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Spectrum of Lymphoma: A Five Years' Experience of Tertiary Care Centre in Eastern Nepal

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Abstract

Background: Immunophenotyping and improvement in classification system of lymphoma gains better epidemiological comparison in incidence and pattern. We aimed to study the spectrum and clinic-epidemiological profile of lymphoma and categorize the type and subtype of lymphoma according to 2008 WHO classification system.

Methods: This hospital-based retrospective, cross-sectional study included all cases of lymphoma diagnosed in a 5-year period from January 2012 to December 2016. Demographic indices and the clinical details provided by various departments were noted in a proforma and the type and subtype of lymphoma were categorized according to 2008 WHO classification system.

Results: There were a total of 47 cases of lymphoma, of which only 68% could be categorized. B cell lineage lymphomas comprised of 61.7% cases and the rest (6.3%) belonged to T cell lineage. Out of these, diffuse large B cell lymphoma (DLBCL) (21.2.% of total lymphoma) was found to be the commonest type of Non-Hodgkin's lymphoma (NHL) followed by classical type of Hodgkin's lymphoma (HL) (12.7% of total lymphoma). The highest number of cases were seen in the 6th decade. The mean age was 48.22 years for NHL and 42.60 years for HL. Male (70.2%) outnumbered female.

Conclusion: Categorization of lymphoma according to the 2008 WHO classification system was achievable in 68% of cases with the aid of various immunophenotyping panels. B cell lineage lymphoma comprised of the majority of cases and DLBCL was seen to be the commonest type of lymphoma. Ancillary technique plays an important role in designating the spectrum of lymphoma.

Keywords: Hodgkin's Lymphoma; Non-Hodgkin's Lymphoma; 2008 WHO classification system

Declarations

Ethics approval and consent to participate: This study was conducted with prior ethical approval from Institutional Review Committee, BPKIHS (Ref. No.: IRC/1029/017).

Consent for publication: Not applicable.

Availability of data and materials: The full data set supporting this research is submitted to the Journal of BPKIHS and will be available upon request by the readers.

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Neoplasm originating in lymphoid tissue consists of various groups of neoplasms including Non-Hodgkin's lymphoma (NHL), Hodgkin's lymphoma (HL), and multiple myeloma (MM) [1]. NHLs are derived from subpopulations of B, T and NK cells, and recent reports also indicate lymphoid derivation of HL [2-4]. Advances in immunophenotyping and improvement in the classification system gains a better epidemiological comparison in the incidence and pattern of lymphoma [5]. In the United States, lymphoma accounts for 5% of new cancer cases and 3.6% of cancer deaths annually [1]. In 2012, NHL was reported as the fourth most common cancer for males in Nepal [6, 7].

In most developed countries, the incidence of NHL is increasing at an annual rate of 4%, indicating a doubling of incidence in every 20 years [8, 9]. Distribution and pattern of lymphoma differ between children and adults. Diffuse large B cell lymphoma (DLBCL) is the most commonly encountered lymphoma in adults. Burkitt's lymphoma (BL) and HL are the predominant childhood lymphomas [10].

The World Health Organization (WHO) classification of neoplasms of the hematopoietic and lymphoid tissues, published in 2001 and updated in 2008, represents a worldwide consensus on the diagnosis, adopted for use by pathologists, clinicians, and basic scientists [11]. Its worldwide acceptance stems from biologically sound underlying principles and from its clinical relevance, practicality, and reproducibility in diverse international settings. Since 2001, the classification has been used in clinical trials and in pathologic and epidemiologic studies and has provided a basis for new genetic and molecular investigations. The major principle of the classification is the recognition of distinct diseases according to a combination of morphology, immunophenotype, genetic, molecular, and clinical features. The disease entities are stratified according to their cell lineage and their derivation from precursor or mature lymphoid cells [12]. This study aims to determine the spectrum and clinic-epidemiological profile of lymphoma in the eastern part of Nepal and categorize the type and subtype of lymphoma according to 2008 WHO classification system.

METHODS

This hospital based retrospective, cross-sectional study included all 47 cases of lymphoma (nodal and extranodal) diagnosed over a period of five years in the histopathology section of the department of Pathology. All lymphoid malignancies diagnosed from 1st January 2012 to 30th December 2016 were identified, clinical details sent from the various departments in biopsy evaluation request form and reports prepared from Pathology Laboratory along with the slides were retrieved from the Pathology department record section of BPKIHS. The biopsy specimen had been fixed in 10% formalin, processed, embedded in paraffin wax and stained with haematoxylin and eosin before being evaluated. The slides were reviewed again. Tumors were analyzed considering the histopathologic spectrum, age, gender, origin and anatomic site. The typing and subtyping according to the 2008 WHO classification system for lymphoid malignancies was done. This data were entered in Microsoft Excel 2010 & converted into SPSS version 11.5 for statistical analysis. For descriptive studies, percentage, ratio, and mean were calculated along with graphical and tabular presentations. Ethical clearance was obtained from the institutional ethical review board of BPKIHS.

RESULTS

A total of 47 cases diagnosed as lymphoma (NHL, 78% and HL, 21.2%) were included. Overall the age ranged from 3 - 82 years; the majority of the cases (8/47) were seen in 6th decade of life. One case each was seen in the children of age 3 and 5 years. Mean age was 48.22 years for NHL and 42.60 years for HL. Male (70.2%) outnumbered females (29.8%). Nodal lymphoma comprised of 61.7% of total cases, out of which about one third (21.3% of total cases) were HL and two thirds (40.4% of total cases) were NHL. Cervical lymph node accounted for 34.0% for the nodal site of NHL followed by inguinal lymph node (10.6%). All the cases of extranodal lymphoma (38.3%) were NHL. Gastrointestinal tract (GIT) and nasopharynx accounted for 21.2% and 10.6% respectively for extra nodal site for NHL. All the GIT NHL was seen in the elderly except for the two adolescents (16 and 18 years) and a child (3 years), all of whom presented with acute abdomen.

Out of 47 total cases, B cell type of lymphoma comprised of 29 (61.7%) cases and 3 (6.3%) cases belonged to T cell type. However, lineage determination in 15 (32%) cases of NHL could not be possible due to unavailability of antibodies so had to be diagnosed only as NHL with the advice of immunophenotyping study.

When categorization of lymphoma was done according to the WHO classification system, the most

common type of NHL was found to be DLBCL type followed by mucosa associated lymphoid tissue (MALT) lymphoma **(Table 1)**. Microscopy of DLBCL revealed diffuse proliferation of large sized immature lymphoid cells and apoptotic cell debri **(Fig. 1)**. Microscopy of MALT lymphoma revealed destruction of gastric gland by proliferation of small to medium sized lymphoid cells **(Fig. 2)**. Proliferation of medium sized lymphoid cells and thin walled blood vessels with membranous CD3 positive cells can be seen in angioimmunoblastic T cell NHL (AITL) **(Fig. 3)**.

Among Hodgkin's lymphoma, the classical type (12.7%) was the most common followed by nodular lymphocyte predominant HL (NLPHL) which accounted for 8.5% **(Table 1)**. Microscopy of classical HL (CHL), mixed cellularity (MC) type revealed mixed population of cells comprising of admixture of inflammatory cell and few classical Reed Sternberg (RS) cells **(Fig. 4)**. Microscopy of NLPHL revealed nodular architectural arrangement comprising predominantly of lymphoid cells and few admixed popcorn (L & H) type of RS cells **(Fig. 5)**. Both DLBCL and CHL were commonly seen in the elderly male patients except for one case of CHL which was found in a 5-year boy.

DISCUSSION

The incidence of lymphoma has increased over the past few years. It ranked twelfth among all cancers worldwide in 1990s [13]. In the United States, it accounts for 5% of new cancer cases and 3.6% of cancer deaths annually [1].

Lymphoma is more prevalent in males compared to females [13]. This finding is similar to our study where male (70.2%) outnumbered females (29.8%). Age of the patient ranged from 3 - 82 years and the majority of the cases (21.2%) were seen in the 6th decade of life. In the study conducted at Amman, Jordan in a total of 485 patients within a period of 5 years, age, gender and lymphoma type were studied. Out of 485 patients, 274 (56.5%) were males. The age ranged from 2 to 90 years [10]. Similarly, in a study from Malaysia conducted over a period of 3 years, the incidence in male was twice that of female. The ages of these patients ranged from 7 to 84 years, with a mean age of 42.1 years. The highest number of cases (22.0%) was in the 6th decade of life [14].

Changing trends are reported in both HL and NHL. The incidence of HL has slightly decreased in

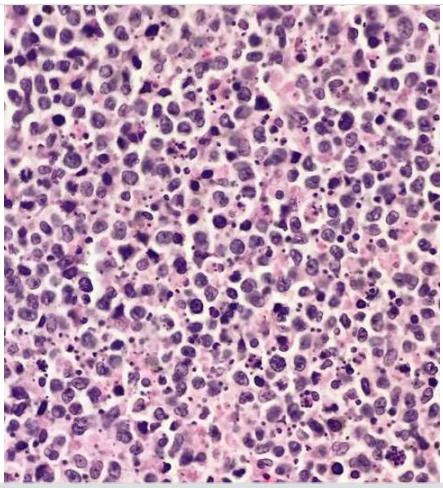

Figure 1: Microscopy reveals diffuse proliferation of large sized immature lymphoid cells and apoptotic cell debri in DLBCL (400X, H & E)

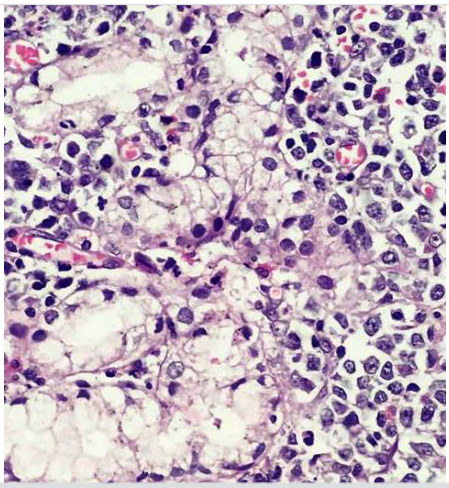

Figure 2: Microscopy reveals destruction of gastric gland by proliferation of small to medium sized atypical lymphoid cells in MALTOMA (400X, H & E)

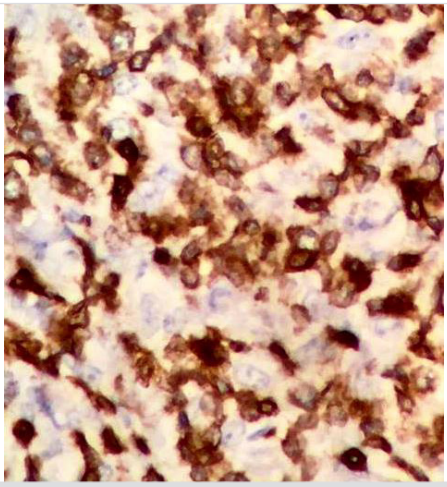

Figure 3: Microscopy reveals membranous positivity of CD 3 in T cell NHL (400X, IHC)

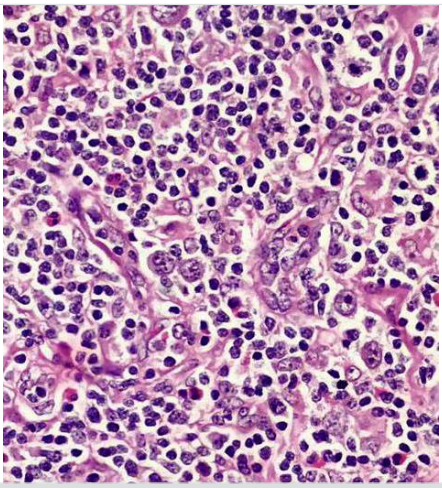

Figure 4: Microscopy reveals polymorphous population of cells and admixed few classical Reed Sternberg cells in Mixed Cellularity HL (400X, H & E)

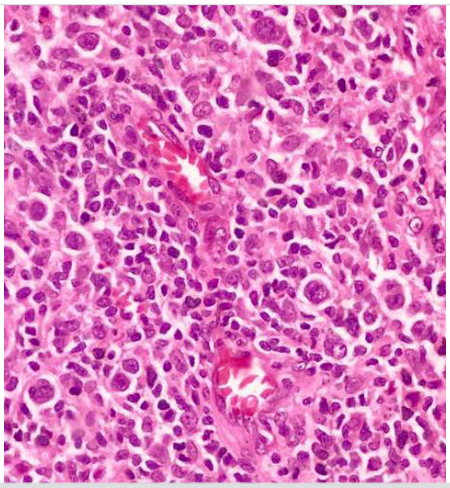

Figure 5: Microscopy reveals mixed population of cells and few admixed popcorn (L & H) type of RS cells in NLPHL (400X, H & E)

recent years, and the diagnosis has shifted from HL to NHL [3]. NHL is on the rise for the past 15 years [10]. It was believed that increment is partly due to emergence of acquired immunodeficiency syndrome related NHL and to a lesser extent by diagnostic improvements [15]. Exposure to occupational chemicals, hair dyes and organic solvents had been identified as possible causes of NHL [9, 10, 15]. In this study, the most common type of lymphoma was NHL (78.7%) than HL (21.2%) though the categorization of lymphoma according to the WHO classification system could be possible only in 68% of cases. These results are closely comparable to several studies conducted in the Middle East region, where the incidence of HL was 33% in Bahrain, 27% in Saudi Arabia, 35% in Oman, but much lower than United Arab Emirates patients where the incidence of HL was 41% [9, 10, 16, 17]. In a report from Malaysia, 91 cases representing 0.35% of total biopsies of the hospital included NHL and HL. The ratio for NHL to HL was 9:1 [14].

The distribution and patterns of lymphoma differed between children and adults in a 5-year study conducted in Jordan [10]. DLBCL is the most commonly encountered lymphoma in adults. BL and HL are the predominant childhood lymphomas [10]. These findings are similar to our study. Burkitt's type NHL though is the most common subtype of childhood malignant lymphoma (ML) in the studies from Jordan and Malaysia [10, 14]. On the contrary, study from east India reported T-cell NHL to be the most common type of childhood ML [18].

In this study the most common type of NHL is DLBCL (21.2%) type followed by MALT lymphoma. DLBCL was reported to be the commonest subtype of adult NHL in several studies [14, 7, 19]. The most common six subtypes reported in 2005 in China included DLBCL, follicular lymphoma (FL), unspecified peripheral T-cell lymphoma (PT-un), precursor T-lymphoblastic lymphoma (T-LBL), extranodal marginal zone B-cell lymphoma of MALT type and B-small lymphocytic lymphoma (B-SLL) [19]. A study from east India concluded that incidence of follicular lymphoma is lower compared to western studies [18]. In Asia, high grade lymphoma is more prevalent and the incidence of FL is low [17]. A study from Sarawak, Malaysia also revealed that DLBCL was the most prevalent NHL subtype [14]. A higher incidence of T NHL is reported in Asia, especially in EBV endemic area such as Japan and some parts of Taiwan [20]. However, the frequency of T NHL is lower in Sarawak [14]. These findings suggest that geographical differences in etiologic or host factors may be responsible for the observed differences in the distribution of cases across NHL subtypes [17]. In this study, categorization according to the WHO classification could be possible only in 68% cases, out of which DLBCL (21.2%) was found to be the commonest type of NHL followed by CHL (12.7%). It could be because of lower prevalence of EBV related T/NK cell lymphomas in our context. A study analysing the reports of 6,382 patients with lymphoma in the Southwest China, mature B cell neoplasms accounted for 56%, mature T and NK cell neoplasms comprised 26%, and precursor lymphoid neoplasms and HL were 5% and 13%, respectively [21].

We found classical type as the most common type

Table 1: Categorization of lymphoma according to WHO classification system (n = 47).

Type	Lineage (L)	Subtype	Frequency	Total
Non Hodgkin's Lymphoma	L not DET	Only NHL	13	15 (32%)
		Only Large Cell Lymphoma	2	
	B Cell	DLBCL	10	19 (40.4%)
		Only B Cell NHL	2	
		MALTOMA	2	
		Mantle Cell Lymphoma	1	
		Burkitts Lymphoma	1	
		Follicular Lymphoma	1	
		CLL/SLL	1	
		TCHRLBCL	1	
	T Cell	EN/NK T Cell Lymphoma	1	3 (6.3%)
		Angioimmunoblastic	1	
		Cutaneous T Cell Lymphoma	1	
Hodgkin's Lymphoma	B Cell	Classical	6	10 (21.2%)
		Lymphoma	4	

CLL/SLL: chronic lymphocytic leukemia/ small lymphocytic lymphoma; DET: determined, DLBCL: diffuse large B cell lymphoma; EN/NK: extranodal/ natural killer; NHL: Non Hodgkin's lymphoma; NLPHL: nodular lymphocyte predominant Hodgkin's lymphoma;TCHRLBCL:T cell histiocyte rich large B cell lymphoma.

of HL (12.8%). A study from Jordan reported that the nodular sclerosis (NS) subtype was the most frequent HL (63.6%); followed by the mixed cellularity (MC) subtype HL (20.3%) [10]. On the contrary, in Oman, the MC appeared in 56% of HL [22]. The study from east India also found that MC was the most common subtype of HL [18]. In the study from Southwest China, MC (76%) was the major subtype of CHL [20]. However, a recent study done in Pakistan in 2008 reported that MC and NS were the main histological subtypes of HL [23]. A comparison of histological appearances of HL in Pakistani and Saudi patients in 2008 showed that MCHL was the commonest subtype among Pakistani patients whereas NSHL was more common among Saudis [24]. The Jordanian experience about HL between Jan 2001 and Dec 2003 also revealed that NS type is the commonest [25].

In the study from Jordan, the incidence of HL peaked at the age of 15-49 years [18]. On the contrary, in the study from Toronto, HL was reported to be rare among children < 5 years of age and relatively rare in the adult population, but is the most commonly diagnosed cancer among adolescents aged 15 to 19 year. In developed countries, there is a bimodal age distribution for HL with a peak in the adolescent/young adult population and again after age > 55 years [26]. This finding is concordant to our study as the mean age for HL was 42.6 years.

Nodal lymphomas comprised of 61.7%, however, extra nodal were found to be 38.3% only in this study. This could be due to small sample size. In the study from Malaysia, the main sites were the lymph nodes (47.2%) and extra nodal sites (46.1%) [27]. Similar findings were also reported from Southwest China where extra nodal lymphomas accounted for almost half of all cases, and the most frequently involved sites were the Waldeyer's ring, the gastrointestinal tract, the sinonasal region and the skin. In addition, the GIT and the nasopharynx were the common sites for extra nodal lymphomas [21]. The common extranodal sites reported from Malaysia for NHL included the GIT, the tonsil, the oral cavity, the testis, the spine and the nose while all the HL were present in the lymph nodes [27]. This finding is concordant to our study where lymph node (predominantly cervical node) was the common site for HL.

We found neck nodes especially the cervical region (34.0%) to be the commonest site followed by inguinal LN (10.6%). Similarly, the GIT (21.2%) followed by the nasopharynx (10.6%) constituted the common sites

for extra nodal lymphoma. Almost similar findings was seen in the Malaysian study in which the majority of lymph node biopsies were from the head and neck region (22.0%), followed by superficial nodes of the axillary and inguinal regions (12.1%), and the mesentery (2.3%) [27].

CONCLUSION

The 2008 WHO classification system categorization of lymphoma could be obtained in 68% of cases with the support of various immunophenotyping panels. B cell lineage lymphoma comprised majority of cases (61.7%) and DLBCL (21.2%) was seen to be commonest type of lymphoma. Ancillary technique has been a helpful tool to allocate the spectrum of lymphoma.

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