ORIGINAL RESEARCH PAPER

Oncology

THE SPECTRUM AND CLINICO-EPIDEMIOLOGICAL PROFILE OF PEDIATRIC SOLID TUMORS AT A TERTIARY CARE HOSPITAL FROM CENTRAL MAHARASHTRA: A RETROSPECTIVE OBSERVATIONAL STUDY.

KEY WORDS: Pediatric Solid tumor, Epidemiologic profile,Outcome of treatment

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ABSTRACT

Background & Aims: The purpose of this retrospective study was to study the epidemiological characteristics and outcomes of children with solid tumours at our institution. **Material And Methods:** 322 paediatric patients aged 0–14 years with histologically confirmed malignancies registered at Government Cancer Hospital(GCH) Aurangabad between Jan2019 to Dec2023 were analysed with regard to demographic status, presenting complaints, investigations, treatment, morbidity, and outcomes. Standard statistical methods were used for analysis. Patients treated as per protocol and necessities. **Result:** Of 322 patients enrolled, 206 (64%) male and 115 (36%) females ,the male-to-female ratio was 1.8, there were no neonate (up to 27 days), 9% were infants and toddlers(28 days–23 months), 40% were younger children (2-5 years), 36% were school going (6-10 years) and 15% were adolescents (11–14 years).Those hailing from urban areas were 71 (22%),while 251 (78%) hailed from rural regions. Most common were retinoblastoma (22%) followed by central nervous system tumours (18%). 78.5% patients went into remission, 2.8% were defaulters,10.55% expired. Of all these patients, 8.3% had a relapse **Conclusion:** The male-to-female ratio observed was greater than that documented in Western countries and India. Significantly higher prevalence of patients in rural regions of central Maharashtra, primarily due to government centre being the sole provider of cancer care in the area. Following Retinoblastoma, the second most prevalent tumour was central nervous system tumours, We have achieved favourable outcomes in cases of retinoblastoma, hepatoblastoma, germ cell tumours, and Wilms' tumour. However, experienced poor outcomes in neuroblastoma, largely due to late presentation.

INTRODUCTION

Cancer in children and adolescents is rare although the overall incidence of childhood cancer has been slowly increasing since1975[1] Worldwide, the annual number of new childhood cancer exceeds 200,000 and >80% of these are from the developing world.[1] Seven out of 10 children with cancer in the resource rich countries are cured, with 5-year survival rates for certain cancers such as Hodgkin's lymphoma and retinoblastoma approaching 95%.[2,3] Recent studies have shown that this success in survival can be replicated in the developing world through shared expertise[4-7] Childhood cancer remains the leading cause of disease-related mortality in children.[8] Malignant solid tumours account for approximately 30% of childhood cancers.[9] The predominant histology of specific solid tumours varies significantly with age.[10]

Dramatic improvements in survival have been achieved in children and adolescents with cancer. Between 1975 and 2010, childhood cancer mortality decreased by >50%.[11] This success can be attributed to several factors. These include enrolment of patients into well-designed prospective clinical trials, systematic collection of tissue to better define the biology of disease, availability of more effective chemotherapy agents, use of multimodal therapy, better supportive care, and more refined diagnostic imaging methods that accurately define the extent of disease.

The increase in cancer prevalence is because of adoption of unhealthy lifestyles, smoking, consumption of calorie dense food, and physical inactivity.[12]

India is also witnessing surge in childhood cancers. As per ICMR-NCDIR national cancer registry, childhood cancers comprise 4% of all reported cancers.[13] This disparity in reporting of data is due to lack of dedicated pediatric cancer centers and non-uniform reporting of data in pediatric cancer registries across the country. Childhood cancer management in low and middle-income countries is characterized by delayed diagnosis and treatment initiation, inadequate or incomplete treatment, and low survival rate. Cancer affects all nations, and therefore, it is an endemic disease with considerable variation in frequency according to the site incidence. The geographical differences in total and site incidences have provided clues of causative factors and especially in separating environmental and ethnic factors from intrinsic factors.

Cancer in children is unique and requires different kinds of care and services for better outcomes, survival, and long-term development. At present, current national health programs and policies are focused on cancer in adults. With considerable reduction in infants and child mortality rates secondary to diarrheal illness and respiratory illness, childhood cancers are emerging as a distinct problem to be dealt upon. Therefore, it is important to know the magnitude of childhood cancers and outcomes throughout the country by maintaining national cancer registry. In this study, we aimed to retro prospectively study the epidemiological characteristics, treatments received, and outcomes of children with solid tumors at GCH, CHH.Sambhajinagar. Based on our study, we could better evaluate the status of our efforts to treat this subgroup of patients and deliver improved care.

MATERIAL AND METHODS:

A retroprospective study was conducted in 322 paediatric patients (children and adolescents up to 14 years of age) with histologically proven solid tumours who were registered at Department of Pediatric oncology of a tertiary care centre from central Maharashtra., for a period of 4 years from January 2019 to December 2023.

A research protocol for this study was approved by the local

Ethics Committee and informed consents were taken from each patient's parent/guardian.

A pro-forma was developed, and patient characteristics with regard to age, sex, locality, residence, type of family, socioeconomic status, clinical presentation, investigations, treatment prescribed, and any morbidity in each case were studied in detail.

Following completion of treatment, the patients were followed up in our outpatient department. The frequency of follow-up visits was according to their individual tumor type and general recommendations. In each visit, a detailed history and physical examination and relevant investigations were done to detect any late side effects of treatment or relapse. The last follow-up studied was till June 2024.

Standard statistical methods were used for statistical analysis

RESULTS

Toal 322 children aged 0-14 years were registered at Government Cancer Hospital(GCH) Aurangabad during the study period.

All subsequent data are for the patients with pediatric solid tumours. There were 64% male and 36% females (M:F ratio was 1.8:1) [Figure 1]. There were no neonates (up to 27 days), 9% were infants and toddlers (28 days–23 months), 40% were younger children (2-5 years), 36% were school going (6-10 years) and 15% were adolescents (11–14 years). There were 78% rural patients and 22% urban patients.

The most frequent were Retinoblastoma (22%) followed by (in descending order)central nervous system tumours (18%) followed by Wilms' tumour (11.5%),Hepatoblastoma (10.9%), primitive neuroectodermal tumour/Ewing sarcoma (10.86%) rhabdomyosarcoma (6.8%), neuroblastoma (6.8%), osteogenic sarcoma (6.2%) and germ cell tumours (5.6%).

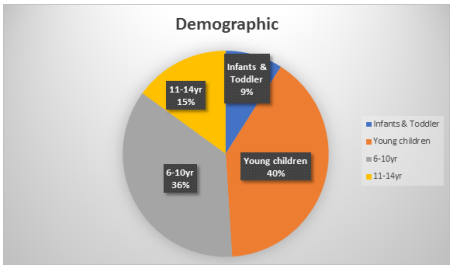

Fig: 1 Demographic details of study population.

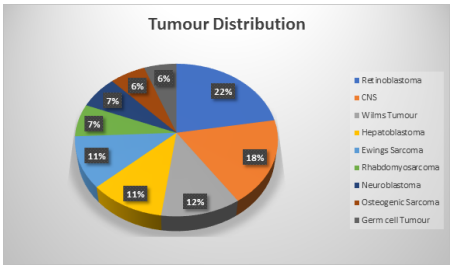

Fig 2: Major tumor distribution

Table 1 shows a comparison of age and gender among study participants.

	Male(%)	Female(%)	Total(%)
RB	27(38)	43(62)	70(21.7)
HBL	23(65.7)	12(34.3)	35(10.9)
EWS	28(80)	7(20)	35(10.9)
OGS	11(55)	9(45)	20(6.2)
RMS	14(63.6)	8(36.4)	22(6.8)
CNS	44(74.6)	15(25.4)	59(18.3)
GCT	11(61.1)	7(38.9)	18(5.6)
WT	25(69.4)	11(30.5)	36(11.2)
NBL	16(72.7)	6(27.3)	22(6.8)
Misc	3(60)	2(40)	5(1.5)
Total	202(63)	120(37)	322(100)

Table 2 shows distribution of common malignancies among study subjects.

	0-2yr()	2-5yr()	6-10yr()	11-14yr()	Total()
RB	10(14.3)	46(65.7)	14(20)	0	70(21.7)
HBL	10(28.6)	19(54.3)	6(17.1)	0	35(10.9)
EWS	1(2.8)	8(22.8)	13(37.1)	13(37.1)	35(10.9)
OGS	0	0	8(40)	12(60)	20(6.2)
RMS	0	3(13.7)	14(63.5)	5(22.8)	22(6.8)
CNS	5(8.5)	17(28.8)	18(30.5)	19(32.2)	59(18.3)
GCT	1(5.5)	2(11.2)	14(77.8)	1(5.5)	18(5.6)
WT	1(2.8)	10(27.8)	23(63.9)	2(5.5)	36(11.2)
NBL	1(4.5)	6(27.3)	13(59.1)	2(9.1)	22(6.8)
Misc	0	2(40)	2(40)	1(20)	5(1.5)
Total	29(9)	113(35.1)	125(38.9)	55(17)	322(100)

Outcome

Among the 322 patients studied, 78.5% patients went into remission,5.62% had partial response, 2.5% were defaulters, 2.8% had stable disease,10.55% expired. Of all these patients, 8.5% had a relapse

Table 3: Overall Outcomes

	Alive(%)	Dead(%)	Relapse(%)	Defaulter (Abandonment) (%)	Total
CNS	45(76.3)	09(15.25)	03(5)	02(3.4)	59(18.3)
RB	65(93)	02(2.8)	02(2.8)	01(1.4)	70(21.7)
NBL	10(45.5)	05(22.7)	06(27.3)	01(4.5)	22(6.8)
WT	24(66.7)	06(16.7)	05(13.9)	01(2.8)	36(11.2)
EWS	32(91)	01(2.8)	02(5.8)	00(-)	35(10.9)
OGS	12(60)	04(20)	03(15)	01(5)	20(6.2)
HBL	30(85.7)	02(5.7)	03(8.6)	00()	35(10.9)
RMS	17(77.3)	03(13.6)	01(4.5)	01(4.5)	22(6.8)
GCT	14(77.8)	02(11.2)	02(11.2)	00(-)	18(5.6)
Misc	04(80)	00(-)	00(-)	01(20)	05(1.5)
Total	253(78.5)	34(10.6)	27(8.4)	08(2.5)	322(100)

Individual Tumour Characteristics

1. **Retinoblastoma (n-70):** They were more common in females (62%) and mostly presented in children in the age group of 2–10 years (85%) followed by children's up to 23 months (14%) and none in the 11–14 years age group. Among these, 63% were unilateral and 38% bilateral.

Most of the tumours were IIRC Group E (58%), followed by Group D (31%), Group C (10%), and Group A (2%).

Most patients went into remission (92%) defaulted (1.5%) relapse (2.8%) and 2.8% expired.

2. **CNS tumours (n-59):** These were more frequent in males (74.6%) and in adolescents (47.8%). The most common histology was astrocytoma (25.64%) and WHO Grade IV (26.9%). Patients defaulted (3.4%), remission was documented in 76%, relapsed 5%, and 15% expired.

3. **Wilms' tumour (n-37):** These constituted 90% of renal tumours. They were more common in males (70%) and mostly presented in children in the age group of 2–10 years (86.4%).

Most of the tumours were diagnosed in Stage III (45.4%), followed by Stage I (29.6%), stage IV (21.2%), and Stage II (3.7%). Most patients went into remission (67%), 2.8% defaulted, relapse 13.5% and 16.1% expired

4. **Hepatoblastoma (n-35):** These were more frequent in

males (66%) and in children in 2–11 years age group (67%) followed by children's up to 23 months (33%) and none among the adolescents. Most patients were diagnosed in Stage III(57%), followed by Stage IV (43%), and none in Stage I/II. Most patients achieved remission (86%) expired 5.7%, relapse 8.5%& none defaulted.

5. **PNET/ES (n-35):** These were more frequent in males (80%) and in adolescents (69%). Localized tumours were marginally more frequent (62.8%) as compared to metastatic disease (37.2%). According to site, 58% were extraosseous, 38% osseous, and 04% in CNS/spine. Most patients' remission was documented in 91%, relapsed in 6% and 2.8% expired.
6. **Germ cell tumours (n-18):** These were more frequent in males (61%)

The most common histologies were yolk sac tumours (35%) and dysgerminoma (25%) followed by mixed germ cell tumour (23%), teratoma (immature 10%,mature 5%), and seminoma (2%).

According to site, 65% were gonadal, 25% were extra-gonadal, and 10% were in CNS/spine (germinomas). Most patients were diagnosed in Stage I/III (41% each) then Stage IV (16%) and Stage II (2.2%). Most of the patients achieved remission (78%) but none defaulted,11% relapsed and 11% expired.

7. **Osteosarcoma (n-20):** These were equally prevalent in males and females. Most were diagnosed in adolescents (80%) and in localized stage (70%). Most patients went into remission (60%), but 5% defaulted, relapsed 15% and 20% expired.
8. **Rhabdomyosarcoma (n-22):** They were more common in males (63%) and in children in the age group of 2–10 years (77%) followed by adolescents (23%) and none in children's up to 23 months. The most common histology was embryonal (60%), followed by alveolar (22%), and pleomorphic (6%) and others (12%). Most of the tumours were diagnosed in Stage IV (47%) Stage II/III (42% each). Most patients went into remission 77%,defaulted 4.5%,relapsed 4.5% and 14% expired.
9. **Neuroblastoma (n-22):** They were more common in males (72%) and mostly presented in children in the age group of 2–10 years (68%) followed by children's up to 23 months (23%) and adolescent in 11–14 years age group (9%). Most of the tumours were diagnosed in Stage IV (73%), followed by Stage III (20%), stage I (7%), and none in Stage II.

Patients had remission 45% , expired 23%, 5% defaulted, and 27% relapse.

10. **Benign tumours (n-5):** These were rare cases – Pheochromocytoma (n-1, remission), giant cell tumour of bone (n-1, remission) inflammatory myofibromatosis (n-1, remission), Langerhans cell Histiocytosis (n-1, remission) and vascular hamartoma (n-1, defaulted).

DISCUSSION

Malignancy is the second most common cause of childhood death in the developed world, accounting for 10%–12.3% of all childhood deaths.[11]

Child health remains a critical health concern in India; however, childhood cancer has not yet received the attention it deserves. Effective management of pediatric tumours necessitates comprehensive epidemiological data regarding these tumours across various geographical regions. In developing nations, as advancements are achieved in the treatment of infectious diseases and nutritional deficiencies, cancer is increasingly recognized as a leading cause of mortality among children.[12,13] In India, cancer is the 9th common cause for the deaths among children between 5 and 14 years of age.[14] The proportion of childhood cancers relative to all cancers reported by Indian cancer registries varied from 0.8% to 5.8% in boys and from 0.5% to 3.4% in girls.[15] There are few studies reporting childhood cancer incidence from cancer registries in Indian states. A recent publication by Satyanarayana et al. provides an updated summary overview of the incidence of childhood cancer on the basis of the 2013 report from the National Cancer Registry Program for the years 2006–2011 that covered 25 population-based cancer registries in India.[16] In low- and middle-income countries, where 80% of children live, the 200,000 children diagnosed with cancer each year have limited access to curative treatment and only about 25% survive.[17] The difference in survival for children diagnosed with cancer between high- and low-income countries continues to widen as curative therapies are developed in the former but not implemented in the latter.[18]

Overall, cancer in childhood is more common among males than females, and the male-to-female ratio in the most resource-rich countries is around 1.2:1.[3,19] However, some cancers such as retinoblastoma, Wilms' tumour, osteosarcoma, and germ cell tumour 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 (PBCRs) except in North East India, and this gives a male-to-female ratio that is much higher than what is seen in the developed world.

PBCR survival data are a better representation of cancer outcomes across India and have been reported from Bangalore and Chennai where the 5-year overall survival for all childhood cancers combined is 37-40%. Approximately two-third of the children for Wilms' tumour and Hodgkins' lymphoma survive for 5 years or more whereas children's with retinoblastoma and germ cell tumours, which are cancers with excellent prognosis in the developed world showed disappointingly low survival and may be related to an advanced stage at presentation and suboptimal chemotherapy regimens used.[21,22]

Our data were collected from GCH, over duration from January 2019 to December 2023 and the overall incidence and prevalence of pediatric solid tumours was consistent with data from other national and international series. The incidence of pediatric cancer including solid tumours in Maharashtra has shown a steady increase over the years. It is not clear whether this is an actual rise or an increase in the proportion of patients seeking health care.

Some Differences Have Also Emerged.

The male-to-female ratio observed was greater than that documented in Western countries and India.

The prevalence of patients is significantly higher in rural regions of central Maharashtra, primarily because the government centre is the sole provider of cancer care in the area.

The distribution of major solid tumours in this region also exhibits notable differences. Following retinoblastoma, the second most prevalent tumour is central nervous system tumours, succeeded by Wilms' tumour (11.2%), primitive neuroectodermal tumour/Ewing sarcoma (10.9%)/ Hepatoblastoma (10.9%), rhabdomyosarcoma (6.8%), neuroblastoma (6.8%), osteogenic sarcoma (6.2%), and germ cell tumours (5.6%).

We have achieved favourable outcomes in cases of retinoblastoma, hepatoblastoma, germ cell tumours, and Wilms' tumour. However, those patients having poor outcomes, particularly in neuroblastoma due to late presentation.

CONCLUSION:

Our study has limitations in that it is a single institution retro-prospective study and has not presented survival data as that would require further prolonged follow-up. This is an area of active research in our institution.

Numerous interconnected factors contribute to the unfavourable prognosis of childhood cancer in India. Insufficient financial resources, a lack of understanding regarding the significance of symptoms, challenges in accessing healthcare, discontinuation of treatment, and a prevalent belief in alternative medicine all lead to late-stage diagnoses.

To enhance the outcomes for childhood cancer patients, it is crucial to tackle these challenges. This can be achieved by elevating educational standards and public health awareness within the community, as well as by training nursing and paramedic personnel to identify these patients at vaccination centres especially Retinoblastoma, and during health visits, thereby facilitating early diagnosis and improved results.

Dedicated and specialized centres equipped with state of the art facility along with trained manpower can achieve the excellent results at par with USA and Europe, where >90% of children are treated in such centers.

Major setback is the poor Turnaround time for advanced diagnostics in resource limited setups, which hampers the outcome due to delay in implementation of treatment and hence the outcome of pediatric cancer patients.

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Nil.

Conflicts Of Interest
There are no conflicts of interest

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