLBCL-ABC	DLBCL-GC	0.342 (NS)	0.065 (NS)	0.065 (NS)	0.078 (NS)
DLBCL-ABC	MCL	0.814 (NS)	0.290 (NS)	0.287 (NS)	0.282 (NS)
DLBCL-ABC	SMZL	0.014*	0.011*	0.291 (NS)	0.061 (NS)
DLBCL-ABC	MZL	0.227 (NS)	0.125 (NS)	0.899 (NS)	0.224 (NS)
DLBCL-ABC	HCL	0.080 (NS)	<0.001*	0.001*	<0.001*
DLBCL-ABC	LPL	0.343 (NS)	0.136 (NS)	0.633 (NS)	0.530 (NS)
DLBCL-ABC	BL	0.685 (NS)	0.528 (NS)	0.565 (NS)	0.670 (NS)
DLBCL-GC	MCL	0.353 (NS)	0.181 (NS)	0.159 (NS)	0.221 (NS)
DLBCL-GC	SMZL	0.003*	0.967 (NS)	0.003*	0.633 (NS)
DLBCL-GC	MZL	0.04*	0.317 (NS)	0.019*	0.252 (NS)
DLBCL-GC	HCL	0.735 (NS)	0.064 (NS)	0.577 (NS)	0.146 (NS)
DLBCL-GC	LPL	0.101 (NS)	0.825 (NS)	0.239 (NS)	0.359 (NS)
DLBCL-GC	BL	0.704 (NS)	0.378 (NS)	0.325 (NS)	0.318 (NS)
MCL	SMZL	<0.001*	0.024 (NS)	0.003*	0.207 (NS)
MCL	MZL	0.017*	0.451 (NS)	0.047*	0.845 (NS)
MCL	HCL	0.027*	<0.001*	0.001*	<0.001*
MCL	LPL	0.210 (NS)	0.342 (NS)	0.831 (NS)	0.960 (NS)
MCL	BL	0.762 (NS)	0.980 (NS)	0.966 (NS)	0.828 (NS)
SMZL	MZL	0.042*	0.088 (NS)	0.158 (NS)	0.253 (NS)
SMZL	HCL	<0.001*	0.002*	<0.001*	0.002*
SMZL	LPL	0.440 (NS)	0.814 (NS)	0.191 (NS)	0.490 (NS)
SMZL	BL	0.036*	0.307 (NS)	0.182 (NS)	0.427 (NS)
MZL	HCL	<0.001*	<0.001*	<0.001*	<0.001*
MZL	LPL	0.810 (NS)	0.526 (NS)	0.522 (NS)	0.893 (NS)
MZL	BL	0.219 (NS)	0.789 (NS)	0.466 (NS)	0.768 (NS)
HCL	LPL	0.019*	0.046*	0.049*	0.013*
HCL	BL	0.459 (NS)	0.009*	0.1 (NS)	0.015*
LPL	BL	0.264 (NS)	0.517 (NS)	0.907 (NS)	0.893 (NS)

*Significant difference. NS=Nonsignificant, CLL=Chronic lymphocytic leukemia, DLBCL-GC=Diffuse large B-cell lymphoma-germinal center, DLBCL-ABC=Diffuse large B-cell lymphoma-activated B cell, HCL=Hairy cell leukemia, SMZL=Splenic marginal zone lymphoma, MCL=Mantle cell lymphoma, MZL=Marginal zone lymphoma, LPL=Lymphoplasmacytic lymphoma, BL=Burkitt lymphoma, WBC=White blood cell, ALC=Absolute lymphocyte count, Hb=Hemoglobin

Table 7: Patients clinical presentation in relation to their age

Clinical notes	*n*	Patients age (year), mean±SD	Median (maximum–minimum)
LAP	49	64.57±14.54	67 (5–92)
Weight loss	3	62.66±1.15	62 (62–64)
Fever	48	57.12±17.67	58.50 (5–80)
Fatigue	46	61.63±14.90	65 (5–80)
Splenomegaly	53	62.07±13.44	63 (26–90)
Pallor	72	59.81±17.11	64 (5–90)
Hepatosplenomegaly	25	60.40±15.98	62 (5–80)
ANOVA		*F* test=1.04 *P*=0.39 (NS)	
Bone pain	2	58.0±9.89	(51–65)
Bleeding	2	29.50±34.64	(5–54)
Backache	1	-	-
Night sweat	1	-	-

NS=Nonsignificant, SD=Standard deviation, LAP=Lymphadenopathy

the methods section. The findings are consistent with the WHO 5th edition and literature reviews, highlighting the diagnostic complexity within resource constraints.[3,7]

In this study, male patients outnumbered females, with an average age of 61 at diagnosis, aligning with Smith *et al.*'s findings in Britain, where males had a higher incidence of mature B-cell lymphomas.[10]

All cases were classified as non-Hodgkin lymphoma (NHL), likely due to the study's focus on FC results, as Hodgkin lymphoma is primarily diagnosed histologically. NHL incidence has risen over the past decade, potentially linked to HIV-related lymphomas, carcinogen exposure, and improved diagnostics, as noted by Paudyal *et al*.[11]

The common subtypes in this study were MZL, MCL, and SMZL. In contrast, DLBCL was the most frequent adult lymphoma in studies from Nepal, Jordan, and China.[11-13] FL was rare, with only one case, whereas it was the second-most common in China.[13] East India reported a lower FL incidence compared to Western countries.[14]

Age significantly influenced diagnoses, with most patients in their 60s. BL primarily affected children, and LPL was observed in patients in their 70s. Gender showed no significant impact. These findings align with Allegra A *et al.*, who noted age related predisposition due to genetic and environmental factors.[15]

Significant age differences were observed among atypical CLL, HCL, BL, DLBCL, MCL, and SMZL, which is consistent with the established data. CLL is commonly diagnosed in older adults (median age 72), HCL at a median age of 55, BL in children and adolescents, DLBCL in those aged 65–74, MCL with a median age of 65, and SMZL at an average age of 67. These patterns agree with studies by Bohn *et al.* and others.[16-21] This significant age difference among various categories of LPD can be attributed to differences in their underlying biology, genetic alterations, immune function, level of B cell maturation, and the cumulative effect of aging on hematopoietic cells.

CBC parameters showed significant variation among categories, with a non-Gaussian distribution. Atypical CLL accounted for 3.3% of cases, characterized by elevated ALC and WBC counts and mildly reduced platelets, aligning with typical CLL features. Disease progression is marked by anemia and thrombocytopenia. Atypical CLL was identified by >10% atypical lymphocytes on PB counts and marker expression patterns (e.g. FMC7 >20%, CD23 <20%).[22]

DLBCL comprised 9.3% of cases, with 6% ABC type and 3.3% GC type, while in the literature, it represented the most common malignant lymphoma. Diagnosis is based on the Hans algorithm.[23,24]

ABC cases showed moderate anemia, reduced platelets, and elevated WBC and ALC, reflecting its aggressive nature, BM infiltration, and systemic inflammation. GC cases exhibited moderate anemia, mild leukocytosis, and a median platelet count of 85.5 × 10^9/L, distinct from MZL and SMZL. ABC and GC cases displayed hematologic differences from SMZL (Hb and WBC values) and HCL (severe pancytopenia typical of HCL). These variations underline the impact of disease aggressiveness and associated factors.[25-28]

MCL showed significant differences from MZL in Hb levels and HCL in all CBC parameters, reflecting its aggressive nature and BM infiltration. MZL is typically indolent and differs from HCL in all CBC parameters.[28,29] SMZL varied from MZL (Hb), likely due to splenic sequestration, and differed from HCL (pancytopenia) and BL (less pronounced anemia unless advanced with BM involvement).[25,28,30]

HCL showed distinct differences from LPL in all CBC parameters and BL in WBC count and ALC, as HCL causes pancytopenia, LPL presents variable WBC counts, and BL being highly aggressive, leads to elevated WBC counts.[27]

Chi-square testing ($P < 0.05$) revealed significant differences in clinical features such as LAP, fever, SMG, and backache, prominent in atypical CLL, MZL, SMZL, and LPL, respectively. Rare features included backache (LPL) and night sweats (MCL). Other clinical features showed no significant variation, aligning with

Table 8: Immunophenotyping of the study disease categories

CDs	Atypical CLL	DLBCL-ABC	DLBCL-GC	MCL	SMZL	MZL	HCL	LPL	BL	χ^2	*P*
CD5											
Negative	0	6 (54.5)	3 (50.0)	2 (4.4)	19 (76.0)	28 (50.9)	23 (95.8)	2 (40.0)	4 (100)	74.43	<0.001*
Positive	6 (100)	5 (45.5)	3 (50.0)	43 (95.6)	6 (24.0)	27 (49.1)	1 (4.2)	3 (60.0)	0		
CD10											
Negative	6 (100)	11 (100)	1 (16.7)	44 (97.8)	25 (100)	55 (100)	15 (62.5)	4 (80)	0	97.20	<0.001*
Positive	0	0	5 (83.3)	1 (2.2)	0	0	9 (37.5)	1 (20)	4 (100)		
CD23											
Negative	4 (66.7)	10 (90.9)	6 (100)	42 (93.3)	20 (80.0)	39 (70.9)	19 (79.2)	2 (40.0)	4 (100)	17.21	0.028*
Positive	2 (33.3)	1 (9.1)	0	3 (6.7)	5 (20.0)	16 (29.1)	5 (20.8)	3 (60.0)	0		
CD200											
Negative	1 (16.7)	6 (54.5)	5 (83.3)	26 (57.8)	12 (48.0)	12 (21.8)	1 (4.2)	2 (40.0)	4 (100)	39.65	<0.001*
Positive	5 (83.3)	5 (45.5)	1 (16.7)	19 (42.2)	13 (52.0)	43 (78.2)	23 (95.8)	3 (60.0)	0		
CD43											
Negative	3 (50.0)	4 (36.4)	2 (33.3)	28 (62.2)	18 (72.0)	39 (70.9)	13 (54.2)	5 (100)	3 (75)	12.44	0.134 NS
Positive	3 (50.0)	7 (63.3)	4 (66.7)	17 (37.8)	7 (28.0)	16 (29.1)	11 (45.8)	0	1 (25)		
CD31											
Negative	3 (50.0)	9 (81.8)	4 (66.7)	31 (68.9)	21 (84.0)	25 (45.5)	3 (12.5)	2 (40.0)	4 (100)	38.96	<0.001*
Positive	3 (50.0)	2 (18.2)	2 (33.3)	14 (31.1)	4 (16.0)	30 (54.5)	21 (87.5)	3 (60.0)	0		
CD11c											
Negative	3 (50.0)	8 (72.7)	6 (100)	36 (80.0)	19 (76.0)	32 (58.2)	0	5 (100)	4 (100)	58.10	<0.001*
Positive	3 (50.0)	3 (27.3)	0	9 (20.0)	6 (24.0)	23 (41.8)	24 (100)	0	0		
Kappa											
Negative	3 (50.0)	8 (72.7)	4 (66.7)	32 (71.1)	13 (52.0)	19 (34.5)	14 (58.3)	1 (20)	3 (75)	18.88	0.015*
Positive	3 (50.0)	3 (27.3)	2 (33.3)	13 (28.9)	12 (48.0)	36 (65.5)	10 (41.7)	4 (80)	1 (25)		
Lambda											
Negative	6 (100)	7 (63.3)	2 (33.3)	32 (71.1)	21 (84.0)	44 (80.0)	19 (79.2)	4 (80)	2 (50.0)	12.29	0.139 (NS)
Positive	0 (0.00)	4 (36.4)	4 (66.7)	13 (28.9)	4 (16.0)	11 (20.0)	5 (20.8)	1 (20)	2 (50.0)		
CD38											
Negative	4 (66.7)	7 (63.3)	1 (16.7)	31 (68.9)	16 (64.0)	41 (74.5)	21 (87.5)	4 (80)	1 (25)	16.82	0.032*
Positive	2 (33.3)	4 (36.4)	5 (83.3)	14 (31.1)	9 (36.0)	14 (25.5)	3 (12.5)	1 (20)	3 (75)		
CD79b											
Negative	1 (16.7)	2 (18.2)	0	5 (11.1)	4 (16.0)	3 (5.5)	0	0	0	8.50	0.38 (NS)
Positive	5 (83.3)	9 (81.8)	6 (100)	40 (88.9)	21 (84.0)	52 (94.5)	24 (100)	5 (100)	4 (100)		
LAIR											
Negative	2 (33.3)	6 (54.5)	5 (83.3)	17 (37.8)	13 (52.0)	27 (49.1)	1 (4.2)	2 (40.0)	3 (75)	23.49	0.003*
Positive	4 (66.7)	5 (45.5)	1 (16.7)	28 (62.2)	12 (48.0)	28 (50.9)	23 (95.8)	3 (60.0)	1 (25)		
IgM											
Negative	2 (33.3)	3 (27.3)	1 (16.7)	20 (44.4)	7 (28.0)	20 (36.4)	19 (79.2)	1 (20)	0	23.15	0.003*
Positive	4 (66.7)	8 (72.7)	5 (83.3)	25 (55.6)	18 (72.0)	35 (63.6)	5 (20.8)	4 (80)	4 (100)		
IgD											
Negative	2 (33.3)	10 (90.0)	2 (33.3)	24 (53.3)	18 (72.0)	34 (61.8)	18 (75.0)	3 (60.0)	3 (75)	12.65	0.124 NS
Positive	4 (66.7)	1 (9.1)	4 (66.7)	21 (46.7)	7 (28.0)	21 (38.2)	6 (25.0)	2 (40.0)	1 (25)		
CD81											
Negative	0	0	2 (33.3)	4 (8.9)	0	3 (5.5)	3 (12.5)	0	2 (50.0)	20.71	0.008 NS
Positive	6 (100)	11 (100)	4 (66.7)	41 (91.1)	25 (100)	52 (94.5)	21 (87.5)	5 (100)	2 (50.0)		
FMC7											
Negative	6 (100)	11 (100)	6 (100)	28 (62.2)	23 (92.0)	49 (89.1)	22 (91.7)	5 (100)	4 (100)	26.59	0.001*
Positive	0	0	0	17 (37.8)	2 (8.0)	6 (10.9)	2 (8.3)	0	0		
CD27											
Negative	1 (16.7)	4 (36.4)	3 (50.0)	24 (53.3)	5 (20.0)	23 (41.8)	7 (29.2)	0	2 (50.0)	13.89	0.085 NS
Positive	5 (83.3)	7 (63.3)	3 (50.0)	21 (46.7)	20 (80.0)	32 (58.2)	17 (70.8)	5 (100)	2 (50.0)		
CD117											
Negative	6 (100)	11 (100)	6 (100)	45 (100)	25 (100)	55 (100)	6 (25.0)	5 (100)	4 (100)	130.75	<0.001*
Positive	0	0	0	0	0	0	18 (75.0)	0	0		

Contd...

Table 8: Contd...

CDs	Atypical CLL	DLBCL-ABC	DLBCL-GC	MCL	SMZL	MZL	HCL	LPL	BL	χ^2	*P*
CD56											
Negative	6 (100)	11 (100)	6 (100)	45 (100)	25 (100)	55 (100)	6 (25.0)	5 (100)	4 (100)	130.75	<0.001*
Positive	0	0	0	0	0	0	18 (75.0)	0	0		

*Significant difference. NS: Nonsignificant difference, CLL=Chronic lymphocytic leukemia, DLBCL-GC=Diffuse large B-cell lymphoma-germinal center, DLBCL-ABC=Diffuse large B-cell lymphoma-activated B cell, HCL=Hairy cell leukemia, SMZL=Splenic marginal zone lymphoma, MCL=Mantle cell lymphoma, MZL=Marginal zone lymphoma, LPL=Lymphoplasmacytic lymphoma, HCL=Hairy cell leukemia, BL=Burkitt lymphoma, Ig=Immunoglobulin, CDs=Communicable diseases

findings in the Justiz Vaillant and Stang internet-based article and Karube's *et al*'s article.[31,32]

Immunophenotyping revealed significant differences in CD5, CD10, CD23, CD200, CD31, CD11c, kappa restriction, CD38, LAIR, IgM, FMC7, CD117, and CD56 expression, aiding diagnosis. CD117 and CD56 were restricted to HCL, potentially referring to molecular heterogeneity and atypical disease behavior requiring further study.

Conclusion

This study highlights the clinical and diagnostic complexity of B-LPDs, emphasizing subtype variations in presentation, immunophenotypic profiles, and age distribution. Accurate differentiation relied on FC, morphology, and ancillary testing, with MZL, MCL, and SMZL being the most common. Immunophenotyping, particularly with markers such as CD5, CD10, CD19, and CD200, was essential for a precise diagnosis. Age-specific patterns and hematologic differences, such as lymphocyte count and Hb levels, reflected biological diversity. The retrospective nature of the study could potentially introduce selection bias, particularly by choosing only reports with complete data. Limited molecular testing and the absence of financial support in this context restricted deeper insights into genetic alterations, and findings may not fully represent populations outside the study's geographical area. Further study is recommended to include more patients with a wider range of involvement and consider molecular diagnostics, therapeutic aspects, and patients' further follow-up.

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Conflicts of interest

There are no conflicts of interest.

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