

## Original Research Article

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# Solid malignant pediatric tumors: a histopathological study

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## ABSTRACT

**Background:** In general, the features of malignancies in children differ biologically and histologically from those of adults with respect to incidence, type of tumor, underlying familial or genetic aberration and tendency to regress spontaneously or cytodifferentiation. In recent years, identification of specific genes, oncogenes, tumor markers and other biological and pathological factors have played an important role in staging and classifying risk categorization of specific tumors as low, intermediate and high-risk lesions.

**Methods:** This study is undertaken to evaluate the incidence and morphological features of solid malignant tumors in children of fifteen years and below. The material for present study is obtained from S. P. Medical College, Bikaner and referred cases. The histopathology slides and paraffin blocks are reviewed.

**Results:** The sections 3-5  $\mu$  thick, are cut and stained by haematoxylin and eosin in all cases and special stains like PAS, MTS, RS done where ever feasible. An analysis of 60 cases of solid malignant tumors of childhood over a period of 5 years are made. The early onset and the embryonal nature of the major pediatric tumors, suggest a prenatal origin and role of genetic factors. Infections, exposure to drugs and chemicals during pregnancy are other contributory factors.

**Conclusions:** Accurate incidence of data is important in the planning and evaluation of clinical trials. Documentation of cases, advanced diagnostic methods like IHC, cytogenetic studies and treatment modalities with close follow up is needed to achieve better statistical evaluation of the problem.

**Keywords:** Histopathology, Malignant, Pediatric, Solid

## INTRODUCTION

Cancer is essentially a disease of adults, yet it is one of the common killers in childhood. In western countries cancer is next only to trauma as a cause of mortality in children under 15 years of age. In India, although infections and malnutrition are the major factors contributing to morbidity and mortality, with the development of preventive and curative measures of treatment, as well as fight against the malnutrition, malignant tumors in children have become the second

biggest killer.<sup>1-3</sup> In general, the features of malignancies in children differ biologically and histologically from those of adults with respect to incidence, type of tumor, underlying familial or genetic aberration and tendency to regress spontaneously or cytodifferentiate.<sup>4</sup> In recent years, identification of specific genes, oncogenes, tumor markers and other biological and pathological factors have played an important role in staging and classifying risk categorization of specific tumors as low, intermediate and high-risk lesions. This concept uses risk factors as predictors of outcomes. Risk-based management allows

the pediatric medical and surgical oncologist to weigh the risks and benefits of treatment for each patient in an effort to maximize survival, minimize morbidity, and improve the quality of life. Hence there is need for accurate histopathological reporting in conjunction with ancillary methods.<sup>5-8</sup>

## METHODS

This study is undertaken to evaluate the incidence and morphological features of solid malignant tumors in children of fifteen years and below. The material for present study is obtained from S. P. Medical College, Bikaner and referred cases for a period of five years from 2012-2016. The clinical history regarding duration of the disease, mode of presentation, symptoms and signs are recorded from the case papers, request forms, patient's history, clinical data along with relevant details obtained from available hospital and departmental records. The histopathology slides and paraffin blocks are reviewed. Gross examination is done carefully noting the size, shape, extent and configuration, nodularity, consistency (solid, cystic or mixed) and torsion. A minimum of 4-5

bits are selected from the representative areas of tumor. The tissue for routine microscopy is preserved and fixed in 10% neutral buffered formalin for 24 hours and processed in automatic tissue processor (Histokinette) and embedded in paraffin. The sections 3-5  $\mu$  thick, are cut and stained by haematoxylin and eosin in all cases and special stains like PAS, MTS, and RT done where ever feasible.

## RESULTS

An analysis of 60 cases of solid malignant tumors of childhood over a period of 5 years is made. The following observations are made: The youngest patient at the time of diagnosis is three days old and diagnosed as immature teratoma. The majority of the tumors in this study occurred between 11-15 years (41.66%), followed by 6-10 years age group (30%) and in 0-5 years age group (28.33%) (Table 1). In the present study 35 (58.33%) malignant tumors are seen in boys and 25 (41.66%) in girls under the age of 15 years, showing male preponderance. Male to female ratio of the incidence of malignant tumors is 1.5:1.

**Table 1: Incidence of malignant tumors in different age groups in relation to sex.**

Sex	0-5 year No. (%)	6-10 year No. (%)	11-15 year No. (%)	Total No. (%)
Male	9 (52.94%)	13 (68.42%)	13 (54.16%)	35 (58.33%)
Female	8 (47.05%)	6 (31.57%)	11 (45.83%)	25 (41.66%)
<b>Total (%)</b>	<b>17 (28.33%)</b>	<b>19 (31.66%)</b>	<b>24 (40%)</b>	<b>60 (100%)</b>

**Table 2: Histological subtypes of tumor with relation to sex.**

Histological subtypes	Male (%)	Female (%)	Total (%)	M:F ratio
Lymphoma	17	6	23 (38.33%)	2.8:1
Hodgkin lymphoma	11	5	16 (26.66%)	
Non-Hodgkin's lymphoma	6	1	7 (11.66%)	
Bone tumors	3	6	9 (15%)	
Osteosarcoma	3	2	5 (8.33%)	
Ewing's sarcoma/PNET	0	4	4 (6.66%)	
Gonadal tumors	4	3	7 (11.66%)	1.33:1
CNS tumors	1	4	5 (8.33%)	1:4
Retinoblastoma	0	2	2 (3.33%)	-
Wilm's tumor	5	0	5 (8.33%)	-
Soft tissue tumors	2	3	5 (8.33%)	2:3
Neuroblastoma	2	0	2 (3.33%)	-
Squamous cell carcinoma eye	1	0	1 (1.66%)	-
Malignant melanoma	0	1	1 (1.66%)	-
<b>Total</b>	<b>35 (58.33%)</b>	<b>25 (41.66%)</b>	<b>60 (100%)</b>	<b>1.5:1</b>

All the cases of present study are sporadic. No associated congenital anomalies are noted in the present study. Histological typing of tumors are depicted in Table 2. Table 2 shows the histological types of the solid

malignant tumors seen in this study. Lymphoma is the commonest pediatric solid malignant neoplasm seen in this study and accounted for 23 cases (38.33%). Bone tumors constitute the second largest group with 9 cases

(15%). This is followed by Gonadal tumors which accounted for 7 cases (11.66%), CNS tumors, soft tissue tumors and Wilm's tumor (5,8.33% each). The relative frequency of other malignant neoplasms is as shown in Table 2.

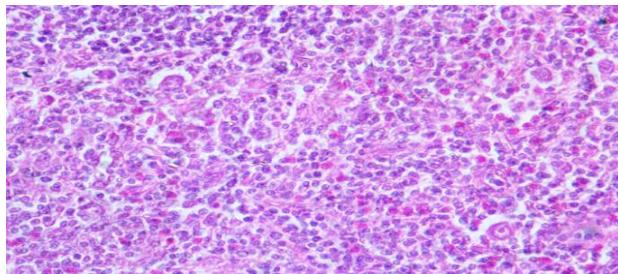
### Lymphoma

Twenty-three cases of lymphoma are diagnosed during the study period. These accounts for 38.66% of all the pediatric malignant solid neoplasms seen in this study. Seventeen cases (73.91%) are seen in males while 6 cases (26.08%) are seen in females. This give a male: female ratio of 2.8:1. Two cases (8.69%) are seen in the 0-5-year age group, 12 cases (52.17%) are seen in the 6-10 year age group while 9 cases (39.13%) are seen in the 11-15 year age group (Table 3).

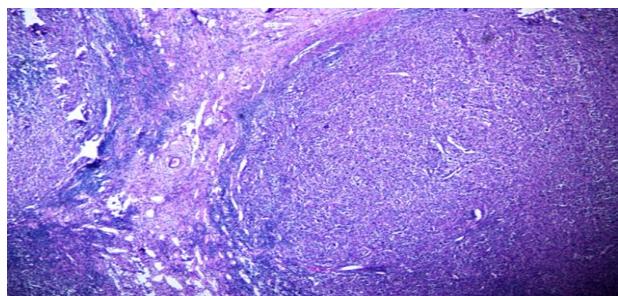
Hodgkin's lymphoma accounts for 16 cases (69.56% of all lymphomas) while other non-Hodgkin's lymphomas account for 7 cases. (30.43% of all lymphomas) (Figure 1-4).

**Table 3: Age and sex wise distribution of lymphoma.**

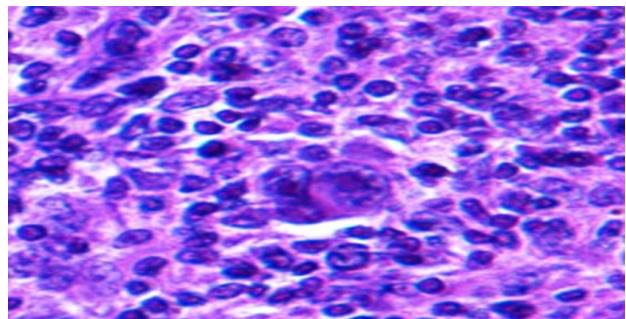
Age group (in years)	Male	Female	Total (%)
0-5	0	2	2 (8.69%)
6-10	10	2	12 (52.17%)
11-15	7	2	9 (39.13%)
<b>Total</b>	<b>17</b>	<b>2</b>	<b>23 (38.33%)</b>



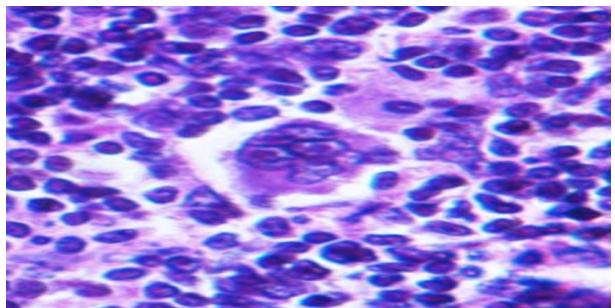
**Figure 1: Lymph node- mixed cellularity Hodgkin lymphoma. High power view (H and E staining) showing several Hodgkin cells with polymorphic lymphoid infiltrate rich in eosinophils.**



**Figure 2: Lymph node- nodular sclerosis Hodgkin lymphoma. Scanner view (H and E staining) showing lymphoid nodules in dense fibro hyaline tissue.**



**Figure 3: Classical reed sternberg cell high power view (H and E staining).**



**Figure 4: Lymphocytic-histiocytic reed sternberg cell. High power view (H and E staining).**

### DISCUSSION

The various malignant tumors of childhood encountered in the present study are compared with similar studies conducted in India and abroad. The malignant tumors of all types are being reported during early life but their common site of origin differ sharply from those of adults, for example Leukemias, CNS tumors, soft tissue tumors, bone and kidney tumors are common sites of origin of malignant tumors in infants and children.

Accurate diagnosis of pediatric small-round cell tumors is important, as disparate approaches to therapy are taken for distinct tumor types. In addition, therapy is also tailored according to patient risk. It has become important to further classify tumors biologically, using cytogenetic or molecular studies to identify chromosome translocations, gene amplification, gene expression patterns, and/or mutations.<sup>9</sup>

The overall incidence of malignant tumors of childhood is more in the males (M: F: 1.5: 1). This observation has been made uniformly in literature by many authors. Male preponderance is noted in all age groups and female preponderance in germ cell tumors by Lee and Lee et al, Miller et al.<sup>10,11</sup> In the present study, the peak occurrence of tumors is found in the 10-15 years age group (40%) similar to the observations of KK Jain (35.5 %).<sup>3,11,12</sup> Whereas Dewani et al and Jussawala and Yeole observed peak occurrence in birth-5 age group as shown in Table 4.<sup>13</sup> The frequency of neuroblastoma, retinoblastoma and Wilms' tumor is strikingly more in children younger than

5 years of age. An increased frequency with age is seen in Non-Hodgkin's lymphoma, Hodgkin's lymphoma, osteosarcoma and Ewing's sarcoma. The early onset and the embryonal nature of many pediatric tumors suggest a prenatal origin, as also seen in our studies.<sup>14</sup>

**Table 4: Comparison of age group distribution of tumors in various studies.**

Series	0-5 years	6-10 years	11-15 years
Jain KK	4.2%	22.2%	35.5%
Dewani	47.2%	40.9%	11.9%
Jussawala	42%	29%	29%
Present study	28.33%	31.66%	40%

Various types of solid malignant tumors are observed in the pediatric age group in the present study, the

lymphomas being the commonest type, followed by soft tissue tumor, germ cell tumor, bone tumors, Wilms' tumor, brain tumor, retinoblastoma and others.

In the present study, the commonest tumors comprised Hodgkin's (11, 16.66%) and non-Hodgkin's lymphomas (10, 15.15%). Similar results were reported by Sonal Sharma et al, and Baneerjee and Walia.<sup>1,15</sup>

The general pattern of pediatric tumors in our center seems to resemble the distribution of pediatric cancers reported from other centers in our country and abroad. Leukemia was the leading type of cancer and malignant tumors were the second most common cancer in several countries. The same findings are noted in our series and Young et al, Pearson et al, Teppo et al and Kusumakumary P et al.<sup>14,16-18</sup>

**Table 5: Histological types of tumor in different series.**

Histological type	Banerjee et al	Venugopal et al	Sharma S et al	Present study
Lymphoma	25.92%	20.95%	21.41%	38.33%
Soft tissue tumors	14.3%	10.4%	7.79%	8.33%
Gonadal tumors	3.8%	4.76%	8.44%	11.66%
Bone tumors	10.52%	3.8%	9.74%	15%
Renal tumors	8.4%	24.76%	19.48%	8.33%
Brain tumors	15.32%	-	9.74%	8.33%
Retinoblastoma	8.7%	-	6.49%	3.33%
Neuroblastoma	4.5%	11.4%	3.89%	3.33%
Others	8.5%	-	20.12%	3.32%
<b>Total</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>

Predominance of Hodgkin's lymphoma over non-Hodgkin's lymphoma correlates with studies made by Mankodi et al, Ramkumar et al and Desai et al.<sup>20-22</sup> Majority of our cases are in 10-15 years. This is similar to observation by SEER, Mankodi et al, and Baneerjee and Walia.<sup>1,20,23</sup> Nodular sclerosis subtype was the commonest subtype in SEER study and age group was 1-5 years in Venugopal et al study.<sup>19,23</sup> Mixed cellularity is the predominant histological subtype in present study and other studies from India and abroad.

Five cases (8.33%) of Wilms' tumor are studied. This is in comparison to study done by Sanyal et al and Sunitha Sharma et al.<sup>24,25</sup> The tumor stage at diagnosis, histological features and patient age are the most important prognostic determinants which have impact on treatment selection and outcome. The Loss of Heterozygosity at chromosome 1p and 16q was associated with increased risk of relapse and death.<sup>26</sup>

In retinoblastoma, no bilateralism or family history is noted in present study. Optic nerve spread indicating bad prognosis was noted by Sang and Albert and Dhir SP.<sup>27,28</sup>

Optic nerve extension and calcification is noted in one of our case.

Neuroblastoma is the commonest tumor of early childhood and is rare beyond the age of ten years.<sup>29</sup> Neuroblastoma, a highly aggressive tumor, was reported to have lower incidence among the Indian children by various authors like Dewani GP, Jussawala DJ and Mangal N.<sup>3,12,30</sup> In the present study the tumor constituted 3.03% of total cases. The neuroblastic tumors NB, GNB, and GN are a spectrum of sympathetic tissue tumors ranging from the very immature and malignant NB to the mature and benign GN. It is the interplay of histologic maturity, genetic composition, and patient features that make NB, GNB and GN an enigmatic group of tumors.

## CONCLUSION

In the present study, histopathological diagnosis could be confirmed with IHC. The frequency of tumors and their distribution is comparable to that reported from other studies. The early onset and the embryonal nature of the major pediatric tumors, suggest a prenatal origin and role

of genetic factors. Infections, exposure to drugs and chemicals during pregnancy are other contributory factors. Accurate incidence of data is important in the planning and evaluation of clinical trials. Documentation of cases, advanced diagnostic methods like IHC, cytogenetic studies and treatment modalities with close follow up is needed to achieve better statistical evaluation of the problem.

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