



RESEARCH ARTICLE

Patterns of lymphoma in Misan city, Iraq: A retrospective observational study [version 1; peer review: 1 approved with reservations, 1 not approved]

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Abstract

Background: Lymphomas represent a biologically and clinically heterogeneous group of neoplasms. They have historically and clinically been divided into two groups, Hodgkin’s lymphoma (HL) and non-Hodgkin’s lymphoma (NHL). This study aimed to identify patterns in lymphomas in Misan city, Iraq, and evaluate the characteristics of this disease.

Methods: A retrospective, observational, single-center study was conducted at Al-Shifaa Oncology Center, Al-Sadder Teaching Hospital, Misan city, Iraq, between 1 April 2016 and 30 April 2018. A total of 80 Misanian participants (48 (60%) men and 32 (40%) women) who had lymphoma were involved in this study. The sources of information were patient files, histopathology reports, and patients’ oncologist reports.

Results: The mean age (±SD) of participants was 36 ±12.8 years. The male to female ratio was 1.5:1. NHL cases were three times more prevalent than HL. The most frequent stage at presentation was stage IV, in 34 (42.5%) participants. The classical subtypes of HL were present in 14 (70%) of HL cases. The diffuse large B-cell lymphoma (DLBCL) subtype was the most common NHL subtype, being recorded for 44 (73.3%) of participants.

Conclusion: Lymphomas were more frequent in men. NHL was more common than HL; one HL case was diagnosed for every three NHL cases. The most common histopathology of HL was mixed cellularity, while DLBCL was the most common subtype of NHL. Most cases presented at an advanced stage, resulting in a late diagnosis.

Open Peer Review

Reviewer Status

| | Invited Reviewers | |
|------------------|-------------------|--------|
| | 1 | 2 |
| version 1 | | |
| 09 Oct 2019 | report | report |

1. **Maria Luisa Moleti**, Sapienza University, Rome, Italy
2. **Wendy Cozen**, University of Southern California, Los Angeles, USA

Any reports and responses or comments on the article can be found at the end of the article.

Keywords

Non Hodgkin lymphoma, Hodgkin lymphoma, Misan, Lymphoid cells, Iraq

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Introduction

The term lymphoma refers to a heterogeneous group of neoplasms that originate from lymphoid cells. The majority (85%) of lymphomas originate from mature B-cells, and 15% derive from the T-cell lineage¹. Historically and clinically, lymphomas have been divided into two groups, Hodgkin’s lymphoma (HL) and non-Hodgkin’s lymphoma (NHL). HL is characterized by the presence of Reed–Sternberg cells, which arise in a single lymph node or chain of lymph nodes and typically spread in a stepwise fashion to anatomically contiguous nodes¹. The crude incidence of HL among Europeans is 2.3 per 100,000 individuals². Young adults aged 20 to 40 years are most commonly affected¹. Histologically, classical HL accounts for 95% of all HL cases¹. The subtypes of classical lymphomas include nodular sclerosis (the most common subtype, comprising 60–65% of cases), mixed cellularity (15–30%), lymphocyte-rich (5%), and lymphocyte-depleted (1%)^{1,3}. HL patients present with peripheral lymphadenopathy, with nodes that are not tender, and with no overlying skin changes^{1,2}. NHL are neoplastic transformations of mature B-, T-, or natural killer cells¹. In children, diffuse large B-cell lymphoma (DLBCL), Burkitt’s lymphoma, and lymphoblastic lymphoma are most common^{2–4}. DLBCL is the most common histological subtype in adults⁴. The incidence increases with age, while a family history of lymphoma, autoimmune disease, human immunodeficiency virus infection, hepatitis C virus seropositivity, and a high body-mass as a young adult have all been identified as risk factors of DLBCL^{4,5}.

Here, we describe a study designed to show patterns of lymphoma among patients in Misan who presented at our center. Since this group of neoplasms are curable diseases, we need to obtain more information about them to get a significant and timely picture about the current lymphoma situation in Iraq, and in Misan in particular.

Methods

Study design

This was a retrospective, observational, single-center study carried out in Misan city, Iraq to identify any patterns in lymphoma prevalence in this governmental administrative area.

Setting

The study was conducted at Al-Shifaa Oncology Center, Al-Sadder Teaching Hospital, Faculty of Medicine, Misan University, Misan city, Iraq, from 1 April 2016 to 30 April, 2018 (Figure 1). The recruitment dates began on the tenth day of each month and continued to the thirtieth day of that month. The period from the first day of the month until the ninth day was the time of patient follow-up. Data were collected on the last day of each month of the study.

Participants

A total of 80 participants (48 men and 32 women) from Misan who were diagnosed with lymphoma were included in this study. The age of participants ranged from 10 years to 80 years. Each patient had been previously diagnosed with lymphoma



Figure 1. Al-Shifaa Oncology Center, Al-Sadder Teaching Hospital at the Faculty of Medicine. Imagery ©2019 Maxar Technologies.

and attended our center for chemotherapy. We included all patients diagnosed with lymphoma without any selectivity (the patients must live in Misan city). Sources of information included patient files, histopathology reports, and patient oncologist reports (these contained all of a patient’s data written by his/her oncologist). Participant follow-up was performed on any day of nine days following a chemotherapy cycle.

Variables

History and investigation results were documented and recorded for each participant in his/her file, including age, type of residency, occupation, sex, diagnosis, stage of lymphoma, subtype of lymphoma, and class of lymphoma.

Data sources/measurement

The main sources of data were patient files and histopathology reports. Data written in the files included a patient’s baseline characteristics, lymphoma baseline characteristics, and all investigations done.

Study size

We obtained this number of participants because we included all individuals with lymphoma without any selection methods.

Ethical considerations

Written informed consent was obtained from all participants, or the parents of those aged less than 18 years, to participate in this study. The Medical Ethical Committee at Al-Shifaa Oncology Center, Al-Sadder Teaching Hospital, Faculty of Medicine, Misan University approved this study (code: 1000552).

Statistical analysis

We used Microsoft Excel (v. 2010) to calculate frequencies and percentages of variables, and also to calculate means and standard deviations (SDs). This study did not have any missing data.

Results

All 80 participants included in this study were examined for eligibility and completion of follow-up. The mean age (±SD) of participants was 36±12.8 years. Half of the participants were in the 31–60 year age group, 24 (30%) of participants were aged >60 years, and just 16 (20%) belonged to the 10–30 year age group. Most participants (53; 67.5%) lived in rural areas, while 27 (32.5%) lived in urban regions. The majority of patients were employed (58; 72.5%). The male to female ratio was 1.5:1 (48 males and 32 females).

NHL was three-times more prevalent than HL, with 60 (75%) and 20 (25%) cases, respectively. Participants most frequently presented with stage IV, in 34 (42.5%) of cases, followed by stage III in 24 (32.5%), stage II in 12 (15%), and stage I in 8 (10%) cases. The classical subtypes of HL were most common, occurring in 14 (70%) cases compared with 6 (30%) cases who had nodular subtypes. The DLBCL subtype was most common among NHL subtypes, being recorded in 44 (73.3%) of cases. Classical HL was subdivided into nodular sclerosis (2; 14.3%), lymphatic-rich subtype (4; 28.6%), and mixed cellularity (8; 57.1%) (Table 1).

Table 1. Characteristics of patients with lymphoma in Misan city, Iraq, April 2016 to April 2018.

| Variable (n=80) | n (%) | |
|-------------------|------------------------------|-----------|
| Age, years | 10–30 | 16 (20) |
| | 31–60 | 40 (50) |
| | ≥ 60 | 24 (30) |
| Residence | Rural | 53 (67.5) |
| | Urban | 27 (32.5) |
| Occupation | Not employed | 22 (27.5) |
| | Employed | 58 (72.5) |
| Sex | Male | 48 (60) |
| | Female | 32 (40) |
| Diagnosis | Hodgkin’s lymphoma (HL) | 20 (25) |
| | Non-Hodgkin’s lymphoma (NHL) | 60 (75) |
| Staging | I | 8 (10) |
| | II | 12 (15) |
| | III | 26 (32.5) |
| | IV | 34 (42.5) |
| HL (n=20) | Nodular | 6 (30) |
| | Classical (CHL) | 14 (70) |
| NHL (n=60) | Diffuse large B-cell | 44 (73.3) |
| | Follicular cell | 4 (6.6) |
| | Mantle cell | 6 (10) |
| | Burkett’s | 2 (3.4) |
| | Peripheral T-cell | 4 (6.6) |
| CHL (n=14) | Nodular sclerosis | 2 (14.3) |
| | Lymphocyte rich | 4 (28.6) |
| | Mixed cellularity | 8 (57.1) |

Discussion

In our study, HL and NHL were recorded in 25% and 75% of cases, respectively, which is consistent with the results of a study conducted in Erbil city, in the north of Iraq⁶. The majority of HL cases presented as the classical subtype (70%), while 30% of cases encountered were of the nodular subtype (30%). The subtypes of classical HL included the nodular sclerosis (NS) subtype (14.3%) and the lymphocyte-rich subtype (28.6%), although the majority of cases comprised the mixed cellularity subtype (57.1%). The most frequent histological subtype of HL was mixed cellularity, which differs from earlier reports from the north of Iraq^{5,6}, but is consistent with earlier reports from nearby countries and India^{7–17}. This changing pattern differs from more recent reports from Saudi Arabia, Jordan, United Arab Emirates (UAE), and Kuwait, where higher relative rates of NS HL were reported, approaching levels seen in the USA and in European countries^{12–17}.

With regard to NHL subtypes, we found that the majority comprised DLBCL, followed by mantle cell, follicular cell, peripheral T-cell, and Burkitt’s lymphoma. According to WHO classifications, DLBCL was also the most common diagnosis

worldwide, at 52.2%, followed by T-cell rich lymphoma¹². The relative proportion of DLBCL seen in the current study is almost twice the proportion seen in the USA and Europe, and is much higher than the proportion reported in India^{2,4,17,18}, but is closer to figures reported from UAE¹⁴, Kuwait¹⁵, Jordan¹³, and Turkey¹⁹.

We found that the majority of lymphoma cases occurred in those aged 31 to 60 years, which was the same as findings in the USA and other countries^{15,18–20}.

The majority of cases in our study presented at stage III or stage IV. Stage IV comprised 42.5% of cases and stage III 32.5%, while the remainder were stage II (15%) and stage I (10%). These results are in agreement with the results of a study by Robert *et al.*²¹.

Limitations of this study include that it was a single-centre study, with a small number of participants, and the participants represent residents of the Misan government administrative area only.

Conclusions

This study showed that in Misan city, Iraq, lymphoma occurs most frequently among males. NHL is more common than HL, and the most common histopathology of HL is mixed cellularity, while DLBCL is the most common histopathology for NHL. Most cases presented with stage III or IV, which reflects delays in diagnosis, and decreases the chance of complete recovery, reflecting a more aggressive course and behavior of the disease.

Data availability

Zenodo: Lymphoma diseases patients patterns in Misan Government, <http://doi.org/10.5281/zenodo.3458806>²².

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Current Peer Review Status: ? ✗

Version 1

Reviewer Report 26 August 2020

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✗ Wendy Cozen

Departments of Preventive Medicine and Pathology, Keck School of Medicine of USC, University of Southern California, Los Angeles, CA, USA

This study describes characteristics of lymphoma patients at a teaching hospital in Misan, Iraq. The subject matter is interesting because the distribution of histologic subtype of lymphoma varies internationally. There is not much known about the distribution of lymphoma types in Iraq so this study will contribute knowledge.

However, the authors miss an opportunity to present more useful data and there are a few problems with the way the paper is written. Comments are below:

1. The representativeness of the lymphoma patients diagnosed at Misan University hospital is unclear. What % of all patients in the region are diagnosed at this hospital? Does the hospital preferentially treat refractory or difficult cases? More details are needed to understand the generalizability of the patients to the Iraqi population.
2. Figure 1 is not necessary.
3. Table 1 - frequencies should be presented by sex.
4. Additional details would be helpful, for example, what is the distribution of germinal center vs. activated B-cell among DLBCL cases? How many of the Hodgkin lymphoma cases are EBV+?
5. The characteristics in Table 1 should be stratified by Hodgkin and non-Hodgkin lymphoma and not lumped together.
6. A pie chart might be a better way to show the histological distributions, perhaps comparing to other countries.

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

No

Are sufficient details of methods and analysis provided to allow replication by others?

No

If applicable, is the statistical analysis and its interpretation appropriate?

No

Are all the source data underlying the results available to ensure full reproducibility?

No

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Epidemiology and pathology of hematologic neoplasms.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Reviewer Report 26 August 2020

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Maria Luisa Moleti

Department of Translational and Precision Medicine, Sapienza University, Rome, Italy

The authors report the results of a retrospective study conducted at Al-Shifaa Oncology Center, Al-Sadder Teaching Hospital, Misan city, Iraq, on 80 lymphoma patients diagnosed and treated from April 2016 to April 2018. The aim of the study was to describe the histopathological and clinical patterns of lymphoma patients from the Misan area.

The important issue of the spectrum of lymphomas in the different geographic areas is the object of several reports and this paper could add new data regarding the Middle East area. However, some comments need to be made.

Introduction

- The Introduction should focus primarily on the topic of different histological lymphoma

subtypes in different geographic areas.

Methods

- Information concerning the Histopathologic Classification system, Stadiation system and stadiation modality, and also the inclusion criteria are not described.
- The methods description is repetitive and unclear and is not completely congruent with the objectives and results of the study. For example:
 - 1) *"The recruitment dates began on the tenth day of each month and continued to the thirtieth day of that month. The period from the first day of the month until the ninth day was the time of patient follow-up. Data were collected on the last day of each month of the study."*
What do the authors mean? It is not clear. Why do the authors mention the follow-up? It is not relevant to this study.
 - 2) *"We included all patients diagnosed with lymphoma without any selectivity (the patients must live in Misan city)"*.
What do the authors mean? It is not clear.
 - 3) *"Study size"*
Can be omitted. It does not make sense; moreover, the authors already mentioned that all diagnosed patients were included.

Results

- The authors could describe the results in a more detailed table, distinguishing the characteristics of the patients with HL and NHL, both for the entire population and also according to the three different age ranges.
- Median age instead of mean age may give more information on the age distribution.
- How many patients are in the pediatric age (<15)? This is relevant because of the different histological distribution of pediatric lymphomas.
- The description of the clinical presentation is missing; it could add interest to the study and could be included in the table.

Discussion

- The authors compare their results to the literature in detail. Other more recent papers on the same topic may be included in the discussion. A table comparing the results of papers reporting the Middle East lymphoma distribution might be interesting.
- Some comments on the low incidence of low-grade lymphomas might be interesting.

References

- In the literature, there are other papers on this topic, for example, Perry, Hematologica 2016, (NHL in the developing world)¹; Gross, Br J. Hematol 2016, (pediatric population in LIC)²; Monabati, Ann. Hematol. 2016 and Mozaheb, Cancer Epidemiology 2011 (data from Iran)³; Saglam, Turkish Journal of Medical Sciences 2018 (data from Turkey).⁵

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Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Not applicable

Are all the source data underlying the results available to ensure full reproducibility?

No source data required

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Pediatric and Young adult hematological malignancies, particularly Hodgkin and non Hodgkin lymphomas,

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

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