



Original Research Article

Apoptotic index as adjuvant in the diagnosis of Non Hodgkin lymphomas

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Abstract

Background: The aim of the study was to analyze the apoptotic index and evaluate its role in various subtypes of Non Hodgkin lymphomas classified by working formulations.

Materials and Methods: This is a retrospective study conducted in the department of pathology. The study included cases diagnosed with Non Hodgkin lymphoma over a three year period, retrieved from the departmental archives. The haematoxylin and eosin stained sections were reviewed. All cases were classified by working formulation into high grade, intermediate grade and low grade lymphomas and the apoptotic index were tabulated and statistically analyzed.

Result: Of the 21 cases of low grade lymphomas, 18 cases showed low apoptotic indices of 2.4% and below, while the rest of the cases showed apoptotic indices greater than 2.4%. There was a great variation in apoptotic indices of intermediate grade lymphomas. Of the 23 cases, 12 cases showed apoptotic indices greater than 2.4% while rest of the 11 cases showed apoptotic indices of less than 2.4%. Among the 13 cases of high grade lymphomas, 10 cases showed high apoptotic indices of greater than 2.4% while rest of the 3 cases showed lower apoptotic indices of less than 2.4%.

Conclusion: Though working formulation classification of Non Hodgkin lymphoma holds good for many cases it has its drawbacks. So by the use of these inexpensive and an effective prognostic indicators along with the working formulation classification it may throw some light on the how a particular subtypes of Non hodgkin lymphoma in a particular patient might behave.

Keywords: Apoptotic Index, Histopathology, Non Hodgkins Lymphoma, Working formulation.

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1. Introduction

Lymphoid neoplasms include various group of tumors of T-cell, B-cell, and NK-cell origin. Worldwide lymphomas rank 6th among all cancers.¹ In India its incidence is on the upsurge with the current figure standing at 5.1 per 100,000 in urban registries. Non-Hodgkin lymphoma (NHL) is a collective term for a heterogeneous group of lymphoproliferative malignancies with differing patterns of behaviour and responses to treatment. The prognosis of NHL depends on the stage, histologic type, and treatment. In lymphomas, immunohistochemistry (IHC) is used to completely phenotype and classify the abnormal population of cells and in classifying, sub-classifying and in predicting the prognosis of several classes of lymphomas. Recent WHO classification

of lymphomas (2024) classifies NHL into B and T cell lymphomas and for this a panel of immunohistochemical markers are to be used. No single antigen is lineage or lymphoma specific and also these panel of immunohistochemical markers are cost effective. The case series study done by Lorenzo leoncini et al² quoted that working formulation classification of lymphomas still holds greater significance. But to date there is no single classification that can predict how a particular tumour in a individual patient might behave. So a need to look at other prognostic indicators becomes necessary. Hence in this study we included apoptotic index as prognostic indicator³ and tried to evaluate its role in various subtypes of Non Hodgkin lymphomas classified by working formulations.

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2. Materials and Methods

This is a retrospective study conducted in the department of pathology. This study included cases diagnosed over a three year period, retrieved from the departmental archives. All cases diagnosed as Non Hodgkin lymphomas during the study period were included. Cases with incomplete records, inadequate tissue or inconclusive diagnosis were excluded. Clinical details were obtained from requisition form and case records. Histopathology slides and paraffin blocks were retrieved from the departmental archives. Where necessary, fresh sections were cut and stained with hematoxylin and eosin. All cases were classified by working formulation into high grade, intermediate grade and low grade lymphomas and the apoptotic index were tabulated and statistically analyzed.

Apoptotic index were calculated by examining H&E slides for apoptotic bodies which are cells with intensely eosinophilic cytoplasm with fragments of dense nuclear chromatin and were then graded. This was done by the method opted by “Y. Soini, P. Pa”a”kko”, and V-P. Lehto” in their study of Histopathological evaluation of apoptosis in cancer.⁴

3. Results

A total of 57 cases were profiled during the study period. Of the 57 cases, maximum number of cases were intermediate grade 2 cases (40.35%) (Table 1) with male predominance (65%) (Figure 1).

Table 1: Distribution of cases

Cases	Number of cases	Percentage of cases
Low grade	21	36.84%
Intermediate grade	23	40.35%
High grade	13	22.80%
Total	57	100%

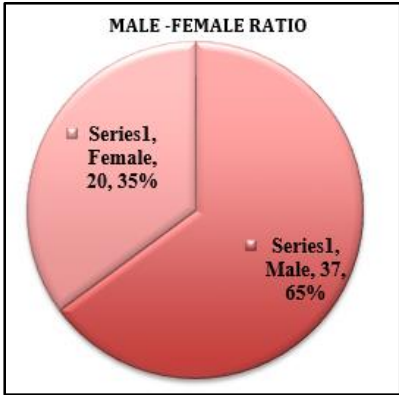


Figure 1: Distribution of cases

These patients of NHL in our study, presented with lymph node enlargement with one cases showing additional lesion in the tonsil and other in skin. Maximum number of patients showed enlarged cervical group of lymph nodes 52.63% (30cases),other nodes involved were inguinal node 21% (12 cases), submandibular node and axillary node 7% each(4 cases),mesenteric node 3 cases(5%) and submandibular node constituting 2 cases (3.5%). The maximum size of enlarged lymphnode was 6cm with minimum size of 0.3cm.

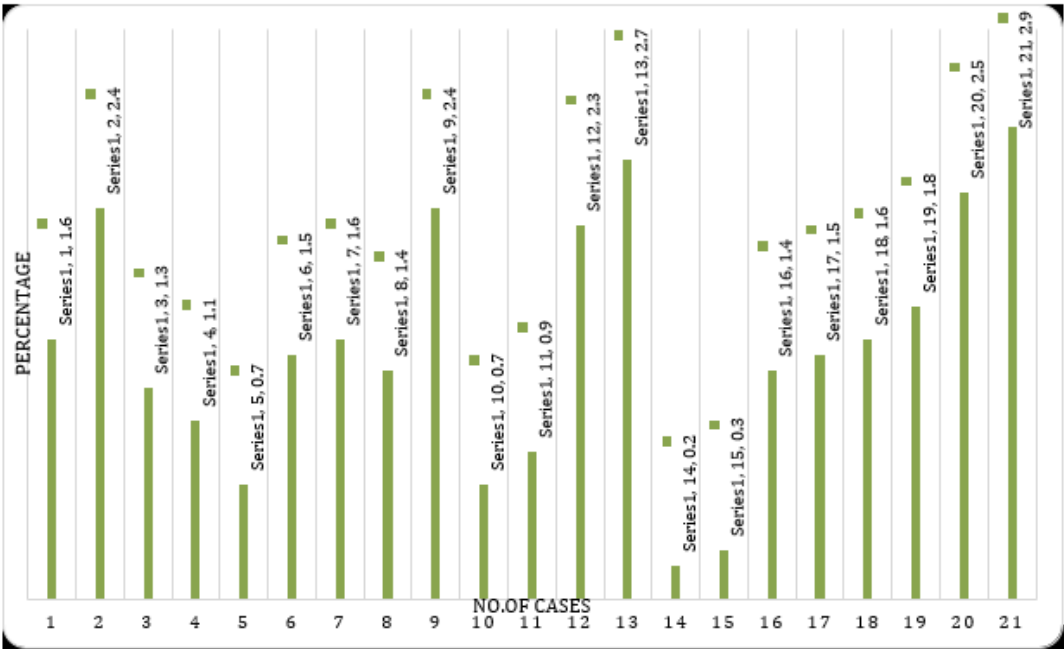


Figure 2: Low grade lymphoma

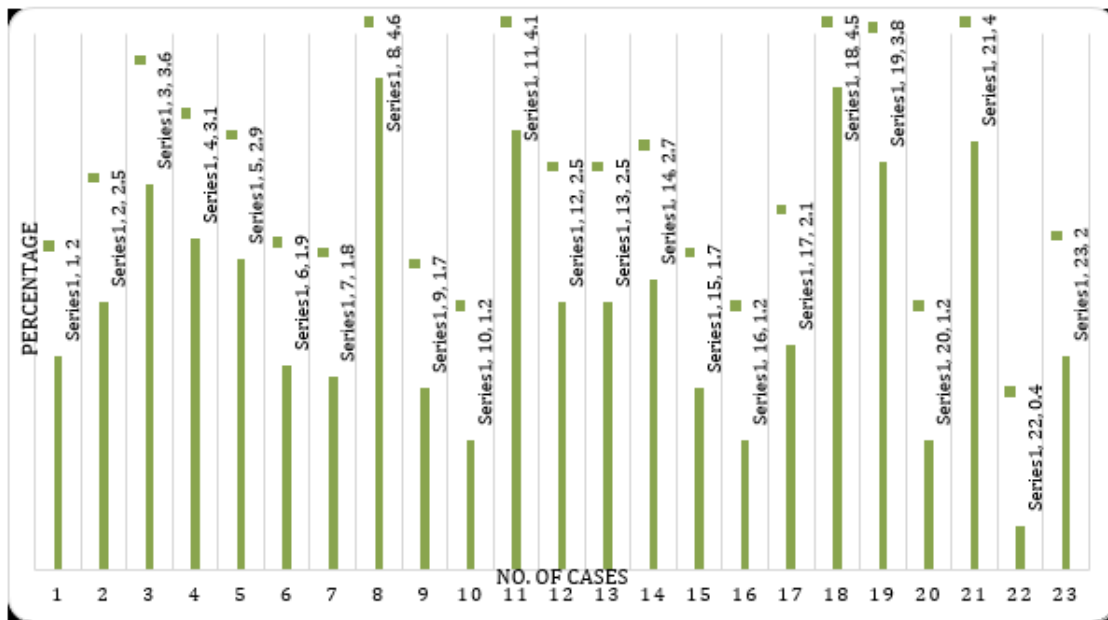


Figure 3: Intermediate grade lymphoma

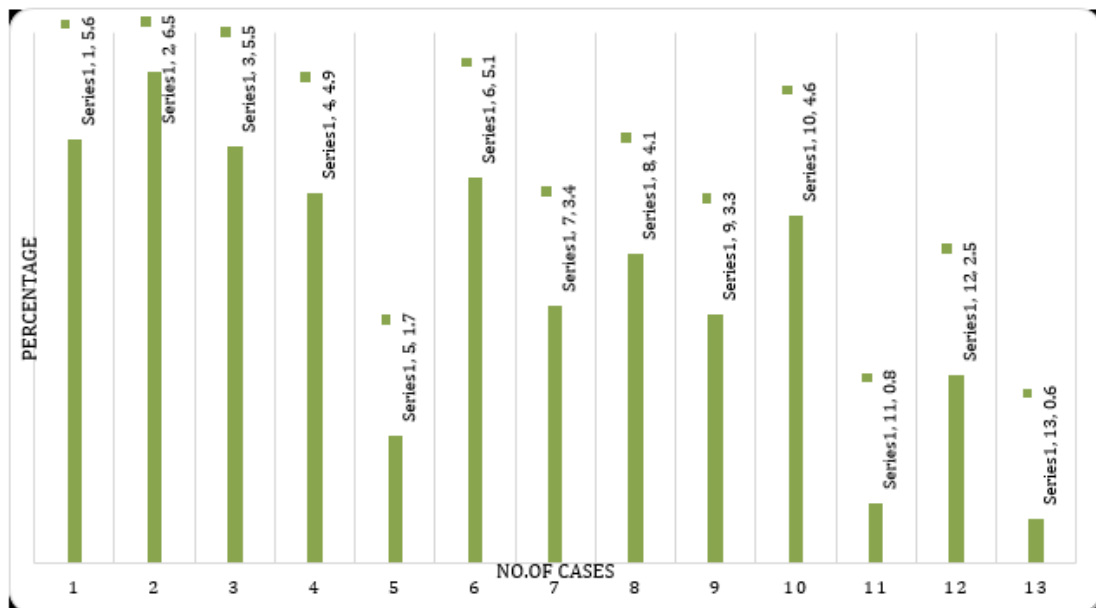


Figure 4: High grade lymphomas

Of the 21 cases of low grade lymphomas, 18 cases showed low apoptotic indices 2.4% and below, while the rest of the cases showed apoptotic indices greater than 2.4%.(Figure 2)

There was a great variation in apoptotic indices of intermediate grade lymphomas. Of the 23 cases, 12 cases showed apoptotic indices greater than 2.4% while rest of the 11 cases showed apoptotic indices less than 2.4% (Figure 3)

Of the 13 cases of high grade lymphomas, 10 cases showed high apoptotic indices of greater than 2.4% while rest of the 3 cases showed lower apoptotic indices of less than 2.4%. (Figure 4)

4. Discussion

Cells undergoing apoptosis modulate their tissue microenvironments. Apoptosis has a role in preventing tumorigenesis,⁵ but paradoxically, higher incidence of apoptosis is linked to aggressive disease in multiple malignancies.⁶⁻¹¹ Indeed, cell loss is significant in aggressive tumors,⁶ and programmed cell death can generate regenerative and reparative tissue responses such as compensatory proliferation and angiogenesis that have strong potential to be causally associated with tumor progression.^{12,13} Catriona A. Ford, et al,¹⁴ demonstrated that the constitutive apoptosis occurring in high-grade B cell lymphoma displays pro-tumor activities by promoting

angiogenesis and the accumulation of tissue-reparatory and growth-promoting macrophages.

Cell proliferation rate and death rate is an important factor for grading neoplasms and predicting their clinical behavior and outcome. This study aimed at analyzing the prognostic significance of apoptotic index in Non-Hodgkin's lymphomas. Though WHO classification holds good, a minimum of 6 immunohistochemical markers are required for classification which is expensive. Hence, in this study we classified NHL by working formulations and assessed the trustworthiness of this classification by applying prognostic indicator like apoptotic indices.

NHL affects all the age groups, commonly involving the elderly. On the basis of data collected by Smith et al,¹⁵ the mean age of the patients were 68 years. In a retrospective analysis of 101 cases of lymphomas by Monoj Kumar Deka et al,¹⁶ 67 patients were male (81%) and 16 were female (19%). The age range was 4 to 88 years with a median age of 53 years. In the present study, mean age of cases with low grade lymphomas were 40 years, intermediate grade lymphomas 27 years and high grade lymphomas 41 years. In our study there was increased incidence in males 65% similar to a study by Leoncini et al.⁷

According to Manzoor Ahmed et al,¹⁷ 78.78% of cases of NHL presented with lymph node enlargement. Among these, 40.5% had generalised lymphadenopathy whereas 24% of patients had cervical lymph node enlargement. Sudipta chakravarthi et al,¹⁸ in their study documented that peripheral lymphadenopathy was noted in 94.7% of cases of NHL. In the current study, the patients of NHL presented with lymph node enlargement with one of the case showing additional lesion in the tonsil and other case in the skin. Maximum number of patients showed cervical group of enlarged lymph nodes which constituted for 52.63% (30 cases). Other nodes involved were inguinal node 21% (12 cases), submandibular node and axillary node 7% each (4 cases), mesenteric node 3 cases (5%), submandibular node 2 cases (3.5%). The maximum size of enlarged node was found to be 6cm with minimum size of 0.3cm.

Leoncini et al⁷ in his study reported that low grade lymphomas had a lower apoptotic indices < 2.4% which is in concurrence with our study which showed that of 21 low grade lymphomas, 18 cases had apoptotic indices of less than 2.4% and 3 cases had apoptotic indices greater than 2.4%. So these cases have an increased chance of behaving as a lower grade with good prognosis and a survival outcome.

Soini et al¹⁹ in his study on "histopathological evaluation of apoptosis in cancer" reported that there is variation in apoptotic indices in varying grades of lymphomas. He also stated that high grade lymphomas and intermediate grade lymphomas show wide range of apoptotic indices from 2.5-8.8. Leoncini et al, in his study has reported that there was a tendency for greater dispersion of cases

towards higher Apoptotic index in high grade than in intermediate grade NHLs. In our study, of 23 cases of intermediate grade lymphomas,

12 cases had apoptotic indices value greater than 2.4% and the remaining 11 cases had a value less than 2.4%.

Roser et al.²⁰ in his study on apoptotic index has shown a direct correlation with the proliferative index, corresponding to a more aggressive clinical course of the disease. In our study, of 13 cases of high grade lymphomas, 10 cases had apoptotic indices ranging from 2.5-6.5% and 3 cases had apoptotic indices value of less than 2.4 %. In our study, all the high grade lymphomas that were classified by working formulation exhibited clearly higher indices for apoptosis indicating the aggressiveness of the tumour.

5. Conclusion

Though working formulation classification of Non Hodgkin lymphoma holds good for many cases it has its drawbacks. So by the use of these inexpensive and an effective prognostic indicator along with the working formulation classification it may throw some light on the how a particular subtypes of Non hodgkin lymphoma in a particular patient might behave. These results have important implications for understanding the fundamental biology of cell death, its roles in malignant disease, and the broader consequences of apoptosis-inducing anti-cancer therapy.

6. Conflict of Interest

None.

7. Source of Funding

None.

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