

Commentary on Clinical Predictors and Prognostic Model for Pediatric Lymphoblastic Lymphoma Treated with Uniform BFM90 Protocol: A Single-Center Experience of 65 Patients from Asia

There are insufficient data on the outcomes and their clinical predictors in pediatric patients with lymphoblastic lymphomas (LBLs). Molecular genetics of pediatric LBLs and acute lymphoblastic leukemia (ALL) overlap to some extent. Risk stratification-directed treatment is the standard of care in the treatment of ALL, and such a risk stratification model has not been developed for the clinical use in LBL patients. To bridge this gap, a retrospective analysis of 65 consecutive patients with pediatric LBL over 15 years, treated with BFM90 protocol, was carried out and the outcomes were assessed in terms of overall survival (OS) and event-free survival (EFS).^[1]

At the end of induction, 57% of patients had a complete remission, 28% had a partial remission, 6% had a progressive disease, and 3% had a stable disease. Treatment-related mortality occurred in three patients overall and 20 patients relapsed. After a median follow-up of 54.57 months, 10-year EFS was 62% and OS was 71%. These outcomes were 15%–20% lower than those reported from developed countries.^[2,3]

On multivariate analysis, three predictors of poor OS and EFS were identified – symptom duration <30 days, white blood cell count >12,000/cumm, and serum albumin <3.5 g/dl. A prognostic model was devised which showed that OS was 92% if no risk factors were present versus 37% if two or three risk factors were present. Twenty percent of patients had two or three risk factors and had poor outcomes both as a result of increased toxicity, higher relapses, and higher deaths (3 out of 14 in the presence of risk factors vs. none in the other group).

Age, sex, presence of mediastinal mass, bulky disease, stage of disease, and elevated serum lactate dehydrogenase were earlier investigated as prognostic markers with variable results. However, the study population and the results were heterogeneous. As majority of patients (90%) of LBL have Stage III/IV disease, stratification of patients into localized and disseminated disease based on stage is not a useful measure in making treatment decisions.

Among novel prognostic markers, molecular profile, minimal residual disease (MRD), minimal disseminated disease (MDD), and use of positron emission tomography (PET) scan were studied in LBLs. Among the molecular markers, the presence of NOTCH1 and FBXW7 mutations was associated with favorable prognosis, while loss of heterozygosity at 6q and PTEN mutations were associated with adverse prognosis. Based on these markers, a prognostic genetic classifier for risk group stratification

for T-cell LBL has been proposed.^[4] MRD was studied as a significant risk factor for relapse. Patients with detectable disease in bone marrow, i.e., MDD by flow cytometry (0.01%), had varying prognosis corresponding to the levels of MDD present.^[5] Postinduction PET-computed tomography (CT) has been shown to improve the ability to detect residual disease, thereby affecting the treatment decisions.^[6]

To conclude, the current study identified useful clinical predictors, which are readily available, inexpensive, and easy to use, that can help predict the outcomes of the patients. This study identifies the need for tailored therapy as per the prognostic score which can help reduce treatment-related mortality and relapses. In future, comprehensive, multicentric, prospective trial incorporating both clinical predictors and novel markers such as molecular profile, MRD, MDD, and use of PET-CT is required to further investigate on a risk-oriented approach in LBL.

Sindhu Chitikela, Deepam Pushpam

Department of Medical Oncology, AIIMS, New Delhi, India

*Address for correspondence: Dr. Deepam Pushpam,
The Medical Oncology Centre, Dr. B.R.A. IRCH, AIIMS,
New Delhi - 110 029, India.*

E-mail: deepampushpam@gmail.com

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