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Morphological classification of childhood acute lymphoblastic leukaemia by French American British (FAB) classification and study of prognosis of pure Burkitt leukemia and Burkitt lymphoma- 02 year study in our institute

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ABSTRACT

Abstract Acute leukemias are a heterogeneous group of neoplasms with differences in clinical course, prognosis and treatment between the groups. Nikolaus Friedreich in 1857 attempt to classify leukemias and categorized leukemias as acute and chronic. FAB classification, classified. Acute lymphoblastic leukemia (ALL) into L1, L2, and L3. In the FAB system, the cut off blast percentage for making a diagnosis of acute leukemia was 30%. and L3 varient of ALL is pure Burkitt leukemia PBL. Both PBL and Burkitt lymphoma/leukemia, presenting with a tumor mass and marrow involvement (BLL), which is associated with a poor prognosis.

Aims and objectives: To classify various types of ALL according to FAB classification and to study prognosis of various types of ALL ie L1, L2 and L3.

Materials and methods: It is a prospective study done over a period of 2 years (July 2017 – June 2019) in M.Y. Hospital. Total 255 cases of ALL included presented with clinical complain of fever ,pallor, weakness, fatigue, infections petechiae , bruising and bleeding manifestation, organomegaly (lymph nodes ,spleen ,liver ,others), bone pain ,tenderness, gum hypertrophy, CNS symptoms and CBC with peripheral smear examination done . Bone marrow aspiration and flow cytometry were done in all cases for the final diagnosis.

Result: Acute lymphoblastic leukaemia (ALL) 255 cases were taken , 35 cases (13%) showed appearances classifiable as type L2 by the French American and British (FAB) cooperative group's criteria, 21 (8.2%) were typed L3, and the remaining 199 (78%) as L1. This study identified L1 varient of ALL show best prognosis and L3 varient of ALL show worst prognosis. Also 21 patients having L3 ALL, which included 9 PBL and 12 BLL cases .Patients with PBL had a significantly better survival than the BLL group. The overall survival of patients with PBL treated with intensive chemotherapy is superior to those with BLL who are similarly treated. Disregarding the patients classified as L3, those with the L1 &L2 variant showed an inferior disease free survival to that of the remainder and more of them failed to remit after receiving "standard" remission induction treatment .These findings confirm earlier reports that FAB L3, ALL is associated with a poor prognosis and that it occurs more commonly in older children. The high remission failure rate is a recent observation and indicates that alternative early treatment may be appropriate for such patients.

CONCLUSION -We have found that when ALL classification done by FAB shows maximum cases were of L1 type followed by L2 type and L3 type or PBL .Also L1 ALL has better prognosis and L3 has worst prognosis and PBL has a favourable prognosis when compared to BLL.

Keywords: lymphoblastic leukaemia (ALL), French American and British (FAB) classification, Pure Burkitt leukaemia (PBL) and Burkitt lymphoma (BLL).

INTRODUCTION

Acute leukemias are a heterogeneous group of neoplasms with differences in clinical course, prognosis and treatment between the groups, with the invent and application of target-based approach to therapy, their classification needs to be precise, facilitating non-overlapping identification of the differing entities, incorporating all the essential and new information. The perspective of the classification of any disease is to treat them

according to their biologic behavior. Nikolaus Friedreich in 1857, attempt to classify leukemias and categorized leukemias as acute and chronic. In 1868, Neumann used the term "myelogenous" to imply that leukemias arise from the bone marrow.[1.] Though the morphological approach to classify acute leukemias has always been in progress, standard criteria to distinguish between myeloid and lymphoid acute leukemias and to subtype them further, based on morphology and cytochemistry were laid down as the first of its kind, in 1976, by the FAB working group.[2,3].Acute lymphoblastic leukemia (ALL) had been classified by FAB into L1, L2, and L3 (Table 1) 7.ALL L3 is equivalent to burkitt lymphoma /leukemia. In the FAB system, the cut off blast percentage for making a diagnosis of acute leukemia was 30%.[2] L3 varient of ALL is pure Burkitt leukemia; PBL. However, leukemic presentation of Burkitt lymphoma in the absence of a mass is uncommon. Both PBL and Burkitt lymphoma/leukemia, presenting with a tumor mass and marrow involvement (BLL), which is associated with a poor prognosis.

Burkitt lymphoma is an uncommon and aggressive mature B-cell neoplasm characterized by high proliferation and MYC translocation. Most cases of Burkitt lymphoma present with tumor masses, with bone marrow involvement typically occurring in the setting of bulky disease. However, rare cases of Burkitt lymphoma may involve only the bone marrow without clinical or radiographic evidence of a tumor mass, so-called pure Burkitt leukemia (PBL). In the past, such patients were considered to have ''L3'' B-lymphoblastic leukemia [3] with a mature phenotype. Patients who present with PBL are classified as having stage IV disease by the Ann Arbor or St. Jude staging systems. Burkitt lymphoma is a highly curable disease when treated with modern intensive chemoimmunotherapy [4]. Clinical studies have found that increased age, black race/ethnicity human immunodeficiency virus (HIV) infection and advanced stage are associated with shorter survival [5,6] In our study we noticed that cases of PBL appear less aggressive than cases of Burkitt lymphoma which present with a tumor mass and bone marrow involvement (BLL) when treated with intensive chemotherapy.

Table 1: FAB classification of acute lymphoid leukemias

L1	: Small, homogenous cells with inconspicuous/1--2 nucleoli
L2	: Large cells with variable size with 1--2 nucleoli
L3	: Large cells, homogenous, finely stippled chromatin with basophilic vacuolated cytoplasm

Table 2: WHO classification of acuteLymphoid leukemias 2001
Precursor B-cell neoplasm
Precursor B-lymphoblastic leukemia
Mature B-cell neoplasm
Burkitt leukemia
Precursor T-cell neoplasm
Precursor T-lymphoblastic leukemia

MATERIALS AND METHODS

It is a prospective study done over a period of 2 years (July 2017 – June 2019) in M.Y. Hospital. Total 255 cases of ALL included presented with clinical complain of fever ,pallor, weakness, fatigue, infections petechiae , bruising and bleeding manifestation, organomegaly (lymph nodes ,spleen ,liver ,others), bone pain ,tenderness, gum hypertrophy, CNS symptoms and CBC with

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peripheral smear examination done . Bone marrow aspiration and flow cytometry were done in all cases for the final diagnosis.

RESULTS AND OBSERVATION Acute lymphoblastic leukaemia (ALL) 255 cases were taken , 35 cases (13%) showed appearances classifiable as type L2 by the French American and British (FAB) cooperative group's criteria, 21 (8.2%) were typed L3, and the remaining 199 (78%) as L1. Bone marrow aspiration of ALL-L1 (figure-1a &1b) shows Small, homogenous cells with inconspicuous/1-2 nucleoli ,ALL-L2 (figure-2a & 2b) shows large cells with variable size with 1-2 nucleoli in and ALL-L3 (figure -3a & 3b) show lymphoblast having intensily basophilic cytoplasm regular cellular features cytoplasmic vaculation with starry sky pattern.

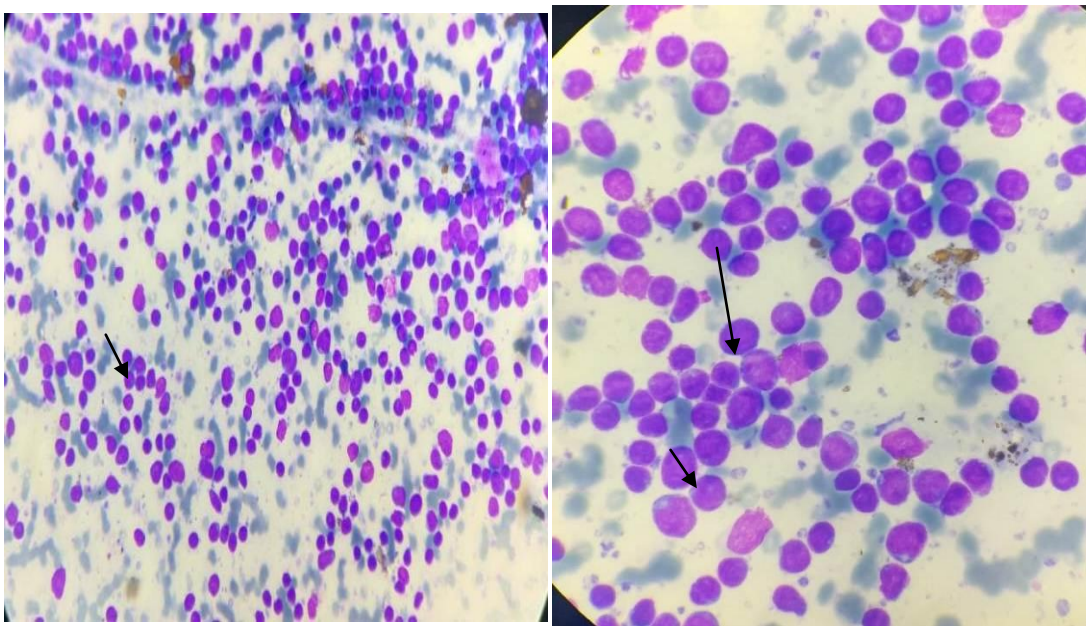

Figure 1a (40X) &1b (100X) ALL L1 –Show hyper cellular marrow with small lymphoblast and inconspicuous nuclei (marked by black arrow)

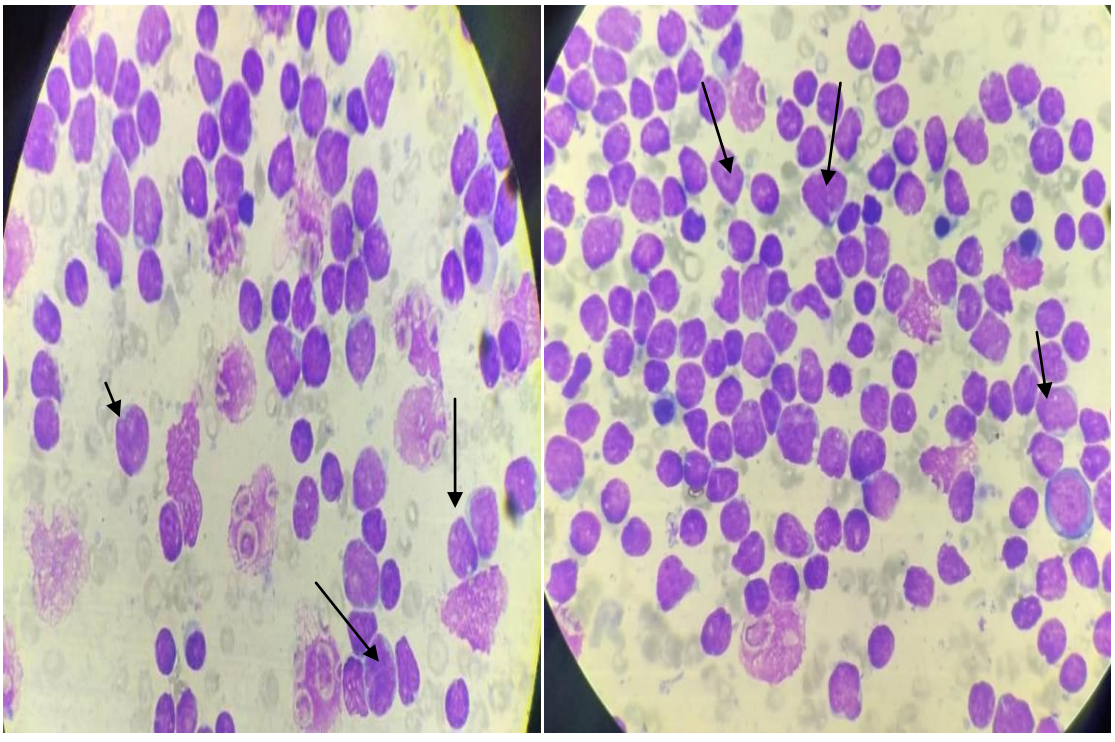

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Figure 2a (100X) &2b (100X) ALL L2 –Show hyper cellular marrow with large cleaved lymphoblast (marked by black arrow)

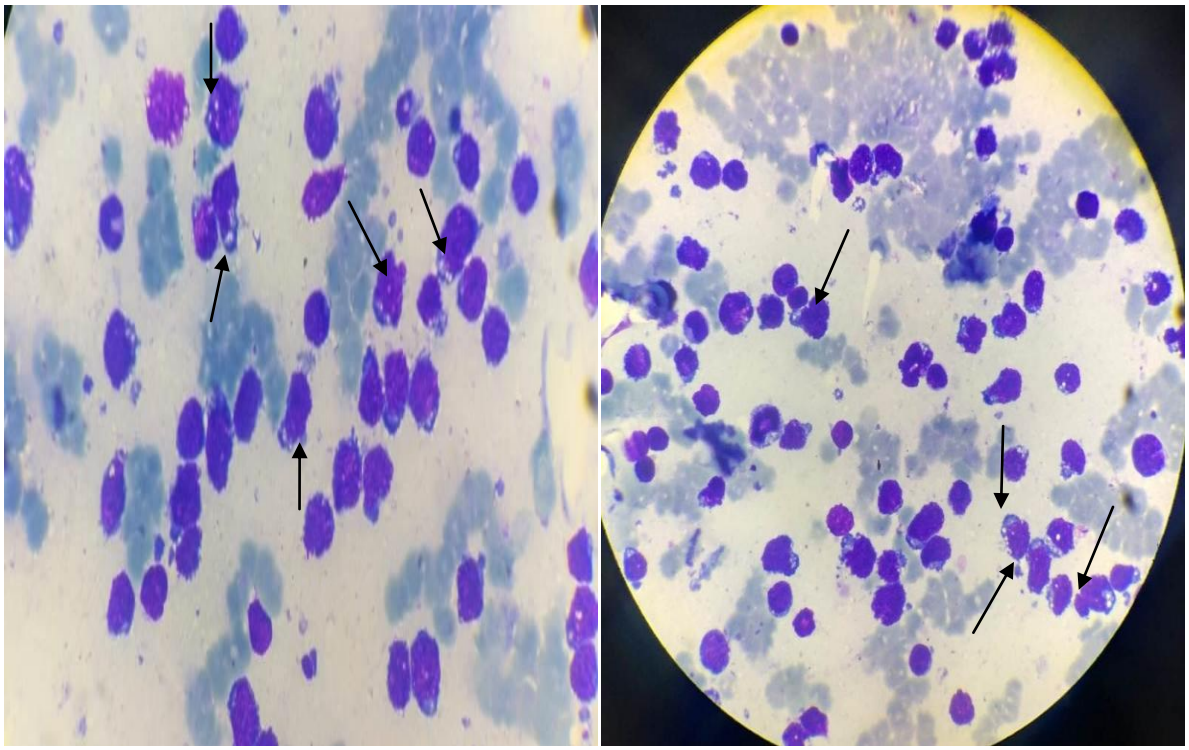
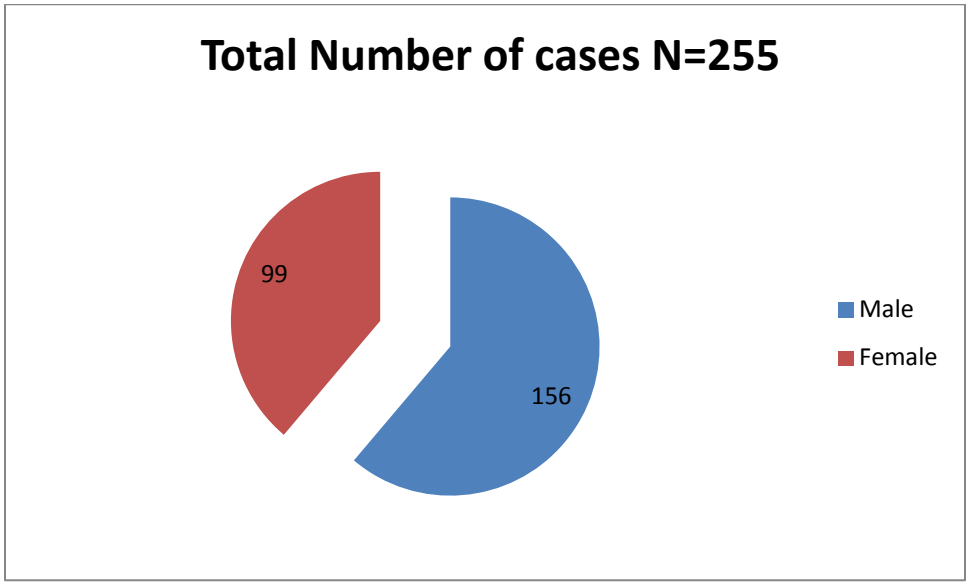


Figure 3a (100X) & 3b (100X) ALL L3 –Hyper cellular marrow showing lymphoblast having cytoplasmic vaculation with starry sky pattern (marked by black arrow)

Graph 1: SEX WISE DISTRIBUTION OF CASES



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Graph 2: AGE WISE DISTRIBUTION OF CASES

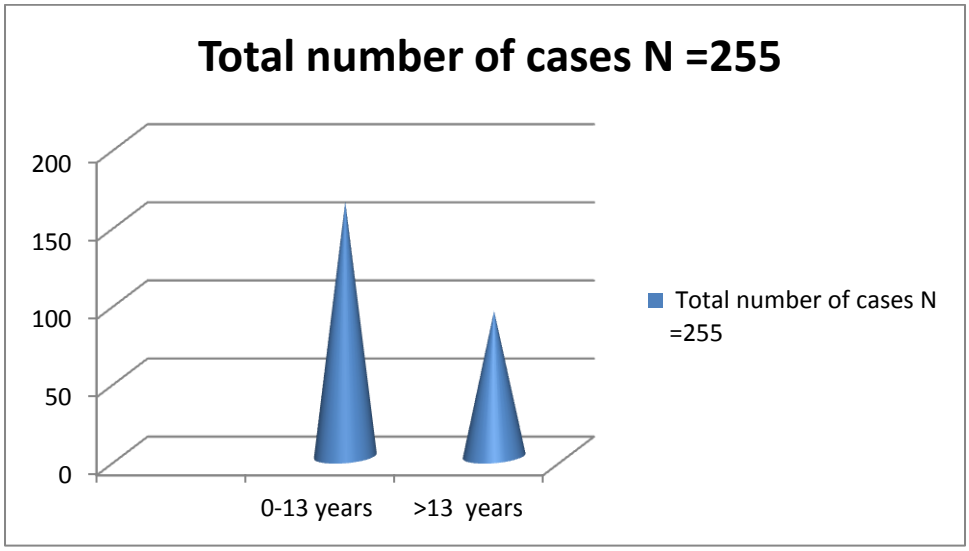

Table 3 Number of cases according to FAB classification of ALL

FAB classification	Cases N=255	Percentage
L1	199	78 %
L2	35	13%
L3 or PBL	9	3.5%
L3 or BLL	12	4.7%

Disregarding the patients classified as L3, those with the L1 &L2 variant showed an disease free survival to that of the remainder and more of them failed to remit after receiving "standard" remission induction treatment .These findings confirm earlier reports that FAB L3, ALL is associated with a poor prognosis and that it occurs more commonly in older children. The high remission failure rate indicates that alternative early treatment may be appropriate for such patients.

DISCUSSION The three morphological groups of ALL defined by the FAB group [7,8] are grossly unevenly distributed. We found a prevalence of 78%, 13%, and 8.2 % for L1, L2, and L3 types, respectively, in a group of 255 consecutive patients. Using the FAB group's scoring system . L2 ALL occurs more commonly in older children, is associated with less profound bone marrow failure, and it also more often does not express the common ALL antigen. Apart from these distinguishing clinical features, there is also a trend emerging for patients with L2 disease to have a worse prognosis compare to L1 disease. The worse prognosis for patients with L2 disease was first noted in 1978 by a Hungarian group3 and later confirmed by Hann et al in the United Kingdom.[9] Viana et al[10] not only indicated that patients with L2 disease had a poorer outlook but noted that more of them were older when compare with L1 disease cases. The clinical importance of ALL FAB type seems to be fairly clear. L2 ALL is a more refractory disease compare to L1 and so is a logical candidate for alternative treatment. We observed in our study which shows L1 ALL has better prognosis and L3 has worst prognosis also PBL has better survival than BLL. Burkitt lymphoma is a curable disease with intensive immunochemotherapy [11,12,13,14]. Both the Ann Arbor and St Jude staging systems consider Burkitt lymphoma with bone marrow involvement to be stage IV, which is associated with a very poor

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outcome[15], with both PBL and BLL included together as stage IV disease. Burkitt lymphoma is the second most common lymphoid neoplasm in HIV-infected patients[16].

CONCLUSION -We have found that when ALL classification done by FAB shows maximum cases were of L1 type followed by L2 type and L3 type or PBL .Also L1ALL has better prognosis and L3 has worst prognosis and PBL has a favorable prognosis when compared to BLL. Our findings suggest that PBL is biologically different from BLL, and should be considered separately from other cases of stage IV Burkitt lymphoma for prognostication and selection of therapy in the future.

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