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The Profile of Childhood Malignancies in Dar es Salaam, Tanzania

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Abstract

Background

Majority of children with cancer live in low- and middle-income countries. The data is scarce on the epidemiology of childhood cancer in these countries. In this study, we enrolled children and adolescents with cancer at the only cancer hospital in Tanzania and determined the epidemiology and HIV infection among this population.

Methodology

This was a descriptive hospital-based study conducted at Ocean Road Cancer Institute in Dar es salaam, Tanzania. Data were collected for eight months (May to December 2010). Participants were enrolled consecutively as they presented to the hospital. Demographic data, HIV status and clinical diagnosis were determined and recorded. Each patient was followed up until a final diagnosis was reached, and investigations for disease staging were completed.

Results

One hundred and fifty-one (151) patients were enrolled in the study. Mean age at presentation was 5.8 years (range 3-17years), and 51.7% of participants were males. Sixty-three per cent (63%) of patients had their diagnoses confirmed by histology or cytology. Retinoblastoma was the most common malignancy (29.1%) followed by Nephroblastoma (11.3%), Burkitt lymphoma (10.6%) and Acute Lymphoblastic Leukemias (10.6%). More than half (58.2%) of patients aged three years or younger had Retinoblastoma. Four patients (2.8%) had HIV infection; three of them with Kaposi's sarcoma and one with Burkitt lymphoma.

Conclusion

Retinoblastoma was the most typical malignancy followed by Wilms tumour, Burkitt lymphoma and acute lymphoblastic leukaemia. The prevalence of HIV infection was very low among patients with the described malignancies.

Key Words: *Childhood Malignancies, Tanzania.*

Background

More than 85% of childhood cancer occur in Low and Middle-Income Countries (LMIC), where resources for health are significantly limited (1, 2). The epidemiology of childhood malignancies is determined by genetics and environmental factors (3-5). Cancers associated with infections such as Burkitt Lymphoma (BL), Hodgkin Lymphoma (HL) and Kaposi's sarcoma (KS) contribute a larger percentage of total cases in LMIC than in high-income countries (HIC) (3, 6).

The pattern of childhood malignancies in Africa is characterized by a high incidence of lymphoma (40%-60%) and a low incidence of leukaemia (2%-8%) (7-10). Two studies done in Tanzania in 1998 and 2000 showed lymphoma to be the leading childhood cancer while bone, germ cell and CNS tumours were rare (11,12). A relative increase of leukaemia has been reported in some studies in Africa (13-15).

HIV infected children are at an increased risk of developing malignancies (16). In Africa childhood malignancies commonly associated with HIV infection are KS and B-cell NHL (17, 18). During the peak of the HIV infection, some countries in Sub Saharan Africa observed a significant increase in paediatric KS (6, 19). Since the year 2000 there are no published studies that describe the profile of childhood malignancies in Dar es Salaam. This study aimed at filling this gap.

Methods

This was a descriptive study conducted at Ocean Road Cancer Institute (ORCI) in the year 2010 when ORCI was the only cancer hospital in Tanzania. ORCI was receiving about 250 - 300 children with cancer per year. We longitudinally enrolled all children and adolescents below 18 years attending ORCI with clinical diagnosis or histologically confirmed diagnosis of malignancy and with parental consent. Consent was sought from children ten (10) years or older. Baseline data was collected for eight (8) months using a structured questionnaire.

Pathological confirmation of diagnosis was done by morphological examination of tissue biopsies, fine needle aspiration (FNAC) or bone marrow aspiration cytology (BMAC). Immunohistochemistry and flow cytometry were not available to aid diagnosis at that time in our hospital. Pre-test counselling for HIV was done to all patients. Data analysis was done using Epi Info and SPSS 16.0 statistical programs. MUHAS Senate Research and Publication Committee, which is the Institutional Review Board issued the ethical clearance and permission to conduct this study was provided by ORCI.

Results

One hundred and fifty-seven (157) patients were recruited in this study; six were excluded (5 non-malignancy, and one (1) died before diagnosis was made).

Demographic characteristics and HIV status of the study participants

The demographic characteristics of the study population are summarized in Table 1. Eventually hundred and fifty-one (151) patients were enrolled in the study and 78 (51.7%) were males. The mean age at presentation was 5.8 years (range 3months-17years). Majority of the patients (82.8%) were ten years old or younger. Out of the 145 patients tested for HIV, only four (4; 2.8%) were positive.

Table 1: Demographic characteristics and HIV status of the study participants

Variables	Number	Per cent
Sex		
Male	78	51.7
Female	73	48.3
Age group (Years)		
≤ 3	55	36.4
4-10	70	46.4
>10	26	17.2
HIV status (n=145)		
Negative	141	97.2
Positive	4	2.8
Parent/Guardian level of education		
No formal	23	15
Primary	92	61.4
Secondary	27	18.1
Diploma and Degree	9	5.5

Types of malignancies noted in this study

Retinoblastoma (RB) was the most typical malignancy seen during the study (29.1%) followed by WT (11.3%), ALL and BL (each 10.6%).

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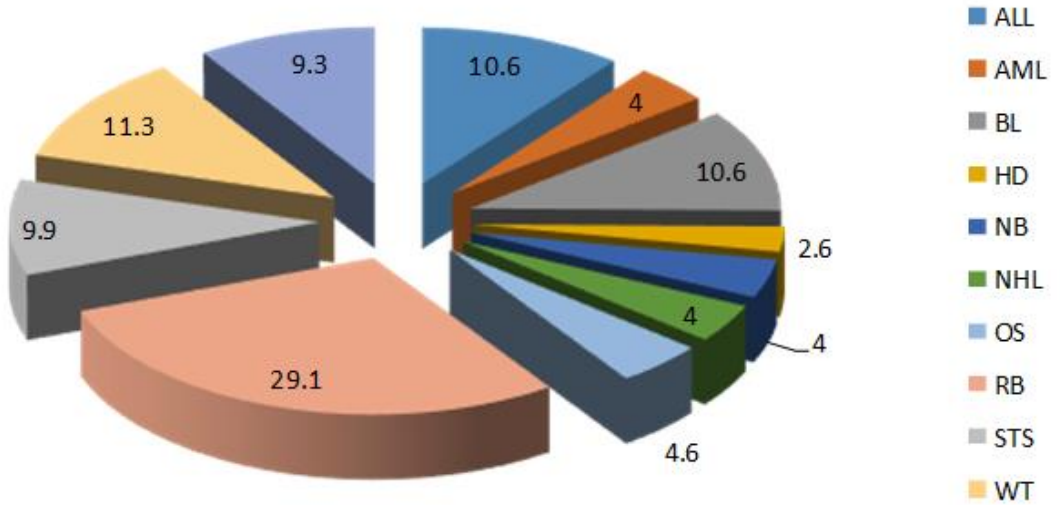
Figure 1: Percent propotion of different types of childhood malignancies



Others included: Squamous cell carcinoma (3), Nasopharyngeal carcinoma (NPC) (3), Hepatocellular carcinoma (HCC) (2), Renal cell carcinoma (1), Ovarian cancer (1), Chronic myelogenous leukaemia (CML) (1) and Uncertain diagnosis (3).

Two (2) of the three (3) patients with Squamous cell carcinoma had Xeroderma Pigmentosa, and one (1) had Ocular, cutaneous albinism. There was no patient with a brain tumour. Age at presentation influenced the type of malignancy. RB, WT and NB accounted for three-quarters of patients three (3) years old or younger; 58.2%, 11% and 7.2% respectively. The pattern of malignancies seen in this study is described in Table 2.

Method of diagnosis of malignancies

The diagnosis was confirmed in 64.2% of patients; 43% by histopathology reports, and 21.2% cytology reports. BMAC diagnosed all haematological malignancies. Histopathology was by morphology alone. Immunohistochemistry and flow cytometry services were not available. RB and WT had less proportion of patients with pathological confirmation of diagnosis, 36.4% and 29.4% respectively.

Table 3 summarizes the proportion of patients with a confirmed diagnosis by the type of malignancy and the diagnostic modality used.

Table 2: Distribution of malignancies by the age of participants

Diagnosis		Age group (years)		
	≤ 3	4-10	>10	Total
	Number (%)	Number (%)	Number (%)	Number (%)
Retinoblastoma	32 (58.2)	12 (17.2)	0	44 (29.1)
Wilms tumour	6 (11.0)	10 (14.3)	1 (3.8)	17 (11.3)
Burkitt lymphoma	1 (1.4)	10 (14.3)	5 (19.2)	16 (10.6)
Acute lymphoblastic leukemia	3 (5.5)	12 (17.2)	1 (3.8)	16 (10.6)
Soft tissue sarcoma	4 (7.2)	8 (11.4)	3 (11.5)	15 (9.9)
Osteosarcoma	0	2 (2.9)	5 (19.3)	7 (4.6)
Neuroblastoma	4 (7.2)	1 (1.4)	1 (3.8)	6 (4.0)
Non- Hodgkin Lymphoma	2 (3.6)	4 (5.7)	0	6 (4.0)
Hodgkin Lymphoma	0	1 (1.4)	3 (11.5)	4 (2.6)
Others	1 (1.8)	7 (10.0)	6 (23.1)	14 (9.3)
Total	**55 (100)**	**70 (100)**	**26 (100)**	**151 (100)**

Table 3: Diagnosis confirmation status by type of malignancy

Diagnosis	Confirmed		Not Confirmed	
	Histology	Cytology	Clinical	Total
	Number (%)	Number (%)	Number (%)	Number (%)
Retinoblastoma	16 (36.4)	0	28 (63.6)	44 (100)
Wilms tumour	5 (29.4)	1 (5.9)	11 (64.7)	17 (100)
Acute lymphoblastic leukemia	0	16 (100)	0	16 (100)
Burkitt lymphoma	9 (56.3)	2 (12.4)	5 (31.3)	16 (100)
Soft tissue sarcoma	12 (80)	1 (6.7)	2 (13.3)	15 (100)
Osteosarcoma	6 (85.7)	0	1 (14.3)	7 (100)
Neuroblastoma	2 (33.3)	2 (33.3)	2 (33.3)	6 (100)
Acute myeloid leukemia	0	6 (100)	0	6 (100)
Non- Hodgkin Lymphoma	3 (50)	3 (50)	0	6 (100)
Hodgkin Lymphoma	4 (100)	0	0	4 (100)
Others	8 (57.2)	1 (7.1)	5 (37.7)	14 (100)
Total	**65 (43.0)**	**32 (21.2)**	**54 (35.8)**	**151 (100)**

Discussion

Retinoblastoma was the most common childhood malignancy seen in this study (29.1%). Previous studies in Tanzania documented RB as the third commonest childhood malignancy contributing to 11% and 13% of reported childhood malignancies (11, 12). A study in Congo has documented RB as the most frequent childhood malignancy with an incidence of 20.1% (6). BL contributed 10.6% of patients seen during this study. From ORCI records, BL used to account for almost 50% of all childhood malignancies seen in a year. Taken together, lymphomas (BL, NHL and HL) are the second most common childhood malignancies. However, lymphoma contribution is smaller as compared to findings from previous studies for which lymphoma formed half of all childhood malignancies (7-10). BL is usually the predominant type of lymphoma in the tropics, including East Africa (6,10,11), which is consistent with our findings. In a study on "Patterns of Distribution of Childhood Cancer in Africa," Bugando Medical Center in Northern Tanzania documented the frequency of Lymphoma as 41%, RB 18%, WT 14%, Leukemia 8% and Neuroblastoma 6% (6).

The observed difference in the proportions of the different types of childhood malignancies seen in this study is most likely a reflection of access to care at ORCI by patients rather than actual differences in the incidence of childhood malignancies in the general population. RB is a slow-growing tumour; hence affected children could still reach ORCI despite various delays in access and receiving care. Children with fast-growing malignancies such as ALL and BL are likely to die if there are delays in accessing care. The lower per cent of RB observed in the previous two studies conducted at MNH (11,12) could be explained by the fact that most RB patients were seen at Comprehensive Community-Based Rehabilitation in Tanzania (CCBRT) hospital and referred to ORCI directly without their documentation at MNH.

Satellite centers have been established in Tanzania, most of these satellite centers offer chemotherapy of BL patients. Therefore, children with this type of malignancies would have accessed treatment from the satellite centers accounting for the decreased contribution of BL in these study findings. However, there could be an actual decrease in BL. A retrospective study in Nigeria in 2009 showed a relative increase of leukaemia with a relative reduction of BL over 30 years (14). Two other studies; one in Sudan and another in Egypt have shown an increase in the frequency of leukaemia whereby in the Sudan study leukaemia (26%) was second to lymphoma (15, 19). In the current study, the proportion of

patients with ALL was similar to that of BL (10.6%). If we excluded RB patients, lymphoma (BL, NHL and HL) would have been the most frequent (24.3%), and followed by leukaemia (20.6%), which compared to previous studies it tallies with a relative increase of leukaemia and a relative decrease of lymphoma. Ewing sarcoma (ES), a rare tumour in African children (20) was seen in one patient only in the current study. This patient had ES of the hip with metastasis. No patients with CNS tumour were seen in this study. A possible explanation is limited access to diagnostic imaging such as MRI, and CT scans hence missed diagnosis. However, the incidence of CNS tumours is believed to be low in Africa (21). The interaction between genetic predisposition and environmental factors (22, 23) could explain the three patients with SCC where two had Xeroderma pigmentosa, and one had ocular, cutaneous albinism.

Mutation in the RB1 gene is associated with hereditary RB, which commonly presents in the first year of life and is often bilateral (22, 23). In this study, all but one, patient below one year had bilateral disease, and decreased to 63.6% in patients below two years. In our setting where genetic studies are not done to determine RB1 mutations, the clinical finding of bilateral RB in patients less than two years can be used as a proxy for hereditary disease. Distinguishing between hereditary and sporadic RB is important because siblings of patients with hereditary RB are at increased risk of developing RB; hence they need regular screening from early infancy.

In this study, only four patients (2.8%) were HIV infected. This is low compared to the 22% found at ORCI in 2005 (unpublished study) and 42.2% in Zimbabwe (24). During the 2005 study at ORCI, there was a selective screening of patients for HIV, therefore determining the actual magnitude of HIV infection was difficult. Patients with HIV associated malignancies were more likely to be screened hence skewing the results towards a higher prevalence of HIV infection. Even though there were few patients with HIV infection, they all presented with commonly described HIV associated malignancies. One patient had bilateral cutaneous nodular KS of the lower limbs, two had generalized mucocutaneous KS, and one had metastatic BL. A study in Malawi showed the prevalence of HIV infection to be 93% for children with KS, 4% for BL and 5% for the remaining cancers combined (25). This is closely similar to the findings of the current study because HIV infection was 100% for KS patients and 6.3% for BL patients. A study in Uganda reported a forty-fold increase in paediatric KS during the AIDS epidemic (26).

In our study, 63.6% of patients had their diagnoses confirmed by histopathology. BMAC diagnosed all patients with leukaemia, but it was often not possible to determine the type of leukaemia with accuracy because flow cytometry was not available. Half of the patients with solid tumours had diagnostic histopathology reports, and the rest of the patients were diagnosed clinically. Sixty-four per cent (64%) of patients with RB did not have histology reports although most of them had undergone enucleation or exenteration. A retrospective study done at CCBRT and ORCI in 2005 had similar findings where almost half of RB patients did not have histology reports (27). Even though clinical diagnosis for RB is acceptable and nearly always accurate, histopathology is essential for staging and to guide further treatment.

Patients with easily accessible tumours such as HL, OS and head and neck tumours had the highest proportion of confirmed diagnoses while intra-abdominal malignancies had the least. This may reflect limited resources in paediatric surgery, anaesthesia, operating theatres and supportive care in general.

Conclusion

Solid tumours were the commonest malignancies followed by leukemia and lymphoma. Two-thirds of the diagnoses were confirmed by histopathology. Only four patients (2.8%) tested positive for HIV infection among the study participants.

Abbreviations

AIDS	Acquired Immunodeficiency Syndrome
ALL	Acute Lymphoblastic Lymphoma
BL	Burkitt Lymphoma
BMAC	Bone Marrow Aspiration Cytology
CCBRT	Comprehensive Community Based Rehabilitation in Tanzania
FNAC	Fine Needle Aspiration Cytology
HIC	High-Income Countries
HIV	Human Immunodeficiency Virus
HL	Hodgkin Lymphoma
KS	Kaposi's Sarcoma
LMIC	Low and Middle-Income Countries
NB	Neuroblastoma

NHL	Non- Hodgkin Lymphoma
OS	Osteosarcoma
ORCI	Ocean Road Cancer Institute
RB	Retinoblastoma
RMS	Rhabdomyosarcoma
STS	Soft Tissue Sarcoma
WT	Wilms tumour

Declarations

Ethics approval and consent to participate

This study received ethical clearance from MUHAS IRB and parents of involved children consented to participate before their child was enrolled in the study.

Availability of data and materials

Data used for this study are available from the corresponding author.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

LC, TK and EK designed the study. LC collected and analyzed data as well as prepared the first draft of the manuscript. All authors read and approved the final manuscript.

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