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A cross-sectional study of the distribution of pediatric solid tumors at an Indian tertiary cancer centre

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ABSTRACT

Background: Pediatric solid tumors include a heterogeneous group of tumors, and the burden of these tumors, especially from resource-challenged countries, is not well described. The aim of this study was to describe the distribution of solid tumors in children in an Indian tertiary cancer center.

Methods: All patients under 12 years of age with histologically confirmed tumors presenting at a tertiary cancer center from January 2014 to January 2019 were identified from the hospital database. Patients with lymphomas, bone, and central nervous tumors were excluded. The demographic profile including age, sex distribution, and the treatment received were recorded for all patients.

Results: The mean age of the eligible 153 patients was 5.7 years with majority (57.3%) in the 0-5 years age group. The male-to-female ratio was 1.6:1 with a male predominance in all tumors except germ cell tumors. Renal tumors were the most common tumors followed by neuroblastoma and soft tissue sarcoma, whereas germ cell and gonadal tumors formed only 8.49% of all tumors.

Conclusions: Extracranial and extraosseous pediatric solid tumors include a wide range of tumors with a predilection for male sex and children below 4 years of age. Wilms tumors, neuroblastoma, and soft tissue sarcomas tumors are the most common tumors.

Keywords: Cancer, Cancer epidemiology, Childhood developing countries, Pediatric solid tumours, Tumour registries, Tumour subtypes

INTRODUCTION

Information regarding the incidence and distribution of a disease in a community is an intricate part of the healthcare planning to guide quality improvement initiatives and policy formulation process. Although there is plenty of data on the incidence and prevalence of infectious diseases in the world, information on epidemiology of malignancies is still lacking. While counties in North America and Europe have stringent population-based cancer registries and cooperative

projects such as Automated Childhood Cancer Information System (ACCIS) and EUROCARE, data reporting in India is still in its infancy, especially for pediatric malignancies.² 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.

To determine the pattern of distribution of pediatric solid tumors, we evaluated all children <12 years of age with extraosseous and extracranial solid tumors.

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METHODS

Institutional Review Board approval and waiver of consent were taken for the study. All patients under 12 years with histologically confirmed disease presenting at Nil Ratan Sircar Medical College and Hospital from January 2014 to January 2019 were identified from the hospital database. Patients without a definite diagnosis of malignancy irrespective of the clinic radiological features and prior therapy for suspected or proven malignancy elsewhere were excluded from the analysis. Patients with central nervous system and bone tumors were also excluded from this study. Similarly, lymphomas and other hematolymphoid disease were also excluded. The age, sex, histopathology, prior treatment, and treatment offered at our hospital were recorded for all patients.

All patients underwent a comprehensive clinical evaluation followed by histological confirmation of the disease except retinoblastoma, which were diagnosed based on clinical and radiological features Radiological investigations included computerized tomogram or magnetic resonance imaging. A dedicated pathologist specializing in pediatric solid tumors established the diagnosis for all the solid tumors. The histological confirmation utilized a biopsy or a fine-needle aspiration cytology as appropriate, and patients who underwent a biopsy elsewhere prior to presentation at our center had the histology reviewed. All treatment decisions were

discussed in a tumor board comprising pediatric medical, surgical, and radiation oncologist, a dedicated pediatric radiologist, pathologist, nuclear medicine, and palliative care physician.

A descriptive analysis was performed to evaluate the age and sex distribution of all tumors. For assessing the relative incidence of a given diagnosis, the frequency distribution and its percentage were calculated. To determine age distribution, patients were divided into three equal age groups, i.e., 5 years or less, 5-9 years, and >9 years, and the distribution between the three age groups was analyzed. Data collection and analysis was performed using SPSS, version 24.

RESULTS

A total of 165 patients have registered in the study period; 18 were found to have no malignancy and 14 patients without histological confirmation of malignancy were excluded. The study cohort, therefore, included 153 patients with a solid tumor (Table1). The mean age was 5.7 years. The male to female ratio was 1.6:1 with 95(62.09%) males and 58(37.90%) females. Majority of the patients (54.90%) were in the 0-5 age group, while a quarter (26.79%) of the patients belonged to the 5-9 years age group. The number of patients in >9-year age group were 27(17.64%).

Mean Age group Age group Gender Age group Type of solid Gender N % age in < 5 year 5-9 years >9 years female tumour male (n%) (n%) (n%) (n%) (n%) years 4.3 33(70.21%) Renal tumour 47(30.7%) 9(19.14%) 5(10.63%) 28(59.57%) 19(40.42%) Neuroblastoma 39(25.49%) 3.9 29(74.35%) 7(17.9%) 3(7.69%) 25(64.10%) 14(35.89%) Soft tissue sarcoma 24(15.68%) 6.7 11(45.83%) 5(20.83%) 8(33.33%) 15(62.5%) 9(37.5%) Germ cell tumour 13(8.49%) 5.8 8(61.53%) 1(7.69%) 4(30.76%) 5(38.46%) 8(61.53%) Liver 10(6.53%) 3.11 7(70%) 1(10%) 2(20%) 7(70%) 3(30%)

Table 1: Distribution of paediatric solid tumour.

Renal tumors were the most common tumors (30.7%) (Table 1) and 85.10% of them were Wilms tumor (Table 2). The non-Wilms tumor included clear cell sarcoma, renal cell carcinoma, renal Ewing sarcoma, malignant rhabdoid tumor, and congenital mesoblastic nephroma. Wilms were the most common accounting for of all the tumors. Neuroblastoma was the second common tumor (25.49%) and (10.4%) showed a predilection for children <5 years of age. Soft tissue sarcomas were the third most common (15.68%) (Table 1). Rhabdomyosarcoma constituted 54.16% and the nonrhabdomyosarcoma formed 45.83% of all the soft tissue tumors (Table 2). The predominant histological types nonrhabdomyosarcoma were extra skeletal Ewing sarcoma, fibromatosis, synovial sarcoma, extrarenal rhabdoid tumors, malignant nerve sheath tumors, inflammatory myofibroblastic tumors, and infantile fibrosarcoma. Rhabdomyosarcoma was predominantly seen in less than 5 years children, while the nonrhabdomyosarcoma was common in more than 9 years age group.

However, there was a male preponderance in both the groups. Germ cell tumors comprised 8.49% of all the tumors with almost an equal distribution at gonadal (53.84%) and extragonadal (46.15%) sites. (Table 2) The gonadal tumors were commonly seen in females above 9 years of age, while the extragonadal tumors were seen in

children <5 years; however, they did not show a gender predilection (Table 2). Liver tumors formed only 6.53% of all the solid tumors and 76% of them were hepatoblastoma. (Table 2) The no hepatoblastoma liver tumors included hepatocellular carcinoma, infantile hepatic hemangioma, mesenchymal hamartoma. Among the 20(13.07%) patients

classified as miscellaneous tumors, thyroid gland, nasopharyngeal, salivary gland, adrenocortical, colon, and pancreatic cancers were seen in decreasing order of frequency. Surgery, either alone or in combination with chemotherapy and/or radiotherapy was offered to more than 80% of the 153 patients.

Solid tumor	Tumor subtype	Frequency	Mean age in years	Age group <4 year	Age group 5-9 year	Age group >10 year	Gender male	Gender female
STS	RMS	13(54.16%)	5.8	7(53.84%)	4(30.76%)	2(15.38%)	9(69.23%)	4(30.76%)
STS	NRSTS	11(45.83%)	7.7	4(36.36 %)	2(18.18%)	5(45.45%)	7(63.63%)	4(36.36%)
Renal	Wilms	40(85.10%)	4.7	29(72.5%)	8(20%)	3(7.5%)	24(60 %)	16(40%)
Renal	Non-Wilms	7(14.89%)	5.4	4(57.14%)	1(14.28%)	2(28.57%)	5(71.42%)	2(28.57%)
GCT	Gonadal	7(53.84%)	8.6	2(28.57%)	1(14.28%)	4(57.14%)	2(28.57%)	5(71.42%)
GCT	Extragonadal	6(46.15%)	2.7	4(66.66%)	1(16.66%)	1(16.66%)	3(50%)	3(50%)
Liver	Hepatoblastoma	7(70%)	3.1	5(71.42%)	1(14.28%)	1(14.28%)	5(71.42%)	2(28.57%)
Liver	Non- hepatoblastoma	3(30%)	6.5	1(33.33%)	1(33.33%)	1(33.33%)	2(66.66%)	1(33.33%)

Table 2: Distribution of histological subtypes of pediatric solid tumors.

DISCUSSION

The exact incidence of most childhood solid tumors in India is not known, despite children <12 years forming 35% of the Indian population. Lack 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 all factor in suboptimal reporting.¹

Although child health continues to be a priority health issue in India, childhood cancer is not yet a major area of focus. Appropriate management of pediatric tumors requires complete epidemiological data of pediatric tumors in different geographical areas. In developing countries, as significant progress is made in treating infectious diseases and nutritional deficiencies, cancer is emerging as a major childhood killer.^{3,4}

This study included patients <12 years of age with histological confirmation of malignancy seen over duration of 5 years. A direct comparison with other studies reporting on pediatric solid tumors is not feasible as these studies have included bone, central nervous system tumors, and even lymphomas.⁵⁻⁸

Renal tumors were the first common tumor and Wilms accounted for 85.10% of all the tumors. Tremendous advances have been made over the past few decades in the treatment of Wilms tumor and evidently, the outcome has significantly improved. Almost 50% of the patients had some form of treatment, predominantly surgery, since renal tumors are unhesitatingly operated by all

cadres of surgeons, including pediatric, general, and urosurgeons. Subsequently, 75% of the patients are referred for adjuvant chemotherapy and radiotherapy and for the treatment of relapsed disease.

The soft tissue sarcomas showed a significant higher incidence in our population when compared with other studies accounting for 18.03% of all tumors. However, this may be a relative increase considering that bone and central nervous system tumor were excluded. There was almost similar distribution of rhabdomyosarcoma and the nonrhabdomyosarcoma in our study; however, there was age difference in their incidence. Rhabdomyosarcoma was common in the <5 years age group, while the nonrhabdomyosarcoma was more common in children >9 years of age. More than 40% with soft tissue tumor had a prior treatment and 80% of these required additional treatment, mostly in the form of revision surgery and/or radiotherapy. The soft tissue tumors due to their presentation as unpresumptuous well-circumscribed masses are often misdiagnosed, and consequently, their evaluation and treatment are suboptimal. We have previously reported 48% of nonrhabdomyosarcoma soft tissue tumors presenting after an unplanned excision, and 46% of these patients had residual disease, thereby necessitating revision surgery.9

The highest incidence (50%) of prior treatment was in patients with germ cell tumor; mostly in the form of surgery, probably due to the easy surgical access especially to the testis and the sacrococcygeal region. The highest incidence of no cancer-directed treatment was with neuroblastoma and liver tumors. The large burden of disease, suboptimal nutritional status, toxicity of the treatment, and poor family

motivation are the prime reasons for no cancer-directed therapy in patients with neuroblastoma. Among the liver tumors, PRETEXT 4 disease, extensive metastases, and hepatocellular carcinoma were the predominant reasons for no cancer-directed treatment. None of the patients with hepatocellular carcinoma in this study could be offered surgery in view of locally advanced and metastatic disease. Patients with initial PRETEXT 4 who did not respond well to preoperative chemotherapy were referred for liver transplant to specialized centers; however, most did not pursue for various reasons. Nonetheless, the outcomes in other patients with hepatoblastoma were favorable.

In India, cancer is the 9th common cause for the deaths among children between 5 and 14 years of age. ¹⁰ The mortality and disability due to cancer can be significantly reduced by early diagnosis and treatment. In order to achieve this, the public health system of the country needs country-specific epidemiological data regarding the disease in the population. ¹ Though the outcomes of all the tumors are not provided, which is a limitation to this study, the distribution patterns of various pediatric solid tumors and the treatment received shows the burden and referral patterns in our institute. An assiduous endeavor of our institution is to provide detailed assessment of individual pediatric solid tumors in the near future to better illustrate the cancer patterns of Indian children.

CONCLUSION

Extracranial and extraosseous pediatric solid tumours include a wide range of tumours with a predilection for male sex and children <4 years of age. renal tumours, neuroblastoma, and Soft tissue tumours are the most common tumours. Public health programs and strategies should be framed using country-specific epidemiological data, for early detection and treatment of disease.

Multiple interrelated factors are responsible for the poorer outlook of childhood cancer in India. Limited financial resources, lack of awareness of the meaning of symptoms, and difficulty in accessing healthcare, abandonment of treatment, and of course, belief in alternative medicines, contribute to advanced stage presentation. It is imperative to address these issues to improve the outcomes of our patients. This can be done by improving the levels of education and public health awareness in the state. Accessibility to health services, especially in adverse weather conditions, however, still remains a challenge. Furthermore, pediatric patients should be treated in dedicated and specialized centres as proved by the excellent results achieved in the USA and Europe, where >90% of children are treated in such centres. Finally, advances in diagnostics including the turnaround time and modalities of treatments need to be implemented to improve the outcomes of our patients.

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Institutional Ethics Committee

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