

The levels of Serum Alkaline Phosphatase and Lactate Dehydrogenase in Hodgkin Lymphoma

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Abstract

Background: Hodgkin's disease (HD) is a neoplastic disease originating in lymphoid tissue, which spreads to lymphoid structures and ultimately nonlymphoid tissues. Lactate Dehydrogenase and Alkaline Phosphatase are increased in blood following membrane cell damage. The aim of this study was to compare Lactate Dehydrogenase and Alkaline Phosphatase levels in children in different stages of Hodgkin's Lymphoma with normal children.

Materials and Methods: In the present study, the sera from 30 patients who suffered from Hodgkin's Lymphoma and were referred to Children's Medical Center, Tehran, Iran as well as 30 normal subjects were collected. The mean age was 7.5 years among patients and 6.8 years in normal subjects. Lactate Dehydrogenase and Alkaline Phosphatase levels were measured using kinetic and colorimetric methods. Data were analyzed using Pearson's correlation coefficient and t- test.

Results: Stages III and IV (advanced stages) were observed in 61.4% of the patients. Lactate Dehydrogenase level among patients was statistically higher in comparison with controls ($P < 0.01$). There was also a statistically significant increase in Alkaline Phosphatase level among patients in comparison with controls ($P < 0.05$). A comparison of both Lactate Dehydrogenase and Alkaline Phosphatase levels among patients with advanced stages (III, IV) and those with initial stages (I, II), revealed elevated levels among patients in advanced stages ($P < 0.001$).

Conclusion: Lactate Dehydrogenase and Alkaline Phosphatase levels might be utilized as markers to determine Hodgkin's lymphoma severity in addition to other markers.

Key words: Lactate Dehydrogenase, Alkaline Phosphatase, Hodgkin's disease.

Introduction

Hodgkin's disease (HD) is a neoplastic disorder originating in lymphoid tissue ¹. HD can cause anemia, leukocytosis, neutrophilia, eosinophilia, lymphopenia and thrombocytosis ². The prognosis of disease depends on the extent and distribution of disease ³, and the classification of the disease, which is established after pathologic examination of a biopsy sample ⁴. Moreover, the measurement of hematological factors such as Erythrocyte Sedimentation Rate (ESR), Copper, Alkaline Phosphatase (ALP), Lactate Dehydrogenase (LDH), iron, zinc, transferrin and ferritin has been proposed in order to help in predicting the prognosis ^{3, 4}. The choice of treatment depends on the age, sex, bulk and the histological subtype of the disease (staging) ^{3, 4}. The staging of the disease usually involves radiologic and blood examination, bone

marrow aspiration and biopsy ^{3, 4}. Generally the Ann Arbor scheme method is used for staging Hodgkin lymphoma (Stages, I, II, III, IV) ^{5, 6, 7}. Some studies have proposed enzymes such as ALP and LDH as strong prognostic factors for HD ⁸. ALP is a hydrolase enzyme responsible for dephosphorylation of molecules, including nucleotides, proteins, and alkaloids, in an alkaline environment ⁹. In humans, ALP is present in all tissues throughout body, but is particularly concentrated in liver, bile duct, kidney, bone, and the placenta ⁹. Thus in patients who suffer from HD, tissue necrosis results in excess ALP release in blood stream ¹⁰. LDH is an enzyme which catalyzes the conversion of lactate to pyruvate which is an important step in energy production inside the cells ¹¹. Many different types of cells in the body contain this enzyme ¹¹. Some

of the organs relatively rich in LDH are the heart, kidney, liver, and muscle tissue ¹¹. As cells die, LDH is released into the blood ¹². Some studies suggest ALP and LDH Levels as prognostic markers in Hodgkin's disease ^{11, 12, 13}. Thus we performed this study to compare the levels of these two enzymes, in patients with different stages of HD, who were referred to Children's Medical Center, Tehran, Iran, as well as normal controls.

Materials and Methods

This study was conducted as a case control study in accordance with the Helsinki Declaration and was approved by the Ethical Committee of Jundishapour University of Medical Sciences, Ahvaz, Iran. Informed consent was obtained from all patients and normal subjects.

Patients

An unrelated to the study group consisted of 30 HD patients, at the time of diagnosis, referred to the Children's Medical Center hospital, Tehran, Iran. Thirty normal subjects were selected as the control group. All patients and normal subjects were at the same range of age (2-13y). Subjects who suffered from liver failure, gastrointestinal discomfort, bone disease, renal failure, cardiovascular disease, hemolytic anemia, pneumonia or sepsis were excluded from the study. The patients' blood cancer and the stage of the disease were confirmed by pathologic examination of biopsy taken from lymphatic nodes and morphological and cytological studies previously described. Patients were subdivided to two groups: group 1 consisted of patients in stages I and II (initial stages), and group 2 consisted of patients in stages III and IV (advanced stages).

Sample preparation

Five ml blood was obtained from each person. Serum was separated and stored at -20 °C.

Analytical methods

ALP levels were determined using colorimetric method and LDH levels were measured using the kinetic method on the basis of P- Nitro Phenyl Phosphate conversion to P- Nitro Phenol. LDH levels were measured using the kinetic method and measurement of UV absorbance of NAD⁺ and NADH₂. Zist Shimi kits (with Co No: 10-503 and 10-533-1), were used to determine both ALP and LDH activities. The normal range of serum ALP was considered: 150-850 international units per liter (IU/L) (for ages under 15 years) ¹⁴. The normal range of serum LDH was defined as: 105 - 333 IU/L ¹⁴.

Statistical analysis

All data were analyzed using the Statistical Package for the Social Sciences (SPSS) software (Version 17, SPSS, Chicago, IL, USA). The correlation between means of continuous variables was analyzed using T-Test.

Results

The mean age was 7.5 years among patients and 6.8 years in normal subjects. The patient group was consisted of 73% males and 27% females. The type of HD based on pathologic findings is summarized in table 1. Table 2 shows the stage of disease among patients. As it can be seen from table 2, 61.4% of patients were at advanced stages of disease and 38.6% of them were at initial stages. There was a significant increase in serum ALP levels among patients in comparison with normal subjects ($p < 0.05$) (Table 3). The mean serum LDH level among patients was also higher than normal subjects with the difference being statistically significant ($p < 0.01$) (Table 3). Comparison of

Table 1: The type of HD based on pathologic findings

Type of HD	Percent
Predominant	16
Nodular Sclerosis	19
Mixed Cellularity	54
Deletion	11

serum ALP based on the stage of disease showed significantly higher levels in advanced stages compared to initial stages ($p<0.001$) (Table 3). Similarly higher serum LDH levels was noticed among patients at advanced stages of disease compared to initial stages ($p<0.001$) (Table 3).

Discussion

Different studies suggest elevated ALP and LDH levels as predicting factors in neoplastic disorders^{1, 2}. Some previous reports are available regarding elevated ALP and LDH levels in HD^{7, 10}. Several other serum markers such as: ESR, Zinc, Copper, Iron, transferrin and ferritin have also been proposed to help the diagnosis or predict the prognosis in HD^{3, 4, 5}. ALP and LDH measurements may increase the sensitivity of HD detection methods and both have been suggested as low cost and sensitive tools to screen HD⁵. Our study revealed both ALP and LDH to be significantly elevated in HD patients compared with normal subjects. That was in agreement with Bien et al. and Jurisic et al. findings^{15, 16}. But Martinow et al. have reported that ALP and LDH increase in HD do not provide independent information to clinical assessment¹⁷. Frequent elevation of ALP enzyme in serum of patients suffering from HD may arise from high utilization of energy by malignant cells¹⁵. The LDH increase probably results from more use of glucose in metastatic tissues and more

converting of glucose in to lactate¹⁶. Our study showed a relation between higher stages of HD and ALP and LDH elevation. Patients in stages III and IV, showed significantly higher ALP and LDH compared with patients in stages I and II. Similarly Jeong et al. showed elevated ALP and LDH among advanced stages of HD¹⁸. By advancing stages of HD, tissues damage increases and this results in more release of ALP and LDH into blood^{15, 16}, which can explain our findings.

Conclusion

The results of the present study propose that Lactate Dehydrogenase and Alkaline Phosphatase levels might be utilized as markers to determine Hodgkin's disease severity in addition to other markers.

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Table 2: The stage of disease among patients

	Stage	Percent	Total Percent
Initial Stage	I	14.3	38.6
	II	24.3	
Advanced Stage	III	32.8	61.4
	IV	28.6	

Table 3: The mean values of ALP and LDH (IU/L)

	Patients	Normal Group	P-Value	Patients in initial stages	Patients in advanced stages	P-Value
ALP	345.5	287.5	<0.05*	307.3	510.4	<0.001*
LDH	517.6	250	<0.01*	340.6	635.2	<0.001*

* significant difference

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