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RESEARCH ARTICLE

IMMUNOPHENOTYPIC PROFILE OF T ACUTE LYMPHOBLASTIC LEUKAEMIA IN A TERTIARY CARE CENTRE - OUR EXPERIENCE

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Abstract

Background: Studying the immunophenotypic profile of T-ALL patients in Kashmir and correlation of various demographic factors.

Methods: 36 patients of all age groups were registered for this study of which 35 were included in the analyses.

Result: 82.86% were males and 17.14% were females. 51.43% had common thymocyte T-ALL, 28.57% had pro T-ALL and 20% had mature thymocyte T-ALL. The average age at presentation was 18.60 years. 51.43% were CD1a positive. CD2 was positive in 70.83%. 88.57% were CD5 positive while 100% were positive for CD7. 42.86% were CD34 positive. The average bone marrow blast percentage was 82.43%. The average peripheral blood TLC was 92.73×10^3 cells/cumm.

Conclusion: This is the first study to report immunophenotypic and demographic profile of T-ALL in Kashmir with the aim to increase understanding of the disease and contributing to more suitable treatment options.

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Introduction:-

Acute leukaemias are the commonest group of cancers in children, both worldwide and in India[11, 2]. Of these, Acute Lymphoblastic Leukaemia (ALL) accounts for 75-80% cases, with 21-50% of these having T-ALL[1]. In Kashmir, two studies on ALL found an incidence of T-ALL of 30.6% (all age groups) and 22.2% (paediatric population)[4, 6]. T-ALL is the disease committed to any stage of T-cell lineage in which patients present with fever, enlarged thymus gland, bleeding, bruising, recurrent infections, tiredness for unknown reason, abdominal pain, and hyperkalaemia related symptoms[7]. A combination of clinical features and multiple laboratory investigations such as immunophenotyping, cytogenetic and molecular studies, are required for diagnosis and prognosis of the disease. Examination of peripheral blood film, bone marrow aspirate/biopsy can help diagnose acute leukaemia. However, morphology alone is not sufficient for accurate diagnosis since there is considerable overlap between morphology of myeloblasts and lymphoblasts and further between B lineage lymphoblasts and T lineage lymphoblasts. Immunophenotyping, using flow cytometry or immunohistochemistry, is the gold standard for exact characterization of blasts. Flow cytometry is reliable and much quicker, with final reports being prepared in a few hours from time of receiving sample.

The immunophenotype reflects thymic T cells which have a distinctive maturation pattern and the blasts show varying maturity. The flow cytometry results revealed that all the patients included in the study were confirmed to

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have T-ALL due to the presence of various T cell markers with absence of B/Myeloid markers. There are no previous papers in the literature that have studied the characteristics of T-ALL in Kashmiri patients. Hence, the full picture of the disease development and outcome in this group is not completely understood. We sought to study and classify the immunophenotype characteristics of Kashmiri patients diagnosed with T-ALL and to correlate the results with age and gender as well as biological factors (peripheral total leukocyte counts and bone marrow blast percentage) to understand the characteristics of the disease in Kashmiri patients. This will guide us to better predict disease outcome and decide a suitable plan of treatment.

Materials And Methods:-

All T-ALL patients were included in this study who had registered in our hospital from October 2015 to September 2020. These totalled 36 cases. All relevant data pertaining to these patients was obtained from the hospital information system database. Informed consent was taken from the patients or their guardians as well as approval from the ethics board of our hospital. Patients with missing data regarding diagnosis or insufficient sample for obtaining results were excluded from the study.

A comprehensive panel of monoclonal antibodies was run for each sample received and patients were divided into three subgroups, based on the World Health Organisation (WHO) Classification i.e. proT (cyCD3+, CD7+, CD1a-, sCD3-), common thymocyte (cyCD3+, CD7+, CD1a+) and mature thymocyte (cyCD3+, CD7+, CD1a-, sCD3+). Results were correlated with demographic factors (age and gender) as well as bone marrow blast percentage and TLC.

Results:-

Out of 36 total cases, 7 were female. However, one female was a case of T-ALL turned Therapy related AML and her previous records of T-ALL diagnosis were unavailable. Hence, she was excluded from the study.

Of the remaining 6 females, 4 (11.43%) were diagnosed with pro T-ALL phenotype, 1 (2.86%) with common thymocyte T-ALL and 1 (2.86%) was diagnosed with mature thymocyte T-ALL phenotype. Of the 4 cases with pro T ALL, 1 was diagnosed as ETPALL (Early T cell Precursor Acute Lymphoblastic Leukaemia) (Table 1).

Among the remaining 29 male cases, 6 (17.14%) were diagnosed with pro T-ALL phenotype, 17 (48.57%) with common thymocyte T-ALL phenotype and 6 (17.14%) with mature thymocyte T-ALL phenotype (Table 1).

Overall, 10 cases (28.57%) were of pro T-ALL phenotype, 18 (51.43%) were of common thymocyte phenotype and 7 (20%) were of mature thymocyte phenotype (Table 1).

	T-ALL subsets				Total
		Pro T-ALL	Common thymocyte T-ALL	Mature thymocyte T-ALL	
Gender	Male count, n	06	17	06	29
	Total, %	17.14	48.57	17.14	82.86
	Female count, n	04	01	01	06
	Total, %	11.43	2.86	2.86	17.14
Total	Total count, n	10	18	07	35
	Total, %	28.57	51.43	20	100

Table 1:- T-ALL=T Acute Lymphoblastic Leukaemia.

The average age of patients with pro, common thymocyte and mature thymocyte T-ALL was 31.4, 12.8 and 14.67 years (6 of 7 cases of mature thymocyte T-ALL as age of one patient was not mentioned in records), respectively. Among female patients, the average age at presentation was 21.83 years and among males, it was 17.3 years. The average age of T-ALL cases as a whole (34 of 35) was 18.60 years.

CD1a was positive in 18 cases of common thymocyte T-ALL (as per definition) (51.43%) and negative in remaining 17 (48.57%) cases of pro and mature thymocyte T-ALL (Fig 1).

CD2 was run in all cases except 11. In the remaining 24 cases, CD2 was positive in 17 (70.83%) and negative in 7 (29.16%). Among the 17 positive cases, 7 cases were of pro T-ALL, 8 were of common thymocyte T-ALL and 2 were of mature thymocyte T-ALL.

CD3, being a lineage marker specific for T cells, was positive in all cases. Cytoplasmic CD3 was not run in 13 cases while surface CD3 was not run in one case. All 13 cases (37.14%) showed surface positivity, 19 cases (54.29%) showed cytoplasmic positivity and 3 cases (8.57%) showed both surface and cytoplasmic positivity.

CD5 was positive in all cases (88.57%) except 4 (11.43%). 17 cases were of common thymocyte T-ALL and 7 cases each were of pro and mature thymocyte T-ALL (Fig 1).

CD7 was positive in every case.

CD34 was positive in 15 cases (42.86%) and negative in 20 cases (57.14%) overall. Among 15 positive cases, 8 were of pro T-ALL, 5 were of common thymocyte T-ALL and 2 were of mature thymocyte T-ALL (Fig 1).

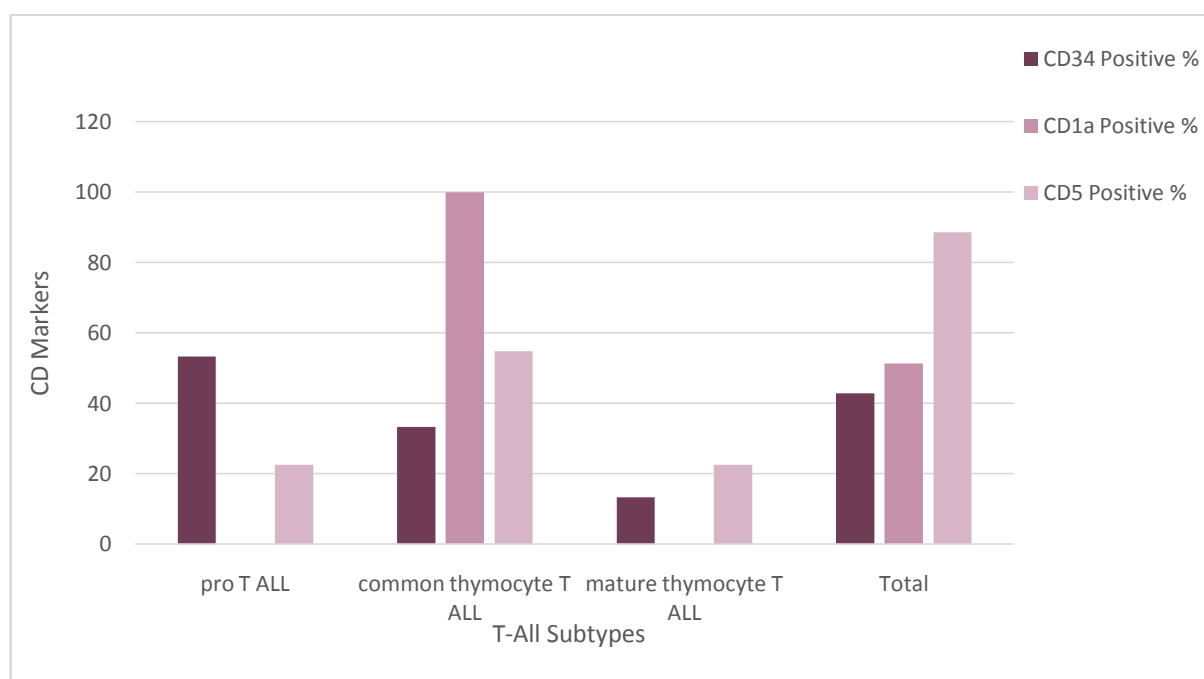


Fig 1:- Expression between CD markers and T acute lymphoblastic leukaemia subtypes.

15 patients did not have marrow reports or flow was done on peripheral blood.

21 patients had marrow reports. The average blast percentage on bone marrow was 82.43%, with the highest being 99% and the lowest being 06%. For pro T-ALL, it was 68.5%. For common thymocyte T-ALL, it was 92.4% and for mature thymocyte T-ALL, it was 86.33%.

The average peripheral blood TLC was 92.73×10^3 cells/cumm, with the highest being 453.1×10^3 and the lowest being 1×10^3 . For pro T-ALL, it was 78.07×10^3 cells/cumm. For common thymocyte T-ALL, it was 60.85×10^3 cells/cumm and for mature thymocyte T-ALL, it was 238.1×10^3 cells/cumm.

Discussion:-

T-ALL is a relatively rare disease and paucity of cases as well as incomplete data documentation at our institution made it even harder to correctly assess this disease in our population. However, using 3 main markers i.e. CD3 (surface and cytoplasmic), CD1a and CD7, we were able to study the immunophenotypic characteristics of this disease according to the WHO classification[5]. The WHO classification segregates T-ALL into three types based on the presence or absence of CD3, CD1a and CD7 i.e., pro T (cCD3+, CD1a-, CD7+, sCD3-), common thymocyte

T-ALL (cCD3+, CD7+, CD1a+) and the mature thymocyte T-ALL (cCD3+, CD1a-, CD7+, sCD3+). CD3 is a lineage determining marker and is therefore positive in all cases.

A study by Pullen et al determined that several of the clinical and laboratory prognostic factors, which are used reliably for B-ALL, are much less predictive in T-ALL (age, TLC, consensus risk group, etc.) [10].

We found that T-ALL is more common among males (82.86%) than females (17.14%) with a male-to-female ratio of 4.83:1, with common thymocyte T-ALL more common (51.43%) than pro and mature thymocyte T-ALL (28.57% and 20% respectively). Our study was at variance with another study which found pre T-ALL cases to be much fewer (4.2%) than T-ALL cases (26.4%)[3].

Of importance is the fact that of the 6 female cases, 4 cases (14.28%) were found to have pro T-ALL including one case of ETPALL and 1 patient each (2.86%) was found to have common and mature thymocyte T-ALL.

The importance of studying the immunophenotypic markers of T-ALL in a given population is their prognostic significance for determining various parameters such as remission rate, event free survival, overall survival, risk of relapse etc.

CD1a was positive in a little more than half of all cases (51.43%). A study in Moroccan children by Lahjouji et al found an excess of the common thymocyte subtype (80.4%) displaying reactivity with CD1a as compared with the frequency reported by others[8].

Among the cases in which CD2 was run, it was found to be positive in 70.83% patients. A study by Uckun et al found a statistically significant correlation between the CD2 antigen positive leukemic cell content of bone marrow and probability of remaining in bone marrow remission, as well as overall event-free survival (EFS)[12].

Cytoplasmic CD3 is a lineage specific marker for T cells. 51.43% cases were positive while 40% showed surface positivity and 8.57% showed both surface and cytoplasmic positivity. CD5, along with CD2 and CD7 is a marker for immature T cells. Majority of the cases (88.57%) were positive. All cases were positive for CD7.

CD34 is a marker for haematopoietic stem cells and was positive in only 34.3% cases. This is in agreement with a study by Pui et al and a couple of other studies which have found expression of this antigen rare/absent by malignant T lymphoblasts [9].

Conclusion:-

This study is the first to report the different immunophenotypes of T-ALL in Kashmir in the English language literature. It is hoped that this study serves as a starting point for further, more detailed studies on this disease in our population eventually leading to better tailored treatment regimens that fit our population characteristics.

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Competing Interests:

None declared.

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