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Clinical Profile and Induction outcomes of Acute Lymphoblastic Leukemia patients.

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ABSTRACT:
BACKGROUND*:*
Acute Lymphoblastic Leukemia(ALL) is characterized by presence of more than or equal to 20% lymphoblasts in the peripheral blood and/or in bone marrow. Incidence in India is 27-52% with skewed male preponderance.It is classified into B cell ALL(75-80%) and T cell ALL(20-25%). Treatment consists of induction, consolidation, maintenance and CNS prophylaxis.Various complications are seen during induction, most common being myelosuppression, tumor lysis syndrome,mucosistis, neuropathy and hyperglycaemia.
METHODS*:*
A total of 42 newly diagnosed ALL patients, who presented to the departement of medical oncology, SVIMS, from November 2023 to December 2024 were recruited including children and adults aged <45 years, with an ECOG PS<2. Detailed history taken and examination was done, bone marrow aspiration was sent for flow cytometric analysis,cytogenetics by RT-PCR and karyotyping done. Baseline investigations were done and started on induction chemotherapy based on age of the patient. Patients were observed for day 8 blast clearance, complications like tumor lysis syndrome,febrile neutropenia,mucositis, thrombotic complications. Post induction response evaluation for morphological remission was done on day 33 of induction or after counts recovery.
RESULTS:
There was equal distribution of pediatric and adult patients(1:1).Male:female ratio was almost 3:1. Most common presenting complaint was fever.Patient who presented with TLC>50000 , had poor prognosis and lower remission rate.those who presented with TLC<50000) had better prognosis.On immunophenotyping, B Cell ALL was more common than T cell ALL.Common cytogenetic abnormalities seen were t(9;22)-Ph+ B-ALL , Hyperdiploidy and complex karyotype).Induction chemotherapy was given to all the 42 patients as per BFM95/ICICLE / GMALL protocol.Day 8 Good prednisolone response higher remission rate.Many complications were noted during induction, most common being febrile neutropenia, hyperglycaemia, tumor lysis syndrome.Overall remission rate in our study was 83.3%.
CONCLUSION:
Identification of various prognostic features at diagnosis and during induction will help us to predict the outcomes of the disease. Favourable factors for higher remission rate in ALL are younger age,TLC <50000, B-Cell ALL, low risk cytogenetics, and day 8 Good prednisolone response.

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I. INTRODUCTION:

According to the Global cancer statistics 2020, a total of 474,519 new cases of leukemia were diagnosed all over the world ,which includes 2.5% of all cancer cases diagnosed in the year.(1)Acute lymphoblastic leukemia (ALL) accounts for 20% of all adult leukemias and is the most common leukemia during childhood (80%) with an estimated prevalence of 3.5 and 2.2 per 100000 male and female population respectively.(2).Acute lymphoblastic leukemia is characterized by the presence of more than or equal to 20%lymphoblasts(early lymphoid precursors) in peripheral blood and/or in bone marrow.ALL is broadly classified based on their cluster of differentiation markers (CD) by flow cytometry into B cell ALL and T cell ALL.(3).Treatment of ALL consists of induction - (to reduce tumour burden and eliminate maximum blasts from bone marrow), consolidation -(further eradication of any residual disease), maintenance therapy (to prevent disease relapse) and extramedullary disease prophylaxis or treatment to prevent CNS relapse.Management in young and fit patients (<40 years) is by Modified BFM 95 protocol or ICICLE protocol consisting prednisolone,vincristine, daunorubicin ,L-asparaginase and intrathecal methotrexate.(5)

while in Older patients (>40 years) , GMALL protocol with prednisolone, vincristine, and daunorubicin is used, L-asparaginase is avoided in older patients. (5)

In Ph positive patients Tyrosine Kinase inhibitors(TKI) Dasatinib or Imatinib are added to conventional chemotherapy protocol. (5)Percentage of blast cells in bone marrow examination at the end of induction is used to determine the response to chemotherapy. <5% blast cells indicates complete remission while >5% indicates refractory disease.(5)

II. AIM:

To study the clinical profile and induction outcomes of acute lymphoblastic leukemia patients presenting to a tertiary care centre.

III. OBJECTIVES:

1. To describe the clinical presentations ,immunophenotypic profile and risk stratification of ALL patients .
2. To study the complications during induction chemotherapy and induction outcomes in ALL patients.

IV. MATERIAL AND METHODS:

It is a hospital based single arm prospective observational study that is being done in patients with immunophenotypically diagnosed ALL patients attending the Department of Medical Oncology ,SVIMS from November 2023 till June 2025.

Inclusion criteria:

1. Newly diagnosed ALL patients
2. Age<50years
3. Performance status-ECOG(Eastern Cooperative Oncology Group) less than 2

Exclusion criteria:

1. Patients with relapsed ALL
2. Performance status-ECOG 2 or more
3. Age>50years
4. Patients with comorbidities like uncontrolled diabetes mellitus, chronic kidney disease,Dilated cardiomyopathy or any heart disease with compromised ejection fraction(EF< 50%), Decompensated liver disease, pre-existing neurological disease.

Detailed history / general physical examination and complete systemic examination was done for all the patients during admission .ECOG performance status was used for assessing general condition of the patient.Flowcytometry was done for the immunophenotypic classification into B -cell ALL and T -cell ALL. Cytogenetic studies for common translocations including t (12;21), t(9;22), t (4;11) and t (1;19) were tested by RT-PCR. Hyperdiploidy was defined as >50 chromosomes and hypodiploidy <44 chromosomes on karyotyping.Data was collected with regard to age, gender, comorbidities, clinical features at presentation, haematological profile at presentation and day 8 Hemogram, flow cytometry, cytogenetics and karyotyping reports from peripheral blood or bone marrow.

CSF analysis was done for assessment of CNS disease on day 8 of induction chemotherapy.(CNS Status I: <5 WBC in CSF without blasts, II: <5 WBC in CSF with blasts, III: CSF >5 WBC in CSF with blasts).Risk stratification was done based onNCI criteria into standard or high risk. Standard risk (Age <10yrs , TLC<50000,B-ALL,absence of high risk cytogenetics, absence of CNS/testicular disease), high risk (Age >10yrs , TLC>50000,T-cell ALL, high risk cytogenetics- t(9;22), MLL,Hypodiploidy,complex karyotype, presence of CNS or testicular disease).Management was by Modified BFM 95 protocol or ICICLE protocol,while in Older patients (>40 years) , GMALL protocol was used. In Ph positive patients Tyrosine Kinase inhibitors(TKI) Dasatinib or Imatinib were added.Prednisolone Response was defined as the cytoreduction (number of blasts per micro lit on day 8 of induction) to a 7 day prednisolone prephase .Patients were prospectively observed for any complications during induction chemotherapy, and also the outcomes at the end of induction chemotherapy.Outcomes:Post induction response evaluation was done on day 33-35 bone marrow examination and the patients will be categorized into complete remission (CR, <5% blasts in the marrow with normal trilineage hematopoiesis) and refractory disease(CR not achieved at the end of induction).

STATISTICAL ANALYSIS:

Data was recorded on a predesigned proforma using Microsoft excel spread sheet.

Statistical analysis was done by statistical software IBM SPSS Statistics (version 26.0) for Windows (IBM Corporation, New York, USA). Percentages were used for categorical variables.For discrete variables, proportions were calculated.Mean ± standard deviation was used for continuous variables.The association between the various qualitative variables were assessed using Chi-square test and quantitative variables were assessed using t-test/ANOVA.p value less than 0.05 was considered significant.

V. RESULTS:

- A total of 42 patients were enrolled in this study till january 2025.Median age in the study group was 19.3 years. Adults and pediatric population were equal. Males were higher with almost 3:1 ratio. Most of them were underweight BMI<18.5 (53.3%)and 25% were obese.Most common presenting feature was fever(76%), other clinical presentations were fatigue,bony pains,bleeding manifestations,dyspnea, and gum hypertrophy.Most common sign was pallor.Hepatomegaly(11.9%)Splenomegaly(23.8%) Hepatosplenomegaly (23.8%)Lymphadenopathy(28.5%). 6 patients of T-ALL had mediastinal mass.40% of patients has Tumor Lysis Syndrome during presentation. Patients were given induction chemotherapy based on the age. 57.1% had TLC >50000/microlitre,54.9% had TLC<50000/microlitre. 69% patients had B cell ALL, 31% had T cell ALL.Most patients had normal cytogenetics and karyotyping(47.6%), 16.6% had t(9;22), 14.2% had hyperdiploidy, 7.1% had complex karyotype, and rest had miscellaneous abnormalities like t(1;19), 7p deletion,t(10;14) and deletion 12p.Of the total 42 patients, 69% patients were high risk, 31 % were stratified to standard risk.27 patients were given BFM95 protocol, 12 were given ICiCLe protocol and 3 were given GMALL protocol. 71% patients had Good Prednisolone Response and rest 29% had Poor Prednisolone Response.Overall Remission rate in this study was 83.3%. Better remission rate was seen with males (86%),TLC <50000 (88.2%),B cell ALL(86.2%) , Hyperdiploidy (100%),normal cytogenetics(90%),Good Prednisolone response(86.6%).Ph+ B-ALL had lower remission rate -71%, complex karyotype-66.6%, t(1;19)-50%.

Variable	p value as per Kruskal Wallis test
Age	0.032
Sex	0.535
BMI	0.236
TLC at presentation	0.039
ALL subtype	0.043
Cytogenetics , karyotyping	<0.001
Chemotherapy protocol	0.067
Day 8 Prednisolone response	0.003

VI. DISCUSSION:

This is an observational prospective study being done in SVIMS medical oncology department from November 2023, still recruiting.A total of 42 patients who fulfilled the inclusion criteria were taken.There was equal distribution of pediatric and adult patients(1:1).Malard et al study showed 2.2:1 ratio.(6).Male:female ratio was almost 3:1. Average ratio in other studies like Reddy et al was 2:1.(7).Most common presenting complaint was fever.This is similar to the study done by Advani et al.(4) .Patient who presented with TLC>50000(57%) , had poor prognosis and lower remission rate.those who presented with TLC<50000 (40% cases) had better prognosis. (Similar to study by advani et al)(8).On immunophenotyping, B Cell ALL was more common than T cell ALL.Common cytogenetic abnormalities seen were t(9;22)-Ph+ B-ALL , Hyperdiploidy and complex karyotype.(9).Induction chemotherapy was given to all the 42 patients as per BFM95/ICICLE / GMALL protocol.Day 8 Good prednisolone response was seen in 71% cases. They had a higher remission rate(86.6%) , similar to other review studies-Terwillinger et al.(10).Many complications were noted during induction, most common being febrile neutropenia, hyperglycaemia, tumor lysis syndrome.

Overall remission rate in our study was 83.3%. The CR rate ranges from 78-93% in a meta analysis published in 2017.(10) (11).9.5%patients did not achieve remission post induction chemotherapy.3patients (7%) expired during induction chemotherapy due to complications.

VII. CONCLUSION:

Age <18 yrs had better prognosis, males had better remission rate(statistically not significant).TLC>50000 had lower remission rate (p value- 0.03).B cell ALL had better prognosis with higher morphological remission.(p-0.043).Based on the cytogenetics, Hyperdiploidy had the best prognosis, Ph+ ALL had worse prognosis(71% remission), and complex karyotype had worst prognosis (50%remission and 1 death).(p<0.001)-statistically very significant.Good prednisolone response had better remission.BFM 95 protocol was seen to have slightly higher remission rate than other two protocols. Identification of various prognostic features at diagnosis and during induction will help us to predict the outcomes of the disease.Favourable factors for higher remission rate in ALL are younger age,TLC <50000, B-Cell ALL, low risk cytogenetics, and day 8 Good prednisolone response.

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