



CLINICO-EPIDEMIOLOGICAL PROFILE OF HEMATOLOGICAL MALIGNANCIES IN PEDIATRIC AGE GROUP IN A TERTIARY CARE CENTRE OF SOUTHERN RAJASTHAN

Pathology

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ABSTRACT

Background: This hematological malignancy comprises a major health problem in the society due to its high mortality and morbidity. There is a need for the accurate estimation of incidence and prevalence of acute lymphocytic leukemia (ALL), and other hematological malignancies in India to estimate the true disease burden and its impact on the population which may help in formulating the guideline which helps in better risk stratification and treatment. Unfortunately, there is a real paucity if epidemiologic data on pediatric cancers in India and particularly in several parts of Rajasthan.

Objectives: To find out the prevalence and other epidemiological distribution of hematological malignancy in pediatric age group patients. Furthermore, it was objected to study hematological profile and bone marrow typing in pediatric patients with hematological malignancies.

Methodology: A prospective observational study carried out over 2 years. Confirmed cases of hematological malignancies were recruited from the pediatric outpatient and inpatient department. Data recorded in the preformed case record form include demographic data, data of clinical history and clinical examination, laboratory findings such as complete blood count, peripheral smear examinations, bone marrow examination for cellularity and differential count, and immunophenotyping.

Observations: ALL is the most common hematological malignancy among pediatric patients in the present study with 156 out of 193 patients (80.82%). Other malignancies are acute myeloid leukemia (AML) (13.98%) and chronic myeloid leukemia (1.55%) and lymphoma (3.62%). Nearly half of the patients were below 5 years of age (59.6%) and males were predominantly affected with frequency of 77.6%. Common clinical features were fatigue, fever, loss of appetite, bone pain, petechies, hepatic and splenomegaly, pallor, and lymphadenopathy.

Conclusion: The most common type of malignancies in pediatric age group is hematological malignancies with predominant variant is ALL. It is commonly affecting age below 5 years with male predominance.

KEYWORDS

Acute lymphocytic leukemia, hematological malignancies, pediatric age

INTRODUCTION

Most frequent childhood cancers arise in the hematopoietic system, central nervous system (CNS), soft tissue, bone, kidney, etc. It is in sharp contrast to adults, in whom skin, lung, breast, prostate, and colon are the most common sites of tumors.[1] Among all these cancers, most frequent cancer in pediatric age group is the hematological malignancy. Worldwide, the annual number of new cases of childhood cancer exceeds 200,000 and more than 80% of these are from the developing world.[2] The reported age of the standardized incidence rate for India ranges from 38 to 124 per million children per year.[3] In India, one study at Tata Memorial Hospital at Bombay, in year 1979, found 271 (75.6%) of total 358 patients with acute lymphoblastic leukemia (ALL) were in pediatric age group with male predominance (70%).[4] The outcome of hematological cancers in terms of long-term survival has significantly improved from 20% to 60% in ALL, from <70% to more than 90% in Hodgkin's disease, from 30% to 70% in non-Hodgkin's lymphoma (NHL), and from 10% to 40% in acute myeloblastic leukemia (AML).[5] This hematological malignancy comprises a major health problem in the society due to its high mortality and morbidity. Unfortunately, there is a real paucity if epidemiologic data on pediatric cancers in India and particularly in Rajasthan. In studies by Marwaha and Kulkarni,[6] it is also stressed on the need for the accurate estimation of incidence and prevalence of ALL and other hematological malignancies in India to estimate the true disease burden and its impact on the population which may help in formulating the guideline. It is important to identify for prognosis and management lacunae in hematological malignancies in the pediatric population for better risk stratification and treatment.

Hence, the study is designed with special interest to find out its prevalence and early diagnosis of the disease, so more and more of this kind of malignancy can be made amenable to the treatment.

METHODOLOGY

It was a prospective observational study carried out by Pathology Department in congruence with Pediatrics in RNT Medical College, Udaipur. These cases include indoor and outdoor cases. Study was done during a period of approximately 2 years (June 2018 to May 2020).

Patients were recruited from outdoor and indoor Department of Pediatrics. Before enrollment in the study, the legal guardians and the patients were clearly explained about the nature of the study. The written informed consent was taken from them before enrollment of the patient in the study. Details of the patients who gave consent were noted down on the preformed case record form. Data of the patients noted were age, gender, clinical histories such as presenting symptoms, past history of any viral infection or similar complaints, family history, history of chronic disease and drug history, clinical examination data such as general examination for pallor, hepatomegaly, splenomegaly, lymphadenopathy, and systemic examination. Clinical investigations such as complete blood count (CBC), peripheral smear examination, bone marrow examination for cellularity and differential count, and immunophenotyping; biochemical examinations such as serum uric acid, serum lactate dehydrogenase, and serum electrolytes. Investigations such as renal function test, cerebrospinal fluid routine, and microscopic examination and radiological examinations were done as per the requirements. In laboratory investigations, the CBC was done by automated cell counter. For peripheral smear examination, blood smear was prepared manually from fresh blood without the use of anticoagulant and stained by Romanowsky stains. For bone marrow examination, the marrow was collected from anterior iliac crest, posterior iliac spines, or in case of infant anteromedial surface of tibia. The stain used for the examination of bone marrow used was Giemsa stain. Some special stains were also utilized for accurate staging of cancer differentiating from another type, like myeloperoxidase (MPO) showing brown color and stain enzyme located in the primary granules of myeloid cells. So, myeloperoxidase (MPO) stains myeloid cells of AML only and not stains lymphoblasts of ALL, which easily differentiate AML and ALL.

RESULTS

The study was carried out by pathology department with the collaboration of pediatric department. During the study duration of 2 years, a total of 193 were diagnosed as having hematological malignancy. The age incidence of hematological malignancy in present study shows that it is highest in 0-5 years of age with 59.6% (115) of all patients [Table 1]. Out of 193 patients, 133 (77.6%)

patients were male and 60 (31.08%) were female. Hence, male to female ratio for hematological malignancy found to be 2.2:1. Table 2 shows frequency and age-wise distribution of various hematological malignancies in pediatric patients. ALL is the most common hematological malignancy among pediatric patients in the present study with 156 out of 193 patients (80.82%). Other malignancies are AML (13.98%) and chronic myeloid leukemia (CML) (1.55%). Lymphoma was seen in 3.62% patients.

Table 1: Age distribution of all the patients

Age(years)	No.	%
0-5	115	59.6
6-10	46	23.8
11-15	32	16.6
Total	193	100

Table 2: Frequency of various hematological malignancies in pediatric patients

Malignancy	Age group (years)			Total number of cases
	0-5	6-10	11-15	
ALL	99(63.5%)	35(22.4%)	22(14.1%)	156
AML	16(59.3%)	6(22.2%)	51(18.5%)	27
CML	0	0	3(100%)	3
Lymphoma	0	5(71.4%)	2(28.6%)	7
Others	0	0	0	0

ALL - Acute lymphocytic leukemia; AML - Acute myeloid leukemia; CML - Chronic myeloid leukemia. Furthermore, most of the patients (99 out of 156) below 5 years had ALL. In CML, all 3 cases are in 11–15 years age group. In lymphoma, 2 cases were of Hodgkin's Lymphoma, which is in 11–15 years age group, and 5 cases were of NHL in 6–10 years group, while AML were distributed evenly throughout in all age groups in pediatric patients. Table 3 shows gender-wise distribution of various hematological malignancies. Out of 156 cases of ALL, 114 were male and 42 were female [Table 3].

Table 3- Sex wise distribution of each malignancy

Malignancy	Male	Female	Total number of cases
ALL	114(73%)	42(26.9%)	156
AML	14(51.9%)	13(48.1%)	27
CML	1(33.3%)	2(66.7%)	3
Lymphoma	4(57%)	3(42.9%)	7

In the present study, the most common presenting symptom was fatigue, which was seen in 98.4% of patients followed by fever in 94.8% of cases. Other symptoms were loss of appetite (90.1%), loss of weight (96.4%), bone pain (56.5%), cough and cold (31.1%), petechiae (29.1%), and CNS symptoms (18.7%).

Table 3 : Clinical symptoms (%) in patients with hematological malignancy signs

Malignancy symptoms	No.	%
Fatigue	190	98.4
fever	183	94.8
Loss of appetite	175	90.1
Weight loss	186	96.4
Bone pain	109	56.5
Cough/cold	96	31.1
Petechiae	56	29.1
CNS symptoms	36	18.7

While most common presenting signs were splenomegaly and pallor, which were seen in 90.2% and 98.9%, respectively, other common signs found were hepatomegaly (74.1%) and lymphadenopathy (29.1%) [Table 4].

Table-4: Clinical signs (%) in patients with hematological malignancy signs

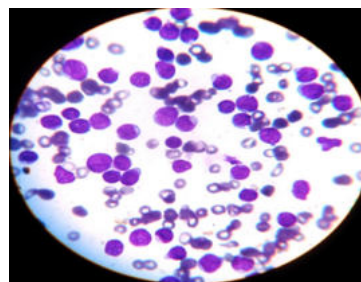
Malignancy signs	No.	%
Splenomegaly	174	90.2
Hepatomegaly	143	74.1
Pallor	185	98.9
Lymphadenopathy	57	29.5

Most of the patients (53.4%) had white blood cell (WBC) count 11,000-50,000/mm³ with 22.80% had >50,000/mm³. Nine patients had WBC count <5000/mm³. (Table-5)

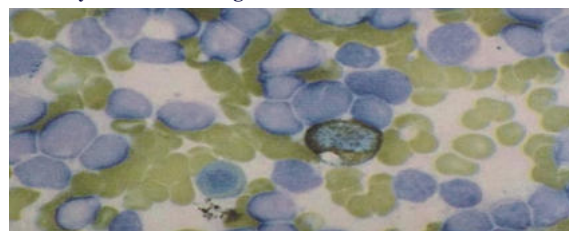
Table 5- Laboratory data in patients with hematological malignancy

Laboratory data	No.	%
Hb(gm%)		
<7	98	50.8
7-11	76	39.4
>11	19	9.8
Total	193	100
WBC count		
<5000	9	4.7
5000-10,000	37	19.2
11000-50000	103	53.4
>50,000	44	22.8
Total	193	100
Platelet count		
<20,000	42	21.8
20,000-100000	129	66.8
<100000	22	11.4
total	193	100

In the present study, total ALL cases were 156, but four cases were in remission. Hence, bone marrow shows normal finding in that cases, but they were known case of ALL-L1.



Figures 1 shows the peripheral smear and bone marrow smear from a 5-year-old child diagnosed as ALL-L1.



peripheral smear stained with Leishman's stain and bone marrow smear stain with negative peroxide smear. (fig.2)

There are small lymphoblasts and homogenous chromatin with scant cytoplasm. Out of remaining 156 cases, L1 type of lymphoblast was seen in 86.44% case, L2 type in 11.86% cases, and L3 type in 1.69% of cases. Hence, L1 is predominant type of lymphoblast in ALL, comprising three-fourth of the cases.

In AML, 10% of cases had blasts of M1 type, 80% had M2 type, and 10% had M3 type of myeloblast. Figure 3 shows peripheral smear of AML case.



It shows myeloblasts with high N: C ratio, prominent nucleoli, and Auer rods in cytoplasm.

DISCUSSION

Hematological Malignancies accounts approximately for one-third of

total cancers occurring in early childhood, with ALL being the most common entity with peak prevalence 2-5 years of age.[7,8] In the present study, within 2 years duration patients from indoor and outdoor departments of pediatrics were screened for hematological malignancies. Among them, 193 patients found various clinical and hematological findings of hematological malignancies.

Similar finding was seen with other studies done by Young *et al.* and Teppo *et al.*[9,10] However, the frequency of leukemia is quite high in the present study as compared to the above-mentioned studies. This difference can be explained by the large number of patients (115) in the age group 0–5 years, in which ALL is the most common malignancy. The studies done in various states of India showed similar findings like present study. A study in West Bengal had incidences of 84% and 16%, respectively, for leukemia and lymphoma.[11] Similarly, studies done in Odisha in 2007 show 90% and 10%, respectively, and in Gujarat in 2010, the incidences for leukemia and lymphoma were 91% and 9%, respectively.[12] While one study in Rajasthan (1991) had reverse finding with incidence of leukemia and lymphoma were 48% and 52%, respectively.[13] The incidence of ALL found in the present study was 80.83%. It shows that more than three-fourth patients in the present study are suffering from ALL. Similarly, data of other countries show the ALL is the most frequently diagnosed malignancy in children, representing nearly one-third of all pediatric cancers.[14]

In the present study, incidence of hematological malignancy was very much high in male patients, i.e., 68.91% of cases were male. Similar findings were seen with other studies done by Das *et al.* and Li *et al.*[16,17]

Presenting signs and symptoms of the patients in the present study were fatigue, pyrexia, anorexia, pallor, splenomegaly, and hepatomegaly, which is seen with similar frequencies in the study by Das *et al.* and Siddaiahgari *et al.*[16,18] Anemia is invariably present in all patients in the present study. Only 1.72% patient in this study and 3% in Das study have hemoglobin level >11 g%. Looking at total count, most of the patients have total count between 10,000 and 50,000.

While interpreting the total count, we should keep leukemoid reaction in mind as it can produce total count in the same range too. Leukemia can be differentiated from leukemoid reaction by examining the peripheral smear and bone marrow.

CONCLUSION

In summary, the most common age group of hematological malignancies in the present study is below 5 years with most common is ALL. Males are commonly affected than females. In ALL, the most common type of lymphoblast seen was L1 type. While in AML, the most common myeloblast was M2 type. The sample size of the study was quite good. However, because of less funding the laboratory evaluation by flow cytometry, karyotyping, and fluorescence *in situ* hybridization analysis could not be done.

Financial support and sponsorship- Nil.

Conflicts of interest- Nil

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