

Epidemiological and Clinical Profile of Hodgkin and Non-Hodgkin Lymphoma in Karbala, Iraq

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ABSTRACT

Background: Lymphoma is a heterogeneous group of malignancies that have their origin in lymphoid tissue, and are broadly grouped into either Hodgkin lymphoma (HL) or non-Hodgkin lymphoma (NHL). Epidemiology, clinical behaviour, and treatment responses of such malignancies differ in geographic regions and human populations. In Iraq, there are limited regional epidemiological data on the lymphoma and, therefore, local studies are necessary to enhance the clinical practice and healthcare planning. Purpose: This research aims to examine the nature of individuals with lymphoma that was treated in the Al-Hussein Medical City in Karbala. We would like to know the types of treatment that were applied to these patients. The target of this study is lymphoma patients and the treatment of lymphomas. What we can learn by studying lymphoma and lymphoma treatment is how to assist lymphoma patients. Methods: The study was a retrospective cross-sectional one as it reviewed the medical records of 80 patients diagnosed with lymphoma during the period of 2018-2023. The data gathered was on demographic details, type and subtype of lymphoma, stage of diagnosis using the Ann Arbor classification, treatment courses and treatment outcome. Findings: The study involved 80 patients who included 61.25% females. Fifty-six patients (70%), and 24 patients (30%), were diagnosed with non-Hodgkin and Hodgkin lymphoma, respectively. The most recurring subtype was diffuse large B-cell lymphoma (DLBCL) which made up 47.5 percent of the total cases. The average age of diagnosis was 50 years (15-82 years). The most common stage of presentation was stage I (27.5%), and stage II (26.25%). R-CHOP (53.75%), and ABVD (32.5) were the most common first-line treatment regimen used in the case of NHL and HL, respectively. In 52.5% of the patients, full remission was attained. Eight point seven five percent of cases received stem cell transplantation. Twenty-seven point five percent of the patients reported a positive family history of malignancy. Conclusion: Non-Hodgkin lymphoma is the most common type of lymphoma in Karbala with the diffuse large B-cell lymphoma being the most common type. R-CHOP, ABVD and other standard treatment programs yielded good remission rates among numerous patients. Even better patient outcomes could be achieved by improving the screening programs and the early referral..

INTRODUCTION

Lymphoma is a heterogeneous collection of haematologic malignancies that results from the clonal development of B-cells, T-cells, and natural killer (NK) cells of lymphocytes at different developmental stages [1]. The prevalence of lymphoma is about 4 -5 percent of all cancers worldwide, and its rate is increasing in most of the low- and middle-income countries [2]. Two major groups, namely, HL and NHL, exhibit considerable disparities in epidemiology, histopathology, clinical manifestations, and prognosis.

NHL represents most cases of lymphoma on a global scale, and the most common subtype on a global scale is diffuse large B-cell lymphoma [DLBCL] [3]. Based on GLOBOCAN 2022 statistics, 544,000 new cases of NHL are estimated worldwide, with a distinct regional disparity [4]. NHL: HL incidence rate ratios in the Middle East are lower than those found in Western populations, with countries in this area attributed to variations in demographics and local environmental exposures [5].

Lymphoma causes a high percentage of the burden of haematological malignancy in Iraq. In a retrospective study of 270 cases of lymphoma in northern Iraq, it was shown that NHL was the most common lymphoma [76%], the most common subtype being DLBCL [52.2%], followed by Burkitt lymphoma [14.6%] [6]. A survey conducted at the Al-Hussein Cancer Centre in Karbala, which covers the Middle Euphrates area, identified 193 patients with HL over eight years, with mixed cellularity being the most common histological subtype [49.74%] and a high

percentage of complete remission [79.27%] [7]. A cross-sectional study of 50 cases in Baghdad proved that HL was 40%, and NHL 60%, and DLBCL was the most common NHL subtype [40%] [8]. Although these sources have been understood, there are few data sources specific to Karbala governorate, which is a significant referral centre for the Middle Euphrates region. There is limited data on this area, and available statistics show that patients from more than one governorate, such as Najaf, Babylon, Al-Qadisiyah, and Al-Muthanna, are referred to the Al-Hussein medical city in Karbala to treat haematological malignancy [7]. Knowledge of local lymphoma trends, treatment patterns, and treatment responses would thus be necessary for clinical judgment and the allocation of health resources.

The current study was conducted to identify the clinical characteristics of patients with lymphoma in Karbala, outline the subtypes and presenting stages, and assess first-line treatment options and their outcomes.

METHODOLOGY

The retrospective cross-sectional study design was adopted. The period considered was between January 2018 and August 2023, during which medical records of lymphoma patients diagnosed and treated at Al-Hussein Medical City in Karbala, Iraq, were reviewed. The extraction of the data was done through a structured data collection tool that retrieved the following variables: patient demographics [age at diagnosis, gender, address], lymphoma type and histological subtype, Ann Arbor clinical stage, B symptoms, comorbidities, laboratory investigations [complete blood count (CBC) and PET/CT imaging], first-line treatment protocol, radiotherapy and the use of stem cell transplantation, treatment response, family history of malignancy, and social history.

Inclusion had to be confirmed histopathologically. Patients with incomplete medical records or unconfirmed diagnoses were excluded. The subtypes of lymphoma were categorized according to the World Health Organization (WHO) classification of lymphoid neoplasms. Both HL and NHL had Ann Arbor staging with the Cotswolds modification. The response to treatment was evaluated according to a pre-existing set of criteria: complete remission [CR] represented the absence of visible disease on imaging, and partial remission [PR] represented a 50% or greater reduction in tumour mass.

The findings were described using descriptive statistics. Frequency and percentage were used to describe the categorical variables. Data was handled in a manner consistent with ethical principles, and patient confidentiality was maintained.

RESULTS

The study involved 80 patients. Table 1 summarizes the demographic and clinical characteristics.

Table 1: Demographic and Clinical Characteristics of the Study Population

Characteristic	n	Percentage (%)
Gender		
Male	31	38.75
Female	49	61.25
Age Group at Diagnosis (years)		
< 30 years	9	11.25
30–45 years	26	32.50
46–60 years	20	25.00
> 60 years	25	31.25
Lymphoma Type		
Non-Hodgkin Lymphoma (NHL)	56	70.00
Hodgkin Lymphoma (HL)	24	30.00

The female-to-male ratio was about 1.6:1, with 49 patients female and 31 male. The average age of diagnosis was

50 years, with a range of 15-82 years. The age group 30-45 years was the most represented [n=26, 32.5%], followed by patients aged 60 years or older [n=25, 31.25%].

In 56 patients [70%], non-Hodgkin lymphoma was detected, and in 24 patients [30%], Hodgkin lymphoma. Regarding the distribution of subtypes [Table 2], the most commonly recorded subtype was DLBCL with 67.86% of cases of NHL [38 patients, or 47.5% of the total population of the study group]. Follicular lymphoma [12.50%] and T-cell lymphoma [7.14%] ranked third and fourth, respectively. In HL, the subtype with the highest prevalence was mixed cellularity [37.50%], with classical HL [unspecified] and nodular sclerosis [29.17% each] ranking 2nd and 3rd, respectively.

Table 2: Distribution of Lymphoma Subtypes

Subtype	n	Percentage (%)
NHL Subtypes		
Diffuse Large B-Cell Lymphoma (DLBCL)	38	67.86
Follicular Lymphoma	7	12.50
T-Cell Lymphoma	4	7.14
Small Lymphocytic Lymphoma (SLL)	1	1.79
Burkitt Lymphoma	1	1.79
Other NHL subtypes	5	8.93
HL Subtypes		
Mixed Cellularity	9	37.50
Classical HL (Unspecified)	7	29.17
Nodular Sclerosis	7	29.17
Non-Classical HL	1	4.17

Table 3 shows the distribution of cases by Ann Arbor stage. Stage I was documented in 22 patients [27.5%], stage II in 21 [26.25%], stage III in 19 [23.75%], and stage IV in 18 [22.5%]. It is interesting to note that 46.25% of the overall cohort had advanced-stage disease [stages III -IV combined]. In the NHL patients, the most common advanced stage was stage IV disease [30.4% of NHL cases], the HL patients were more likely to be diagnosed at lower stages, with stage I and II of the disease taking up 75% of cases.

Table 3: Distribution of Ann Arbor Stage by Lymphoma Type

Stage	Total n (%)	NHL n (%)	HL n (%)	Overall (%)
Stage I	22 (27.5%)	14 (25.0%)	8 (33.3%)	27.50
Stage II	21 (26.25%)	11 (19.6%)	10 (41.7%)	26.25
Stage III	19 (23.75%)	14 (25.0%)	5 (20.8%)	23.75
Stage IV	18 (22.5%)	17 (30.4%)	1 (4.2%)	22.50
Total	80 (100%)	56 (100%)	24 (100%)	100

Most frequent clinical manifestations were lymphadenopathy [lump], fever, night sweats, and weight loss- all of which are B symptoms. B symptoms were also common in NHL as well as HL patients. A percentage of the patients were found to have comorbidities, and the most prevalent were hypertension [HTN], diabetes mellitus [DM], and ischaemic heart disease [IHD]. Only 22 patients [27.5%] reported a positive family history of malignancy.

Figure 1 shows the spread of lymphoma types and the percentage of HL and NHL in the population under study.

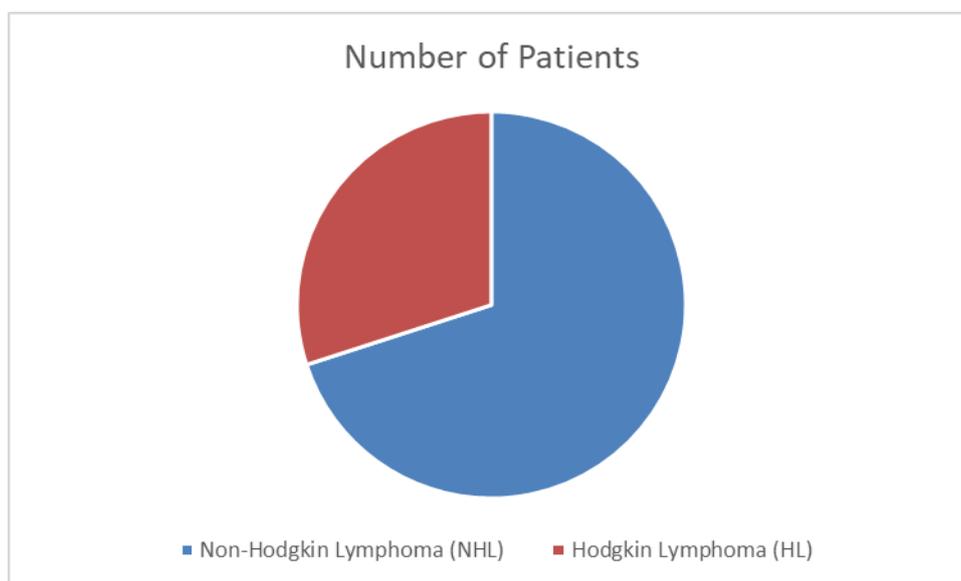


Figure 1. Distribution of lymphoma types among the study population (n=80)

Table 4 describes the treatment modalities and outcomes. The most commonly used first-line regimen was R-CHOP and its variations, which were used in 43 patients [53.75%], mainly used in NHL. The use of ABVD was used in 26 patients [32.50%], which is the regular first-line therapy of HL patients. Rituximab in combination with bendamustine [RB] was used in 7 patients [8.75%], mainly for indolent lymphomas. There were a few cases of using other regimens, such as CHOP, R-DHAP, and pembrolizumab (Keytruda). There was the use of radiotherapy in 3 patients [3.75%] and stem cell transplant in 7 [8.75%].

42 patients [52.5] achieved complete remission, and 19 patients [23.75] achieved partial remission. The response to treatment was not measured or ongoing among the remaining patients [23.75%] when data were collected. A second-line therapy was established in some patients who responded partially or not, and stem cell transplantation was developed in some of the relapses or refractory cases.

Table 4: Treatment Modalities and Outcomes

Treatment / Outcome	n	Percentage (%)
First-Line Treatment		
R-CHOP (incl. variants)	43	53.75
ABVD	26	32.50
Rituximab + Bendamustine (RB)	7	8.75
Other (CHOP, R-DHAP, Pembrolizumab)	4	5.00
Radiotherapy	3	3.75
Stem Cell Transplantation	7	8.75

Treatment Response		
Complete Remission (CR)	42	52.50
Partial Remission (PR)	19	23.75
Not Yet Assessed / Ongoing	19	23.75

DISCUSSION

This paper reports the clinical characteristics and treatment response of 80 lymphoma patients referred to Al-Hussein Medical City, Karbala, a tertiary oncology centre serving the broader Middle Euphrates region of Iraq. The trend of NHL [70%] versus HL [30%] in the current cohort is in line with trends across Iraq and the Middle East. A three-to-one ratio of NHL to HL was reported by Mjali et al. in a study based on Misan city, with NHL predominantly at stage IV [9]. On the same note, Yaqo et al. reported that NHL accounted for 76% of lymphomas in the northern part of Iraq, and the most common subtype was DLBCL [6]. NHL preponderance was also reported in the Al-Tae et al. Baghdad study at a rate of 60, with 40% of NHL cases being DLBCL [8].

The predominant subtype in the current cohort was DLBCL [67.86% of NHL, 47.5% overall], consistent with worldwide and regional data sets. DLBCL accounts for 25-30% of total lymphoma diagnoses worldwide and is the most frequent aggressive B-cell malignancy [10]. The NHL classification study indicated that, in the Middle East scenario, 52% of NHL cases in Sulaimaniyah Province, Iraq, were DLBCL, and 54.02% of NHL cases at Al-Hussein Cancer Centre, Karbala (Mjali et al. [4,11]). The uniformity in the prevalence of DLBCL across different Iraqi groups highlights similarities in biological and potentially environmental factors.

In HL, the most common subtype was mixed cellularity [37.50%], consistent with the Karbala HL study by Mjali [2021], which also found mixed cellularity as the most common subtype [49.74%] [7]. Conversely, the most frequent HL type in the West, 60-65 percent of all cases, is nodular sclerosis [12]. The comparatively higher incidence of mixed cellularity in this study and in cases from regional Iraq may be due to the younger age of onset of HL in the region and the possibility that mixed cellularity HL is more closely associated with Epstein-Barr virus [EBV] infection in developing nations [13].

The female preponderance [61.25] is one of the most remarkable observations in the current study, as a male preponderance is usually reported in the literature on lymphoma in Iraq and the region. The studies by Mjali et al. and Yaqo et al. showed male predominance in the populations with HL and NHL, respectively [6,7]. This observed female dominance may in part be due to referral patterns to Al-Hussein Medical City and variations in health-seeking behaviour across the governorates. It can also reflect the presence of patients from Babylon, Najaf, Wasit, and other governorates who came to receive treatment at this centre, which can bias the gender composition of the cohort.

The average age at diagnosis was 50 years, and the 30-45-year age group had the highest percentage [32.5%]. This is in line with reports in the region. A mean age of 27.17 years, specifically for HL, was recorded in the Karbala HL study, which is typical of the bimodal age distribution of HL with a young adult peak [7]. In the present study, the wider age distribution is due to the inclusion of HL and NHL, as the latter has a higher incidence peak among older adults and middle-aged people. DLBCL and extranodal NHL in the north of Iraq were also found to be more frequent in adults, which confirms the age distribution in this area [6].

The staging data showed that the disease was in an early stage (stages I-II) in 53.75 percent of all the cases reported and at an advanced stage (stages III-IV) in 46.25 percent. The distribution is widely in line with the regional findings. Stage II is the most frequent presenting stage in the Karbala HL series [40.93%], with fairly good results [7]. Still, in NHL, the presentation stage is more advanced around the world; in the current group, stage IV was the most prevalent among NHL patients [30.4% of NHL], which is why timely diagnosing and more intensive access to staging tests including PET/CT are important.

The most prevalent first-line treatment regimen was R-CHOP [rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone], and it was given to 53.75% of all patients. This is in line with existing international recommendations, which consider R-CHOP the standard treatment for DLBCL and numerous other aggressive B-cell NHLs [14]. The use of ABVD [adriamycin, bleomycin, vinblastine and dacarbazine] was used in 32.50 percent of the patients, which is indicative of its use as the corner stone of HL treatment [15]. The remission rate was 52.5%, which is generally similar to the 79.27% CR rate in the HL-only Karbala series by Mjali [7], a difference understandable given that advanced NHL cases had a lower CR rate. The therapeutic practices were evolving with the use of rituximab-based regimens and, in a few instances, pembrolizumab in patients with resistant or relapsed disease only.

The current study has several weaknesses that should be mentioned. Since it is a retrospective review, the quality

of the clinical records was a determinant of data completeness. The documentation of some patients was incomplete, especially regarding treatment response, and they were classified as continuing or as those who had not been evaluated. Further subgroup analysis was not possible due to the lack of molecular profiling data, including cell-of-origin classification of DLBCL. Also, the study group includes patients referred from several governorates, which might not necessarily reflect the epidemiology of lymphoma in Karbala alone. Future multicentre trials that incorporate molecular diagnostics will be needed to define outcomes better.

CONCLUSION

In Karbala, the most common histological type is NHL subtype, and the most common type is the DLBCL. Hodgkin lymphoma is often diagnosed at earlier stages, with the mixed cellularity subtype being the most common. The most common first-line regimens are standard R-CHOP in NHL and ABVD in HL, and remission is achieved in most cases. A presentation at the beginning of the stage is associated with better results. These findings are important in showing that there should be region-specific lymphoma registries, increased access to diagnostic facilities such as PET/CT and immunohistochemistry, and synchronised public health strategies to enable earlier diagnosis and optimised treatment outcomes across the Middle Euphrates region of Iraq.

RECOMMENDATIONS

It is recommended that a special lymphoma registry be established to cover Karbala and the Middle Euphrates area, enabling future epidemiological surveillance.

In addition, the regional oncology centers should provide more access to advanced staging techniques like PET/CT scans and complete immunohistochemistry studies. Educational programs in public health should be undertaken to make the people of Iraq more aware of the symptoms of lymphomas, especially lymphadenopathy, night sweats, and weight loss without an apparent cause, in order to encourage people to come for treatment at the earliest.

Risk stratification of DLBCL and other aggressive lymphomas should be made easier by the introduction of molecular diagnostic techniques like cell of origin and genetic profiling. Further studies should be undertaken to find strong survival data and the effectiveness of the treatment regimens in the long term for the Iraqi patients..

REFERENCES

1. The current study was conducted to identify the clinical characteristics of patients with lymphoma in Karbala, outline the subtypes and presenting stages, and assess first-line treatment options and their outcomes.
2. METHODOLOGY
3. The retrospective cross-sectional study design was adopted. The period considered was between January 2018 and August 2023, during which medical records of lymphoma patients diagnosed and treated at Al-Hussein Medical City in Karbala, Iraq, were reviewed. The extraction of the data was done through a structured data collection tool that retrieved the following variables: patient demographics [age at diagnosis, gender, address], lymphoma type and histological subtype, Ann Arbor clinical stage, B symptoms, comorbidities, laboratory investigations [complete blood count (CBC) and PET/CT imaging], first-line treatment protocol, radiotherapy and the use of stem cell transplantation, treatment response, family history of malignancy, and social history.
4. Inclusion had to be confirmed histopathologically. Patients with incomplete medical records or unconfirmed diagnoses were excluded. The subtypes of lymphoma were categorized according to the World Health Organization (WHO) classification of lymphoid neoplasms. Both HL and NHL had Ann Arbor staging with the Cotswolds modification. The response to treatment was evaluated according to a pre-existing set of criteria: complete remission [CR] represented the absence of visible disease on imaging, and partial remission [PR] represented a 50% or greater reduction in tumour mass.
5. The findings were described using descriptive statistics. Frequency and percentage were used to describe the categorical variables. Data was handled in a manner consistent with ethical principles, and patient confidentiality was maintained.
6. RESULTS
7. The study involved 80 patients. Table 1 summarizes the demographic and clinical characteristics.
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9. Table 1: Demographic and Clinical Characteristics of the Study Population
10. Characteristic n Percentage (%)
11. Gender
12. Male 31 38.75
13. Female 49 61.25
14. Age Group at Diagnosis (years)
15. < 30 years 9 11.25

16. 30–45 years 26 32.50
17. 46–60 years 20 25.00
18. > 60 years 25 31.25
19. Lymphoma Type
20. Non-Hodgkin Lymphoma (NHL) 56 70.00
21. Hodgkin Lymphoma (HL) 24 30.00
22. The female-to-male ratio was about 1.6:1, with 49 patients female and 31 male. The average age of diagnosis was 50 years, with a range of 15-82 years. The age group 30–45 years was the most represented [n=26, 32.5%], followed by patients aged 60 years or older [n=25, 31.25%].
23. In 56 patients [70%], non-Hodgkin lymphoma was detected, and in 24 patients [30%], Hodgkin lymphoma. Regarding the distribution of subtypes [Table 2], the most commonly recorded subtype was DLBCL with 67.86% of cases of NHL [38 patients, or 47.5% of the total population of the study group]. Follicular lymphoma [12.50%] and T-cell lymphoma [7.14%] ranked third and fourth, respectively. In HL, the subtype with the highest prevalence was mixed cellularity [37.50%], with classical HL [unspecified] and nodular sclerosis [29.17% each] ranking 2nd and 3rd, respectively.
24. Table 2: Distribution of Lymphoma Subtypes
25. Subtype n Percentage (%)
26. NHL Subtypes
27. Diffuse Large B-Cell Lymphoma (DLBCL) 38 67.86
28. Follicular Lymphoma 7 12.50
29. T-Cell Lymphoma 4 7.14
30. Small Lymphocytic Lymphoma (SLL) 1 1.79
31. Burkitt Lymphoma 1 1.79
32. Other NHL subtypes 5 8.93
33. HL Subtypes
34. Mixed Cellularity 9 37.50
35. Classical HL (Unspecified) 7 29.17
36. Nodular Sclerosis 7 29.17
37. Non-Classical HL 1 4.17
38. Table 3 shows the distribution of cases by Ann Arbor stage. Stage I was documented in 22 patients [27.5%], stage II in 21 [26.25%], stage III in 19 [23.75], and stage IV in 18 [22.5%]. It is interesting to note that 46.25% of the overall cohort had advanced-stage disease [stages III -IV combined]. In the NHL patients, the most common advanced stage was stage IV disease [30.4% of NHL cases], the HL patients were more likely to be diagnosed at lower stages, with stage I and II of the disease taking up 75% of cases.
39. Table 3: Distribution of Ann Arbor Stage by Lymphoma Type
- | Stage | Total n (%) | NHL n (%) | HL n (%) | Overall (%) |
|---------------|-------------|------------|------------|-------------|
| 41. Stage I | 22 (27.5%) | 14 (25.0%) | 8 (33.3%) | 27.50 |
| 42. Stage II | 21 (26.25%) | 11 (19.6%) | 10 (41.7%) | 26.25 |
| 43. Stage III | 19 (23.75%) | 14 (25.0%) | 5 (20.8%) | 23.75 |
| 44. Stage IV | 18 (22.5%) | 17 (30.4%) | 1 (4.2%) | 22.50 |
| 45. Total | 80 (100%) | 56 (100%) | 24 (100%) | 100 |
46. Most frequent clinical manifestations were lymphadenopathy [lump], fever, night sweats, and weight loss—all of which are B symptoms. B symptoms were also common in NHL as well as HL patients. A percentage of the patients were found to have comorbidities, and the most prevalent were hypertension [HTN], diabetes mellitus [DM], and ischaemic heart disease [IHD]. Only 22 patients [27.5%] reported a positive family history of malignancy.
47. Figure 1 shows the spread of lymphoma types and the percentage of HL and NHL in the population under study.
48. Figure 1. Distribution of lymphoma types among the study population (n=80)
49. Table 4 describes the treatment modalities and outcomes. The most commonly used first-line regimen was R-CHOP and its variations, which were used in 43 patients [53.75%], mainly used in NHL. The use of ABVD was used in 26 patients [32.50%], which is the regular first-line therapy of HL patients. Rituximab in combination with bendamustine [RB] was used in 7 patients [8.75%], mainly for indolent lymphomas. There were a few cases of using other regimens, such as CHOP, R-DHAP, and pembrolizumab (Keytruda). There was the use of radiotherapy in 3 patients [3.75%] and stem cell transplant in 7 [8.75%].
50. 42 patients [52.5] achieved complete remission, and 19 patients [23.75] achieved partial remission. The

response to treatment was not measured or ongoing among the remaining patients [23.75%] when data were collected. A second-line therapy was established in some patients who responded partially or not, and stem cell transplantation was developed in some of the relapses or refractory cases.

51. Table 4: Treatment Modalities and Outcomes

Treatment / Outcome	n	Percentage (%)
53. First-Line Treatment		
54. R-CHOP (incl. variants)	43	53.75
55. ABVD	26	32.50
56. Rituximab + Bendamustine (RB)	7	8.75
57. Other (CHOP, R-DHAP, Pembrolizumab)	4	5.00
58. Radiotherapy	3	3.75
59. Stem Cell Transplantation	7	8.75
60. Treatment Response		
61. Complete Remission (CR)	42	52.50
62. Partial Remission (PR)	19	23.75
63. Not Yet Assessed / Ongoing	19	23.75

64. DISCUSSION

65. This paper reports the clinical characteristics and treatment response of 80 lymphoma patients referred to Al-Hussein Medical City, Karbala, a tertiary oncology centre serving the broader Middle Euphrates region of Iraq. The trend of NHL [70%] versus HL [30%] in the current cohort is in line with trends across Iraq and the Middle East. A three-to-one ratio of NHL to HL was reported by Mjali et al. in a study based on Misan city, with NHL predominantly at stage IV [9]. On the same note, Yaqo et al. reported that NHL accounted for 76% of lymphomas in the northern part of Iraq, and the most common subtype was DLBCL [6]. NHL preponderance was also reported in the Al-Tae et al. Baghdad study at a rate of 60, with 40% of NHL cases being DLBCL [8].
66. The predominant subtype in the current cohort was DLBCL [67.86% of NHL, 47.5% overall], consistent with worldwide and regional data sets. DLBCL accounts for 25-30% of total lymphoma diagnoses worldwide and is the most frequent aggressive B-cell malignancy [10]. The NHL classification study indicated that, in the Middle East scenario, 52% of NHL cases in Sulaimaniyah Province, Iraq, were DLBCL, and 54.02% of NHL cases at Al-Hussein Cancer Centre, Karbala (Mjali et al. [4,11]). The uniformity in the prevalence of DLBCL across different Iraqi groups highlights similarities in biological and potentially environmental factors.
67. In HL, the most common subtype was mixed cellularity [37.50%], consistent with the Karbala HL study by Mjali [2021], which also found mixed cellularity as the most common subtype [49.74%] [7]. Conversely, the most frequent HL type in the West, 60-65 percent of all cases, is nodular sclerosis [12]. The comparatively higher incidence of mixed cellularity in this study and in cases from regional Iraq may be due to the younger age of onset of HL in the region and the possibility that mixed cellularity HL is more closely associated with Epstein-Barr virus [EBV] infection in developing nations [13].
68. The female preponderance [61.25] is one of the most remarkable observations in the current study, as a male preponderance is usually reported in the literature on lymphoma in Iraq and the region. The studies by Mjali et al. and Yaqo et al. showed male predominance in the populations with HL and NHL, respectively [6,7]. This observed female dominance may in part be due to referral patterns to Al-Hussein Medical City and variations in health-seeking behaviour across the governorates. It can also reflect the presence of patients from Babylon, Najaf, Wasit, and other governorates who came to receive treatment at this centre, which can bias the gender composition of the cohort.
69. The average age at diagnosis was 50 years, and the 30-45-year age group had the highest percentage [32.5%]. This is in line with reports in the region. A mean age of 27.17 years, specifically for HL, was recorded in the Karbala HL study, which is typical of the bimodal age distribution of HL with a young adult peak [7]. In the present study, the wider age distribution is due to the inclusion of HL and NHL, as the latter has a higher incidence peak among older adults and middle-aged people. DLBCL and extranodal NHL in the north of Iraq were also found to be more frequent in adults, which confirms the age distribution in this area [6].
70. The staging data showed that the disease was in an early stage (stages I-II) in 53.75 percent of all the cases reported and at an advanced stage (stages III-IV) in 46.25 percent. The distribution is widely in line with the regional findings. Stage II is the most frequent presenting stage in the Karbala HL series [40.93%], with fairly good results [7]. Still, in NHL, the presentation stage is more advanced around the world; in the current group, stage IV was the most prevalent among NHL patients [30.4% of NHL], which is why timely diagnosing and more intensive access to staging tests including PET/CT are important.
71. The most prevalent first-line treatment regimen was R-CHOP [rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone], and it was given to 53.75% of all patients. This is in line with existing international recommendations, which consider R-CHOP the standard treatment for DLBCL and

numerous other aggressive B-cell NHLs [14]. The use of ABVD [adriamycin, bleomycin, vinblastine and dacarbazine] was used in 32.50 percent of the patients, which is indicative of its use as the corner stone of HL treatment [15]. The remission rate was 52.5%, which is generally similar to the 79.27% CR rate in the HL-only Karbala series by Mjali [7], a difference understandable given that advanced NHL cases had a lower CR rate. The therapeutic practices were evolving with the use of rituximab-based regimens and, in a few instances, pembrolizumab in patients with resistant or relapsed disease only.

72. The current study has several weaknesses that should be mentioned. Since it is a retrospective review, the quality of the clinical records was a determinant of data completeness. The documentation of some patients was incomplete, especially regarding treatment response, and they were classified as continuing or as those who had not been evaluated. Further subgroup analysis was not possible due to the lack of molecular profiling data, including cell-of-origin classification of DLBCL. Also, the study group includes patients referred from several governorates, which might not necessarily reflect the epidemiology of lymphoma in Karbala alone. Future multicentre trials that incorporate molecular diagnostics will be needed to define outcomes better.

73. CONCLUSION

74. In Karbala, the most common histological type is NHL subtype, and the most common type is the DLBCL. Hodgkin lymphoma is often diagnosed at earlier stages, with the mixed cellularity subtype being the most common. The most common first-line regimens are standard R-CHOP in NHL and ABVD in HL, and remission is achieved in most cases. A presentation at the beginning of the stage is associated with better results. These findings are important in showing that there should be region-specific lymphoma registries, increased access to diagnostic facilities such as PET/CT and immunohistochemistry, and synchronised public health strategies to enable earlier diagnosis and optimised treatment outcomes across the Middle Euphrates region of Iraq.

75. RECOMMENDATIONS

76. It is recommended that a special lymphoma registry be established to cover Karbala and the Middle Euphrates area, enabling future epidemiological surveillance.

77. In addition, the regional oncology centers should provide more access to advanced staging techniques like PET/CT scans and complete immunohistochemistry studies. Educational programs in public health should be undertaken to make the people of Iraq more aware of the symptoms of lymphomas, especially lymphadenopathy, night sweats, and weight loss without an apparent cause, in order to encourage people to come for treatment at the earliest.

78. Risk stratification of DLBCL and other aggressive lymphomas should be made easier by the introduction of molecular diagnostic techniques like cell of origin and genetic profiling. Further studies should be undertaken to find strong survival data and the effectiveness of the treatment regimens in the long term for the Iraqi patients.