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Patterns of Care of Childhood Cancers in India

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Abstract

Management of childhood cancers in India has seen a new high in last few decades due to collaborative efforts of Physicians and organizations- both governmental and non-governmental. However, care is still heterogenous in this vast country. The problems span from a lack of data to programs for tackling cancers at the community level and lack of awareness among parents and physicians on childhood cancers, along with a nihilistic attitude and stigma attached to cancers even in this digital era. In this article, we describe the milestones in the development of Pediatric Oncology as a specialty, of cancer registries, of diagnostic armamentarium, access to affordable drugs, and, palliative care for children with cancers in India, that perhaps reflects care in other developing countries.

Keywords: childhood cancers, patterns of cancer care, cancers in India, pediatric cancer care, cancers in developing nations

1. Introduction

1.1 Epidemiology of childhood cancers in India

Pediatric cancers have never been an area of attention of cancer control in India, as majority of cancers occur in adults. Globally, it is reported that up to 85% of pediatric cancers occur in the developing world with a 5-year survival rate of less than 10%. On an average, in India, pediatric cancers account for less than 5% of all cancer cases. Nearly 45,000 new cancer cases are diagnosed in children every year in India. The main focus in pediatric care has been on control and reduction of infectious disease related mortality, which is in striking contrast with the developed world [1].

More than 0.2 million cases of childhood cancers are diagnosed across the globe every year. In the developed world, majority of these are cured, with a 5-year survival rate of 95%. However, the first step towards the control of childhood cancers in developing countries like India is to find out the incidence of cancers, to take directed measures in terms of control and treatment facilities. The main sources of such data are cancer registries [2].

Compared to the West, with average incidence of 75 to 150 childhood cancers per million children, the average incidence of childhood cancers in India is high. The age standardized incidence of cancers in India in the age group 0–14 years is highest in the Chennai Urban registry (124/million children) and lowest in the Ahmedabad rural registry (38/million children). The reasons for higher incidence

in urban areas as compared to rural areas are not clear. However, cancer contributes to only 2% of cancer related deaths in childhood as per available data. It was never a priority, in comparison to infectious diseases control, the main cause of mortality among children in India. Another contrast with developed world is the preponderance of cancers in boys, except in North-East India. The main reason is probably gender bias in seeking healthcare. However, the reasons for disproportionately higher rate of Hodgkin's disease in male children, up to 20 times more incidence than in females, are not known [3, 4].

1.2 The challenge: the great divide and an unmet need

One decade ago, the estimated gap between the developed and developing world in the survival rates in pediatric cancers was about 60–70% - a great divide. The reasons are many.

Because of high prevalence and mortality due to infectious diseases in children in India than cancer mortality - 58% of all deaths in the age group of 5–14 years, and half of these are due to diarrhea and pneumonia - and improved outcomes of infectious diseases by simple medication that can be delivered at peripheral centers, the emphasis has been high in this domain.

The Pediatric Hematology and Oncology (PHO) chapter of Indian Academy of Pediatrics (IAP) was established in 1987, with a focus on capacity building through training initiatives across all aspects of childhood cancers. Its flagship program was the *Indian National Training Program in Practical Paediatric Oncology*.

In order to foster collaborative efforts in childhood cancers, both in terms of uniformity of care as well as shared databases, Dr Bharat Agarwal, Dr Purna Kurkure and Dr Anupam Sachdeva formed *Indian Paediatric Oncology Group* InPOG in 2008. The emphasis now was clearly on clinical trials and research.

The Indian Pediatric Hematology Oncology Group (IPHOG) was formed in 1987 at the 24th Annual Conference of the *Indian Academy of Paediatrics* at Madras, with an intention of identifying and overcoming the barriers and to bridge the gap, by addressing factors leading to the decreased survival of children with cancers.

Some of the identified barriers were: delayed diagnosis, nihilism about childhood cancers, abandonment of treatment, lack of experience, inadequate infrastructure to treat emergent toxicities, expectation of cure, and, unwillingness to opt for retreatment at relapse [5].

Practical solutions that are already being followed by some institutions in India are as follows:

- i. Educating primary care providers, especially pediatricians, about the diagnosis of childhood cancers and early referral to specialized centers
- ii. Twinning, a process of collaboration between a hospital in a developing country with another in the developed world
- iii. Establishing a reliable blood component support system
- iv. Training nursing staff and other valuable trained human resources like social workers
- v. Measures to prevent abandonment after diagnosis of cancer in a child by providing logistic support in the form of transportation and free shelter to the family as well as employment with modest wages to parents

- vi. A systems for reminding and follow up with the parents of a child shortly after missing the scheduled visit
- vii. Fellowship and other training programs in medical colleges with well-established pediatrics departments
- viii. Countering nihilism and misinformation by untrained or improperly trained health care workers, emphasizing curability in the majority

2. Cancer registries

Cancer registration, an essential part to decipher patterns presentation, care and outcomes research, was started in India only in 1960s, in a small way. Until 1964, data was gathered through cancer surveys to estimate the incidence and trends. This was grossly inadequate for any conclusions and meaningful planning of need based services.

The first registry in India was started in Bombay (current Mumbai) in 1964 followed by Pune in 1973 and then in Aurangabad in late seventies [6]. However, cancer registration as a complete coordinated program was started only in 1982, with the Indian Council for Medical Research (ICMR) taking steps towards establishing the National Cancer Registry Program (NCRP).

The beginning was humble with three population based and three hospital-based registries, which is now expanded to 36 population based and over a hundred hospital-based cancer registries.

We have come a long way in these 6 decades. The existing registries cover about only 15% of the country's population [7]. We still lack population-based registries in some of the bigger states like Andhra Pradesh, Uttar Pradesh, Odisha and Rajasthan, where we depend on hospital-based registries. Cancer registration is not mandatory in our country. Collection in population-based registries is also through active methods, involving lot of time and manpower.

To overcome these hurdles, ICMR, through the establishment of National Centre for Disease Informatics and Research (NCDIR), initiated a program called, Cancer Atlas, to fill in these gaps, by abstracting information directly from pathology labs in Hospitals and Medical colleges, where, up to 85% of the cancer cases are confirmed microscopically. Another welcome step is that cancer case reporting is now mandatory in the states like Kerala, Karnataka, Gujarat and Manipur.

Relying on Population Based Cancer registries may be grossly insufficient to estimate the burden of cancer in children. Lack of awareness among public, particularly parents, to recognize and report symptoms likely to be from cancer in children, lack of accessible pediatric cancer services in many parts of the country, financial constraints of the family, resulting in dropout from treatments or even death before being seen at a specialized facility for treatment, are some glaring lacunae. As such, the burden estimated may not reflect the actual scenario in Indian society. India shares this common problem with other countries. The same is detailed in UICC's outreach program for childhood cancers called "My Child Matters"TM.

To help in this aspect, a few Voluntary and non-governmental organizations (NGO) are reaching out to maintain databases of pediatric cancers in India, such as the Jiv Daya Foundation from Dallas, USA, that funds a cloud based program called "Indian Pediatric Oncology Database" [8].

Type of cancer	Most common presentation Symptoms and Features of disease	Reason for late diagnosis and Barriers in completion of treatment	Estimated 5-year Survival in India from available data
Acute Lymphocytic Leukemia and Acute Myeloid Leukemia [9–11]	<ul style="list-style-type: none"> • 40-50% of all pediatric malignancies • Anemia, Fever • Late age at Diagnosis, Poor prognostic T cell type and High-risk cytogenetics are common compared to west 	<ul style="list-style-type: none"> • Symptoms often mistaken for more common nutritional Deficiency • Misconceptions about word, Blood cancer • Fear of invasive procedures like Intrathecal chemo and Bone marrow examination 	ALL: 45–81% AML: 35.5% (North India) Induction Mortality: 18%
Lymphoma <ul style="list-style-type: none"> • Hodgkin's and Non-Hodgkin's lymphoma [12–14] 	<ul style="list-style-type: none"> • HL: Lymph nodal swellings • NHL: Abdominal symptoms, Constitutional Symptoms and lymphadenopathy • Mixed cellularity type is most common in Hodgkin's disease and Burkitts is most common in NHL 	<ul style="list-style-type: none"> • Often mistaken for more common disease, Tuberculosis • Many patients are empirically started on ATT • Steroids are often used in peripheral centers without a diagnosis 	Hodgkin's Lymphoma:90% NHL: Early stage: 91% Advanced stage 61%
Central Nervous system tumors [15]	<ul style="list-style-type: none"> • Headache, vomiting and seizures • Most common types are Astrocytoma and medulloblastoma • Higher incidence of Craniopharyngioma compared to West. 	<ul style="list-style-type: none"> • Non-specific in younger children • Symptoms are missed and misdiagnosed as Meningo-Encephalitis and treated in those lines before referral to oncology centers • Very limited number of centers with Pediatric Neuro imaging and reporting facilities 	Data Not available
Retinoblastoma [16]	<ul style="list-style-type: none"> • 6-10% of all childhood tumors • Mean age at presentation is 29–34 months • Leukocoria, strabismus, proptosis, visual loss and red eye. 	<ul style="list-style-type: none"> • Lack of awareness of symptoms among parents leads to delay in medical attention • Not willing of enucleation 	5 years OS: South India: 92% North India: 63%
Neuroblastoma [17]	<ul style="list-style-type: none"> • 4-8% of all pediatric malignancies • Predominant abdominal disease 	<ul style="list-style-type: none"> • Delay in presentation • up to 80% present in advanced stage 	3 year OS: Early stage:60.7% Advanced stage: 35.7%
Wilms Tumor [18]	<ul style="list-style-type: none"> • Abdominal mass 	<ul style="list-style-type: none"> • Late presentation and advanced stage at diagnosis • Lack of expertise and trained staff in peripheral centres, specially pediatric surgery 	5 year OS: 70–85%

Table 1.
Charateristics of common childhood cancers in India.

2.1 Pediatric oncology as a sub-specialty

Although India is making rapid strides in the development in several areas like agriculture and space technology, there is glaring deficiency and disparity in delivering much needed primary medical care. While this is in part due to the difficult to reach terrain of this vast sub-continent, the main reasons appear to be a reluctance of the well trained doctor to serve remote areas due lack of basic civic amenities. Lack of political will, compounded by lack of awareness of the curability and pessimism about cancer in both law makers themselves, as well the medical fraternity further worsen the problem (**Table 1**).

This pessimism is predominant in pediatric cancers as there are insufficient points of care. Most cancers are under diagnosed due to lack of adequate diagnostic facilities, and, when diagnosed, are treated by pediatricians with limited knowledge about oncology, or adult oncologists with limited knowledge about pediatric cancers.

2.2 Specialized childhood cancer centers

The first pediatric oncology center was established in 1970, at the Cancer Institute, Chennai, by Professor V Shanta, a great visionary in the field of cancer education and training. Another landmark is the establishment of first dedicated Pediatric Oncology Unit in Mumbai at the Tata Memorial Hospital, in the 1990s, by Prof. Shripad Banavali. This center also pioneered the training program and award of a sub-specialty doctoral degree pediatric oncology. The main advantage of such dedicated centers is access to advanced diagnostic services like Immunophenotyping, PET CT, cytogenetics, blood component therapy and trained nurses manning clinics catering to venous access devices [19].

In early 2000, pediatric oncology developed as a specialized branch in India. It is the combined responsibility of academicians in various pediatric departments to build and develop a sustainable pediatric oncology program. The reasons are obvious: it is still not sustainable for a pediatric oncologist to restrict practice to just pediatric oncology, in the community. The earnings from care of only childhood cancer patients being meager, most practice non-malignant hematology as well as general pediatrics. Medical Oncologists with a training in pediatric oncology happily practice both adult and pediatric oncology.

2.3 Development of pediatric cancer society – and ISMPO

The Indian Association of Cancer Chemotherapists was founded in the early 60s by surgeons who practiced adjuvant chemotherapy for their operated patients. Most of its members were eminent cancer surgeons like Dr. Roy Choudhury of Kolkata and Dr. N C Mishra of Lucknow. It was renamed as the Indian Society for Medical and Pediatric Oncology at an annual conference of the Society in Ahmedabad, Gujarat, in late 80s (personal communication, Professor Pankaj M Shah – Former Director, Gujarat Cancer and Research Institute). Cancer oriented pediatricians still band together as the pediatric oncology sub chapter of the Indian Academy of Pediatrics.

Along with ISMPO, several other Oncology Networks like ICON (Indian Cooperative Oncology Network), and INPOG (Indian National Pediatric Oncology Group) help of pediatric oncologists in collaborating across the nation and with experts abroad to share ideas, knowledge, and expertise.

Childhood cancer care in India - then and now.

There is a drastic improvement in the outcomes of childhood cancers over the past two decades ago. The reasons are many, including dedicated training programs,

establishment of pediatric cancer centers, and, most importantly adoption and collaboration of treatment protocols from the developed world.

One such example of collaboration is adoption of the acute lymphoblastic leukemia and lymphoma protocols developed by Prof Ian Magrath of the National Cancer Institute, USA, specifically for the developing world [MCP 841 & MCP 842 protocols]. With the guidance from Prof. Magrath's International Network for Cancer Treatment and Research (INCTR), the outcomes of the patients on this protocol improved by three times from 20 to 60%. The protocol also paved the way for adequate platelet transfusion protocols mandating intramuscular l-asparaginase as well as immunophenotyping of acute lymphoblastic leukemia and lymphoma into cALLa positive and T cell leukemias [20, 21].

2.4 Volunteers and non-governmental agencies

There are several volunteer groups and non-governmental organizations (NGOs) that provide much needed help to the patient and family who travel to a city from the moffusil. The St. Jude's Children Homes specialize in establishing homes in or near the premises of major childhood cancer treatment centers, in cities, for housing the child with family as a unit, throughout the course of its treatment. Several organizations also provide technical, logistic and financial assistance with travel, food, shelter, paperwork as well as drugs.

2.5 Awareness programs for pediatricians

The Pediatric Oncology sub-chapter of the Indian Academy of Pediatrics created a training program for pediatricians, called NTP-PPO (National Training Program – Practical Pediatric Oncology). Over the years, through this program, nearly 50 workshops have been conducted and about 2000 pediatricians have been trained to identify, diagnose, and refer children with cancers to appropriate centers. Pediatricians are also trained in management of febrile neutropenia, venous access and maintenance chemotherapy. Since most of them practice in the community, their services are often of paramount importance in ensuring continuity of care.

There are other programs for intensive pediatric oncology training, such as a one-year program by IAP and 2-year Fellowship by the National Board of Examinations, which works under the aegis of Ministry of Health and Family Welfare, Government of India [22].

2.6 Overcoming delay in referral

Delay in referral is a big hindrance for timely management of pediatric cancers. Some delay is due to logistics: not so easy to negotiate monsoon inundated roads in remote rural areas. A sheer lack of awareness even among radiologists and orthopedic specialists is one reason for delay in diagnosis of Ewing's Sarcoma and Osteosarcoma, which are often treated as tubercular osteomyelitis [22].

2.7 Access to medicines - generics

There are several early obstacles in access to essential medications for cancer patients in India. Several attempts were made by the government to bridge this gap. One such successful attempt was providing access to generics. The other big step is

inclusion of some of antineoplastic drugs like imatinib in the Essential Medicines List (EML). In many states, such as Andhra Pradesh, Tamil Nadu, Rajasthan and Kerala, the government has evolved schemes like the *Arogyasri*, which ensure that the entire treatment of all childhood cancers is completely free for all those below the poverty line by all modalities. The state of Andhra Pradesh has even included free hematopoietic stem cell transplantation in its program for children below poverty line. The recently introduced Health Scheme of the Government of India, *Ayushman Bharat*, will hopefully be of help to children with cancer in states where this is operational. A major drawback of both these schemes is the large amount of paperwork and prior sanction that is needed for preauthorisation, for the mode of treatment as well as for every new cycle. Another drawback is the limitation both in the choice of regimen as well as the cost of drugs. A final drawback is lack of subsidy for the tests needed to prove the diagnosis and stage the disease. Since there is no health insurance cover for the child from the 'middle class', the financial impact on the parent's pocket is unusually heavy – leading to abandonment [23].

2.8 Development in palliative care

Pediatric palliative care is in a naïve state in most parts of the world, and so is in India. With very few dedicated pediatric palliative care centers and many cultural barriers, provision of palliative care is still mostly rudimentary [24].

A bright example for such development in India is collaboration between Nawaj Mehdi Jung (MNJ) Hospital in Telangana State with the Canadian branch of International Network for Cancer Treatment and Research in 2007 [25]. Such an exercise to prevent and treat pain in the children diagnosed with cancer irrespective of the end point resulted in enrolment of more pediatric patients, reduction in dropouts from treatment and those lost to follow up, with an increase in survival. In India, it is estimated that 1.6 million pediatric patients with various ailments are in need of pediatric palliative care. However, it will be a difficult task to train enough personnel to be able to serve this population. A first step towards such goal is the initiation of training program in MNJ hospital. In 2010, the Indian Association of Palliative Care (IAPC) established a separate pediatric palliative care unit in the state of Maharashtra, in collaboration with the International Children Palliative Care Network (ICPCN) [26].

3. Conclusions

India, along with other low and middle income countries, has been the hub spot for leading the developments in management of pediatric cancers. Together, these countries account for nearly 90% of all diagnosed childhood cancers across the globe. In India, majority of population is from rural areas, where, awareness about symptoms of childhood cancer symptoms, the knowledge of diagnosis and even referral among physicians is low, contributing to avoidable delays in instituting treatment, with resultant inferior cure rates. Prohibitive costs in private sector coupled with unavailability of facilities in public sector, render outcomes to be very poor even in cancers like Hodgkin's lymphoma that are otherwise curable by simple protocols. Although there are policies at national level addressing the prevention and control of cancers as a whole, there is no special emphasis on pediatric cancers. However, there is light at the end of tunnel in the form of several schemes, like coverage of pediatric cancers under the newly -launched *Ayushman Bharat* scheme, a universal health policy initiated by central government, and several central

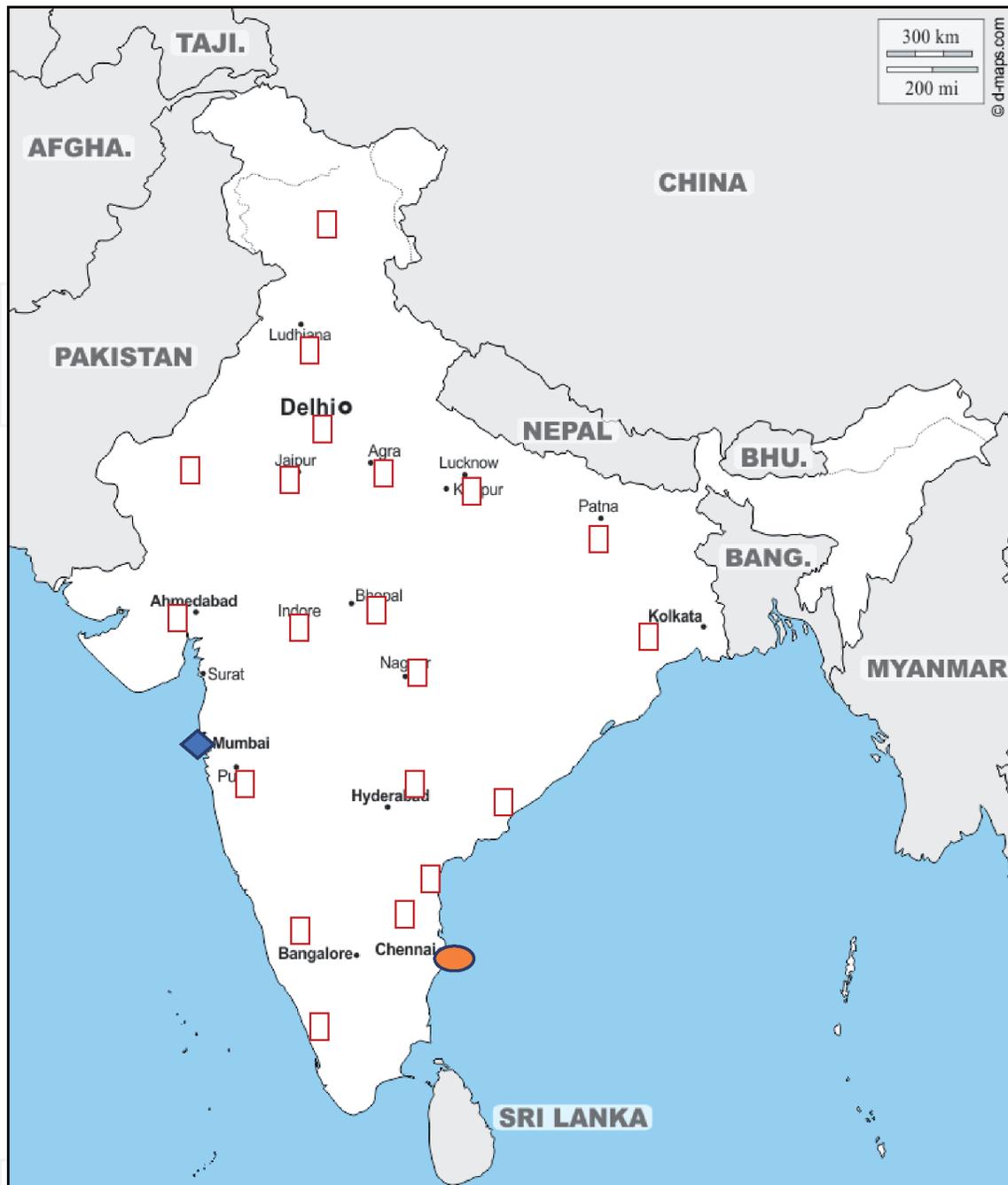


Figure 1. Pediatric oncology centers in India in various decades.  First pediatric cancer center in India 1970's: Chennai;  Second pediatric cancer Center in India 1990's: Mumbai;  Pediatric oncology services currently available in India.

government schemes providing funds for treatment of childhood cancers. However, this is just a beginning and there is a long way to go to build patient centric care for children with cancer, spread of health literacy among the public and developing centers with skilled staff where patient and family are treated with dignity.

India, which is the fastest growing nation among developing countries in terms of human resources, development and cancer incidence in children should lead by example by improving quality of care and accessibility to Cancer care to children, in particular. Finally, it is especially important to remember that pediatric oncology departments as standalone units cannot serve and deliver comprehensive care required by a child. Collaboration between pediatricians, radiologists, surgeons, anesthetists, neurosurgeons, urologists, psychiatrists and other subspecialties would help in achieving the quality of care.

4. Common Childhood cancer in India and their characteristics

There is severe paucity in the data of exact incidence, prevalence, morbidity, mortality, and survivorship data of pediatric cancers in India. However, based on the available registry data, both population based and hospital based, the most common malignancies diagnosed in India in children are Leukemias, Lymphomas, CNS tumors, Retinoblastoma and Malignant Bone Tumors (**Figure 1**).

Conflict of interest

The authors declare no conflict of interest.

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