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Epidemiology of Hodgkin's disease and Non-Hodgkin's Lymphomas (ICD-O: M-959-972), Period: 2013-2017

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Abstract

Background: GLOBOCAN estimates the rank of Non-Hodgkin Lymphomas are 13th and Hodgkins Lymphoma are 28th most prevalent cancers in India during 2018. No recent update in the epidemiology of these lymphomas has been performed in our country. We diagnosed 974 new lymphomas during the period beginning January 1, 2013 and ending December 31, 2017 in our centre.

Findings: The most frequent lymphoma was diffuse large B cell lymphoma, followed by follicular lymphoma and then classic Hodgkin's disease. The male: female ratio is 1.2:1. Diagnosis by age showed that non-Hodgkin's lymphoma is by far more frequent in the 61-80 years old patients. On the other hand, classic Hodgkin's lymphoma is more frequent in the 20-40 years old population.

Conclusion: The present study demonstrated that Non-Hodgkin Lymphoma (NHL) accounting for 68.0% was the most common and Hodgkin Lymphoma (HL) 32.0% with all sub-types of all Lymphoid Hematopoietic Malignancies (HLM cases). Our results are very similar to those published by other centers in Europe and United States.

Keywords: Epidemiology, Hodgkin's Lymphoma, Non-Hodgkin's Lymphoma

Introduction

Hematologic malignancies (HMs) are a heterogeneous group of diseases of diverse incidence, prognosis, and etiology. Most population based studies on the incidence of HMs have grouped these diseases into broad categories: Hodgkin versus non-Hodgkin lymphoma, acute versus chronic, and lymphatic versus myeloid leukemia [1, 2].

Lymphoid and hemopoietic malignancies as a group constitute one of the important cancers in India, as elsewhere in the world. While information on incidence and mortality of these cancers, and that on survival, are available from most developed countries, there are very few reports describing this experience in developing ones. The GLOBOCAN 2018 estimates that there will be worldwide 18.1 million new cases of cancer and 9.6 million deaths from cancer in 2018. Cancer is an important cause of morbidity and mortality worldwide, in every world region [1]. One in 5 men and one in 6 women worldwide develop cancer during their lifetime, and one in 8 men and one in 11 women die from the disease according to the World Health Organization. The number of new cases for non-Hodgkin lymphoma (NHL) will be 509,590 (2.8%) is the 13th rank and deaths case 248,724 (2.6%) and Hodgkin lymphoma (HL) case will be 79,990 (0.4%) is the 26th rank and deaths 26,167 (0.3%) worldwide respectively; it is estimated that nearly one-half of the cases and over one-half of the cancer deaths in the world will occur in Asia in the year 2018 [1]. Studies conducted both in North America and in Central and South America have shown that the incidence of NHL has been increasing over time, particularly in the elderly, with the incidence being higher in men and in white individuals [2-8]. The subtypes that have increased most in frequency are diffuse large B-cell lymphoma, accounting for 30%-40% of all cases of lymphoma [4,7], and immunoblastic lymphoma [4]. In Brazil, the incidence of NHL in men can be as high as 9.1 cases per 100,000 inhabitants, with B-cell lymphomas being the most common subtype, accounting for 37% of NHL cases. Of these, diffuse large B-cell lymphomas are the most common [7].

On the other hand, HL is a rare form of cancer, with an incidence rate in Canada of around 3 per 100,000 inhabitants. Although the outcome is often favorable, some patients fail to respond satisfactorily to standard treatment [8]. HL is much more common in children over ten years of age. The disease is known to allow a bimodal peak with first peak at 15-20 years and in those of year's 15-19 ages its incidence is almost twice that of NHL [9]. The prognosis and treatment of NHL depend on the subtype, stage and associated comorbid conditions. While adequate information is available on the epidemiology of NHL from developed nations. Lymphoid and hemopoietic malignancies as a group constitute one of the important cancers in India, as elsewhere in the world. Cancer registration in India was initiated in 1964 and expanded since 1982, through initiation of the National Cancer Registry Program (NCRP) by the Indian Council of Medical Research. NCRP [10] currently has twenty-nine population based registries and twenty-nine

hospital based registries. This source provides fairly complete and reliable incidence data. The GLOBOCAN 2018 estimates the burden of cancer in India among both sexes will be: incidence cases 11, 57,294 and mortality cases 7, 84,821 with non-Hodgkin lymphoma (NHL) 28,110 (2.4%) is the 11th rank and deaths case 23,510 (3.0%) and Hodgkin lymphoma (HL) case will be 9,115 (0.79%) is the 26th rank and deaths 5,714 (0.73%) respectively [1].

We have made an attempt to review the epidemiology of Lymphoid Hematopoietic Malignancies (LHM) in the past 5 years at a tertiary centre of Gurugram in Haryana based on age, sex and the type of malignancy with further sub typing wherever possible.

Search and Selection Criteria

We searched PubMed, Scopus, Google Scholar, and references from relevant articles using the search terms "Lymphoid Hematopoietic Malignancies" 'lymphoma', 'NHL', 'India', 'epidemiology' and 'incidence'. We also accessed the website of the International Agency for Cancer Research and reviewed all the online databases 'GLOBOCAN', 'Cancer Incidence in Five Continents' and other publications contains information on cancer in India [1, 12-15].

Materials and Methods

This was a cross-sectional, descriptive prevalence study conducted within the referral facility for this micro-region, the Fortis Memorial Research Institute, in the city of Gurugram, Haryana, India. The sample population consisted of patients diagnosed with different subtypes of non-Hodgkin or Hodgkin lymphoma between January 2013 and December 2017, whether still alive or deceased. All the patients registered at the facility with an immunohistochemical diagnosis of one of the several subtypes of lymphoma were included. Those without immunohistochemical confirmation were excluded from the study. A total of 974 cases of all lymphoid neoplasms diagnosed with different sub-types of Non-Hodgkin or Hodgkin lymphoma during the 5-year study period beginning January 1, 2013 and ending December 31, 2017 were registered. The data was collected from the Hospital Based Cancer Registry (HBCR) and utilized for this study. For each year newly identified lymphoid neoplasm case, patient demographic data, including age and sex, and information on the tumor histologic type, primary site, and immunophenotype were collected. All the recorded data details are entered in Microsoft Excel data sheet. The information collected is cross-checked for completeness. The data is checked and validated by using quality control programs/tools for cancer registries of International Agency for Research on Cancer (IARC) for avoiding duplication and any unlikely combination of age, sex, site and morphology and other factors in the data base. The primary site and morphology data were coded using the International Classification of Diseases for Oncology, third edition **[11]**. Information on other variables was coded according to the international guidance. Our Hospital is a tertiary hospital, which has a referral population around 4, 00,000 patients. It is considered a highly qualified centre in hematologic disorders.

Statistical analysis

Collected Data was analyzed using Statistical Package for Social Sciences (SPSS) version23.0. The statistical methods applied include and cross tabulations such as frequency counts, percentage, mean and Chi-square test were applied to identify relationship between variables.

Classification

The classification of lymphomas divides into B-cell, T-cell and NK-cell neoplasms, i.e. non-Hodgkin lymphomas (NHL) and Hodgkin lymphomas (HL). The World Health Organization (WHO) classifies 49 subtypes of Hodgkin lymphoma (HL) and non-Hodgkin lymphomas (NHL); where Hodgkin Lymphoma have 13 subtypes and NHL have 36 subtypes; 21 of B-cell and 15 of T-cell type with different clinical, morphological and immunogenic features, reflecting the stage of maturation of the B- and T-lymphoid cells from which the neoplasm has originated**[11]**.

Results

During 2013 to 2017, a total of 15,148 of new cancer cases were registered. Of these 974 (6.4%) primary lymphoid hematopoietic malignancies (LHM) were registered. The incidence of lymphoid hematopoietic malignancies increased yearly between 2013 and 2017. A male predominance was observed in the incidence of lymphoid hematopoietic malignancies (n = 619, 63.6%) as compared to females (n = 355, 36.4%). The sex ratio was 573 females to 1,000 males. A highly significant difference was observed among the total cancer cases & lymphoid hematopoietic malignancies between 2013 and 2017 when sex was taken into consideration, in which the frequency was higher in males compared with females ($\chi 2$ test, chi-square statistic is 28.2005; p-value is < 0.00001 and highly significant at p <.01) significant. Table 1 & Fig.1 depicts the year-wise distribution of total number of new cancer cases versus all lymphoid hematopoietic malignancies cases.

Table 1: Distribution of total number of new cancer cases versus all lymphoid hematopoietic malignancies cases.

Year	New cancer cases				LHM cases				% between Total & LHM cases
	Male	Female	Total	%	Male	Female	Total	%	
2013	832	658	1490	9.8	86	32	118	12.1	0.78
2014	1191	966	2157	14.2	99	54	153	15.7	1.01
2015	1888	1587	3475	22.9	164	85	249	25.6	1.64
2016	2013	1685	3698	24.4	90	75	165	16.9	1.09
2017	2381	1947	4328	28.6	180	109	289	29.7	1.91
Total (2013-17)	8305	6843	15148	100.0	619	355	974	100.0	6.43
%	54.8	45.2	100.0		63.6	36.4	100.0		
The chi-square statistic is 28.2005; p-value is < 0.00001 and Significant at p <.01.									

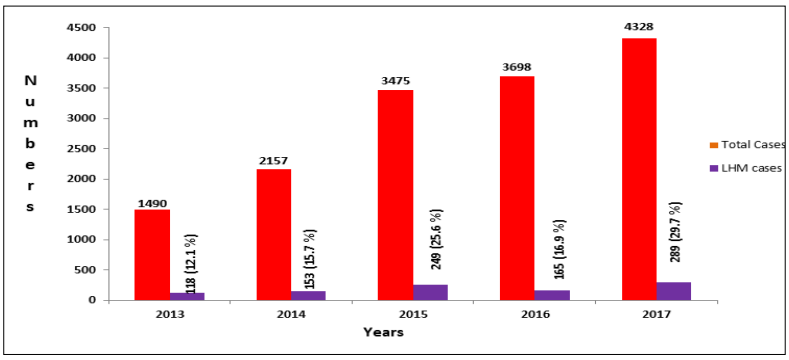

Fig 1: Year-wise distribution of total cancer cases with primary LHM cases

Table 2: Number of LHM cases by broad age groups and sex, period: 2013-2017

Ages	Male	Female	Total	%
0-10 **(Paediatric)**	41	8	49	5.0
11-20	53	24	77	7.9
21-30	75	47	122	12.5
11-30 **(Young Adults)**	128	71	199	20.4
31-40	84	52	136	14.0
41-50	78	40	118	12.1
51-60	102	85	187	19.2
31-60 **(Middle Adults)**	264	177	441	45.3
61-70	109	69	178	18.3
71-80	77	30	107	11.0
61+ Geriatric	186	99	286	29.3
Total	619	355	974	100.0

The incidences of LHM cases are more common in middle adults (31-60 years) (n=441; 45.3%) followed by geriatric age (61+ years) (n=285; 29.3%) and young adults (11-30 years) (n= 199; 20.4%) patients were higher than those in paediatric patients.

Table 3 depicts the distribution of primary Lymphoid Hematopoietic Malignancies (LHM) by sex**.** The number of lympholiferative disorders diagnosed in our center between January 2013 and December 2017 was 974, 619 males and 355 females. The male: female ratio is 1.7:1. A non-significant difference was observed in lymphoid hematopoietic malignancies between 2013 and 2017 when sex was taken into consideration, in which the frequency was higher in males compared with females ($\chi 2$ test, the chi-square statistic is 0.05 and the *p*-value is 0.806507 P>0.05) not significant.

Table 3: Distribution of primary Lymphoid Hematopoietic Malignancies (LHM) by sex

Hodgkin/ Non-Hodgkin	Male	Female	Total	%	Chi-square statistic
Hodgkin	200	112	312	32.0	Not significant 0.806507 (at p <.05)
Non-Hodgkin	419	243	662	68.0	
Total	619	355	974	100.0	
%	63.6	36.4	100.0		

Table 4: depicts the frequency of subtypes of Hodgkins Lymphoma (HL) & Non-Hodgkin Lymphoma (NHL) by sex according to the World Health Organization classification in a population sample at the Fortis Memorial Hospital, Gurugram, Haryana, India, 2013-2017 (n=974 patients). Overall, there were 619 males (63.6%) and 355 females (36.4%). With respect to age, 285 (29.3%) were > 60 years of age and 689 (70.7%) were <60 years of age. The youngest of these patients were 2 years old and the oldest 89 years old, with a mean age of diagnosis 46.3 years.

In relation to the Hodgkin Lymphoma (HL) accounted for most of the cases (n=312; 32.0%), males were 200 (64.1%) and females were 112 (35.9%) with a sex ratio of 560 females to 1000 males; only eight subtypes were catalogued: Hodgkin lymphoma, NOS HL (n = 264; 27.1%), mixed cellularity HL (n=18; 1.8%), lymphocyte – rich HL (n = 13; 1.3%), nodular sclerosis HL (n = 12; 1.2%), lymphocyte-depletion HL (n=2; 0.2%), granuloma HL (n=1; 0.1%), nodular lymphocyte HL (n=1; 0.1%) and classical nodular sclerosis HL (n=1; 0.1%).

Rest of the cases were Non-Hodgkin Lymphoma (NHL) accounted (n = 662; 68.0%), males were 419 (63.3%) and females were 243 (36.7%) with a sex ratio of 580 females to 1000 males; only eighteen subtypes were catalogued: B-cell NHL, NOS HL (n = 304; 31.2%), large B-cell NHL (n=161; 16.5%), lymphoma NOS (n = 75; 7.7%), mature T cell lymphoma (n =22; 2.3%), mantle cell lymphoma (n=16; 1.6%), Burkitt lymphoma (n=10; 1.0%), marginal zone B-cell lymphoma (n=6; 0.6%), anaplastic large cell lymphoma (n=4; 0.4%), small B lymphatic lymphoma (n=3; 0.3%), precursor B-cell lymphoblastic & T-cell lymphoblastic lymphoma (n=7; 0.7%), large B-cell mediastinal lymphoma

(n=2; 0.2%), T-cell angioimmunoblastic lymphoma (n=2; 0.2%). NK/T-cell lymphoma (n=2; 0.2%), large B-cell diffuse immunoblastic lymphoma (n=1; 0.1%), splenic marginal zone B-cell lymphoma (n=1; 0.1%) and cutaneous T-cell lymphoma (n=1; 0.1%) (Figure 2).

Most patients were <60 years of age in both the NHL (n= 689; 70.7%) and the HL (n=416; 42.7%) groups. Similarly, males were predominant in both groups, male patients having NHL (n=619; 70.7%) and HL (n= 273; 87.5%). Figure 2 describes the distribution of cases of lymphoma according to their subtype.

In relation to the subtypes of Hodgkins Lymphoma, lymphoma (NOS) was the most prevalent subtype, representing 264 of the 312 cases (84.6%), males were 168 (53.8%) and females were 96 (30.8%). This was followed by the mixed cellularity subtype with 18 cases (5.8%), males were 14 (4.5%) and females were 4 (1.3%) and lymphocyte rich subtype 13 cases (4.2%), males were 9 (2.9%) and females were 4 (1.3%) and by nodular sclerosis subtype 12 cases (3.8%) respectively.

In relation to the subtypes of Non-Hodgkin Lymphoma, large B-cell lymphoma (NOS) was the most prevalent subtype, representing 304 of the 662 cases (45.9%), males were 181 (27.3%) and females were 123 (18.6%). This was followed by the diffuse, large B-cell subtype with 161 cases (24.3%), males were 99 (15.0%) and females were 62 (9.4%) and lymphoma (NOS) subtype 75 cases (11.3%), males were 51 (7.7%) and females were 24 (3.6%) and by follicular lymphoma (NOS, gr-1 to 3) 45 cases subtype (6.8%), males were 28 (4.3%) and females were 17 (2.6%) and mature T-cell lymphoma subtype 22 cases (3.3%), males were 17 (1.7%) and females were 5 (0.8%) and by the mantle cell subtype 16 cases (2.4%), males were 14 (2.1%) and females were 5 (0.8%) and Burkitt lymphoma was also one of the most prevalent subtypes, with 10 cases (1.5%), males were 8 (1.2%) and females were 2 (0.3%).

Table 4: Frequency of histologic sub-types of Hodgkin's lymphoma & Non-Hodgkins lymphoma according to the WHO classification by sex, period: 2013-2017

ICD-O	Histology/Morphology	Total		Male		Female		< 60 yrs		Mean age at diagnosis	
		n	%	n	%	n	%	n	%	Year	Range
Category- Hodgkin D (All) with Subtype		312	32.0	200	64.1	112	35.9	273	87.5		
9650	Hodgkin Lymphoma, NOS	264	27.1	168	63.6	96	36.4	229	86.7	36.5	3-86
9652	Hodgkin Lymphoma, mixed cellularity	18	1.8	14	77.8	4	22.2	17	94.4	23.1	4-62
9651	Hodgkin Lymphoma, lymphocyte-rich	13	1.3	9	69.2	4	30.8	11	84.6	29.3	6-67
9663	Hodgkin lymphoma, nodular sclerosis	12	1.2	4	33.3	8	66.7	12	100.0	25.5	15-43
9653	Hodgkin Lymphoma, lymphocyte depletion	2	0.2	2	100.0	0	0.0	2	100.0	20.2	8-38
9661	Hodgkin granuloma	1	0.1	1	100.0	0	0.0	1	100.0	34.0	N/A
9659	Hodgkin Lymphoma, nodular lymphocyte	1	0.1	1	100.0	0	0.0	0	100.0	68.0	N/A
9665	Classical Hodgkin lymphoma, nodular sclerosis	1	0.1	1	100.0	0	0.0	1	100.0	25.0	N/A
Category- Non- Hodgkin D (All) with subtype		662	68.0	419	63.3	243	36.7	416	62.8		
9591	Malig. Lymphoma, non-Hodgkin (NOS), B-cell	304	31.2	181	59.5	123	40.5	183	60.2	52.8	3-86
9680	Malig. Lymphoma, large B-cell, diffuse	161	16.5	99	61.5	62	38.5	100	62.1	51.7	2-84
9590	Malig. Lymphoma	75	7.7	51	68.0	24	32.0	50	66.7	49.9	25-71
9702	Mature T-cell lymphoma	22	2.3	17	77.3	5	22.7	18	81.8	45.0	6-80
9673	Mantle cell lymphoma	16	1.6	14	87.5	2	12.5	10	62.5	61.1	39-89
9687	Burkitt lymphoma (NOS)	10	1.0	8	80.0	2	20.0	10	100.0	19.2	3-53
9699	Marginal zone B-cell lymphoma	6	0.6	3	50.0	3	50.0	3	100.0	58.8	29-80
9714	Anaplastic large cell lymphoma, T cell	4	0.4	3	75.0	1	25.0	4	100.0	28.0	15-41
9670	Malig. Lymphoma, small B lymphatic	3	0.3	2	66.7	1	33.3	1	100.0	68.8	47-81
9728	Precursor B-cell lymphoblastic lymphoma	3	0.3	3	100.0	0	0.0	3	100.0	11.8	5-26
9727	Precursor cell lymphoblastic lymphoma (NOS)	2	0.2	2	100.0	0	0.0	2	100.0	25.5	12-35
9729	Precursor T-cell lymphoblastic lymphoma	2	0.2	2	100.0	0	0.0	2	100.0	15.0	
9679	Mediastinal large B-cell lymphoma	2	0.2	0	0.0	2	100.0	2	100.0	40.5	27-60
9705	Angioimmunoblastic T-cell lymphoma	2	0.2	2	100.0	0	0.0	1	50.0	55.5	41-61
9719	NK/T- cell lymphoma	2	0.2	2	100.0	0	0.0	2	100.0	40.5	29-51
9684	Malig. Lymphoma, large B-cell, diffuse, immunoblastic	1	0.1	1	100.0	0	0.0	1	100.0	56.0	N/A
9689	Splenic marginal zone B-cell lymphoma	1	0.1	1	100.0	0	0.0	1	100.0	51.0	N/A
9709	Cutaneous T-cell lymphoma	1	0.1	0	0.0	1	100.0	1	100.0	58.0	N/A
Category- Follicular Lymphoma/ with subtype		45	4.6	28	62.2	17	37.8	22	48.9		
9690	Follicular lymphoma (NOS)	35	3.6	22	62.9	13	37.1	19	54.3	58.4	25-71
9695	Follicular lymphoma, grade1	6	0.6	3	50.0	3	50.0	1	16.7	65.5	48-76
9691	Follicular lymphoma, grade 2 (mixed cell)	2	0.2	2	100.0	0	0.0	0	0.0	69.5	61-78
9698	Follicular lymphoma, grade 3 (B cell)	2	0.2	1	50.0	1	50.0	2	100.0	58.5	58-59
Grand Total of Hodgkin and Non-Hodgkin Lymphoma		974	100.0	619	63.6	355	36.4	689	70.7	2.0	2-89

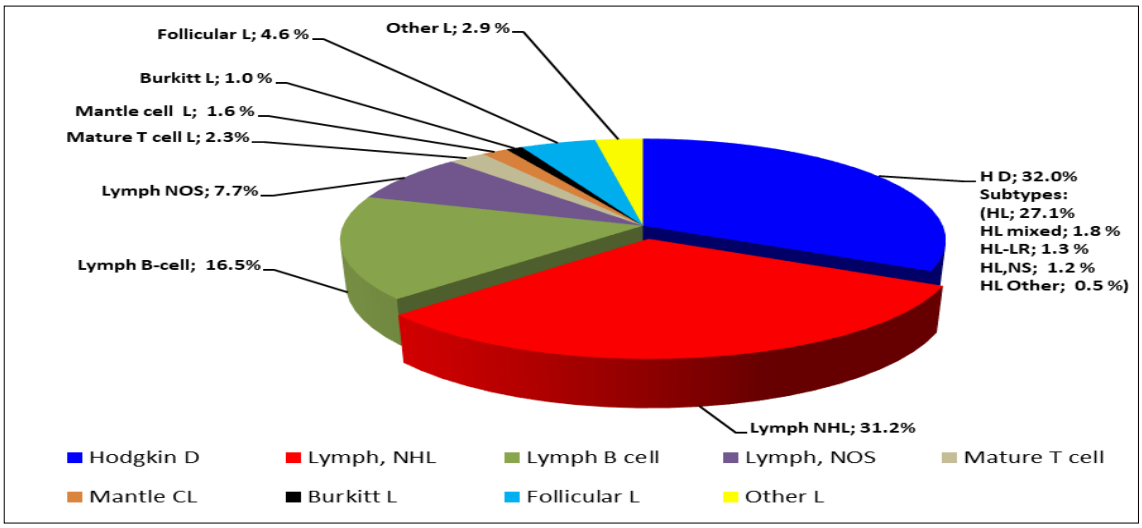

Fig 2: % of Non-Hodgkin's lymphoma & Hodgkins lymphoma malignancies: Both Sexs, Period: 2013-2017

Discussion

Epidemiological studies on lymphomas have been conducted around the world. However, with respect to developing countries with different socioeconomic, occupational, psychological, ethnic and even climatic conditions, prevalence and incidence rates, as well as the distribution of the subtypes, may vary, as can prognosis and survival [16-22].

Despite recent advances in new therapeutic chemotherapy regimens for lymphoma, epidemiological studies worldwide are few and almost absent in India. We considered very important to update the epidemiology of lymphomas in our center with the aim to focus our investigational efforts in the most prevalent type. Our results are not so different from the other series published if we consider only the frequencies.

The present study demonstrated that Non-Hodgkin Lymphoma (NHL) accounting for 68.0% was the most common and Hodgkin Lymphoma (HL) 32.0% with all sub-types of all HLM cases. We found that HM incidence was generally lower in women than men; this is a well-known phenomenon [9, 10]. There is a very similar work published by Omoti *et al*. 2012 [19] the differences between our results and theirs are the male: female ratio which is of 1.7:1 in our data and 1.6:1 in theirs.

The epidemiological profile of the current sample is in agreement with the existing literature regarding the greater prevalence of the subtypes of non-Hodgkin lymphoma and of male patients. Nevertheless, in this study, the prevalence of cases in patients under 60 years of age was much higher for the majority of the most prevalent subtypes of NHL. Although conflicting with some previous reports [3, 6-7, 13, 21, 23-25] these findings are in agreement with some major studies that have reported a greater incidence in individuals under 60 years of age in less developed countries of Central and South America, Africa and Asia [18-20, 26-30]. In relation to Hodgkin lymphomas, a greater frequency of cases in individuals under 60 years of age was indeed expected, particularly for the classic mixed cellularity HL subtype that, according to the literature, tends to be more equally distributed among the different age groups at diagnosis [19, 21, 23, 30, 31-33]. This was indeed the case, with 40% of cases occurring in individuals over 60 years of age compared to 7.15% for cases of the classic nodular sclerosis subtype.

Conclusion

In conclusion, the present study provided the pattern of HLM distribution and frequency in a tertiary hospital of Gurugram, India for the first time, to the best of our knowledge. It was not possible to state risk factors of HLM other than those reviewed and analyzed from the hospital based records; thus, a logistic regression model was not necessary, since the aim of this study was to analyze the frequency of haematological malignancies registered in a tertiary hospital of Gurugram, India. The results revealed that NHL occurred more frequently in elderly people (>50 years of age), whereas HL was more common in middle adults (<50 years old) compared with all other analyzed groups. Overall, there was a progressive increase in the occurrence of HLM between 2013 and 2017, and males were more frequently affected compared with females, but the difference was not significant. In addition, increased life expectancy and improved treatment options have also led to the reduced frequency of some disorders and the predominance of others.

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Conflict of interest

None

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