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STUDY OF HAEMATOLOGICAL MALIGNANCY IN PAEDIATRIC PATIENTS

Pathology

Dr. Hitendra Barot MD, Assistant Professor, Department of Pathology, B. J. Medical College and Civil Hospital, Asarwa, Ahmedabad 380016, Gujarat, India.

Dr. Rahul Sinha* MD, Senior Resident, Department of Pathology, B. J. Medical College and Civil Hospital, Asarwa, Ahmedabad 380016, Gujarat, India.*Corresponding Author

Dr. Mitali Das MD, Department of Pathology, B. J. Medical College and Civil Hospital, Asarwa, Ahmedabad 380016, Gujarat, India.

ABSTRACT

Introduction: Haematological malignancy comprises a major health problem in the society due to its high mortality and morbidity. It is of clinical importance to diagnose these malignancies early so that proper intervention may be undertaken. The present study is an attempt to study prevalence of paediatric haematological malignancy in our tertiary care centre. **Material and method:** This study comprised of a total 124 cases of paediatric patients during a period of approximately 2 years (June 2016 to September 2018) in a Tertiary Care Centre, Ahmedabad, Gujarat. These cases include indoor and outdoor cases.Relevant proper clinical history was obtained. Lab parameters were obtained from internal Lab Informatics Services. Peripheral smear, Bone Marrow Examination and Special Stain (PAS and MPO) were done as per indication. **Result and conclusion:** In our study we found that ALL is commonest haematological malignancy in paediatric age (81.45%). 0-5 years is most frequent age group affected by haematological malignancy (50.8%). Male to female ratio is 1.8:1. Only 2 cases of CML was found only in age group 11 to 15 years(both female). 3 cases of lymphoma was found in 6 to 10 years, 1 case in 11 to 15 years. No case of CML, lymphoma was found in age 0 to 5 years. The commonest sign were pallor (91.13%) and splenomegaly (87.90%) followed by hepatomegaly (59.68%) and lymphadenopathy (22.58%).The most common type of lymphoblast seen in ALL was L1 type, and most common myeloblast seen in AML was M2 type.

KEYWORDS

Paediatric, Hematologic, Leukaemia, Lymphoma, CML

INTRODUCTION:

Haematological malignancy comprises a major health problem in the society due to its high mortality and morbidity. Unfortunately, there is a real paucity of epidemiologic data on paediatric cancers in India.

In studies by Marwaha and Kulkarni [7], it is also stressed on the need for the accurate estimation of incidence and prevalence of acute lymphoblastic leukaemia and other haematological malignancies in India to estimate the true disease burden and its impact on the population which may help in formulating the guideline[3].

Most frequent childhood cancers arise in the haematopoietic 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 tumours[5]. Among all these cancers, most frequent cancer in paediatric age group is the haematological malignancy[5].

Worldwide, the annual number of new cases of childhood cancer exceeds 2,00,000 and more than 80% of these are from the developing world. The reported age of the standardized incidence rate for India ranges from 38 to 124 per million children per year[2].

In India, one study at Tata Memorial Hospital at Mumbai, 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%)[7] .The outcome of haematological 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) in 10 to 40% in acute myeloblastic leukemia (AML)[1] . It is important to identify haematological malignancies for prognosis and management lacunae in the paediatric 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. Considering the study subject for the area of Ahmedabad, we studied the paediatric patients coming to our teaching institute in Ahmedabad for better view of study.

Material and method:

This study comprised of a total 124 cases of paediatric patients during a period of approximately 2 years (June 2016 to September 2018) in a Tertiary Care Centre, Ahmedabad, Gujarat. These cases include indoor and outdoor cases.

Clinical details and Peripheral smear examination:

1. Descriptive cross-sectional study of cases including detailed clinical data of age, sex, clinical features, biochemistry and radiological findings of the patients were obtained from laboratory information system.
2. Peripheral blood was drawn from all study subjects under aseptic precautions in EDTA vaccutainers. A complete haemogram was performed using Horiba pentra XLR automatic Haematological analyzer (five-part differential).
3. Peripheral smear examination was done with slides stained in Giemsa stains.

Bone marrow aspiration and biopsy:

1. Bone marrow aspiration was done from anterior iliac crest/posterior iliac spines, anteromedial surface of tibia especially in infant.
2. In small babies, marrow was withdrawn from the medial aspect of the upper end of the tibia just below the level of the tibial tubercle
3. In older children, the tibial cortical bone is usually ercle. too dense and the marrow within is normally less active.
4. Sternal puncture in children should be avoided because the bone is thin and the marrow cavities are small

Special Stain :

1. Periodic acid Schiff (PAS) stain was used to differentiate ALL from AML which gives characteristic block cytoplasmic positivity in ALL.
2. Myeloperoxidase (MPO) stains blasts in cases of AML. It was used to differentiate between AML and ALL.

Ethical considerations:

All procedures performed were in accordance with the ethical standards of the institution.

Observation and result:

Total of 124 cases were diagnosed as having haematological malignancy out of about three lakh paediatric cases, which include both outdoor and indoor patients. So, our hospital-based prevalence of haematological malignancy is 42 cases per 1 lakh paediatric population.

We have studied incidence of various haematological malignancies in paediatric patiens, age-wise distribution of malignancies, sex wise distribution of including male: female ratio, percentage of signs and symptoms in patients, various laboratory parameters and blast type on

bone marrow examination.

Table 1: Various haematological malignancies in paediatric patients

Haematological Malignancy	No. of cases	Percentage (%)
ALL	101	81.45
AML	17	13.71
CML	02	1.61
CLL	00	-
LYMPHOMA	04	3.23
Total	124	100

As table and graph shows, among all the haematological malignancies, we found 101 cases of ALL, 17 cases of AML, 2 cases of CML and 4 cases of lymphoma. So, ALL is the leading malignancy in paediatric age group comprising total of 81.45% of all cases.

Table 2: Age wise distribution

Age Group	No. of cases	Percentage (%)
0-5 Years	63	50.80
6-10 Years	33	26.61
11-15 Years	28	22.58
Total	124	100

So, it suggests highest incidence in 0-5 year of age group.

Table 3: Sex wise distribution

Sex	No. of case	Percentage (%)
Male	81	65.32
Female	43	34.67
Total	124	100

Out of 124 cases, 81 cases found in male and 43 cases in female, which comprise 65.32% and 34.67% of total cases respectively.

In our study M:F ratio is 1.8:1, suggesting disease is more common in male sex.

Table 4: Age wise distribution of each haematological malignancy

Malignancy	Age Group						Total No. of cases
	0-5 Years		6-10 Years		11-15 Years		
	No. of Cases	%	No. of Cases	%	No. of Cases	%	
ALL	56	55.44	24	23.76	21	20.79	101
AML	7	41.17	5	29.41	5	29.41	17
CML	-	-	-	-	2	100	2
LYMPHO MA	-	-	3	75	1	25	4
Total	63	-	32	-	29	-	124

Age wise distribution of each haematological malignancy show that out of 101 cases of ALL, 56 cases are in age group 0-5 year comprising 55.44% of total cases of ALL, while in 6-10 years and 11-15 years age group, ALL found in 24 cases and 21 cases respectively, which comprise 23.76% and 20.79% of total cases of ALL in respective age group. This indicates ALL is more common in age group 0-5 years (55.44%).

In our study among total AML cases 41.17% cases are in age group 0-5 years. 29.41% of total cases of AML, found in age group 6-10 years and another 29.41% of total cases found in age group 11-15 years.In CML both the cases are in 11-15 years age group.In lymphoma 3 cases are in 6-10 years group and 1 case in 11-15 years age group.

Table 5: Sex wise distribution of each malignancy

Malignancy	Male		Female		Total No. of cases
	No. of Cases	%	No. of Cases	%	
ALL	70	69.30	31	30.69	101
AML	8	47.05	9	52.94	17
CML	-	-	2	100	2
LYMPHOMA	3	75	1	25	4
Total	81	65.32	43	34.67	124

70 cases were male and 31 cases were female in ALL comprising 69.30% and 30.69% of total ALL cases, suggest ALL is more common in male.In AML, 47.05% cases were male and 52.94% cases were female, while in CML both the cases were female and lymphoma 75% and 25% cases were male and female respectively.

Table 6: Blast typing of ALL and AML cases in bone marrow examination

	Blast Type	No. of cases	Percentage (%)
Lymphoblast (among total cases of ALL)	L1	86	72.90
	L2	13	11.01
	L3	02	1.70
Myeloblast (among total cases of AML)	M0	-	-
	M1	02	1.70
	M2	12	10.16
	M3	03	2.54
	M4	-	-
	M5	-	-
	M6	-	-
	M7	-	-
Total		118	100 %

Total ALL cases were 101 but 4 case were in remission, so bone marrow shows normal finding in that cases but they were known case of ALL-L1. Out of 118 Cases, L1 type of lymphoblast was seen in 72.90% case' L2 type in 11.01% cases and L3 type in 1.70% cases. This indicate that L1 in predominant type of lymphoblast in ALL, comprising 3/4th of the cases.

We observe 1.70% blast of M1 type, 10.16% of M2 type and 2.54% of M3 type of myeloblast. Two cases of chronic phase of CML and three cases of lymphoma do not show increased marrow blast. Only one case of NHL show bone marrow involvement.

Table 7: Clinical signs (%) in patients with haematological malignancy

Sign	No. of Cases	Percentage (%)
Splenomegaly	109	87.90
Hepatomegaly	74	59.68
Pallor	113	91.13
Lymphadenopathy	28	22.58

Commonest signs were pallor and splenomegaly comprise 91.13% and 87.90% of cases respectively, followed by hepatomegaly in 59.68% and lymphadenopathy in 22.58% of cases.

Table 8: Symptoms in patients with haematological malignancy

Symptoms	No. of Cases
Fatigue	101
Fever	89
Loss of appetite	82
Weight Loss	93
Bone Pain	55
Cough / Cold	40
Petechiae	22
CNS Symptoms	19

We can see that the most common symptom is fatigue in total of 101 cases among 124 cases followed by weight loss, fever, loss of appetite in and so on.

DISCUSSION:

Total 124 paediatric patients were diagnosed with haematological malignancy and findings obtained are discussed with other studies here. Studies include following findings

TABLE 9 – Haematological malignancy incidence

Haematological malignancy	Prajapati et al (India)[11]		Michel et al (Switzerland)[10]		Present Study	
	No of cases	%	No of cases	%	No of cases	%
	156	100	721	100	124	100
Leukemia	147	94.23	520	72.12	120	96.77
Lymphoma	9	5.77	201	27.88	4	3.23

According to this table, leukemia is the leading haematological malignancy in paediatric age group. In our study, we found 96.77% leukemia, that is comparable to study done by Prajapati et al and Michel et al in which prevalence was 94.23% and 72.12% respectively.

Table 10: Clinical features

Clinical Features	K. Das[4]	Prajapati et al[12]	Present Study

Fatigue	80%	84.4%	81.45%
Fever	79%	77.5%	71.77%
Anorexia	25%	44.8%	66.13%
Weight Loss	25%	36.2%	75.00%
Bone Pain	34%	29.3%	44.35%
Bleeding / petechiae	34%	25.8%	17.74%
Pallor	92%	81%	91.15%
Splenomegaly	63%	82.7%	87.90%
Hepatomegaly	70%	65.5%	59.68%
Lymphadenopathy	72%	36.2%	22.58%

Comparison study shows that, fatigue, fever, pallor, hepatosplenomegaly are cardinal manifestation and physical signs.

Table 11: Laboratory data values

	Values	K. Das[4]	Prajapati et al[12]	Present Study
Hb (gm%)	<7	66%	68.96%	56.45%
	7-11	31%	29.32%	38.71%
	>11	03%	1.72%	4.84%
Platelet Count (per cumm)	<20,000	-	20.68%	25.81%
	20,000-99,999	-	60.36%	59.68%
	>1 Lakh	-	18.96%	14.52%
Total WBC Count (per cumm)	<5,000	17%	1.72%	4.03%
	5,000-9,999	15%	8.62%	21.77%
	10,000-49,999	42%	62.06%	45.16%
	>50,000	26%	27.60%	29.03%

It is clear that anemia is invariably present in all patients. Only 4.84% patient in our study and 3% in K. Das study have Hb level >11 gm%.

Table 12: Incidence of cancer in various states

Type of cancer	Mumbai (1998)	Rajasthan (1991)	West Bengal (2003)	Banglore (1996)	Kerala (2000)	Orissa (2007)	Gujarat (2010)	Present Study (2011)
Leukemia	80%	48%	84%	77%	70%	90%	91%	96.77%
Lymphoma	20%	52%	16%	23%	30%	10%	9%	3.23%

As per this table in all study cases of leukemia are more than lymphoma except in Rajasthan where the cases of lymphoma are more[4,8,11].

CONCLUSION AND SUMMARY:

1. A study of haematological malignancies were undertaken at Tertiary Care Centre, Ahmedabad, Gujarat for approximately 2 year (June 2016 to September 2018) to know the incidence of different types of haematological malignancies, its morphology, its age and gender wise distribution, related clinical features and its correlation with other studies.
2. Total 124 cases of haematological malignancies were studied from June 2016 to September 2018.
3. Our hospital-based prevalence of haematological malignancy is 42 cases per 1 lakh paediatric population. Though it may not be the exact value of prevalence in Ahmedabad, but it may reflect the prevalence of hematological malignancy in paediatric population as larger number of patients coming to our hospital.
4. Acute lymphoblastic leukaemia (ALL) is the leading malignancy in paediatric age group comprising total of 81.45% of all cases.
5. Majority of cases (50.80%) in age group 0-5 years, 33 cases in age group 6-10 years, 28 cases in age group 11-15 year comprising 50.80%, 26.61% and 22.58% of cases respectively.
6. 81 cases were found in male and 43 cases in female, which comprise 65.32% and 34.67% of total cases respectively with M:F ratio is 1.8:1, suggesting disease is more common in male sex.
7. ALL is more common in age group 0-5 years (55.44%). Half of total AML cases are in age group 0-5 years.
8. Most common symptom was fatigue in total of 101 cases among 124 cases followed by weight loss, fever, loss of appetite in and so on.
9. Majority of patients had anaemia in total of 95.16% of patient. Maximum cases have total WBC count between 10,000-49,999 per cumm. In this study leucocytosis is more common than leukopenia. Majority of patients had platelet count between 20,000 - 1 Lakh (59.68%)
10. Most of the patients had increased S.LDH and S.uric acid levels.
11. Bone marrow findings in majority of cases were of hypercellularity and out of 118 Cases, L1 type of lymphoblast was seen in 72.90% cases indicate that L1 in predominant type of lymphoblast in ALL, comprising 3/4th of the cases. M2 type blasts were most common among AML cases.
12. The observation made from the current study has shown maximum number of cases in age group between 0-5 years and with male predominance.
13. Among all haematological malignancies ALL is the most common malignancy.
14. It is seen that among cases of ALL, the most common type of lymphoblast seen was L1 type. While in AML, the most common myeloblast was M2 type.
15. The study though of small sample size, does bring out facts which were also brought out by various other authors. However, laboratory evaluation by flow cytometry, karyotyping, and fluorescence *in situ* hybridization analysis help aid in further classification of haematological malignancies. It calls for further study and research in the field of haematologiccal malignancy which has remained still not completely curable even at this stage.

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