

Farrago of Pediatric Solid Malignancies from a Tertiary Care Centre in Northeast India: A Retrospective Analysis

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Abstract

Background: Worldwide, the annual number of new childhood cancer exceeds 200,000 and >80% of these are from the developing world. Cancer remains the leading cause of disease-related mortality in children.

Aim and Objective: This study aimed to throw light on the prevalence and pattern of pediatric solid malignancies at a tertiary care center in Northeast India.

Materials and Methods: A retrospective analysis of pediatric solid malignancies in the age group of 0–14 years was carried out over a period of 1 year in the department of pathology.

Results: Forty-five cases of pediatric solid malignancies were identified. The mean age of the study group was 7.7 years with the peak age incidence in the >9–14 years of age group, and male to female ratio being 1.1:1. The top tumors in the list were lymphomas (20%), retinoblastomas (13.3%), soft-tissue sarcomas, and germ cell tumors (11.1% each), bone sarcomas and neuroblastomas (8.9% each), and central nervous system tumors (6.9%). Lymphomas and retinoblastomas were, respectively, the most common solid malignancies in boys and girls. Equal sex distribution was detected in bone sarcomas, neuroblastomas, and salivary gland tumors, while the other tumors exhibited gender predilection. Epithelial malignancies such as salivary gland carcinoma, nasopharyngeal carcinoma, and rarer ones such as adrenal cortical carcinoma were also chronicled.

Conclusion: Accurate diagnosis of these entities aided by meticulous histopathological evaluation serves as a medium for compilation of data regarding these malignancies. Information provided by this study can aid in reflecting the tumor burden and boosting the public health-care strategies.

Key words: Cancer, Childhood, Pattern, Histopathology, Lymphoma

INTRODUCTION

Children are not merely adults, and the diseases they contract are not merely variants of adult disease. Neoplasia of childhood is one such “disease” which occupies a numerically important group leading to untimely deaths in the growing age group and taking a heavy toll in terms of lives. Neoplasia

in childhood are unique to, or at least take distinctive forms in this stage of life. Only 2% of all malignant tumors occur in infancy and childhood; nonetheless, cancer is a leading cause of death in children aged 4–14. Neoplastic disease accounts for approximately 9% of all deaths in this cohort.^[1] About 30.76% of the Indian population falls in the 0–14 years of age group.^[2] The overall incidence rates of childhood cancer across the world vary between 75 and 150 per million children per year, while the reported age of the standardized incidence rate for India ranges from 38 to 124 per million children per year, amounting to 1.6–4.8% of all cancers in India.^[3] In the developing world childhood cancers are yet to be recognized as a major pediatric illness due to several other competing causes of death such as diarrheal illness and respiratory illness. However, due to

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considerable reduction in infant and child mortality rate, it is emerging as a distinct entity to be dealt with. Rapid and accurate diagnosis of childhood tumors and hematological malignancies has become increasingly important as more specific chemotherapeutic regimes have evolved. The prognosis of malignancy in children depends primarily on the tumor type, extent of disease at diagnosis, and rapidity of response to treatment. Data reporting in India is still in its nascent stage, especially for pediatric malignancies. Cancer registries that document the incidence of disease are plagued by poor reporting from government hospitals and no reporting by many of the private practitioners, with some population based studies reporting an incidence of just over a 1000 cases in 10 years. To enhance this data, this study was undertaken as an endeavor to depict the prevalence and pattern of pediatric solid malignant tumors presenting at a tertiary care center in Northeast India.

MATERIALS AND METHODS

A retrospective analysis of pediatric solid malignancies was carried out over a period of 1 year in the department

of pathology at a tertiary care center in Northeast India following all the guidelines of the institutional ethics committee. Only those cases in children between the age group of 0 and 14 years with conclusive and unequivocal diagnosis were included in the study. Details of age, gender, and other relevant clinical information were collected from the medical records. The hematoxylin and eosin stained slides sectioned from formalin fixed paraffin embedded tissues and the immunohistochemistry stained slides were retrieved from the archives in the department of pathology and evaluated.

RESULTS

The study consisted of 45 cases of solid pediatric malignant tumors who had presented at our institute during a period of 1 year [Table 1]. The annual incidence rate of pediatric solid malignancies was 0.8% of total pediatric admissions. The mean age of the childhood solid tumors was 7.7 years with the peak age incidence in the >9–14 year age group (44.4%). Male cases (24, 53.3%) outnumbered females (21, 46.7%). The most common pediatric solid malignancy was

Table 1: Distribution of histological subtypes of pediatric solid malignancies

SL No.	Tumor type	Frequency, n (%)	Mean age, years	Age group, n (%)			Gender, n (%)	
				0–4 years	>4–9 years	>9–14 years	Male	Female
1.	Lymphoma	9 (20)	9.9	1 (11.1)	3 (33.3)	5 (55.6)	8 (88.9)	1 (11.1)
(a)	T-Lymphoblastic lymphoma	5 (55.6)	10	0	3 (60)	2 (40)	4 (80)	1 (20)
(b)	DLBCL	2 (22.2)	13	0	0	2 (100)	2 (100)	0
(c)	Classical Hodgkin lymphoma	2 (22.2)	6.5	1 (50)	0	1 (50)	2 (100)	0
2.	Retinoblastoma	6 (13.3)	4.3	3 (50)	3 (50)	0	1 (16.7)	5 (83.3)
3.	Soft tissue sarcoma	5 (11.1)	10	0	1 (20)	4 (80)	5 (100)	0
(a)	Rhabdomyosarcoma	2 (40)	11	0	0	2 (100)	2 (100)	0
(b)	Ewing Sarcoma/PNET	1 (20)	5	0	1 (100)	0	1 (100)	0
(c)	Fibrosarcoma	1 (20)	12	0	0	1 (100)	1 (100)	0
(d)	Synovial sarcoma	1 (20)	11	0	0	1 (100)	1 (100)	0
4.	Germ cell tumor	5 (11.1)	10.6	1 (20)	0	4 (80)	1 (20)	4 (80)
(a)	Yolk sac tumor	2 (40)	8.5	1 (50)	0	1 (50)	1 (50)	1 (50)
(b)	JGCT	1 (20)	11	0	0	1 (100)	0	1 (100)
(c)	Dysgerminoma	1 (20)	13	0	0	1 (100)	0	1 (100)
(d)	MMGCT	1 (20)	12	0	0	1 (100)	0	1 (100)
5.	Neuroblastoma	4 (8.9)	4.75	2 (50)	2 (50)	0	2 (50)	2 (50)
6.	Bone malignancies	4 (8.9)	4.75	0	0	4 (100)	2 (50)	2 (50)
(a)	Ewing sarcoma/PNET	2 (50)	11.5	0	0	2 (100)	0	2 (100)
(b)	Osteosarcoma	2 (50)	13.5	0	0	2 (100)	2 (100)	0
7.	CNS malignancies	3 (6.9)	12.5	1 (33.3)	2 (66.7)	0	0	3 (100)
(a)	Medulloblastoma	2 (66.7)	3	1 (50)	1 (50)	0	0	2 (100)
(b)	Immature pineal teratoma	1 (33.3)	8	0	1 (100)	0	0	1 (100)
8.	Wilms' tumour	2 (4.4)	2	2 (100)	0	0	0	2 (100)
9.	LCH	2 (4.4)	5.25	1 (50)	1 (50)	0	2 (100)	0
10.	Salivary gland carcinomas	2 (4.4)	14	0	0	2 (100)	1 (50)	1 (50)
(a)	Mucoepidermoid carcinoma	1 (50)	14	0	0	1 (100)	0	1 (100)
(b)	Adenoid cystic carcinoma	1 (50)	14	0	0	1 (100)	1 (100)	0
11.	Hepatoblastoma	1 (2.2)	1	1 (100)	0	0	0	1 (100)
12.	UN NPC	1 (2.2)	8.5	0	1 (100)	0	1 (100)	0
13.	Adrenal cortical carcinoma	1 (2.2)	13	0	0	1 (100)	0	1 (100)
14.	Total	45	7.7	12 (26.7)	13 (28.9)	20 (44.4)	24 (53.3)	21 (46.7)

DLBCL: Diffuse large B cell lymphoma, JGCT: Juvenile granulosa cell tumour, MMGCT: Malignant mixed germ cell tumour, CNS: Central nervous system, LCH: Langerhans cell histiocytosis, UN NPC: Undifferentiated non-keratinizing nasopharyngeal carcinoma

the lymphomas (20%), followed by retinoblastoma (13.3%), soft-tissue sarcomas (STS), and germ cell tumors (11.1% each); bone sarcomas and neuroblastomas (8.9% each), and central nervous system (CNS) tumors (6.9%) completed the top five. Moreso, lymphomas were the most common solid malignancy in boys, while retinoblastoma topped the list in girls. Equal sex distribution was detected in the sarcomas of bone, neuroblastomas, and salivary gland tumors, while other tumors exhibited sex predilection [Figure 1]. Lymphomas comprised nine cases, out of which seven were Non-Hodgkin lymphomas (NHL) and two were Hodgkin lymphomas (HL). As far as the overall age incidence of lymphoma was concerned, most of the cases (5) were in the >9–14 years of age group (55.6%), with NHL accounting for four of those. The 0–4 years of age group reported the lowest incidence, with only one case of HL and none of NHL in that category. Lymphomas showed a predilection for boys, with the male to female ratio being 8:1. NHL constituted six out of the total eight cases in males as well as for the lone female case. With regards to the histologic type, the predominant sort was T-lymphoblastic lymphoma (5 cases, 71.4%), followed by diffuse large B-cell lymphoma (2 cases, 28.6%). Both the HL belonged to the mixed cellularity group. While bone marrow involvement was not detected in both the cases of HL, three out of seven cases of NHL (42.9%) evinced metastasis to the bone marrow.

The present study involved six cases of retinoblastoma, accounting for 13.3% of the total cases. Retinoblastoma was the most common solid tumor in girls, with five female cases. STS came joint third, comprising five cases (11.1%), all of them occurring in boys. Majority of those patients (4 cases) were above 9 years, an overwhelming incidence rate of 80% in the >9–14 year age group. Morphologically,

the five cases of STS comprised two cases of embryonal rhabdomyosarcoma and one case each of fibrosarcoma of the hand, synovial sarcoma of the scalp and extraskelatal Ewing sarcoma/Primitive neuroectodermal tumor (ES/PNET) of the shoulder. Germ cell tumors (GCT) totalled five cases (11.1%), ranking joint third along with STS. All the GCTs were of gonadal origin, comprising two cases of yolk sac tumor, and one case each of dysgerminoma, juvenile granulosa cell tumor and malignant mixed germ cell tumor. Neuroblastoma numbered four cases (8.9%) and had an equal sex distribution, with the male cases occurring in the >4–9 years of age group and the female cases in the 0–4 years of age group. Bone marrow involvement was detected in three out of the four cases. Bone malignancies equalled neuroblastoma cases (4 cases, 8.9%), two cases each of osteosarcoma (both in males) and ES/PNET (both in females). CNS tumors accounted for three cases (6.9%), comprising two cases of medulloblastomas and one case of immature pineal teratoma. Wilms tumor comprised 2 cases in the present study (4.4%), both involving the left kidney. Completing the list were two cases each of Langerhans cell histiocytosis (LCH), and salivary gland malignancies (adenoid cystic carcinoma and mucoepidermoid carcinoma), followed by lone case each of hepatoblastoma, adrenal cortical carcinoma (ACC), and non-keratinizing undifferentiated nasopharyngeal carcinoma.

DISCUSSION

Data regarding the incidence of childhood solid tumors is limited. Although children <15 years comprise 31% of the Indian population, the exact incidence of most childhood solid tumors in India is not known. Lack

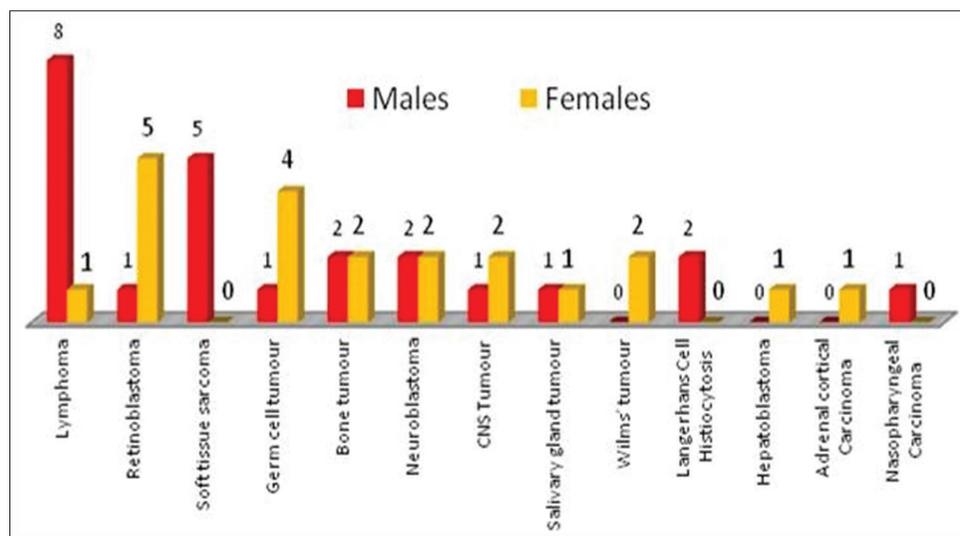


Figure 1: Gender distribution of pediatric solid malignancies in the study

of information among patients and parents about the signs and symptoms of childhood cancer, relying on nonmedical forms of treatment, lack of finances, untrained professionals at a primary care center, lack of laboratory and diagnostic imaging equipment, poor data collection, and reporting infrastructure all lead to suboptimal reporting.^[4] Appropriate management of pediatric tumors requires complete epidemiological data of pediatric tumors in different geographical areas. In India, cancer is the 9th common cause for the deaths among children between 5 and 14 years of age.^[5] Indian cancer registries have reported the proportion of childhood cancers relative to all cancers in the range of 0.8–5.8% in boys and 0.5–3.4% in girls.^[6] The present study collected a database of pediatric malignant solid tumors from a tertiary care center in the most north eastern part of India with the aim of analyzing the patterns and frequency of these tumors.

The 45 cases of pediatric solid malignancies in this study formed 0.8% of all pediatric admissions in the hospital. This finding is quite in agreement with that of the results of Upadhyay *et al.* and Miglani *et al.*^[7,8] The slightly increased incidence rate in the present series can be a reflection of the rising trend of childhood solid tumors in our country. The peak age incidence was in >9–14 years of age group (44.4%), which is comparable to that found by Jain *et al.*, Gupta *et al.*, and Sharma *et al.* [Table 2].^[8-10] Embryonal tumors such as neuroblastoma, Wilms tumor,

and retinoblastoma occurred mainly in the 0–4 years of age group, while the >9–14 years of age group mainly consisted of lymphomas, sarcomas, germ cell tumors, and carcinomas. The overall incidence of childhood malignant tumors is more in males (male to female ratio of 1.1:1). This observation has been made uniformly in literature by many authors.^[6,8-17] However, some tumors such as retinoblastoma, Wilms tumor, and germ cell tumors tend to show a slight female preponderance. The reported incidence of childhood cancer in India in males (39–150 per million children per year) is higher than in females (23–97 per million children per year) in all population-based cancer registries except in Northeast India.^[9]

The pattern of pediatric solid malignancies in various studies has been enlisted in Table 3. Most of the studies arrayed including the current one depict lymphomas as the most common childhood solid tumors. Shah *et al.*, Agboola *et al.*, and Ibrahim *et al.* also bear witness to that.^[18-20] The incidence in the current context was 20%, which is almost similar to the findings of Sharma *et al.* and Upadhyay *et al.*^[6,17] In fact, Hesham *et al.* in a study of 155 solid pediatric malignancies from Egypt discerned a rather high incidence (48.4%) of lymphomas.^[13] The distribution of NHL and HL varies among different series [Table 4]. Some have found NHL to be in the majority,^[13,21-24] while in some studies HL predominated.^[9,12,14] NHL was more common in the present series. Majority of the lymphoma patients were in the >9–14 year age group, which is similar to the observation by Surveillance, Epidemiology, and End Results (SEER), Mankodi *et al.*, Jain *et al.*, and Baneerjee *et al.*^[8,11,25,26] Moreover, it can be stated that lymphoma does not spare any age group. Lymphoid neoplasms predominated in boys, with the male to female ratio varying in different series.^[6,8,9,11-14] Contrary to the west, lymphoblastic lymphomas and diffuse large B cell lymphomas supersede Burkitt/Burkitt-like lymphoma among NHLs. In the present series retinoblastoma totalled six cases, accounting for an incidence of 13.3%. The incidence of this tumor ranges from 1.7 to 38.9% in

Table 2: Peak age incidence group of pediatric solid malignancies in various studies

SL. No.	Series	Peak age incidence group
1.	Miglani <i>et al.</i>	0–5 years
2.	Bannerjee <i>et al.</i>	0–5 years
3.	Jain <i>et al.</i>	10–13 years
4.	Gupta <i>et al.</i>	11–15 years
5.	Pandey <i>et al.</i>	10–14 years
6.	Hesham <i>et al.</i>	0–4 years
7.	Memon <i>et al.</i>	0–4 years
8.	Sharma <i>et al.</i>	12–19 years
9.	Present study	>9–14 years

Table 3: Distribution of histological tumour types of pediatric solid malignancies in various series

SL. No.	Tumor type	Bannerjee <i>et al.</i> (%)	Venugopal <i>et al.</i> (%)	Sharma <i>et al.</i> (%)	Gupta <i>et al.</i> (%)	Sharma <i>et al.</i> (%)	Memon <i>et al.</i> (%)	Hesham <i>et al.</i> (%)	Pandey <i>et al.</i> (%)	Present study (%)
1.	Lymphoma	25.9	20.95	21.4	38.3	---	15.9	48.4	31.4	20
2.	Retinoblastoma	8.7	---	6.5	3.3	2.6	38.9	---	5.9	13.3
3.	Soft-tissue sarcoma	14.3	10.4	7.8	8.3	12.2	9.7	5.2	6.5	11.1
4.	Germ cell tumor	3.8	4.8	8.4	11.7	14.5	2.6	---	9.8	11.1
5.	Bone tumor	10.5	3.8	9.7	15	11.9	5.3	4.5	7.2	8.9
6.	Neuroblastoma	4.5	11.4	3.9	3.3	4.9	---	29	4.6	8.9
7.	CNS tumor	15.3	---	9.7	8.3	25.7	10.6	1.9	1.96	6.9
8.	Wilms tumor	8.4	24.8	---	8.3	8.9	13.2	9.7	18.3	4.4
9.	Miscellaneous	8.6	---	20.1	3.3	5.3	7	1.3	5.23	15.6

CNS: Central nervous system

various series, with a study from Pakistan reporting it as the most common pediatric tumor.^[6-12,14,17] Nevertheless, retinoblastoma is the most common intraocular childhood malignancy. The frequency of STS as well as the gender predilection in the present series was quite in agreement with the findings of the other series.^[10,14,16] Embryonal rhabdomyosarcoma was the most common STS in children. Other series of works such as Prathap *et al.*^[27] also have found a similar preponderance of rhabdomyosarcomas [Table 5]. The incidence of malignant GCTs in the present series was 11.1%, which is almost comparable to that of the series of Upadhyay *et al.* and Gupta *et al.*^[6,9] All the GCTs were of gonadal origin, whereas Qureshi *et al.* recorded an almost equal distribution at gonadal and extragonadal sites.^[15] Neuroblastoma is the most common tumor of early childhood and is rare beyond the age of 10 years. It is a highly aggressive tumor and was reported to have lower incidence among the Indian children by various authors such as Dawani *et al.*, Jussawala *et al.*, and Mangal *et al.*^[28-30] Three of the four cases of neuroblastoma in the current study had metastasized to the marrow at the time of presentation. The incidence of marrow involvement ranges from 25.4 to 70% in various series.^[31-34] Bone malignancies tend to affect the slightly older children, and the discovery in the present series correlated with that. The authors proclaimed the incidence of these tumors to be 8.9%, while other studies have broadcast it in the range of 3.8–17.9%.^[6,9-14,16,17] Similar to other observations, osteosarcoma and ES/PNET were the most common bone malignancies in the current context. The low incidence of CNS in the

current study was due to the lack of dedicated neurosurgery services at our center. Nevertheless, in contrast to western studies, the incidence of CNS tumors in Indian studies is less. Medulloblastoma is promulgated as the most common CNS pediatric malignancy. Majority of the Wilms tumors in almost all the series occurred in the first 5 years of life, which was in accordance with the finding in the present study. However, most of the other Indian studies disclosed a higher incidence than ours.^[7,10-12,14,17] LCH is an uncommon disease. The annual incidence is about five cases per 1 million population, with most cases occurring in childhood. There is a male predilection, with a male-to-female ratio of 3.7:1.^[35] Epithelial malignancies are portrayed by most series in the 10–14 years of age group, a similar reflection as ours. Mucoepidermoid carcinoma is the most common malignant salivary gland tumor in children. Epithelial malignancies adumbrated in other studies besides the ones outlined in ours are follicular thyroid carcinoma, colorectal adenocarcinomas, pancreatic adenocarcinomas, hepatocellular carcinoma, and squamous cell carcinoma of the eye. Among the rarer malignancies perceived in our study were hepatoblastoma, nasopharyngeal carcinoma, and ACC. Hepatoblastoma, though rare, is the most common childhood liver malignancy. Approximately 100 cases are diagnosed yearly in the USA. The most recent SEER data for the period 2002–2008 demonstrates that the highest incidence of hepatoblastoma is in the 0–4 years of age group, with 10.5 and 5.2 cases per million children <1 and 1–4 years.^[36] Nasopharyngeal carcinoma has an infrequent incidence rate in children. It rarely appears in children under 14 years of age, and the annual incidence rate in the United Kingdom is 0.25 cases per 1 million inhabitants. It does make up 20–50% of all primary malignant nasopharyngeal tumors in children though.^[37] A single case of a rare tumor, ACC was relayed in our study. ACC is a rare neoplasm with an incidence in children of 0.3/million under 15 years of age. They have a bimodal peak; the first one is in the fourth and fifth decades of life and the second one in the first decade, and demonstrate a slight female predilection.^[38] Bannerjee *et al.*, and Sharma *et al.* also chronicled ACC in their series.^[11,17]

Table 4: Incidence of non-Hodgkin lymphoma and Hodgkin lymphoma in various series

SL. No.	Series	Incidence	
		Non-Hodgkin lymphoma (%)	Hodgkin lymphoma (%)
1.	Pandey <i>et al.</i>	13.7	17.6
2.	Gupta <i>et al.</i>	11.7	26.7
3.	Hesham <i>et al.</i>	31	17.4
4.	Memon <i>et al.</i>	2.6	9.7
5.	Present study	15.6	4.4

Table 5: Pattern of soft-tissue sarcomas in various series (in descending order from 1 to 3)

SL. No.	Series	Tumor type		
		1	2	3
1.	Prathap <i>et al.</i>	Rhabdomyosarcoma	Fibrosarcoma	Leiomyosarcoma, Liposarcoma
2.	Upadhyay <i>et al.</i>	Rhabdomyosarcoma	Fibrosarcoma	Angiosarcoma
3.	Sharma <i>et al.</i>	Rhabdomyosarcoma	Synovial sarcoma	
4.	Qureshi <i>et al.</i>	Rhabdomyosarcoma	Extraskeletal Ewing sarcoma/PNET	Fibromatosis
5.	Pandey <i>et al.</i>	Rhabdomyosarcoma	Malignant fibrous histiocytoma	DFSP
6.	Memon <i>et al.</i>	Rhabdomyosarcoma	Fibrosarcoma, Chondrosarcoma	Fibrous histiocytoma
7.	Sharma <i>et al.</i>	Extraskeletal Ewing sarcoma/PNET	Rhabdomyosarcoma	---
8.	Present study	Rhabdomyosarcoma	Extraskeletal Ewing sarcoma/PNET, Fibrosarcoma, Synovial sarcoma	---

Accurate diagnosis of pediatric malignancies is important, as disparate approaches to therapy are implemented for distinct tumor types. In addition, therapy is also tailored according to patient risk. The tremendous role of histopathological examination and ancillary studies such as immunohistochemistry, cytogenetic, and molecular analysis in the veracious recognition of the pediatric solid malignancies cannot be understated. The mortality and disability due to cancer can be considerably reduced by early diagnosis and treatment. In order to achieve this, the public health system of the country necessitates country-specific epidemiological data regarding the disease in the population. Moreso understanding the geographic variations in pediatric cancer may contribute to advances in knowledge about etiologic factors.

CONCLUSION

The incidence of childhood solid malignancies observed in this study is not glaringly different from other studies in India and abroad. Neoplasms involving lymphoid tissues, retina, soft tissues, gonads, and bone were among the most common pediatric tumors. Embryonal tumors transpired mainly in the 0–4 year age group, while the >9–14 year age group encompassed mainly of lymphomas, sarcomas, germ cell tumors, and carcinomas. The major limitation of this study was that it was a single institute retrospective analysis conducted during a short span of time with limited number of cases. It was essentially a hospital study which does not claim of the population at large. Yet it was a humble endeavor to assess the incidence and pattern of the dissimilar malignant childhood solid tumors in this part of the country. Cognizance of these patterns and variances will contribute to advances in knowledge about etiologic factors, raise awareness about the global nature of pediatric neoplasms and their histologic distribution and enable public health programs and strategies to be framed using country specific epidemiological data, for early detection and treatment of these deadly pediatric solid malignancies.

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