

An Insight into Childhood Malignancy

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Abstract

Childhood cancers represent a significant public health concern, affecting a vulnerable population with unique biological and developmental characteristics. The aim of this article is to describe the main causes and different types of malignancies in childhood. By understanding the contributing factors towards malignancy in childhood one can plan for the preventive measures and early diagnosis and treatment modalities can be adopted. Even though the treatment patterns have improved, people are still unaware about the symptoms which cause increased mortality and morbidity. This article reviews the prevalence and types of childhood cancers, emphasizing the need for a comprehensive understanding of their etiology. When identified at an early stage, childhood cancer can be partially cured. A recent report from the National Cancer Registry Program (NCRP) in India revealed that cancers in children aged 0–14 constituted 4.0% of all cancer cases. The Population Based Cancer Registry in Delhi recorded the highest age-adjusted incidence rate (AAR), with 203.1 per million in boys and 125.4 per million in girls.

Keywords: Childhood cancers, Pediatric malignancies, Early diagnosis, Preventive measures, Treatment modalities, Symptoms of childhood cancer, Pediatric oncology

INTRODUCTION

While childhood cancers are uncommon, they represent a significant source of illness and death among children below the age of 15. Malignancies are difficult to detect in children because the signs and symptoms are nonspecific and mimic many common disorders. Pediatric malignancies differ from that in adults since they are more aggressive and consequently more responsive to chemotherapy [1]. This article reviews the prevalence and types of childhood cancers, emphasizing the need for a comprehensive understanding of their etiology. As per WHO data. Every year, 400,000 children and adolescents receive a cancer diagnosis. While cancer stands as a leading cause of childhood mortality in developed nations, it remains secondary to infections in causing death in developing countries [2]. The challenge of pediatric malignancies derives from the broad spectrum of complex diseases, all with their own biology and natural history. The optimal and creative integration of different therapies into their management requires a sophisticated understanding of the disease as well as the adverse effects. Pediatric malignancy gives the ear to oncologists because each new patient opens a new world into which the doctor must not only enter but be successful. As the survival rates for pediatric cancers improve with modern technologies, we will be having an increased population of young adults who are cancer survivors [3].

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REVIEW OF LITERATURE

A study was conducted with an aim to find out the profile of childhood cancers in western Orissa, India for a period of two years (2005-2007). The pediatric population (0-14 years of age), which was diagnosed to have malignancy, in the Department of Pathology, V.S.S Medical College, Sambalpur, Orissa, India was the study group. The result shows that Pediatric malignancies comprise 4.4% of the

cancer load of all the age groups. The incidence of different variants, based on the International Classification of Childhood Cancer (ICCC), showed leukemia as the commonest cancer, to constitute 45.45% of the total cancer load, followed by soft tissue sarcomas -11.82%, malignant bone tumors-10%, lymphomas- 8.17%, retinoblastomas- 5.45%, neuroblastomas-4.55%, Wilms' tumor- 4.55%, germ cell tumors -4.55%, CNS neoplasms- 3.64%, hepatoblastomas- 0.91% and squamous cell carcinomas of the skin- 0.91%, in the decreasing order of their frequencies. The age distribution showed an incidence of 31.82% in the 0-4 years age group, 24.55% in the 5-9 years age group and 43.64% in the 10-14 years age group. The sex ratio showed a male predominance.

A study conducted with the aim to find out the epidemiology of tumors in children in a region below <14 years age who presented to tertiary care Cancer hospital, Bhopal, M.P. for period of four years (2015- 2018) as shown in Methodology: All children with cancer, aged 1-14 years diagnosed by mean of histological and cytological examination during a period of 4 years were reviewed. The result showed that during the period of four years 275 patients were diagnosed as having pediatric malignancies. According to year wise distribution, the highest incidence of cases was found in 2016 (32.72%). The highest number of cases, 96(35%) were in the 10-14 years of age group and mean age was 7.43 with SD 4.0. Male were affected more than females with ratio of 2.66:1. It was observed that hematological malignancies were more common 172(62.54%) than the non-hematological malignancies 103(37.45%). Leukemia 150 (54.54%) is the most common pediatric cancer amongst which Acute lymphoblastic leukemia is the most common hematological malignancy. Overall, it was found that the most common cancer group in the present study were leukemia (54%) followed by lymphoma (8.36%), Brain tumor's (7.27%) and Sarcoma (7.27%). The study concluded that although the exact incidence rate cannot be provided by this hospital-based study, the information is useful in showing distribution patterns of childhood malignancy in this region [4,5]. Childhood cancers have different characteristics than those occurring among adults and are described as cancers occurring below 15 years of age. In developed countries, its incidence is relatively rare but it's a leading cause of death. More than 80% of childhood cancers occur in low- and middle-income countries. Based on data from population-based cancer registries under National Cancer Registry Program, in this commentary, the author described the incidence and pattern of Childhood cancers in India and its implications.

Symptoms of Childhood Cancer

It is difficult to detect cancer in children as they are rare compared to adults.

Some symptoms are:

- Continued, unexplained weight loss.
- Headaches, often with early morning vomiting
- Increased swelling or persistent pain in the bones, joints, back, or legs
- Lump or mass, especially in the abdomen, neck, chest, pelvis, or armpits.
- Development of a whitish appearance in pupil of the eye or changes in the vision
- Recurrent fevers not caused by infections.
- Excessive bruising or bleeding (often sudden)
- Noticeable paleness or prolonged tiredness

Prevalence of Childhood Cancers

Childhood cancers are relatively rare compared to cancers in adults, accounting for approximately 1% of all cancer diagnoses. However, their impact on affected families is profound. A thorough analysis of these cancer types provides a foundation for exploring potential causes [6,7].

The modified relative occurrence rates of prevalent types of childhood cancer are as follows: Leukemias, brain and spinal tumors, lymphomas, and sympathetic nervous system tumors (Neuroblastoma) are among the most frequent. Kidney (Wilms) tumors, as well as soft tissue and bone

sarcomas, also rank high in childhood cancer cases. For instance, neuroblastomas are more prevalent during infancy. The incidence of bone cancers sharply increases in the age group of 11 to 15, aligning with the adolescent growth spurt [8].

The majority of pediatric cases of acute leukemia, neuroblastoma, Wilm's tumor, retinoblastoma and primary liver cancer occur below the age of 5 years. Hodgkin and non-Hodgkin lymphoma and bone marrow tumors occur frequently in children over 10 years old. At all ages, boys are affected more frequently than girls. Progress in diagnostic techniques, comprehensive treatment approaches, judicious application of chemotherapy, and enhanced supportive care have significantly enhanced survival rates. Currently, more than 70% of childhood cancers are effectively treatable. Genetic factors. A growing body of evidence suggests that genetic factors play a crucial role in the development of childhood cancers [9,10].

Environmental Exposures

Environmental factors, including exposure to carcinogens, ionizing radiation, and certain chemicals, have been implicated in the development of childhood cancers. Prenatal exposures and those occurring during early childhood are of particular concern. This section reviews notable studies linking environmental factors to specific childhood cancers [11].

Maternal and Perinatal Factors

Maternal health during pregnancy and perinatal factors may influence a child's susceptibility to cancer. Topics explored in this section include maternal age, smoking during pregnancy, gestational exposures, and birth weight. These factors need to be understood to take necessary preventive measures.

Infectious Agents

Few infectious agents are responsible for cancer. For example, Human papillomavirus (HPV), Epstein-Barr virus (EBV), and human immunodeficiency virus (HIV) are examples of infections that may contribute to the development of specific childhood malignancies.

Future Directions

Advances in genomics, molecular biology, and epidemiology offer promising avenues for further research into the causes of childhood cancers. To formulate effective planning for preventive measures in childhood malignancies, there should be much research work in this field. Also, clinicians, researchers and policy makers together put the effort.

Few of the Pediatrics malignancies Leukemia

According to estimates from GLOBOCAN (<http://globocan.iarc.fr>), India sees nearly 25,000 children diagnosed with cancer annually, with approximately 9,000 of them having leukemia. Even with these conservative projections, it suggests that there could be 90,000 children with leukemia in India over a decade. Leukemia is a malignant condition resulting from the abnormal clonal proliferation of hematopoietic cells, causing disruptions in normal marrow function and various manifestations of leukemia. Globally and in India, leukemia represents the most frequently diagnosed category of childhood cancers, with over 95% being of the acute type. Significantly, there has been substantial progress in treating acute lymphoblastic leukemia, achieving a 5-year overall survival rate of 90% in high-income countries. Acute Lymphoblastic Leukemia constitutes 75% of Leukemias [12].

Acute Myeloid Leukemia

Approximately 20% of children with Leukemia present with AML. The disease occurs throughout the pediatric age range, with greater frequency in newborn and adolescence. Young children with Down syndrome exhibit a heightened occurrence of Acute Myeloid Leukemia (AML). Initial symptoms involve paleness, fatigue, bleeding, infections, and fever. In comparison to Acute Lymphoblastic Leukemia (ALL), the presence of organ enlargement at the time of diagnosis is less frequent.

Brain and Central Nervous System (CNS) Tumors

Childhood malignancies involving the brain and central nervous system (CNS) rank as the second most prevalent. Commonly encountered tumors include medulloblastoma, gliomas, and ependymomas. Genetic syndromes (e.g., neurofibromatosis), prenatal exposure to certain medications, and ionizing radiation have been linked to an increased risk of CNS tumors in children.

Few examples for Supratentorial tumors are Astrocytoma, Malignant gliomas, Craniopharyngiomas, Embryonal tumors, Pineal region tumors and meningiomas. Examples of Infratentorial tumors are Medulloblastoma, Brainstem glioma and Ependymoma. The high technology in CT scan and MRI have improved the diagnosis modalities. Modern neurosurgical techniques also have improved the conditions [13].

Neuroblastoma

Neuroblastoma originates from embryonic neural crest cells found in the peripheral sympathetic nervous system. It stands as the most frequent solid tumor outside the brain in childhood, contributing to 15% of deaths related to cancer. Neuroblastoma occurs only rarely in adolescents and adults. More than one third of patients are diagnosed before the age of 1 year, whereas fewer than 5% of patients are present after the age of 10 years.

Neuroblastoma primarily affects young children, with around 90% of cases being identified before the age of 5, and nearly 50% diagnosed within the initial 2 years of life. While the condition may be present from birth, it typically remains unnoticed until the tumor starts to enlarge and exert pressure on nearby organs.

Cancer cells have the ability to rapidly spread to various parts of the body, including lymph nodes, liver, lungs, bones, the central nervous system, and bone marrow. Approximately 70% of children diagnosed with neuroblastoma will exhibit metastatic disease. While the exact causes remain unclear, genetic factors, including hereditary forms of the disease, and alterations in specific genes such as MYCN, have been implicated. Additionally, maternal smoking during pregnancy may contribute to an increased risk [14].

Wilms Tumor

Wilms tumor is an embryonal neoplasm with three distinct components: blastemal, epithelial, and stromal elements. These elements can display diverse patterns of aggregation or lines of differentiation. The overall pathological characteristics of Wilms tumor involve its common presentation as a single tumor on one side, although there is a possibility of multicentric growth and bilateral occurrence. The tumor typically appears solid, with lobulated features and a lack of calcification.

Approximately 8% of Wilms tumor cases are diagnosed in children under the age of 5, and the occurrence is comparable between boys and girls. Certain genetic syndromes (e.g., WAGR syndrome) and abnormalities in genes like WT1 are associated with an elevated risk of Wilms tumor. Prenatal exposure to certain substances and maternal age may also play a role.

Rhabdomyosarcoma

Rhabdomyosarcoma stands as the predominant soft-tissue sarcoma observed in children under 15 years of age. Nearly half of these cases are diagnosed below the age of 5 years and two thirds by 10 years of age [15].

Bone tumors

Osteogenic sarcoma and Ewing's sarcoma are the primary categories of bone tumors prevalent among children and adolescents. Both the tumors occur more commonly during second decade of life and show male predominance.

Retinoblastoma

Retinoblastoma is a type of eye cancer that originates in the retina, which is the delicate lining located on the inner surface of the eye. While it typically occurs in young children, there are rare instances of retinoblastoma developing in adults. There is increased frequency of retinoblastoma in some developing countries especially Latin America, Africa and Asia including India. Children with hereditary retinoblastoma are at exceptionally high risk of developing multiple primary cancers, especially osteosarcoma and soft tissue sarcomas.

Specific site Malignancies

Bladder and Prostate Rhabdomyosarcoma

Bladder and prostate Rhabdomyosarcoma combined represent approximately one half of genitourinary RMS. The predilection of bladder RMS for males and the bladder trigone often make it impossible to determine the origin of these tumors.

Pretesticular

Para testicular Rhabdomyosarcoma is less common than bladder/prostate RMS. Patients generally present with a painless scrotal mass. Scrotal ultrasound is generally the first diagnostic test that confirms a mass in the scrotum.

Vagina and vulva

Rhabdomyosarcoma of the vagina and vulva is rare accounting for 3 % of pediatric RMS, Vaginal RMS occurs in very young children, 90% younger than 5 years of age. Vulvar tumors may be initially mistaken as an infected Bartholin's gland.

Uterus and Cervix

Uterine and cervical RMS are less common than vaginal RMS. They occur predominantly in adolescent girls near puberty with a mean age of 13. Patients may present with a pedunculated polyp protruding from the cervix or with diffuse intramural involvement of the uterus and/or cervix and even invasion of adjacent organs, bleeding is common.

Para meningeal

Para meningeal RMS accounts for approximately 15% of pediatric RMS and 40-50% of head and neck RMS.

Other sites of Rhabdomyosarcoma are trunk, Retroperitoneal, Perineal and Hepatobiliary Tree.

DISCUSSION

The pediatric population (0-14 years of age) constitutes 32.4% of the total population of India. Cancer in children is an emerging major childhood killer. Malignant neoplasms are the third commonest causes of death in the 1 to 4 years age group and the second commonest causes of death in the 5 to 14 years age group. These are histologically very diverse, and it has been firmly established that the classification of childhood cancer should be based on the morphology of the cancer cells. Conclusion: The frequency of different diseases which are detected at a particular centre is not an exact reflection of the disease spectrum of that population, but it can give a rough estimation of the trend. There exist regional and geographic differences in the incidence and the histologic types of pediatric cancers. Community awareness about pediatric malignancy is very much required in the present scenario [16].

CONCLUSION

The problem of severe illness due to malignancy and death in children poses a tremendous challenge to the pediatric specialists as well as to the family members. After finishing treatment, it is crucial for individuals who have survived childhood cancer to undergo follow-up care for ongoing health monitoring. Every survivor should be provided with a treatment summary and a care plan for

survivorship. While individuals who have overcome any form of cancer may experience health issues months or even years post-treatment—referred to as late effects—childhood cancer survivors face a particular concern due to the potential for profound and enduring physical and emotional consequences resulting from childhood cancer treatments. The nature of late effects depends on factors such as the cancer type, the child's age, the treatment method, and other considerations. Awareness about malignancies in children will help the community to get treatment earlier and hence the complications can be minimized.

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