ORIGINAL RESEARCH PAPER

Oncology

KEY WORDS: Pediatric leukemia, Central Maharashtra, Clinico-epidemiological features.

CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF CHILDHOOD LEUKEMIAS FROM A TERTIARY CARE CANCER CENTER IN CENTRAL MAHARASHTRA.

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ABSTRACT

Introduction: As there is increasing burden of childhood leukemias, key step in caring for these children is estimating the current burden of childhood leukemia in India, understanding the clinico-epidemiological features, and assessing survival trends, as there is a scarcity of data on this topic. **Objectives:** This retrospective observational study aims to determine the clinico-epidemiological profile, complications, and outcomes of leukemia in pediatric patients representative of Central Maharashtra over a five-year period. **Materials And Methods:** We analyzed the clinico-epidemiological features and treatment responses of all leukemia cases aged 1-12 years from the hospital-based cancer registry of a tertiary care cancer center in Central Maharashtra, covering the years 2019 to 2023, with data analysis conducted in December 2024. Complications during hospitalization were also recorded. **Results:** Out of 265 leukemia patients, 213(80%) were included in the study as they continued follow-up. Of these, 126(59%) were male and 87(41%) were female, with 109(51%) being younger than 5 years of age. Acute lymphoblastic leukemia(ALL) was the most common immunophenotype, affecting 168(78%) patients, with 134(80%) cases being B-ALL, treated using the Modified BFM(Berlin-Frankfurt-Münster)-90 protocol. The most common symptom was fever(155,72%), the most frequent sign was hepatomegaly(164,76%), and the most prevalent complication was febrile neutropenia(136, 63%). Of the 168 ALL cases, 115(68.6%) achieved complete remission and survived, 26(15%) relapsed, and 37(22%) patients died. **Conclusion:** In this study, males were more commonly affected than females (1.4:1), particularly among children under 5-years-of-age. Fever was the most common symptom, and hepatomegaly was the most common sign. B-ALL was the most frequent type and showed improved survival rates compared to other immunophenotypes. Of the 168-ALL cases, 68.6% survived in complete remission, while 22% of patients died. In conclusion, this study provides valuable evidence and epidemiological insight into the incidence and outcomes of childhood leukemias, particularly in low-and middle-income countries(LMICs).

INTRODUCTION:

Leukemias are the most prevalent type of childhood cancer worldwide, accounting for 25 to 30% of cases in India[1]. Remarkable progress in the treatment of acute lymphoblastic leukemia (ALL) has resulted in a 5-year overall survival rate of up to 90% in high-income countries[2]. However, advancements in the treatment of myeloid leukemias have been less significant, with 5-year survival rates remaining steady at around 70%[3]. There is a lack of comprehensive, long-term data on the clinico-epidemiological characteristics and survival trends of childhood leukemia in India.

Several prospective multi-center studies under the guidance of the Indian Paediatric Oncology Group (InPOG) have been initiated to collect data on childhood leukemias. The goal of this study is to explore the clinico-epidemiological profile and complications of childhood leukemias in Central India. The data collected from our center will provide valuable baseline information to support such collaborative efforts.

MATERIALS AND METHODS:

This retrospective observational study was conducted on a population representative of central Maharashtra. Data was collected from January 2017 to January 2022, with analysis performed in March 2024. After obtaining approval from the institutional ethical committee, we included children aged 1 to 12 years diagnosed with both acute and chronic leukemias. We excluded infants, children older than 12 years, patients lost to follow-up, and those diagnosed with lymphoma, aplastic anemia, or myelodysplasia.

A total of 213 children with leukemia were included, and informed consent was obtained from their parents or guardians. Information was gathered on demographic characteristics, a detailed history of initial symptoms, and clinical examination findings. Nutritional status was assessed through height, weight, and BMI measurements, which were plotted on growth charts to evaluate for malnutrition. Laboratory investigations included complete blood count, peripheral smear, blood sugar, renal function tests (blood urea, serum creatinine), serum electrolytes (sodium, potassium, phosphorus, calcium), liver function tests, serum uric acid, serum lactate dehydrogenase, serum viral markers, and urine analysis. Imaging modalities such as chest radiographs, abdominal sonography, and echocardiography were performed.

Diagnosis And Specific Therapy:

Children suspected of leukemia based on symptoms and signs were confirmed through bone marrow aspiration. Acute leukemia was diagnosed by the presence of >20% blasts in bone marrow or peripheral blood[4], while chronic myeloid leukemia (CML) and juvenile myelomonocytic leukemia (JMML) were diagnosed according to specific criteria[5]. Cerebrospinal fluid (CSF) analysis for malignant cells was performed for all ALL cases. Bone marrow aspiration and CSF tapping were carried out after obtaining informed consent from the parents. Diagnosis was confirmed by flow cytometric analysis of peripheral blood or bone marrow aspirate, and immunophenotyping was performed using flow cytometry. Cytogenetic and karyotyping samples were also sent.

Patients were treated with chemotherapy, cranial radiotherapy, G-CSF, IV antibiotics, blood transfusions, and other supportive treatments as needed. ALL patients were

treated according to the Modified BFM (Berlin-Frankfurt-Münster)-90 protocol after risk stratification[6]. Acute myeloid leukemia (AML), excluding acute promyelocytic leukemia (APML), was treated with the 7+3 regimen and hematopoietic stem cell transplant (HSCT)[7]. APML was treated according to the APML-4 protocol[8], CML with tyrosine kinase inhibitors (Imatinib)[9], and JMML with Azacitidine followed by HSCT[10]. Regular follow-up examinations were conducted during the hospital stay, and any complications were documented and treated. Outcomes were classified as complete remission, relapse, death, or abandonment of treatment.

Statistical Methods:

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS version 24.0, IBM Corporation, USA) for MS Windows. Descriptive statistics were calculated for each variable. Continuous data are presented as mean ± standard deviation (±2 SD). The Pearson Chi-square test was used to assess significance, with p-values less than 0.05 considered statistically significant.

RESULTS:

A total of 265 children diagnosed with leukemia were enrolled in the study, with 213 (80%) continuing their follow-up. Of these, 75% were from rural areas and 25% from urban areas. The gender distribution showed that 59% were male and 41% were female, with a male-to-female ratio of 1.4:1. Among the participants, 109 children (51%) were between 1-5 years of age, and 104 (49%) were aged 5-12 years. The mean age was 4.84 years, with a standard deviation of ±2.78 years. The youngest child was 1 year old, the oldest was 12 years old, and the median age was 4 years.

Of the 168 (78%) cases of acute lymphoblastic leukemia (ALL), 134 (62%) were B-ALL, and 34 (16%) were T-ALL cases. Acute myeloid leukemia (AML) accounted for 38 (19%) children, juvenile myelomonocytic leukemia (JMML) for 1 (0.4%), and chronic myeloid leukemia (CML) for 6 (2.6%). Among the children, 40% were underweight, and 5% were overweight for their age. The most common initial symptom was fever, reported by 155 (72%) children, followed by loss of appetite, observed in 148 (69%) children (Figure 1). Hepatomegaly (77%) was the most frequent sign, followed by splenomegaly (69%) as the second most common sign (Figure 2). Regarding hemoglobin levels, 46 (21%) children had a value of <7 gm/dl, 93 (43%) had hemoglobin levels between 7-11 gm/dl, and 74 (34%) had levels above 11 gm/dl. White blood cell (WBC) counts were below 100,000/mm^3 in 153 (71%) children, with hyperleukocytosis (WBC >100,000/mm^3) found in 60 (28%). Platelet counts showed that 57 (26%) children had less than 20,000/mm^3, 77 (36%) had between 20,000-50,000/mm^3, and 79 (37%) had more than 50,000/mm^3. The median values for hemoglobin, WBC, and platelets were 8.9 gm/dl, 38 x10 /L, and 52 x10 /L, respectively.

The most common complication observed in the study was febrile neutropenia, which affected 136 (63%) children, followed by sepsis in 129 (60%) children. Neurological complications included vincristine-induced neuropathy in 10 (5%) children, while cerebral venous sinus thrombosis (CVST) and methotrexate encephalopathy were each seen in 2 (0.9%) children. The majority (123, 57%) of children were hospitalized for 1-4 weeks, 70 (32%) stayed for 4-6 weeks, and 20 (11%) had prolonged hospital stays of more than 6 weeks. Of the 213 children, 155 (72.7%) survived, while 27.3% succumbed to the disease.

DISCUSSION:

This study included 213 children diagnosed with leukemia, comprising ALL, AML, CML, and JMML. Among them, 59% were male, and 41% were female, with a male-to-female ratio of 1.4:1, which is consistent with the findings of Guru et al., who reported 78.1% boys and 21.9% girls[13]. Leukemia affects children of all age groups, but in our study, the most common age group was between 1-5 years (51%), similar to Siddaiahgari et al., who reported 79.61% in the same age range[14]. A significant majority of patients (75%) came from rural areas, which may reflect the fact that this government cancer center serves a predominantly rural population in central Maharashtra, offering free healthcare services. Over 40% of the children in this study were underweight, likely due to limited access to proper nutrition, which contrasts with findings in Western populations[15].

Fever was the most common presenting symptom, seen in 155 (72%) of patients, followed by loss of appetite in 148 (69%), which aligns with Siddaiahgari et al., who reported fever in 92.23% of cases, followed by pallor in 87.38%[14]. Hepatomegaly was the most common physical sign, observed in 164 (76%) of children, followed by splenomegaly in 146 (68%). Neurological manifestations were rare, occurring in only 2 (0.9%) children. These findings are similar to Manisha B et al., who also identified hepatomegaly as the most common sign[16]. In contrast, Mishra et al. reported splenomegaly as the most common sign, followed by hepatomegaly and purpura, which may be due to a larger sample size and the inclusion of adults[17].

Febrile neutropenia (63%) was the most common complication, followed by sepsis (60%), which is consistent with our findings. However, Hassan et al. noted treatment-related toxicities as the most common complication, likely due to their longer study period, spanning nearly 17 years[18].

In our study, 168 (78%) of the patients had ALL, with 134 (62%) being B-ALL and 34 (16%) T-ALL. Similarly, Pandian et al. observed 85.7% of patients with B-ALL and 14.3% with T-ALL[19]. Mukhopadhyay et al. reported a near-equal distribution, with T-ALL in 50.4% and B-ALL in 47.3% of cases, which could be explained by the inclusion of both children and adults in their study[20]. Forty-three percent of patients had a hemoglobin level of <7 gm/dl, similar to the findings of Teuffel et al.[21]. Most children (71%) had WBC counts below 100,000/mm^3, with 28% showing hyperleukocytosis (>100,000/mm^3), which is comparable to Kong et al.'s findings of 19.2%[22]. Severe thrombocytopenia (<20,000/mm^3) was seen in 26% of patients, which is consistent with Shalal et al.'s study, where 25.5% of cases had severe thrombocytopenia[23]. Regarding hospitalization duration, 57% of patients stayed for 1-4 weeks, and 32% stayed for 4-6 weeks, similar to the findings of Hassan et al., who reported that 97.8% of cases had hospital stays of less than 4 weeks[18].

CONCLUSION:

This study shows that the incidence and clinico-epidemiological characteristics of childhood leukemia in central Maharashtra are similar to those reported in other Indian studies. ALL was the most common hematological malignancy (78%), with B-ALL accounting for 80% of cases. The majority of ALL cases occurred in children under 5 years of age (51%), with a male predominance. Fever (72%) was the most common symptom, hepatomegaly (76%) the most common sign, and febrile neutropenia (63%) the most frequent complication. B-ALL had better survival rates compared to other subtypes. Among the 168 children with ALL, 65.5% survived in complete remission, 15% relapsed, and 22% died.

There is a notable gap in prospective multi-center studies on childhood leukemia, particularly in ALL and AML. However, initiatives like InPOG-ALL-15-01 are advancing clinical trials in India. The success of trials like MCP-841, which improved survival rates from less than 20% to nearly 60%, demonstrates that clinical trials and treatment protocols tailored to India's needs can make a significant difference. This highlights the

importance of understanding the disease burden through collaborative data collection, as protocols used in high-income countries may not yield the same outcomes in LMICs like India. Sharing our center's experience and outcomes, especially with the Modified BFM-90 ALL protocol, plays a crucial role in improving survival rates and reducing mortality and morbidity in childhood leukemia.

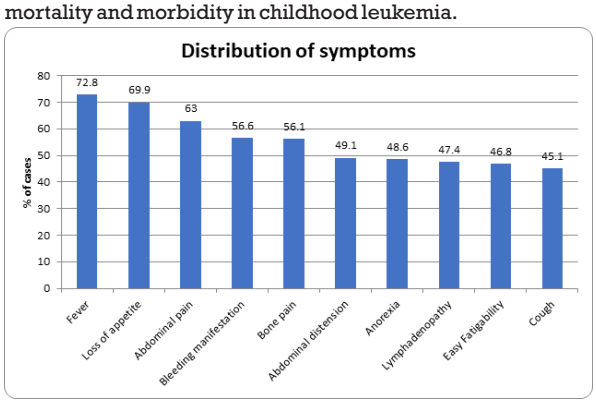

Figure 1) Distribution Of Symptoms On Presentation Among Cases Studied.

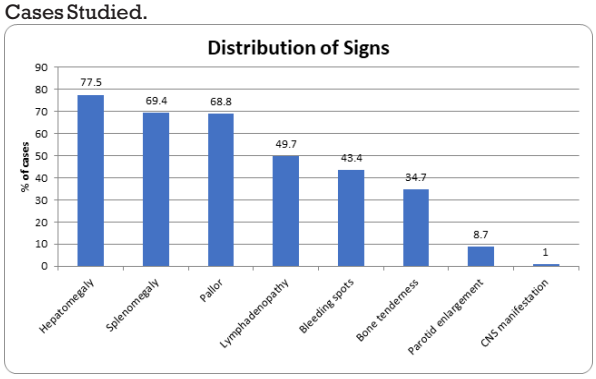

Figure 2) Distribution Of Signs In Cases Studied.

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