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Research Paper

Patterns of Solid Childhood Neoplasms in Jimma University Medical Center, Southwest Ethiopia – A Histopathologic Approach

A research paper submitted to Department of Pathology, Jimma University; in partial fulfillment of the certificate of specialization program in pathology

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List of Acronyms

- **DFSP:** Dermatofibrosarcoma Protuberance
- **FMoH:** Ethiopian Federal Ministry of Health
- **G.C.:** Gregorian calendar
- **HL :** Hodgkin Lymphoma
- **IACR:** International Association of Cancer Registries
- **IARC:** International Agency for Research on Cancer
- **ICCC-3:** International Classification of Childhood Cancer 3rd Edition
- **ICD-O:** International Classification of Disease for Oncology
- **IHC:** Immunohistochemistry
- **JUMC:** Jimma university Medical Center
- **M:F:** Male to Female Ratio
- **NCCP:** National Cancer Control Program
- **NHL:** Non Hodgkin Lymphoma
- **PI:** Principal investigator
- **SD:** Standard Deviation
- **WHO:** World Health Organization

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Abstract

Introduction: Cancer is among the most common cause of morbidity and mortality worldwide. Children are not spared, however, the burden of childhood cancer is either unknown or neglected in developing countries. Childhood malignancies deserves separate analyses.

Objective:- To determine the patterns of childhood neoplasms in Jimma university medical center, Southwest Ethiopia.

Methods: - A retrospective study design was employed from September 2013 to August 2017. All children under the age of 15 years with histologically confirmed diagnosis of neoplasia were selected, data was collected, cleaned, grouped and analyzed by SPSS version 20.

Results: - There were 140 cases of childhood solid neoplasms among 59.3% were malignancies. The majority of malignancies occurred in age group 0 – 4 years (38.6%) and 10 – 14 years (34.9%).The majority of malignancies (81.2%) were from rural area. The most common extracranial solid malignancies were retinoblastoma (27.7%), soft tissue sarcomas (21.7%), lymphomas (10.8%), nephroblastoma (9.6%) and malignant bone tumors (9.6%).

Discussion and Conclusion: - The magnitude of solid childhood malignancy was increasing during the study period. Overall retinoblastoma, soft tissue sarcomas and lymphomas accounted for around 60% of solid childhood malignancies. Embryonal tumors are found to be common in under 5 children. The frequency of epithelial and malignant melanoma, gonadal germ cell tumors and bone malignancies increases with age. Burkitt's lymphoma, Kaposi's sarcoma and neuroblastomas are less frequent while soft tissue sarcomas are more frequent in the study area.

Key terms: - childhood malignancy/cancer/, childhood neoplasms, benign, malignant

1. INTRODUCTION

1.1. Background of the Study

Cancer /neoplasm/ is defined as an abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of the normal tissues and persists in the same excessive manner after cessation of the stimuli which evoked the change (1). Based on their characteristics neoplasms can be benign or malignant. Even though there is high incidence of cancer in adults; children are not spared (1). Generally, the distribution of different types of cancer – according to age, sex, and organ or involved anatomic sites– revealed variation in pattern (2; 3; 4).

Cancer is among the most common cause of morbidity and mortality worldwide. According to GLOBOCAN, there were 14.1 million new cases and 8.2 million deaths and 32.6 million people living with cancer in 2012 worldwide (5). The mortality rates are 8% to 15% higher in developing countries than the developed countries (6).

According to Ethiopian Federal Ministry of Health, cancer accounts for about 5.8% of total national mortality (6). Based on data from Tikur Anbessa Specialized Hospital; it is estimated that the annual incidence of cancer is around 60,960 cases and the annual mortality is over 40,000 (i.e. 72%) (6). The high rate of mortality is primarily due to different reasons. About 80% patient seek therapy in advanced stage. Despite the higher prevalence of fatal cancers like HCC; problems of availability and accessibility of diagnostics and treatment; poorly structured referral system; scarcity of cancer specialists could result in long waiting time. Thereby these reinforce tumor progression in the meantime (6; 7).

In children above the age of 4 years, cancer is the second most common cause of mortality in United States, following accidents (1). “Even more agonizing than the mortality rate is the emotional and physical suffering inflicted by cancers.” (1). Over one-third of patients experience clinical anxiety and depression. Cancer is also distressing for the family, profoundly affecting both the family’s daily functioning and economic situation (6; 8).

1.2. Statement of the problem

The overall worldwide incidence of childhood cancer increased from 124 in 1980s to 140.6 per million person-years in 2001 – 10 in the aged group 0–14 years (9). Greater than 40% of the African population is under the age of 15 years (10). However, in many low-income and middle-income countries the burden of childhood cancer is either unknown or neglected (9). This is partly because all cancers in pediatric age group account from <1% (in Nigeria) to about 10% (in Rwanda) of the overall cancer burden (3; 11; 12).

Out of over 200,000 childhood cancer diagnosis globally, over 80% are from developing countries (3; 11). Associated with the rapid increase in the youth population in developing countries, this figure is expected to increase to 90% in the next decade (10; 13; 11).

In 2014, over 98 million people were living in Ethiopia (14). Out of the total number, 44.7% are under the age of 15 and 40% is under the age of 5 (15). Approximately 6,000 pediatric cancers are diagnosed yearly in Ethiopia according to data from Tikur Ambesa Hospital (16).

Fortunately, about 70% of childhood cancers are sensitive to treatment with 5 year survival rates of greater than 80% in developed countries (17; 8; 10; 18). The risk of recurrence after treatment within 20 years is approximately 8% (19).

Even though cure is possible in resource poor settings with simple and safe protocols, more than 70% (close to 100% based on some studies) die of the disease due to lack of access to treatment or unaffordability (16; 11; 15). Under funding of the limited pathology services in African countries together with the lack subspecialties in pediatric malignancies; suboptimal and inconsistent tissue processing; and lack of immunohistochemistry (IHC) are associated with the poor outcome of childhood malignancies (10). Moreover the health system of Ethiopia and other low income countries, majorly focuses on infectious diseases and malnutrition (6; 16).

1.3. Justification and Significance of the study

Despite its sensitivity to therapy, there is higher rate of mortality from childhood cancer. In order to tackle this major public health problem, Jimma University, located in South west region of Ethiopia, had established pediatric oncology ward in Jimma University Medical Center (JUMC).

Since oncology centers in Ethiopia are a very recent developments; population based cancer registries are either absent or on their infancy. Studies also show only 11% of sub-Saharan Africans were covered by population-based cancer registries. Considering only high-quality registry data, these value drops to 1% (2).

Based on the World Health Organization's global cancer control strategy; the Ethiopian FMOH launched the first step for effective National Cancer Control Plan (NCCP) for 2015/16 to 2019/20 G.C. The plan aims to decrease Morbidity and mortality from cancer mainly through; (I) Primary prevention; (II) early detection of cancer; and (III) Diagnosis and treatment of cancer (6). Yet the NCCP prioritize and give due attention to cancers common in adulthood.

Thus, this study will provide information regarding the magnitude of the problem by determining the frequency and patterns of solid childhood malignancies according to sex, age groups and residency. Thereby, it will help to define priorities thereby improve the service quality. It will also serves as a baseline study for further research and as an input for the policy makers.

2. LITERATURE REVIEW

Distribution of Childhood malignancies shows variability with sex, age, histologic type, anatomic site and geographic region. The classification, staging and prognostic indicators of childhood malignancies have peculiar characteristics and deserve separate analysis (2; 3; 4; 10; 17).

2.1. Distribution by age and sex

Worldwide the incidence of childhood malignancy is variable with sex, age, regions and histologic type. Overall there is slightly higher male preponderance with M:F ratio of 1.17:1. In India the highest sex ratio (M: F = 1.7:1) was observed in the age group of 5–9 years. In females renal tumors, epithelial tumors¹ and gonadal tumors are more common (9). The Age Specific Rate (AGR) is higher in under five years old children than those aged 5–9 years and 10 – 14 years (16; 9; 17).

2.2. Distribution by Type of tumor

Globally, in the age group 0-14 years; leukemias, CNS tumors and lymphomas are the most common cancers in descending order. Bone tumors and soft tissue sarcomas represent 4.7% each and epithelial tumors for 3.8% (9).

Worldwide in under five years old children leukemias account for 36.1%; CNS tumors for 17.2%; Neuroblastoma for 12.5%; renal tumors for 8.9%; lymphoma for 5.3% of all cancer; Epithelial tumors and melanoma represented for 0.9%. CNS tumors represents 26.3% of cancers in the age group 5 – 9 years and 20% of cancers between age 10 – 14 years (9).

Unlike other regions, in Sub-Saharan Africa Kaposi sarcoma, represent 46% of soft tissue sarcomas in this age group which is associated with HIV epidemics (20; 21). Burkitt's lymphoma is the commonest cancer in West Africa (21; 11).

¹In this study Epithelial neoplasms comprise all other types of carcinoma (e.g. adrenocortical, thyroid, nasopharyngeal, skin), except those occurring in kidney, liver, and gonads.

Table 2-1 Summary of different literatures done on Histopathologic pattern and frequency of solid malignant child hood tumors in different countries (regions) of Africa.

	African Country			
	Nigeria (11)	Ethiopia (16)	Zimbabwe (21)	Egypt (22)
Region	Zaria	Gondar, (Northwest Ethiopia)	National Cancer Registry	east delta of Egypt ²
Study Period	2006 – 2013	2010 to 2013	2000-2009	2004 to 2008
M:F Ratio	1.4:1	2.4:1	1.3:1	1.5:1
Age	---	7 ± 4	---	5.6±3.04
0 – 4 years	57.9%	26.8%	42.3%	60%
5 – 9 years	31.7%	32.4%	29.2%	27.7%
10 – 14 years	10.3%	36.6 %	28.4%	12.3%
Acute Leukemia	12.2%	60.6%	8.9%	---
Lymphoma	20.8% ³	---	13.5%	48.4% ⁴
Burkitt’s Lymphoma	15.7%	---	2%	---
CNS tumors	2.1%	4.2%	6.1%	1.9%
Neuroblastoma	4.7%	7%	---	29%
Renal Tumors	11.5%	18.3%	16.2%	9.7%
Retinoblastoma	34.5%	1.4%	13%	---
Germ cell and gonadal tumors	1.1%	---	---	---
Bone Tumor	0.9%	1.4%	5.5%	4.5%
Hepatic Tumors	0.4%	2.8%	---	1.3%
Other Epithelial tumors	3.3%	---	13.2%	---
Soft tissue Sarcoma	8.4%	4.2%	21.6%	5.2%
Kaposi Sarcoma	1.4%	---	15.7%	---
Rhabdomyosarcoma	7%	4.2%		5.2%
Total number Cases	426	71	1,766	155

²Studied the pattern of malignant solid tumors and lymphomas

³NHL 1.6% + 3.5% HL

⁴NHL 31% + 17.4% HL

Table 2-2 Summary of different literatures done on Histopathologic pattern and frequency of solid malignant child hood tumors in different non-African countries (regions).

	Country			
	Bangladesh (3)	Canada (8)	Korea (23)	Yemen (24)
Region	Dhaka(as part of NICRH ⁵)	National	National	Hadhramout
Study Period	2005 – 2009	1992 – 2006	1993 - 2011	2002 – 2014
M:F Ratio	1.6:1	1.12:1	1.2:1	1.4:1
Age	9.48±2.66	---	---	7.34 ± 4.18
0 – 4 years	30.9%	46%	42.6%	31%
5 – 9 years	31.4%	26.1%	25.2%	35%
10 – 14 years	37.7%	27.9%	32.2%	33.7%
Acute Leukemia	14.3%	32.5%	34.2%	23%
Lymphoma	24.2%	11.2%	10.7%	24%
Burkitt’s Lymphoma	3.6%	---	---	
CNS tumors	3.7%	19.9%	14%	15%
Neuroblastoma	---	7.3%	7.1%	
Renal Tumors	6.8%	5.7%	3.5%	5.4%
Retinoblastoma	17.4%	2.4%	2.7%	4.7%
Germ cell and gonadal tumors	3.7%	3.3%	7.6%	---
Bone Tumor	7.3%	4.5%	5.9%	5.2%
Hepatic Tumors	1.3%	1.5%	2.2%	1.4%
Other Epithelial tumors	19.3%	3.8%	4.2%	13.1%
Soft tissue Sarcoma	---	6.2%	5.5%	5.9%
Others	2%	1.7%	2.3%	2.5%
Total Cases	1,250	13,211	15,113	406

To summarize, both tables (table 1&2) clearly depicted that the pattern of distribution of solid childhood malignancies are different across various geographic region. This implies, the top priority (common) childhood malignancies differ from country to country.

Source: ⁵National Institute of Cancer Research and Hospital(NICRH); a hospital based study

3. OBJECTIVES

3.1. General objective

- ✓ To determine the patterns of childhood neoplasms in Jimma university medical center, Jimma, Southwest Ethiopia between September 2013 and August 2017 G.C.

3.2. Specific objectives

1. To determine the distribution of solid childhood Neoplasms by sex, age groups and address
2. To assess the distribution of solid childhood neoplasms according to their biologic behavior
3. To identify the distribution of solid childhood malignancies by histologic type

4. METHODS AND MATERIALS

4.1. Study area:

Jimma University Medical Center (JUMC) is located in Jimma, Oromia region – in south western part of Ethiopia – 352 km away from the capital Addis Abeba. JUMC is the only referral teaching hospital in this region. It is believed to serve about 15 million people in the south western part of the country with a catchment area of 17,500 km (25).

The department of pathology annually receives over 1,200 biopsy samples from different departments that serve child with malignancy. These includes department of pediatrics, pediatric oncology, surgery, gynecology, ophthalmology, maxillofacial surgery and dermatology. Therefore, the biopsy registry logbook in the department of pathology of JUMC, is a good representative resource that worth utilization.

4.2. Study design and period

A Hospital based cross sectional study design was employed from September 2013 to August 2017 G.C.

4.3 Source population

All children under the age 15 whose biopsy samples had been sent to the Department of Pathology of JUMC in the study period.

4.3.1 Study population

All children aged below 15 years with histologically confirmed diagnoses of solid childhood malignancy from September 2013 to August 2017 G.C. were included in this study.

4.4. Eligibility criteria

4.4. 1 Inclusion criteria:

- ✓ children under the age of 15 years with histologic diagnosis of solid malignant tumor in the study period

4.4.2 Exclusion criteria:

- ✓ Hematologic malignancies
- ✓ Repetitive biopsy reports of the same case e.g. incisional biopsies that are followed by excisional biopsies
- ✓ Unclear histological diagnosis
- ✓ Request forms with one or more undocumented variables

4.5. Study Variables

Dependent variables

- ✓ Histopathologic diagnosis

Independent variables

- ✓ Age
- ✓ Sex
- ✓ Address

4.6. Sampling technique and Data source

Non probability sampling technique (convenience) is used. All children under the age of 15 years, during the 5 years study period, were selected from the biopsy registry log book and copied into a separate format. The original histopathology report was retrieved from hard copy and soft copy archives using the corresponding biopsy accession number in the format. Study subjects were picked according to the histologic diagnosis and inclusion and exclusion criteria. Eligible study subjects were provided a unique study number.

4.7. Data collection

The data were collected using a well prepared checklist according to International Classification of Childhood Cancer, third Edition (ICCC3) and different literatures (2; 4; 26). Study number, basic demographic data, histopathologic group of the solid childhood malignancies together with common histopathologic variants was recorded in the checklist. Collection of data were done by one general practitioners and two pathology residents.

4.8. Data quality control

The collected data was rechecked for completeness and accuracy by the principal investigator according to their biopsy accession number and study ID number.

4.9. Data processing and Analysis

The collected data were coded according to the checklist and entered into software, Statistical Package for Social Sciences (SPSS) statistics software version 20. Specific histological diagnoses were grouped according to ICC3 and coded accordingly. The coded data was rechecked for completeness and accuracy as well as for any exclusion criteria. Concomitantly, specific histologic diagnosis of each study subject was recorded in a separate table in order to trace the specific histopathologic variant.

Tumor distribution is analyzed by age groups, sex, histological types and residency. Mainly descriptive statistics was used in the analysis. Percentages, means, standard deviation, ratios in the form of tables, cross-tabulations and charts are used to describe and compare the findings. Pearson's R is used to assess the degree of association between different variables.

4.10. Ethical Consideration

The research were conducted after approval of the proposal by Research and Ethics Committee of Jimma University, JUMC board and the Department of Pathology. The collected data are kept confidential.

4.11. Operational definition

- **Benign childhood neoplasm** = tumors that are not recurrent or progressive according to ICD-O classification occurring below the age of 15 years (9; 26).
- **Childhood cancers /malignancy/** = defined as a diverse array of malignant or borderline neoplasm in children below the age of 15 years.
- **Rural** = patients living out of Jimma
- **Solid childhood neoplasms** = benign or malignant childhood neoplasms
- **Urban** = Patient living in Jimma city

4.12 Dissemination of results

The findings of the study will be presented to department of pathology and to all concerned bodies such as department of pediatrics, oncology, ophthalmology, surgery, maxillofacial, public health etc. A copy of the study will be given to library periodicals and the department of pathology. Meanwhile room to present on research conferences and publish the paper on scientific journals will be actively sought.

5. RESULT

There were about 5,536 biopsy cases documented in the log book between September 2013 and August 2017. Among these 461 (8.3%) were found to be under 15 years of age. One hundred forty (140) cases were solid neoplasms that comprise of 51.4% male and 48.6% female with a male to female ratio of 1.06:1. The mean age of patients was 8.0 years (SD±4.3). Fourteen percent of the cases had no documented address. Among cases with documented addresses 83.3% live rural setting.

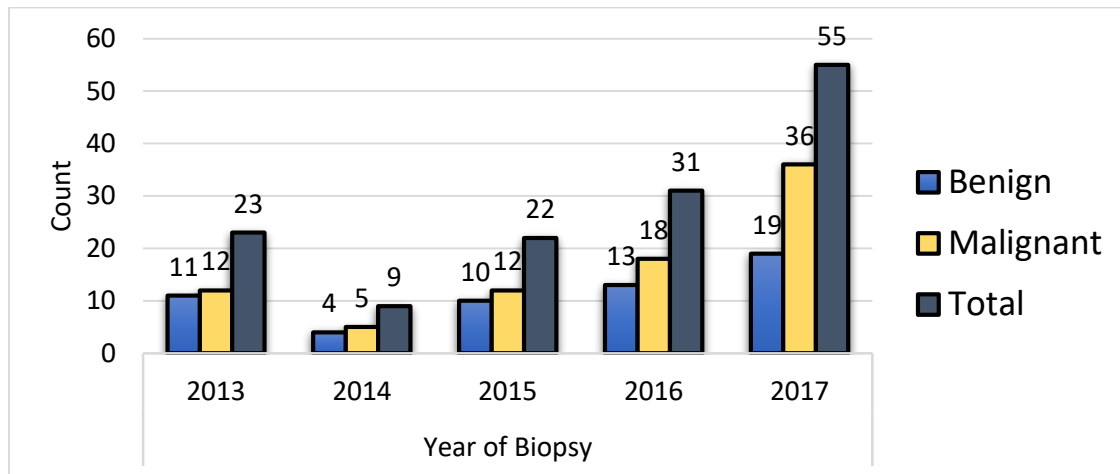


Figure 5-1 Benign and malignant solid childhood neoplasms over 5 years period; in JUMC, Jimma, Southwest Ethiopia between 2013 and 2017 G.C.

The distribution of all solid childhood neoplasms according to different age groups showed that most are between 10 – 14 years 68 (48.6%); followed by 0 – 4 years 42 (30%) and the rest were in the age group 5 – 9 years (Table-3). But in children above the age of ten years, 39 (68.4%) of neoplasms are found to be benign (Table 4).

Generally solid childhood neoplastic conditions are composed of 57 (40.7%) benign; 83 (59.3%) malignant conditions (Figure -2). Malignant tumors account for 76.2% and 73.3% of cases below the age of 5 years and 5 – 9 years age group respectively. Whereas, only 42.6% of case above the age of 10 years are malignant (Table 4). There association between age under 10 years and malignancy ($p = 0.00$).

The age group 10 – 14 years account for 68.4% of all benign tumors (Table 4). The male to female ratio of benign childhood neoplasm is 0.85:1. Among benign solid neoplasms the most common tumors are soft tissue tumors 27 (47.5%); bone tumors 17 (29.8%) and ovarian tumors 5 (8.7 %) mainly comprising of mature cystic teratomas (see table 5).

Table 5-1. Cross tabulation of solid childhood neoplasms and age group; in JUMC, Jimma, Southwest Ethiopia during 2013 –2017

ICCC3 Category	Age category			Total
	Under 5 years	5 – 9 years	10 – 14 years	
lymphoma	1	6	2	9 (6.4%)
Neuroblastoma and other peripheral nerve sheath tumors	1	0	2	3 (2.1%)
Retinoblastoma	17	4	2	23(16.4%)
Renal tumors	6	1	1	8 (5.7%)
bone tumors	1	4	20	25 (17.9%)
Soft tissue and other extraosseous tumors	12	11	22	45 (32.1%)
Germ cell tumors and neoplasms of gonads	2	1	8	11 (7.9%)
epithelial neoplasms and malignant melanomas	2	3	11	16 (11.4%)
Total	42 (30%)	30 (21.4%)	68 (48.6%)	140 (100%)

Table 5-2. Distribution of benign and malignant solid childhood neoplasms according to age groups; in JUMC, Jimma, Southwest Ethiopia between September 2013 and August 2017

Category	Benign	Malignant	Total
Under 5 years	10	32	42
	23.8%	76.2%	100%
5 – 9 years	8	22	30
	26.7%	73.3%	100
10 – 14 years	39	29	68
	57.4%	42.6%	100%
Total	57 (40.7%)	83 (59.3%)	140 (100%)

Table 5-3. Cross tabulation of benign solid childhood tumors and age group; in JUMC, Jimma, Southwest Ethiopia between September 2013 and August 2017

ICCC3 Category	age category			Total
	Under 5 years	5 – 9 years	10 – 14 years	
Soft tissue	7	6	14	27(47.5%)
Hemangioma	3	5	5	
Fibroblastic tumors	1	0	5	
Lipoma	2	0	2	
Other	1	1	2	
bone tumors	0	2	15	17 (29.8%)
Central giant cell granuloma	0	0	5	
Ossifying fibroma	0	0	4	
Osteochondroma	0	0	3	
Others	0	2	3	
ovarian tumors	1	0	4	5 (8.7%)
Mature teratoma	1	0	3	
serous cystadenoma	0	0	1	
epithelial neoplasms	1	0	5	6 (10.5%)
Ganglioneuroma	1	0	1	2 (3.5%)
Total	10 (17.5%)	8 (14%)	39 (68.4%)	57 (99.9%)

The distribution of malignant solid childhood tumors according to age groups showed; 32 (38.6%) belong to the age group 0 – 4 years; 29 (34.9%) in the group 10 – 14 years and 22 (26.5%) in 5 – 9 years age groups (Table 5). The mean age of the patient was 6.89 years (SD±4.17) years. The male to female ratio for solid malignant neoplasms is 1.18:1. Most of the children with malignancy came from the rural areas (81.2%).

Retinoblastoma was the most prevalent malignant neoplasm 23 (27.7%); followed by soft tissue 18 (21.7%); Lymphoma 9 (10.8%); nephroblastoma 8 (9.6%) and bone 8 (9.6%).

Retinoblastoma was the most common malignancy (27.7%) solid childhood malignancy in JUMC during the study period. About 73.9% of cases belonged to under 5 years old age group. The male to female ratio was 1.3: 1.

Malignant soft tissue tumors are the second most common solid childhood malignancy. Among soft tissue sarcomas; 5 (27.8%) were rhabdomyosarcoma, 4 (22.2%) were borderline vascular neoplasms and 3 (16.7%) of the cases were spindle cell sarcomas.

There were 9 cases (10.9%) of Lymphoma. Among 4 (44.4%) cases of Hodgkin Lymphoma (HL) and 4 (44.4%) cases of Non-Hodgkin Lymphoma (NHL) and a single case of Burkitt 's lymphoma were found. Seven out of nine patients with diagnosis of lymphoma were found to be males.

Table 5-4. Distribution of solid childhood Malignancies according to age group; in JUMC, Jimma, Southwest Ethiopia between September 2013 and August 2017

ICCC3 Category	Age category			Count(%)	Mean age (±SD)	M:F
	Under 5 year	5 – 9 years	10 – 14 years			
Retinoblastoma	17	4	2	23(27.7%)	4.1 (±2.32)	1.3:1
Soft tissue sarcomas	5	5	8	18(21.7%)	7.92 (±4.39)	0.8:1
Rhabdomyosarcomas	3	2	0	5		
Spindle cell sarcomas	1	1	1	3		
Borderline Vascular tumors	1	1	2	4		
Lymphoma	1	6	2	9(10.9%)	7.33(±3.16)	3.5:1
NHL	0	2	2	4		
HL	0	4	0	4		
Burkitt's Lymphoma	1	0	0	1		
Nephroblastoma	6	1	1	8 (9.6%)	4.25 (±2.54)	1:1
bone tumors	1	2	5	8 (9.6%)	9.19(±4.40)	1.67:1
Osteosarcoma	0	2	3	5		
Ewing sarcoma	1	0	2	3		
Germ cell tumors and neoplasms of gonads	2	1	4	7 (8.4%)	8.6 (±5.42)	0.2:1
Ovary	1	1	4	6		
Testis	1	0	0	1		
Neuroblastoma	0	0	1	1 (1.2%)		
epithelial neoplasms and malignant melanomas	0	3	6	9 (10.9%)	10.1 (±3.85)	1.5:1
Skin Cancer	0	0	1	1		
Melanoma	0	1	1	2		
Papillary thyroid Ca	0	1	1	2		
Mucoepidermoid Ca (Parotid)	0	1	1	2		
Adenocarcinoma (colon)	0	0	1	1		
Total	32	22	29	83 (100%)	6.89 (±4.17)	1.18:1
M:F for age categories	1.46:1	1.2:1	0.93:1			

6. DISCUSSION

This study provides information about the pattern of solid childhood tumors by age groups, sex, residency, behavior of the tumor and histopathologic types. Among all solid childhood neoplasms, malignant tumors accounts for 59% of cases. According to the biopsy report from the department of pathology, JUMC, the prevalence of solid childhood malignancies was increasing from September 2013 to August 2017 G.C. However the rapid raise of malignant conditions in the last year (2.4 times that of the first year of the study period) is most probably due to the increment patient flow associated with the beginning of pediatric oncology treatment in JUMC.

Benign tumors account for 40.7% of solid childhood neoplasms in this study. About 25% of solid tumors in children under the age of ten years are benign. In contrary 57.4% of solid tumors above the age of ten are benign ($p = 0.00$). Most of benign tumors (68.4%) occur in the age group 10 – 14 year age group.

Benign soft tissue tumors account for 47.5% of benign childhood tumors in this study. Studies also showed that unlike adults benign mesenchymal tumors are common in children (1). The study found out that hemangiomas contribute for nearly half of all benign soft tissue cases. Most of them were excised from head and neck, upper limb and shoulder areas. All of the cases were above the age of 2; among which about 77% of them were above the age of ten years. Unlike other literatures which stated that over one third of childhood vascular tumors are diagnosed before the age of one; all of the benign vascular tumors were above the age of 2 years in this study (27; 1). Cases of fibroblastic and nerve sheath tumors (fibromyxoma, schwannoma and neurofibroma), and lipomas are also commonly seen.

Benign bone tumors accounting for 29.8% of benign solid childhood tumors. The most commonly affected age group were the 10 – 14 years. About 53% of reported bone tumors were central giant cell granulomas and ossifying fibromas of either maxilla or mandible.

Osteochondromas also occur in lesser frequency (17.6%). The higher frequency of benign head and neck childhood neoplasms is probably due to increased patient flow to the solo Maxillofacial Department of JUMC in Southwest region.

Generally the male to female ratio for malignant childhood tumors was 1.18:1.0. This ratio is similar to the global figures (9). The highest sex ratio (M:F = 1.46:1) was observed in the age group 0 – 4 years. Germ cell tumors are common among females while lymphoma and bone tumors are more common in males. Most of the children with malignant tumors came from the rural areas (81.2%) which might be the reflection Ethiopian population distribution (28).

The majority of childhood malignancies occur in age group 0 – 4 years (38.6%) and 10 – 14 years (34.9%). Embryonal tumors such as retinoblastoma, nephroblastoma and rhabdomyosarcomas are more common in under five years old children (72.2%). There were two cases of malignancy in children below the age of one year; immature ovarian teratoma (2 month old) and PNET Ewing sarcoma (5 months old). Whereas in children above the age of 5 years; epithelial and malignant melanoma (all of the cases), malignant bone tumors (87.5%), soft tissue sarcomas (72.2%) and gonadal germ cell tumors (71.4%) are found in more frequency. These results were similar with other studies done in Zimbabwe (21; 17).

The most common malignant tumors were retinoblastoma (27.7%), soft tissue sarcomas (21.7%), lymphomas (10.8%), nephroblastoma (9.6%) and malignant bone tumors (9.6%). These results are relatively similar with those reported from Nigeria where Retinoblastoma (34.5%), Lymphoma (20.8%), nephroblastoma (11.5%), soft tissue sarcomas (8.4%) and Neuroblastoma are common (11). In contrast, in Korea the most common malignancies were CNS tumors (14%), Germ cell tumors (7.6%), Neuroblastoma (7.1%) and bone tumors (5.9%) (23). In Zimbabwe the top three childhood malignancies are soft tissue tumor (21.6%), nephroblastoma (16.2%) and Lymphoma (13.5%) (21). While Lymphoma (24%), CNS tumors (15%) and epithelial tumors (13.1%) are the most common solid childhood malignancies in Yemen (24). These reveals the variability of the distribution of solid childhood malignancies with different geographic regions

Retinoblastoma was the most common childhood tumor affecting 27.7% of children with solid malignancies. It usually afflicts the age group 0 – 4 years (73.9%) with mean of 4.1 years (± 2.32). Most of patients (73.1%) come from rural area. The study result corresponds with the findings observed in Nigeria, where retinoblastoma was found to be the most common malignancies among children (11). In most of the developed countries retinoblastoma accounts for 2.5 - 4% of all childhood cancers (8; 21). The frequency of retinoblastoma in this study is higher than records of most countries (9; 3; 8; 21; 23; 24). These could be due to the higher

patient flow towards JUMC Ophthalmology department that serves as the only referral center in the region over the study period; accompanied by the initiation of Pediatric Oncology treatment.

Soft tissue tumors account for 21.7% of all childhood malignancy. The frequency of soft tissue sarcomas is less than 10% in most studies (21; 9). Among malignant soft tissue tumors rhabdomyosarcomas contribute for 27.8% of cases in this study. All cases of rhabdomyosarcomas were found in children below the age of 10 years. Embryonal and alveolar histologic types were reported from biopsies taken from thigh, bladder and Oropharyngeal mass. Borderline soft tissue tumors such as hemangioendothelioma, hemangiopericytoma, solitary fibrous tumor and infantile myofibromatosis account for 38.9% childhood soft tissue sarcomas in this study. Cases of Spindle cell sarcomas (16.7%) include DFSP and Fibromyxoid sarcoma. Unlike reports of childhood malignancies in Sub-Saharan Africa, Kaposi sarcoma is not common in the study area (9; 21).

Lymphoma was the third most common malignancy in this study. Two third of cases afflict the age group 5 – 9 years followed by 10 – 14 years age group. Similarly study in Zimbabwe showed most cases of lymphoma occurred in age group 5 – 9 and 10 – 14 years (21). There were only 9 cases (10.8%) of lymphomas comprising 4 cases of HL and NHL each. In contrast to reports from West Africa, where Burkitt's account for over 15% of all childhood malignancies, there is low incidence of Burkitt's lymphoma in this study (11; 21). However the issue of small sample size cannot be ignored.

Bone tumor contributes for eight cases (9.6%) of all childhood malignancies in this study. The mean age was 9.19 (SD±4.40). Five out of eight cases belonged to osteogenic sarcoma (All of them were above the age of 5). The rest of the cases were Ewing sarcoma.

There were also eight cases of nephroblastoma (9.6%) in this study. Reports showed 98% of patients with nephroblastoma are younger than 10 years (29). Likewise, in this study, seven out of the eight cases were under the age of 10 years with peak age of 2 – 5 years. The mean age at diagnosis was 3.4 years and 5.1 years for males and females respectively. However other studies showed mean age of 3.1 and 3.6 years for males and females respectively (29). The marked difference in female group is principally due to the small sample size composed of three under five female children admixed with a single case of a 10 years old female patient.

Limitation

- Leukemia, CNS and intrathoracic tumors and are not included in the study due to lack of sample flow and inconsistency of the sample flow over the study period. As a result, only extracranial solid childhood tumors are included in this study. The reader should also take into consideration that most of the frequencies and percentages used for comparison are taken from literatures comprising these tumors.

7. CONCLUSION

There are increasing cases of solid childhood neoplasms over the study period. Generally three out of five cases are malignant solid tumors. Approximately three quarter of solid tumors in under 10 years old children are malignant. In contrast, more than half of solid tumors in above 10 years old children are benign. Early childhood (0 – 4 years) and periadolescence (10 – 14 years) are age groups with the highest peaks of malignancy. Embryonal tumors – retinoblastoma, nephroblastoma and rhabdomyosarcomas – are common in under 5 children. While as children age epithelial and malignant melanoma, gonadal germ cell tumors and bone malignancies with succeeding years.

From the findings, Retinoblastoma, soft tissue sarcomas and lymphomas accounted for more than half (3/5) of solid childhood malignancies in this study. Unlike the low frequency of soft tissue sarcomas reported in most studies; there is higher proportion of cases in the study area. On the other hand Burkitt's lymphoma, Kaposi's sarcoma and neuroblastomas are less frequent as compared to other countries. Further prospective studies with set values have to be done in order to include all childhood malignancies.

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9. Annex

Check list

Table 9-1. Check list of the demographic and major histopathologic diagnostic groups according to the International Classification of Childhood Cancer, 3rd edition (ICCC3) (4; 2; 26)

General Information		Year of Dx _____ Number of biopsies seen annually _____ Biopsy No _____
Histologically confirmed diagnosis _____ _____		
S. No.	Variable	Code and response
1.	Age	1. 0 – 4 years 2. 5 – 9 years 3. 10 – 14 years
2.	Sex	1. Male 2. Female
3.	Place of residency	1. Urban 2. Rural

Morphologic Type of tumor	Code
1. Lymphomas and reticuloendothelial neoplasms	1
1.1. nonHodgkin lymphoma except Burkitt	1
1.2. Hodgkin lymphomas	2
1.3. Burkitt lymphoma	3
1.4. Miscellaneous lymphoreticular neoplasms	4
1.5. Unspecified lymphomas	5
2. Neuroblastoma and other peripheral nervous cell tumors	2
2.1. Neuroblastoma and ganglioneuroblastoma	1
2.2. Other peripheral nervous cell tumors	2
3. Retinoblastoma	3

4. Renal tumors	4
4.1. Nephroblastoma and other nonepithelial renal tumors	1
4.2. Renal carcinomas	2
4.3. Unspecified malignant renal tumors	3
5. Malignant bone tumors	5
5.1. Osteosarcomas	1
5.2. Chondrosarcomas	2
5.3. Ewing tumor and related sarcomas of bone	3
5.4. Other specified malignant bone tumors	4
6. Soft tissue and other extraosseous sarcomas	6
6.1. Rhabdomyosarcomas	1
6.2. Fibrosarcomas, peripheral nerve sheath tumors, and other fibrous neoplasms	2
6.3. Kaposi sarcoma	3
6.4. Other specified soft tissue sarcomas _____	4
6.5. Vascular neoplasm	5
7. Hepatic Tumors	7
7.1. Hepatoblastoma	1
7.2. Hepatocellular carcinoma	2
8. Germ cell tumors and neoplasms of gonads	8
8.1. Malignant gonadal germ cell tumors	1
8.2. Gonadal carcinomas	2
8.3. Other and unspecified malignant gonadal tumors	3
9. Other malignant epithelial neoplasms and malignant melanomas	9
9.1. Thyroid carcinomas	1
9.2. Nasopharyngeal carcinomas	2
9.3. Malignant melanomas	3
9.4. Skin carcinomas	4
9.5. Other and unspecified carcinomas	5
10. Others _____	10
11. CNS Tumors and miscellaneous intracranial and intraspinal neoplasms	11

Table 9-2 Age distribution of common small round blue cell tumors in JUMC, Jimma, Southwest Ethiopia between 2013 and 2017

	Under age of 5 year	Above age 5 year
Retinoblastoma	17	6
Nephroblastoma	3	2
Rhabdomyosarcoma	6	2
Ewing sarcoma	1	2
Neuroblastoma	0	1
Total	27	13

Table 9-3 Age distribution of common malignant childhood neoplasms in JUMC, Jimma, Southwest Ethiopia between 2013 and 2017

Under age of 5 years	5 – 9 years	10 – 14 years
Retinoblastoma (17)	Lymphoma (6)	Soft tissue sarcomas (8)
Nephroblastoma (6)	Soft tissue sarcomas (5)	epithelial neoplasms and malignant melanomas (6)
Soft tissue sarcomas (Rhabdomyosarcomas) (5)	Retinoblastoma (4)	bone tumors (5)