International Journal of Pathology; 2010; 8(1): 9-12

Original Article

Serum Lactate Dehydrogenase 2 Isoenzyme as Marker of Bone Marrow Infiltration in Non Hodgkin Lymphoma

Naghmana Mazher, Zafar Iqbal, Naumaan Aslam, Seema Mazher

Objective: To assess the level of serum lactate dehydrogenase 2 (LD2) in the patients of NHL with and without bone marrow infiltration.

Introduction: Lactate Dehydrogenase (LDH) is commonly increased in patients with haemopoietic malignancies and has been shown to be of prognostic value in patients with Non- Hodgkin lymphoma (NHL) especially. Serum LD2 isoenzyme level was determined in already diagnosed 60 patients of NHL.

Aims and Objectives: Patients were divided into two groups, 30 patients with bone marrow infiltration (group B) and remaining without infiltration (group C). The values were compared with 20 healthy age and sex matched contrtols (groupA). The estimations were made prior to the institution of chemotherapy.

Results: LD2 level was significantly raised in NHL patients compared with controls. There was also significant difference when the values were compared between the patients of NHL with and without bone marrow infiltration. The levels showed positive correlation with the extent of the disease.

Conclusion: We conclude that the above mentioned non invasive parameter is useful indicator of the extent of the disease.

Keywords: Non- Hodgkin Lymphoma, mucosa associated lymphoid tissue, Hodgkin Disease, Lactate Dehydrogenase.

Introduction

Lymphomas are the malignancies of lymphoreticular system.[1] Lymphoma arises when lymphocytes become malignant and accumulate either by duplicating faster than normal or they can live longer than normal lymphocytes. In malignant lymphomas the majority of the cells are frozen at a single stage of normal differentiation.[2,3] Two broad types of lymphomas are named as Hodgkin disease (HD) and Non Hodgkin lymphoma (NHL) .[4,5]

In NHL, primary manifestation of disease occur outside the bone marrow at the site of normal lymphoma homing lymph node, spleen, MALT (mucosa associated lymphoid tissue) or anywhere. Lymphomas outside lymph node and spleen are referred to as extranodal lymphomas. In NHL when the disease involves the bone marrow, the disease is said to be advanced to stage IV.

In NHL patients may present with localized and generalized peripheral lymphadenopathy, indistinguishable on clinical grounds from Hodgkin disease but major constitutional symptoms such as fever, night sweats or weight loss occur less commonly in NHL than in HD.[6-9]

NHL constitutes an intimidating and extended family of lymphoid neoplasm encompassing diverse B-cell malignancies of lymph node follicle and several less common T-cell proliferations, plus a smattering of macrophage malignancies.

After the histological diagnosis of malignant lymphoma, staging defines the extent and the location of the disease on which treatment protocol depends.[10]

Patients who do not respond to conventional therapy may benefit from investigational approaches. Among the biological markers, the most important is Lactate Dehydrogenase which reflects the proliferative activity and invasive potentials of lymphoma.[11,12]

Lactate Dehydrogenase (LDH) has molecular weight of 135,000 Daltons. It is a zinc containing enzyme. LDH catalyzes the reversible oxidation of lactate to pyruvate. It is expressed at higher levels

Correspondence Address
Dr. Naghmana Mazher
Post Graduate Medical Institute, Lahore

Article Received : February 20, 2010
Acceptance Date: August 22, 2010

when lymphocytes are dividing or when cells are distressed or damaged.

Elevating LDH is an indication of disease progression.[13] Sharp increase can indicate transformation. LDH has five isoenzymes which differ slightly in structure. LDH2 is concentrated in lymphocytes.

Materials and Methods

It was a cross sectional study conducted on 80 subjects irrespective of age and sex divided into following groups as follows.

Group A: Normal healthy controls (n=20)

Group B: Patients of NHL without bone marrow infiltration (n=30)

Group C: Patients of NHL with bone marrow infiltration (n=30)

These cases were selected from Lahore General Hospital, Lahore, Institute of Nuclear Medicine and Oncology (INMOL), Lahore, Services Hospital, Lahore, Mayo Hospital, Lahore and Jinnah Hospital, Lahore.

Newly diagnosed cases of NHL by lymph node biopsy prior to the institution of chemotherapy were selected. The patients with history of myocardial infarction, renal failure, hepatic dysfunction, skeletal muscle disease, hemolytic anemia, malignancy of any other system cerebrovascular accident, infectious mononucleosis andIntestinal infarction were excluded.

Serum lactate Dehydrogenase 2 (LDH2) isoenzyme level was measured by Agarose Gel Electrophoresis at Centre of Excellace in Molecular Biology (CEMB), Lahore. The results were analyzed by using Student's 't' test.

Results

In controls mean serum LD2 level was 29.1 ± 4.08%, in group B was 39.83 ± 2.09% while in group C it ranged from 52.53 ± 4.47%.

Table I: LD2 Levels In Controls and NHL

Parameter		Controls (n = 20)	Non infiltration (n = 30)	P value
LD2	(%)	29.1 ± 4.08	39.83 ± 2.09	< 0.001 *

Very highly significant

The difference between the mean levels of the controls and patients groups, as well as between the NHL patients with and without bone marrow infiltration was highly significant (P<0.00) (Tables I,II,III and Figures I,II,III). In 6(20%) cases with leucocytosis LD2 values ranged from 54-60% with mean value of 57.5 ± 2.07%. Highest values (60 & 59%) were noted in 2 (7%) cases with peripheral spill over. The cut off limit of serum LD2 among group B & C derived from the data was 45%. The cases with infiltration showed values above this cut off limit.

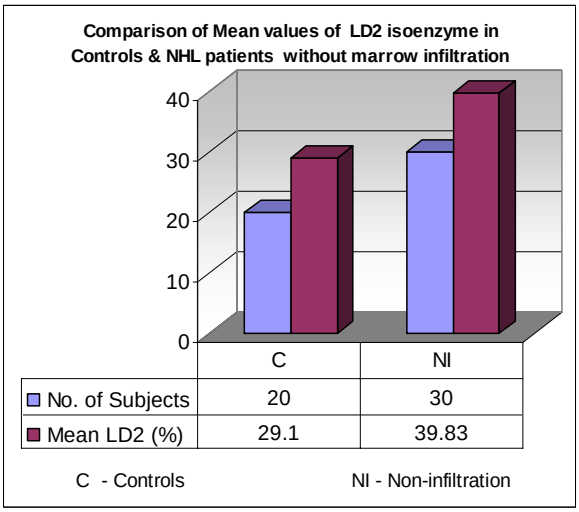

Figure I: Comparison of mean values of LD2 isoenzyme in controls and NHL patients without marrow infiltration.

Table II: LD2 Levels In Controls And NHL Patients With Bone Marrow Infiltration

Parameter	Controls (n = 20)	Infiltration (n = 30)	P value
LD2 (%)	29.1 ± 4.08	52.53 ± 4.47	<0.001*

*Very highly significant

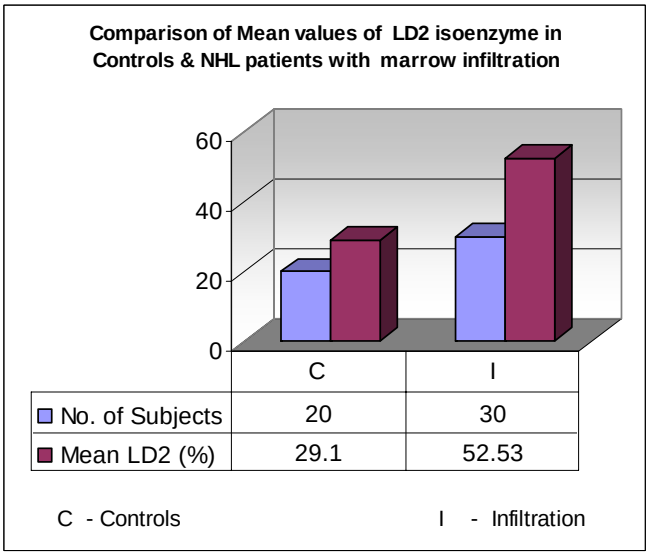

Figure II: Comparison of mean values of LD2 in controls and NHL patients with marrow infiltration

Table III: Comparison Of LDH2 In Patients Of Non-Hodgkin's Lymphoma

Parameter	Non infiltration (n = 30)	Infiltration (n = 30)	P Value
LD2 (%)	38.83 ± 2.52	52.53 ± 4.47	<0.001*

*Very highly significant

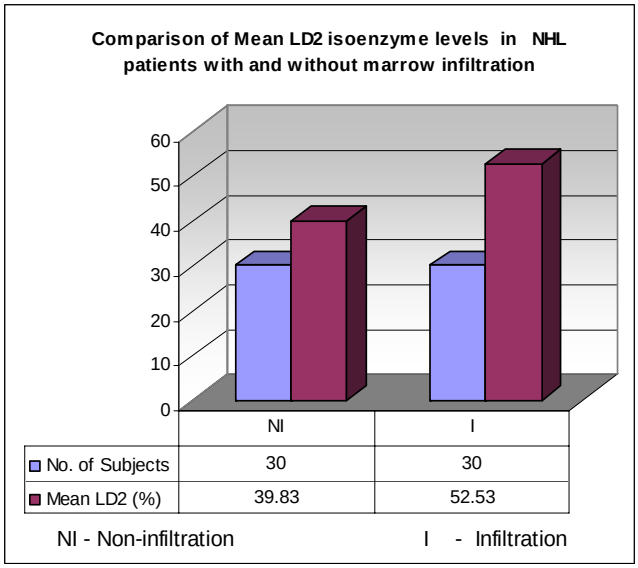

Figure III: Comparison of mean LD2 isoenzyme levels in controls and NHL patients with and without marrow infiltration

Discussion

In the present study mean LD2 level in controls was 1.51±0.43%. In patients of NHL without bone marrow infiltration mean level was 2.41±0.48%. While in NHL patients with bone marrow infiltration it was 3.9±0.7%. Mean LD2 level was significantly raised in NHL patients with and without bone marrow infiltration as compared to controls (p<0.001). Similar observations were reported by Csako1982, Rotenberg 1983. Paule 1984, Maruyam 1994, Dumontet 1999, Boufia 2004.

Csako 1982 stated that highest LD2 isoenzyme activity is helpful to evaluate the tumor burden and prognosis in patients of NHL.[14] According to Rotenberg 1983 elevated serum LD levels with predominance of LD2 may be early and the only sign of occult malignant lymphoma.[15]

Dumontet 1999 commented that there are some characteristic serum LD isoenzyme profiles in patients with NHL and some of these specific alterations may help to refine the prognostic value of total serum LDH.[18]

Boufia 2004 said that LD2 appear to be a biochemical marker of the tumor process and of cellular differentiation. Increase in LD2 was a sign of evolution towards a more aggressive phase of the disease. There are characteristics alterations in serum LD2 levels in patients with NHL.[19]

Boufia 2004 also reported that among 160 patients 49% had increased serum LDH. The analysis of LD isoenzyme profiles in all patients showed increased percentage of isoenzyme 2 in patients with NHL (both at diagnosis and at relapse) which shows superiority of LD2 isoenzyme estimation over total LDH. This also shows that former is more reliable indicator of malignant potential in NHL.

Conclusion

In view of above observations it was concluded that LD2 isoenzyme was raised in 58% of the NHL patients, with a considerable rise in patients with bone marrow infiltration. So LD2 isoenzyme can serve as an indicator of extent of disease.

Being a non invasive parameter it can be used to assess the proliferative activity and invasive potentials of lymphoma.

References

1. En: wikipedia.org/wiki/lymphoma.
2. Zinzani PL. Lymphoma: diagnosis, staging, natural history, and treatment strategies. SeminOncol 2005; 32: 4-10.
3. Dolores A, Rajdev L. Non-Hodgkn's lymphoma. American Society of Clinical Oncology 2004.
4. Weber AL, Rahemtullah JA. Hodgkin and non-Hodgkin lymphoma of the head andneck: clinical, pathologic and imaging evaluation. Neuroimaging Clin N Am 2003; 13(3): 371-92.
5. Sukpanichnant S. Analysis of 1983 cases of malignant lymphoma in Thailand according to the World Health Organization classification. Hum Pathol 2004; 35(2): 224-30.
6. Karin ZC, Jose SR, Antonio CA, Maria RR. Prognostic factors in non-Hodgkin's lymphoma. Sao Paulo Med J 2000;118(1): 7-12.
7. Skunca Z, Gveric-Krecak V, Dominis M, Planinc-Peraica A, Jaksic B. Non-Hodgkin's lymphoma: clinical symptoms, therapy and prognosis in 37 patients. Acta Med Croatica 2003; 57(4): 261-7.
8. Bai CM, Yang T, Xu Y, Zhang W, Liu XL, Zhu YL, Chen SC, Shen T. Clinical analysis of 32 primary intestinal non-Hodgkin's lymphoma. ZhonghuaZhong Liu ZaZhi 2006; 28(2): 142-4.
9. Rao DS, Said JW. Small lymphoid proliferations in extranodal locations. Arch Pathol Lab Med 2007; 131(3): 383-96.
10. Morra E. The biological markers of non- Hodgkin's lymphoma: their role in diagnosis, prognostic assessment and therapeutic strategy. Int J Biol Markers 1999; 14(3): 149-53.
11. Economopoulos T, Papageorgiou S, Dimopoulos MA, Pavlidis

N, Tstalas C, Symeonidis A et at. Non-Hodgkin's lymphoma in Greece according to the WHO classification of lymphoid neoplasms.A retrospective analysis of 810 cases.ActaHaematol 2005; 113(2): 97-103.

12. Escalon MP, Liu NS, Yang Y, Hess M, Walker PL, Smith TL, Dang NH. Prognostic factors and treatment of patients with T- cell non-Hodgkin's lymphoma. Cancer 2005; 103(10): 2091-2098.
13. Zhou SY, Shi YK, He XH, Zhang P, Dong M, Huang DZ, Yang JL, Zhang CG, Liu P, Yang S, Feng FY. Treatment effect of DICE regimen on patients with relapsed or refactory intermediate and highgrade non- Hodgkin's lymphoma. Ai Zheng 2005; 24(4): 465-9.
14. Csako G, Magrath IT, Elin RJ. Serum total and isoenzymelactate dehydrogenase activity in American Burkitt's lymphoma patients. Am J ClinPathol 1982; 78(5): 712-7.
15. Rotenberg Z, Weinberger I, Fuchs Y, Erdberg A. Davidson E, Agmon J. Belinson Medical Centre, Israel 1983.
16. Paule B, Francoual J, Lindenbaum A, Derrieux C, Russo C, Gerbert D, Leluc R. Lactate dehydrogenase isoenzyme activity in malignant haematological diseases. Biomed Pharmacother1984; 38(1): 62-5.
17. Maruyama F, Ezaki K, Okamoto M, Miyazaki H, Wakita M, Nomura T, Tsuzuki M, Kojima H, Sobue R, Matsui. Incresed blood cell destruction during vigorous regeneration of bone marrow after CAMBO-VIP chemotherapy for non-Hodgkin's lymphoma.RinshoKetsueki 1994; 35(2): 114-9.
18. Dumontet C, Drai J, Bienvenu J, Berard EN, Thieblemont C, Bouafia F, Bayle F, Moullet I, Salles G, Coiffier B. Profiles and prognostic values of LDH isoenzymes in patients with non-Hodgkin's lymphoma. Leukemia 1999; 13(5): 811-7.
19. Bouafia F, Drai J, Bienvenu J, Thieblemont C, Espinouse D, Salles G, Coiffier B. Profiles and prognostic values of serum LDH isoenzymes in patients with haematopoietic malignancies. Bull Cancer 2004; 91(7-8): 229-40.

Announcements

1. The 35th National PAP conference is planned in November 2010 at King Edward Medical College Lahore from 5-7th November. Last date for submission of abstract is October 5, 2010

2. A symposium on “Global issues local solutions” is planned by Shaukat Khanum Memorial Hospital, Lahore from 25th to 27th November 2010. Last date of Submission of abstract is 31st August 2010.

3. The schedule of Monthly workshops of Histopathology in PIMS Islamabad are as follows

    - October 30, 2010 Mediastinum, Thyroid and parathyroid glands
    - December 8, 2010 Gastrointestinal tract, Peritoneun and Retroperitoneum
    - January 29,2011 Respiratory System
    - February 26, 2011 pancreas, Adrenal Gland Paraganglia, Pituitary Gland
    - March 26, 2011 Male Reproductive System
    - April 30, 2011 Breast