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Research Article

PATTERN OF PEDIATRIC MALIGNANCY – 8 YEAR EXPERIENCE

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Abstract :

Pediatric malignancies are a leading cause of disease related death among children. The causes of pediatric cancer are not well understood. It is a retrospective analysis conducted in J.N. Medical College AMU Aligarh with pediatric population (0-14 year of age) from 1997 to 2004 (8 years). Pediatric malignancies comprise 4.8% of cancer load of all age group. The incidence of different type of malignancies was at par in comparison to their studies. (KusumKumary at, Arora all ect). The age distribution showed higher incidence in second age group in females and third age group in males. In this study most of the patients (82%) were from rural areas. The sex ratio showed a male predominance. These type of studies can provide us a rough picture of pediatric malignancies for the planning of their treatment and awareness of the people.

Keywords *:* Pediatric Cancer, Pattern

INTRODUCTION

Cancer is the leading disease-related cause of death among children in the United States.(1) The types of cancers that most frequently develop in children are different from the most common adult cancers. For example, although leukemia, lymphoma, and brain/other nervous system (brain/other nervous system [ONS]) cancers account for more than half of all childhood cancers, they account for less than 10% of cancer cases in adults. In addition, etiologic differences and genomic variations within even the same cancer type suggest that the childhood and adult cancers may be discrete diseases.(2) These observations warrant a specific focus on pediatric cancers.

The causes of most childhood cancers are unknown, and for the most part these diseases cannot be prevented. The overall incidence of pediatric cancer rose about one-third from 1975 to 2010, from 12.5 to 16.8 cases per 100,000 populations. For the period of 1993 to 2010, cancer incidence among children aged 0−19 years increased 0.6% per year.(3) In the individual racial/ethnic groups tracked by NCI's Surveillance, Epidemiology, and End Results (SEER) Program, a rise in incidence over the last two decades is apparent in whites, Asians/Pacific Islanders, and Hispanics. In African American children, incidence rates have risen significantly since 1998. The incidence of cancer is higher in Hispanic and white children than in children of other ethnicities/races.

Cancer in children and adolescents is rare and biologically very different from cancer in adult (4). It is estimated that about 148000 cancers occurred during 2008 in children aged 0-14 years in less - developed regions (5). In India cancer is the 9th common cause for the deaths among children between 5 to 14 years of age (6). 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(7).

Although cancer in children is rare, it is the leading cause of death by disease past infancy among children in the United States. In 2014, it is estimated that 15,780 children and adolescents age 0 to 19 years will be diagnosed with cancer and 1,960 will die of the disease in the United States(8).

The most common types of cancer diagnosed in children and adolescents are leukemia, brain and central nervous systems tumors, lymphoma, rhabdomyo sarcoma, neuroblastoma, wilms tumor, bone cancer and gonadal (testicular and ovarian) germ cell tumors.

As of January 1, 2010, there were approximately 380,000 survivors of childhood and adolescent cancer (diagnosed at ages 0 to 19 years) alive in the United States (8). The number of survivors will continue to increase, given that the incidence of childhood cancer has been rising slightly in recent decades and that survival rate overall are improving.

The pediatric population (0-14 year of age) constitutes 32.4% of total population of India(9) cancer in children is an emerging major childhood killer malignant neoplasm are the third commonest cause of death in the 1-4 years of age group and the second commonest cause of death in the 5 to 14 years are group(10). Pediatric neoplasm constitute 3.7-4% of all the cancers according to data which was available from the population based registries at Bangalore, Bombay and madras as was studied by kusumakumary et al(11). In us it is abow-2% according to Singh and Silverman(12).

Geographic differences in the occurrence of childhood cancers have also been described by some authors (12-13). From the viewpoint of cancer control, particularly in the context of developing countries like India, there is a need to detect cancers at an early, curable stage of the disease. The five year survival rate for certain cancers like Hodgkin's lymphoma and retinoblastoma is now 95% in resource-rich countries (14). Worldwide the annual number of new cases of childhood cancer exceeds 200000 and more than 80% of these are from the developing ward. Seven out of 10 children with cancer in the resource rich countries are cured. Their late presentations may be due to many factors which include lack of awareness and socioeconomic conditions, to some extent.

Marked differences were found in the age distribution of various cancers. The frequency of ALL, neuroblastoma, Wilm’s tumor, retinoblastoma and hepatoblastoma were strikingly more in children younger than 5 years of age. An increased frequency with age was seen in non-Hodgkin’s lymphoma, Hodgkin disease, osteosarcoma and Ewings sarcoma. The early onset and the embryonal nature of many pediatric tumors suggest a prenatal origin.

Male predominance is a salient feature of many childhood tumors. Sex ratio also varies with site. The male excess is particularly marked in neoplasms of lymphoid origin i.e., in ALL, NHL and HD which represent over one-third of all tumors. Environmental factors like exposure to carcinogens at work or smoking habits may be contributing to excess of cancer in adult males, but such an explanation cannot account for the excess of cases seen in male children. Genetic difference in immune function may be responsible for the increased incidence of lymphoid tumors in males. The female excess seen in germ cell tumors may be

due to earlier development of ovarian tumors than testicular tumors, but no convincing explanation is given for increased incidence of sacrococcygeal teratomas in girls.

There are reports of geographic differences in the incidence and frequency of cancer in children. Data available from population based cancer registries at Bangalore, Bombay and Madras show that 3.7 to 4% of all cancers is constituted by pediatric neoplasms(11). In Dibrugarh in the north eastern India and Chandigarh in the north western India the frequency was 2% and 4.8% respectively(12). The proportion of childhood cancers seems to be high compared to that of developed countries where there is a lower proportion of children in the population. The international comparison of cancer frequency and incidence are potentially biased by variability in diagnosis, classification and differential access to medical care and incomplete registration and hence has to be interpreted with caution.

Most cancers in children, like those in adults, are thought to develop as a result of mutations in genes that lead to uncontrolled cell growth and eventually cancer. In adults, these gene mutations are often the result of exposure to environmental factors, such as cigarette smoke,asbestos, and ultraviolet radiation from the sun. However, environmental causes of childhood cancer have been difficult to identify, partly because cancer in children is rare, and partly because it is difficult to determine what children might have been exposed to early in their development.

Many studies have shown that exposure to ionizing radiation can damage DNA, which can lead to the development of childhood leukemia and possibly other cancers. For example, children and adolescents who were exposed to radiation from the World War II atomic bomb blasts had an elevated risk of leukemia (10), and children and adults who were exposed to radiation from accidents at nuclear power plants had an elevated risk for thyroid cancer (11). Children whose mothers had x-rays during pregnancy (that is, children who were exposed before birth) and children who were exposed after birth to diagnostic medical radiation from computed tomographyscans also have an increased risk of some cancers (12).

Studies of other possible environmental risk factors, including parental exposure to cancer-causing chemicals, prenatal exposure to pesticides, childhood exposure to common infectious agents, and living near a nuclear power plant, have so far produced mixed results. Whereas some studies have found associations between these factors and risk of some cancers in children, other studies have found no such associations (8,13-15). Higher risks of cancer have not been seen in children of patients treated for sporadic cancer (cancer not caused by an inherited mutation) (16).

Malignant neoplasms are rare in children. Its impact on children’s lives varies with its incidence, diagnosis, therapy, mortality and survival at different places and time childhood cancer are unique in the sense that they arise from embroyonal cells, respond to treatment rapidly and the survival has improved dramatically over the last two decades due to aggressive combined modality management(17-18). Improvements in survival have also been shown to be associated with increased centralization of management.

Cancer is an important cause of mortality in many of the economically developed nations of the world. More than 10% of all deaths in children below 15 years of age are caused by malignant disease in developed countries. In the developing world childhood cancers are yet to be recognized as a major pediatric illness due to several others. Competing causes of death like diarrheal illness and respiratory illness(19).

MATERIAL AND METHOD:

This retrospective study included all the patients attended the department of radiotherapy J. N. Medical College, Aligarh during 8 years from June 1997 to June 2004. All of the cases were histopathologically proven between 0-14 years of age.

Information were collected in the form of age, name, sex, site of tumor and diagnosis. All the cases were analysed critically in respect of epidemiology.

RESULT :

In the present study, 266 cases of paediatric malignancies were detected, which constituted 4.8% of the total cancer cases in all the age groups, which was comparable to the findings of other studies, like 4.5% in Kusumakumari et al's study and Jussawalla and Yeole's study which showed that they formed 3.5% of the total cancer load(5),(9). But in the literature which was reviewed by Bhalodia et al, in 2011, paediatric tumours were found to constitute 2% of all the malignancies (10). According to Arora et al, in 2009, the incidence of cancer in India varied between 1.6-4.8% (8). So, our finding fell in this range. In contrast to this, the incidence in the United States was found to be only 2% (6).The international comparison of the cancer frequency and the incidence varies due to a variability in the diagnosis, classification and the differential access to the medical care.

In our study Majority of patients were the residents of rural areas 218 (82%) where as urban dwellers accounted only 46 (18 %) cases.

TABLE :- 1 Distribution according to age group.

Total no	Male	Female	Rural	Urban
264	146	120	218 (82%)	46 (18%)

Case records pertaining to the age group 0-14 years were analyged to find out the descriptive clinical profile of these patients. Histological diagnosis was confirmed by our pathologist in all cases.

TABLE :- 2

Age	Male	Famale
0-5 year	30(20.5%)	25 (20.8%)
6-10 year	48 (32.8%)	60 (50%)
11-14 year	68 (46.5%)	35 (29.1%)
	146	120

Total number of patients registered in our department during this 8 years period was 266 and accounted about 4.8% of total neoplastic disease (266/5526) out of 266, 146 patients were males and 120 (45.1%) were females most common age group was 11-14 years is males 68 (46.5%). In females most common age group was 6-10 years 60 (50%)

Table :- 3 Incidence of cancer & childhood cancer

Year	Total No. of Patients	Male	Female
1997	415	10	7
1198	587	11	9
1999	660	15	13
2000	695	18	15
2001	702	22	18
2002	745	25	21
2003	763	21	18
2004	959	24	22
	5526	146	120

Table :- 4 Distribution According to disease

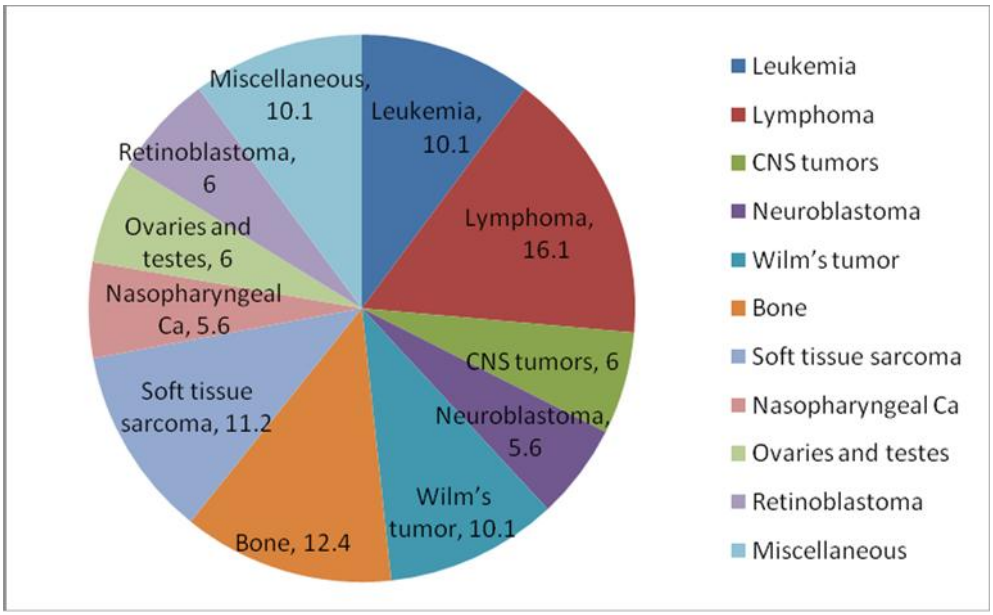
Disease	**Total No**	**No. of patients male**	**Female**
Leukemia	27 (10.1%)	15 (10.2%)	13 (10.8%)
Lymphoma	43 (16%)	24 (16.4%)	19 (15.8%)
CNS tumors	16 (6%)	10 (6.8%)	6 (5%)
Neuroblastoma	15 (5.6%)	8 (5.4%)	7 (5.8%)
Wilm's tumor	27 (10.1%)	19 (13%)	8 (6.6%)
Bone tumor	33 (12.4%)	18 (12.3%)	15 (12.5%)
Soft tissue sarcoma	31 (11.2%)	15 (10.2%)	16 (13.3%)
Ovaries and testis	16 (6%)	10 (6.8%)	6 (5%)
Retinoblastoma	16 (6%)	9 (6.1%)	7 (5.8%)
Nasopharyngeal ca	15 (5.6%)	7 (4.7%)	8 (6.6%)
Miscellaneous	27 (10.1%)	13 (8.9%)	14 (8.3%)
	266	146	120

The commonest malignant disease in the children was lymphomas constituting about 43 (16.1%) in which non Hodgkins lymphoma was more commoner in comparison to Hodgkins lymphoma was more common in comparison to Hodgkins lymphoma (68%/32%).

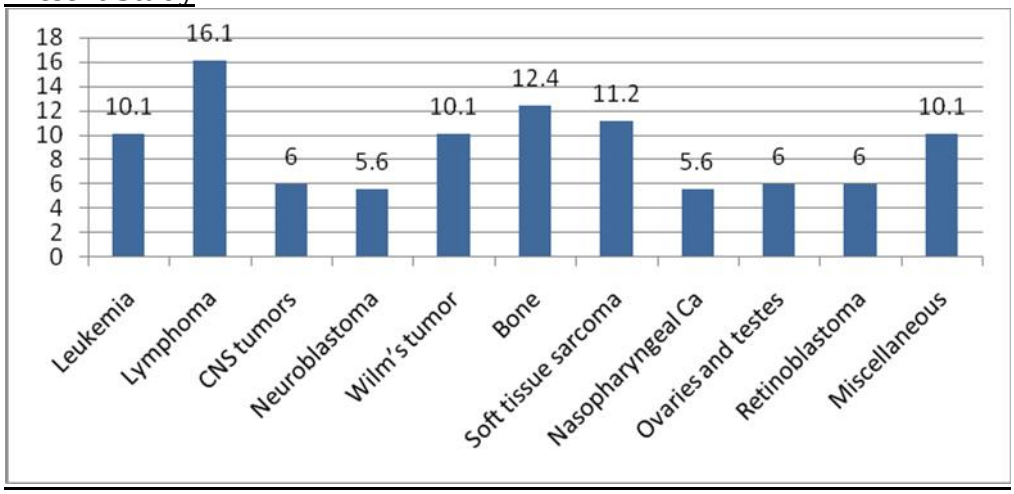
Due to limited treatment facility in our hospital for the treatment of acute leukemia, registration of leukemia was less (10.1%) in comparison to other studies.

Table :- 5 Comparison with other study

Disease	Young *et al.*(6) US White	Pearson *et al.*(7) UK	Teppo *et al.*(8) Finland	McWhirter *et al.*(10) Australia	Kusuma kumary et al Present data	Present Study
Leukemia	33.8	20.4	32.8	20.6	30	10.1
Lymphoma	10.6	8.7	8.6	10.3	10	16.1
CNS tumors	19.2	16.6	21.5	21	19.3	6
Neuroblastoma	7.7	7.5	3.3	7.4	5.1	5.6
Wilm's tumor	6.3	5.4	7.4	6.6	5.4	10.1
Bone	4.5	4.8	4.7	5.3	5.4	12.4
Soft tissue sarcoma	6.8	8.5	3.6	-	6.6	11.2
Nasopharyngeal Ca	-	-	-	-	-	5.6
Ovaries and testes	-	-	1.8	-	-	6
Retinoblastoma	2.7	3.1	3	3.1	4.5	6
Miscellaneous	8.2	11.9	13.3	14	10.3	10.1



Present Study



DISCUSSION:-

Childhood cancer is the leading causes of disease related death among children and adolescents (ages 1-19 years) in the United States, although cancer among children in rare. The causes of childhood cancer are not well understood.

Survival rates for most childhood cancers vary widely across cancer types. Survival rates for some cancers have improved in recent years and overall more than 80 percent of children and adolescents who are diagnosed however for some childhood cancer types, survival remains low.

The causes of most childhood cancers are not exactly known. Almost 5 percent cancers in children are caused by an inherited mutation.

Most cancers in children like those in adults are thought to develop as a result of mutations in genes that lead to uncontrolled growth.

Incidence of germ cell tumor was about 11% in which majority were testicular and ovarian tumor. Which was 6% little higher in comparison to other studies.

Ewing's sarcoma and osteosarcoma were two commonest form of bone tumor. In which ewings sarcoma was more common than osteosarcoma (18/15). Significant number of nasopharyngeal carcinoma cases was registered 15 (5.6%) in our department.

However environmental causes of childhood cancer have been difficult to identify partly because cancer in children is rare and partly because it is difficult to determine what children might have exposed to early in their development. Many studies have shown that exposure to ionizing radiation can damage DNA which can lead to the development of childhood leukemia and possibly other cancers children and adolescents who were exposed to radiation from the world war II atomic bomb blasts had an elevated risk of leukemia and children and adults who were exposed to radiation from accidents at nuclear power plants had an elevated risk for thyroid cancer. Children whose mothers have X-Ray during pregnancy also have an increased risk of some cancers.

The maximum number of paediatric malignancy cases were observed in the third age group in males, and second age group in females, which was at par with the findings of other studies (9),(11).

In all the paediatric age groups, leukaemia was found to be the most common type of cancer, which was lesser in comparison our study to other studies because of limited treatment facility for hematogical malignancy in our hospital. (5),(11),(14),(16),(17). Lymphoma were the most common malignancies in which was 16.4% in males and 15.8% in females. Most of the studies. including the present study. revealed a male predominance [Table -6].

Table :- 6 Comparison of overall M to F ratio with other studies

Sl. No.	Studies M/F ratio	M/F Ratio
1	Jussawalla et al., Bombay, 1988 [8]	1.7
2	Mangal et al., Rajasthan, 1991 [18]	1
3	Das et al., West Bengal, 1994 [16]	2
4	Nandakumar et al., Bangalore, 1996 [11]	1.8
5	Grovas et al., Ncdb, UU, 1997 [19]	1.2
6	Martin et al., Cuba, 1997 [12]	0.98
7	Gutierrez et al., Mexico, 1997 [20]	1.6
8	Ocana et al. Mexico, 2004 [14]	1.1
9	Bryan et al., Vellore, 2011 [21]	4
10	Bryan et al., Usa , 2011 [21]	1.1
11	Bhalodia et al., Gujarat, 2011 [10]	1.3
12	Present Study, 2007 Kusumakumary et	2.34
13	Our Study	1.2

The male predominance in our country could be due to the extra attention which is given to the male child as a result of cultural factors [8]. According to Kusumakumary et al, male predominance is a salient feature of many childhood tumours. The male excess is particularly marked in the neoplasms of lymphoid origin, possibly due to the genetic differences in the immune function.

Comparison of the relative frequencies of childhood cancer with those of other studies in India and outside India has been shown in [Table -7].

A significant number of cases of nasopharyngeal carcinoma has been registered 15 (5.6). This may be due some genetic mutation or environmental factor.

The percentage of the CNS neoplasms in present study was 6%, which was comparable to the finding of study conducted in Gujrat 2010. A higher incidence was observed in other studies from India and other countries [18]. This is probably due to the inadequate facility for paediatric neurosurgery at our hospital. The incidence of soft tissue sarcoma was 11.2% in present study which was comparable to other regional studies of India.

Table :- 7 Comparison of incidence of pediatric malignancies with studies in India.

Types of cancer	Bombay (1988) [9]	Rajasthan (1991) [18]	West Bengal (1994) [16]	Bangalore (1996) [11]	Kerala (2000) [5]	West Bengal (2003) [17]	Gujarat (2011) [10]	Orissa 2007	Our Study
Leukemia	31.8	26	36	29	30	39.1	44.18	45.5	10.1
Lymphoma	10.7	32	9.5	19	10	10.8	16.27	8.2	16.1
CNS Neoplasm	12.2	1.6		13.2	19.3		6.97	3.6	6
Neuroblastoma		13		4.7	5.1	1.7	6.97	4.5	5.6
Retinoblastoma	6.3	1.2	32.6	3.8	4.5	19.2		5.5	6
Renal Tumour	6.1	16	4.2	5.1	5.4	10	9.3	4.5	10.1
Hepatic Tumour				0.9				0.9	-
Malignant Bone Tumours	8.9		5.8	3.4	5.4	5	2.32	10	12.4
Soft Tissue Sarcoma			5.2	4.7	6.6	11.2	2.32	11.8	11.2
Germ Cell Tumour		5.7	5.2	2.9	2.9			4.5	6
Carcinoma				5.5				0.9	-
Nasopharyngeal Ca									5.6
Miscellaneous	15.3	4.5	1.5	3.8	13.8	2.5	11.67		10.1

The incidence of retinoblastoma in present study (5.6%) was in accordance with that which was observed by Jussawalla et al., (6.3%), Nandakumar et al (3.8%), Kusumakumary et al (4.5%) and Ocana et al., who found a 4.3% incidence [5,9,11,14]. The studies from West Bengal showed significantly higher frequencies of 32.6% and 19.2% which were observed by Das et al. and Chaudhuri et al respectively [16,17]. Retinoblastoma runs in families and a higher incidence was associated with older paternal age, which increased the frequency of the mutation [16]. Most of the studies from outside India showed a lower frequency of retinoblastoma. It was found to be more prevalent in India than in the western countries (Breslow et al.,) [7].

Retinoblastoma is caused by an inherited mutation in a gene called RB. Inherited mutations associated with certain familial syndromes such as Li Fraumeni Syndrome, Beck with Wiedemann Syndrome, Fanconi anemia syndrome, etc. also increase the risk of

childhood cancer. Genetic mutations that cause cancer can also arise during the development of fetus in the womb.

Malignant bone tumours constituted 12.4% of the cases in the present study and this finding was at par with Jussawalla et al's finding, whereas it was slightly higher than that in most of the other studies, where it was found to vary from 2.32%-5.8% [9].

Conclusion :

Worldwide, the annual number of new cases of childhood cancer exceeds 200,000 and more than 80% of these are from the developing world. [5] Seven out of 10 children with cancer in the resource-rich countries are cured, with a five-year survival for certain cancers, for example, Hodgkin's disease and retinoblastoma, now 95%. [6,7] Recent studies have shown that this success in survival can be replicated in the developing world through twinning programs and shared expertise. [8-11] As we make progress in reducing infection-related childhood deaths in India, it is no longer acceptable to ignore children with cancer, who have an increasing likelihood of cure with appropriate treatment. A fundamental step in caring for these children is to estimate the current burden of childhood cancer in India and to understand how the occurrence and outcome of the disease varies across the country.

To conclude the pattern and frequency of childhood cancer which are detected at a particular center is not an exact reflection of disease spectrum of that area, but it can give a estimated trend of disease of that area. It can help us to assess the magnitude of the disease in our country.

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