

## **Histopathological Pattern of Pediatric Malignant Tumors and Survival Rate at Kilimanjaro Christian Medical Centre, Tanzania from 2013 to 2015**

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### **Authors' contributions**

*This work was carried out in collaboration between all authors. Author SK designed the study, wrote the protocol and wrote the first draft of the manuscript. Authors SM and RP contributed on the design of the study and analysis. Authors AM and BTM participated in study design, data collection supervision and analysis and reviewed the final manuscript. All authors read and approved the final manuscript.*

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### **ABSTRACT**

**Background:** Childhood malignant tumors are among diseases that cause death to children below 14 years. Although it is the second most common cause of death in children in developed countries, its magnitude in Africa is not well known.

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**Aim:** To determine the proportion of pediatric malignant tumors and the immediate outcome among children attending Kilimanjaro Christian Medical Centre in Tanzania.

**Study Design:** Retrospective – hospital based study.

**Place and Duration:** Kilimanjaro Christian Medical Centre, Pathology department, 3 years.

**Methodology:** Microscopic slides from January 2013 to December 2015 were retrieved from archives and evaluated at a magnification of 40x, 100x and 200x for histological features, diagnosis and disease grading. The findings were confirmed by the pediatric pathologist and concluded on the diagnoses and the grade. The tumors were graded into well-differentiated and undifferentiated. Parents/guardians were contacted through phone calls to establish progress of their children to assess the six-month survival rate.

**Results:** Among 84 studied patients' slides, 43 (51.2%) were from males with the median (IQR) age of 4.5 (2.3-9.3) years while 50 children (59.5%) were under five years of age. Retinoblastoma 21 (25%) was the most common malignant tumor followed by Squamous cell carcinoma and Sarcoma comprising 13 (15.5%) each. Among 75 children other than patients with leukemia, 42 (56.0%) had well differentiated and 33 (44.0%) had undifferentiated malignant tumors. Forty-one (97.6%) of the patients with well-differentiated malignant tumors survived within six months from the date the specimen was taken. The overall six-month survival rate was 84.5%. Thirteen patients (15.5%) died during the six-month period of follow up.

**Conclusion:** Retinoblastoma was the most common malignant tumor affecting children <14 years in northern Tanzania. The overall six-month survival rate was high when early detection of childhood malignancies is practicable.

*Keywords: Histopathological pattern; pediatric; malignant tumor; tumor differentiation.*

## 1. INTRODUCTION

Pediatric malignant tumors are among the leading killers in children below 14 years in the developed world, while in Africa it is not even ranked among the top ten causes of death [1]. Histologically, childhood malignancies manifest in different types including Retinoblastoma, Squamous cell carcinoma, Nephroblastoma, Leukemia, and Sarcoma. Inheritances of genetic susceptibility or spontaneous mutations have shown greater association with causes of cancer in children, because of the rapid cell proliferation that occurs at young ages [2]. However, the genetic basis for the most common types of childhood cancers has not been established except for retinoblastoma and Wilm's tumor [2].

The prevalence of pediatric malignancies varies between developed and developing countries. In Europe, Latin America and the USA, Leukemia has been reported as the leading malignant tumor [3-5] while in Africa, Lymphomas and Leukemia are the leading malignant tumors in children [6]. In Tanzania a study at the Ocean Road Cancer Institution indicated that retinoblastoma was the leading malignant tumor among pediatric malignancies [7].

Children suffering from different types of malignancies have different survival rates and these differ between developed and developing countries. In developed countries the survival

rate is higher (> 75%) [8] than in developing countries (<55%) [9]. This may be associated with availability of different diagnostic methods and treatment.

Generally, little is known about the types of malignant tumors among children attending tertiary hospitals in northern Tanzania and their outcomes, therefore this may lead to limitation in management and hence increase malignant tumor related morbidity/mortality in children. This study was carried out to determine the proportion and survival rate of pediatric malignant tumors at Kilimanjaro Christian Medical Centre in northern Tanzania between 2013 and 2015. Findings from this study will assist in the development of appropriate management protocol in relation to tumor types.

## 2. METHODOLOGY

### 2.1 Study Site

The study was conducted at Kilimanjaro Christian Medical Center; a referral, consultant, research and teaching hospital located in Moshi in northern Tanzania with a bed capacity of over 650. It provides medical services to a population of approximately 15.7 million people from Tanga, Kilimanjaro, Arusha and Manyara Regions. It processes and examines approximately 2,953 histology/cytology specimens per year for both adults and children.

## 2.2 Data Collection

This was a retrospective hospital – based study. Structured data collection forms were used to collect information. All children with malignancy aged 3 months to 14 years diagnosed by means of histology/cytology examination were recruited in the study. Microscopic slides, stained with Haematoxylin and Eosin were retrieved from archives and examined under 40x, 100x and 200x magnification for histological features to diagnose and grade the disease. The tumors were graded into well-differentiated and undifferentiated tumors. A pediatric pathologist who was on site reviewed and confirmed the histological presentations and differentiation, and together with the corresponding author concluded the diagnosis and grade of the tumor. Identified cases were contacted through their parents or guardians to establish their progress. Patients who had complete data were included in the study.

## 2.3 Data Analysis

Data analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0. Descriptive statistics were used to summarize numerical data. The association between variables was analyzed using Chi-square test for categorical data. Odds of events were tested using Odds Ratio (OR) at 95% Confidence Interval (CI). Survival rate was calculated by direct method whereby the survival was expressed in terms of the percentages of cases alive at the time of specimen collection, and who were still alive within six months after specimen collection.

## 3. RESULTS

A total of 101 patients were recruited in the study, of whom 17 (16.8%) were excluded from the study due to incomplete data. Out of 84 patients with malignancy 43 (51.2%) were males with the median (IQR) age of 4.5 (2.3-9.3) years (range= 0.25 - 14 years) while 50 children (59.5%) were under five years of age. Among 84 patients, 34 (40.5%) were from Kilimanjaro and 31 (36.9%) were from Tanga and Arusha regions. Others 19 (22.6%) were from Manyara, Singida, Shinyanga, Mwanza, Dodoma, Rukwa, Kigoma and Kenya (Table 1).

The most common clinical presentation was swelling (63.1%) followed by pain (10.7%) in the affected region or organ (Fig. 1).

**Table 1. Demographic characteristics (N=84)**

Variable	No. (%)
<b>Sex:</b>	
Male	43 (51.2)
Female	41 (48.8)
<b>Age (years):</b>	
Median (IQR)	4.5 (2.3-9.3)
Under 5	50 (59.5)
5 - less than 10	16 (19.0)
10 – 14	18 (21.4)
<b>Region:</b>	
Kilimanjaro	34 (40.5)
Arusha	23 (27.4)
Tanga	8 (9.5)
Other	19 (22.6)

The most commonly affected organ was the eye with 26 (31.0%) followed by skin with 19 (22.6%), (Fig. 2).

The most common malignant tumors were retinoblastoma 21 (25.0%), Squamous cell carcinoma 13 (15.5%) and sarcoma 13 (15.5%). Sarcoma included Rhabdomyosarcoma 4 (4.8%), Kaposi's sarcoma 2 (2.4%), spindle cell sarcoma 3 (3.5%) and osteosarcoma 4 (4.8%). The remaining 8 (9.5%) included basal cell carcinoma, urothelial carcinoma, melanoma and adenocarcinoma (Fig. 3).

Among 75 children with tumor differentiation, 42 (56.0%) had well differentiated malignant tumors while 33 (44.0%) had undifferentiated tumors (Fig. 4, A-B and Fig. 5 A-B). In 9 Leukemia cases tumor differentiation was not done, as differentiation is not applicable.

The majority of Sarcoma 9 (69.2%), leukemia 6 (66.7%) and retinoblastoma 11 (52.4%) were undifferentiated tumors. Sarcoma was two times more likely to be undifferentiated as compared to retinoblastoma,  $P = 0.48$  (Table 2).

Forty-one (97.6%) of the patients with well-differentiated malignant tumors survived within six months from the date the specimen was taken. Patients with undifferentiated pediatric malignancies were 13.1 times more likely to die within six months after specimen collection than those with well differentiated (OR, 13.1; 95% CI, 1.5-111.2;  $P < .009$ ), (Table 3).

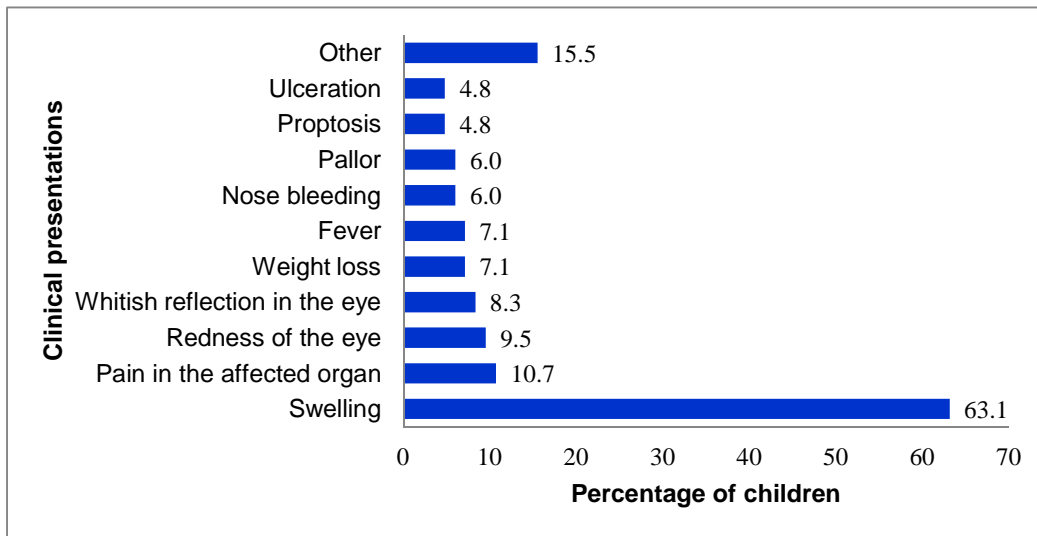


Fig. 1. Distribution of clinical presentations (N=84)

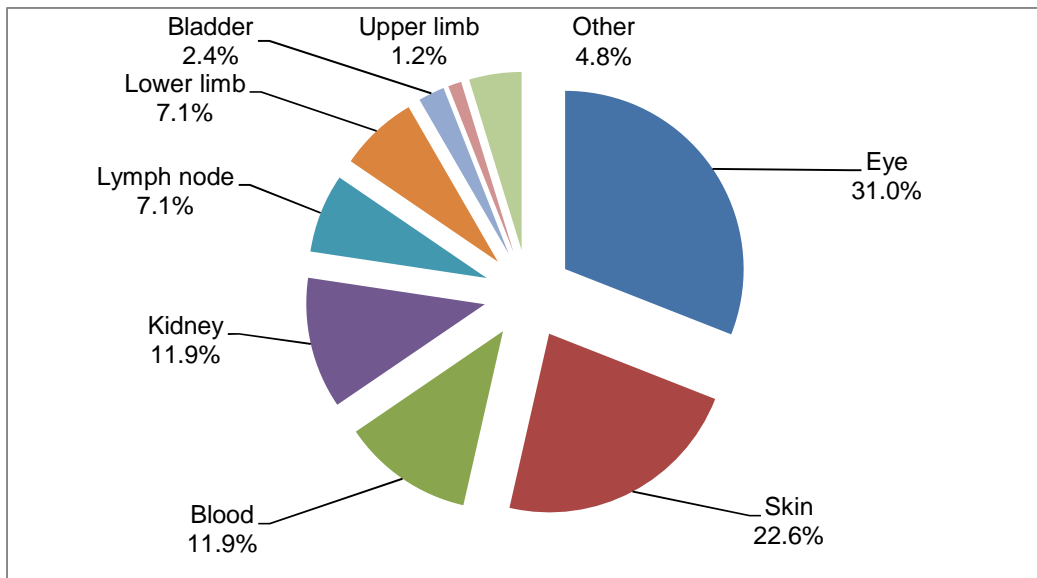


Fig. 2. Organs affected (N=84)

Table 2. Distribution of tumor differentiation according to the type of pediatric malignancy (N=75)

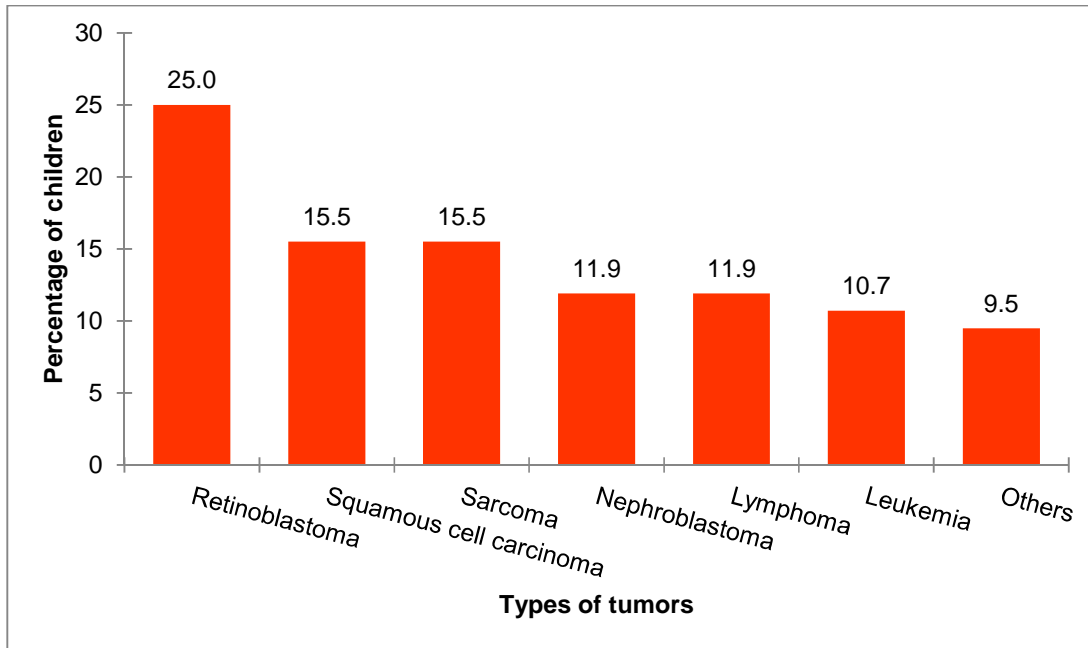
Type of malignant tumor	Tumor differentiation		OR (95% CI)	*P-value
	Undifferentiated	Differentiated		
Retinoblastoma	11 (52.4%)	10 (47.6%)	1.0	
Squamous cell carcinoma	1 (7.7%)	12 (92.3%)	0.1 (0.0-0.7)	0.01
Sarcoma	9 (69.2%)	4 (30.8%)	2.0 (0.5-8.8)	0.48
Nephroblastoma	3 (30.0%)	7 (70.0%)	0.4 (0.1-1.9)	0.28
Lymphoma	4 (40.0%)	6 (60.0%)	0.6 (0.1-2.8)	0.70
Others	5 (62.5%)	3 (37.5%)	1.5 (0.3-8.0)	0.70

\*Fisher's exact P-value, N (%)

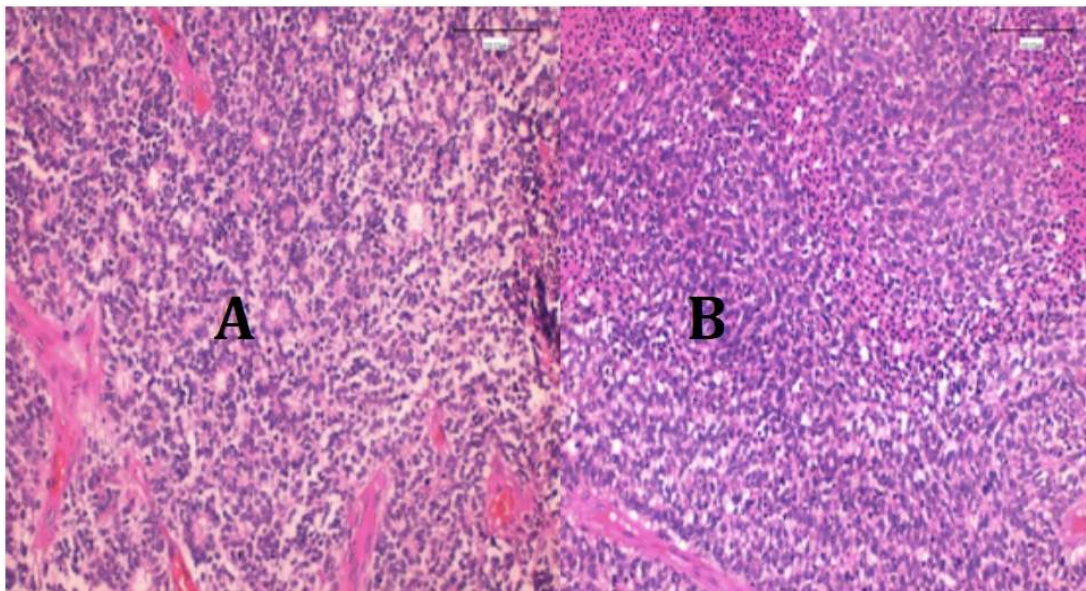
**Table 3. Histological differentiation vs. six-months survival rate (N=75)**

Histological differentiation	Outcome at six months		OR (95% CI)	*P-value
	Died	Alive		
Undifferentiated	8 (24.2%)	25 (75.8%)	13.1 (1.5-111.2)	0.009
Differentiated	1 (2.4%)	41 (97.6%)		

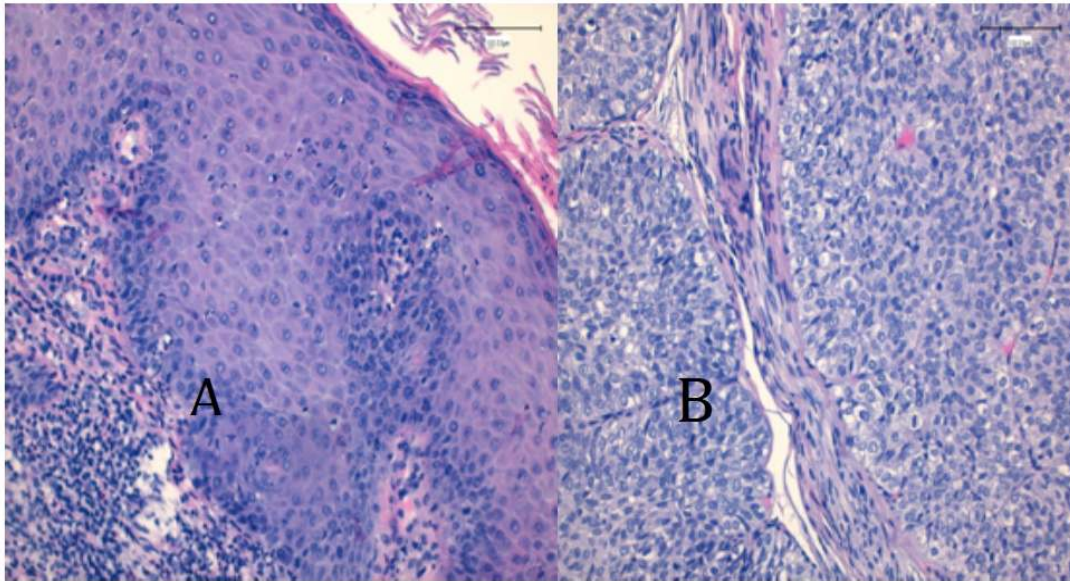
\*Fisher's exact P-value, N (%)



**Fig. 3. Distribution by histopathological diagnosis of malignant tumors (N=84)**



**Fig. 4. Well-differentiated retinoblastoma from a 4 year-old male patient (A), undifferentiated retinoblastoma from a 1 year-old male (B), original magnification X 200**



**Fig. 5. Well-differentiated squamous cell carcinoma from a 10 year-old female (A), undifferentiated squamous cell carcinoma from a 12 year-old male (B), original magnification X 200**

#### 4. DISCUSSION

Retinoblastoma was the most common malignant tumor followed by squamous cell carcinoma. The frequency of retinoblastoma was almost similar with findings from a previous study [7] at Ocean Road Cancer Institute in Tanzania. However, it differs with a study conducted in Pakistan (38.9%) [10]. This may be due to the difference in social demographic and genetic susceptibility within Asia and Africa.

The current study has indicated that the Squamous cell carcinoma was the second most common malignant tumor among pediatric malignancies. A study conducted in Tanzania [7] found a very low frequency of Squamous cell carcinoma. Most of the patients with Squamous cell carcinoma in the current study were patients with Xeroderma pigmentosa and albinism who frequently attended dermatology clinic at KCMC. The Regional dermatology-training centre at KCMC frequently conducts outreach and special targeted programs, which contribute to majority of the patients being referred for surgery at the institution. A biopsy specimen is normally taken to confirm the diagnosis and predict prognosis. This can explain the higher number of squamous cell carcinoma cases in our study.

With regards to tumor differentiation, approximately half of the patients had well-

differentiated tumors. The majority of the undifferentiated malignant tumors were sarcoma and retinoblastoma. This may be attributed by the fact that these tumors tend to have embryonic origin such as retinoblastoma or early childhood presentation within rapid growing cells, which in others cases might have been diagnosed at late stages of the disease [11].

The overall six-month survival rate in this study was high. However, the results are incomparable to findings of a study conducted in South Africa [9] where the survival rate was found to decrease with an increase in the duration of follow up. The higher survival rate observed in this current study is likely to be associated with short duration of follow up.

In our study, most of the patients with well-differentiated malignant tumors survived within six months from the date the specimens were taken. This means patients with undifferentiated malignancies were 13.1 times more likely to die within six months after specimens were taken than with well differentiated ones. This finding conforms to a common trend that well differentiated malignant tumors have higher survival rates as compared to undifferentiated ones [11].

Leukemia had the lowest survival rate due to lack of treatment protocol and medication in our set

up which necessitates referral to Muhimbili National hospital in Dar es Salaam where the treatment was offered. However, the majorities of participants were unable to access care due to financial constraints and could not travel to Dar es Salaam for proper treatment (this came up during phone follow up for survival data). Moreover, delays in seeking and receiving care for patients with malignancy as well as diagnosis challenges may have a major impact on initiation of treatment and hence low survival rate [12].

## 5. CONCLUSION

Retinoblastoma and squamous cell carcinoma are the most common malignant tumors among pediatric malignant tumors biopsied at Kilimanjaro Christian Medical Centre. The overall six-months survival rate is high when early detection of childhood malignancies is practicable.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

The ethical approval was sought and obtained from Kilimanjaro Christian Medical University College Research and Ethics Committee, with the Certificate number 920. The permission to conduct the study at KCMC was sought from the Department of Anatomy and Neuroscience, Department of Pathology and Department of Dermatology. Confidentiality was maintained throughout the research period.

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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