

A COMPARISON OF HISTOLOGICAL APPEARANCES OF HODGKIN'S DISEASE IN PAKISTANI AND SAUDI PATIENTS

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Background: Hodgkin's disease (HD) is a relatively rare lymphoma that affects younger as well as older persons. It is reported in the Western as well as Asian studies that HD is a rare disease in developing world. It is commoner in males in most of the countries and shows a bimodal pattern of age. The commonest subtype is nodular sclerosis in the west and mixed cellularity in the eastern and developing countries. The present study compares eight years' data of HD as regard age, sex, site of anatomical presentation and subtypes according to WHO classification among Pakistani and Saudi patients. **Methods:** This retrospective comparative study included 211 cases of HD from various institutions of Lahore, Pakistan; and 78 cases retrieved from the data of King Abdul Aziz Hospital and Oncology Centre, Jeddah, Saudi Arabia. **Results:** The analysis of both data of HD showed lack of bimodal age pattern and was common among younger age. Male was the dominating sex. Cervical group of lymph nodes was the commonest presenting site. Mixed cellularity HD (MCHD) was the commonest subtype among Pakistani patients whereas Nodular Sclerotic HD (NSHD) was more common among Saudis. **Conclusion:** A comparison of the pattern of Pakistani and Saudi data of HD showed lack of bimodality in both. The male sex predominated. Morphologically the MCHD and NSHD were the commonest subtypes in Pakistani & Saudi patients respectively.

Keywords: Hodgkin's Disease, Lymphoma,

INTRODUCTION

Hodgkin's disease (HD) is a relatively uncommon heterogenous lymphoreticular disorder that affects both younger and older persons.¹ Its incidence varies with age, geographical distribution and social class. Aetiologically the role of infectious agents, such as Epstein-Barr virus (EBV), familial clustering and individuals with specific human leukocyte antigen (HLA) types support genetic predisposition.² HD is less common in coloured racial/ ethnic groups than in whites. It has been reported to be specifically rare in Asians.³ Although a bimodal distribution of age has been generally reported by various workers⁴⁻⁶ from western countries and some Middle Eastern countries⁷, this pattern is not observed in this part of the world, i.e., Indian subcontinent⁸. Hence diverse trends have been reported between younger and older people in cases of Hodgkin's disease.^{6,9} The sex incidence among whites of US form about 63% of males; in Denmark 59% and in U.K the mortality data indicates a higher sex ratio of 66%.¹⁰⁻¹² A Saudi study from Riyadh reported a much higher male preponderance of 70.4% whereas female formed 29.6%¹³; similarly a report from Pakistan shows a male to female ratio of 33:1.⁸

As regard the morphological subtypes the REAL/WHO classification recognises a basic distinction between lymphocytic rich HD and classic HD (CHD). CHD has been classified into four subtypes; lymphocytic predominant, nodular sclerosing, mixed cellularity and lymphocytic depletion. This subtyping reflects the difference in

clinical presentation, behaviour, morphology and phenotype.¹⁴ The essential requirement for the diagnosis of HD is the presence of 'Reed Sternberg' type of giant cells in an appropriate cellular background of lymphoid cells and histiocytes. The frequency of subtypes of HD is variable according to geographical distribution. In various developed and industrialised western countries nodular sclerosing HD supercedes the other types, whereas in developing countries the mixed cellularity is the commonest type.¹⁵ The pattern in Asia except Japan shows preponderance of mixed cellularity HD, followed by nodular sclerosis type HD.^{8,16-19}

The present study was aimed at analysing the cases of HD in two tertiary care teaching hospitals, a private laboratory in Lahore, Pakistan; and the data from a tertiary care public hospital and Oncology Centre in Saudi Arabia. The age, sex, location and the histological typing of HD were considered from the point of view of a comparison in Pakistan and Saudi Arabia.

SUBJECTS AND METHODS

A total of 211 cases of Hodgkin's Disease (HD) were retrieved from the data of the department of Pathology, King Edward Medical University Lahore, Pakistan; a private clinic (Polytest clinic) Lahore, and the Department of Histopathology, Lahore Medical & Dental College, Lahore for the years 1999 to 2006. The data of another 78 cases of diagnosed HD was retrieved from the records of King Abdul Aziz Hospital & Oncology Centre at Jeddah, Saudi Arabia for the years June 1996 to June 2003. The data extraction proforma included name, age, sex,

nationality (in case of Saudi Arabia), lymph node groups or organs involved at presentation and the morphological diagnosis of HD.

The data included patients of all ages and both sexes. The histological diagnoses were made by at least two pathologists at King Edward Medical University and private clinic at Lahore. In case of Saudi data the diagnoses were made by three pathologists. The data from both countries were then analysed using above mentioned parameters collected in the data proforma. The data was analysed using STATA 8.2. Frequencies, percentages and graphs are given for qualitative variables. Pearson chi square and Fisher exact test were applied to observe associations between qualitative variables. A *p*-value of <0.05 was considered as statistically significant.

RESULTS

The present study was carried out in Lahore, Pakistan and in Jeddah, Saudi Arabia after retrieving the data of HD among the cases of lymphoma. A total of 211 cases were collected from various sources in Lahore, and a total of 78 cases of HD were retrieved from the data of lymphomas from the records of histopathology department of King Abdul Aziz hospital & Oncology Center, Jeddah. These cases were received from a period of eight years in both centers i.e. from 1999 to 2006, and 1996 to June 2003 respectively. The data analysis was performed for age, sex, lymph node groups and organs involved at presentation and the morphological diagnosis of HD was made using REAL / WHO classification for the subtypes of HD. A comparison of age groups, sex and morphological types is also drawn.

This age distribution of HD in the data from Lahore varied between 3 and 75 years with median age of 21.383. The age range in Saudi data was between 4 and 78 years with a mean age of 25.883. The largest number of cases (n=143, 67.77%) occurred during the first three decades. It tapered as the age advances and becomes least common after the age of 50 years. This is true both for Pakistani & Saudi data. Statistically no significant association could be observed between age groups and number of

patients in Pakistani & Saudi data. Their *p*-values in various age groups were: 0–10:<0.7663; 11–20:<0.5124; 21–30:<0.2599; 31–40:<0.4621; 41–50:<0.4071; 51–60:<0.5674; 61–70:<0.1653; and in 71–80:<0.4598. Among the 211 cases in the data from Lahore, the male sex dominated (n=159, 75.25%) with female forming 24.64% (n=52). The male to female ratio is 3:1. Similar sex dominance was observed in the Saudi data of HD. The males formed 69.23% (n=54); whereas females were 30.76% (n=24) having a sex ratio of 2.25:1. (Table-1)

Among males and females of both groups (sex wise), no significant association between the males and females was found. The males in the combined data had a *p*-value of <0.2942 (insignificant) and in females of both groups <0.2941 (insignificant).

The nodal involvement was found to be most common both in Pakistani (n=200, 94.78%) and Saudi data (n=71, 91.02%). The cervical involvement was the commonest site in both. The extra nodal involvement was 3.79% (n=8); and 3.31% (n=7) respectively (Table-2). The morphological subtypes included lymphocytic predominant, nodular sclerosing, mixed cellularity and lymphocytic depletion types. Mixed cellularity HD was the commonest type (n=146) forming 69.19% in Pakistani data, the nodular sclerosis followed it (n=39, 18.48%). The lymphocytic predominant constituted 8.53% (n=18) whereas lymphocytic depletion was the least common i.e. 2.84% (n=6). In Saudi data, nodular sclerosing HD was the commonest type forming 53.85% (n=42 of 78) and mixed cellularity followed it, i.e., 32.05% (n=25 of 78). The lymphocytic predominant formed 14.10% (n=11 of 78). No case was diagnosed as lymphocytic depletion type among Saudi patients. (Figure-1) A significant association was observed between cases of MCHD in both Pakistani and Saudi groups. *p*<0.000 (69.19% and 32.05% respectively) as the cases of MCHD in Pakistani data are found to be more than in Saudi data. Regarding the NSHD subtype a significant association was observed between Pakistani & Saudi cases. *p*<0.000 (18.48% & 53.85% respectively); as the cases of NSHD are more in Saudi data.

Table-1: Age & Sex Distribution in Pakistani & Saudi patients

Age (Year)	Pakistani Data (211 Cases)			Saudi Data (78 Cases)		
	No. Patients	M (%)	F (%)	No. Patients	M (%)	F (%)
0–10	30 (14.21)	20 (66.66)	10 (33.33)	10 (12.85)	8 (80)	2 (20)
11–20	68 (32.22)	55 (80.88)	13 (19.11)	22 (28.20)	12 (54.54)	10 (45.45)
21–30	45 (21.32)	33 (73.33)	12 (26.66)	12 (15.38)	9 (75)	3 (25)
31–40	28 (13.27)	20 (71.42)	8 (28.57)	13 (16.67)	10 (76.92)	3 (23.07)
41–50	20 (9.47)	16 (80)	4 (20)	12 (12.82)	8 (80)	2 (20)
51–60	10 (4.73)	7 (70)	3 (30)	5 (6.41)	3 (60)	2 (40)
61–70	6 (2.88)	4 (66.66)	2 (33.33)	5 (6.41)	3 (60)	2 (40)
71–80	1 (0.47)	1 (100)	0 (00)	1 (1.28)	1 (100)	0 (00)
No age	3 (1.42)	2 (66.66)	1 (33.33)			
Total:	N=211	159 (75.35)	52 (24.64)	N=78	54 (69.23)	24 (30.76)

Males: *p*<0.2942 (insignificant); Females: *p*<0.2941 (insignificant)

Note: *p*-values of age groups are shown in results (all insignificant)

Table-2: Presenting sites of Pakistani and Saudi patients

Location→	Pakistani Data (n=211)	Saudi Data n=78	
	No: (%)	No: (%)	p-value
Nodal			
Cervical	108 (51.11)	38 (48.7)	0.7160
Axilla	31 (14.69)	8 (10.26)	0.3278
Inguinal	20 (9.47)	6 (7.69)	0.6386
Mediastinal	2 (0.94)	5 (1.28)	0.7996
Abdominal	15 (7.10)	4 (5.13)	0.5484
Generalised	24 (11.37)	8 (10.27)	0.7914
Para aortic	---	2 (2.56)	
Extra Nodal			
Liver	---	2 (2.56)	
Spleen	3 (1.42)	1 (1.28)	0.9279
Breast	---	1 (1.28)	
Intestinal (ileum)	6 (1.88)	3 (3.85)	0.3325
Testis	1 (0.47)	---	
Kidney	1 (0.47)	---	
	211	78	

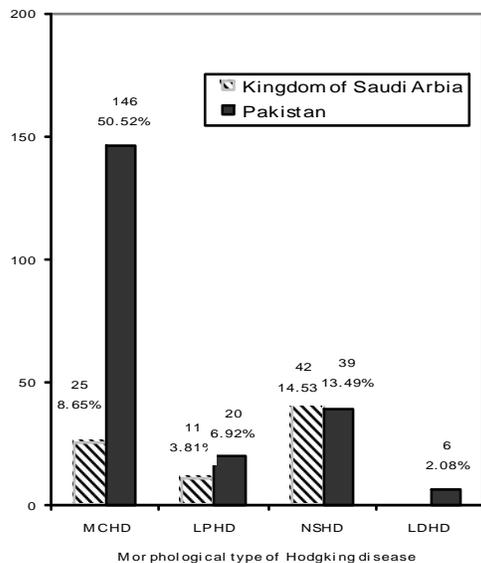


Figure-1: A comparison of the morphological subtypes of Hodgkin's disease, in Pakistani & Saudi data

DISCUSSION

The age distribution of Hodgkin's disease has a distinct pattern in most of the western communities and in some Middle East countries. A bimodal distribution of age has been generally reported by various workers from the western countries⁴⁻⁶ and some Middle East countries.⁷ However, this bimodal age pattern has not been observed in Pakistan⁸; whereas on the contrary the HD tapers after the age of 50. In fact in the present study in Pakistan & Saudi Arabia as the age advances (after 30 years) the incidence of HD falls rapidly. In the present study the average age in Pakistani patients was less and maximum cases of HD occurred during the first three decades; so is the case in Saudi patients from Jeddah— an eastern province of Saudi Arabia.

Among the 211 cases of HD in the data from Lahore, the male sex dominated forming 75.25% (n=159) and female forming 24.64% (n=52). The male to female ratio is 3:1. A similar sex dominance was observed in the Saudi patients among whom males formed 69.23 % (n=54); and females were 30.76% (n=24) with a sex ratio of 2.25: 1. In the western studies the sex incidence among whites of US formed about 63% of males; in Denmark 59% and in UK 66%.¹⁰⁻¹² A Saudi study from a western province reported a male incidence of 70:40%; this is closer to our study in the Saudi data (male= 69.23%) but definitely less than in Pakistani data from Lahore (male 75.25%).^{8,13} This is also supported by a study from Greece.²⁰ That is a relatively less industrialised country of Europe.

As regard the distribution of HD, commonest anatomical site in the present study was cervical lymph nodes (51.11%, n=108) among Pakistani patients; and 48.7% (n=38) in the Saudi data. The morphological analysis according to REAL/WHO classification revealed that the commonest subtype of HD was mixed cellularity HD forming 69.19% (n=146), this is followed by nodular sclerosis (18.48%, n=39), and lymphocytic predominant type (8.53%, n=20), and the least common was noticed to be lymphocytic depletion type (2.84%; n=6). The Saudi data on the other hand showed nodular sclerosis being 53.85% (n=42), followed by mixed cellularity HD being 32.05% (n=25) and lymphocyte predominant HD 14.1% (n=11). Lymphocytic depletion type of HD was not diagnosed in any Saudi patient. In another previous study from Riyadh, Saudi Arabia located in the western province and geographically situated about 1000 km away from the eastern city of Jeddah where our Saudi study was carried out, the dominant subtype of HD was mixed cellularity (59.3%) followed by nodular sclerosis.¹³

Majority population of Jeddah consists of economically rather poor class expatriates. Hence there might be a difference in the aetiologies of HD. Nodular sclerosis is more common in certain eastern countries¹⁶⁻¹⁷, whereas in others mixed cellularity predominates.²¹ Similarly mixed cellularity HD is more prevalent in Pakistan⁸. In the present study we also experienced a similar pattern in the data from Lahore. It may be pointed out that the high incidence of mixed cellularity HD is identical both in children¹⁸ and adults.⁸ Although generally speaking in industrialised countries the nodular sclerosis HD is more common than the other subtypes; however some western studies also showed predominance of mixed cellularity subtypes.^{20, 22}

Similarly a German study reported a slight dominance of mixed cellularity (43.8%) followed by

nodular sclerosis.²³ This refutes the reports which plead that nodular sclerosis HD is the dominant type in industrialised western countries, Germany is however a highly industrialised country. A Brazilian cross sectional histopathological study²⁴ covering four university hospitals, on the other hand showed the pattern similar to industrialised countries reporting nodular sclerosis HD being the commonest type forming 69.2%, and mixed cellularity only 21.1%.

Lymphocytic predominant formed 4.1% and lymphocytic depletion being 4.6%. This study is consistent with our data from Jeddah, Saudi Arabia except the prevalence of lymphocytic depletion forming 4.6% of 1025 Brazilian cases. However this & other above mentioned reports are contrary to our findings in the data analysed from Lahore, Pakistan, where the frequency of subtypes is different.

CONCLUSION

This study compares the data of Hodgkin's disease from Pakistan and Saudi Arabia for a period of eight years. The pattern of bimodality of age was not seen in both centres and the HD was more common during the 2nd, 3rd and 4th decades followed by a sharp decline. Mixed cellularity HD was the commonest type in Pakistani patients, whereas NS was the commonest type in Saudi patients in Jeddah centre. This change in pattern may be the result of, perhaps, different aetiological factors both infective & environmental, along with a highly variable expatriate population forming a majority in Jeddah.

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