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The prevalence of lymph proliferative disorders in a group of Iraqi patients and its relation to blood indices parameters

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SUMMARY

Abstract: Lymphoproliferative Disorders (LPDs) are a group of neoplasms affecting various cells within lymphoid system. Each type has different treatment and prognosis.

Objective: To measure the prevalence of LPDs in a sample of Iraqi patients delineating its specific phenotypes in terms of their prevalence and male to female ratio.

Design: Cross sectional study.

Materials and methods: Cross sectional study that is done at National Centre of Haematology from November 2019 till March 2020 on 64 patients who were diagnosed to have one subtype of MPDs. Blood samples were taken from them and analysed to get complete blood count using automated electronic counter (Haematology auto-analyser-BECKMAN COULTER, ACT. 5 diff. USA). Blood film, Bone marrow aspirate and biopsy were analysed for each patient. Data were presented in frequencies and percentages and analysed using Chi-Square, student t test and ANOVA test when applicable using Graph pad 8 software and p=0.05 as significance level.

Results: CLL is the most common pathologic type that accounts for (42.2%), followed by follicular lymphoma (23.4%), mantle cell lymphoma (10.94%), B-cell lymphoblastic leukaemia/lymphoma (9.38%), lymphoma (4.69%), Splenic Marginal Zone Lymphoma (4.69%) and T-cell NHL (4.69%). LPDs were more prevalent in males apart from Hodgkin's lymphoma.

Discussion and Conclusion: LPDs is a group of many lymphoid neoplasms that vary in their prevalence. The prevalence observed in our population is greatly different form the cited literature. This could be explained by the low number of patients in our sample.

Key words: LPDs, Hodgkin's ,CLL, mantle cell

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INTRODUCTION

Lymph Proliferative Disorders (LPDs) refer to several conditions listed in the WHO classification in which lymphocytes are produced in excessive quantities [1, 2]. They typically occur in people who have a compromised immune system. They are sometimes equated with "immunoproliferative disorders", but technically lymph proliferative disorders are a subset of immunoproliferative disorders, along with hypergammaglobulinemia and paraproteinemias.

Types

Lymphoproliferative disorders are a set of disorders characterized by the abnormal proliferation of lymphocytes into a monoclonal lymphocytosis. The two major types of lymphocytes are B cells and T cells, which are derived from pluripotent hematopoietic stem cells in the bone marrow. Individuals who have some sort of dysfunction with their immune system are susceptible to develop a lymph proliferative disorder because when any of the numerous control points of the immune system become dysfunctional, immunodeficiency or deregulation of lymphocytes is more likely to occur. There are several inherited gene mutations that have been identified to cause lymph proliferative disorders; however, there are also acquired and iatrogenic causes [3].

X-linked lymph proliferative disorder: A mutation on the X chromosome is associated with a T cell and natural killer cell lymph proliferative disorder.

Autoimmune lymph proliferative disorder: Some children with autoimmune lymph proliferative disorders are heterozygous for a mutation in the gene that codes for the Fas receptor, which is located on the long arm of chromosome 10 at position 24.1, denoted 10q24.1 [4]. This gene is member 6 of the TNF-Receptor Superfamily (TNFRSF6). The Fas receptor contains a death domain and has been shown to play a central role in the physiological regulation of programmed cell death. Normally, stimulation of recently activated T cells by antigen leads to co-expression of Fas and Fas receptor on the T cell surface. The engagement of Fas by Fas receptor results in apoptosis of the cell and is important for eliminating T cells that are repeatedly stimulated by antigens [5]. As a result of the mutation in the Fas receptor gene, there is no recognition of Fas by Fas receptor,

leading to a primitive population of T cells that proliferates in an uncontrolled manner [2].

Other inherited causes: Boys with X-linked immunodeficiency syndrome are at a higher risk of mortality associated with Epstein-Barr virus infections, and are predisposed to develop a lymph proliferative disorder or lymphoma. Children with Common Variable Immunodeficiency (CVID) are also at a higher risk of developing a lymph proliferative disorder. Some disorders that predispose a person to lymph proliferative disorders are Severe Combined Immunodeficiency (SCID), Chediak-Higashi syndrome, Wiskott-Aldrich syndrome (an X-linked recessive disorder), and ataxia-telangiectasia. Even though ataxia telangiectasia is an autosomal recessive disorder, people who are heterozygotes for this still have an increased risk of developing a lymph proliferative disorder [6].

Acquired causes: Viral infection is a very common cause of lymph proliferative disorders. In children, the most common is believed to be congenital HIV infection because it is highly associated with acquired immunodeficiency, which often leads to lymph proliferative disorders [7].

Iatrogenic causes: There are many lymph proliferative disorders that are associated with organ transplantation and immunosuppressant therapies. In most reported cases, these cause B cell lymph proliferative disorders; however, some T cell variations have been described. The T cell variations are usually caused by the prolonged use of T cell suppressant drugs, such as sirolimus, tacrolimus, or ciclosporin [8]. The Epstein-Barr virus, which infects >90% of the world population, is also a common cause of these disorders, being responsible for a wide range of non-malignant, pre-malignant, and malignant Epstein-Barr virus-associated lymph proliferative diseases.

AIM

To measure the prevalence of LPDs in a sample of Iraqi patients delineating its specific phenotypes in terms of their prevalence and male to female ratio.

MATERIALS AND METHODS

Cross sectional study that is done at National Centre of Haematology from November 2019 till March 2020 on 64 patients who were diagnosed by a specialist hematopathologist to have one subtype of MPDs. Blood samples were taken from them and analysed to get complete blood count using automated electronic counter (Haematology auto-analyser-BECKMAN COULTER, ACT. 5 diff. USA). Blood film, Bone marrow aspirate and biopsy were analysed for each patient.

The study protocol was approved by our institutional review board and conformed to the principles of the Declaration of Helsinki. After obtaining formal written consent from each patient. The data were prepared as frequencies, relative frequencies. Blood samples were taken from them and analysed in terms of blood indices which include RBSs, WBCs, and platelets.

STATISTICAL ANALYSIS

Analysis of data was carried out using the available statistical package of SPSS-25 (Statistical Packages for Social Sciences-version 25). Data were presented in simple measures of frequency, percentage.

RESULT

Sixty-four patients were enrolled in this study Males 40 (62.5%) and females 24 (37.5%) The male to female ratio in general is 1.66.

The analysis of bone marrow biopsy as shown in table 1, reveals the hematologic phenotypes predominantly as LPD mostly CLL (26 cases) followed by follicular lymphoma (14 cases) prevalent (24 cases).

The distribution of LPD cases according to sex and male to female ratio (shown in table 2). LPDs are more prevalent in males except for Hodgkin's lymphoma.

The final diagnosis of LPD cases in terms of frequency and percentage after performing bone marrow biopsy (Table 3).

Tab. 1. Hematologic phenotypes according to the analysis of bone marrow biopsy

	BM biopsy
B-cell lymphoblastic leukemia/ lymphoma.	2
Diffuse Large B-cell Lymphoma	1
Follicular Lymphoma	14
Hodgkin lymphoma proved by immunohistochemistry	3
LPD mostly CLL	26
LPD mostly lymphoplasmocytic lymphoma	1
Lymphoblastic lymphoma	2
Mantle cell Lymphoma	7
NHL	1
NHL (splenic type)	1
Small cell lymphoma, CLL	1
Splenic marginal zone lymphoma	2
T-cell lymphoblastic lymphoma	1
T-cell NHL	2

Tab. 2. The frequency of LPD diseases in terms of male and female patient's number and the male to female ratio

Diagnosis	Male	Female	Male to Female Ratio
B-cell lymphoblastic leukemia/lymphoma.	4	2	2
CLL	16	11	1.45
follicular lymphoma	10	5	2
Hodgkin's lymphoma	1	2	0.5
mantle cell lymphoma	5	2	2.5
Splenic Marginal Zone Lymphoma	2	1	2
T-cell NHL	2	1	2

Tab. 3. The final diagnosis of LPD diseases in terms of frequency and percentage

Diagnosis	Frequency	Percentage (%)
B-cell lymphoblastic leukemia/ lymphoma	6	9.38
CLL	27	42.19
follicular lymphoma	15	23.44
Hodgkin's lymphoma	3	4.69
mantle cell lymphoma	7	10.94
Splenic Marginal Zone Lymphoma	3	4.69
T-cell NHL	3	4.69

DISCUSSION

This paper presents contemporary sex-specific incidence, prevalence and survival estimates for more than 20 lymphoma subtypes, providing much needed 'real-world' data to better inform practitioners and researchers. To our knowledge, this is the first time (in Iraq) that reliable population-based epidemiological data for several clinically meaningful lymphoma subtypes have been presented side-by-side. The benefits of this are immediately apparent. Within categories that are often lumped together, outcome varied markedly from one subtype to another; patients with some disease subtypes tending to have near normal lifespan, whereas those with others often died rapidly from their disease. Furthermore, strong differences between males and females were observed with respect to subtype prevalence frequencies, as well as age at cancer onset. Such differences have clear implications not only for etiological hypotheses and clinical practice, but also for health service planning.

Some malignancies of lymphoid cells almost always present as leukaemia (i.e., primary involvement of bone marrow and blood), while others almost always present as lymphomas (i.e., solid tumours of the immune system). However, other malignancies of lymphoid cells can present as either leukaemia or lymphoma. In addition, the clinical pattern can change over the course of the illness. This change is more often seen in a patient who seems to have a lymphoma and then develops the manifestations of leukaemia over the course of the illness.

In our study the male to female ratio is 1.66. Globally, LPDs are well known of being more common in males than females [6] in one study it was found to be 1.4.

Focusing on specific diseases we can notice that male are more affected than females except for HL (Hodgkin's lymphoma) (Table 10) which is 0.5. The findings of HL being more common in females could be attributed to low number of recruited patients. Moreover, In HL sex ratio is age dependent, i.e. child less than 5 year, the male to female ratio is 5.3 [9].

Smith et al. reported in his study that HL sex ratio of 1.41 [10]. While Cartwright et al. reported an HL sex ratio of 1.49 [11].

Regarding B-cell lymphoblastic leukaemia/lymphoma, the male to female ratio in our study is 2 as compared to another study which has shown the ratio of 1.39 [10]. There was no T-cell lymphoblastic leukaemia in our patient's sample.

CLL is more prevalent in males with a sex ratio of 1.45. This ratio is compatible with other results reported by Cartwright et al [11] who has found a sex ratio of 1.4. The Cancer Statistics of USA for 2013 has shown a male to female ratio of 1.34 [12].

Follicular lymphoma in our study has shown to be male dominant with a male to female ratio of 2. Which is much higher as compared with other study showing the ratio of 0.95 [10]. US data study has shown that ratio varies from 1.2-1.6 depending on race whether white, black or Asian [13]. Another study shows there is no significant difference in incidence between males and females [14]. This disparity could be attributed to low number of cases in our study.

Mantle cell lymphoma shows a high prevalence in males versus females of 2.5. This is compatible with US statistics showing a male/female ratio varying from 2.5, 1.9 and 1.8 for white, black and Asian populations respectively [13]. Similarly, a British study has reported a male/female ratio of 2.57 [10].

Splenic marginal zone lymphoma results show male/female ratio to be 2. This is much higher to the US data that shows the ratio of 1, 1.1 and 1.2 for white, black and Asians respectively [13]. On the other hand, the British study reported the male/female ratio of 1.65 [10].

T-cell NHL is more prevalent n males with a male/female ratio of 2. This is close to the US data showing the ratio of 1.8, 1.7 and 1.6 for white, black and Asian populations respectively [13]. The British data reported a male/female ratio of 1.55 [10].

Regarding the percentage of specific diseases from the whole prevalence of LPDs, we have found that CLL constitutes 42.19%. This is close to the American data of cancers that shows CLL accounting for 37% (2020).

B-cell lymphoblastic leukaemia/lymphoma has prevalence in our sample as 9.38%. This is much lower than a study which reported the ratio of 19.34% [15].

Regarding follicular lymphoma the prevalence in our sample is 23.44%. It reflects much higher prevalence as compared with the American data of cancer which reported the prevalence of 13% [13].

Hodgkin's lymphoma prevalence is 4.69% which is much lower than the American data of cancer that reported the prevalence of 8% [13]

Mantle cell lymphoma prevalence is 10.94%. As compared with Danish data it accounts for 1.87% to 6.42% [16]. Another study reported the prevalence of 3.74% [15].

Splenic Marginal Zone Lymphoma accounts for 4.69% of our sample. This is close to other studies who reported the prevalence to be <2% of all LPDs [2, 12, 17].

T-cell NHL accounts for 4.69% of patients. This is close to other study showing the prevalence to be 4.74% [15].

CONCLUSION

LPDs are a group of many lymphoid neoplasms that vary in their prevalence. The prevalence observed in our population is greatly different form the cited literature. This could be explained by the low number of patients in our sample.

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