SUMMARY & CONCLUSION

The Bone marrow microenvironment is a complicated system of accessory or stromal cells which produce a mesh work of extra cellular matrix (ECM), glycoproteins and cytokines to sustain hemopoiesis.

Cytokines are protein substances that are secreted by cells to affect by autocrine / paracrine mechanisms other types of cells and so it resembles the message between different types of cells. The affected cells can translate the cytokines message into an action such as proliferation, differentiation and apoptosis.

From the above, we aimed by this research to clarify the diagnostic and prognostic aspect in estimating some elements of BM microenvironment, including cytokines (IL3, IL6, TNFα), adhesion molecules (sCD44, L-selectin), extracellular matrix (fibronectin) and stromal cell, in 20 patients at diagnosis (before treatment) and re-estimated after being in complete remission (after treatment), and this was compared with 10 normal persons as a control group.

Complete history was taken and all laboratory, radiological and histopathological investigations that confirm the diagnosis of the cases were performed.

BM cellularity was increased in 55%, while it was normal in the remaining 45% of NHL patients at diagnosis. BM marrow stromal cells (reticular cells, macrophages, fibroblasts) were increased in 55% of NHL patients at diagnosis, while in remission reticular cells and macrophages

were increased in only 20% of cases and fibroblasts were increased in 15% only of examined biopsies specimens.

Marrow infiltration was presented by 75% of patients with focal infiltration in 53.3%, followed by diffuse and paratrabecular patterns in (46.7% and 26.6%) respectively.

The mean values BM of TNFα, IL-6 and IL3 were found to be significantly increased in NHL patients at diagnosis in comparison to control group and lower to near their normal levels in remission with no statistical difference when compared to control group.

The mean values of BM plasma cytokines (TNFα, IL-6 and IL3) were significantly increased in:

a) Patients with B-symptoms than those without B-symptoms at diagnosis and in remission.
b) Patients with extranodal sites > 1 than those with extranodal sites ≤ 1 at diagnosis and in remission
c) Patients with T-cell lymphomas than those who had B-lymphoma at diagnosis and in remission in (TNF-α and IL-6) and at diagnosis only in IL3.

Moreover the mean values of BM plasma TNF-α and IL-3 were significantly increased in patients with high IPI than those of intermediate / high and intermediate / low and low IPI score at diagnosis and in remission.

Patients with BM TNFα level > 50 pg / mL was associated with 1.5 folds higher frequencies of B-M invasion at diagnosis.

Patients with BM plasma IL-6 > 28 were associated with 2.8 and 5.4 folds higher frequencies of BM invasion and B-symptoms respectively at diagnosis.

BM plasma TNFα, IL3 and IL-6 showed strong positive correlations with serum LDH, β_2 microglobulin, ESR and IPI.

The mean values of BM plasma adhesion molecules (sCD44 and L-selection) were found to be significantly increased in NHL patients at diagnosis (Group I) when compared to control group, while it lowered to near their normal levels in remission but still higher than their levels in controls with no statistical significant difference.

The means values of BM plasma adhesion molecules (sCD44 and L-selectin) were significantly increased in :-

a) Patients with extranodal sites > 1 than those with extranodal site ≤ 1 at diagnosis and in remission
b) Patients with high grade lymphomas than those of intermediate and low grade lymphomas.
c) Patients with high IPI than those of intermediate / high and intermediate / low and low IPI score at diagnosis and in remission in BM sCD44 and at diagnosis only in BM L-selectin.

Moreover, the mean value of BM plasma sCD44 was significantly increased in :-

a) Patients with B-symptoms than those without B-symptoms at diagnosis in remission.

b) Patients with BM involvement than those without BM involvement.
c) Patients with T-cell lymphomas than those who had B-cell lymphomas at diagnosis and in remission.

Patients with BM plasma L-selectin > 8ug/mL were associated with 4.8 folds higher frequencies of BM invasion, while patients with BM plasma sCD44 > 280 ng/mL were associated with 2.8 and 4.7 folds higher frequencies of BM invasion and B-symptoms respectively at diagnosis.

The mean value of BM plasma fibronectin was significantly decreased in NHL patients at diagnosis when compared to that of controls, while in remission, it was more increased than group I, but still lower than its level in control group with no statistical significant difference.

The mean value of BM plasma Fibronectin was found to be significantly decreased in :-

a) Patients with extranodal sites >1 than those who had extranodal sites $\leq$1 at diagnosis and in remission.
b) Patients with BM involvement than those without BM involvement at diagnosis only.
c) Patients with T-cell lymphomas than those who had B-cell lymphomas at diagnosis and in remission.

The mean values of serum LDH and β_2 microglobulin were significantly increased in NHL patients at diagnosis (before treatment), as compared to those of controls, while in remission their mean values were significantly lower than their levels in diagnosis but still higher than their levels in controls with no significant difference between them.

Serum LDH and β_2 microglobulin were associated with 6.27 and 3.90 folds higher frequencies of BM invasion and B-symptoms respectively.

From the above data, we can concluded that BMM including BM cytokines (TNFα, IL-3 and IL-6), BM adhesion molecules (sCD44 and L-selectin) and BM extracellular matrix fibronectin are good indicators of disease activity and regression, so they considered good prognostic factors in NHL patients. They were improved in remission, so they can use to follow up of patients during remission.