

# Non-Hodgkin lymphoma in Jordan

## *Types and patterns of 111 cases classified according to the WHO classification of hematological malignancies*

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### ABSTRACT

**Objective:** Non-Hodgkin lymphoma (NHL) is one of the most frequent malignancies in Jordan. The aims of this study are: 1. To classify NHL cases in Jordan, using the new World Health Organization (WHO) classification system, 2. To identify the most common types of NHL in Jordan, and 3. To compare lymphoma types and patterns in Jordan with those in surrounding countries and the West.

**Methods:** We studied all NHL cases, diagnosed during 1996 through to 1999 inclusive, at 2 major medical centers in Jordan, in order to identify their main types and patterns. One hundred and eleven cases of confirmed NHLs were reexamined and immunophenotyped in the year 2000, at the Department of Pathology, Jordan University of Science and Technology, Irbid, Jordan, using an immunohistochemical panel of antibodies, including CD3, CD15, CD20, CD30, CD43, CD45 and CD45RO. Confirmed NHL cases were reclassified according to the recently proposed WHO system of Hematological Malignancies.

**Results:** The median age of NHL cases was 44-years

(range 2-85). The vast majority of cases were of B-cell phenotype; only 14% of the cases were T-cell lymphomas. Most of the cases were of the aggressive intermediate to high-grade large cell type. Diffuse large B-cell lymphoma (DLBCL) comprised 53% of NHLs and 62% of B-cell NHLs. Indolent lymphomas were uncommon, comprising 14% of all NHL cases. Twenty-nine cases were seen among patients less than 20-years. Burkitt lymphoma represented the largest group (55%) of the childhood NHLs followed by diffuse large cell and lymphoblastic types.

**Conclusion:** Indolent lymphomas are rare in Jordan and account for less than 15% of all NHLs. Aggressive lymphomas; on the other hand, account for the majority of NHLs in Jordan. Burkitt lymphoma affected children less than 10-years of age with a median of 4.5-years. These observations indicate that NHLs in Jordan have different type distribution and patterns from those seen in the West.

Saudi Med J 2004; Vol. 25 (5): 609-614

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Jordan is a Middle-Eastern developing country located in the so called "lymphoma belt." The geographic boundaries of this "belt" extend from

Western Asia to the Middle East to Northern Africa. Countries located in the "lymphoma belt" are reported to have a high incidence of malignant

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Received 29th September 2003. Accepted for publication in final form 9th February 2004.

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lymphoma (ML). It is not clear, however, whether the frequency and incidence rates of ML in these countries are higher than those of western countries, since no reliable statistics exist in these countries. Recent reports from the Jordan Cancer Registry have indicated that hematopoietic neoplasms (lymphomas and leukemias) are the most common malignancies among Jordanian males and the second most common malignancies among Jordanian females.<sup>1,2</sup> Malignant lymphomas ranked third among malignancies affecting Jordanian males and second among malignancies affecting females. Despite this fact, studies regarding lymphoma in Jordan are limited.<sup>3-11</sup> In addition, no studies exist of patterns and types of ML lymphoma in Jordan, using the recent lymphoma classification systems, including the Revised European American Lymphoma (REAL) system<sup>12</sup> or the proposed World Health Organization (WHO) Classification of Hematological Malignancies,<sup>13</sup> which is largely based on the REAL system. This is a histopathological and immunohistochemical study of non-Hodgkin lymphoma (NHL) in Jordanian patients. The aims of this study were: 1. To classify NHL cases in 2 major medical centers in Jordan, using the new WHO classification system, 2. To identify the most common types of NHL in Jordan, and 3. To compare lymphoma types and patterns in Jordan with those in surrounding countries and the West.

**Methods.** This was a retrospective study of all NHL cases diagnosed in the Pathology Departments at the Jordan University of Science and Technology (JUST) and Basheer Hospital (BH), from 1996 through to 1999 inclusive. The Pathology Department at JUST is located in Irbid, Jordan and is the chief provider of surgical pathology services to the entire North of Jordan. The BH Pathology Department is located in Amman, Jordan, and is a main provider of surgical pathology services in the Central and Southern regions of Jordan. Both pathology departments are the 2 largest in Jordan, receiving approximately 30% of surgical pathology specimens of the country.

**Histopathologic studies.** Paraffin blocks of all ML cases diagnosed at JUST and BH from January 1996 through to December 1999 were retrieved. Four-micron thick paraffin sections were stained with Hematoxylin and Eosin. Slides were histologically re-examined by 2 hematopathologists (NMA and HSK) at the Department of Pathology at JUST in the year 2000. The diagnoses were confirmed and re-classified using morphologic and immunophenotypic findings, according to the WHO classification.<sup>13</sup> The total number of cases diagnosed as ML and retrieved from the Pathology Department's archives of both medical centers was 212. After histological review and

immunohistochemical staining, 15 cases (6.8%) were excluded. Five cases were excluded due to insufficient amount of diagnostic tissue in the paraffin blocks. The diagnosis in 10 cases was changed into "atypical lymphoid proliferation" or non-lymphoid undifferentiated malignant neoplasm. Eighty-six cases of Hodgkin disease were not included in this study leaving a final number of 111 NHL cases.

**Immunohistochemical studies.** Immunologic classification of ML cases was performed by immunohistochemical staining of formalin-fixed paraffin-embedded 4 micron-thick sections, using previously described methods. Leukocyte markers used included antibodies against the leukocyte common antigen (CD45), the T-cell antigens CD3, CD43 and CD45RO (UCHL1), the B-cell antigen CD20 (L26), in addition to the Hodgkin's markers CD15 (Leu-M1) and CD30 (BerH2). Autoclaving was used for antigen recovery. All antibodies were obtained from DAKO (Glostrup, Denmark).

**Results.** Table 1 shows the main types of NHL cases, including their proportion, age and sex distribution of patients. The median age of NHL patients was 43.5-years, with a range of 2-85-years. Figure 1 illustrates the age distribution of the cases and of the 4 most common subtypes of NHLs. The age distribution of all patients was as follows: 27.9% of patients were 20-years or younger, 18.2% ranging from 21-40-years-old, 37.4% ranging from 41-60-years-old, and 16.3% older than 60-years. The most frequent NHL type in the youngest age group (20-years or less) was Burkitt's lymphoma (55%) followed by diffuse large B-cell lymphoma (28%) and lymphoblastic lymphoma (17%). Males were more affected than females, with a M:F ratio of 1.4:1.

**Site of presentation.** Most of NHL cases (55%) were nodal in location, with the most frequent biopsy location being the cervical lymph nodes, followed by axillary lymph nodes. Extranodal lymphomas, summarized in Table 2, accounted for 43% of the cases; the most common extra-nodal sites were the stomach (26%), followed by small and large intestine (17%), tonsils and pharynx (13%), and mediastinum (7%). Three additional cases involved lymph nodes and extranodal sites at the time of presentation.

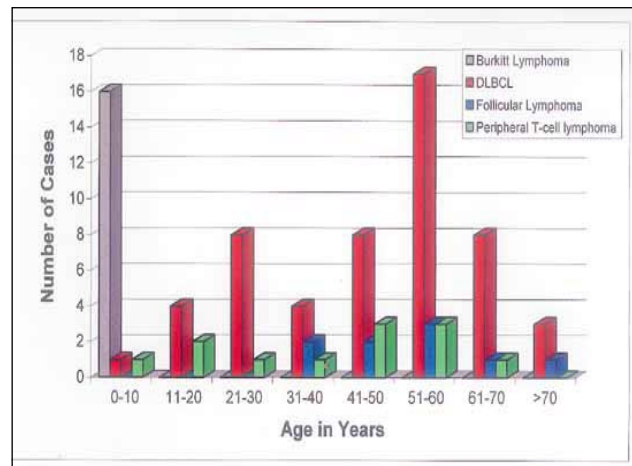
**B-cell non-Hodgkin's lymphoma.** The majority of NHL cases were of B-cell lineage (86%), while the remaining 14% were of T-cell lineage. Indolent lymphomas comprised 14% of all NHL and 16% of B-cell NHL cases, with follicular center cell lymphomas being the most common low grade B-cell NHL type (8%), followed by marginal zone lymphoma (4%) and small lymphocytic lymphoma (2%). Indolent lymphomas affected adults with an

**Table 1** - Distribution of 111 non-Hodgkin's lymphoma cases according to phenotype, histologic types, patients' sex, age and site.

Diagnosis	N	Age range (med.)	M:F	Nodal/ Extranodal
<b>B-cell lymphomas</b>				
SLL	2	50-65	2:0	2/2*
Marginal zone	4	38-55	3:1	0/4
Follicular	9	40-71 (55)	4:5	9/0
Mantle	3	35-70	3:0	3/0
Diffuse large cell	59	5-85 (52)	1.3:1	34/25
Lymphoblastic	2	6-16	1:1	1/1
Burkitt	16	2-10 (4.5)	2.4:1	6/10
<b>T-cell lymphomas</b>				
Anaplastic large cell	2	50-55	2:0	2/1†
Diffuse large cell	10	5-65 (32)	2:1	6/4
Lymphoblastic	4	4-74 (5)	1/3	1/3
<b>Total</b>	<b>111</b>	<b>2-85 (43.5)</b>	<b>1.3</b>	<b>64/50</b>
M:F - male to female, SLL - small lymphocytic lymphoma, * 2 cases of SLL had lymph node and splenic involvement at the time of presentation † one case presented with simultaneous skin and lymph node involvement				

age ranging from 38-71-years, and a median age of 51-years. All 9 cases of follicular center lymphoma had a nodular pattern and were composed of either predominantly small cleaved lymphoid cells (grade I) [5 cases] or mixed small and large lymphoid cells (grade II) [4 cases]. None of the follicular NHL cases were of predominant large lymphoid cell type (grade III). All cases of marginal zone lymphoma were extranodal gastric lymphomas of mucosa associated lymphoid tissue (MALT) type. The diagnosis of the 3 cases of mantle cell lymphoma was mainly based on the histological and immunohistochemical findings. In one of these cases, flow cytometric study was performed, showing the neoplastic B-cells to express CD5, with strong surface light chain immunoglobulin expression and lack of CD23. The majority of B-cell NHL cases (84%) were of intermediate to high-grade histologic types. Diffuse large B-cell lymphoma (DLBCL) was the most common type of B-cell NHL accounting for 53% of NHLs and 62% of B-cell NHLs, and was seen in all age groups. The distribution of DLBCL patients among different age groups was as follows: 20-years-old and younger 9%, 21-40-years-old 23%, 41-60-years-old 47% and older than 60 years 21%. Burkitt lymphoma (BL) was the most common B-cell lymphoma of the pediatric age group. All BL cases were 10-years-old or younger with a median age 4.5-years. More than 62% of BL cases were located in intraabdominal locations (intestinal, mesenteric), while the remaining cases were located in the head and neck region.

**T-cell non-Hodgkin's lymphoma.** Table 1 shows the 16 cases of T-cell NHL cases, and their

**Figure 1** - Age distribution of the 4 most common non-Hodgkin lymphomas in Jordan. Diffuse large B-cell lymphoma (DLBCL) was the most common type seen in Jordan affecting all age groups; similarly peripheral T-cell lymphoma involved all age groups. Follicular lymphomas were seen only in adults, whereas, all Burkitt lymphoma cases occurred in children 10-years-old or younger.

distribution according to histologic types, patient's sex, age range, median age and nodal or extra nodal location. Four (25%) of these patients were less than 20-years-old. Twelve (75%) of the T-cell NHL cases were classified as peripheral T-cell lymphoma. Histologically, 10 of these cases (63%) had either a diffuse large cell pattern (9 cases) or a mixed small and large cell pattern (one case). CD30 positive anaplastic large cell lymphoma was seen in 2 patients, 50 and 55-years-old. T-cell lymphoblastic lymphoma accounted for 25% of all T-cell NHLs; 3 cases were seen in children, 4-6-years-old, and one in a 71-year-old female.

**Discussion.** During the last 40-years, it has been recognized that ML is one of the most frequent malignancies in Jordan.<sup>4</sup> The earliest study of cancer in Jordan reported that ML was the third most frequent malignant neoplasms in the country during the sixties.<sup>4</sup> However, until the recent establishment of the National Jordan Cancer Registry, there were no reliable statistical studies of cancer in general and ML in particular. Only a few studies exist on the incidence, types and patterns of lymphoma in Jordan.<sup>6,7</sup> Most of these studies were carried out using older morphology-based lymphoma classification systems, such as the Rappaport or working formulation systems, which did not include immunophenotypic features of ML cases. In the last 10-years, there have been major advances in the classification, diagnosis and treatment of ML. The current study deals with the common types of ML in Jordan, classified according to the recently published WHO system,<sup>13</sup> with comparison of ML

**Table 2** - Characteristics of 47 extranodal non-Hodgkin lymphomas according to site of involvement, age, phenotype, sex and histopathologic type.

Site	n of cases	T-cell	B-cell	Range years	Median age	M:F	Histopathologic type
Gastric	12	0	12	38-79	55	6:6	DLBCL 8; MZL 4
Intestine	7	0	7	2-32	6	2:5	BL 4; DLBCL 2; lymphoblastic 1
Tonsils and pharynx	6	0	6	2-65	37	2:4	DLBCL 4; BL2
Head (jaws, parotid, orbit, postnasal)	5	1	4	3-55	10	5:0	DLBCL 3; BL 1; DLTCL 1
Back and chest wall	3	0	3	38-59	42	2:1	DLBCL 3
Mediastinum	3	3	0	4-71	4	1:2	Lymphoblastic 3
Other sites	11	3	8	4-70	61	5:6	DLBCL 6; DLTCL 3; BL 2
<b>Total</b>	<b>47</b>	<b>7</b>	<b>40</b>	<b>2-85</b>	<b>39</b>	<b>23:24</b>	
M:F - male to female, DLBCL - diffuse large B-cell lymphoma; MZL - marginal zone lymphoma BL - Burkitt lymphoma, DLTCL - diffuse large T-cell lymphoma							

patterns in children and adults between Jordan, the surrounding middle-eastern countries and the West.

According to the recent 1997 report by the Jordan Cancer registry, ML represents 10.2% of all cancers in Jordan,<sup>2</sup> which is considerably higher than their proportion in the United States of America (USA), which is around 4%.<sup>14</sup> The annual incidence rate for ML as reported by the Jordan Cancer Registry in 1997 is 13.0/100000,<sup>2</sup> with a rate of 4.4/100000 for Hodgkin disease, and 8.6/100000 for NHL. We believe that these rates may be slightly underestimated due to non- and misdiagnosis and under-reporting of ML cases. The incidence of ML in Jordan seems to be lower than that of the USA, which is 13.7/100000 for NHL and 3.1/100000 for Hodgkin disease.<sup>15,16</sup> However, long term monitoring of cancer cases is required before accurate estimates of ML incidence in Jordan are determined. As elsewhere in the world, NHL cases are more common in Jordan than Hodgkin disease cases. Similar to western countries, NHL in Jordanian patients tended to be more common in males, and to involve mostly adults. However, the median age at diagnosis of Jordanian NHL patients (44-years) was less than that observed in the West (55-years).<sup>17</sup> Eighty-six percent of NHL cases in Jordan were of B-cell type, which is within the rates of 80-90% reported in the world, except for the Far Eastern countries.<sup>18</sup> It appears that indolent lymphomas are uncommon in Jordan, comprising only 14% of our B-cell lymphomas. This is markedly different from what is observed in the USA, where low grade lymphomas comprise up to 49% of NHL cases,<sup>17,19</sup>

but is similar to figures observed in nearby middle eastern countries, such as Kingdom of Saudi Arabia<sup>20</sup> and Oman,<sup>21</sup> and elsewhere in the world, such as Italy<sup>22</sup> and China.<sup>23,24</sup> Follicular center cell lymphoma was the most frequent type of low-grade lymphoma, comprising approximately 8% of NHL in this series, as compared to 20-25% in the USA.<sup>17,22,23</sup> Small lymphocytic lymphoma comprised of less than 2% of NHL cases, as compared to 15% in the USA.<sup>17,19</sup> As expected, patients with low-grade lymphomas were all adults, and more likely to be males. Most cases of NHL in this study were of the aggressive intermediate to high-grade types. DLBCL was the most common type of NHL, comprising 53% of all NHL cases and more than 62% of NHL cases of B-cell lineage. Diffuse large B-cell lymphoma (DLBCL) involved all age groups, and was the most frequent type of ML in adults with a peak incidence between 50 and 60-years of age. However in the childhood cases, DLBCL was the second most common NHL exceeded only by BL. In children, BL was the most frequent type of ML, followed by DLBCL and lymphoblastic lymphoma. Burkitt lymphoma cases in this series almost exclusively involved children, and were located in the abdomen or head and neck region. The median age for BL cases seen in this study was 4.5-years, a younger age than that seen for this lymphoma in the West. This finding, however, is in agreement with observations made in the past from Jordan and neighboring countries.<sup>9,11,25,26</sup> Extranodal presentation was seen in 47 cases and additional 3 cases had simultaneous nodal and extranodal presentation.

Gastrointestinal lymphomas represented the largest group of group of extranodal NHLs, a finding in agreement with the literature.<sup>27-29</sup> Interestingly, 3 mucosal associated lymphoid tissues (MALT) sites including stomach, intestine and pharynx represented 56% of extranodal sites seen in this series. Gastric lymphomas were the most frequent extranodal lymphomas representing more than one quarter of all extranodal NHLs. This finding is in agreement with the reports from the West<sup>27-29</sup> and from our own group's findings on gastrointestinal lymphomas,<sup>11</sup> but contradicts earlier reports from the Middle East, which claimed that intestinal lymphomas were commoner than gastric lymphomas.<sup>30,31</sup> The number of cases of immunoproliferative small intestinal disease were seen in this study. This is also in agreement with our previous report, which indicated the extreme rarity of this entity in Jordan.<sup>11</sup>

The types and patterns of lymphoma in this study are most likely representative of the majority of Jordanians diagnosed with NHL in Jordan, as this group includes all cases diagnosed at 2 major medical centers during a 4-years period. These 2 medical centers serve almost all of the Government hospitals in the entire regions of Jordan. The above results may be a reflection of the patient population of these 2 centers, since the vast majority of these patients belong to the lower socioeconomic classes of the Jordanian society. It may be interesting to compare these findings to those of NHL patients of higher socioeconomic classes, who are mainly diagnosed in the private sector.

In conclusion, this study provides a brief overview of the main types of non-Hodgkin lymphoma cases in Jordan, with some of their epidemiological patterns. Classification of NHL cases in this study used the most recent classification systems of lymphoid neoplasms, but was mainly based on morphologic and immunophenotypic features of these tumors. Further, studies of NHL in Jordan are needed, with emphasis on their epidemiological, cytogenetics, molecular features, and association with different environmental factors and clinical behavior.

## References

1. Jordan Cancer Registry. Cancer Incidence in Jordan 1996 Report. Amman (JO): Ministry of Health; 1998. p. 8-10, 22-23.
2. Jordan Cancer Registry. Cancer Incidence in Jordan 1997 Report. Amman (JO): Ministry of Health; 2000. p. 27-29, 41-42, 60-62.
3. Kalbian V. A case of Burkitt's lymphoma in an Arab child from Jordan. *Int J Cancer* 1967; 2: 603.
4. Khalidi RH. A pattern of cancer incidence in Jordan 1965 - 1969 with a discussion. *Jordan Med J* 1972; 7: 30-40.
5. Dajani YF, Al-Jitawi S. Primary gastrointestinal lymphoma in Jordan. *Trop Geogr Med* 1983; 35: 375-379.
6. Tarawneh MS. Non-Hodgkin's lymphomas in Jordanians: a histopathological study of 231 cases. *Hematol Oncol* 1986; 4: 91-99.
7. Tarawneh MS, Madanat F, Khalaf MA, Awidi AS, Shamayleh AM, Amr SS et al. Hodgkin's disease in Jordanian children: a study of 26 cases. *Clin Oncol* 1984; 10: 21-25.
8. Amr SS, Tarawneh MS, Jitawi SA, Oran LW. Malignant neoplasms in Jordanian children. *Ann Trop Paediatr* 1986; 6: 161-166.
9. Madanat FF, Amr SS, Tarawneh MS, El-Khateeb MS, Marar B. Burkitt's lymphoma in Jordanian children: epidemiological and clinical study. *J Trop Med Hyg* 1986; 89: 189-191.
10. Madanat FF. MOPP therapy in children with Hodgkin's disease. *Am J Pediatr Hematol Oncol* 1989; 11: 407-410.
11. Almasri NM, Al-Abbadi M, Rewaily E, Abulkhail A, Tarawneh MS. Primary gastrointestinal lymphomas in Jordan are similar to those in Western countries. *Mod Pathol* 1997; 10: 137-141.
12. Harris NL, Jaffe ES, Stein H, Banks PM, Chan JK, Cleary ML et al. A revised European-American classification of lymphoid neoplasms: a proposal from the International Lymphoma Study Group. *Blood* 1994; 84: 1361-1392.
13. Harris NL, Jaffe ES, Diebold J, Flandrin G, Muller-Hermelink HK, Vardiman J et al. The World Health Organization classification of hematological malignancies report of the Clinical Advisory Committee Meeting, Airlie House, Virginia, November 1997. *Mod Pathol* 2000; 13: 193-207.
14. Silverberg E, Lubera J. Cancer statistics, 1987. *CA Cancer J Clin* 1987; 37: 2-19.
15. Boring CC, Squires TS, Tong T, Montgomery S. Cancer statistics, 1994. *CA Cancer J Clin* 1994; 44: 7-26.
16. Weisenburger DD. Epidemiology of non-Hodgkin's lymphoma: recent findings regarding an emerging epidemic. *Ann Oncol* 1994; 5 Suppl 1: 19-24.
17. National Cancer Institute sponsored study of classifications of non-Hodgkin's lymphomas: summary and description of a working formulation for clinical usage. The non-Hodgkin's Lymphoma Pathologic Classification Project. *Cancer* 1982; 49: 2112-2135.
18. Warnke RA, Weiss LM, Chan M, JKC, Cleary ML, Dorfman RF. Tumors of the lymph nodes and spleen. Atlas of tumor pathology, fascicle 14. 3rd series. Washington (DC): Armed Forces Institute of Pathology; 1995. p. 53-62.
19. Siebert JD, Mulvaney DA, Potter KL, Fishkin PA, Geoffroy FJ. Relative frequencies and sites of presentation of lymphoid neoplasms in a community hospital according to the revised European-American classification. *Am J Clin Pathol* 1999; 111: 379-386.
20. Thomas JO, Abdelaal MA. Malignant lymphoma in western province of Saudi Arabia. *East Afr Med J* 1995; 72: 355-358.
21. Bamanikar S, Thunold S, Devi KR, Bamanikar A. The pattern of malignant lymphoma in Oman. *J Trop Med Hyg* 1995; 98: 351-354.
22. Hoppe RT. The non-Hodgkin's lymphomas: pathology, staging, treatment. *Curr Probl Cancer* 1987; 11: 363-447.
23. Ng CS, Chan JK, Lo ST, Poon YF. Immunophenotypic analysis of non-Hodgkin's lymphomas in Chinese. A study of 75 cases in Hong Kong. *Pathology* 1986; 18: 419-425.
24. Harrington DS, Ye YL, Weisenburger DD, Armitage JO, Pierson J, Bast M et al. Malignant lymphoma in Nebraska and Guangzhou, China: a comparative study. *Hum Pathol* 1987; 18: 924-928.
25. Isaacson P, Al-Dewachi HS, Mason DY. Middle Eastern intestinal lymphoma: a morphological and immunohistochemical study. *J Clin Pathol* 1983; 36: 489-498.
26. Ladjadj Y, Philip T, Lenoir GM, Tazerout FZ, Bendisari K, Boukheloua R et al. Abdominal Burkitt-type lymphomas in Algeria. *Br J Cancer* 1984; 49: 503-512.

27. Rudders RA, Ross ME, DeLellis RA. Primary extranodal lymphoma: response to treatment and factors influencing prognosis. *Cancer* 1978; 42: 406-416.
28. Freeman C, Berg JW, Cutler SJ. Occurrence and prognosis of extranodal lymphomas. *Cancer* 1972; 29: 252-260.
29. Franssila KO, Jaser N, Sivula A. Gastrointestinal non-Hodgkin's lymphoma. A population-based clinicopathological study of 111 adult cases with a follow-up of 10-15 years. *APMIS* 1993; 101: 631-641.
30. Al-Bahrani ZR, Al-Mondhiry H, Bakir F, Al-Saleem T. Clinical and pathologic subtypes of primary intestinal lymphoma. Experience with 132 patients over a 14-year period. *Cancer* 1983; 52: 1666-1672.
31. Salem P, El-Hashimi L, Anaissie E, Geha S, Habboubi N, Ibrahim N et al. Primary small intestinal lymphoma in adults. A comparative study of IPSID versus non-IPSID in the Middle East. *Cancer* 1987; 59: 1670-1676.

