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A Clinicopathological Study of Spectrum of Pediatric Malignancies in North India Region

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Abstract
Background: *Childhood cancers constitute less than 1 % of all cases of cancer. However, inspite of being rare they have provided insights into the epidemiology, genetics , etiology and treatment of pediatric malignancies .The aim of this study is to understand the burden of childhood malignancies in our region, along with morphological & Clinicopathological correlation*
Material & Methods: *This study was performed on the patients of the age group 0-14 years, during a period of 3 years (2011-2014).*
Result: *A total 120 malignancies were studied in the range of 0 month- 14 years with 70 boys (58%) and 50 girls (42 %). In general the malignancies were common in males than females. the male : Female Ratio of childhood malignancies was 1.4:1*
Haematological malignancies were the commonest constituting 28.33 % each, followed by bone tumor and retinoblastoma 11.66% each, where as spindle cell neoplasm being 8.33 %, CNS tumor & Wilm's tumor 5.0% each.

Introduction

Malignant neoplasm are rare in children, yet it is an important cause of childhood mortality in many of the economically developed nations of the world. It is second major cause of childhood mortality after accidents (>10 %)

Childhood Malignancies differ from adult malignancies in many aspects, Such one most important aspect of childhood malignancy which affects their clinical course, treatment and prognosis in that they arise from embryonic cells or cells in replications. So the childhood tumors are better considered as cancer of growth and adult malignancies as cancer of aging. Also childhood malignancies are mostly due to inherited or spontaneous mutations in cells in replication whereas in adults, environmental carcinogens play the major role.

In the developing world, childhood cancers are fastly emerging along with other public health problems.

Like other malignancies, a timely diagnosis of childhood malignancies can affect the course of illness and its prognosis. Apart from clinical features, routine biochemical examination and radiological investigation, FNAC with the help of

CT and ultrasound is an important tool in rapid and accurate diagnosis of childhood malignancies. Although Histopathological examination is confirmatory tool in diagnosis, but biopsy may not be always possible sometimes and in such circumstances, FNAC, due to its high accuracy is highly supportive to radiological diagnosis and thus helpful in guiding the clinician. Present study is aimed

- Study the morphological and clinicopatho-logical correlation of pediatric tumors and to evaluate the accuracy of FNAC and compare the result with histopathological diagnosis in available cases

Material & Methods

This study was done in SMS Medical college jaipur in Department of Patholgy. This study was carried on various paediatric malignancy (0-14 years).

Cytology smear is immediately fixed in 95 % ethyl alchol for a minimum period of 15 minutes and stained by rapid papanicoloau techniques, hematoxylin and eosin, and may grunwald giemsa stains.

For histopathology Routine Hematoxylin and Eosin staining was done

Peripheral smears are prepared from EDTA samples or finger prick and stained with leishman stain. Bone marrow smears are received from clinical departments and stained with leishman stain and giemsa stain

Observation

In present study, 120 cases of paediatric malignancies are studied under the age group 0-14 years. The following observations were made.

Table: 1 Age & Sex wise distribution of Pediatric Malignancies

Age Group (Years)	Male	Female	Total
0-5	24	12	36
6-10	18	10	28
11-14	28	28	56
Total	70	50	120

Table 1 shows that the most of the pediatric malignancies were seen in the age group 11-14 years followed by 6-10n years.

It also shows that pediatric malignancies were more common in males than females in all age group. The Male: Female ratio of childhood malignancies is 1.4 : 1

This table also shows that most of the pediatric malignancies were seen in the age group 11-14 years followed by 6-10 years.

Table: 2 Age wise distribution and modality of diagnosis of Pediatric malignancies

Age Group (Years)	Modality of Diagnosis			Total
	Histopathology	Cytology	Haematology	
0-5	26	04	06	36 (30%)
6-10	10	06	12	28(23.33%)
11-14	26	14	16	56(46.66%)
Total	62(51.66%)	24(20%)	34(28.33%)	120

Table 2 shows that out of 120 cases of pediatric malignancies 62 cases (51.66%) were diagnosed by histopathology, 34 cases (28.33%) by hematology and 24 cases (20 %) were diagnosed by cytology.

Histopathologically diagnosed cases were 18 malignant lymphomas including 12 non hodgkin's lymphoma & 6 hodgkin's Lymphoma followed by 14 cases of retinoblastoma, 6 each of wilm's tumor, ES/PNET, CNS tumours & osteogenic sarcoma while only 4 cases of malignant spindle cell neoplasm and a 2 cases of mucopiodermoid carcinoma .

On FNAC 8 cases each of NHL and Hodgkin's disease, 6 of soft tissue spindle cell neoplasm and 2 cases of osteogenic sarcoma were diagnosed.

All the cases of Leukemia were diagnosed by PBF and / or bone marrow examination and included 26 cases of ALL, 6 of AML and 2 cases of Juvenile CML.

Table : 3 Sex –wise distribution of pediatric malignancies

S.no	Types of childhood	Male	Female	Total	(%)	Male: Female
1.	Leukemia	14	20	34	28.33	0.7 : 1
2.	Lymphoma Non Hodgkins Lymphoma Hodgkins Lymphoma	26 18 08	08 02 06	34 20 14	28.33 16.66 11.66	3.25 :1 9:1 1.33:1
3.	CNS tumors	4	2	6	5.0	3:1
4.	Retinoblastoma	10	4	14	11.66	2.5:1
5.	Wilm's Tumor	04	02	06	5.0	3:1
6.	Bone tumor Osteogenic Sarcoma ES/PNET	02 02 0	12 06 06	14 08 06	11.66 6.66 5.0	1:6 1:3 -
7.	Malignant spindle cell neoplasm	10	0	10	8.33	-
8.	Mucoepidermoid carcinoma	0	02	02	1.66	-
	Total	70	50	120	100	1.4 : 1

Table 3 shows that the leukemia and lymphoma comprised equal number of cases (28.33%) which is followed by 11.66 % each of retinoblastoma and bone tumors, CNS and Wilm's tumors each comprised of only 5 % of total cases.

CNS tumors included four cases of medulloblastoma and two cases of low grade astrocytoma.

Table 3 also shows that the childhood malignancies were more commonly seen in male than female except bone tumors which is far more common in females.

Table: 4 Age & Sex wise distribution of leukemias

Age group(Yr.)	Male	Female	Total (%)	Male:Female
0-5	02	04	06 (17.64 %)	1:2
6-10	06	06	12(35.28%)	1:1
11-14	06	10	16(47.05%)	0.6:1
Total	14	20	34	0.7:1

Table 4 shows that most cases of leukemia were seen in the age group 11-14 years (47.05 %) followed by 6-10 years (35.25 %) and 0-5 years (17.64 %) and it also shows that acute leukemia is more common in female than in male children.

Table: 5 Incidence of Leukaemia (Sex –wise distribution)

Type	Male	Female	Total (%)	Male:Female
ALL	12	14	26 (76.47 %)	0.85:1
AML	02	04	06 (17.64 %)	0.50:1
Juvenile CML	02	0	02(5.8%)	-

Table 5 shows that the most common type of leukemia in children was ALL which comprises 76.47 % of total cases of leukemia followed by AML (17.64%). It also shows that both ALL and AML are more commonly seen in females than males Two cases of juvenile chronic myeloid leukemia has been encountered in present study.

Table: 6 Sex wise incidence of solid Pediatric tumors

S.no	Type	Male	Female	Total(%)
1.	Lymphoma	26	8	34(39.53)
2.	CNS tumors	04	02	06(6.97)
3.	Bone tumors	02	12	14(16.27)
4.	Retinoblastoma	10	04	14(16.27)
5.	Wilm's tumor	04	02	06(6.97)
6.	Soft tissue tumor	10	0	10(11.62)
7.	Mucoepidermoid carcinoma	0	02	02(2.32)
	Total	56	30	86

Table 6 shows that most common type of solid pediatrics malignancies was lymphoma (39.53%) which is followed by bone tumour and retinoblastoma (16.27% each), soft tissue tumor (11.62 %), CNS tumors (6.97 %) and Wilm's tumor (6.97 % each) and only one of Mucoepidermoid carcinoma (2.32%)

Table: 7 Age-wise distribution of paediatric malignancies

Type of childhood malignancies	Age group (0-5 years)	Age group (6-10 years)	Age group (11-14 years)
Leukemia	06 (16.66%)	12(42.85%)	16(28.57%)
Lymphoma	06 (16.66%)	10(35.71%)	18(32.41%)
CNS tumors	02(5.55%)	02(7.14%)	02(3.57%)
Soft tissue tumor	02(5.55%)	0	08(14.28%)
Retinoblastoma	14(38.88%)	0	0
Kidney Tumor	06(16.66%)	0	0
Bone tumors	0	02(7.14%)	12(21.42%)
.Mucoepidermoid carcinoma	0	02(7.14%)	0

Table 7 shows that most of the cases of Leukemia and lymphoma were seen in the age group 11-14 years while the CNS tumors were more commonly seen in age group 0-5 years.

It is also clear from the table that all the cases of retinoblastoma and Wilm's tumors were seen in the age group 0-5 years while all the cases of bone tumor were seen out of the age 5 years

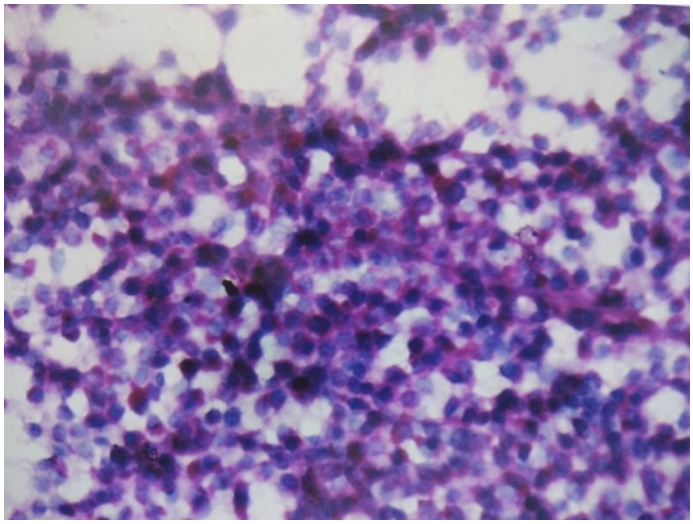

Figure 1 Ewing sarcoma –FNAC Smear Showing Hypercellular Smear Having Bimodal Population (400x,Pas Stain)

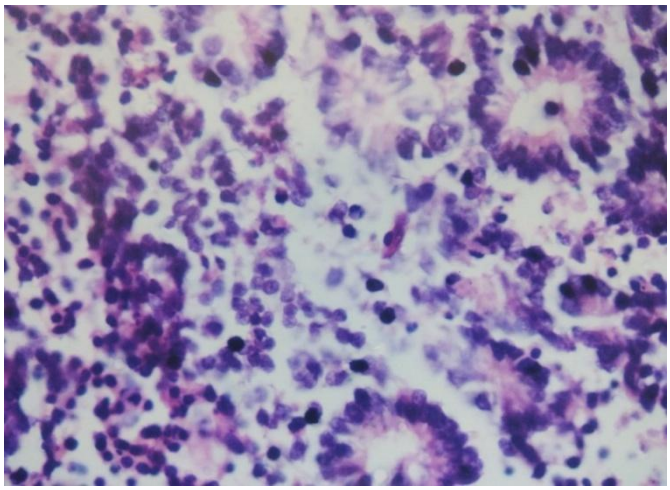

Figure 2: Retinoblastoma – H&E Stain Show Flexner –Wintersteiner Rossete (400x)

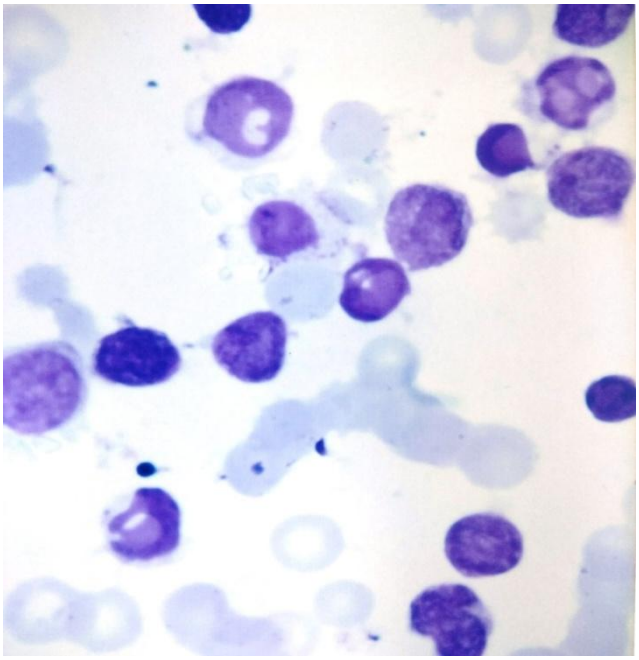

Figure 3: AML- PBF Smear Showing Myeloblast with Prominent Nucleoli (Oil Immerson)

Discussion

Present study was conducted in the Department of Pathology, SMS Medical College, Jaipur, over a period of 3 years. It comprised of an analysis of 120 pediatrics malignancies

All these cases were reviewed as regards to incidence, age and sex distribution, nature and pattern. The result observed have been compared with similar studies done in India and abroad.

Comparison of relative proportion of pediatric malignancies in different age group with other studies

Study	Relative proportion of pediatric malignancies in different age group with other studies		
	0-5	6-10	11-14
SEER(1975-1995)	47.37%	25.32%	27.31%
Present Study (2008-2010)	30.00%	23.33%	46.66%

In our study, proportion of pediatric malignancies in the age group *6-10 years* is 23.33 % which is almost equal to the SEER study (25.32%)

The table shows that the incidence was more in age group 11-14 years in our study. in contrast to the SEER study which shows that the incidence was more in 0-5 years age group

Comparsison of Male:Female ratio of Childhood malignancies with other studies

S.Singh et al India ,1988	AK Rathi et al India 2005	M. Tevfik Dorak USA 2009	Present study 2008-2010
2.1:1	2.64:1	1.22:1	1.44:1

The incidence was more common in males than females when all cases of childhood malignancies were taken into account in present study (1.4:1) which is slightly higher than study from USA (1.22:1) and lower than the study by S.Singh et al (2.1:1) and AK Rathi et al (2.64:1) [1].

But when only leukemia cases were compared for M:F ratio , our study shows female predominance regarding childhood ALL (0.85:1) and AML (0.5:1) where as in SEER study [2] there is male predominance in childhood ALL but equal M:F ratio regard to AML.

Comparison of relative Frequency of Leukemia subtypes in total number of pediatric malignancies with other studies

Leukemia	SEER (1975-1995)	Present Study (2008-2010)
ALL	24.50%	21.66%
AML	3.20 %	5.01 %
Total	27.70 %	26.67 %

Relative frequency of ALL and AML in our study was 21.66 % and 5.01 % respectively which was comparable to the SEER study.

The frequency of childhood Acute Leukemia among all pediatric malignancies in our study was26.67 % which is almost similar to the SEER study (27.70 %)

Incidence of various solid Pediatric malignancies by different studies

Disease	USA (%)	UK (%)	Mumbai Yeole et al(3) (%)	Delhi Arya LS et al(4) (%)	Present study (%)
Lymphoma	12.3	8.7	12.65	11.5	39.53
CNS tumors	19.1	16.6	17.6	21.0	6.97
Wilm's tumor	6.5	5.4	5.25	3.3	6.97
Bone tumor	4.8	4.8	3.85	3.3	16.27
Soft tissue tumor	6.3	8.5	4.3	3.8	6.97
Other	10.1	16	19	11.8	18.60

Lymphoma contributed 39.53 % of cases in the current study which was higher than all the other studies. This may be due to relative low incidence of CNS tumors in our study (6.97 %) which seems to be due to less number of registration of pediatric neurosurgery cases in our institution.

The incidence of wilm's tumor, soft tissue tumor and other malignancies were comparable to that of other studies (Table : 4)

Comparison of Age incidence in different Pediatric malignancies with SEER study

Type of childhood malignancies	0-5 years		6-10 years		11-14 years	
	SEER 1975-1995	Present 2008-2010	SEER 1975-1995	Present 2008-2010	SEER 1975-1995	Present 2008-2010
Leukemia	36.10 %	16.66 %	33.40 %	42.85%	21.80%	28.57%
Lymphom	3.90 %	16.66%	12.90%	35.71%	20.60%	35.71%
CNS tumor	16.60 %	5.55 %	27.70 %	7.14 %	19.60 %	3.57 %
Retinoblastoma	6.30 %	3 8.88%	0.50 %	0 %	0.10 %	0 %
Kidney tumor	9.70 %	16.66 %	5.40 %	0 %	1.10 %	0 %
Bone tumor	0.60 %	0 %	4.60%	7.14 %	11.10 %	21.42 %
Soft tissue tumor	5.60 %	5.55 %	7.50 %	0 %	9.10 %	10.71 %
SNS tumors	14.30 %	0%	2.70 %	0 %	1.20 %	0 %
Miscellaneous	6.90 %	0 %	5.30 %	7.14 %	15.40 %	0 %

Leukemia was the commonest malignancy in the age group 0-5 years and 6-10 years and results were comparable with those of SEER study.

In our study the frequency of lymphoma was comparatively high in all age group if we consider only the solid malignancies which might be due to lack of pediatric neurosurgery in our institution and hence less CNS tumors biopsies received to our department.

Our study was comparable to SEER study where all the cases of retinoblastoma and wilm's tumor have their occurrence under the age group of 5 years.

The incidences or CNS tumors in our study was lower in all age groups as compared to SEER study while bone tumors were least common below five years compatible with the SEER study.

Comparison of type of childhood Malignancies with other studies

Type of childhood Malignancies	Kusum kumara Et al , India (%)	Banglore Registry ICMR 1990-1996 (%)	Mumbai Registry ICMR 1990-1996 (%)	Delhi Registry ICMR 1990-1996 (%)	Chennai Registry ICMR 1990-1996 (%)	Kuntal Et al West Bangal 2003 (%)	A K Rathi Et al 1996-2005 (%)	Present study 2008-2010 (%)
Leukemia	30.00	27.15	32.20	29.05	33.15	39.10	6.57	28.33
Lymphoma	10.00	11.30	13.05	13.50	20.50	10.80	11.58	28.33
CNS Tumor	19.30	12.85	17.20	14.20	11.40	-	31.08	5.0
Retinoblastoma	4.50	4.20	3.90	5.00	6.75	19.20	14.10	11.65
Wilm's tumor	5.40	6.15	4.65	5.70	4.20	10.00	4.16	5.00
Soft tissue tumors	6.60	4.50	5.20	4.10	4.70	11.20	11.85	8.33
SNS tumors	5.10	4.70	4.60	4.90	3.85	1.70	2.56	0
Bone Tumors	5.40	7.75	5.20	5.80	3.65	5.00	8.33	11.66
Miscellaneous	13.70	21.50	14.00	17.75	12.07	3.00	9.77	1.66

In the present study hematological pediatric malignancy was the commonest malignancy i.e . Lymphoma and leukemia (28.33 % each) having equal incidence followed by retinoblastoma and bone tumor (11.66 %), soft tissue tumor (8.33 %) CNS tumors (5.0 %). Our results were comparable to most other Indian studies as shown in Table 6 (30 % by Kusum Kumari et al. 27.15 % by Bangalore ICMR registry, 32.20 % by Mumbai ICMR Registry, 29.05 % by Delhi ICMR Registry)

The frequency of Wilm's tumors in current study was 5.0 % of all pediatric malignant neoplasm which was also comparable to other Indian studies (5.40 % by Kusum Kumari et al[5], 6.15 % Bangalore Registry, 4.65 % by Mumbai Registry,

5.70 % by Delhi Registry). Similarly incidence of malignant soft tissue tumor in our study were comparable with other Indian studies as shown in Table 6.

The Present study showed that Lymphoma contributed 28.33 % of childhood malignancies which was much higher than all other Indian studies (10.00 % by Kusum Kumari et al. 11.30 % by Bangalore ICMR registry, 13.05 % by Mumbai ICMR Registry, 13.50 % by Delhi ICMR Registry, 10.80 % by kuntal et al[6] , 11.58 % by AK Rathi et al) whereas CNS tumor in our study showed relatively low frequency (5.0%) as compared to all others Indian studies.

Comparison of various childhood malignancies with studies abroad

Type of Childhood Malignacis	Young et al USA white (%)	C Stiller UK (%)	Pearson et al UK (%)	C.C. Vathare et al (%)	SEER Study (%)	Present Study (%)
Leukemia	33.80	35.00	20.40	35.63	31.50	28.33
Lymphoma	10.60	11.00	8.70	10.34	10.70	28.33
CNS tumors	19.20	28.00	16.60	18.39	20.20	5.0
Retinoblastoma	2.70	2.70	3.10	4.59	3.10	11.65
Kidney tumors	6.30	6.00	5.40	4.59	6.30	5.0
Bone tumors	4.50	2.90	9.80	-	4.50	11.66
Soft tissue tumors	6.80	3.70	8.50	5.74	7.00	8.33
SNS tumors	7.70	6.00	7.50	6.89	7.80	0
Miscellaneous	8.40	4.70	25.00	13.83	8.90	1.66

In the present study Leukemia was the commonest malignancy (28.33%) and the results were comparable to all the foreign studies (33.80% by Young *et al* [8], 35.00% by Stiller *et al* UK [9], 35.63% by C.C. Vathare *et al*, 31.50% by SEER study).

The results for the Wilm's tumor & soft tissue tumors were almost similar to the other foreign studies as shown in Table 7.

Our study shows higher frequency of Lymphoma among all solid pediatric malignant neoplasm while CNS tumors accounted for a lower number of cases when compared with other studies from abroad.

Conclusion

It can be concluded from our study that pediatric malignancies contribute a significant childhood health problem in our region affecting all pediatric age group but more prevalent in the age group 11-14 years. Incidence was more commonly seen in males than female except for leukemia & bone tumors. Hematological malignancies were the commonest followed by retinoblastoma, bone tumors, soft tissue tumors, CNS tumors & Wilm's tumors. The results were comparable with other studies.

FNAC is an important, safe & effective tool in early diagnosis although histological examination is confirmatory. Though not available in our institution, cytogenetics & molecular genetics may further aid in confirmation of the diagnosis.

PBF is a rapid & simple method for initial assessment of leukemia based on morphology of leukemic cells however cytochemistry, cytogenetics, Immunocytochemistry & molecular genetics are of special value.

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