

Pediatric Lymphomas: A five year experience at a tertiary care hospital

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ABSTRACT

Objectives: To determine the frequency of lymphomas in children in our population and to compare it with national and international studies.

Materials and methods: A retrospective analysis was carried out on children under 18 years of age diagnosed with lymphoma in the duration of five years from 2006 till date, at the Histopathology Department of CH & ICH, Lahore. All the cases were re-evaluated and different morphological features were noted. Immunohistochemical stains were applied wherever required.

Results: A total of 198 cases of lymphoma were reported. NHL was diagnosed in 70 cases (35.3%). Out of these, lymphoblastic lymphoma were seen in 38 cases (54.28%), whereas 19 cases (27.14 %) were of Burkitts lymphoma (BL), 11 cases (15.71%) were of Diffuse Large B Cell Lymphoma (DLBL) type and 1 case (1.42%) each of Anaplastic Large Cell (ALCL) and Follicular Lymphoma. The age range of the cases under study is from 8 months to 16 years with male to female ratio of 2.4: 1. There were 128 (60.3%) cases of Hodgkin's Lymphoma (HL), among which Mixed Cellularity Type (MC) is more common (n=108, 84.3%). The age range is from 1-14 years with male to female ratio of 9.2:1.

Conclusion: Hodgkin Lymphomas of MC Type are far more common than NHL in children with predominance of males.

Key words: Lymphomas, tumours, children, malignant

INTRODUCTION

Children's Hospital and Institute of Child Health (CH&ICH) Lahore, being a tertiary care hospital, cater a wide range of pediatric histopathology specimens from all over the province. We present here a single institutional retrospective study on lymphomas in children upto 18 years of age. Lymphomas are the malignant neoplasms of lymphoid lineage broadly classified as either Hodgkins (HL) or Non Hodgkin's Lymphoma (NHL). In children, lymphomas account for 13% of all childhood tumours¹ and are considered as the third most common pediatric cancer worldwide^{2,3}.

The NHL represents a multitude of discrete types of lymphoid neoplasia each with its own molecular pathogenesis, distinctive pattern of clinical behavior and therapeutic response^{4,5,6}. In pediatric population, NHL is usually diffuse, extranodal, high grade, and has different classification in contrast to that of adults^{7,8}.

The modern classifications of REAL and WHO rely on the constellation of cytologic, immunological, phenotypic, genotypic, and clinical characteristics of NHL^{9,10}. In children there are mainly three primary subtypes of NHL namely BL, lymphoblastic and large

cell lymphomas^{6,11}. Lymphoblastic lymphomas are categorized as Precursor T and Precursor B type, while large cell lymphomas are divided into large B and large T cell type. Lymphomas of B cell origin express surface immunoglobulin of IgM type and B cell specific antigens CD19 and CD20^{12,13} whereas, T cell lymphomas express CD7, CD5, CD1, CD3, CD4, CD8 and CD2^{2,3}.

HL is a distinct primary solid tumor of the immune system that shows wide variation in incidence among different geographic regions and various races¹⁴. The first report on HL in children was presented by Thomas Hodgkin in 1832². Epidemiology suggests an infectious etiology with Epstein Barr Virus (EBV) in up to 40% of cases. The B-cell nature of the pathognomonic Hodgkin and Reed-Sternberg (HRS) cells has been documented¹⁴.

The importance of the current study is that it documents the relative distribution of various types of lymphoma in a geographical area in comparison with other studies. It is hoped that it will contribute towards a better understanding of predisposing factors for Malignant Lymphoma (ML) in this part of the world.

MATERIALS AND METHODS

The present study is a retrospective analysis of all cases of lymphomas less than 18 years of age reported in the duration of approximately five years

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from 2006 till date, at the Histopathology Department of CH & ICH, Lahore. History and data regarding age, sex, site and size of the tumours was retrieved from medical records. Routine H/E stained slides were re-evaluated and different morphological features were noted. Immunohistochemical stains including CD3, CD20, CD15 and CD30 were applied wherever required.

RESULTS

A total of 198 cases were reported, out of which NHL was diagnosed in 70 cases (35.3%). Out of these, lymphoblastic lymphoma was seen in 38 cases (54.28%) with positive CD3 staining (Fig 2), whereas 19 cases (27.14%) were of CD20 positive BL, 11 cases (15.71%) were of DLBL with positive staining of CD20 and 1 case (1.42%) each of CD30 positive ALCL (Fig 3), and follicular lymphoma. The age range of the cases under study is from 8 months to 16 yrs with mean of 10.4 yrs with most of the cases seen in the age group of 5-10 yrs with the exception of DLBL of which out of 7 cases, 4 were

seen in the age group of >10 years (Table 1). Regarding gender distribution majority of cases were seen in males (n=41, 58.5%) with male to female ratio of 2.4: 1 (Table 1). There is predominant involvement of nodes by NHL, however, few cases were also seen in extranodal sites like salivary glands, mediastinum, genitalia and even heart as well (Fig 1).

HL was diagnosed in majority of cases (n=128, 64.6%), among which MC type is the most common (n=108, 84.3%) followed by Nodular Sclerosis (NS) (n=16, 12.5%) and lymphocyte depleted (LD) (n=3). There was only a single case (0.78%) of lymphocyte rich (LR) and no case of lymphocyte predominant (LP). The age range is from 1-14 yrs with mean of 9.2 yrs and majority of cases being in the age group of 5-10 years. However, there were 2 cases of LD which were seen in age group of less than 5 yrs (Table 2). There is preponderance of males (n=105, 82%) with male to female ratio of 9.2:1 (Table 2). All the cases were seen in lymph nodes.

Table 1: Frequency and clinical characteristics of Non-Hodgkins Lymphoma in the present study

	Lymphoblastic	BL	DLBL	ALCL	Follicular
Frequency	38 (54.28)	19(27.14)	11(15.7)	01(0.78)	01(0.78)
Gender distribution					
Males	26	06	07	01	01
Females	12	13	04	--	--
Ratio	2.16:1	0.46:1	1.75:1	1:0	1:0
Age distribution					
>5yrs	06	03	--	--	01
5-10yrs	25	13	04	01	--
<10yrs	07	03	07	--	--

Table 2: Frequency and clinical characteristics of Hodgkins Lymphoma in the present study

	MC	NS	LD	LR
Frequency	108(84.3%)	16(12.5%)	03(2.34%)	01(0.78%)
Gender distribution				
Males	98	05	01	01
Females	10	11	02	--
Ratio	9.8:1	0.45:1	0.5:1	1:0
Age distribution				
>5yrs	14	04	02	--
5-10yrs	76	09	01	01
<10yrs	18	03	00	--

Fig 1: Extra Nodal Distribution of NHL

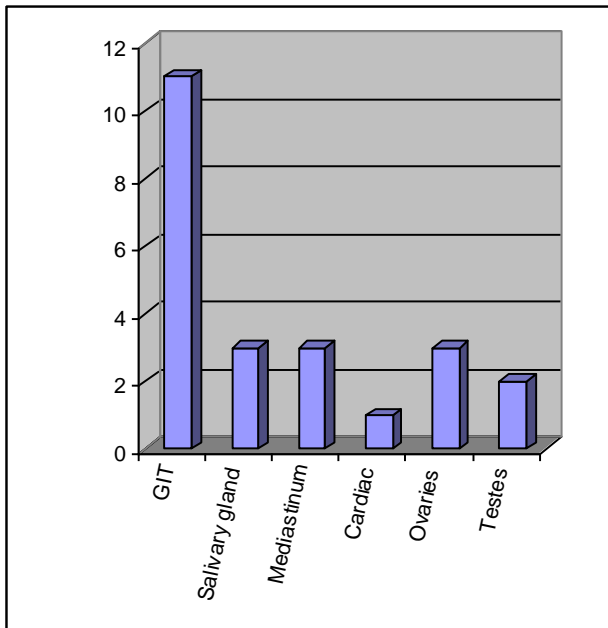


Fig 2 : Lymphoblastic Lymphoma with increased mitotic rate and inconspicuous nucleoli X 250

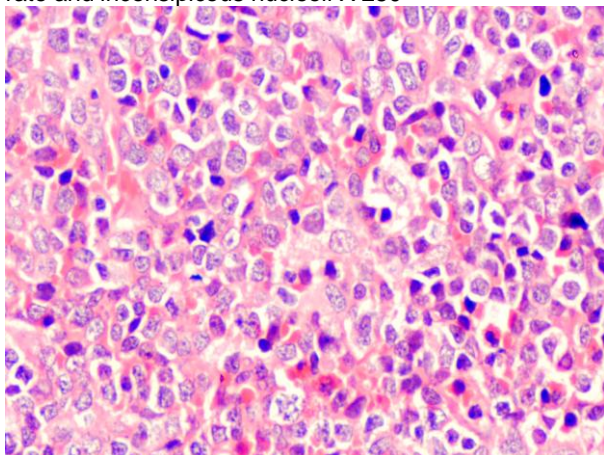


Fig 3: CD30 strongly positive in ALCL X 200

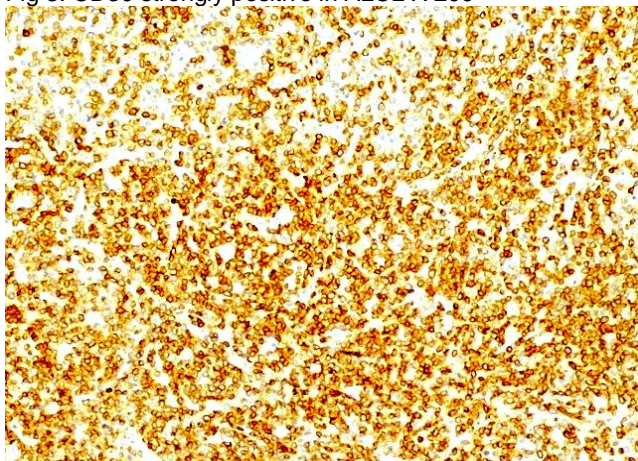
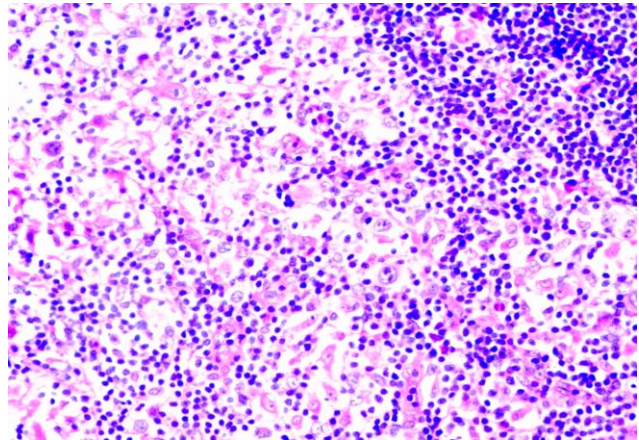


Fig 4:RS cells seen present against reactive background X 100



DISCUSSION

The incidence of lymphoma is increasing worldwide largely contributed by NHL¹⁵. They rank fifth in cancer incidence in United States, and are increasing at a rate of almost 7% per year¹⁶. However, Pakistan falls into a low risk region for NHL both in males and females, graded 1 on a scale of 1-5¹⁷. This observation is similar to ours as majority of our cases were HL with only 70 cases (35.3%) of NHL of the total 198 cases (Table 1). In contrast to the present study, Mushtaq et al and Abdullah et al observed NHL more frequent than HL in Pakistan^{18,19}.

In Saudi Arabia, AL Nazar et al also observed that majority of cases were of HL (n=20, 28.1%) in the pediatric population²⁰.

Regardless of age or histology, males have a higher incidence than females^{5,20}. NHL is considered to be most common cancer in males in Northern Pakistan²¹ and 9th most common malignant neoplasm among males in Karachi/Sindh²². In western countries there is also predominant involvement of males²³. These observations are similar to the present study in which we also found males to be predominantly involved in NHL (Table 1).

We observed that majority of NHL were found in the age group of 5-10 yrs with the mean of 10.4yrs (Table 1). However, Gualco observed most of the cases of NHL in slightly older age group (15-18 yrs) as compared to our study²³.

According to Percy et al, BL is much more common in males, with the highest incidence between the ages of 5 years and 14 years⁸. This finding is in contrast to ours as we observed BL mainly in females between 5-10 years of age (Table 1). In the present study lymphoblastic lymphoma was diagnosed in 38 cases (54.28%), being majority of them in males and in age group of 5-10 yrs (Table 1). We observed most of the NHL in the nodes with few

cases seen in extranodal sites (Fig 1). However, BL was mainly found in GIT, whereas Shah et al in Pakistan and Al Sawami in Yemen observed most of the cases of NHL as extranodal^{2,6}. Amongst the extranodal sites, gut was the most frequent site for these malignant tumors similar to our observation.

In our study population, HL was the major group (n=128, 64.6%) with majority of the subtype of MC (n=108, 84.3%) (Fig 4, Table 2). There are some studies in middle east and India, where MC appears to be more common subtype of HL^{2,18,24}. However multiple research workers depict NS to be more common followed by MC^{23,25,26,27,28}.

Most of cases of HL were diagnosed in the age group of 5-10 years (Table 2), similar to the observation by Srina et al in Thailand, Togo in Mali and Patridou^{29,30,31} as well as other developing countries^{9,31,32,33}. In United States, majority of cases were diagnosed in older age group^{26,34}.

Regarding gender distribution of HL in the present study, it was noticed that majority of cases were seen in males with Male to Female ratio of 9.2:1. Similar to the observation by Togo and other developing as well as developed countries^{26,27,33}. All cases were seen in lymph nodes. A study in Saudi Arabia also had predominant involvement of males and no extranodal involvement by HL². We were unable to determine the prognosis of these patients and observe the effects of chemotherapy on different types of ML.

CONCLUSION

Our results show that among NHL, there is a high frequency of lymphoblastic lymphomas followed by abdominal BL. HL were the predominant tumours amongst the malignant lymphomas affecting majority of males diagnosed in our region, where the MC as the most frequent HL, similar to the trend in some other Middle East countries.

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