Original paper

Clinical & Pathological Pattern of Hodgkin Lymphoma in Middle Euphrates Region of Iraq

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Abstract

Background: Hodgkin lymphoma (HL) is one of the most common malignancies affecting the young Iraqi patients. This disease has diversified pathologies and clinical stages. **Aims:** To evaluate the clinical & pathological pattern of patients with HL in Middle Euphrates region of Iraq. **Materials & Methods:** A retrospective descriptive study conducted at Al- Hussein cancer center in Karbala province of Iraq between February 2012 and June 2020.
Results: There were 193 patients with HL, 103 were male, 90 were female, M:F ratio was 1.14:1. Mean age at presentation was 27.17 years. Cervical lymph nodes was the common site for presentation (74.09%). Stage II was the most frequent stage (40.93%) while stage I was the least frequent (11.92%). Of classical HL type the mixed cellularity subtype was the most common one (49.74%), while the nodular lymphocyte predominant was representing (1.55%) only. A majority of our patients (79.27%) achieved complete remission post first line treatment.
Conclusion: The distribution of HL is mostly in young patients, the disease usually presented in early stage with very good response to treatment.
Key words: Hodgkin lymphoma, Pattern, Middle Euphrates, Iraq

Introduction

Hodgkin lymphoma (HL) is a wide spread lymphatic malignancy, accounting about 11 % of all lymphoid malignancy, distinguished by the presence of Reed-Sternberg cells, a giant malignant lymphatic cells.(1) Worldwide more than 79000 new cases were diagnosed, leading to more than 26 000 death in 2018.(2)

HL generally presented with involvement of peripheral lymph nodes but liver, lung & bone marrow may be infiltrated by the disease. At the same time, B symptoms (fever > 38°C, > 10% weight loss over 6 months, night sweats) may be also presented.(3)The Ann Arbor staging system is commonly used for HL staging. Stage I presented with single lymph node area with or without local extra nodal involvement, stage II presented with two or more lymph nodes area on the same side of the diaphragm, stage III presented with lymph nodes involvement on both sides of diaphragm while stage IV presented with disseminated infiltration of extra-lymphatic sites. A letter A or B may added to the stage, A referring to the absence of B symptoms while letter B referring to the presence of B symptoms.(3) HL is classified according to World Health Organization (WHO) into: a nodular lymphocyte predominant subtype which represents about 5% of cases & a classical HL that represents 95% of cases and includes several subtypes: nodular sclerosis, mixed cellularity, lymphocyte predominant and lymphocyte depleted.(4) Reed Sternberg cells of HL are CD15 & CD30 positive and oftentimes CD20 negative. While nodular lymphocyte predominant is CD30 & CD15 negative and CD20 & CD 45 positive. Seldom CD3 (which is T cells and natural killer marker) represented in HL.(5, 6)

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ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) chemotherapy regimen ± radiation is a common protocol for early and advance stage HL meanwhile autologous stem cell transplantation was kept for relapse or refractory patients only.[7] While R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone) is an effectual protocol for nodular lymphocyte predominant patients.[8]

This is the first statistical study of HL in Middle Euphrates region. It can help to provide basic information, assess the progress in recent years and to develop future lymphoma treatment strategies in this area of our county.

Materials and Methods

This is a retrospective descriptive study conducted in Al-Hussein cancer center in Karbala on HL patients diagnosed between February 2012 and June 2020. Our center was established in November 2011 with oncology & hematology wards. It covers not only Karbala population but other patients from Middle Euphrates region in Iraq are also referred to this center for solid & hematological malignancy treatment.[9,10] All patients were diagnosed according to the WHO classification by tissue biopsy and confirmed by immunohistochemistry markers. Immunhistochemical panel in our province using a panel of antibodies against CD30, CD15, CD20, CD3 and CD45. All patients are staged according to Ann Arbor classification by computed tomography (CT scan) or by positron emission tomography (PET) scan while bone marrow assessment was used in advanced and bulky disease only. Data provided information about the gender of patients, age, stage, years of diagnosis, histopathological classification of HL, treatment protocols and treatment outcomes. This study was approved by the review ethical committee of Karbala teaching hospital.

Results

There were 193 patients enrolled in our study, with mean age was 27.17 years, median age was 24 years and age range was (4-78 years). There were 103 male patients (53.37%) and 90 were female patients (46.63%) with male to female ratio= 1.14:1. Cervical lymph nodes were the most site involved 143 patients (74.09%) followed by mediastinum 18 patients (9.33%) , abdominal lymph nodes 15 patients (7.77%) , axillary lymph nodes 13 patients (6.73%) , inguinal lymph nodes 2 patients (1.04%) and extra lymphatic 2 patients (1.04%). B symptoms presented in 123 patients (63.73%) & 14 patients (7.25%) were bulky disease (bulky mediastinal disease or > 10 cm adenopathy). Majority of our patients presented with stage II 79 patients (40.93%) followed by stage III 57 patients (29.53%), stage IV 34 patients (17.62%) and stage I 23 (11.92%). Bone marrow was involved in 17 patients (8.81%) as shown in (table 1).

Mixed cellularity was the most histopathological type with 96 patients (49.74%), followed by nodular sclerosis 79 patients (40.93%), lymphocyte predominant 8 patients (4.15%), lymphocyte depleted 7 patients (3.63%) and nodular lymphocyte predominant 3 patients (1.55%) as shown in (figure 1). Regarding CD markers, CD 30 was positive in 187 patients (96.89%), CD 15 was positive in 174 patients (90.16%), CD 45 was negative in all patients, CD 20 was positive in 3 patients (1.55%) and CD 3 was positive in 6 patients (3.11%) as shown in (table 2). From 193 patients there were 130 patients (67.36%) received chemotherapy alone while 63 patients (32.64%) received chemotherapy plus radiotherapy, only 16 patients (8.29%) undergo ASCT. Majority of patients (98.44%) received ABVD protocol while 3 patients (1.56%) with nodular lymphocyte predominant received R-CHOP protocol. There were 153 patients (79.27%) achieved complete remission, 31 patients (16.06%) relapsed, while 11 patients (5.70%) were refractory (table 3).

Table 1. Patients characteristics on presentation

Age, years	
Mean	27.17
Median	24
Range	4-78
Gender	
Male	103 (53.37%)
Female	90 (46.63%)
B symptoms	
Present	123(63.73%)
Absent	70 (36.27%)
Bulky disease	
Yes	14 (7.25%)
No	179 (92.75%)
Site	
Cervical	143 (74.09%)
Mediastenal	18 (9.33%)
Abdominal	15 (7.77%)
Axillary	13 (6.73%)
Inguinal	2 (1.04%)
Extra lymphatic	2 (1.04%)
Stage	
I	23 (11.92%)
II	79 (40.93%)
III	57 (29.53%)
IV	34 (17.62%)
Bone marrow involvement	
Yes	17 (8.81 %)
No	176 (91.19 %)

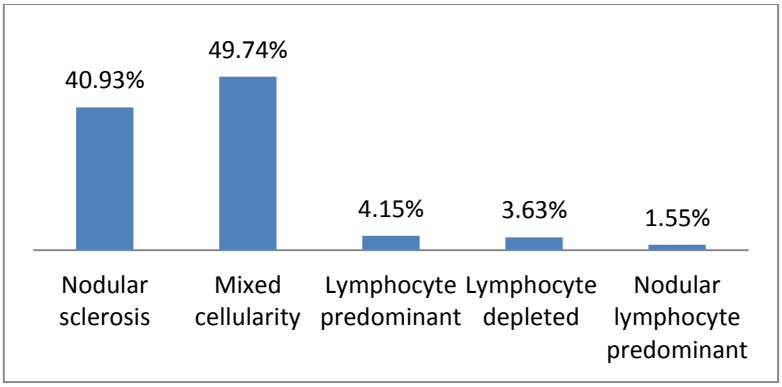

Figure 1. Pathological pattern of HL patients

Table 2. CD expression in HL patients

	Positive N (%)	Negative N (%)
CD 30	187 (96.89%)	6 (3.11%)
CD 15	174 (90.16%)	19 (9.84%)
CD 20	3 (1.55%)	190 (98.45%)
CD 45	0 (0.00%)	193 (100%)
CD 3	6 (3.11%)	187 (96.89%)

Table 3. Frontline treatment details

	N (%)
Treatment details	
Chemotherapy alone	130 (67. 36%)
Chemotherapy + RT	63 (32.64%)
ASCT	16 (8.29%)
Chemotherapy protocol details	
ABVD	190 (98.44%)
R-CHOP	3 (1.56%)
Treatment outcomes	
Complete remission	153 (79.27%)
Relapse	31 (16.06%)
Refractory	11 (5.70%)

RT = Radiotherapy, ASCT = Autologous stem cells transplant, ABVD = Doxorubicin, Bleomycin, Vinblastine, Dacarbazine, R-CHOP = Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, Prednisolone.

Discussion

HL has distinctive epidemiological features. The difference in occurrence according to the age, sex, race and socioeconomic status indicates that both genetic and environmental factors may play a role in the pathogenesis of HL.[11] In our province lymphoma represents the second most common malignancy after breast cancer presenting more than 8% of registered cases.[12] Mean age of our patients was 27.17 years with (male to female ratio= 1.14:1). Being Iraqi has a high percent of young population (> 58% of population under 25 years old) so it was not unusual to find that most of patients with HL in this study below 30 year old.[9] Male predominant was also seen in previous studies in northern Iraq, Jordan, Saudi Arabia and United States. [13-17]

Cervical lymph nodes were the most common site for involvement in our study that can be explained by seeking early medical advice by our patients. These findings agreed with many other studies in the US , Saudi Arabia and Armenia.[16-18] B symptoms presented in 63.73% of patients, which is close to a study done by Shamoon et al., in Iraq while it is higher than in Pakistan (55%) and lower than Saudi Arabia where B symptoms presented in more than 80% of patients.[16,19, 20] Bone marrow was involved in (8.81%) of patients which is close to India, higher than in German study where bone marrow was infiltrated only in 4.8% of patients.[21,22] In the same time our results were lower than in Pakistan and Saudi Arabia where 15.7% & 14.3% of patients respectively presented with bone marrow infiltration.[16,20]

A majority of cases in our study were stage II, which is consistent with other studies in Iraq while in countries such as Saudi Arabia and Pakistan, the disease was more advance.[13,16,19, 20]

Classical HL represents the majority of cases (98.45%) while nodular lymphocyte predominant represents only (1.55%) which is close to results in the north of Iraq and the US.[14,17] Mixed cellularity was the most common cHL subtype, same results were obtained in Jordan , Saudi Arabia, India, Pakistan and Kenya.[15,16,20,21,23] Meanwhile nodular sclerosis was the most frequent type in north Iraq , United States ,Germany, Latin America and Hong Kong.[13,17,24-26]

The diagnosis was confirmed by IHC staining in which CD 15, CD30 was done for all patients and they were positive together in about 90% of cases and this was agreed with study in north Iraq.[14] CD 20 was positive in (1.55%) of patients close to north Iraq and Germany where less than 5% were positive and lower than India where CD20 was expressed by 15.61% of the cases.[14, 27, 28]

Due to its better toxicity profile, ABVD has become the standard chemotherapeutic regimen used to treat cHL in the United States of America.[17] Therefore it was the most common used protocol for classical HL in our center and other centers in Iraq.[14,19] About 79.27% of our patients achieved remission, 16.06% relapse, while only 5.70% were refractory. These findings are close to a study done in north Iraq and Asian countries such as Malaysia but lower than developed countries in Asia such as Hong Kong this may be explained by shortage in resources in our war torn country.[14,19, 26, 29]

Conclusion

In our study classical HL represents the majority of cases while mixed cellularity is the most frequent subtype, most of our patients presented in early stages and most common site involved was in the neck, 63.73% of patients had B symptoms. Almost our patients had CD30 and CD15 positive by immunohistochemistry. Treatment outcomes were good in our center where 79.27% of patients achieved remission. Unique pattern of HL in Middle Euphrates region highlights the need for future studies in other parts of Iraq with larger number of patients to understand the lymphoma dissemination in this country.

Declaration

Conflict of Interest

The authors declare that there is no conflict of interest.

Authors Contribution

All authors listed have made a substantial, direct, intellectual contribution to the work and approved it for publication.

Funding

None.

Data Availability

All data sets analyzed in the study are included in the manuscript and presented as tables.

Ethics Statement

Selected topic was accepted by scientific committee; official acceptance was taken from health authorities to conduct this study. Collected information was kept confidential.

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