

ORIGINAL ARTICLE

PATTERN OF PAEDIATRIC MALIGNANCIES IN A TERTIARY CARE HOSPITAL IN NORTHERN PAKISTAN

Tanveer Ashraf, Tariq Ghafoor*, Saman Tanveer**

Department of Paediatrics, CMH Lahore Medical College, Lahore, *Department of Paediatric Oncology, CMH, Rawalpindi, **Army Medical College, Rawalpindi, Pakistan

Background: Out of 200,000 new cases of childhood cancer worldwide, 80% are from developing countries. This study was conducted to evaluate pattern and frequency of malignant diseases among children, in northern Pakistan. **Methods:** This retrospective hospital based study was carried out at Paediatric Oncology Department of Combined Military Hospital Rawalpindi from 1st January 2012 to 30th June 2017. All new patients below 15 years of age with confirmed diagnosis of malignant diseases were included. Medical records of patients were analyzed and frequencies were calculated according to diagnosis, sex and age. **Results:** A total of 1,087 new patients, 734 male and 353 female, were included in the study. Mean age was 5.5±3.5 years. Majority of children (47.8%) were in age group 1–5 years, followed by age group 5–10 years (31.9%). Acute Lymphoblastic Leukaemia (ALL) was the commonest malignancy seen in 38.2% of patients. Other common malignancies were Acute Myeloid Leukaemia (AML) 15.5%, Hodgkin Lymphoma 7.4%, Non-Hodgkin lymphoma 5.4%, Wilms' tumour 6.1%, Neuroblastoma 4.6%, Rhabdomyosarcoma 3.8%, Retinoblastoma 3.5% and Brain tumours 3.5%. Among infants (<1 year age), Acute leukaemia and Wilms' tumour were more common. Overall male to female ratio was 2:1. Almost all tumours were more prevalent in males except Ewing Sarcoma (M/F 1:1.08) and Wilms' tumour (M/F 1:1). **Conclusion:** Acute Lymphoblastic Leukaemia is the commonest paediatric malignancy in our population. It is in accordance with other regional and international studies. We have relatively higher frequency of AML and lower frequency of brain tumours.

Keywords: Children, Cancer, Pattern, Pakistan, Acute Lymphoblastic Leukaemia, ALL

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INTRODUCTION

Childhood cancers account for 1% of total malignancies in developed countries but 3–8% in under developed world.^{1,2} This may be due to relatively higher proportion of children in population of these countries or because of higher incidence of malignant disorders due to genetic or environmental factors.³ Out of 200,000 new cases of childhood cancer worldwide, 80% are from developing countries.⁴

Cancer is second only to trauma and accidents as leading cause of deaths in children in North America and Western Europe.⁵ In Pakistan and other developing countries, infections like diarrhoea and pneumonia still remain the major contributor to childhood mortality.⁶ That is why our health care system is more concerned about improvement in management of these diseases. As we make progress in reducing infection-related childhood deaths, it is no longer acceptable to ignore children with cancer, who have an increasing likelihood of cure with appropriate treatment.

In order to improve paediatric oncology services, we have to first estimate the burden of childhood cancer and to understand how the occurrence and outcome of disease varies across the country. National tumour registry and population based studies are of vital importance in achieving that goal.⁷

In absence of population based national or regional tumour registries, hospital based studies can

give us insight into the pattern and relative frequencies of different types of malignant disorders and variation among different age and gender groups.⁸ In Pakistan, we do not have an organised national cancer registry⁹, therefore as first step we should organise data of individual paediatric oncology centres. We have carried out this study with the aim to have basic information about various malignancies among children in our region and to compare it with other national and international studies.

PATIENTS AND METHODS

It is a retrospective hospital based study, carried out at paediatric oncology department of Combined Military Hospital Rawalpindi, the largest paediatric oncology unit in northern Pakistan. Most of our patients were from northern Punjab, Khyber Pakhtunkhwa province, Gilgit Baltistan region and State of Azad Jammu & Kashmir. This is the only oncology centre in the region treating Acute Myeloid Leukaemia in children.

All new cases of malignant diseases in children up to 15 years of age, reporting to this department from 1st January 2012 to 30th June 2017 were included. Patients presenting with non-malignant disorders like aplastic anaemia, haemophagocytic lymphohistiocytosis (HLH) and Langerhan cell histiocytosis (LCH) were excluded. Children having relapsed disease were also exclude. Relevant information regarding patients' age,

sex and final diagnosis was collected from review of medical record.

Patients were divided in 4 age groups, <1 year, >1–5 years, >5–10 years and >10 years. Frequency of different malignancies was calculated along with variation AMONG different age and gender groups. Data was analysed on SPSS-16, and $p \leq 0.05$ was considered statistically significant.

RESULTS

Out of 1,426 new patients admitted during above mentioned period of 5½ years, 1,087 children fulfilled inclusion criteria whereas 339 children were excluded from the study. There were 734 males and 353 females.

Acute Lymphoblastic Leukaemia (ALL) was the most common malignancy, seen in 38.4% of patients. Other common malignancies were Acute Myeloid Leukaemia (AML) 15.5%, Hodgkin Lymphomas 7.4%, Wilms’ tumour 6.1%, Non-Hodgkin lymphoma 5.4%, Neuroblastoma 4.6%, Rhabdomyosarcoma 3.8%, Brain tumours 3.5%, Retinoblastoma 3.5% and Ewing sarcoma 2.3%. Table-1 shows frequency and percentage of all malignancies seen in our patients.

Table-1: Frequency of various Malignancies

	Frequency	Percent
Acute Lymphoblastic Leukaemia	417	38.4
Acute Myelocytic Leukaemia	169	15.5
Hodgkin Lymphoma	80	7.4
Wilms’ tumour	66	6.1
Non Hodgkin Lymphoma	59	5.4
Neuroblastoma	50	4.6
Rhabdomyosarcoma	41	3.8
Brain Tumour	38	3.5
Retinoblastoma	38	3.5
Ewing Sarcoma	25	2.3
Germ Cell Tumours	24	2.2
Bi-phenotypic Acute Leukaemia	17	1.6
Infant ALL	15	1.4
Hepatoblastoma	14	1.3
Osteosarcoma	7	0.6
Juvenile Myelomonocytic Leukaemia	6	0.6
Nasopharyngeal Carcinoma	5	0.5
Chronic Myeloid Leukaemia (Ph +)	4	0.4
NR-STs (Nonrhabdoid soft tissue sarcoma)	3	0.3
NR-STs (Infantile Fibrosarcoma)	2	0.2
NR-STs (synovial sarcoma)	2	0.2
GIST (Gastrointestinal stromal tumour)	1	0.1
Hepatocellular Ca	1	0.1
Malignant Melanoma	1	0.1
Others-AML+Ewing sarcoma	1	0.1
Pancreatic Neuroendocrine Tumour	1	0.1
Total	1087	100.0

Mean age of patients was 5.5±3.5 years. Majority (47.5%) of patients were in 1–5 years age group. Hodgkin lymphoma, brain tumours and Ewing sarcoma were more prevalent in children between 5–10 years age and osteosarcoma among children >10 years age.

Among 80 infants less than 1 year of age, common malignancies were acute leukaemia (28.8%), Wilms’ tumour (16.2%), Retinoblastoma (12.5%), Neuroblastoma (11.2%) and Hepatoblastoma (10%).

Overall male to female ratio (M:F) was 2.08:1. There was no significant difference in M:F ratio among different age groups (Table-2). All common malignancies were more prevalent in males ($p < 0.05$) except Ewing sarcoma (M/F= 1:1.08) and Wilms’ tumour (M/F= 1:1) (Table-3).

Table-2: Age and Gender distribution of patients

Gender	Age Groups				Total
	Infant <1 year	1–5 years	5–10 years	>10 years	
Female	28	173	105	47	353
Male	52	351	240	91	734
Total	80	524	345	138	1087
M:F Ratio	1.85:1	2.02:1	2.28:1	1.93:1	2.07:1

Table-3: Male to female ratio of common paediatric malignancies

Type of Malignancy	Gender	No.	Percent (95% CI)	p
ALL	Male	293	70.3 (65.6–74.6)	<0.001
	Female	124	29.7 (25.4–34.4)	
AML	Male	108	63.9 (56.2–71.1)	<0.001
	Female	61	36.1 (28.9–43.8)	
Hodgkin Lymphoma	Male	65	81.3 (71.0–89.1)	<0.001
	Female	15	18.8 (10.9–29.0)	
Non-Hodgkin Lymphoma	Male	45	76.3 (63.4–86.4)	<0.001
	Female	14	23.7 (13.6–36.6)	
Rhabdomyosarcoma	Male	30	73.2 (57.1–85.8)	0.005
	Female	11	26.8 (14.2–42.9)	
Neuroblastoma	Male	35	70.0 (55.4–82.1)	0.007
	Female	15	30.0 (17.9–44.6)	
Hepatoblastoma	Male	12	85.7 (57.2–98.2)	0.01
	Female	2	14.3 (1.8–42.8)	
Brain tumours	Male	23	60.5 (43.4–76.0)	0.26
	Female	15	39.5 (24–56.6)	
Wilms’ Tumour	Male	33	50.0 (37.4–62.6)	1.00
	Female	33	50.0 (37.4–62.6)	
Ewing Sarcoma	Male	12	48.0 (27.8–68.7)	1.00
	Female	13	52.0 (31.3–72.2)	

DISCUSSION

Most common malignancy in our patients is Acute Lymphoblastic Leukaemia (ALL) accounting for 38.4% of total. Most of other studies from developed and under developed world have also reported the same pattern.^{3,10,11}

Acute Myeloid Leukaemia (AML) is the second most common disease (15.5%) in our study. This finding is not in conformity with published literature.^{11,12} It may be because of referral bias, as our department is the only centre in Northern Pakistan, treating AML in children. Referral bias may be the likely reason for another unusual finding, the lower frequency of Central Nervous System (CNS) tumours (3.5%). In our hospital, most of CNS tumours are managed by department of Neurosurgery and Radiation Oncology and relatively

fewer children report to our centre. In developed world, CNS tumours are the second most common childhood cancer (22–25%) and lymphomas a distant third (10%).^{10,11} In contrast, in our setup lymphomas exceed CNS tumours. Not only is the proportion of lymphomas higher, but Hodgkin Lymphoma (HL) exceeds non-Hodgkin lymphoma (NHL), a pattern opposite to that seen in the developed world. Like Pakistan, Hodgkin lymphoma is common in India.³ In Bangladesh, NHL is more common than HL.¹³ Most of the studies from Africa show much higher frequency of NHL due to higher incidence of Burkitt Lymphoma.^{14–16} In India, frequency of CNS malignancies varies from 7.6% to 14.7% in different regions³ whereas in Bangladesh it is closer to our results at 4.4%.¹³ In Iran, various studies have found CNS tumours to be second most common malignancy, after leukaemia.¹⁷

Retinoblastoma accounts for 3.5% of our patients, similar to frequency seen in most of developed world.¹¹ Other countries of our region including India and Bangladesh have much higher prevalence of eye tumours in children.^{3,13} In Bangladesh, Retinoblastoma is second most common malignancy after leukaemia. One explanation given for higher incidence in these two countries is that eye tumours are relatively easy to recognise and diagnose, as compared to haematological and CNS malignancies that present with non-specific symptoms. A lower frequency in our study does not favour that explanation.

Ewing sarcoma is the commonest (2.3%) bone tumour in our study. Osteosarcoma is much less frequent (0.6%) and seen in older children. This is in contrast to most regional and international studies that find osteosarcoma as the commonest bone tumour.^{10,13}

In our study, overall male to female ratio (M:F) is 2:1. Paediatric malignancies are more prevalent among boys as compared to girls and this fact has been observed in studies across the world. In developed countries, overall male to female ratio is 1.2:1.^{3,10} However, some cancers like retinoblastoma, Wilms' tumour, osteosarcoma and germ cell tumour are actually more common in females.¹¹ Studies from developing countries have found relatively higher M:F ratio.^{15,18–20} Previous studies from Pakistan have also shown increased preponderance in males.^{2,21}

In our study gender disparity is even higher than other developing countries. Arora and Eden³ analysed thirteen population based cancer registries from India and have found variable M:F in various regions. In Delhi region M:F for Hodgkin Lymphoma (HL) was 11.8:1 whereas in Mumbai it was 3.1:1. Similar variation was reported for ALL, AML and Bone tumours.³ In our patients M:F for HL was 4.3:1 ($p < 0.001$). It is higher than all other countries except few regions in India. More studies are needed to figure out the reason for such a significant male predisposition.

We had 14 cases of Hepatoblastoma, 12 males and 2 females with M:F of 6:1 ($p = 0.01$). This ratio is much higher as compared to other published studies. Hossein *et al*¹³, from Bangladesh have reported >3:1 M:F in Hepatoblastoma and Acute Leukaemia. In our study, Ewing Sarcoma is the only tumour among common malignancies that is more prevalent among females (M:F = 0.9:1). Wilms' tumour was equal among males and females (1:1). These findings are in conformity with other published studies.^{3,11}

Mean age of our patients was 5.5±3.5 years. Most of children were in age group >1–5 years, followed by >5–10 years. Infants (age <1 year) account for 7.4% of total patients. Infantile leukaemia, Wilms' tumour, retinoblastoma, neuroblastoma and hepatoblastoma are common malignancies among infants. Osteosarcoma, Non-Rhabdoid soft tissue sarcomas and Nasopharyngeal carcinomas were seen in older children and adolescents. This pattern of age distribution is in conformity with other international studies from developed and developing countries.^{3,10,11}

There are a few limitations of our study. It is a hospital based single centre study and has referral bias regarding AML and CNS tumours.

CONCLUSION

Acute Lymphoblastic Leukaemia is the most frequent paediatric malignancy in our population. Hodgkin Lymphoma is more common than NHL and lymphomas as a group account for most common solid malignancy in our children. Childhood cancers are more prevalent among males except Ewing sarcoma and Wilms' Tumour. Larger multicentre studies and population based cancer registries are needed to have better insight in pattern and incidence of these diseases.

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Address for Correspondence:

Dr Tanveer Ashraf, Consultant Paediatrician, CMH Lahore Medical College, Abdul Rahman Road, Lahore Cantt.

Cell: +92-323-6111875

Email: tanveer760@gmail.com

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