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# BETA-2-MICROGLOBULIN AS A MARKER OF EXTENT OF DISEASE IN NON-HODGKIN LYMPHOMA

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**ABSTRACT**

***Introduction:*** *Lymphomas are the malignancies of lymphoreticular system. These malignant lymphocytes accumulate either by duplicating faster than normal or they can live longer than normal. Malignant lymphomas represent clonal malignancies in which the majority of the cells are frozen at a single stage of normal differentiation. Two broad types of lymphomas are named as Hodgkin disease and Non-Hodgkin lymphoma. Serum Beta 2 microblobulin (β2m) is commonly increased in patients with haemopoietic malignancies and have been shown to be of prognostic value in patients especially with Non-Hodgkin lymphoma (NHL).* ***Materials and Methods:*** *Serum β2m level was determined in already diagnosed (n=60) patients of NHL. They were divided into two groups, 30 patients with bone marrow infiltration (group B) and the remaining without infiltration (group C). The values were compared with 20 healthy age and sex matched contrtols (group A). The estimations were made prior to the institution of chemotherapy.* ***Results:*** *β2m level was significantly raised in NHL patients compared with controls. There was also a 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. We* ***conclude*** *that the above mentioned non invasive parameter is a useful indicator of the extent of the disease.*

***Key Words****: Non-Hodgkin Lymphoma, mucosa associated lymphoid tissue, Beta 2 microglobulin, Enzyme Linked Immunosorbent Assay.*

## INTRODUCTION

Lymphomas are defined as malignancies of lymphoreticular system.[1,2] Malignant lymphomas represent clonal malignancies in which majority of the cells are frozen at a single stage of normal differentiation.[3]

About 85% of lymphomas are of B-cell origin and 15% of T-cell origin. B-cell originate and mature (differentiate) in the bone marrow while T-cells also start in the bone marrow but they differentiate and mature in the thymus gland. In non-Hodgkin lymphoma (NHL) primary manifestations of disease occur outside the bone marrow at the site of normal lymphocytes homing lymph nodes, spleen, MALT (mucosa associated lymphoid tissue) or anywhere. Lymphomas outside lymph node and spleen are referred to as extranodal lymphomas.

A patient with NHL may present with localized and generalised peripheral lymphadenopathy[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. Once histological diagnosis of malignant lymphoma has been established, it is mandatory to determine extent of disease so that treatment protocol may be decided.[10]

Patients at high risk for failure with conventional therapy may benefit from investigational approaches. The biological markers of NHL are distinguished in three categories: serological, immunophenotypic and molecular markers. The clinical importance of biological markers in NHL is based on their support of morphological diagnosis, their role in staging and prognostic assessment. Among the most important serological markers Beta-2-microglobulin ($\beta_2$m) reflects the tumour load.

$\beta_2$m is a low molecular weight polypeptide, non-covalently linked to the heavy chain of class 1- histocompatability antigens which are shed with cell turnover. It is plentiful on the surface of lymphocytes. Increased production or destruction of the cells causes $\beta_2$m levels in the blood to increase.[11,12] This study was conducted to assess the level of serum $\beta_2$m in the patients of NHL with and without bone marrow infiltration.

## PATIENTS AND METHODS

It was a cross sectional study carried out on 80 subjects (irrespective of age and sex) divided into following groups.

Group A: Normal healthy controls (n=20)

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

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

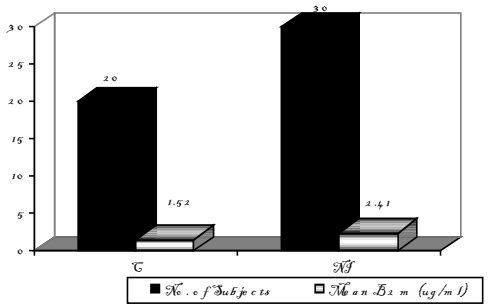
The cases were selected from Lahore General Hospital, Institute of Nuclear Medicine and Oncology (INMOL), Lahore, Services Hospital and Mayo Hospital, Lahore.

Newly diagnosed cases of NHL by lymph node biopsy prior to the institution of chemotherapy of both sexes and all age groups were selected for the present study. The patients with the history of myocardial infarction, renal failure, hepatic dysfunction, skeletal muscle disease, haemolytic anaemia, malignancy of any other system, cerebrovascular accident, Infectious mononucleosis and intestinal infarction were excluded.

Serum β-2m was measured by Enzyme Linked Immunosorbent Assay (ELISA) technique. The results were analysed by using Student's 't' test.

## RESULTS

In controls mean serum $\beta_2$m level was 1.52 ± 0.43 µg/ml. Mean serum $\beta_2$m level in group B patients was 2.41 ± 0.48 µg/ml whereas in group C it was 3.93 ± 0.71 µg/ml. 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 were highly significant (P<0.00) (Tables 1,2,3 and Figs 1,2,3). In 6 cases with lymphocytosis β2m value ranged from 4.5-5.23 µg/ml with mean value of 4.91 ± 0.27 µg/ml. Highest values (5.23 and 5.2 µg/ml) were noticed in 2 (7%) cases with peripheral spill over. The cut off limit of serum $\beta_2$m among group B & C derived from




C - Controls NI – Non-infiltration

**Fig. 1:** *Comparison of mean values of $\beta_2$m in Controls and NHL patients without marrow infiltration.*

**Table 1:** *β2 Microglobulin level in controls and NHL patients without bone marrow infiltration.*

| Parameter | | Controls (n = 20) | Non Infiltration (n = 30) | P value |
|---|---|---|---|---|
| β2m | (µg/ml) | 1.52 ± 0.43 | 2.41 ± 0.48 | < 0.001* |

* Very highly significant

**Table 2:** *β2- Microglobulin level in controls and NHL patients with bone marrow infiltration.*

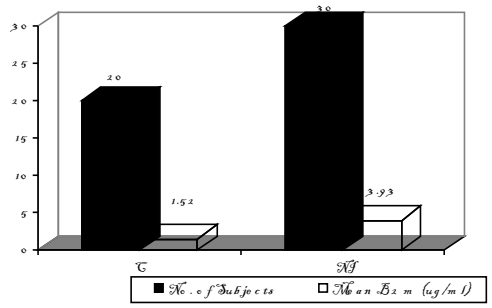
| Parameter | Controls (n = 20) | Infiltration (n = 30) | P value |
|---|---|---|---|
| β2m (µg/ml) | 1.52 ± 0.43 | 3.93 ± 0.71 | < 0.001* |

* Very highly significant

**Table 3:** *Comparison of β2m in patients of non-hodgkin's lymphoma.*

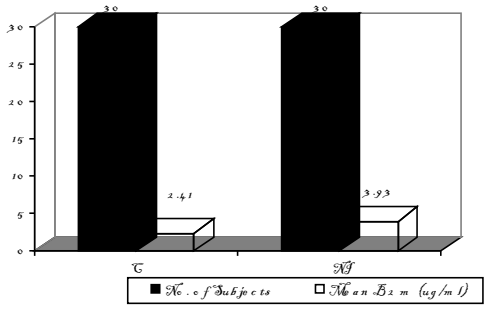
| Parameter | Non Infiltration (n = 30) | Infiltration (n = 30) | P value |
|---|---|---|---|
| β2m (µg/ml) | 2.41 ± 0.48 | 3.93 ± 0.71 | < 0.001* |

* Very highly significant




C - Controls I – Infiltration

**Fig. 2:** *Comparison of mean values of $\beta_2$m in Controls and NHL patients without marrow infiltration.*




NI – Non-infiltration I – Infiltration

**Fig. 3:** *Comparison of mean $\beta_2$m levels in NHL patients with and without marrow infiltration.*

the data was 3.0 µg/ml. The cases with infiltration showed values above this cut off limit.

In this study β2m level ranged from 1-1.88 µg/ml in four cases of stage I and was 2.0-2.42 in 8 patients of stage II, whereas in eighteen patients from stage III its range was 1.99-3.29 µg/ml.

## DISCUSSION

Mean β2m 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 various other workers.[14-16]

According to Melillo β2m seems to reflect tumour burden of malignant cells.[17] In other studies it was commented that β2m was among the most important serological markers which reflect tumour load. It has been reported that β2m can be helpful to assist the diagnosis of NHL.[16,21] In this study β2m level ranged from 1-1.88 µg/ml in four patients of stage I and was 2.0-2.42 µg/ml in eight patients of stage II.[16,21] On the other hand in 18 patients from stage III its range was 1.99-3.29 µg/ml. As far as the range of β2m in patients with stage III is concerned it was found to be slightly lower than stage II. The lower value in the range in stage II patients may be due to the fact that some of the patients in this stage presented earlier in the out patient department clinics and so were investigated for the serological markers at earlier time.

Similar observations were made by Hagberg[22] who reported β2m level greater than 3.0 µg/ml in 15% of patients with stage I and II and in 65% of those with stage III and IV. It seems that β2m level was elevated with progression of disease. Level of β2m also showed an increase in mean values with the advancing stage of NHL. According to Roberto et al[23] β2m concentration >3.3 mg/l had an unfavorable outcome. It was reported that in tumour stage I β2m concentration was 1.65 ± 0.45 µg/ml and in stage II it was 2.41 ± 0.65 µg/ml.[24] The level in stage III and IV was 3.48 ± 1.15 µg/ml and 5.49 ± 1.99µg/ml respectively. In stage III and IV β2m levels were significantly higher than normal.

Our results are similar the observations already made in other reports.[22,24,25]

In view of above observations it was **concluded** that β2 m was raised in 55% of NHL patients with marked increase in stage IV disease. So β2m can be considered as a marker of tumor burden. Being a non invasive parameter it can be used to assess the tumour burden in NHL patients.

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