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Original article

Incidence and Mortality Rates of Hodgkin's Lymphoma in the Western Region of Libya

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Keywords.
Cancer, Hodgkin's Lymphoma, Non-Hodgkin's Lymphoma, Mortality Rate, Survival Rate.

ABSTRACT

Hodgkin lymphoma (HL) is a malignant disorder of the lymphatic system and represents an important subgroup of lymphoid neoplasms, which also include non-Hodgkin lymphoma (NHL), plasma cell neoplasms, and lymphoid leukemias. Differences in cancer incidence, mortality, diagnosis, and treatment outcomes between developed and developing countries highlight the need for local epidemiological studies. Due to the limited availability of documented research on lymphomas in Libya, this study aimed to investigate the incidence, clinical characteristics, and outcomes of HL patients while also presenting a rare familial case involving affected siblings. This retrospective documentary study was conducted using records from the oncology centers of Sabratha and Misurata between September 2023 and January 2024. A total of 872 lymphoma patients were reviewed, of whom 357 were diagnosed with HL. Male patients constituted a slightly higher proportion of HL cases than females, with mean ages of 36.83 and 34.91 years, respectively. Most HL cases originated from Misurata, followed by Tripoli and Khums. The highest disease frequency was observed among individuals aged 9–40 years, while fewer cases were recorded among older age groups. The overall mortality rate among lymphoma patients was low, with 19 deaths recorded among the 872 cases. Among HL patients, mortality was slightly higher in females than in males. The findings are consistent with international reports indicating a higher incidence of HL in males and a predominance of disease occurrence in younger adults. The study confirms important epidemiological and clinical characteristics of HL and NHL in Libya and emphasizes the need for further research to better understand the causes, risk factors, and prognosis of Hodgkin lymphoma, particularly in relation to its increasing epidemiological trends.

Introduction

The lymphomas comprise a heterogeneous group of cancers with diverse etiologies, treatment pathways, and outcomes [1, 2]. Importantly for research, awareness of the similarities and differences among the different subtypes emerged only recently, as biological knowledge about the connections among these intricate cancers, bone marrow, immune system, and cellular and genetic basis of malignant transformation grew [1-4].

The primary cause of lymphoma is unknown. Many factors that can increase its risk include age, sex, autoimmune diseases, and a diet rich in meat [5]. However, the contribution of different risk factors to lymphoma development may vary in different regions. On the other hand, the frequency of lymphoma and its clinical characteristics may vary in different regions. Additionally, many competing classifications had been used until a consensus classification, the Revised European-American classification (1994), and subsequently, the WHO classification (2001, with a revision in 2008) were proposed and accepted as the global standard [3, 4, 6].

Males consistently have higher age-standardized rates and numbers than females for both non-Hodgkin lymphoma (NHL) and Hodgkin lymphoma (HL), with the discrepancies being slightly more pronounced in less developed parts of the world [7]. In the NHL, as age increases, so do the age-specific male and female rates; nevertheless, as age increases, so does the divergence between the male and female rates. In contrast, there are two peaks in the HL incidence distribution: one in young adults and one in the elderly. In adulthood, there is a noticeable male excess; nevertheless, the forms of the two curves are significantly different, with the females having a little earlier peak and a deeper dip. These patterns demonstrate how HL is made up of several disease entities, each with unique descriptive characteristics [2, 8].

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A recent study in Libya conducted by Jbireal et al. (2022), there were 6.4 new cases of lymphoma per 100,000 people. This number is divided into 2.6 HL and 3.8 NHL. The frequency of lymphoma in Libyans is closely associated with middle age; the mean age of cases is 43 years old, and about 60% of cases occur in people between the ages of 20 and 60 [9].
According to epidemiology, industrialized and poor nations differ greatly in cancer incidence and mortality [10-12]. Variations in access to resources (including new therapies and technologies for diagnosis and monitoring) and other aspects of the quality and accessibility of cancer treatment, early detection, and prevention could account for the discrepancy in survival [11, 13, 14].
Additionally, HL ranks 26th and 27th, respectively, in terms of frequency among malignant malignancies worldwide, with an estimated 83 000 new cases and 23 000 deaths [15]. However, HL is more common in men and is one of the most common cancers in teenagers and young adults in several countries [16, 17]. The disease's genesis is not entirely understood. It is commonly associated with EBV among immunocompromised individuals (eg, due to HIV infection) and transplant-related immunosuppression [16, 18], while certain subtypes are also associated with family history [19].
Furthermore, family aggregation studies and population registry data clearly support a genetic component that is inherited, even if the etiology of HL is still very diverse. Siblings and monozygotic twins of afflicted patients have been shown to have a higher risk of getting HL. Additionally, multi-case families have been found to have genetic anticipation, which is the phenomenon when a disease manifests at an earlier age or with higher severity in subsequent generations [20].
The total heritability of HL is estimated to be around 28% based on extensive registry data from large-scale Swedish and Danish cohorts using a threshold-liability model [20, 21]. First-degree relatives of HL patients have a 3.1-fold higher chance of getting the same cancer, according to these thorough familial aggregation analyses (Relative Risk [RR] = 3.1; 95% CI, 1.8–5.3). Remarkably, cross-subtypic analysis shows that a family history of chronic lymphocytic leukemia (CLL) is associated with a significant 2.1-fold increase in risk (RR = 2.1; 95% CI, 1.2–3.8), whereas a family history of non-Hodgkin lymphoma (NHL) does not significantly increase HL risk (RR = 1.3; 95% CI, 0.9–1.8) [21].
As a result, both local and international data show an increasing frequency of HL and NHL; nevertheless, documented epidemiological, diagnostic, and therapeutic research is severely lacking in Libya. In order to fill this knowledge gap, this study postulates that HL is extremely common in western Libya and that, as a result of socioeconomic constraints and deteriorating healthcare infrastructure, its overall survival rate is below international standards. By comparing data from two significant regional oncology centers, Sabratha Oncology Institute (SOI) and Misurata Oncology Institute (MOI), the study seeks to ascertain local incidence and survival rates in order to assess these theories.

Methods

Study area and design

This is a retrospective, documentary, and screening study of Hodgkin's lymphoma cases diagnosed and recorded during the period from 2012 to 2022 in the two main Libyan oncology institutes (Sabratha and Misurata Oncology Institutes, SOI and MOI).

Data collection

All data have been collected throughout multiple visits to both oncology centers during the period from August 2023 to December 2023. The collection of various data relied on the electronic patient registration system in both centers. The processes of data tabulation, organization, examination, and statistical analysis were carried out during the period from the end of December 2023 to March 2024 under the supervision of those responsible for the patient registration system in both oncology centers.

Statistical analysis

The data obtained were tabulated as mean ± standard deviation (SD) and were subjected to statistical analysis to determine the level of significance as described by Steel et al. (1997) [22]. Chi-Square test was used for comparison of lymphoma type distribution between genders. Independent-samples t-test for comparison of mean age between males and females. Fisher's exact test was used to evaluate whether there is a significant difference in the distribution of lymphoma types among deceased patients. Differences were considered significant when $P \leq 0.05$. All the statistical analyses were done using the software program of Statistical Package for the Social Sciences (SPSS (2015) Version 22 program for Windows).

Results

Of the 872 cases of lymphoma, 398 (45.6%) were female, and 474 (54.3%) were male. Non-Hodgkin lymphoma made up 60.3% and 57.5% of cases, respectively, while Hodgkin lymphoma accounted for 39.6% of male cases and 42.4% of female cases. Gender and lymphoma subtype did not significantly correlate ($\chi^2 = 0.675$, $p = 0.411$) (Table 1).

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Table 1. Gender distribution and number of cases (HL/NHL) registered in both oncology institutes.

Gender	No. of cases: HL/ (%)	No. of cases: NHL/ (%)	Total/ (%)	P value
F	169 (42.4%)	229 (57.5%)	398 (45.6%)	-
M	188 (39.6%)	286 (60.3%)	474 (54.3%)	0.411
Total	357 (40.9%)	515 (59%)	872 (100%)	-

Chi-square test: $\chi^2 = 0.675$, *df = 1, P = 0.411*

The current study has demonstrated that the most cases of HL came from Misurata with a percentage of (23.38%) followed by Tripoli (17.46%) and Khums (13.8%). On the other hand, with regard to the distribution of NHL among the population at the same period, the study has demonstrated that throughout the total number of (872) lymphoma patients, 515 of them were suffering from NHL. The highest percent of NHL patients came from Tripoli (19.34%), followed by Misurata (16.25%) and Sabratha with a percent of (8.32%) (Figure 1).

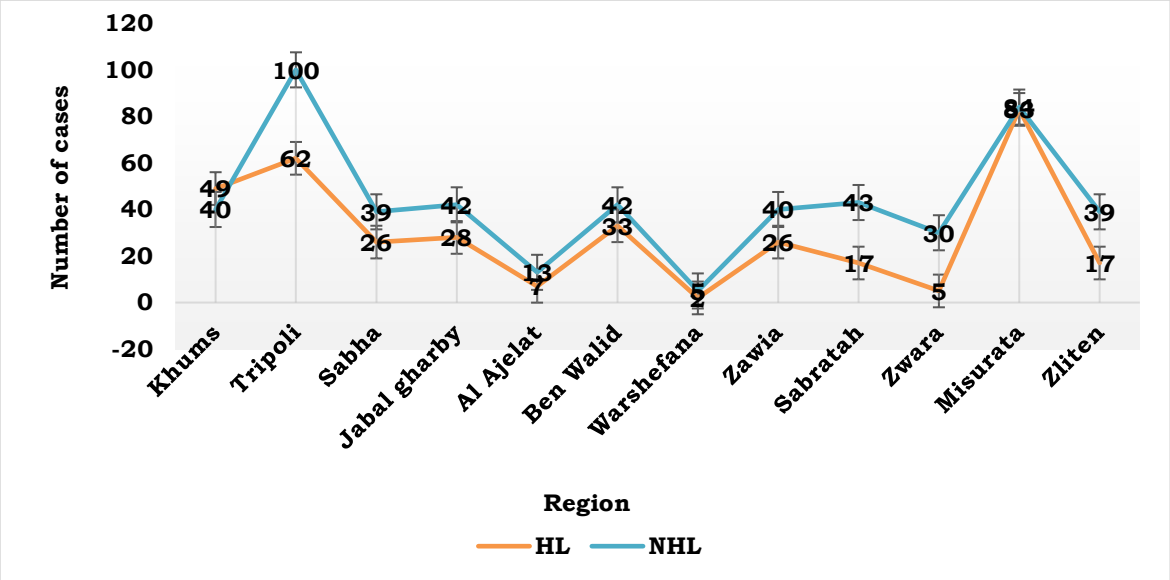

Figure 1. Registered number of lymphoma cases (HL/NHL) and percent according to the geographical regions of Libya during the period from 2012-2022.

Remarkably, with regard to the distribution of lymphoma patients according to the age of patients, the current study observed that the highest percent of patients suffering from HL was among patients (male and female) who are belonging to the group of (9-40) years old followed by patients within the age group of (41-70) years old and few patients within the age group of (71-100) years old (Figure 2).

In contrast, the distribution of NHL patients was different. The highest number of them belonged to the age group of (41-70) years old (males and females). The next highest number of NHL patients belonged to the age group of (9-40) years old, whereas the fewest number of them were within the age group of (71-100) years old, although the number of patients belonging to this age group is also high.

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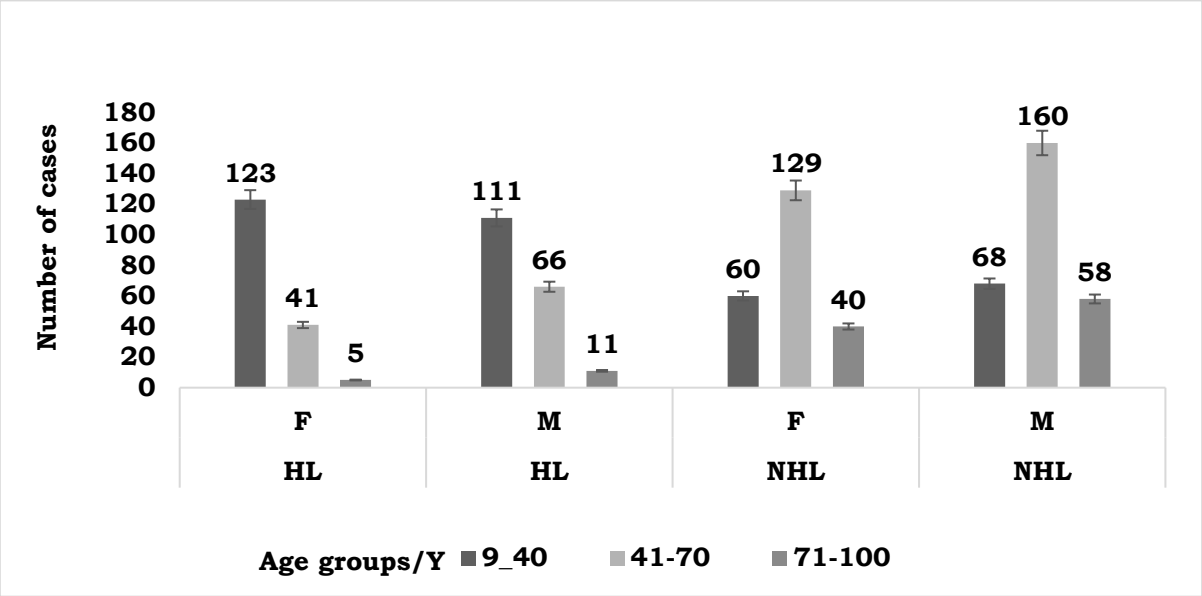

Figure 2. Distribution of lymphoma patients (HL/NHL) according to age groups.

Mortality rate of Lymphoma disease.

Nineteen deaths, or 2.17% of all cases of lymphoma, were reported throughout the study period (2012–2022). Of these, 11 (2.3%) were male, and 8 (2.0%) were female. For both males (81.8%) and females (62.5%), NHL was the leading cause of mortality. However, there was no significant gender difference in the distribution of lymphoma types among died patients (Fisher's exact test, p = 0.648) (Table 2).

Table 2. Known and recorded deaths during 2012–2022 according to lymphoma type and gender.

Gender	HL, n (%)	NHL, n (%)	Total deaths, n (%)	P value
Female	3 (1.7)	5 (2.18)	8 (2.0)	
Male	2 (1.0)	9 (3.1)	11 (2.3)	0.648*
Total	5 (1.4)	14 (2.7)	19 (2.17)	

**Fisher's Exact Test.*

The mortality rate was higher among NHL patients (2.7%) than HL patients (1.4%). NHL cases showed an approximately twofold greater risk of death compared with HL cases (Relative Risk; RR = 1.94). Moreover, the mortality rate among NHL patients (2.7%) was nearly twice that observed among HL patients (1.4%), indicating a substantially poorer outcome for NHL during the study period. On the other hand, the odds of death (OR) among NHL patients were approximately twice those observed among HL patients (OR = 1.97) (Table 3).

Table 3. Comparison of mortality rates according to lymphoma type and gender among registered cases (2012–2022).

Lymphoma type	Total cases	Deaths	Mortality rate (%)
HL	357	5	1.4
NHL	515	14	2.7
Female	398	8	2.0
Male	474	11	2.3
Relative Risk (RR):1.94; Odds Ratio (OR): 1.97			

Discussion

Growing awareness of lymphoma and its different types in recent years has led to an increase in the frequency of these malignancies, with comprehensive classifications based on the histological subtype reported by cancer registries worldwide. On the other hand, the incidence of Hodgkin lymphoma differs according to age, gender, sex, and geography. Hodgkin lymphoma is more common in men [23], teenagers and young adults [24], people with a history of Epstein-Barr virus infection [25], HIV/AIDS [26], autoimmune illnesses [27], environmental exposure [28], cigarette smoking [29], and family history.

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The current study found that male predominance is in line with the global epidemiological features of lymphoma. Both HL and NHL are more common in males than in females, according to a number of studies. This discrepancy has been explained by biological, hormonal, genetic, and environmental variables. Differences in immunological modulation, occupational exposures, and vulnerability to environmental and viral risk factors connected to lymphomagenesis have been associated with male predominance [30]. This result is consistent with recent epidemiological data from Italy based on the Global Burden of Disease 2023 project, which found that males had a greater prevalence of both HL and NHL but did not discover significant sex-related variations in the relative distribution of lymphoma subtypes. Males made up for 60.3% of HL cases and 55.7% of NHL cases in that study, exhibiting a trend comparable to the current study [31].

The current study's finding that NHL predominates over HL in both genders is likewise in line with data from other countries. NHL is a complex collection of neoplasms with a wide range of clinical and pathological features, and it accounts for most lymphoid malignancies globally. According to global analyses, NHL continues to be a major contributor to cancer morbidity and death across many populations, accounting for far more cases of lymphoma than HL [32, 33]. In a similar vein, a recent investigation of trends in adult HL incidence in the US revealed a consistent male preponderance in HL incidence over the course of the research, while the size of the difference varied by age group and histological subtype. These results corroborate the conclusion that there are sex-related variations in the incidence of lymphoma, but these variations may not always result in notable variations in the distribution of HL and NHL among individuals who have been diagnosed [34]. The multidimensional nature of lymphoma formation and the necessity of further research examining additional demographic, environmental, and genetic factors of lymphoma occurrence in Libya are highlighted by the fact that gender was not substantially linked with lymphoma subtype.

Significant regional variance was seen throughout the research area in the geographic distribution of lymphoma cases. In most regions, NHL was therefore more prevalent than HL. While HL cases were most common in Misurata (81 cases) and Tripoli (62 cases), NHL cases were most common in Tripoli (100 cases) and Misurata (84 cases). These results could be explained by these cities' greater populations, easier access to oncology care, and more extensive cancer registration programs. International studies have shown similar trends, with metropolitan areas typically reporting more cancer cases due to better diagnostic and reporting capabilities [35, 36]. In contrast, the lowest frequencies of lymphoma were observed in Warshefana region, which may reflect a smaller population size, limited healthcare access, or underreporting of cases.

The age-specific distribution found in this study is in line with current global epidemiological data on lymphoma trends. Most HL cases in both males (111 cases) and females (123 cases) were diagnosed in the younger age group (9–40 years). This result is consistent with recent data showing that HL usually peaks before the age of 40 years and frequently affects teenagers and young adults. According to a population-based analysis conducted in the United States by Aslani et al. (2024), the incidence of HL is still highest among younger people, especially those between the ages of 20 and 39, which reflects the disease's distinctive bimodal age distribution. On the other hand, the current investigation found that the frequency of HL significantly decreased in older age groups, confirming earlier findings that younger populations are most affected by HL [34].

On the other hand, NHL was more common in people between the ages of 41 and 70, with females (129 cases) and males (160 cases) showing the highest rates. This pattern is consistent with previous worldwide research showing that NHL incidence rises progressively with age and peaks in middle-aged and older populations. According to Huang et al. (2024) and Li et al. (2021), immunological senescence, chronic inflammation, cumulative genetic alterations, and extended exposure to environmental and occupational toxins make aging one of the biggest risk factors for NHL [37, 38]. However, the current study's higher mortality rate among NHL patients is in line with recent international research that found that NHL patients had worse survival outcomes than HL. Advances in chemotherapy, immunotherapy, and risk-adapted treatment regimens have resulted in dramatic gains in HL survival, with long-term survival rates reaching 85% in many countries [35].

On the other hand, NHL is a diverse group of cancers with varying biological behavior and prognosis, which raises death rates globally [38]. Despite improvements in treatment, NHL still accounts for a higher percentage of lymphoma-related mortality, according to recent worldwide research [37]. Similarly, after controlling for disease features and treatment variables, studies from North America and Europe have found no significant gender-related variations in lymphoma-specific mortality [31, 39]. However, the high rate of NHL-related fatalities emphasizes the necessity of ongoing initiatives to enhance early diagnosis, risk assessment, and treatment results for NHL patients.

The comparison of mortality rates revealed that patients with NHL experienced a higher mortality rate than those with HL. The calculated relative risk (RR = 1.94) and odds ratio (OR = 1.97) indicate that NHL patients had nearly twice the risk of death compared with HL patients. This finding is consistent with recent studies reporting better survival outcomes for HL, largely due to advances in risk-adapted treatment protocols and the generally favorable prognosis of the disease, whereas NHL encompasses a heterogeneous group of malignancies with variable and often more aggressive clinical behavior [38, 40]. Regarding gender, mortality was slightly higher among males than females, although the difference was relatively small. Similar observations have been reported in recent epidemiological studies, where male patients often demonstrate

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marginally poorer outcomes, potentially due to differences in disease biology, comorbidities, and healthcare-seeking behavior [34, 37, 41].

Conclusion

The current study gives a complete review of lymphoma patterns in Libya based on cases documented in two oncology facilities between 2012 and 2022. NHL was more prevalent than HL and accounted for the majority of cases across most demographic and geographic categories. A little male predominance was noted; however, no significant correlation was discovered between gender and lymphoma subtype. HL occurred more commonly among younger persons, whereas NHL predominated in middle-aged and older adults, confirming recognized global epidemiological trends. Although mortality rates were generally modest, patients with NHL had greater rates than those with HL. Additionally, mortality was higher in NHL compared to HL, with a nearly twofold increased risk, while only a slight gender difference was observed. These results provide important epidemiological information about lymphoma in Libya and emphasize the need for better registration procedures, enhanced cancer surveillance systems, and additional population-based research to find potential genetic, environmental, and healthcare-related factors influencing the incidence and prognosis of lymphoma.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Data availability

The data underlying the findings can be obtained from the corresponding author.

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