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BMH Med. J. 2018;5(2):37-42 **Research Article**

Profile of Malignancies in Children Under 2 Years of Age- Study From a Tertiary Care Cancer Center in South India

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Abstract

Aim: Pediatric cancers are characterized by high cure rate and rarity of cancers of epithelial origin. There's a significant heterogeneity in the histologic variants of pediatric cancers as we consider different age groups. This study aims at analyzing the profile of malignancies in children under two years of age.

Materials and methods: This is a retrospective data analysis done over a period of five years starting from January 2009, at a cancer center in South India. Histopathological confirmation was made mandatory for all cases. Malignancies were classified based on the International Classification of Childhood Cancer.

Results: Males were more commonly affected. Acute leukemia was the most common malignancy in this age group followed by Wilms tumor and neuroblastoma. Treatment refusal/abandonment rate was relatively high with 37% opting out.

Keywords: Malignancies in Children

Introduction

Pediatric malignancies are unique in several aspects including their origin from embryonal cells [1], rapid response to therapy and high rate of survival as compared to adult cancers which mainly arise from epithelial cells and are associated with dismal prognosis. Though pediatric malignancies constitute only 1% of all cancers in the US, they are the second commonest cause of mortality in children, in this region. The scenario is different in India and many other resource-limited countries, where the incidence of pediatric malignancies is on the rise - forming 3.7% - 4% of all cancers [2]. At the same time, cancer is not a major cause of death in children in these countries, as there are other remediable causes of death like infection and diarrhea, to be addressed [3].

The heterogeneity of pediatric malignancies is substantial. They arise from lymphoreticular system, CNS, connective tissues or viscera. Even the most common malignancies have significant clinical,

biological and regional variability owing to environmental and genetic differences. The common cancers that occur in older children are strikingly different from those in younger ones and their response to treatment also varies [4,5]. While the common cancers that occur in the older children are leukemia, lymphoma and brain tumor, the younger ones show preponderance to neuroblastoma and Wilms tumor along with leukemia. Although there are several studies which describe the epidemiological profile of pediatric malignancies, the literature review shows a paucity of studies on cancers of infants and children in the younger age group in particular. This study aims at analyzing the frequency of occurrence of various malignancies in children under two years of age in a tertiary care cancer center in South India. Cancer therapy in a resource-limited country like India faces many challenges including the cost of treatment, late presentation, limited access to cancer care delivery centers and lack of parental education. As a result, treatment refusal/ abandonment is a major limiting factor against achieving high cure rate in pediatric malignancies in these countries. This study also focuses on the treatment refusal/abandonment rate in children under two years with cancer.

Materials and Methods

It is a retrospective data analysis conducted at a tertiary care cancer center. The study population includes all pediatric malignancies under 2 years of age, registered at this institute, during the period January 2009 to December 2013. The details included in the study were collected from case records, hospital cancer registry and also during follow up. The diagnosis was achieved by various clinical, hematological, radiological and histopathological methods. After a detailed history and clinical examination, hematological studies like peripheral smear, bone marrow aspiration study, flow cytometry and cytogenetic studies were performed in case of hematological malignancies. FNAC followed by cytological studies were done in solid tumors and histopathological studies were done where a biopsy was taken. Histopathological confirmation was made mandatory for all tumors except some surgically inaccessible CNS tumors and retinoblastomas that are not enucleated. Malignancies were classified based on International Classification of Childhood Cancer (ICCC) which was given by Kramarova and Stiller in 1996 [6]. The data collected were analyzed using SPSS version 20.

Results

The total number of pediatric patients registered during the period was 2640, out of which 421 cases (16%) were under 2 years of age. Among them, 175 (41.5%) were infantile malignancies and 246 (58.5%) in the 1-2 year group. Males were more in number in both age groups with the male: female ratio being 1.70:1. It is clear from **Table I** that male: female ratio is highest in the infants' group (2.1:1).

Table I: Distribution of malignancies on the basis of gender

	<1YR	1-2YRS	TOTAL
MALE	119(68%)	146(59%)	265(63%)
FEMALE	56(32%)	100(41%)	156(37%)
TOTAL	175	246	421
M:F RATIO	2.1:1	1.46:1	1.70:1

The most common malignancy in both age groups were acute leukemias, the total being 181 (43%). There were 147 cases (35%) of acute lymphoblastic leukemia (ALL), 29 cases (7%) of acute myeloid leukemia (AML), five cases of juvenile myelo monoblastic leukemia (JMML) and one case of myelodysplastic syndrome (MDS). The prevalence of ALL is less in the infantile group when compared to the second group, whereas that of AML is slightly higher among infants. Acute **Anoop**

leukemias were followed by Wilms tumor with 51 cases (12.1%). In the infants' group, the second commonest malignancies were Wilms tumor and neuroblastoma with 21 cases each (12%) while the second group had Wilms tumor as the second commonest tumor with 30 cases (12.2%).

The incidence of other malignancies in the decreasing order of frequency is - Neuroblastoma - 43 (10.2%), Rhabdomyosarcoma (RMS) - 27 (6.4%), Germ cell tumor (GCT) - 22 (5.2%), Retinoblastoma - 20 (4.8%), Brain tumors - 19 (4.5%), Lymphomas - 17 (4.1%), Hepatoblastoma - 14 (3.3%), Ewing sarcoma / PNET -14 (3.3%) and LCH - 6 (1.4%). Some of the malignancies showed strong association with a particular gender. For example, most of the brain tumors (84%) were seen in boys and they formed 6% of all malignancies in boys as against a 1.9% in girls. At the same time, GCT, JMML and Ewing sarcoma showed a relatively higher incidence among girls. While considering the treatment refusal/ abandonment rate, it was found to be 37% in the study population with both age groups showing comparable values. The refusal rate was highest for AML and Hepatoblastoma and least for Hodgkin Lymphoma, LCH, WT, and RB. Incidence of each malignancy in the two age groups and the whole cohort is depicted in **Table II**.

Table II: Incidence of each malignancy age group wise.

Diagnosis	<1 year		1-2 years		Whole series	
	Number	%	Number	%	Number	%
ALL	45	25.7	102	41.5	147	34.9
WT	21	12.0	30	12.2	51	12.1
NB	21	12.0	22	8.9	43	10.2
AML	13	7.4	16	6.5	29	6.9
RMS	16	9.1	11	4.5	27	6.4
GCT	6	3.4	16	6.5	22	5.2
RB	9	5.1	11	4.5	20	4.8
BT	7	4.0	12	4.9	19	4.5
NHL	7	4.0	8	3.3	15	3.6
HB	8	4.6	6	2.4	14	3.3
ES	9	5.1	6	2.4	14	3.3
LCH	2	1.1	4	1.6	6	1.4
JMML	5	2.9	0	0.0	5	1.2
NRMS	4	2.3	0	0.0	4	1.0
HD	2	1.1	0	0.0	2	0.5
MDS		0.0	1	0.4	1	0.2
HCC		0.0	1	0.4	1	0.2
TOTAL	175	100.0	246	100.0	421	100

ALL - Acute lymphoblastic leukemia; WT - Wilms tumor; NB - Neuroblastoma; AML - Acute myeloid leukemia; RMS - Rhabdo myo sarcoma; GCT - Germ cell tumor; RB - Retinoblastoma; BT - Brain tumor; NHL - Non Hodgkin lymphoma; ES - Ewing sarcoma; LCH - Langerhan cell histiocytosis; JMML - Juvenile myelomonoblastic leukemia; NRMS - Non-rhabdomyo sarcoma; HD - Hodgkin disease; MDS - Myelo dysplastic syndrome; HCC - Hepato cellular carcinoma

Discussion

The frequency of occurrence of various forms of malignancies in our series shows a marked difference with that of older children. ALL, similar to older children, remains as the most common

malignancy and its frequency (34.9%) is comparable to that in older children. The four most common cancer types among infants as well as 1-2 year group are similar. This shows that both these groups share somewhat similar biology of cancer. At the same time, there's a striking difference between the proportion of ALL in the two groups with infants showing low incidence. All cases of JMML and majority of soft tissue sarcomas were confined to infants.

In contrast to older children in whom brain tumors and lymphomas are the commonest forms of malignancies after leukemias, their incidence is far less in the study cohort. Instead, Wilms tumor and neuroblastoma show high incidence in our study population.

Due to the paucity of literature on the profile of malignancies in this particular age group, we couldn't make any comparisons with similar studies. However, we made an attempt to compare the results with studies on infantile malignancies which is depicted in **Table III**.

Table III: Frequency of malignancies among infants from various studies.

Ping Yang et al Taiwan 2009[7]	Robinowicz et al Israel 2013[8]	Ries et al US 1999[9]	Birch & Blair UK 1992[4]	Our Study
Leukemia(25.6 %)	NB(35%)	NB(28%)	NB(22%)	Leukemias(43%)
RB(17.1%)	Leukemias(15.9%)	Leukemias(17%)	Leukemias(19.6%)	WT(12.2%)
NB(14.6%)	BT(10.7%)	BT(13%)	BT(18%)	NB(8.9%)
BT(11%)		GCT(6%)	RB(17%)	RMS(6.4%)

RB - retinoblastoma; NB - neuroblastoma;BT-brain tumor; RMS - rhabdomyosarcoma; GCT - germ cell tumor

It is clear from the table that neuroblastoma is the commonest form of cancer in infants in the west followed by leukemias and brain tumors. Whereas, data from Taiwan, similar to our study, shows that leukemias are far common in this region and neuroblastomas are only third in incidence. In comparison to all four studies, the incidence of brain tumors is much less in our series whereas that of Wilms tumor is markedly high. This reflects the geographical variation in the biology of infantile malignancies. Another possibility could be solid tumors being detected late and not reaching oncology centers in low and middle-income countries, while leukemias seeking proper treatment as they are detected early [10,11]. As the data used in our study is from a single center and no population-based data is available, we cannot conclude this as the general trend in this region. Still, it can serve as a rough estimate of the trends in the population. Population-based studies will help in assessing the exact pattern of cancers in this age group and planning health strategies.

Table IV: Comparison of distribution of malignancies among infants based on gender

	Ping Yang et al Taiwan 2009[7]	Robinowicz et al Israel 2013[8]	Birch& Blair UK 1992[4]	Our Study
Male	40	155	134	265
Female	42	154	108	156
M:F Ratio	0.95	1.04	1.25	1.7

While comparing the male:female ratio, it is evident that the proportion of males affected is much higher in our study population. If we consider the infantile malignancies alone, the ratio is even more (2.1). We cannot be sure that the incidence of cancer in this age group is really high among males or is it simply because of the fact that more males are being taken for treatment. Although there is a markedly high incidence of brain tumors among males and that of JMML, GCT and Ewing sarcoma

in females, we couldn't establish any such trend while analyzing other studies.

The treatment refusal/abandonment rate among low and middle-income countries (LMIC) is found to vary from 25- 50%. The refusal rate in our series is found to be 37% which is in line with this observation. While both age groups show almost similar rates of refusal, there is considerable variation in case of individual malignancies. The factors that result in refusal/abandonment of treatment are multifactorial. Previous studies have shown that financial constraints and lack of parental education are the most important factors resulting in refusal of treatment [12,13]. A study conducted by Slone et al in Zambia showed that mother's educational status and proximity to treatment center are the other factors influencing treatment completion [3].

Conclusion

There is considerable variation in the occurrence of childhood malignancies in different age groups. Unlike western countries, acute leukemia remains as the most common malignancy among infants and young children. However, being a single-center study, this cannot be extrapolated to the population. The treatment abandonment rate is relatively high and is contributed by a plethora of factors. It should be ensured that more children adhere to proper treatment by implementing appropriate socio-economic support to the affected families.

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