REVIEW OF LITERATURE
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Knowledge about lymphoid neoplasia was nil till 1832 when Thomas Hodgkin read a paper before the Medico Chirurgical Society in London on some morbid appearances of the absorbent glands and spleen, and then in 1865, the paper of Mr. Hodgkin's was supported by Wilks, in which he described glands showing white deposits like suet, scattered throughout and he named the morbid entity after the fully deserved name of Mr. Thomas Hodgkin as "Hodgkin's disease".

In 1878, Greenfield drew attention to the finding of large multinuclear cells in those lymphnodes and in 1892, Mr. Goldman, pointed out the frequency of local eosinophilia in these lymphnodes. Though Sternberg discovered initially the typical mirror nucleated giant cell, it was fully described by Reed in 1902 & laid the basis of the full fledged histological diagnosis of Hodgkin's disease & it was here that Hodgkin's and lymphosarcoma, the two tumours of lymphnodes were distinctly separated.

In 1863, Virchow & then in 1893, Kundrat described another lymphnode neoplasm as lymphosarcoma with its two sub types as lymphocytic & lymphoblastic.
It was only in 1913, that Ewing described a primary tumour arising out of the reticulum cells of lymphnodes. Oberling in 1928, suggested this name as a tumour of bone marrow. It was termed as Retothelosarcoma of lymphnodes by Roulet in 1930. However its very existence was denied by Symmers in 1938, but in 1941, warren, and Picana said that it does occur though quite rare.

In 1925, by Brill, Beehr, Rosenthal and then later by Symmers in 1927, described another variety of lymphnode neoplasm. During the second & third decade of the present century it became clear to many observers that these numerous diseases existed within the broad limits of primary tumours of lymphnodes.

A lot of confusion was prevailing regarding the exact classification & description of these tumours. Since then there has been a constant effort on the part of both Pathologists & Physicians and now by immunologists to give a clearcut description of each of these tumours & their classification with conceptual understanding.

Harrison in 1960, commented that there is still a certain amount of confusion surrounding this group of diseases and workers in past have applied
countless name to a relative small number of entities & even now a bewildering number of synonyms are in daily use.

Willis in 1960, started his noteworthy chapter dealing with lymphoid tumours with opening gambit of "no where in pathology has a chaos of names, so clouded clear concepts, as in the subject of lymphoid tumours". He commented that most of the confusion has resulted largely from the failure to recognise frankly certain intrinsic difficulty in the subject & the confusion, regarding the histogenetic relationship of the components of lymphoid tissue, lymphocyte & reticulo-endothelial frame work.

It was seen realised that the prevailing confusion can be removed by recognising that they are derived by divergent differentiation from a primitive mesenchymal stem cell.

Boyd, 1961, classified these tumours based on the type of the cell, from which they arise. Root (1963), gave an account of classification of malignant lymphomas and their characteristic features.

In 1966, Anderson while giving a concise classification commented that "It is not clear
as to what extent these minute subdivisions of malignant lymphomas are of clinical importance.

He divided lymphnode neoplasms into four groups and kept Hodgkin's as a separate class.

I. Non Hodgkin's lymphomas.
   A. Giant follicular lymphoma
   B. Lymphosarcoma
   C. Lymphatic leukemia.
   D. Reticulum cell sarcoma

II. Hodgkin's disease.

Jackson & Parker subdivided Hodgkin's group in three subclasses depending upon the histological type with a clinical and prognostic value.

   i. Paragranuloma
   ii. Granuloma
   iii. Sarcoma

These being in order of increasing malignancy however it did not bear the promise that it claimed initially and it was realised that it does not provide much prognostic significance.

Butler & Luke reclassified Hodgkin's disease into six classes which were later modified in the conference held at Rye in Paris in 1965, in which need for a standardised clinical staging, classification for Hodgkin's disease was emphasised and the final four
classes. Classification was approved which is as following

i. Lymphocytic predominance

ii. Nodular sclerosis

iii. Mixed cellular

iv. Lymphocytic depletion

The above classification which at the moment is in the current International use is of great clinical and prognostic value and gives best histoclinical correlation. This is in order of increasing malignancy.

In the Non-Hodgkin's group, there used to be three types,

i. Lymphosarcoma

ii. Giant follicular lymphoma &

iii. Reticulum cell sarcoma

Lymphosarcoma was further subdivided into lymphocytic & lymphblastic type. It was entirely histological and did not bear any clinical or prognostic correlation.

Rappaport (1966) has come forward with a classification which bear clinical and prognostic correlation and is currently in usage. It is as follows —
I. Lymphocytic
   a. Well differentiated lymphocytic lymphoma
      N-WDLL  D-WDLL
   b. Intermediate/moderately differentiated lymphocytic lymphoma
      N-MDLL  D-MDLL
   c. Poorly differentiated lymphocytic lymphoma
      N-PDLL  D-PDLL

II. Histiocytic
    N-HL   D-HL

III. Mixed cellular
     N-MC   D-MC

IV. Undifferentiated
    N-UL   D-UL

The nodular and diffuse type is based on the presence or absence of nodularity in the microsections of tissue. The original lymphoblastic lymphosarcoma is now classified in poorly differentiated lymphocytic lymphoma and reticulum cell sarcoma is grouped into histiocytic type.

The histiocytic type, as compared to the lymphocytic one, shows an initial localised behaviour, spread is late yet prognosis is poor.

Nodular variety has a better prognosis as compared to diffuse variety in all types.

During the last few years there has been a tremendous change in our understanding about lymphomas
mainly because of the renewed knowledge about the immunology.

Malignant lymphomas are neoplasms of the immune system but the terminology and classifications employed during the past decades bear no relationship to our modern understanding of the immune system of the human body. The traditional classifications & terminology were proposed on the basis of suspected cellular derivation & presumed degree of differentiation long before recent advances in immunology were made.

The term reticulum cell sarcoma & lymphosarcoma have been applied in an extraordinary variable fashion & achieved a meaningless status, by preventing effective comparison of results from different centres.

The classification of Happle, though bore prognostic correlation yet preceded the advances in immunology & also lacks conceptual relevance.

It is now generally agreed from studies of experiments conducted that there are two functioning lymphocytic systems in the body.

i. The 'T-cell' or Thymic dependent system of the cellular immunity.

ii. The 'B-cell' or Bursal equivalent (Thymic independent) or lymphocytic system of humoral immunity.

A third lymphocytic system a 'Non T or B' cell system may exist and account for marrow stem cell for which they proposed 'U-cell' (undefined cell) as the representative type.

The cells of T & B lymphocytic systems have got separate functions to perform & have constant distribution. T-lymphocyte circulate 4-6 times a day and account for about 70% of peripheral blood lymphocytes while 20-25% are B-cells.

These T cells are found in the para-cortical areas of lymphnodes, perivascular region of spleen & in small foci in G.I.T.

B-cells concentrate in follicular centres of lymphnodes, spleen, lamina propria of G.I.T. & inter-spaces in bone marrow. Even this classification, which is not at the moment in International usage is acknowledge to be deficient and must await further correlative morpholo-
gical & functional studies. However this provided a working basis on which recent lymphoma studies could begin from an immunological standpoint.

I. B-cell
   - Small lymphocyte (B)
   - Plasmacytoid lymphocyte
   - Follicular center cell (FCC)
     - Small cleaved
     - Large cleaved
     - Small noncleaved
     - Large noncleaved
   - Immunoblastic sarcoma
   - Hairy cell leukaemia

II. T-cell
   - Small lymphocyte (T)
   - Convoluted lymphocyte
   - Cerebriform lymphocyte
     (Sezari, Mycosis fungoides)
   - Immunoblastic sarcoma (T)
   - Lymphoepitheloid cell

III. Histiocytes

IV. U-cell

The National Cancer Institute, USA in 1982 proposed a working formulation which amalgamates the good points of all the systems of classification
which facilitates an easy clinical comparison of case reports & therapeutic trials. It is as follows-

I. Low Grade
   A. Malignant lymphoma
      small lymphocytes, consistent
      with CLL, plasma cytoid.
   B. Malignant lymphoma, follicular
      predominantly small cleaved cell, diffuse areas & sclerosis.
   C. Malignant lymphoma, follicular mixed.
      small cleaved & large cell, diffuse areas & sclerosis.

II. Intermediate grade
   D. Malignant lymphoma, follicular
      predominantly large cell
      diffuse areas, sclerosis.
   E. Malignant lymphoma, diffuse
      small cleaved cell, sclerosis.
   F. Malignant lymphoma, diffuse
      Mixed. Small & large cell, sclerosis.
   G. Malignant lymphoma, diffuse
      -Large cell,
      -Cleaved cell
      -Non cleaved cell
      -Sclerosis.
III. High Grade

H. Malignant lymphoma

Large cell, immunoblastic
plasma cytoid
Clear cell
polymorphous
Epitheloid cell component

I. Malignant lymphoma

Lymphoblastic
convoluted cell
non convoluted cell

J. Malignant lymphoma

small non-cleaved cell
Burkitt's
Follicular areas

K. Miscellaneous

Composite
Mycosis fungoides
Histiocytic
Extramedullary plasmacytoma
Unclassifiable
Other

Along with the efforts on the part of pathologists, Clinicians have also sweated constantly in order to classify the lymphoma clinically into various stages, mainly based on their extent of involvement of the body because over which they held their line of treatment.
In 1947, Graver suggested a three stage classification based on Anatomic distribution of the disease in the body. Again in 1950 Peter slightly modified these stages. Since then Peter and Middlemis (1958) Eson & Russel (1963), Fayos et al (1965), Desai (1965) & Lukes et al (1966) have classified into number of stages. Now the classification currently in use is given by Saul. A. Rosenberg (1970) which is a modification over Ann Arbor classification. It is as follows:

**Clinical Classification**

**Stage I**

Disease limited to one anatomic region or two contiguous anatomic regions on the same side of diaphragm.

**Stage II**

Disease in more than two anatomic regions or in two non continuous regions on the same side of diaphragm.

**Stage III**

Disease on both sides of diaphragm but not extending beyond the involvement of lymphnode, spleen or Waldeyer's ring.

**Stage IV**

Involvement of bone marrow, lung parenchyma, pleura, liver, skin, kidney, G.I.T. or any organ in addition to lymphnodes, spleen or Waldeyer's ring.
All stages are classified as A & E depending on the absence or presence of systemic symptoms. They are (I) Significant history of fever, (II) Pruritus, (III) Night sweats, (IV) Significant weight loss in last six months. Though this staging is proposed for Hodgkin's lymphoma it is in use for Non-Hodgkin's lymphomas as well.

The diagnosis of malignant lymphomas can be definitely established only by the histological examination of the tissue involved. In majority of these cases coming to us, present with superficial nodes. However they may be of value in diagnosis but cannot give us an accurate idea about the correct stage of the disease, because superficial nodes may be just the outward manifestation of an internal occult lesion.

Symmers in 1924, has stated that in Hodgkin's disease, primary involvement of abdominal & thoracic lymphonodes combined, is ten times more common than the primary involvement of cervical lymphnodes.

Ewing supported the idea of the internal occult lesions. The correct clinical staging has very important role because that guides our line of treatment.

Constantly efforts has been concerted towards correct clinical staging and then it was realised
that apart from detailed physical examination, X-ray chest, retroperitoneal lymphangiography & bone marrow examinations are an integral part of an examination. Staging laparotomy may also be done alternatively. This is an standard procedure but still limited to Western Hospitals. When it is performed, the laparotomy should always be complete and include at least two needle biopsies of each lobe of liver, a wedge biopsy of the liver edge, biopsies of suspicious area, splenectomy and biopsies of selected lymph nodes in the retroperitoneal area marked in the lymphangiogram, prior to operation. Nodes in the portahepatis also should be biopsied. Alternative to staging laparotomy is laparoscopy.

After the reports of these pieces correct staging is made and treatment started. This is very important because of effective methods of Radiotherapy and Chemotherapy in lymphomas, which has considerably improved the quality & quantity of the life of these patients, is available.

Humkin, Ronald et al in March 1974, reviewed 84 cases of non-Hodgkin's lymphoma with staging laparotomy and occult abdominal spread was located in 56%, splenic hilar in 54% paraaortic in 40% and spleen in 34%.

**HODGKIN'S DISEASE**

The dominant histologic change in Hodgkin's disease involves the reticulum cells of R.E. system. The
lymphatic elements donot take an active part in the hyper plasia in most cases and often are diminished in number. It might reasonably be expected that an organ rich in R.E. tissue such as bone marrow would be commonly involved in the disease.

Stiener in 1943 in his comprehensive review of the subject suggested that bony lesions might develop in one of three ways -

i. Direct invasion from contiguous lymphogranulomatous mass.

ii. By haematogenous spread.

iii. By primary origin in the bone marrow.

Krumshar in 1931, reported a case of Hodgkin's disease of Bone marrow & spleen without apparent involvement of lymphnode.

The reported incidence of bone or bone marrow involvement in Hodgkins disease is very variable particularly in studies based on clinical evidence alone. Stiener (1943) determined an average incidence of 8.3%. Lesions of bone most frequent involving the spinal column & pelvis were noted in 23% of Jackson & Parker studies. Similar lesions were detected in 14.8% of Hodgkins disease cases reported by Vieta in 1942.

Steiner 1943, noted an average incidence of 28.3% of bony lesions in 547 reported autopsies; but
observed that the incidence reported from any series apparently depended on the thoroughness of skeletal examination. The vertebrae, pelvis, ribs, sternum, skull & humerus were most commonly involved. 63.70% of sternal sections contained lymphogranulomatous lesions. He also observed that there was no basis for the impression that skeletal lesions come only as a late manifestation of the Hodgkin's disease.

Cooper & Watkins in 1949, concluded on the basis of smears of aspirated marrow that this tissue was of little use in evaluation of patients with Hodgkin's disease or in follicular lymphoma. In 1950, Cooper & Co-worker began study of section of marrow & came to opposite conclusion.

Genupool J.L. & Meyer, K. (1966) concluded after studying the bone marrow involvement in malignant disease that bone marrow aspiration & sections of bone marrow were complementary in patients with carcinoma & malignant lymphoma. Section biopsy was alone of value in Hodgkin's disease and neither technique was of value in patients with reticulum cell sarcoma. They studied 42 patients with Hodgkin's disease where 11 (26%) of biopsies were positive. Three of the positive cases had suggestive aspirations. Two additional sugg-
estive aspirations were present where biopsy were negative.

The first reference to the presence of Reed Sternberg cells in the peripheral blood was made by Issacs (1944) Ludmann & Spear (1957) showed photomicrographs of such cells in the case of known Hodgkin's disease.

Steiner (1943) has seen that Reed Sternberg cells were exclusively found at sites where there was tenderness on pressure and presternal oedema present (Varadi 1955).

Bayrd et al 1954 stated that it is only in the acute form of the disease, that the Reed Sternberg cells are present in the bone marrow. In Pool et al series where bone marrow positive, survival period ranged from 1 week - 12 months. As a whole they concluded that patient with acute or subacute form of illness are likely to yield Reed Sternberg cells in the aspirated bone marrow.

Varadi (1965) reported single case in which sternal aspiration yielded a specimen containing many lymphocytes & large basophil cells with large nuclei, and large blue nuclear cells which he classified as Reed Sternberg cells. Rohr & Hegglin identiﬁed Reed Sternberg cells in the specimens of marrow in a case of Hodgkin's disease.
John E. Ultman (1966) while presenting his paper in a symposium over Hodgkins disease held that frequency of involvement of different lymphonodes is as follows:

Cervical 60-80%, Axillary 6-20%, Inguinal 6-12%,
Mediastinal 6-11%, retroperitoneal, spleen & liver are less commonly involved in early cases.

It emphasised that for accurate staging of the Hodgkin's disease, following studies are considered desirable.

1. Adequate surgical biopsy, reviewed by an experienced pathologists.
2. A detailed history, recording the absence or presence of and duration of fever, unexplained sweating & its severity, unexplained pruritus, and unexplained weight loss.
3. A careful detailed physical examination, special attention to all node bearing areas, including waldeyer's ring & determination of size of liver & spleen.
4. Necessary laboratory procedures -
   a. Complete blood count, including ESR.
b. Serum alkaline phosphatase
c. Evaluation of renal function.
d. Evaluation of liver function.
5. Radiological studies.
   a. Chest roentgenogram (Posteroanterior, lateral view).
   b. Bilateral lower extremity lymphangiogram.
   c. CT scan of abdomen with or without ultrasonography.
   d. View of skeletal system to include thoracic, lumbar vertebrae, the pelvis, proximal extremities & any areas of bone tenderness.

Following procedures for the staging of Hodgkin's disease required under certain conditions -
   a. Whole chest tomography if any abnormality is noted or suspected on the routine chest X-ray.
   b. Bone marrow biopsy (needle or open) in the presence of i.e. i. am elevated alkaline phosphatase.
      ii. unexplained anaemia or other blood count depression.
      iii. other evidence of bone disease (scan or X-ray).
   c. Exploratory laparotomy & splenectomy, if management decision will depend on the identification of abdominal disease.

Some useful ancillary procedures are also, applied for staging of Hodgkin's disease.
   a. Skeletal scintigrams
   b. Hepatic & spleen scintigrams
   c. Gallium whole body scans
d. Serum chemistries to include serum calcium & uric acid for over all management of patient.

e. Estimates of the patients delayed hypersensitivity of tuberculin type.

Number a,b,c, can not be used as evidence of Hodgkin's disease without biopsy confirmation.

Though staging of disease, as discussed above, is important in determine the prognosis yet there are additional factors of prognostic importance which should also be considered -

i. Age of patient (disease more progressive in older patients).

ii. Sex (Markedly bad prognosis in males).

iii. Duration of symptoms before diagnosis is made (longer the duration better the prognosis).

iv. Exact location of presenting lymphnode.

v. Exact histological type.


John E. ultman (1966) also observed that fever was present in 32-50% of cases, Pruritus in 10-15% of cases, and asthemia in almost all the cases. Bone marrow involvement was found in 60% of autopsies. However during disease number of patients who exhibited bony lesions were less than 30%.
His observation also tells us that disease tends to remain in stage I, IIa, & IIb in younger & female patients, where as in older & males it tends to present with late stage III or IV.

Regardless of the stage of disease presence of systemic symptoms is a bad sign.

Webb, Upogi, & Silver (1970) emphasised that accurate clinical staging is important due to advent of effective super voltage radiotherapy & combination chemotherapy for the advanced cases.

Rosenberg (1971) emphasising the bone marrow examination because the better outlook of patients of metastasis treated by new super voltage radiations & combination chemotherapy showed in his study that of all the patients reviewed.

Mayers & Co-workers (1974) studied bone marrow involvement & survival of as many as 174 patients. Out of them 19 had positive bone marrow, 11 showed Reed Sternberg cells, 4 varying degree of fibrosis, 6 with malignant cells with focal involvement & 13 with diffuse involvement. Anaemia found with equal frequency in both positive & negative cases.

Ferrant et al (1975) observed 14 cases positive out of 38 while doing comparative study of radiotherapy, bone scanning and a bone marrow biopsy.
Donnan I. O'Carroll et al (1976) did bone marrow trephine biopsy on 107 previously untreated patients with Hodgkin's disease. 15 patients (14%) exhibited bone marrow involvement. These consisted of 2 of 3 patient (67%) with lymphocyte depletion, 6 of 27 patients (22%) with mixed cellularity. 5 of 64 patients (8%) with nodular sclerosis & 2 were unclassified. Typical Reed Sternberg cells were found in the trephine biopsy in 13 of 15 patients & mononuclear Reed Sternberg variant in remaining 2. Bone marrow involvement was the only evidence of stage IV disease in 10 of the 15 patients.

Thomas, V Colby et al (1981) studied (clinico-pathological) 659 cases and observed that nodular sclerosis was the most common pattern (60%) with the best total survival. Lymphocyte predominance had the best relapse free survival. The cellular phase of nodular sclerosis was found to have an overall survival and some clinical features more akin to mixed cellularity Hodgkin's disease.

Lee N. Newcomer et al showed that 18 patients with bone involvement were identified from a series of 124 consecutive patients with combined modality therapy with advanced stage/relapse of Hodgkin's disease. Pain at the site of involvement was noted in 14 patients.
11 patients had night sweats, fever or weight loss. Neurological deficit was associated with in 4 patients. Spinal root compression was documented in 3 patients and left facial nerve palsy occurred with skull involvement in 1 patient.

Ketawy A., Dinshaw et al (1984) did retrospective analysis of 441 patients with Hodgkin's disease seen at Tata Memorial Hospital, Bombay & found that bone marrow biopsies in 242 patients were found to be little value in stage I & II. Thirty of 34 patients with positive bone marrow biopsy were in clinical stages III b & IV. Whereas 24 of these 34 patients showed mixed cellularity & lymphocytic depletion pattern.

Non-Hodgkin's lymphoma

By original definition, lymphosarcoma lacks the systemic character of Hodgkin's disease & leukaemia, arising as a apparently local change in lymph node tissue, it seeks to extend by local invasion, by contiguous growth through lymph channels & by formation of true metastatic lesions in distant organs.

Lymph vessels have not been demonstrated in bone marrow but small accumulations of lymphatic tissue along the small arteries have been described by most investigators. Lymphosarcoma might
arise in the bone marrow but this structure would seem no more likely to become secondarily involved than would any other organ.

Suger Baker & Graver noted in 1940 clinical evidence of bony involvement of 9.7% of 197 cases of lymphosarcoma. In 1% the process appeared to arise in bone marrow.

Ellis, Jensen & co-workers (1964) found bone marrow positive in 23% cases of lymphosarcoma & 5% of reticulum cell sarcoma. Lymphosarcoma was first described by Kundrat in 1893. In 5-10% of patients with this disease extensive marrow involvement & a leukemic blood picture developed preterminally.

Issac in 1937 pointed out the difference between lymphosarcoma cell leukaemia & acute & chronic lymphatic leukaemia. He also pointed out a number of cytological differences between lymphosarcoma cells in blood & lymphocytes.

Schwartz in 1965, pointed out the criteria of diagnosis of lymphosarcoma cells leukaemia, while reviewing 23 patients as follows—
i. Significant involvement of bone marrow (lymphocytic elements making 50% of marrow count).
ii. L.S.A. cells in peripheral blood.
iii. Evidence of marrow dysfunction i.e. anaemia, neutropenia & thrombo-cytopenia.
Schwitzer & Kosa (1970) told that lympho-sarcoma cell leukaemia represents a poorly differentiated lymphocytic lymphoma which has involve the peripheral blood & bone marrow.

Abhimanyu, Garg, Ramesh Dewar, et al (1985) done a retrospective analysis of 238 patients of Northern India. They found most common histologic type encountered was diffuse histiocytic lymphoma (39%), followed by (DPDLL) diffuse poorly differentiated lymphocytic lymphoma (29%) and diffuse mixed histiocytic and lymphocytic lymphoma (9%). Nodular lymphoma constituted 9% of all Non Hodgkin's lymphoma.

A lower frequency of nodular lymphomas, a lower median age of onset (45 yrs.) and a higher male to female ratio (4.5:1) as compared to Western countries was observed.

Vineiquerra a Silver (1971) studied 75 patients with lymphosarcoma, 47 (68%) had positive marrow. Of importance, 40 of such patients had their stage increased from I to IV. They utilized both needle & aspiration bone marrow biopsy. They recommended bone marrow examination as an integral part of the investigation of these patients with lymphoma, irrespective of the clinical stage of the disease process.
Stephen & Rosenberg & others (1972) reviewed 218 patients with non Hodgkin's lymphoma which were classified by Rappaport classification. They found positive bone marrow as follows -

(They utilised all three types of bone marrow biopsy).
- Open technique of 96 patients studied - 17 patients (18%) were positive.
- Needle technique of 141 patients studied - 22 (16%) were positive.
- Aspiration technique of 195 patients studied - 11 (6%) were positive.
- Only 2 cases of I & II stage showed marrow involvement.
- Histiocytic lymphoma very uncommonly had positive bone marrow where as lymphocytic & mixed variety had frequent positive bone marrow.

Incidence of bone marrow involvement was not correlated with nodular or diffuse pattern but patients with nodular lymphoma survived longer than with diffuse variety.

Frieddick & clera, Bloomfield and others in 1974, did bone marrow biopsy in 108 patients with non Hodgkins lymphoma to evaluate incidence, degree and pattern as related to their histology, 44 cases showed marrow involvement. N-PDLL, (Nodular poorly differentiated lymphocytic lymphoma), exhibited more frequent marrow involvement than did D-PDLL, (Diffuse poorly differentia-
ted lymphocytic lymphoma) 27 out of 40 positive cases showed focal while rest 13 cases showed diffuse involvement 24 positive cases showed lesser degree of involvement than rest 16 cases. Reticulum cell sarcoma exhibited markedly less tendency to involve the bone marrow initially.

Jenskin & Brown (1975) correlated the clinical staging of 34 patients of non hodgkin's lymphoma with staging after laparotomy and splenectomy and found the following results.

Clinical Stage I - 7 cases were reduced to 6 after above procedure.

IIa - 12 cases were reduced to 8 after above procedure.

IIb - 6 cases were reduced to 2 after above procedure.

III - 5 cases were increased to 10 after above procedure.

IIIB - 2 cases were increased to 5 after above procedure.

IV - 2 cases were increased to 3 after above procedure.

Benzam et al (1975) found in an retrospective study of 550 patients with non Hodgkin's lymphoma, only 17 (3%) presented with severe leukopenia or thrombocytopenia due to bone marrow involvement.
Richard S. Stein, John E. Ultmann et al (1976) studied 121 patients with non Hodgkin's lymphoma to evaluate the incidence of bone marrow involvement. He found that involvement of bone marrow was dependent on both histologic type and the extent of extremedullary disease. It was observed most frequently in patients with poorly differentiated lymphocytic lymphoma (60%) but was not observed in 36 patients of all histologic types whose clinical evaluation and/or laparotomy revealed diseases in stage I or II. Among 56 patients with poorly differentiated lymphocytic lymphoma in stage III & IV, exclusive of marrow involvement. Disease was observed in 40 patients (71%). These observations together with the results of previously reported therapeutic trials suggest that staging laparotomy and total nodal radiotherapy alone may be of limited value in P-DLL, when clinical evidence of stage III or IV is present.

V. Maitreyan et al (1987) studied bone marrow infiltration by bone marrow biopsy and/or aspiration in 85 untreated patients with established non Hodgkin's lymphoma. Marrow involvement was found in 32 of 85 patients (37.6%) being more frequent with low grade (70.8%) as compared to high grade (20.8%) histology, 23 of these 32 patients (71.9%) were upstaged by said procedure and they contended that bone marrow biopsy is
a useful clinical tool in the initial investigation & staging of patients with malignant lymphomas.

C.S. Soman & Elizabeth K. Abraham (1968) looked the bone marrow biopsy of 163 patients of Non Hodgkin's lymphoma. Among these 58 patients (35.6%) showed evidence of involvement. Highest frequency of involvement was seen in well differentiated lymphocytic lymphoma & lowest in histiocytic type. Among the various patterns of marrow involvement the interstitials variety was the most frequent. Bone marrow biopsy was superior to aspiration in identifying marrow involvement.