Original Article

Clinico-pathological profile of Hodgkin's lymphoma in children

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Introduction : Hodgkin's lymphoma is a type of lymphoma characterized clinically by the spread of disease from one group of lymph nodes to another and by the development of systemic symptoms with advancement of disease. Pathologically, it is characterized by the presence of Reed-Sternberg cells. With early detection survival rate of the disease is around 90%.

Objective: The principal purpose of this study was to assess the clinico-pathological features of the Hodgkin's lymphoma in children (n – 30).

Method: A retrospective study was carried out with 30 Paediatric patients of Hodgkin's lymphoma in the department of Paediatric Haematoncology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from October 2008 to March 2009 . Clinical features of Hodgkin's lymphoma were assessed among these patients. Histopathological features of individual cases were also assessed.

Result: Wide spectrum of clinical presentation like swelling of lymph nodes (most common cervical lymph nodes 100% cases), fever (80%), weight loss (70%), Vomiting (20%), Oedema (6.7%) and Jaundice (3.3%) were found. Majority patients were in advanced stage and B symptoms at the time of presentation. ESR was high in 70% cases. Mean Hb concentration was 8.14 ± 1.89 gm/dl with a range from 5.50-12gm/dl. Serum LDH was high in 60% cases. Out of all the Hodgkin's lymphoma patients 20% were lymphocyte predominant and 80% were mixed cellularity type.

Conclusion : Most common clinical presentations in patients of our study were lymphadenopathy, fever and weight loss. Other presenting features were vomiting, oedema and jaundice. Majority patients have advanced stage disease. 80% were mixed cellularity type and 20% were lymphocyte predominant variety.Clinical presentations are similar to other previous studies.

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Introduction

Hodgkin's lymphoma has a bimodal incidence curve; it occurs most frequently in two age groups, the first being young adulthood (age 15–35) and the second being in those over 55 years[1].

Overall, it is more common in males, except for the nodular sclerosis variant, which is more common in females. The annual incidence of Hodgkin's lymphoma is about one in 25,000 people and the disease accounts for slightly less than 1% of all cancers worldwide. The incidence of Hodgkin's lymphoma is increased in patients with HIV infection[2].

Patients with Hodgkin's lymphoma may present with the following symptoms: painless enlargement of one or more lymph nodes, rubbery in consistency and frequently involved cervical and supraclvicular regions (80-90%). The spleen is pathologically involved in 30% to 45% of patients with Hodgkin's disease at diagnosis, although, conversely, approximately 35% to 50% of patients with Hodgkin's disease and clinical splenomegaly do not have pathologic involvement documented at staging laparotomy[3,4]. Approximately one third of the patients may have disease-related symptoms, including B symptoms and pruritus.

In classic Hodgkin disease (Hodgkin's lymphoma), the neoplastic cell is the Reed-Sternberg (RS) cell.

Classical Hodgkin lymphoma (excluding nodular lymphocyte predominant Hodgkin's) can be sub-classified into 4 pathologic subtypes (Nodular sclerosing CHL, Mixed-cellularity subtype, Lymphocyte rich and Lymphocyte depleted) based upon Reed-Sternberg cell morphology and the composition of the reactive cell infiltrate seen in the lymph node biopsy specimen.

Literature review revealed very little information focusing on clinico- pathological feature of Hodgkins Lymphoma in children. This paucity of information and absence of a national cancer registry system in Bangladesh led us to conduct this study.

Objectives

To assess the clinico pathological features of Hodgkins Lymphoma among 30 children.

Methodology

A retrospective study was conducted in the department of Paediatric Haematooncology of BSMMU, Dhaka from October 2008 to March 2009. Patients who were attended or admitted in the department of paediatric Haematoncology of BSMMU during the period of August 2005 to July 2008 was enrolled in this study.

Patients of age group 1–15 years of both sexes with only histo-pathologically proven lymphoma were included in the study. Those less than 1 year and more than 15 years were excluded from the study. The estimated final sample size was 30 through purposive sampling technique.

Data were collected using a preformed data collection sheet . Base line information was collected from the patients register book (2005-2006) of the department of Paediatric Haematoncology of BSMMU.

All data were then systematically furnished in preformed data collection form. Quantitative data were expressed as mean and standard deviation and qualitative data were expressed as frequency distribution and percentage. Statistical analysis was done by using computer software SPSS 15 for windows.

Result and observationents

In this retrospective study total 30 patients of histopathologically proven Hodgkin disease were included. Among them, majority (60%) were of the age group 5-10 years and 30 % were <5 years, 10% belong to more than 10 years. Mean age of the study patients was 7.05 ± 2.62 years (Table-1).

Table I: Distribution of the patients by age

Age (in year)	No. of Patients	Percent
≤5	9	30.0
5-10	18	60.0
>10	3	10.0
Total	30	100.0
Mean ± SD (Range)	7.05 ± 2.62	(3.5-12.0)

In this study we found that most of the children were male (60%) and 40% were female (Fig. 1) and (70%) patients were from middle socio economic class and only 30% were from lower socio-economic class. (Table II)

Table II : Distribution of the socio-economic status

Socio-economic status	Frequency	Percent
Low	9	30.0
Middle	21	70.0
Total	30	100.0

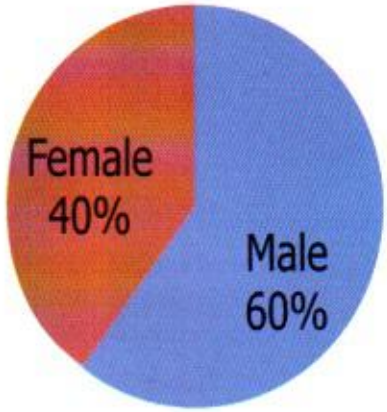

Fig. 1 : Distribution of Patients by sex

All of the study patient (100% of respondents) presented with swelling of lymph nodes, 80% had fever and 70% presented with weight loss, 20% with vomting, 6.7% with edema and 3.3% with Jaundice.

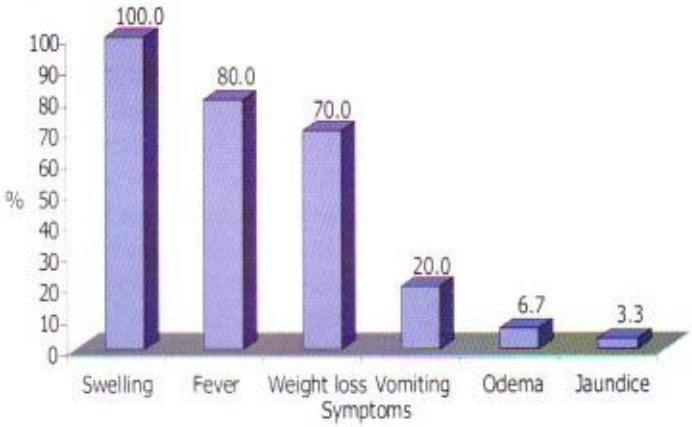

Fig. 2 : Distribution of Patients by Symptoms

This study showed that commonest site of involvement were cervical lymph nodes (100%) followed by inguinal nodes (30.0%), hylar represent 30% and paraaortic 10%. (Fig. 3)

Out of all patients 56.7% reported stage III & IV disease and 43.3% stage I & II diseases. B symptoms reported 80.0% (25) cases of all stages (Table III).

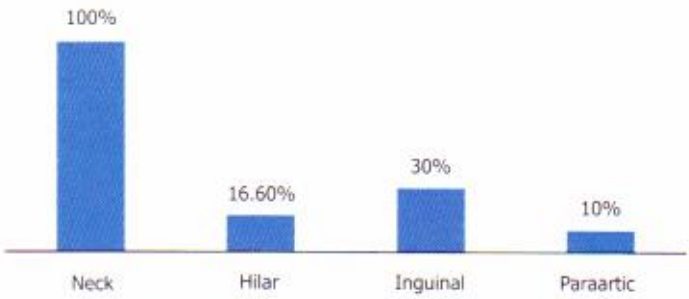

Fig. 3 : Distribution of lymphnode site involvement

Table III : Stage at Presentation

	Frequency	Percentage
Stage I	5	16.6
• IA	2	6.6
• IB	3	10.0
Stage II	8	26.6
• IA	1	3.3
• IB	7	23.3
Stage III	12	40.0
• IA	1	3.3
• IB	11	36.6
Stage IV	5	16.6
• IA	1	3.3
• IB	4	13.3

This study showed that splenomegaly (26.6%) was more commonly found than hepatomegaly (16.6%) (Table- IV).

Table IV : Distributionof extranodal involvement

Extranodal area	No. of Patients	Percent
Hepatomegaly	5	16.6.0
Splenomegaly	8	26.6.0

Haematological and Biochemical parameter of the study patient showed that ESR were high in 70% cases and serum LDH was abnormal in 60% cases. (Table V)

Table V: Distribution of Patients by ESR & LDH

	ESR		LDH	
	No. of Patients	Percent	No. of Patients	Percent
Normal	9	30.0	12	40.0
High	21	70.0	18	60.0
Total	30	100.0	30	100.0
Mean ± SD (Range)	58.80 ± 40.80	7±115	434.50 ± 158.25	255±820

Mean haemoglobin (Hb) of the study patient was 8.14±1.89, WBC count was 7633.33 ± 1357, mean serum urea was 28.50 ± 4.76, mean serum creatinine was 0.58±0.15 and mean SGPT was 27.67 ± 7.77. (Table VI)

Table VI: Distribution by lab/biochemical parameter

Variables	Mean ± SD	Range
Hb (gm/dL)	8.14 ± 1.89	5.50-12.00
WBC	7633.33 ± 1357.82	5000-10000
SGPT	27.67 ± 7.77	15-36
Urea	28.50 ± 4.76	20-35
S. Creatinine	0.58 ± 0.15	0.25-0.85

According to histological features 20% of the study patients were lymphocyte predominant and 80% were mixed cellularity type. None was found as Lymphocyte depleted or Nodular sclerosing type (Table VII).

Table VII: Distribution by histological features

Histological variant	Frequency	Percent
Lymphocyte predominant	6	20.0
Lymphocyte depleted	0	0.0
Mixed cellularity	24	80.0
Nodular sclerosing	0	0.0

Discussion

Analysis of data of this study shows mean age of the study subjects were 7.05 ± 2.62 years, ranging from 3.5 to 12.0 years. 30 % of the respondents were in the age group of 5 years and majority (60%) was in the age group of 5-10 years. Only 10% cases were of age group >10 years.

The data from the study by IARC, on cancer incidence in five continents, for the year 1988 to 1992. Study populations over 4.5 million, suggests that Hodgkin's lymphoma, has a bimodal peak at ages 15–34 years and over 60 years in most European, American, Hispanic and Australian populations with incidence rates less than 1.46 per 100,000 in the age group 0 to 14 years and around 6 per 100,000 per year in the over-60-year-olds[5].

Siddiqui N et al. studied that the clinico-epidemiological profile of Hodgkin's lymphoma (HL) in Pakistan. Six hundred and fifty eight histopathologically confirmed cases of HL were identified. Patients ranged in age from 1 year - 84 years. The mean age at presentation was 23.8 years. Three hundred and twenty cases (48.6%) belonged to age group < 18 years and 338 cases (51.4%) were > 18 years of age[6].

In current study 60% of the children were male and 40% were female. Cartwright and Watkins (2004)[7], in their review presented the age-standardized (World) incidence rates/100 000/year for Hodgkin's disease is higher (maximum 1.46) in males than female (maximum 0.78) [5, 7].

It has been suggested that risk of Hodgkin's lymphoma may be linked to social class background in childhood. Positive associations between Hodgkin's lymphoma and correlates of higher social class have been reported in studies of children

and young adults[8]. In our study 70% of patients were belonged to middle class family and 30% of the patients were of lower socio-economic class.

Most common presentation of our patients were swelling of lymph nodes.100% of patients presented with swelling of cervical lymphadenopathy, other site included supraclavicular mediastinal, inguinal and para-aortic. B symptoms present in majority of cases, 80% had fever and 70% with weight loss. Other presenting features were undue vomiting (20%), oedema (6.7%), and Jaundice (3.3%).

In Siddiqui et al.[6] series the majority of patients (81.2%) presented with cervical lymphadenopathy.

Ramani A et al.[9] reported that out of 103 patients with lymphomas, Fever and superficial lymphadenopathy were the commonest presenting features and 'B' symptoms were present in over 60% of both groups[7].

According to Howard Terebalo, patients with Hodgkin's lymphoma may present with the following symptoms: painless enlargement of one or more lymph nodes which felt rubbery in consistency and frequently involved cervical and supraclvicular regions (80-90%), splenomegaly (30%)[3]. In our series, splenomegaly26.6% cases and hepatomegaly was found in 6.6% cases.

Hepatomegaly (5%), Hepato-splenomegaly, Pain after alcohol consumption[4], nonspecific back pain has been reported in some cases of Hodgkin's lymphoma. About one-third of patients with Hodgkin's disease may also present with systemic symptoms, including low-grade fever; night sweats; unexplained weight loss of at least 10% of the patient's total body mass in six months or less, itchy skin (pruritus)[4].

Clinical staging was done at the time of diagnosis. majority of the patients, 56.7% were stage III & IV diseases and 43.3% stage I & II diseases among them 80% presented with B symptoms. Ramani A et el[11] reported that out of 103 patients with lymphomas 31 (30.1%) had Hodgking's lymphoma. Among them 64.5% of HL presented in stages III & IV of the diseases. Siddiqui N et el[6] Early stage I & II disease was present in 43.9% patients at presentation, while 56.1% patients presented with advanced stage III & IV.

On histopathological study, 20% of our cases were diagnosed as lymphocyte predominant 80% were mixed cellularity type and none was of lymphocyte depleted or nodular sclerosis type. According to Ho et al[10], the nodular sclerosing subtype was commonest in females (5 out of 8 cases) and for males, the commonest was mixed cellularity (10 out of 18 cases)[10]. In Siddiqui et al.[6] series, histopathologically, mixed cellularity (MC) constituted 63.8% of cases, followed by nodular sclerosis (NS) 19.9%, lymphocyte predominant (LP) 7.3% and lymphocyte depleted (LD) 1.2%.

In 70.0% cases ESR was high and Mean Hb concentration was 8.14.14 ± 1.89 gm/dl Serum LDH was high in 60.0% cases, Mean (±SD) blood urea level was 28.50 ± 4.76, S. creatinine 0.58± 0.15, SGPT was 27.67 ± 7.77 and mean WBC count was 7633.33 ± 1357.82. All of these were within their normal limit.

Conclusion

In this study we found that most common clinical presentations in patients of our study were lymphadenopathy, fever and weight loss. Other presenting features were vomiting, oedema and jaundice. Majority patients have advanced stage disease. 80% were mixed cellularity type and 20% were lymphocyte predominant variety.Clinical presentations are similar to other previous studies.

Limitation of this study is that smaller sample size (30) was used to evaluate and analyze the clinico-pathological pattern. Immuno-phenotyping could not be done and association with EBV, HIV or other viruses was not observed.

Further epidemiological study in large scale is recommended to evaluate the clinicopathological pattern in Bangladesh. More systemic assessment as well as CT scan or MRI confirmation is needed to explore the involvement of other internal organs.

References

1. Mauch P, James A, Volker D, Richard H, Laurence W. Hodgkin's Disease. Lippincott Williams & Wilkins, USA, 1999, pp. 62-64.
2. Biggar RJ, Jaffe ES, Goedert JJ, Chaturvedi A, Pfeiffer R, Engel's EA. Hodgkin lymphoma and immunodeficiency in persons with HIV/AIDS. Blood 2006;108 (12): 3786–91.
3. Aisenberg AC, Qazi R. Abdominal involvement at the onset of Hodgkin's disease. Am J Med 1974;57:870
4. Desser RK, Moran EM, Ultmann JE. Staging of Hodgkin's disease and lymphoma: Diagnostic procedures including staging laparotomy and splenectomy. Med Clin North Am 1973;57:479
5. IARC. Cancer Incidence in Five Continents, vol. VII. IARC Scientific Publications (no. 143): Lyon, 1997.
6. Siddiqui N, Ayub B, Badar F, Zaidi A. Hodgkin's lymphoma in Pakistan: a clinico-epidemiological study of 658 cases at a cancer center in Lahore. Asian Pac J Cancer Prev. 2006;7(4):651-5.
7. Cartwright RA, Watkins G. Epidemiology of Hodgkin's disease: a review. Hematol Oncol 2004; 22: 11–26.
8. Alexander FE, Ricketts TJ, McKinney PA. Community lifestyle characteristics and incidence of Hodgkin's disease in young people. Int J Cancer 1991; 48: 10–14.
9. Ramani A, Kumar KA, Rao KK, Vidyasagar MS, Kundaje GN. Clinico-pathological profile of lymphomas in south India: a prospective rural referral hospital study of 103 cases. J Assoc Physicians India. 1992;40(4):282-3.
10. Ho FC, Todd D, Loke SL, Ng RP, Khoo RK. Clinico-pathological features of malignant lymphomas in 294 Hong Kong Chinese patients, retrospective study covering an eight-year period. Int J Cancer. 1984;34(2):143-8.