ALL is a heterogeneous hematologic disease characterized by the proliferation of immature lymphoid cells in the bone marrow, peripheral blood, and other organs.

ALL represents 75% to 80% of acute leukemias among children, making it the most common form of childhood leukemia; by contrast, ALL represents approximately 20% of all leukemias among adults.

The cure rates and survival outcomes for patients with ALL have improved dramatically over the past several decades, primarily among children. Data from the SEER database have shown a 5-year overall survival (OS) of 86% - 89% for children.

The diagnosis of acute leukemia (AL) is based on clinical and laboratory data. The laboratory evaluation of patients suspected of having acute leukemia (AL) is complex.

The French-American-British (FAB) cooperative group, first broadly classified acute leukemias based on morphology of blast cells as seen on Wright- or Wright-Giemsa-stained bone marrow smears and a variety of cytochemical stains.

However, morphological diagnosis of acute leukemia may be incorrect up to 9%.

This led to the introduction of flow cytometry immunophenotyping (FCI), and the FAB classification was modified to incorporate these, mainly to distinguish acute myeloid leukemia from acute lymphoblastic leukemia.

In 2001, the 3rd edition of the WHO classification of AL formally introduced the requirement for immunophenotyping and cytogenetic studies for the diagnosis.

The 2008, 4th edition of the WHO classification, added additional cytogenetic disease groups for AML and ALL, introduced the category of mixed-phenotype acute leukemia (MPAL), and included provisional entities of AML that were based on gene mutation studies.

The 2016 WHO classification continued to define some disease entities by a combination of morphologic, immunophenotypic, and molecular genetic changes, but some gene mutations and cytogenetic abnormalities, although not disease defining, offer significant prognostic information.

Laboratory data include a CBC with morphologic assessment of blood and bone marrow, karyotype, appropriate molecular genetic and/or fluorescent in situ hybridization (FISH) testing, and immunophenotyping.

The flow cytometry panel should be sufficient to distinguish AML, T-cell acute lymphoblastic leukemia (T-ALL), B-cell precursor ALL (B-ALL), and acute leukemia of ambiguous lineage on all patients with AL.

ALL can be broadly classified into 3 groups based on immunophenotype, which include precursor B-cell ALL, mature B-cell ALL, and T-cell ALL. Among children, B-cell ALL constitutes approximately 88% of cases; in adult patients, B-ALL represent approximately 75% of cases (including mature B-cell ALL that constitutes 5% of adult ALL), whereas the remaining 25% comprise T-ALL.

Within the B-cell lineage, the profile of cell surface markers differs according to the stage of B-cell maturation, which include early precursor B-cell (early pre-B-cell), pre-B-cell, and mature B-cell ALL.

Early pre-B-cell ALL is characterized by presence of terminal deoxynucleotidyl transferase (TdT), expression of CD19/CD22/CD79a, and the absence of CD10 or surface immunoglobulins.

Pre-B-cell ALL is characterized by presence of cytoplasmic immunoglobulins and CD10/CD19/CD22/CD79a expression and was previously termed common B-cell ALL due to the expression of CD10.

Mature B-cell ALL shows positivity for surface immunoglobulins and clonal lambda or kappa light chains, and is negative for TdT. CD20 may be expressed in approximately 50% of B-cell ALL in adults, with a
higher frequency (>80%) observed in mature B- ALL.

T-cell ALL is typically associated with the presence of cytoplasmic CD3 (T-cell lineage blasts) or cell surface CD3 (mature T cells) in addition to variable expression of CD1a/CD2/CD5/CD7 and expression of TdT. CD52 may be expressed in 30% - 50% of T- ALL in adults.

Hematologic malignancies related to ALL include AL with ambiguous lineage, such as mixed phenotype acute leukaemias (MPAL).

MPAL include bilineage leukemias, in which 2 distinct populations of lymphoblasts are identified, with 1 meeting the criteria for acute myeloid leukemia. Another type of MPAL is the biphenotypic type, in which a single population of lymphoblasts expresses markers consistent with B-cell or T-cell ALL, in addition to expressing myeloid or monocytic markers.

Myeloid-associated markers such as CD13 and CD33 may be expressed in ALL, and their presence does not exclude this diagnosis.

In developing countries, leukemia is most common among childhood cancers and it constitutes 3–10%. Leukemias account for 0.15–0.6% of the total medical admissions in many general hospitals in India.

Acute myeloid leukemia (AML) accounts for approximately 20% of AL in children and 80% AL in adults.

In India childhood cancer constitutes less than 5% of the total burden of cancer. Approximately 45,000 children are diagnosed with different types of cancer every year.

ALL is the most commonly reported childhood malignancy and accounts for 30% of all cancers diagnosed in children under 15 years, with B-cell ALL representing about 88% of cases. A Hospital Based Cancer Registry Report of ICMR (2004–2006) reported that acute leukemia is the most common childhood cancer with an estimated prevalence of up to 60 to 85% of all leukaemia’s.

The present article by Rajkumar and Vijay from the Kidwai Institute in Bangalore has studied the immunological subtypes of ALL at their center. All cases of Acute Leukemia where flow cytometric analysis was done during a period of 4-year from January 2012 to August 2015 were included in this retrospective study.

1425 cases were acute Leukemias (70.02%), 918(64.42%) were acute lymphoblastic Leukemia, (Adult ALL were 317 (34.5%) and paediatric ALL were 601 (65.46%); 688 were B-ALL (74.94%) AND 230 T ALL (25.05). In 601 children with ALL, B-ALL were 480(79.86%) and T-ALL were 121 (20.13%). In 317 adults, with ALL, B-ALL were 208(65.6%) cases and T-ALL were 109 (34.38%). In both adults and children ALL, B-ALL was the most common subtype. AML comprised of 487 (34.17%), MPAL (mixed phenotypic acute leukemia) comprised of 21(1.47%).

Their findings are consistent with most reported studies including from India.

A number of Indian studies have been carried out, which have taken into account clinical, morphological features, immunophenotyping, cytochemical and FISH, though the numbers in each study have not been large.

The advantage of the present study is the large number they have been able to analyse. However being a retrospective study no other information regarding the other parameters are mentioned.

The Department of Pathology, Gujarat Cancer and Research Institute, Ahmedabad, conducted a study from January 2015 to December 2015. 455 AL patients were enrolled, of which 184 (40.4%) diagnosed as AML, 214 (47%) as B-ALL, 55 (12.1%) as T-ALL, and 2 (0.4%) as MPAL by morphology, cytochemistry, and immunophenotyping.

Another study from Lok Nayak Hospital, Delhi, studied 100 newly diagnosed consecutive cases of AL from 2011 - 2013. Flow cytometry was performed on peripheral blood/bone marrow aspirate on Beckman Coulter flow cytometer (FC500) using a panel of markers comprising CD10, CD19, CD20, CyCD22, CyCD3, CD2, CD5, CD7, CD13, CD33, CD117, CD11c, CD34, HLA-DR and CD45.

Based on morphology, cytochemistry and immunophenotyping 57 cases of ALL and 43 cases of AML were diagnosed. Amongst ALL cases, 46 were B-ALL and 11 were T-ALL.

A prospective study was conducted in Department of Hematology, PGIMER, Chandigarh. All consecutively diagnosed cases of ALL for a period of 2 years (July 2010 to June 2012) were included. They had 303 Pediatric cases (<15 years) and 207 adult cases (>15 years).

Of the 303 pediatric case 85 % (257/303) were classified as B- ALL and 15 % (46/303) patients were identified as T- ALL.

Similar results have been published from the Institute of Child Health and Hospital for Children, Chennai.

Today most centers and treating physicians follow international guidelines for the diagnosis and treatment of various disorders. With advances in diagnostic tests and emerging new treatment strategies it is mandatory for us to keep up with these advances even in resource poor settings.

A number of Indian studies have carried out immunophenotyping with cost effective panels especially designed for resource constraints. With the advent of large laboratory chains, it is now possible to carry out these tests even in small centres that do not have in house facilities.
Thus, with the wider availability of the tests, it has become the standard of care today to carry them out prior to starting treatment. The tests themselves though expensive are a fraction of the cost of the overall treatment of a leukaemia. They in fact help to prognosticate and risk stratify the patients thus ensuring optimum utilization of resources.

Most treating oncologists and haematologists do a full diagnostic workup routinely; unfortunately with the wealth of material we have, publications are still meagre, a situation which we should try to overcome.

Conclusion

In conclusion, the authors should be commended for the effort of publishing the study with a large number of patients. However, there are a number of Indian studies who have provided more comprehensive data, albeit with smaller numbers.

An ideal way to project our Indian data would be for large institutions to come together and pool their data. This would help us to identify the unique problems we face in diagnosis, management and outcomes and help to give insight into future course of action.

References

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