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The Incidence Rate of Non-Hodgkin's Lymphoma in Saudi Arabia: An Observational Descriptive Population Based Epidemiological Study from the Saudi Cancer Registry (2006–2016)

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Abstract

BACKGROUND: Non-Hodgkin's lymphoma (NHL) consists of several hematologic malignancies arising from B, T lymphocytes or natural killer lymphocytes, and nearly 85–90% originates from B lymphocytes.

AIM: This current study illustrates frequency of diagnosed NHL cases, age-standardized incidence rate (ASIR) and crude incidence rate (CIR) by age group, year of diagnosis and administrative regions for identifying the distribution, pattern, and real condition of NHL in Saudi Arabia.

METHODOLOGY: In this study, an epidemiological analysis of NHL cases is conducted on registered cases between 2006 and 2016 from Saudi cancer registry (SCR). For statistical analysis, t-test, sex ratio, Kruskal–Wallis and descriptive statistics were performed by SPSS version 20.0.

RESULTS: A total of 8019 NHL cases were documented from reported from January 2006 to December 2016. Among males, Riyadh region had the highest overall ASIR at 7.9 followed by Eastern region at 6.9/100,000 males and lowest overall ASIRs were observed in Jazan and Hail region at 3.5, and the Northern region at 3.9/100,000 males. The highest overall ASIR among females was reported in the Riyadh region at 6.9 and Eastern region at 5.2/100,000 females and lowest overall ASIR was documented in the Jazan region at 2.2, followed by Hail at 2.4. The overall age-standardized incidence sex ratio of NHL was found to be 1.3/100,000 in Saudi Arabia.

CONCLUSION: This study concluded an increase in CIRs and ASIRs NHL among Saudi population. Highest overall ASIRs for NHL among males and females from 2006 to 2016 were documented in Riyadh and Eastern region. While, lowest overall ASIRs among males and females were documented in the Jazan and Hail region.

Introduction

Non-Hodgkin's lymphoma (NHL) consists of several hematologic malignancies [1] arising from B, T lymphocytes or natural killer lymphocytes, and nearly 85–90% originates from B lymphocytes [2]. It consists of a broad range of cancers of the immune system ranging from indolent to aggressive types [3]. Among most common cancers, NHL ranked as 10th in males and 12th in females worldwide, with 248,724 deaths and 509,590 new cases estimated in 2018 [4]. There are more than 60 different subtypes of Non-Hodgkin lymphoma. These subtypes are grouped according to the cell where it starts, as B-cell lymphomas or T-cell lymphomas. About 85 percent NHL cases are B-cell lymphomas and 15 percent cases are T-cell lymphomas. The majority of B-cell lymphomas are either diffuse large B-cell lymphoma (DLBCL) or follicular lymphoma (FL). Other subtypes of B-cell lymphomas are [5].

- Mucosa-associated lymphatic tissue (MALT) lymphoma
- Small cell lymphocytic lymphoma/chronic lymphocytic leukemia (SLL/CLL)
- Mantle cell lymphoma (MCL)
- Mediastinal (thymic) large B-cell lymphoma
- Lymphoplasmacytic lymphoma and Waldenstrom macroglobulinemia
- Nodal marginal zone B-cell lymphoma
- Splenic marginal zone lymphoma
- Extranodal marginal zone B-cell lymphoma
- Intravascular large B-cell lymphoma
- Primary effusion lymphoma
- Burkitt lymphoma
- Primary central nervous system lymphoma.

T-cell lymphomas can be aggressive (fast-growing) or indolent (slow growing). Common subtypes of T-cell lymphomas include:

- Peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS)
- Cutaneous T-cell lymphoma (Sézary syndrome and mycosis fungoides)
- Anaplastic large cell lymphoma
- Angioimmunoblastic T-cell lymphoma

Globally, the incidence of NHL varies considerably across the world, with the highest incidence observed in Lebanon (23.35/100,000

people; 95% UI: [20.19–27.08] in 2017), followed by Australia (15.95/100,000 people; 95% UI: [14.1–17.89]) and New Zealand (15.73/100,000 people; 95% UI: [14.117.89]). The lowest incidence was observed in Iraq (1.49/100,000 people, 95% UI: [1.35–1.64] in 2017), followed by Kyrgyzstan (1.68/100,000 people; 95% UI [1.51–1.84]) and Bangladesh (1.71/100,000 people; 95% UI: [1.42–2.01]) [6].

NHL incidence is linked with large temporal and geographic variability across the world, however this inherent etiological heterogeneity unmasked some risk factors. Lifestyle and environmental factors such as obesity and particular occupational exposures and genetic factors like a family history of NHL are associated with risk of developing NHL [7], [8]. Helicobacter pylori, Hepatitis C virus, and Epstein–Barr virus associated infections are well established risk factors for NHL development [9]. In patients infected with HIV, the chances of developing NHL are higher because of immunosuppression [10]. A case-control study showed that male with diabetes, low monthly income, previous exposure to chemical and absence of regular exercise found to be at higher risk of developing NHL [11], [12].

The current study was intended to analyze the epidemiological parameters of age standardized incidence rates (ASIR) and crude incidence rates (CIR) of NHL categorized by age group, year of diagnosis and different regions of Saudi Arabia for identification and discussing the NHL distribution. Therefore, the detailed observational epidemiological study was conducted to examine the distribution of NHL cases recorded in the Saudi cancer registry (SCR) between 2006 and 2016.

Materials and Methods

We conducted an observational retrospective population based epidemiological study on NHL, which was based on the data from cancer registry by the ministry of health, Saudi Arabia [13]. This study did not require ethical clearance as the data regarding NHL diagnosed cases from January 2006 and December 2016 in administrative region of Saudi Arabia is publically open and easily available by the SCR annual reports [14]. SCR offered a comprehensive report from 2006 to 2016 for 13 administrative regions, incidence with number of cases in percentage, ASIR and CIR stratified by year of diagnoses, administrative regions and gender. In this study, only Saudis (citizens of Saudi Arabia) were included and non-Saudi residents were excluded from the study[15]. For statistical analysis, SPSS version 20.0 (IBM Corporation, Armonk, NY, USA) was used. In different regions of Saudi Arabia, ASIR and CIRs from the SCR reports for the year 2006 to 2016 were recorded and calculated the difference between them to investigate the trend of NHL in females and males. Independent-samples t-test was used for comparing ASIR and CIR of NHL among males and females. We also conducted a nonparametric Kruskal–Wallis H-test for correlating ASIR and CIRs of NHL between different regions of Saudi Arabia. In addition, male/female ratio of NHL was also determined from CIR, age-specific incidence rate (AIR) and ASIR stratified by year of diagnosis, age group, and administrative regions. The overall percentage of stage distribution of NHL from 2006 to 2016 was also identified in Saudi male and female. Stages of cancer from SCR were categorized into distant, localized, unknown, and regional stage [16].

Results

NHL among males

In the SCR reports, a total of 4669 NHL cases were recorded between January 2006 and December 2016. 351 cases (7.5%) of NHL were documented in the year 2006. There was increase of 2.5% in the number of NHL cases from 2006 to 2016. From 2006 to 2016, overall number and percentage of NHL among males were 424 cases (9.1%) per year (Tables 1 and 2).

The average number and percentage were calculated on stratifying the NHL cases according to age groups between 2006 and 2016. 5 years were set as the class width of the age groups and included age groups from 0–4, 5–9, 10–14, to 75 years and over. Males in the age group of 75 years and more were most often affected with NHL (59 overall cases per year; 13.9%) followed by the age group of 70–74 and 65–69 years (34 overall cases per year; 8%). Lowest percentage and overall number of NHL cases were observed in the age group of 10–14 years followed by 0–4 and 5–9 years (Figure 1a and b).

We observed highest overall age specific incidence rate (AIR) of NHL cases from 2006 to 2016 among males of the age group of 75 years and over (47.7), followed by 70–74 (36.1) and 65–69 (28.5)/100,000 males. However, the age-specific incidence male/female ratio was highest in the age group of 0–4 and 5–9 at 3, followed by 15–19 at 2/100,000. Age groups from 20 to 75 years and over demonstrated nearly similar age-specific incidence sex ratio (Figure 2).

The CIRs of NHL cases in Saudi males were categorized by the year of diagnosis from 2006 to 2016/100,000 males, found an increase from 2006 to 2007, 2008 to 2009 then a minor increase from 2010–2011 to 2012–2013 and decrease from 2015 to 2016. CIR of 4.1/100,000 males was observed in 2006. The highest CIR of 5/100,000 males was estimated in the year 2015. Moreover, the overall CIR of NHL cases from 2006 to 2016 was 4.4 (95% CI, 4.2–4.6) (Figure 3). We also applied the two independent sample t-test on CIR among males

Table 1: Number and percentage of non-Hodgkin's lymphoma in males during 2006–2016

Years	0–4	5–9	10–14	15–19	20–24	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75+	All ages	Percentage
2006	6	21	11	12	22	7	19	25	27	21	24	23	22	27	27	57	351	7.5
2007	17	18	15	23	16	21	18	31	26	37	25	17	29	43	35	47	418	9
2008	14	19	13	16	14	12	19	23	25	25	27	27	27	30	35	44	370	7.9
2009	10	8	18	22	18	26	23	12	27	29	27	31	29	34	35	73	422	9
2010	12	14	12	18	20	22	21	29	30	28	30	19	30	33	32	57	407	8.7
2011	15	18	14	17	15	26	19	19	19	34	38	42	29	37	31	59	432	9.3
2012	13	8	8	24	17	23	16	28	28	26	32	31	30	36	45	59	424	9.1
2013	13	17	7	16	25	20	21	25	20	32	35	35	33	39	35	62	435	9.3
2014	12	9	12	25	27	26	19	25	22	28	24	38	31	29	37	74	438	9.4
2015	25	27	14	25	28	26	32	27	30	30	45	44	32	26	34	58	503	10.8
2016	14	17	11	16	25	29	30	28	30	34	34	33	41	39	28	60	469	10
Total	151	176	135	214	227	238	237	272	284	324	341	340	333	373	374	650	4669	100
Overall	14	16	12	19	21	22	22	25	26	29	31	31	30	34	34	59	424	9.1
Percentage	3.2	3.8	2.9	4.6	4.9	5.1	5.1	5.8	6.1	6.9	7.3	7.3	7.1	8	8	13.9	100	

Table 2: Number and percentage of Non-Hodgkin's lymphoma in females between 2006 and 2016

Years	0–4	5–9	10–14	15–19	20–24	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75+	All ages	Percentage
2006	5	5	4	11	9	8	11	15	16	16	17	21	26	17	25	28	234	7
2007	9	6	6	13	17	10	15	13	12	22	19	19	23	28	28	45	285	8.5
2008	5	6	5	8	10	22	14	13	20	23	20	36	32	27	26	37	304	9.1
2009	3	2	5	11	14	16	16	13	15	23	31	24	23	25	29	37	287	8.6
2010	2	9	4	12	8	20	15	15	15	16	30	27	33	30	28	32	296	8.8
2011	7	5	8	8	17	20	11	22	15	22	23	21	25	30	33	45	312	9.3
2012	3	8	12	8	13	16	15	15	17	23	32	34	22	28	35	35	316	9.4
2013	3	4	3	12	8	18	13	14	17	24	32	29	30	30	29	45	311	9.3
2014	3	5	7	7	13	12	17	17	28	12	34	29	38	23	23	39	307	9.2
2015	8	5	10	9	15	11	16	26	15	30	17	43	26	24	26	45	326	9.7
2016	5	5	8	5	25	7	14	23	17	24	36	32	53	38	27	53	372	11.1
Total	53	60	72	104	149	160	157	186	187	235	291	315	331	300	309	441	3350	100
Overall	5	5	7	9	14	15	14	17	17	21	26	29	30	27	28	40	305	9.1
Percentage	1.6	1.8	2.1	3.1	4.4	4.8	4.7	5.6	5.6	7	8.7	9.4	9.9	9	9.2	13.2	100	

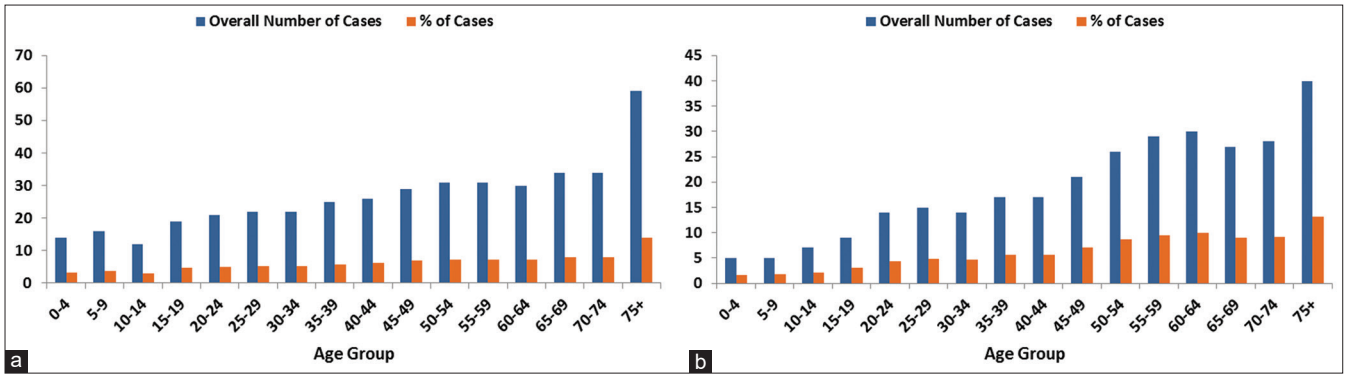

Figure 1: a) Graphical representation of overall number and percentage of Non-Hodgkin's lymphoma in males during 2006–2016. b) Graphical representation of number and percentage of Non-Hodgkin's lymphoma in females between 2006 and 2016.

and females and observed that males had significantly higher CIR as compared to females [t(20) is 10.454, p < 0.0001]. The overall crude incidence male/female ratio per 100,000 males from 2006 to 2016 was 1.4.

We also calculated the overall CIR of NHL stratified by the regions of Saudi Arabia per 100,000 males from 2006 to 2016. The highest overall CIR for NHL cases was observed in Riyadh at 5.4, followed by Baha and Makka region at 4.6/100,000 males. It was observed that the Kruskal–Wallis analysis was statistically significant for these regions in other areas of Saudi Arabia (p < 0.001). Jazan and Northern region documented lowest overall CIR at 2.6 and 2.7, respectively. Moreover, Jazan showed th highest crude incidence male/female ratio at 1.7, followed by Baha and Madinah at 1.6 (Figure 4).

The ASIR of NHL categorized by the year of diagnosis per 100,000 males from 2006 to 2016 was estimated from the SCR. An increase was observed from 2006 to 2007, decrease in 2008, followed by increase in 2009, decrease in 2010 and then decrease from 2015 to 2016 (Figure 5). The ASIR of 7/100,000 males was the highest rate documented in the year 2007 and the lowest at 5.5/100,000 males in 2014. In addition, the overall ASIR of NHL per 100,000 males from 2006 to 2016 was 6.2 (95% CI: 5.9–6.5). The overall age-standardized incidence sex ratio was found to be 1.3. We also applied independent sample t-test on ASIR between males and females and observed that ASIRs were significantly higher in males as compared to females [t(20) is 7.365, p <.0001].

We also investigated the overall ASIR of NHL stratified by the different regions of Saudi Arabia from 2006 to 2016/100,000 males. Riyadh region had the highest overall ASIR at 7.9/100,000 males, followed by Eastern region at 6.9 (Figure 6). It was found that Kruskal–Wallis analysis was statistically significant for these regions than other areas of Saudi Arabia (p < 0.001). The lowest overall ASIRs were observed in Jazan and Hail region at 3.5, and the Northern region

Overall age specific incidence rate of NHL cases from 2006 to 2016 per 100,000			
Age group	Male	Female	AIR sex ratio
0–4	1.2	0.4	3
5–9	1.5	0.5	3
10–14	1.2	0.7	1.7
15–19	2	1	2
20–24	2.1	1.5	1.4
25–29	2.5	1.7	1.5
30–34	2.9	1.9	1.5
35–39	4	2.7	1.5
40–44	5	3.3	1.5
45–49	7	5.3	1.3
50–54	9.2	8.2	1.1
55–59	12.1	12.1	1
60–64	16.4	16.9	1
65–69	28.5	21.9	1.3
70–74	36.1	31.4	1.1
75+	47.7	31.4	1.5

AIR: Age-specific incidence rate, NHL: Non-Hodgkin's lymphoma.

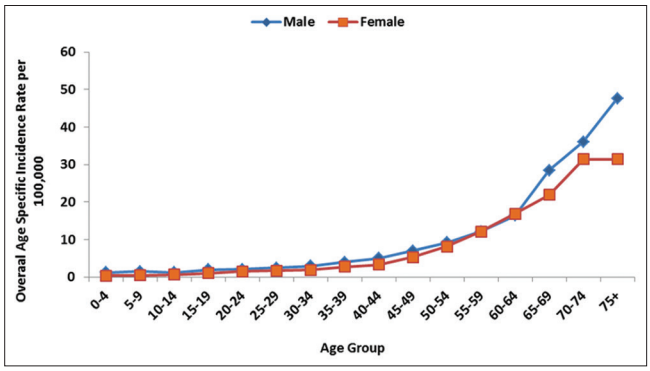

Figure 2: Overall age specific incidence rate of non-Hodgkin's lymphoma cases from 2006 to 2016/100,000 among male and female

Overall crude incidence rate of NHL per100,000			
Region	Male	Female	CIR sex ratio
Asir	4.4	2.9	1.5
Baha	4.6	2.9	1.6
Madinah	4.3	2.7	1.6
Jazan	2.6	1.5	1.7
Qassim	3.5	2.5	1.4
Hail	3	2	1.5
Jouf	3.9	2.7	1.4
Najran	3.2	2.4	1.3
Riyadh	5.4	4.3	1.3
Northern Region	2.7	2	1.4
Makka	4.6	3.5	1.3
Tabuk	3.2	2.4	1.3
Eastern Region	4.4	3.4	1.3

CIR: Crude incidence rate, NHL: Non-Hodgkin's lymphoma.

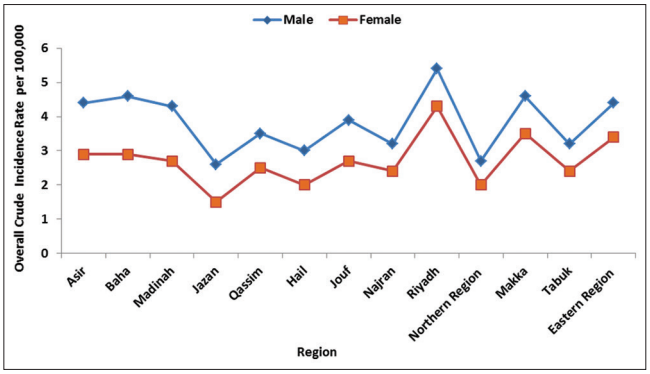

Figure 4: A overall crude incidence rate of non-Hodgkin's lymphoma cases per 100,000 among males and females according to administrative regions during 2006–2016

at 3.9/100,000 males. Furthermore, Jazan region demonstrated highest age-standardized incidence sex ratio per 100,000 males at 1.6, and Hail and Baha at 1.5, respectively (Figure 6).

To analyze the NHL pattern among different administrative regions of Saudi Arabia, differences in CIRs and ASIRs between 2006 and 2016 were calculated (Table 3). Highest CIR between 2006 and

CIR of NHL per100,000			
Years	Male	Female	CIR sex ratio
2006	4.1	2.7	1.5
2007	4.7	3.3	1.4
2008	4.1	3.4	1.2
2009	4.6	3.2	1.4
2010	4.3	3.2	1.3
2011	4.4	3.2	1.4
2012	4.2	3.2	1.3
2013	4.3	3.1	1.4
2014	4.4	3.2	1.4
2015	5	3.3	1.5
2016	4.6	3.8	1.2
Mean	4.4	3.2	1.4
Median	4.4	3.2	1.4
SD	0.28	0.26	0.1
95% CI: Mean	4.2–4.6	3–3.4	

CIR: Crude incidence rate, CI: Confidence interval, SD: Standard deviation, NHL: Non-Hodgkin's lymphoma.

Age-standardized incidence rate of NHL per100,000			
Year	Male	Female	ASIR sex ratio
2006	6.6	4.8	1.4
2007	7	5.1	1.4
2008	6	5.4	1.1
2009	6.8	5.1	1.3
2010	6.2	5.2	1.2
2011	6.4	4.8	1.3
2012	6.2	4.7	1.3
2013	6.1	4.6	1.3
2014	5.5	4	1.4
2015	5.9	4.1	1.4
2016	5.6	4.9	1.1
Mean	6.2	4.8	1.3
Median	6.2	4.8	1.3
SD	0.47	0.43	0.11
95% CI: Mean	5.9–6.5	4.5–5.1	

ASIR: Age-standardized incidence rate, NHL: Non-Hodgkin's lymphoma, CI: Confidence interval, SD: Standard deviation.

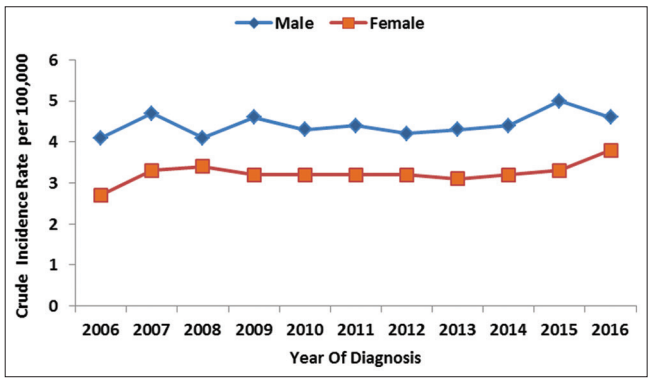

Figure 3: Crude incidence rate of non-Hodgkin's lymphoma per 100,000 among males and females during 2006–2016

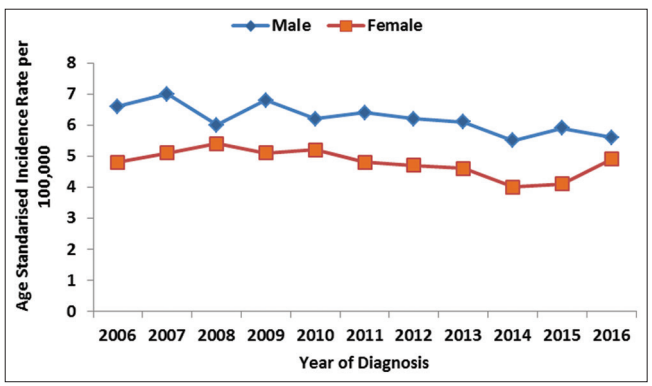

Figure 5: Age-standardized incidence rate of non-Hodgkin's lymphoma per 100,000 among males and females

Overall age standardized incidence rate of NHL from 2006 to 2016			
Region	Male	Female	ASIR sex ratio
Asir	5.4	3.9	1.4
Baha	5.1	3.4	1.5
Madinah	5.8	4.1	1.4
Jazan	3.5	2.2	1.6
Qassim	4.6	3.7	1.2
Hail	3.5	2.4	1.5
Jouf	5.5	3.9	1.4
Najran	4.7	3.8	1.2
Riyadh	7.9	6.9	1.1
Northern Region	3.9	3.3	1.2
Makka	6	4.9	1.2
Tabuk	6.6	4.8	1.4
Eastern Region	6.9	5.2	1.3

ASIR: Age-standardized incidence rate, NHL: Non-Hodgkin's lymphoma.

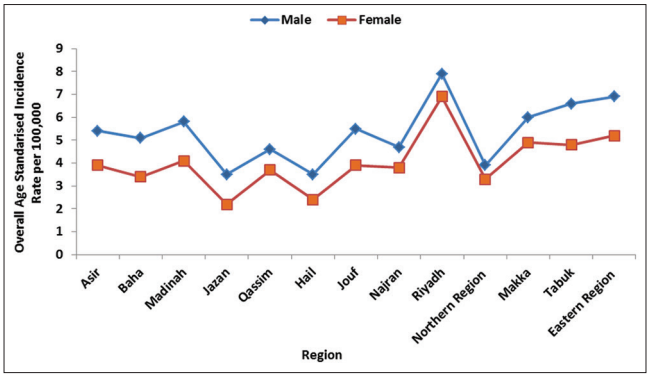

Figure 6: A overall age-standardized incidence rate of non-Hodgkin's lymphoma cases per 100,000 among males and females according to administrative regions during 2006–2016

2016 was documented in females in Qassim region and greatest change in ASIR was found in Northern region among females.

From 2006 to 2016, the overall percentage of stage distribution of NHL among males was also calculated. It was observed that most frequently diagnosed cases of NHL was found at the distant stage (44.2%), followed by localized (24.6%), unknown (17.2%), and regional stage (14%) (Figure 7).

NHL among females

From the SCR, a total of 3350 NHL cases was found between January 2006 and December 2016 (Table 1b). From 2006 to 2016, incidence of the number of NHL cases was increased. In the year 2006, 234 cases (7%) were documented and reported an increase of 4.1% in number of NHL cases in 2016. From 2006 to 2016, the overall number and percentage of NHL in females were 305 cases (9.1%) per year.

Females in the age group of 75 years and over were most frequently affected by NHL (40 overall cases per year, 13.2%), followed by age group of 60–64 years (30 overall cases per year, 9.9%). Lowest percentage of NHL cases was observed in the age group of 0–4 and followed by 5–9 years and 10–14 years (Figure 1a and b).

From 2006 to 2016, females showed high overall age-specific incidence rate in the age groups of 75 years and over, 70–74 at 31.4, 65–69 at 21.9 and 60–64 at 16.9/100,000 females (Figure 2). The CIRs of

Table 3: The difference in crude incidence rate and age-standardized incidence rate between 2006 and 2016

Region	Sex	CIR/ASIR	2006	2016	Difference
Asir	Male	CIR	3.3	5.5	2.2
		ASIR	4.3	6.5	2.2
	Female	CIR	2	4	2
		ASIR	3.2	5.3	2.1
Baha	Male	CIR	4.4	6.6	2.2
		ASIR	6	7.2	1.2
	Female	CIR	1.7	4.1	2.4
		ASIR	1.9	3.5	1.6
Madinah	Male	CIR	4.2	3.5	−0.7
		ASIR	5.5	4	−1.5
	Female	CIR	4	2.5	−1.5
		ASIR	6.9	3.8	−3.1
Jazan	Male	CIR	1.8	2.8	1
		ASIR	2.5	4.3	1.8
	Female	CIR	1.1	2	0.9
		ASIR	2.1	2.6	0.5
Qassim	Male	CIR	3.3	2.4	−0.9
		ASIR	4.1	2.8	−1.3
	Female	CIR	0.9	3.7	2.8
		ASIR	2	4.5	2.5
Hail	Male	CIR	1.3	3.4	2.1
		ASIR	1.8	3.9	2.1
	Female	CIR	0.4	1.1	0.7
		ASIR	0.4	1.2	0.8
Jouf	Male	CIR	5.5	3.2	−2.3
		ASIR	4.8	4.6	−0.2
	Female	CIR	3.1	2.7	−0.4
		ASIR	5.2	4.1	−1.1
Najran	Male	CIR	4.3	3.7	−0.6
		ASIR	4.8	3.8	−1
	Female	CIR	1.1	2.3	1.2
		ASIR	1.8	3.4	1.6
Riyadh	Male	CIR	4.5	5.4	0.9
		ASIR	7.6	7	−0.6
	Female	CIR	3.9	4.3	0.4
		ASIR	6.9	6.3	−0.6
Northern region	Male	CIR	2.4	4.9	2.5
		ASIR	2.8	5	2.2
	Female	CIR	0	2.1	2.1
		ASIR	0	2.8	2.8
Makka	Male	CIR	4.3	4.4	0.1
		ASIR	6.2	5.2	−1
	Female	CIR	2.8	4.4	1.6
		ASIR	3.8	5.2	1.4
Tabuk	Male	CIR	3.7	4.9	1.2
		ASIR	7.4	7.5	0.1
	Female	CIR	2.6	2.3	−0.3
		ASIR	5.8	3.3	−2.5
Eastern province	Male	CIR	4.5	5	0.5
		ASIR	7.8	6.6	−1.2
	Female	CIR	3	4.4	1.4
		ASIR	5.1	6.4	1.3

ASIR: Age-standardized incidence rate, CIR: Crude incidence rate.

NHL cases in Saudi females upon stratifying according to year of diagnosis from 2006 to 2016/100,000 females, showed slight increase from 2006–2008, remain stable from 2009 to 2015 and then increase in 2016 (Figure 3). In 2006, CIR of 2.7/100,000 females was estimated. CIR of 3.8/100,000 females was the highest rate reported in the year 2016. The overall CIR of NHL per 100,000 females from 2006 to 2016 was found to 3.2 (95% CI, 3–3.4) In addition, we also calculated the overall CIR of NHL stratified by the different regions of Saudi Arabia per 100,000 females (Figure 4). The highest overall CIR for NHL at 4.3/100,000 females was observed in the Riyadh region, followed by the Makka region at 3.5/100,000 females. It was found that the result of Kruskal–Wallis was statistically significant for these regions in comparison to other areas of Saudi Arabia ($p < 0.001$). Jazan region reported the lowest overall CIR at 1.5 and Hail and Northern Region at 2/100,000 females.

The ASIR of NHL among Saudi females was categorized by the year of diagnosis in Saudi Arabia, from 2006 to 2016 from the SCR (Figure 5).

Overall percentage stage distribution of NHL in males				
Years	Localized	Regional	Distant	Unknown
2006	16.5	16.5	35	31.9
2007	23.7	13.6	42.3	20.3
2008	14.6	14.6	44.3	26.5
2009	18.5	16.6	41.5	23.5
2010	22.1	18.7	45	14.3
2011	26	14	43	17
2012	28.8	12.5	46.5	12.3
2013	22	9	50	19
2014	27.9	13.9	47.7	10.5
2015	32	12.3	47.3	8.3
2016	38	12	44	6
Mean	24.6	14	44.2	17.2

NHL: Non-Hodgkin's lymphoma.

Overall percntage stage distribution of NHL in females				
Year	Localized	Regional	Distant	Unknown
2006	15.8	17.5	34.6	32.1
2007	21.4	18.2	36.8	23.5
2008	18.8	14.8	42.1	24.3
2009	16.4	18.1	41.1	24.4
2010	27	16.9	38.9	17.2
2011	31	14	38	17
2012	27.8	13.6	48.1	10.4
2013	26	12	45	17
2014	30.9	12.7	46.9	9.4
2015	30.4	13.8	44.8	11
2016	37	12	41	10
Mean	25.7	14.9	41.6	17.8

NHL: Non-Hodgkin's lymphoma.

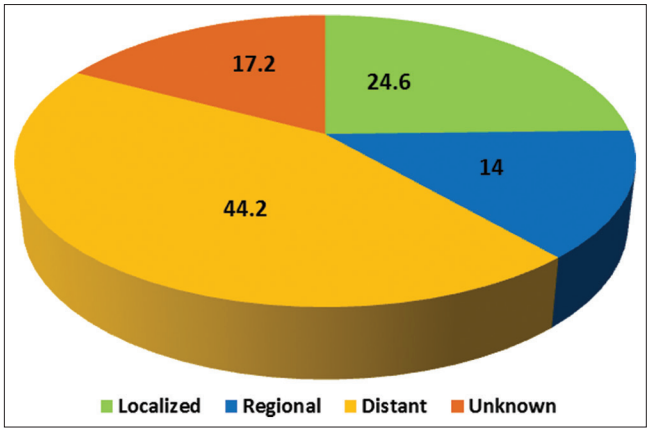

Figure 7: Overall percentage stage distribution of non-Hodgkin's lymphoma in males during 2006–2016

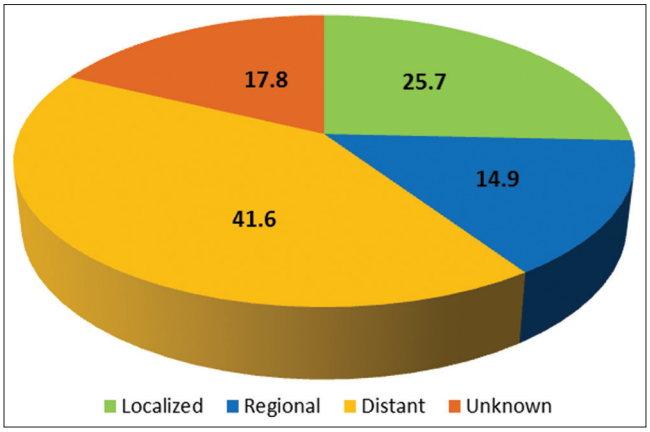

Figure 8: Overall percentage stage distribution of Non-Hodgkin's lymphoma in females during 2006–2016

We observed increase from 2006 to 2008, slight decrease in 2009, then again decrease in 2011–2014, followed by increase in 2015 and 2016. The highest ASIR was reported at 5.4/100,000 females in the year 2008 and lowest at 4/100,000 females in 2014. The overall ASIR among Saudi females from 2006 to 2016/100,000 females was 4.8 (95% CI, 4.5–5.1). We also calculated the overall ASIR from 2006 to 2016 among females stratified by different region of Saudi Arabia (Figure 6). The highest overall ASIR was reported in the Riyadh region at 6.9 and Eastern region at 5.2/100,000 females. It was found that Kruskal–Wallis test was statistically significant for these regions in comparison to other areas of Saudi Arabia ($p < 0.001$). Jazan region at 2.2 documented the lowest overall ASIR, followed by Hail at 2.4/100,000 females.

The overall percentage of stage distribution of NHL from 2006 to 2016 was also calculated among females (Figure 8). NHL was most frequently diagnosed at distant stage (41.6%), followed by localized (25.7%) and unknown stage (17.8%). NHL was diagnosed at a lower percentage in regional stage (14.9).

Discussion

The CIR and age-standardized incidence rate (ASIR) of NHL cases are required to be investigated and updated in different regions of Saudi Arabia. The present study is aimed to examine the CIR and ASIR pattern among NHL cases from 2006 to 2016 in Saudi Arabia. To the best of our knowledge, this is the first descriptive epidemiological study analyzing the spatial/temporal distribution of NHL from 2006 to 2016 in women and men in different regions of Saudi Arabia, which is based on the PubMed database. In this study, we have identified the actual state of NHL trend and explored importance of NHL in Saudi Arabia population.

In the present study, highest overall ASIRs for NHL among males from 2006 to 2016 were observed in Riyadh and Eastern region. The most possible justification is that the males of these regions are greatly exposed to risk factors linked with NHL than in other regions. In addition, rise in ASIR for NHL among males in Riyadh and Eastern region can also be linked with other factors such as lifestyle habits, environmental, and genetic risk factors. Hence, detailed epidemiological analysis is required that will provide better understanding of key risk factors linked with increase of ASIR for NHL in Riyadh and Eastern region. Other probable reasons for the high value of incidence rate includes occurrence of industries in these regions [17], advanced healthcare facility and its accessibility and Vitamin D deficiency [18]. A study suggested about the deficiency of vitamin D in 83.6% of Arabian population [19]. In the Saudi University students, 100% severe deficiency of Vitamin D was found [20]. Previous studies suggested that decreased vitamin D serum level was linked with increased risk of NHL development [21], [22]. The lowest overall ASIR

among males were documented in the Jazan and Hail region may be because of the presence of particular protective factors in this region than the higher ASIRs regions. Other possible reasons may include lesser industrialization, less health-care facility and its accessibility, less westernization and less screening than in regions with higher incidence.

Riyadh is the highly affected region with obesity in Saudi Arabia, having 35% obesity prevalence in comparison to Jazan having prevalence at 2% [23]. Hence, significantly higher rates were observed in Riyadh as compared to other regions. A meta-analysis of observational study by Mitri *et al.* suggested that individuals having diabetes were at higher risk of developing NHL in comparison to individuals without diabetes [24], [25]. A national survey conducted by Saudi Ministry of Health in 2013 found that in Riyadh region, diabetes prevalence was 20 times more as compared to Jazan region. Our finding reported the lowest overall ASIR of NHL in Jazan and highest overall ASIR in Riyadh among males and females indicating that diabetes prevalence may be the reason for rise in ASIR in Riyadh and decrease in Jazan region [23], [26]. Investigation of these factors in case of NHL may give better insight of this disorder and may be useful in reducing its burden.

According to GLOBOCAN 2018 estimates, incidence rates of NHL per 100,000 were highest in Australia and New Zealand (16.4), Northern America (14.8), and Northern Europe (13.5), whereas Middle Africa (3.2) and Central America (4.6) had the lowest incidence rates among males. Among females, similar geographical trend was found. Northern America had the highest incidence rate at 10.4, while the lowest rates were observed in Middle Africa at (2.8). NHL ranked as fourth major reason of cancer incidence in Bahrain, Oman, Egypt, Sudan and Qatar. NHL ranked as 5th and 9th most common cancer in further 87 countries [4]. In a study it was found that NHL cancer among Saudi men show increasing trends. The region of Riyadh, the Eastern region, and Makkah had the highest overall CIRs and ASIRs. Jazan, Hail, and Baha had the lowest. The greatest differences in the ASIR of NHL among Saudi men from 2001 to 2008 were found in Jouf [27], [28]. A variable increase in the number of cases was observed. The study found that the survival trends are comparable with those from Western countries [29].

In spite of the lack of time distribution and geographic data regarding NHL, we aimed to study the trends and patterns NHL between 2006 and 2016 in population of Saudi Arabia. Results of this descriptive epidemiological study would help in making better public health policy for NHL in Saudi Arabia and may be useful in making future hypothesis of possible NHL risk factors in the most frequently affected region by prospective epidemiological studies that detect the association of disease and exposure.

Conclusion

This study concluded an increase in CIR and ASIR NHL among Saudi population. Highest overall ASIRs for NHL among males and females from 2006 to 2016 were documented in Riyadh and Eastern region. While, the lowest overall ASIRs among males and females were documented in the Jazan and Hail region. Further studies are required for the identification of potential risk factors associated with NHL in Saudi population.

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