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HIGH INCIDENCE OF LYMPHOMA IN IRAN WITH PARTICULAR ATTENTION TO ABDOMINAL LYMPHOMA

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The absence of a cancer registry renders the estimations of the incidence of various cancers difficult. However, isolated reports from the Middle East indicate that there is a high incidence of lymphoma in this area (2, 4, 6, 7, 13, 20, 21, 22, 23, 38, 39).

Lymphoma occurs more frequently in immunodeficiency syndromes (11, 17, 24) and after treatment with immunosuppressive agents (41, 42) Some forms of lymphoma are associated with specific viruses (15, 16),while others are accompanied by immunoglobulin abnormalities (8,9,12,26,35, 36, 43) Immunological factors have been related in the pathogenesis of lymphoma (1, 13, 34).

The present study was aimed at confirming the increased frequency of malignant lymphoma in Iran through a retrospective analysis of the pathologically confirmed cases.

MATERIALS

Case records were analysed from data available at the Taj Pahlavi

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Cancer Institute. The Institute has an associated 150 bed hospital, and also serves a 650 bed general hospital. In addition to local patients, there were referrals from all parts of the country.

During an 18-year period (1956-74), 85,000 surgical specimens were received out of which 30,641 were malignant tumors (36%). Lymphomas formed 8.7% (2675 cases) of all the malignancies. This was the third commonest neoplasm following cancer of skin and carcinoma of esophagus.

Since the population under study was not representative of any particular region of the country, age-standardization was not attempted. Thus, the incidence of lymphoma was estimated as the frequency of cases diagnosed as lymphoma compared with other neoplasms at the Institute. The diagnosis in each case was based upon surgical resection and classified as lymphosarcoma (L.S.), reticulum cell sarcoma (R.C.S.) and Hodgkins disease (H.D.). Cases of Chronic Lymphatic Leukemia and Giant Follicular Lymphoma were not included.

In order to determine if there has been a change in the incidence of lymphoma in recent years, the material was divided into two series, one covering lymphoma cases collected in the first 16 years, and the second covering data from the last 2 years.

RESULTS

Relative incidence of lymphoma in relation to all malignant tumors:

During an 18-year period, from 1956 to 1974, 30,641 malignant tumors were surgically resected from separate individuals and assessed pathologically. A diagnosis of malignant lymphoma was made in 2,675 cases. Thus the lymphoma group formed 8.7% of all tumors and was the third commonest malignancy seen at this Institute. (Fig. 1); skin cancer and carcinoma of esophagus were seen more frequently.

During the first 16-year period, there were 2328 cases of lymphoma and in the last two year period, 347 cases of lymphoma were recorded (Table I). Using these data, it is apparent that the incidence of lymphoma at this Institute is about 150 cases per year.

Incidence of histologic types of malignant lymphoma:

Analysis of the total number of lymphomas collected during the 16-year period, 1956-1972, revealed 2328 cases (Fig. 2). The commonest type was L.S. with 865 cases forming 37.2% of the total. There were 759 cases of H.D. i.e. 32.6%, and 704 cases of R.C.S., 30.2%. In contrast, in t he two-year period, 1972-1973, (Fig. 3) out of a total of 347 malignant lymphomas, 136 (39.2%) had H.D. which was now detected as commonly as L.S. i.e. 39.2%. During same period only 75 cases (21.6%) of R.C.S. were seen.

In a comparative analysis of the last 2-year period with the preceding 16 years, there appeared to be a decrease in the incidence of R.C.S. of 8.6% and a corresponding increase of 6.6% in cases of H.D. This observation was in accordance with a relative increase in cases of H.D.. referred to this Institute or a recent increase in histological diagnosis of H.D. compared to R.C.S.

Age incidence at time of resection

A comparison of the age incidence of lymphoma according to the age at the time of surgical removal in the 16-year period, 1956-1972, with the 2-year period, 1972-1974, is illustrated in Figs.4 and 5. The percentage incidence is based upon the proportion of individuals presenting with one type of lymphoma in a 10-year age group in relation to the total number of patients who suffered from corresponding tumors. It may be concluded from Figs. 4 & 5 that the incidence of L.S. increases steadily to a maximum in the 41-50 year age group and then declines. This age distribution is similar for the two periods of study. The age incidence of R.C.S. in the first 16-year period reveals two peaks, one in the 21-30 age group and the other in the 41-50 group. In contrast,the incidence of this tumor seen in the latter 2-year period appears to have a single peak in the 41-50 age group. Hodgkin's Disease appeared to have the highest incidence in the 21-30 age group in the 16 year observations and then declined gradually.

In contrast more recent figures suggest a peak incidence in the 11-20 age group constituting 26.5% of all cases of H.D.seen during the two-year period, and a second peak in the 41-50 age group that is 18.4% of all Hodgkin's cases seen over this 2-year period.

Sex distribution of lymphoma:

Our data are suggestive of preponderance of lymphoma in males (Table II). In general, for all types of lymphoma the males outnumbered females twice or more. The ratios were higher in the 2-year period than in the 16-year period.

Anatomic Distribution of Malignant Lymphoma:

The anatomic distribution was related to the site of resection or biopsy, and is illustrated in Figs. 6 & 7 for the first 16 years and the last 2 years respectively.

Table III shows the percentage frequency of the site of resection in relation to the type of lymphoma. For all lymphomas collected in the first 16 years, in 56.9% the first diagnosis was made from cervical lymph node biopsy, 16.3% abdominal node biopsy, 8% axillary, 8.8% inguinal, 1.2% thoracic and 8.8% others. During the last 2-year period of study, from all cases of lymphoma, comparable results were as follows: 61.9% cervical, 16.4% abdominal, 8.4% axillary, 10.1% inguinal

and 3.2% thoracic.

It may be concluded that in the two periods of study, an abdominal lymph node histological diagnosis was the second commonest following cervical nodes.

Although the site of biopsy of the involved lymph node is not always indicative of the primary lesion, in cases of thoracic and abdominal lymph node biopsies, these sites would probably represent the primary lesion, since superficial node biopsy would have been preferred if available. This would then imply that our relative incidence for thoracic and abdominal (in particular) lymph node involvement is most probably the same as the relative incidence for the site of origin.

The histologic types of lymphoma in abdominal nodes appeared with the following frequencies (both 16- and 2-year periods combined):L.S. (47.6%), R.C.S. (33.5%) and H.D. (18.2%).

DISCUSSION

The high incidence of lymphoma in Iran has been reported previously (Table IV). Habibi (22) studying the records collected from various laboratories in Tehran noted that 8.1% of all malignant tumors were lymphoma. In the three observations reported from Shiraz,the incidence varied from 7.6 % (23) and 10.2% (7) to 12.1% (13). It is

apparent that much of the material used in the Shiraz studies was derived from a common source.

In the present study, from a total of 30,641 malignant tumors collected at the Taj Pahlavi Cancer Institute, 2,675 cases were classified as malignant lymphoma; an incidence of 8.7% which corresponded to the results obtained by Habibi (22). The number of referrals of lymphoma patients at this Institute was about 150 cases per year, which was 1.5 times more frequent than the results of Habibi (22), and 3.75 times that of Shiraz. Thus, it is apparent that lymphoma is seen more commonly in Tehran.

Malignant lymphoma was the third commonest malignancy in our series next to cancers of skin and esophagus respectively. The high incidence of esophageal cancer in our records is in contrast to reports from Shiraz (7,23) and is explained by the high proportion of referrals from the Caspian area, a region with a known high incidence. (25, 27).

Lymphoma was the second commonest malignancy in 2 reports (7, 23) and the third commonest in another report (22) from Iran.

Lymphoma also occurs in high frequency in other regional countries. In Afghanistan, Sobin (38) using data based upon surgical patholo-

gical material collected during a 2½ year period found 57 cases of lymphoma from a total of 550 malignant tumors; an incidence of 10.36%. Tabara (39) has reported an incidence of 11.3% from Lebanon.

Histologically, the most common type of lymphoma seemed to be L.S. followed by H.D. and R.C.S. respectively (Table I). In the last 2 years (1972-74), there appeared to be an increase in total cases of H.D., with a corresponding decrease in R.C.S. This could either be due to a real increase in the incidence of H.D., or an increase in diagnosis of cases of H.D. which were previously classified as R.C.S.

The incidence of L.S. was found to increase steadily to a maximum in 41-50 year age group and then decline. For R.C.S. the same thing was noticed except for another smaller peak in the 21-30 age group seen only in the 16-year period of study. Cases of H.D., in contrast to the other types, occurred more frequently in the early age: in the 16 year observations the peak was in 21-30 year age group; while in the 2-year period 2 peaks were found; the taller being in the 11-20, and the other in 41-50 age group. In general, all lymphoma types appear to occur at an earlier age in Iran and the sex ratio is in favor of men.

In the present study although we were unable to forward more definitive figures to show the actual incidence of primary gastrointestinal lymphoma,

our data were nevertheless, suggestive of a high occurence of primary abdominal lymphoma. The lymphomatous abdominal nodes were the second commonest (next to cervical), and formed 16.27% of all the malignant lymphomas in our series. In other reports from Iran (7 ,13) gastrointestinal lymphomas constituted about one quarter of all lymphomas. Rappaport (34) has shown that in seven out of eight cases of small intestinal lymphoma, the mesenteric nodes were involved; in addition, he has reported lymphoma having started from the mesenteric nodes in 2 cases. These observations support our notion that our figures for lymphomatous abdominal nodes may at least represent the minimal incidence of primary abdominal lymphoma in this area.

Previous reports from Iran and other Middle Eastern countries have shown primary small intestinal lymphoma to be a common malignancy in this region (2, 3, 7, 13,18,23,28,31,32,33,34, 37, 38). This entity appears to have few characteristics regarding the clinical presentation, age incidence, site of involvement , and histology which differentiates it from its "Western" counterpart (2, 14, 28, 32, 34). It was first reported from Israel (14, 31), soon followed by reports from other countries on the Southern and Eastern shores of the Mediterranean Sea (hence the term 'Mediterranean Type' of lymphoma) (37). However, other reports from Iran (13, 28), Iraq (2, 3), South Africa (29) etc. are suggestive that not only this condition is not restricted to the Mediterranean area, it may not even be an ethnic disease.

Previous reports have emphasized intestinal lymphoma as a late complication of celiac sprue (5, 19, 40). With rarity of celiac sprue in Iran (10), this condition does not seem to be a likely predisposing factor here. Although Dutz, et al (13) have emphasized the role of syndrome of infantile diarrhea and marasmus in the orphanage infants, such historical background has not been substantiated in most of our cases (unpublished data).

Recent findings of association of Alpha-heavy chain disease (8,9, 12, 26,30,36, 43) and giardiasis (13, 28) with primary small intestinal lymphoma, as well as the observation of increased incidence of lymphomas in immunodeficiency syndromes (11, 17 , 24) and following treatment with immunosuppressive agents (41, 42) have raised the possibility of some congenital or acquired type of immunodeficiency which together with chronic antigenic stimuli might predispose to development of lymphoma (13, 34).

Only a coordinated prospective study may determine which of the mentioned observations are actually involved in the pathogenesis of this disorder.

Table I. Comparison of lymphoma-types in the two periods of study

Year	Total No. Lymphomas	L.S.	R.C.S.	H.D.
1956 - 71	2328	865	704	759
% Total		37.2	30.2	32.6
1972 - 74	347	136	75	136
% Total		39.2	21.6	39.2

Table II. Sex distribution of lymphoma

1956 - 1972	Total	Male	Female	Ratio
All lymphomas	2328	1610	718	2.4
Lymphosarcoma	865	625	240	2.6
Retic. Cell Sarcoma	704	459	245	1.9
Hodgkin's Disease	759	526	233	2.3
1972 - 1974				
All Lymphomas	347	256	91	2.8
Lymphosarcoma	136	100	36	2.8
Retic. Cell Sarcoma	75	55	20	2.8
Hodgkin's Disease	136	101	35	2.9

Table III. Primary Site of Surgical Resection

1956 - 1972	Cervical	Abdominal	Axillary	Inguinal	Thoracic	Others
Total	56.9	16.3	8.0	8.8	1.2	8.8
Lymphosarcoma	52.3	21.4	5.0	10.4	1.3	9.6
Retic.Cell Sarcoma	52.4	19.0	6.3	8.2	0.7	13.4
Hodgkin's Disease	66.3	8.0	12.9	7.6	1.5	3.7
1972 - 1974	**Cervical**	**Abdominal**	**Axillary**	**Inguinal**	**Thoracic**	**Others**
Total	61.9	16.4	8.4	10.1	3.2	- -
Lymphosarcoma	55.2	17.6	10.3	11.8	5.1	- -
Retic. Cell Sarcoma	57.3	18.7	10.7	8.0	5.3	- -
Hodgkin's Disease	71.3	14.0	5.1	9.6	- -	- -

Table IV. Incidence of Lymphoma in relation to total number of Neoplasia seen in Tehran & Shiraz

Author	Period of Study	Region	Total No. Neoplasms	Total No. Lymphoma	Lymphoma % of Neoplasms	Incidence Lymphoma/Yr.
Habibi (1970)	1940-64	Tehran	28069	2276	8.1	94.8
Haghighi et al (1971)	1963-68	Shiraz	3295	234	7.6	39.0
Dutz et al (1971)	1960-69	Shiraz	3006	364	12.1	40.4
Barekat et al (1971)	1962-69	Shiraz	3275	350	10.2	43.8
Mojtabai et al (1973)	1956-73	Tehran	30641	2675	8.7	149.8

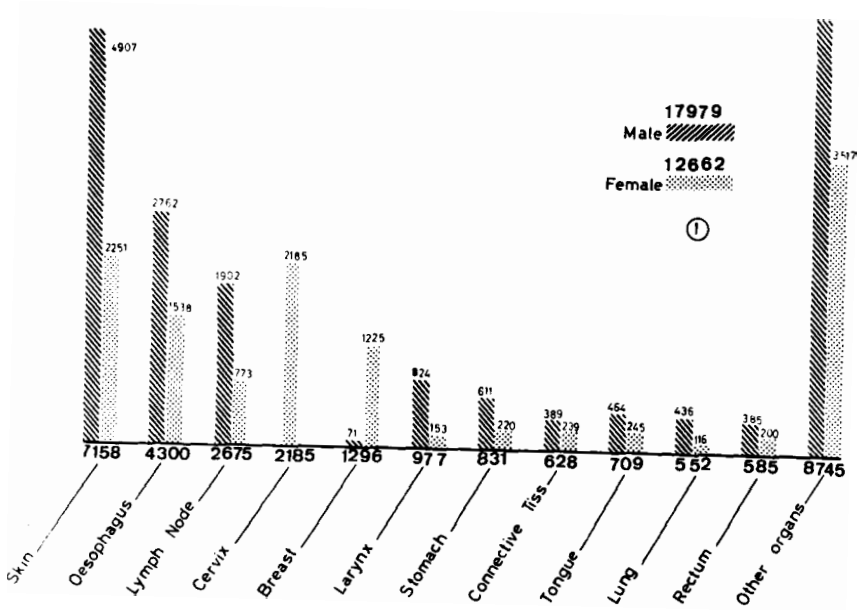

Fig. 1. Relative incidence of 30641 cancer cases seen from 1956 to 1974 at Taj Pahlavi Cancer Institute in relation to site of surgical resection and sex

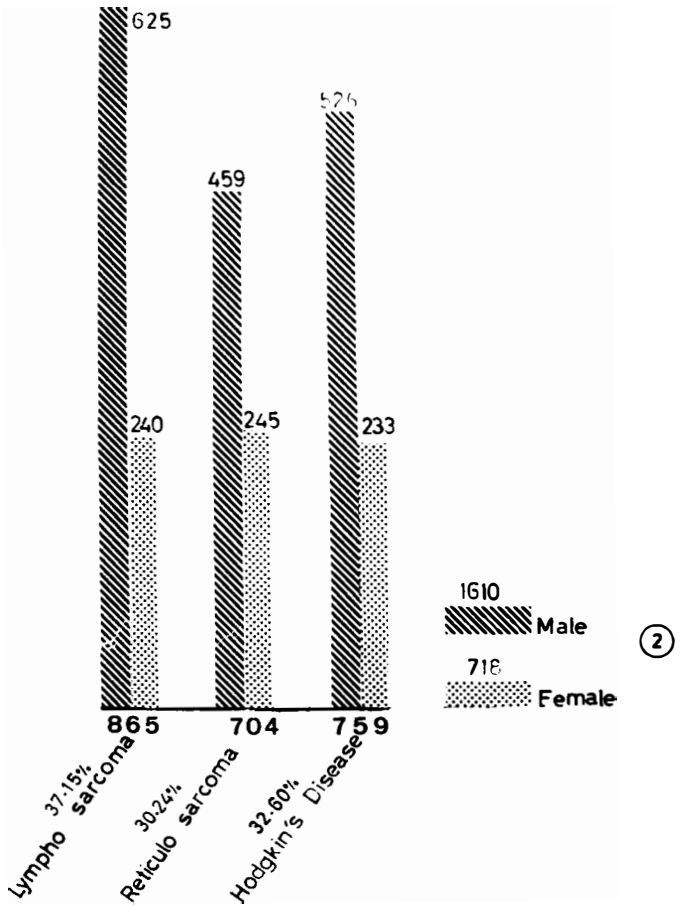

Fig. 2. Ratio of lymphomas according to histologic types and sex. 1956-72

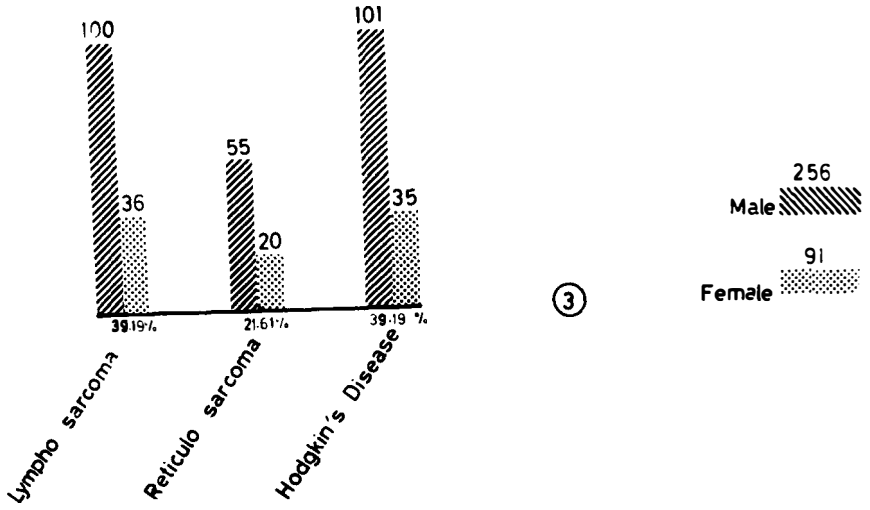

Fig. 3. Ratio of lymphomas according to histologic types and sex. 1972-74.

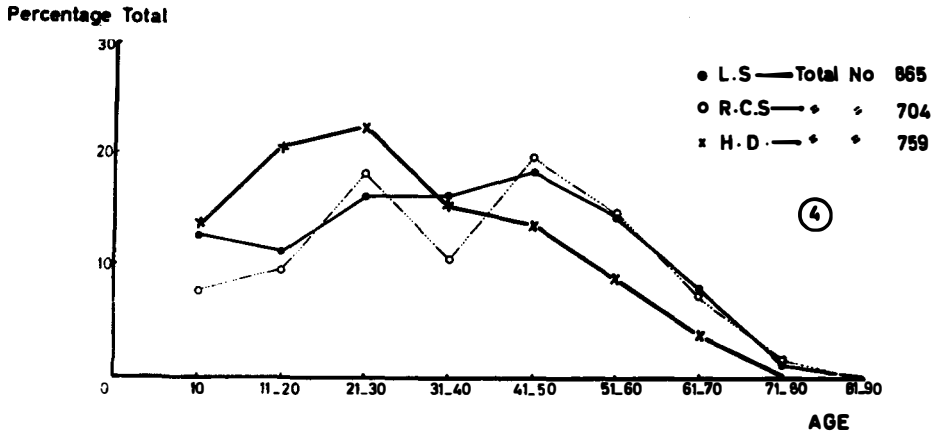

Fig. 4. Age distribution of lymphoma types in relation to percentage total in 10 yearly age groups. 1956-1972.

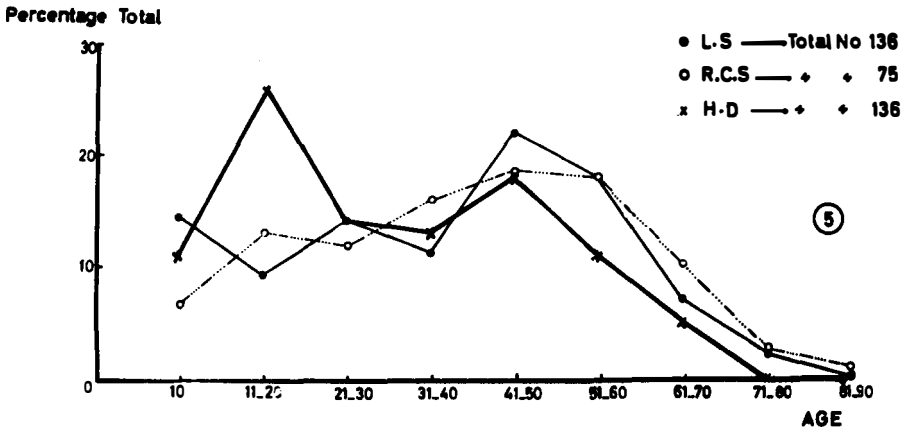

Fig. 5. Age distribution of lymphoma types in relation to percentage total in 10 yearly age groups. 1972-1974.

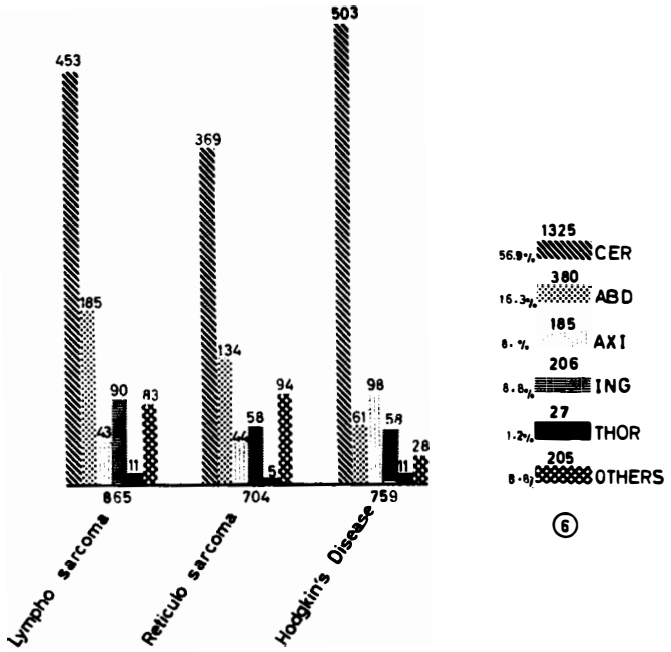

Fig. 6. Bodily distribution of lymphoma types according to site of surgical resection. 1956-1972.

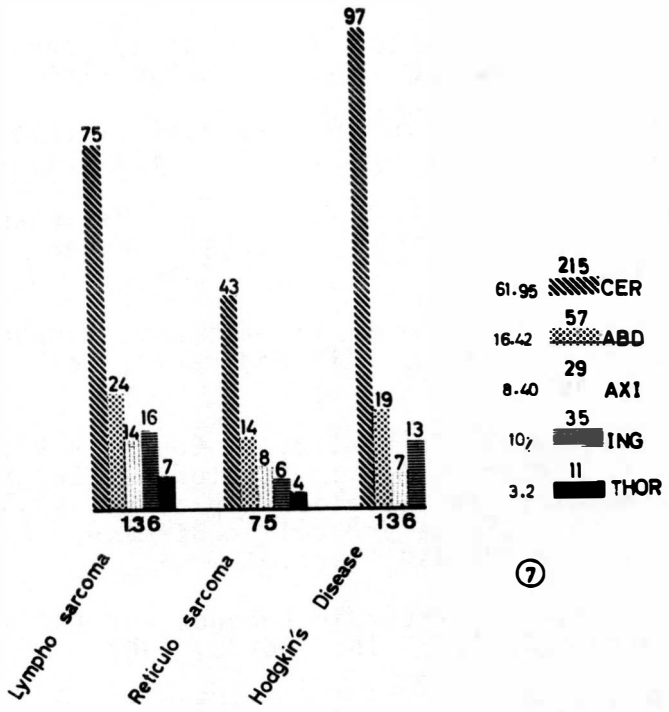

Fig. 7. Bodily distribution of lymphoma types according to site of surgical resection. 1972-1974.

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