Section: Pathology

Original Research Article

HEMATOLOGICAL PROFILE OF T AND B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA CASES IN A TERTIARY CARE HOSPITAL: A 2 YEAR STUDY OF 100 CASES

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Abstract

Background: There has been an increasing trend in the incidence of acute lymphoblastic leukemia cases since 1990. ALL was the number one cause of DALYs (disability adjusted life years) and deaths in India in 2019 for both boys and girls aged 0 to 20 years. We aim to analyze the prevalence of both cell types (B & T) of acute lymphoblastic leukemias in our demography, with specific clinicopathological correlations.**Materials and Methods:** Patients with a provisional diagnosis of acute leukemia, from in and out patient departments of Pediatrics, Medicine and Medical Oncology and those received in department of Pathology-Madurai Medical College were selected. Samples of blood and bone marrow smears of total 102 cases of acute lymphoblastic leukemia for 2 years were analysed. **Results:** Overall, 79.4% were of pediatric age group and 20.6% were of adult category. The mean age of presentation was 10.4 years. ALL commonly presented in the male gender with 69 cases compared to 31 cases of females. Analysis of the hematological profiles showed that Mean hemoglobin concentration was 8.75 g/dl. Around 45.1% patients presented with leucopenia and leucocytosis was seen only in 15.7%. Nearly half of the patients (45.1%) had normal platelet count. Of the 102 cases, 4 patients had relapse and 2 were defaulters. **Conclusion:** The study of hematological profile of 102 cases of acute lymphoblastic leukemia in the demography of South Tamilnadu is an attempt to analyse the prevalence and remission rates of this population.

INTRODUCTION

Acute lymphoblastic leukemia (ALL)/lymphoblastic lymphoma (LBL) is a clonal hematopoietic stem cell disorder of B or T cell origin. The World Health Organization (WHO) 2017 classification system categorizes these disease entities under precursor lymphoid neoplasm which includes 4 distinct entities: B-ALL/LBL not otherwise specified (NOS); B-ALL/LBL with recurrent genetic abnormalities; T-ALL/LBL; and NK-ALL/LBL.[1] According to the Global Burden of Disease Study 2019, there was a global increase in cases of ALL from 66,810 cases in 1990 to 153,320 cases in 2019.[2] New ALL cases increased by 1.29% worldwide with a critical rise in cases among older individuals.[2] In India, the incidence of leukemias for the past 29 years has steadily increased, accounting for 6.8% as of 2019.[3] ALL was the number one cause of DALYs (disability adjusted life years) and deaths in India in 2019 for both boys and girls aged 0 to 20 [3]. Patients with leukemia in resource limited settings in India often have a worse prognosis due to low awareness, late detection and limited access to affordable treatment options. [4] Therefore we aim to analyze the prevalence of both cell types (B & T) of acute lymphoblastic leukemias in our demography, with specific clinicopathological correlations in order to provide valuable insights into the recent shifting patterns in leukemias.

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MATERIALS AND METHODS

Place of study- Department of Pathology, Madurai Medical College, Tamil Nadu
Type of study- Prospective and retrospective
Study period -2 years
Sampling methods- Patients with a provisional diagnosis of acute leukemia, from in and out patient departments of Pediatrics, Medicine and Medical Oncology and those received in department of Pathology-Madurai Medical College were selected.
Study population –102 cases of acute lymphoblastic leukemias
Sample collection- Blood, bone marrow smears.
Inclusion criteria

1. All cases confirmed as acute lymphoblastic leukemia by flow cytometry.
2. All cases being treated for acute lymphoblastic leukemia

The study was conducted after approval from institutional ethical committee in the Department of Pathology, Madurai Medical College, Tamil Nadu from Oct 2022 to Nov 2024. Total of 102 cases of flow cytometry confirmed ALL were selected from department of Pathology, Madurai Medical College. Available case history and clinical details such as - Hemoglobin, WBC count, Platelet count and various hematological indices were evaluated using automated analyzer. Peripheral blood/bone marrow smear was made on clean glass slides with fresh blood samples; Air dried unfixed smears were flooded with Leishman stain for a period of 2 minutes, and then added twice quantity of buffered distilled water for next 2-7 minutes. The stained smears were examined under the microscope. A diagnosis of acute leukemia was made if blasts were > 20% in the bone marrow sample. Lineage and immunophenotyping of the leukemia cases as B or T was done by flow cytometry in new cases. Follow up cases on treatment were also handled in a similar fashion, to detect relapse. The protocol followed to treat the ALL cases was Modified BFM (95/2002) protocol.
Data analysis: Statistical analysis was performed using V.25.0 Statistical Package for the Social Sciences (SPSS). Continuous variables were expressed as mean and standard deviation. Categorical variables were expressed as frequency and percentage with 95% confidence interval. Chi-square test and Fisher's exact test (when expected frequencies were <5) were used to find out the association between categorical variables. The significance level was set at <0.05 in all cases. The multivariable analysis includes the variables which are associated with the outcome in bivariate analysis.

RESULTS

The study included 102 cases of ALL with 89 B-cell and 13 T-cell immunophenotype [Table1]. Overall, 79.4% were of pediatric age group and 20.6% were of adult category. The mean age of presentation was 10.4 years. ALL commonly presented in the male gender with 69 cases compared to 31 cases of females. Analysis of the hematological profiles showed that 44% of patients had moderate anemia and 26% had severe anemia during presentation. Mean hemoglobin concentration was 8.75 g/dl [Table2]. Around 45.1% patients presented with leucopenia – WBC count less than 4000 cells/cu.mm whereas 39.2% did have a normal WBC count. Mean WBC count was 9782.35 cells/cu.mm. Leukocytosis was seen only in 15.7% [Table3]. Nearly half of the patients (45.1%) had normal platelet count. Mean platelet count was 133769.6 cells/cu.mm[Table4]. Of the 102 cases, 4 patients had relapse and 2 were defaulters [Table 5].

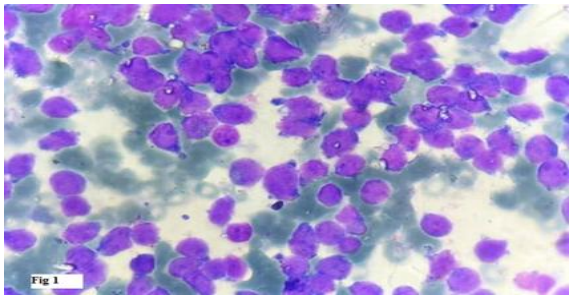

Figure 1: Bone marrow aspiration smears showing sheets of lymphoblasts (oil immersion, 100X)

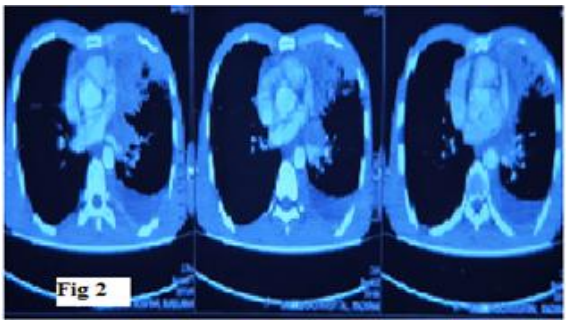

Figure 2: CT thorax with mediastinal mass and arch of aorta encasement

Table 1: Type of ALL.

Type	Frequency	Percentage
B cell ALL	89	87.3
T cell ALL	13	12.7
Total	102	100.0

Table 2: Haemoglobin levels

Haemoglobin (g/dl) & anemia	Frequency	Percentage
Hb >12	25	24.5

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Hb 9-11 (mild)	6	5.9
Hb 7-9 (moderate)	44	43.1
Hb 4- 6 (severe)	26	25.5
Hb < 4 (very severe)	1	1.0
Total	102	100.0

Table 3: WBC count

Total count (cells/mm3)	Frequency	Percentage
< 4500	46	45.1
4500 - 11000	40	39.2
>11000	16	15.7
Total	102	100.0

Table 4: Platelet levels

Platelet count(cells/mm3)	Frequency	Percentage
<10000	1	1.0
10000 - < 50000	22	21.6
50000 - <1 lakh	24	23.5
1 lakh - <1.5 lakh	5	4.9
1.5 lakh - 4 lakh	46	45.1
> 4 lakhs	4	3.9
Total	102	100.0

Table 5: Outcome category

Category	Frequency	Percentage
Remission	96	94.1
Relapse	4	3.9
Default	2	2.0
Total	102	100.0

Table 6: Association between the patient characteristics and the outcome

Patient characteristics	Remission	Relapse	p Value
Sex			
Male	15 (15.3 %)	2 (50 %)	0.068
Female	4 (4.1 %)	0	
Male child	50 (51%)	2 (50 %)	
Female child	29 (29.6%)	0	
Type of ALL			
B cell	86 (87.8 %)	3 (75 %)	0.425
T cell	12 (12.2 %)	1 (25 %)	
Hemoglobin (g/dl)			
Normal (12)	24 (24.5 %)	1 (25 %)	0.411
Mild (9-11)	5 (5.1 %)	1 (25 %)	
Moderate (7-9)	43 (43.9%)	1 (25 %)	
Severe(4-6)	25 (25.5%)	1 (25 %)	
Very severe(<4)	1 (1%)	0	
WBC(cells/mm3)			
<4500	43 (43.9%)	3 (75%)	
4500 - 11000	40 (40.8 %)	0	0.428
>11000	15 (15.3 %)	1 (25 %)	
Platelet (cells/mm3)			
< 10000	1 (1 %)	0	0.151
10000 – < 50000	20.4 (20 %)	2 (50 %)	
50000 - < 1 lakh	23 (23.5%)	1 (25%)	
1 – < 1.5 lakh	5 (5.1%)	0	
1.5 - -4 lakh	45 (45.9%)	1 (25%)	
> 4 lakh	4 (4.1%)	0	

With reference to the association between the patient characteristics and the outcome ,categorical variables were associated with the outcome using Chi-square test and Fisher's exact test (when expected frequencies were <5) [Table 6]. The significance level was set at <0.05 in all cases. No statistically significant difference was observed. The treatment outcome is not dependent on the age, sex, type of ALL or the hematological values.

The multivariable backward regression model shows multivariable analysis and includes the variables which are associated with the outcome in bivariate analysis [Table 7].On the basis of bivariate analysis, the following variables are associated with the outcome such as, age, type of leukemia, hemoglobin levels, WBC count and platelet count. The final model reveals that the most variable are independent of the outcome as their significance P>0.05.

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Table 7: Multivariable regression model to predict the outcome based on independent variables

Independent variables	Beta (β)	SE (β)	p-value
Age	0.022	0.030	0.459
Hemoglobin	0.064	0.187	0.731
WBC	0.000	0.000	0.567
Platelet	0.000	0.000	0.888
Type of ALL	144	1.607	0.929

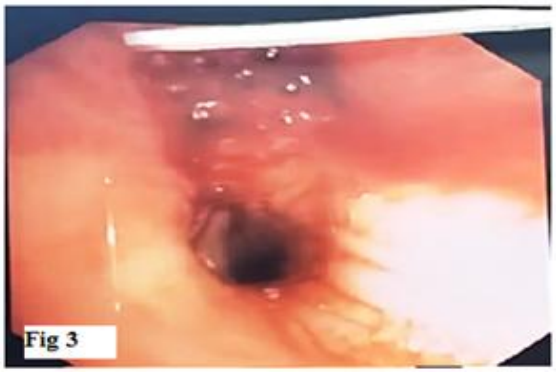

Figure 3: Bronchoscopy showing mucosal irregularity

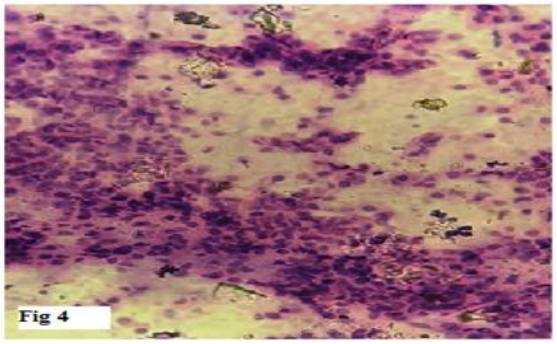

Figure 4: Bronchoalveolar lavage fluid showing atypical lymphoid cells (high power, 40X)

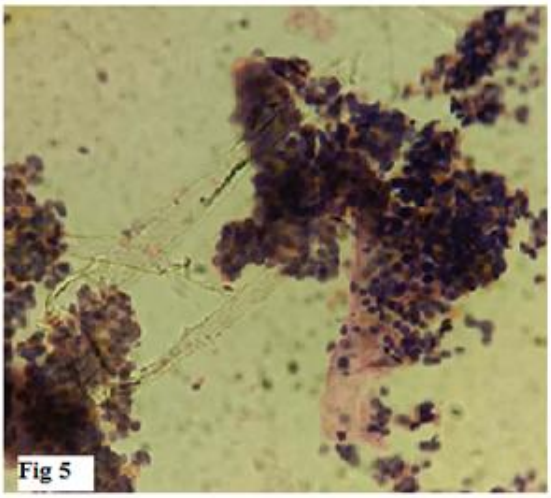

Figure 5: Pleural fluid cytology showing clusters atypical lymphoid cells (high power, 40X)

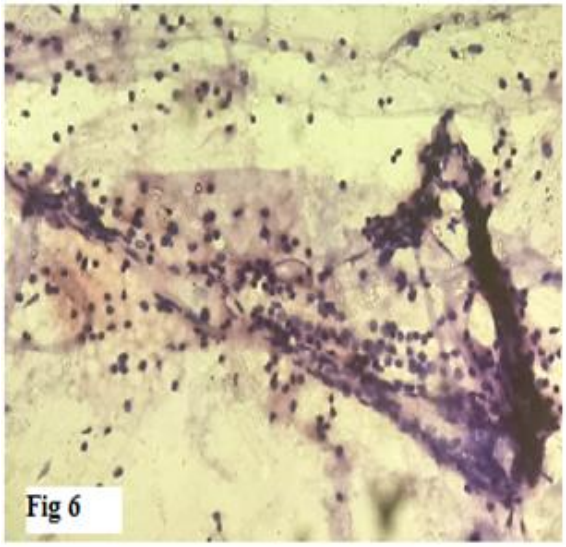

Figure 6: Axillary node FNAC smears showing sheets of atypical lymphoid cells (high power, 40X)

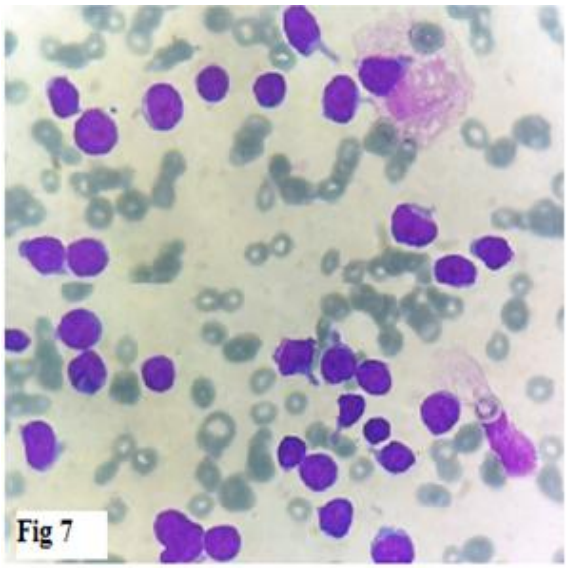

Figure 7: Peripheral smear showing lymphoblasts with scanty cytoplasm and coarse chromatin (oil immersion, 100X)

DISCUSSION

Acute lymphoblastic leukemia is a neoplasm of precursor lymphoid cells committed to the B cell or T cell Lineage.[5]It is the second most common acute leukemia in adults.[6] ALL is characterised by the presence of small-to-medium sized blast cells with scant cytoplasm, moderately condensed to dispersed chromatin & inconspicuous nucleoli involving the bone marrow and blood.[5]A diagnosis of ALL is essentially made only when there are >20% blasts in

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marrow [Figure 1].[5]Haematological parameters show a diverse presentation during diagnosis and during treatment. Patients may present with bone marrow failure (anemia, thrombocytopenia, neutropenia), with normal, increased or decreased WBC count.The overall remission rate is >95% in children and 60 – 85% in adults.[5]Infancy, older patient age, higher WBC count, slow response to initial therapy as assessed by morphological examination of blood and bone marrow and minimal residual disease proven by flow cytometry are all associated with worse prognosis.[5]So strict follow up of these patients is essential to prevent relapse and further management.

In this study, a total of 102 cases have been diagnosed as acute lymphoblastic leukemia, based on clinical features, hematological parameters, morphology of leukemic cells and their immunophenotype. In our study, males were the most commonly affected (69.4%) which was comparable to Shuchismita S et al, [7] (2022) where 61.7% were males. This was also consistent with similar studies.[8-11]B cell ALL was more frequent (87.3%) which was similar to Bhattacharyya et al (2013), where out of 60 cases of ALL , 68.3% turned out to be B cell ALL and Dakka N et al(2007) with 67% B cell ALL.[9,11] The mean age of presentation in our study was 10.4 years which was roughly similar to 11 years in Gupta DG et al(2023).[10] Mean hemoglobin concentration of our study was 8.75 g/dl. This was nearly similar to Gupta DG et al (2023) where the mean hemoglobin was 7.9g/dl.[10] In the present study 94.1% had remission after induction, comparable to 93.4% remission rate in Garg et al (2023).[12] This was liken to 83–95% remission rate in children with ALL at the end of induction at various centers across India, as reported in a review by Arora et al(2016).[13] Complete remission was obtained in 88% and 84% of B-ALL and T-ALL, respectively and relapses after 1 year occurred in 30% and 37% of cases, respectively in the study by Dakka N et al.[11] This rate was high compared to our study with a relapse rate 3.9%, though our study did have few cases lost to follow up. The relapse was found to occur in males predominantly in our study.

We would like to highlight one case that we encountered with a unique presentation. A 35 – year – old male presented with complaints of acute onset cough, hemoptysis, and breathlessness. CT thorax revealed a mass lesion in anterior & middle mediastinum with encasement of arch of aorta and left pulmonary artery along with left upper lobe consolidation [Figure 2]. Bronchoscopy of left upper division bronchus showed extrinsic compression with mucosal irregularity [Figure 3]. Bronchoalveolar wash cytology revealed clusters of atypical lymphoid cells [Figure 4]. Pleural fluid cytology also showed similar atypical lymphoid cells [Figure 5]. Following this, a complete blood workup along with an axillary node fine needle aspiration was done. The cytology smears from the axillary node were composed of atypical lymphoid cells [Figure 6]. The peripheral smear [Figure 7] and bone marrow showed 60% and 90% blasts respectively. Flow cytometry confirmed a diagnosis of T cell – acute lymphoblastic leukemia (CD 45-99%, cytoplasmic CD3 – 99%, CD 5-98%, CD 7-98%).

The challenges we faced in a resource limited setting was the inability to do genetic studies like FISH/PCR and ploidy analysis due to financial constraints. Also, determination of MRD (minimal residual disease) levels in this population would provide an insight into prognosis and risk of relapse.

CONCLUSION

The study of hematological profile of 102 cases of acute lymphoblastic leukemia in the demography of South Tamil Nadu is an attempt to analyse the prevalence and remission rates of this population. We hope this data would provide further insights into correlation with genetic analysis and molecular rearrangements of such cases in the future.

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