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CLINICO-EPIDEMIOLOGICAL PROFILE OF PEDIATRIC HEMATOLOGICAL MALIGNANCIES. INSIGHTS FROM A TERTIARY CARE CENTRE IN JAIPUR RAJASTHAN, INDIA

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ABSTRACT

Background: Childhood malignancy is among the leading causes of mortality in the paediatric population in developed countries. The incidence of haematological malignancy is increasing globally. Among childhood malignancies, haematological malignancy is the most common. Our study was aimed to study the current clinicoepidemiological pattern and the exact burden of haematological malignancy in Rajasthan so that proper guidelines can be formulated for its early diagnosis and treatment.

Materials and Methods: A hospital based prospective observational study was conducted in which data were collected from the newly diagnosed haematological malignancies admitted in the hospital during the study period and clinicoepidemiological profile of each case was analysed.

Results: 107 cases were included in the study among which the most common haematological malignancy was leukaemia. B-ALL was the most common leukaemia comprising 81.30 % of cases. The most common age affected was between 0-5 years which constituted 56.07% cases. The male to female ratio of haematological malignancy was found to be 1.9:1. Hindus 90.7% (97 cases) were more affected than Muslim 9.3% (10 cases). 7 patients of ALL were born out of consanguineous marriage. The most common presenting symptom was fever which was seen in 93.5% of patients followed by swelling in 30.8% of cases while the most common presenting signs were pallor 100% f/b hepatomegaly (77.6%) and splenomegaly (61.7%). Anemia was seen in 100% patients and among them 50.5 % of patients had severe anemia (< 7 gm %). Most of the patients (43.92%) had WBC count between 5000-49,999 per mm 3 while most of the patients (67.3%) had platelet count between 20,000 to 99,999 per mm3. Rural region and urban region had almost equal distribution of haematological malignancy. Rajasthan had the highest representation constituting 91.6% of cases. In which Jaipur had the highest share (23.5% cases). Most of the patients belonged to lower middle income group (53.3%) according to modified Kuppuswamy scale. On comparing haematological malignancy with father's occupation, most patient's father were farmers (38.3%) and 19.6 % were labourer.

Conclusion: The most common haematological malignancy was leukaemia among which B- ALL was the most common type. The most common age group affected was 0 to 5 years. Males were more affected. From the present

study, it was concluded that the etiology for the haematological malignancy may be multifactorial for which a study on a larger scale is needed.
Keywords: Clinicoepidemiological profile, haematological malignancy, multifactorial, modified Kuppuswamy scale.

INTRODUCTION

Childhood malignancies are the second leading cause of mortality in the paediatric population in developed countries.[1] In the year of 1857, Virchow probably was the first to classify leukemia. On the pathologic distribution of tumour he distinguished splenic and lymphatic forms of leukemia.[2] The incidence of leukemia has increased considerably and this rise is noticeable because of improved statistics, better case findings with novel technologies which lead to better diagnosis and treatment methods. The incidence of leukemia found to be varying from different geographical areas according to their life styles, economic conditions, and poverty rate.[3] The incidence and clinical presentation of many haematological cancers in India is relatively lower and differs from that seen in western world due to health awareness and availability of health care delivery system.[4]

In view of increasing incidence of the childhood malignancy there is a need for a more effective and time sensitive approach for the diagnosis and intervention. Early diagnosis of the childhood malignancy provides us adequate time to plan for treatment and optimize patient prognosis. The most common childhood malignancy in paediatric age group is haematological malignancy and it comprises a major health problem in the society due to its high mortality and morbidity. Unfortunately there are very few epidemiological data on haematological malignancy in India and particularly in Rajasthan.

In the developing countries, a lot of effort has been devoted to reduce the child mortality from non malignant conditions such as malnutrition, diarrhoea, respiratory diseases, and many other infective causes. Haematological malignancy also requires urgent attention so that early diagnoses can be done and therapeutic interventions may be undertaken. One of the important steps in this regard is conducting epidemiological studies to determine the incidence of paediatric malignancies in different regions of the country. This will help the health professionals of a particular region to look out for the more common malignancies in that part. Provision of better health care is the ultimate goal of such epidemiological studies. In detailed review of literature we found only few studies which measured the burden of haematological malignancies in Rajasthan.

Hence there is a need to know the exact burden of these haematological malignancies in Rajasthan so that proper guidelines can be formulated for its early diagnosis and treatment. It will also help to develop appropriate infrastructure and allocation of proper funds.

RESULTS

The age wise incidence of haematological malignancies in present study shows that it is highest in 0-5years age group with 56.07% (60 cases) of all patients. The male to female ratio for haematological malignancy was found to be 1.9:1 (Table-1). ALL is the most common haematological malignancy among paediatric patients in present study with 95 patients out of 107 patients (88.78%) with B-ALL comprising 87 cases (81.30%) and T-ALL comprising 7 cases (6.54%). Other malignancies are AML 4 cases (3.74%) 2 cases of relapse (1.9%); HL 7 cases (6.54%) [Table-2]. Furthermore, most of the patients; 56 out of 87 in age group 0-5 yrs had ALL.

Hindus 90.7% (97 cases) were more affected than Muslim 9.3% (10 cases). 7 patients of ALL were born of consanguineous marriage. In the present study, the most common presenting symptom was fever which was seen in 93.5% of patients followed by swelling 30.8% of cases while most common presenting signs were pallor 100% f/b hepatomegaly (77.6%) and splenomegaly (61.7%) [Table-3].

Among lab findings, anemia was seen in 100% patients and among them 50.5 % of patients had severe anemia (< 7 gm %). These findings are correlating with clinical examination, which showed pallor in 100% patients. Most of the patients (43.92%) had WBC count between 5000-49,999 per mm3 while most of the patients (67.3%) had platelet count between 20,000 to 99,999 per mm3 [Table-4]

In the present study, most of the haematological malignancy (51.4%) was from rural region and 48.6% was from urban region. Most of the cases (91.6%) were from Rajasthan, 5.6 % from UP, 1.9% from Haryana and 0.9% from MP. Among Rajasthan, Jaipur district had the most cases (23.5%) while least was from Kotputali and Jhalawar district (1% each).

In the present study, most of the patients belonged to lower middle group (53.3%) according to modified Kuppuswamy scale [Table-5]. On comparing haematological malignancy with father's occupation, most patient's father were farmer (38.3%), 19.6 % were labourer. 3 cases of ALL patients had positive family history of malignancy. 9 cases had positive viral association, 7 cases had EBV association and 2 cases had HCV association.

In the present study, 87.9 % treatment was ongoing, 4.7% expired during the treatment, 3.9% had successfully completed the treatment, and 1.9%

cases were relapse while 1.9% patient abandoned the treatment (Table-6).

Table 1: Age and sex wise distribution of study subjects

AGE GROUP (YEARS)	NUMBER OF CASES	PERCENTAGE OF CASES	MALE	FEMALE
0 TO 5	60	56.07	41(68.3%)	19(31.7%)
6 TO 10	23	21.50	15(65.2%)	08(34.8%)
11 TO 15	22	20.56	13(59%)	9(41%)
>15	2	1.87	1(50%)	1(50%)

Table 2: Frequency of various hematological malignancies in study subjects

	Age (n=107)				Total
	0 to 5 Years	6 to 10 Years	11 to 15 Years	> 15 Years	
B-ALL	55	18	13	1	87
	91.67	78.26	61.9	50.00	81.3
T-ALL	1	1	5	0	7
	1.67	4.35	22.73	0.00	6.54
AML	3	0	0	1	4
	5.00	0.00	0.00	50.00	3.74
B-ALL RELAPSE	0	0	2	0	2
	0.00	0.00	4.55	0.00	1.9
HODGKIN LYMPHOMA	1	4	2	0	7
	1.67	17.39	9.09	0.00	6.54
NON HODGKIN LYMPHOMA	0	0	0	0	0
	0.00	0.00	0.00	0.00	0.00
Total	60	23	21	2	107
	56.07	21.50	20.56	1.87	100.00

Table 3: Symptoms and Signs observed among study subjects

SYMPTOMS	NUMBER OF CASES (%)
• FEVER	**100(93.5%)**
• BLEEDING	**14(13.1%)**
• BONE PAIN	**18(16.8%)**
• SWELLING	**33(30.8%)**
• VOMITTING	**9(8.4%)**
• COUGH/CORYZA	**9(8.4%)**
• SEIZURES	**0(0%)**
• SKIN NODULES	**0(0%)**
• GUM SWELLING	**3(2.8%)**
• ABDOMINAL SWELLING	**12(11.2%)**
CLINICAL SIGNS	
• PALLOR	**107(100%)**
• JAUNDICE	**5(4.7%)**
• SKIN NODULES	**16(15.0%)**
• BLEEDING	**17(15.9%)**
• EDEMA	**11(10.3%)**
• LYMADENOPATHY	**50(46.7%)**
• BONY TENDERNESS	**18(16.8%)**
• SPLENOMEGALY	**66(61.7%)**
• HEPATOMEGALY	**83(77.6%)**
• RENOMEGALY	**2(1.9%)**

Table 4: Laboratory findings observed among study subjects

LABORATORY FEATURE	VALUE	NUMBER OF CASES (%)
1. HEMOGLOBIN (GM %)	<7	54(50.5%)
	7-11	52(48.6%)
	>11	1(0.9%)
2. HIGHEST WBC (PER MM3)	<5000	17(15.9%)
	5000-49,999	47 (43.92%)
	>50,000	43(40.2%)
3. PLATELET COUNT (PER MM3)	<20,000	30(28.0%)
	20,000-99,999	72(67.3%)
	>1 LAKH	5(4.7%)

Table 5: Distribution of hematological malignancies according to socio-economic status observed among study subjects

Socioeconomic status	Frequency	Percent
<5 LOWER (V)	28	26.2
11-15 LOWER MIDDLE (III)	57	53.3
16-25 UPPER MIDDLE (II)	18	16.8
5-10 UPPER LOWER (IV)	4	3.7
Total	107	100.0

Table 6: Hematological malignancy and outcome

OUTCOME	Frequency	Percent
ABANDONED	2	1.9
COMPLETED	4	3.7
EXPIRED	5	4.7
ONGOING	94	87.9
RELAPSE	2	1.9
Total	107	100.00

DISCUSSIONS

In the present study, leukemia was the most common haematological malignancy accounting for about 87.85% cases. Similar finding was found with other studies done by Prajapati zankhana et al, Dasgupta senjuti et al and Mittal aditi et al.[5,6,7] The frequency of leukemia is quite high in the present study as compared to some studies done by Mittal aditi et al. This difference can be explained by the large number of patients [56.07%] in the age group 0-5 years, in which ALL is the most common malignancy.

The incidence of ALL found in the present study was 88.78%. Similar findings were shown by studies done by Prajapati zankhana et al and Dasgupta senjuti et al. In the present study, the most common age group affected by haematological malignancy was 0-5 years which accounted for 56.07 %. Similar findings were seen in studies done by Prajapati zankhana et al, Dasgupta senjuti et al. While one study done in Rajasthan done by Mittal aditi et al, the most common age group affected was between 15 to 18 years. In our present study, the highest incidence was high in male patients accounting for 65.4% cases. Similar findings were seen with other studies done by Prajapati zankhana et al, Dasgupta senjuti et al and Mittal aditi et al.

In the present study, the most common presenting symptoms was fever which was seen in 93.5% of patients while the most common presenting symptom in study done by Prajapati zankhana et al was fatigue followed by fever and in study done by Mishra renu et al,[8] constitutional symptoms were the most common clinical symptom.

The most common presenting signs was pallor 100% followed by hepatomegaly (77.6%) and splenomegaly (61.7%) while the most common sign in study done by Prajapati zankhana et al was splenomegaly (82.7%) and in the study done by Mishra renu et al the most common sign was splenomegaly (56.36%) and hepatomegaly (52.72%).

Anemia is invariably present in all patients in the present study. Similar finding was seen in studies done by Prajapati zankhana et al and Jatav J et al.[9] In the present study, 50.5 % of patients had severe anemia (< 7 gm %) while in the study done by Prajapati zankhana et al severe anemia constituted in 68.96% cases. Similar findings were seen in study conducted by Jatav J et al. Most of the patients (43.92%) had WBC count between 5000-49,999 per mm3 while similar findings were seen in studies done by Prajapati zankhana et al and Jatav J et al. Most of the patients (67.3%) had platelet count between 20,000 to 99,999 per mm3; similar findings were seen in study done by Prajapati zankhana et al which accounted for 60.36 % and Jatav J et al.

In the present study, most of the patients belonged to lower middle group (53.3%) according to modified Kuppuswamy scale. Similar finding was seen in study done by Hashemizadeh H MSc et al,[10] in Iran which accounted for 35%.

In the present study, most of the haematological malignancy (51.4%) was from rural region and 48.6% was from urban region. Similar findings were seen in study conducted by Dasgupta senjuti et al, in which majority (72.3%) of the patients were residents of rural areas whereas urban dwellers accounted for 27.5 % cases. A study conducted by Nasir et al,[11] showed that out of 149 patients, 62.42% belonged to rural areas and 37.58% belonged to urban areas. These findings are in agreement with Kong et al,[12] who reported that children born in rural areas showed significantly increased risk of death from cancer.

In the present study, on comparing haematological malignancies according to religion Hindus 90.7% (97 cases) were more affected than Muslim 9.3% (10 cases). Similar findings were seen in a study done by Laishram R. S. et al,[13] in which Hindus had the maximum number of cases (64.1%) followed by Christians and least number in Muslims.

In the present study, most of the cases (91.6%) were from Rajasthan, 5.6 % from Uttar Pradesh, 1.9% from Haryana and 0.9% from Madhya Pradesh. Among Rajasthan, Jaipur district had the most cases (23.5%) while least was from Kotputali and Jhalawar district (1% each). A study done by

Asthana smita et al,[14] showed that lymphoma and leukemia cases were maximum in North region of India. However we could find no studies which showed the district wise distribution of haematological malignancies in Rajasthan.

On comparing haematological malignancy with father's occupation, most patients' father were farmer (38.3%), 19.6 % were labourer while the remaining patient's father occupation. In a study conducted by Hashemizadeh H MSc et al in Iran, childhood leukemia was compared with high risk jobs of father. The type of high risk job in most of the ALL group were farming (74%) and 26% was painting. Similarly in a case control study conducted by Perez-Saldivar ML et al,[15] in Mexico City showed that among the children of fathers who were exposed to a high level of carcinogenic substances at work, there seemed to be a greater risk of developing ALL. Occupations that remained as risky occupations were insurance agent, farmer, machinery operator and builder.

In the present study, a total of 8 cases had history of consanguinity. Among these, 7 patients of ALL were born of consanguineous marriage while 1 case AML had history of consanguinity. In a study done by Nasir et al, patients were explored on the parental consanguinity basis and showed following categories of first cousin (38%), second cousin (21%), first cousin once removed (2%), bradri (19%), distant relations (11%), and unrelated spouses (9%), respectively and found that consanguinity was an important risk factors in the occurrence of Leukemia. In a similar study done by Yasmeen and Ashraf (2009) et al,[16] showed that acute lymphoblastic leukemia which comprised 32% of all cancers in their study, consanguinity was seen in 47% of cases.

In the present study, 3 cases of ALL patients had positive family history for carcinoma among all study subjects.2 cases had a positive family history for carcinoma neck while one case had positive family history of carcinoma oral cavity. However all the study subjects with positive family history for carcinoma had ALL. Similar findings were observed in study conducted by Bener, A et al.[17] In this study, the family history of cancer was overall more often positive in cases than in controls, 39 of 117 and 22 of 117, respectively .The family history of carcinoma was more common in patients with ALL than in Hodgkin and Non Hodgkin lymphoma. In this study stomach carcinoma was more prevalent of all tumors in the relatives of subjects (ALL, 7; HL, 2; NHL, 3).

In the present study, 9 cases had positive viral association, 7 cases had EBV association and 2 cases had HCV association. Similar findings were observed in a study done by Deng w et al,[18] which showed that 101 out of 162 children with ALL were positive for EBV, a positive rate of 62.35%, indicating a high rate of EBV infection in children with ALL.

In the present study, 87.9 % treatment was ongoing, 4.7% expired during the treatment, 3.9 % have successfully completed the treatment and 1.9% cases were B-ALL relapse while 1.9% patient abandoned the treatment.

CONCLUSION

In the present study, the most common haematological malignancy was leukemia among which B- ALL was the most common type. The most common age group affected was 0 to 5 years. Male was more affected than females. Hindus were more affected than Muslim. From our study we could determine the most common symptoms and signs. Different lab findings were elaborated from the study. The distribution of haematological malignancy among rural and urban was almost equal so an association could not be established between the two. Our hospital being a renowned tertiary care centre in Northern India we had cases not only from Rajasthan but also from nearby state like MP, UP and Haryana. Almost all the districts had nearly uniform distribution of haematological malignancy. However a study on large scale should be done in Rajasthan as the exact load of malignancy can be determined. The lower middle group was the most affected group according to socioeconomic status. So, the parents' education, family's income might have a direct or indirect relation in the occurrence of haematological malignancy for which a study on a large scale needs to be done. A direct relation between the father's occupation and occurrence of haematological malignancy couldn't be established as the study subjects had no direct exposure to carcinogens. Some association between consanguinity and haematological malignancy was established which suggests that there may be some genetic predisposition. There was some association between the viral infection and the occurrence of haematological malignancy which might even play a major role on the prognosis and treatment outcome of the malignancy. Hence it can be concluded that the etiology for the haematological malignancy may be multifactorial for which a study on a larger scale is needed.

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