ORIGINAL ARTICLE

PATTERN AND OUTCOMES OF CHILDHOOD MALIGNANCIES AT UNIVERSITY OF GONDAR HOSPITAL, ETHIOPIA : NONCONSECUTIVE CASE SERIES

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ABSTRACT

Background : *Childhood malignancy is an increasingly significant problem in low income countries. Despite the burden of the disease, little is known about patterns and outcomes of childhood malignancies in Ethiopia..*

Objective : *To describe the pattern and outcome of childhood malignancies at a teaching hospital in Northwest Ethiopia*

Methods*: A nonconsecutive case series of children aged ≤14 years admitted with the diagnosis of any malignant cancer to University of Methods: A nonconsecutive case series of children aged ≤14 years admitted with the diagnosis of any malignant cancer to University of Gondar Hospital from September 2011 to September 2014. University of Gondar Hospital is a tertiary care teaching and referral hospital in northwest Ethiopia.*

Results*: The total number of admissions to the Pediatrics ward during the study period was 4,400. Medical records of 142 cases were reviewed and 110 (2.5%) cases were selected for the study. 67.3 % of them were male. Patient age ranged from 5 months to 14 years (median 6.5 years, IQR 3.2-12.0 years). The peak age at diagnosis was 10 -14 years. Acute lymphoblastic leukemia was the commonest type of malignancy, comprising 30% of cases. Final diagnosis was made by fine needle aspiration for forty-six cases (41.8%). Thirty-nine percent abandoned treatment and 11% died. Multi-organ failure secondary to severe sepsis was the immediate cause of death in 33% of deaths.*

Conclusion and recommendation: *Malignancies represent a significant proportion of admissions. Acute lymphoblastic leukemia is the commonest type of malignancy. Further research is required to determine best practices for the management of pediatric malignancies.*

1. Background

An estimated 80-85% of pediatric cancer cases occur in the global south, where the 5-year survival can be less than 10% (1). Despite the tremendous burden that these diseases place on health care systems, relatively little is known about pediatric malignancies and the manner of presentation in Ethiopia. Africa bears a great burden of childhood cancer. Cancer is now curable in developed countries as survival rates approach 80%, but in Africa,>80% of children still die without access to adequate treatment(2) .The costs of treatment, diagnostic investigations, meals and hospital stay are borne by patients and their families. Because no coordinated cancer registry exists in Ethiopia, few studies have explored the incidence of pediatric malignancies and to our knowledge none have reported outcomes from our region. This study

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aimed to describe baseline characteristics for patients with childhood malignancies diagnosed at University of Gondar Hospital (UGH) in Northwest Ethiopia. UGH is a tertiary care government-funded referral hospital with a catchment area of 5 million people (3). The department of pediatrics and child health is the only site treating children with malignancies in northwestern Ethiopia. Children with malignancy receive chemotherapy based on protocols for treatment of malignancies in our country. In addition, surgery will also be done for non-advanced cases of solid tumor. Different types of supportive cares are also given.

2. Methods

A nonconsecutive case series was performed on medical records of one hundred ten cases. One physician retrieved the admission registration book for children aged ≤ 14 years with diagnosis of malignancy admitted to UGH between September 2011 and September 2014. Cases for whom a medical record was available and either a histopathologic or radiographic diagnoses of malignancy was made were included in the study. Cases who had presented with a relapse or for a follow-up visit were excluded from analysis. Data was collected using a pretested data extraction form. Hand-written data was checked for completeness and accuracy and transcribed into a computer database. Means and standard deviation or medians and inter-quartile ranges were calculated for continuous variables. Frequency percentages were calculated for categorical variables. All statistics were generated using Epi-info version 7.0. Ethical approval for this study was obtained from the UGH internal review board.

3. Results

155 patients with malignancies were identified from the pediatric ward's admission-discharge log books.142 cases had medical records available; the remaining 13 charts had been lost. 32 cases did not fulfill the inclusion criteria 110 cases were selected for analysis.

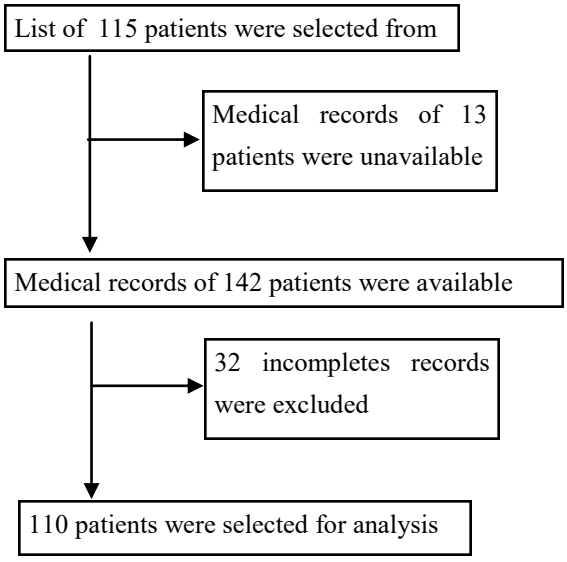

Figure 1. Study Flow

Of 110 cases, 74 (67.3%) were males (Figure 2). Patient age at diagnosis ranged from 5 months to 14 years, 36.4% of cases presented between 10-14 years, 30% presented between 1-4 years, 29% between 5-9 years and 4.5% presented <1 year. The median age was 6.5 years (IQR: 3.25-12).

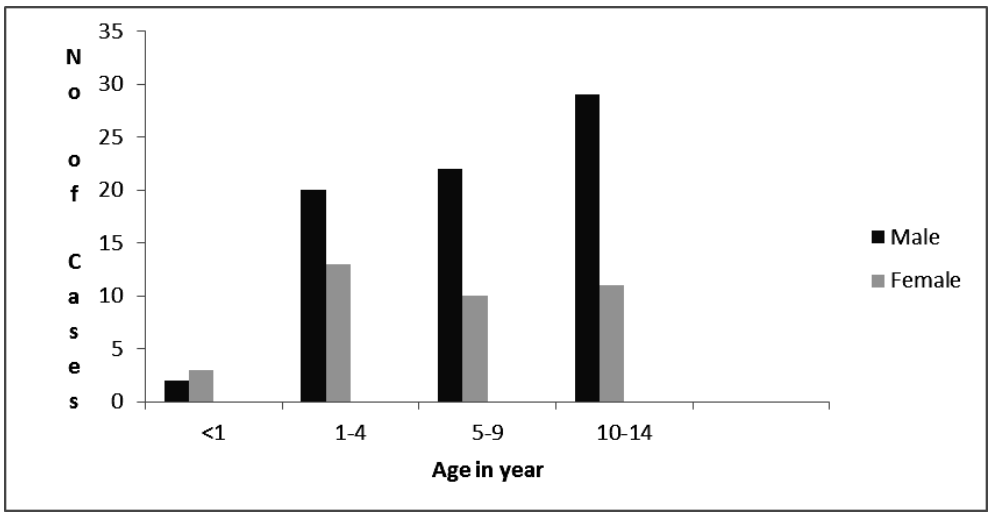

Figure 2: Gender distribution by age group among children with childhood malignancies at University of Gondar, September 2011-september 2014

Female patients were younger at diagnosis, with median age of 5.0 years (IQR: 2.0-11.5) versus 7.0 years (IQR: 4.0-12.0) for males. Most patients came from rural areas (56.4%). 26% of patients presented with severe acute malnutrition (weight for height less than 70%, mid upper arm circumference less than 11 cm or edema of both feet) 22% had moderate acute malnutrition (weight for height between 80-70%, MUAC 11-12.5) and 20% were under weight (weight for age less than 5th centile) (Figure 3). 71% presented with duration of illness of more than 30 days before diagnosis. Patients from rural areas presented with a mean duration of illness of 3.3±4.2 months while the duration of illness for patients from urban area was 2.7 ±4.3 months.

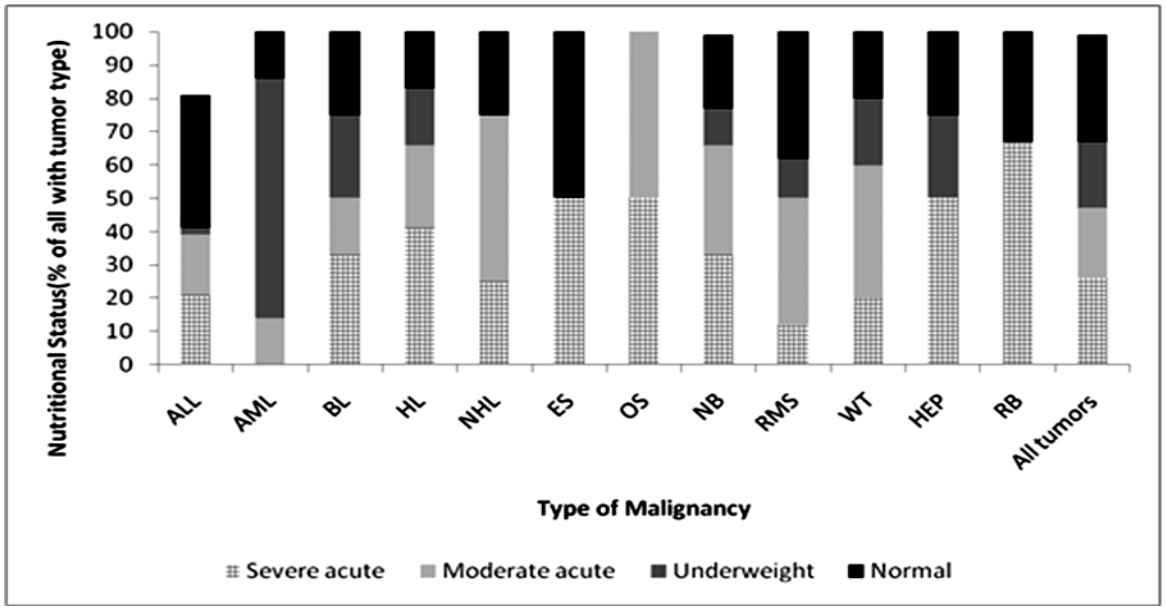

Figure 3: Nutritional Status of children diagnosed with childhood malignancy at University of Gondar, September 2011-September 2014

Among clinically diagnosed malignancies, acute lymphoblastic leukemia (ALL) accounted for the majority (37%), followed by Hodgkin lymphoma (HL) and rhabdomyosarcoma (RMS) (10% each) of the cases. Acute myelogenous leukemia (AML) and malignant bone tumors were not considered clinically (Table 1).

Table 1: Demographic characteristics of patients with malignancies among children age ≤ 14 years admitted to Gondar University Hospital, September 2011-September 2014

	Age (years)				
Sex	**< 1**	**1-4**	**5-9**	**10-14**	**Total**
Male	2(1.8%)	20(18%)	22(20%)	29(26%)	73(66%)
Female	3(2.7%)	13(12%)	10(9%)	11(10%)	37(34%)
Total	5(4.5%)	33(30%)	32(29%)	40(36%)	110(100%)

Final diagnosis was made by fine needle aspiration(FNAC) for 46 cases (42%), Bone marrow aspiration (BMAC) for 39 cases (35.4%), tissue biopsy for 11 cases (10%) and imaging modalities for 27 cases (24.55%). A combination of FNAC and imaging were used in 20 cases (18.18%), whereas biopsy and Imaging were used for 2 cases (1.82%). 7 cases (6.4%) were diagnosed after combining imaging results and clinical considerations (Table 2).

Table 2: Modalities used to diagnose childhood malignancy at Gondar University Hospital, September 2011-September 2014

Type	Method of diagnosis (%)				
	BMAC	FNAC	Biopsy	Imaging	Clinical
ALL	30 (90)	2	--	--	41(37)
AML	7(100)	--	--	--	--
BL	--	10 (83)	--	--	--
HL	--	9 (75)	--	--	12(11)
NHL	--	2 (50)	1 (25)	--	9(8)
ES	--	1 (50)	1 (50)	--	--
OS	--	2 (100)	--	--	2(1)
NB	--	8 (89)	1 (11)	--	9(8)
RMS	--	3 (38)	4 (50)	1 (12.5)	11(10)
WT	--	3 (60)	1 (20)	1 (20)	7(6)
HEP	--	4 (100)	--	--	3(2)
RB	--	--	3 (100)	--	3(2)
CNST	--	--	--	3 (100)	3(2)
PTC	--	2 (100)	--	--	1(0.9)
MISC	1 (25)	1 (25)	--	--	9(8)
Total	38	47	11	5	110(100)

ALL=acute lymphoblastic leukemia; AML=acute myelogenous leukemia; BL=Burkitt's lymphoma; BMAC=bone marrow aspiration cytology;FNAC=fine needle aspiration cytology;NHL=non-Hodgkin's lymphoma; HL= Hodgkin's lymphoma; OS=osteosarcoma; ES=Ewing's sarcoma; NB=neuroblastoma; RMS=rhabdomyosarcoma; WT=Wilm's tumor; HEP=hepatoblastoma; RB=retinoblastoma; CNST=central nervous system tumor; PTC=papillary thyroid carcinoma

Plain X-ray was the most frequently used imaging method, in 98 cases (89.09%) of radiographically-confirmed cases.

Among pathologically diagnosed malignancies, leukemias, accounted for 33 cases (30%). Among the leukemias, ALL was more prevalent than AML (30% vs 6.4%). Lymphomas were the second most prevalent malignancies, accounting for 28 cases (25.4%). Burkitt Lymphoma and Hodgkin Lymphoma were the most common type of lymphomas, each accounting for 11% of the malignancies, followed by Non-Hodgkin Lymphoma 3.6%.

From the total of 110 patients 104 (94.5%) were offered treatment in the hospital and 5 (4.5%) were referred to higher treatment center. Of those who started treatment in the hospital 21 (20%) patients were discharges against medical advice, 18(20%) patients absconded before being formally discharged, 26(25%) patients did not appear for the scheduled follow up care and treatment. Only 2(1.8%) patients were declared cured and

discharged from care. Until the time of completion of data collection 19(18%) patients were on treatment. 12(11%) patients died during their hospital stay. Multi-organ failure secondary to severe sepsis was considered the immediate cause in 4(33%) cases, and respiratory failure due to brain metastasis was considered for 3(25%) cases.

4. **Discussion**

In this study malignancies accounted for 2.5% of all admissions to the pediatric ward this figure has increased from a previous report in 1992 (0.66%,(4)) and is consistent with a similar report in 2010 (2.8%, (5)). The figure is comparable to that for other Ethiopian hospitals (3.1%,(6)) and a hospital in Ghana(1.6%). Malignancies in our study disproportionately affected males in 2:1 ratio. This finding agrees with other studies from the global south (4, 6-9). This gender disparity is believed to reflect cultural and economic factor elsewhere (10). This ratio was found to be lower(1.14:1) in developed countries (11).

In our study, more than half of the patients were from rural areas. This agrees with findings from other studies in Africa (6, 12) and may reflect the underlying population distribution; in northwest Ethiopia, 85% of the population lives in a rural area.

On average, patients in our study were sick 3 months prior to diagnosis of malignancy, and that delay ranged as high as 2 years. Almost three quarters presented with duration of illness of more than a month before diagnosis, and a longer wait time was observed among rural patients. This may be due to lack of transportation, lack of money to get transportation and delay in early referral of patients from rural areas. The time to diagnosis in our study was lower than that reported in other Ethiopian hospitals (23 weeks (6)). In our study, the highest number of malignancies was detected among children age 10-14 years. This differs from studies in Ethiopia, Nigeria, India and Australia, in which peak incidence occurs from 0-4 years (4, 6, 11, 13). This may be due to the difference in the cancer types among different countries.

In our study almost half of patients had moderate or severe wasting and this high rate of wasting might contribute to poor outcome in children with malignancies. Cases with malnutrition have lower survival rates than well - nourished patients(14).Nutritional status may have a role in the carcinogenesis by causing immune deficiency, also by inadequate intake of antioxidants(15).

In our study 87% of patients had cytopathologic or histopathologic confirmation of malignancy. The relatively high proportion may be because our center is a teaching and referral hospital where relatively pathological service is better than other centers in the country. In a Namibian study a rate of 91% were recorded (16). Australian study showed that 95.4% of childhood cancers were histologically verified (11). Studies have shown that

CT scan have affected the management of about 30% of patients with cancer. Most of the children with cancer living in developing countries could not profit from those advanced diagnostic facilities because of the cost (10). In our study only 10% of the patients had CT scan. This low rate of imaging among cancer patients is mainly due to economical reason.

In our study, leukemias accounted for 30% of malignancies. This finding differs from other studies in Ethiopia, which reported lymphomas and Wilms tumor as most prevalent malignancies (4) (6). Lymphomas, and in particular Burkitts lymphoma, are the most commonly encountered malignancies elsewhere in Africa (8, 17, 18). This finding is consistent with findings from developed countries (11, 19, 20).

The second most common observed malignancy was lymphoma (25.4%), in agreement with reports from Latin America and Asian countries(13, 21) and in contrast to developed countries, where CNS tumors were reported to be more common than lymphomas (22, 23) .Burritt and Hodgkin Lymphoma were the most commonly encountered lymphomas, followed by other Non Hodgkin Lymphoma. This dominance of Burkitt's lymphoma among childhood lymphomas parallels other findings from Africa (8, 17, 18). In the third place of frequency neuroblastomas were more common than African countries (6, 17). The third most common childhood cancers reported from Sudan and Nigeria were Nephroblastomas (17, 18), whereas in developed countries, lymphomas were in the third place (13, 22, 23) . The prevalence of Wilms tumor and retinoblastoma as evident in our study is in accord with the pattern from other studies from Africa and USA, (18, 22). This shows that these tumors are prevalent in children less than 5 years of age. Besides a two year study (2005-2006) at Black Lion Hospital, Addis Ababa showed the common malignant cancers in children in descending order of frequency were Wilm's tumor, leukemias, lymphomas and rhabdomyosarcoma (6).

There were only 3 cases (2.73%) of CNS tumors; all of them were diagnosed clinically and using CT scan finding. This low frequency of CNS tumors is mainly because our center did not have the neuroimaging and neurosurgery facilities required for diagnosis. This finding is in agreement with other findings from resource-poor countries (18, 24).

In our study, 11% of patients died during admission. ALL, RMS, and retinoblastoma in aggregate accounted for three-quarter of inpatient death. Multi-organ failure secondary to severe sepsis, respiratory failure secondary to CNS metastasis, and status epilepticus were described as the proximate causes of death in three-quarters of cases. The study under-estimates overall mortality, since almost 65% of patients left the hospital before treatment was complete or were lost to

follow-up. The relatively high rate of attrition is likely explained by the large cost of hospital stay for cancer patients, the expensive investigation cost and unavailability of chemotherapeutic drugs in the hospital pharmacy. Further investigation is required to determine the reasons for attrition and the true short- and long- term mortality among patients with pediatric malignancy.

This study has several limitations. First ,patient records could not be retrieved for 9% of study patients. Although a systemic connection between diagnosis and loss is unlikely, incomplete records likely affect the accuracy of our report. Second, histopathologic diagnosis was not performed for 15% of the study patients, forcing us to rely on clinical diagnoses made by the admitting team. This may affect the accuracy of the figures. Third, a large proportion of patients were discharged against medical advice, disappeared from the treatment center, or lost to follow-up. This likely affected the precision and accuracy of our mortality analysis.

Pediatric malignancies are important and increasing cause of admission to our hospital. Children with cancer at our facility are more likely than those in other African centers to have leukemias and present between the ages of 10-14 years. Strategies are required to decrease abandonment of treatment, improve supportive care, and establish appropriate follow-up among children with cancer at our hospital. A cancer registry in Ethiopia is essential to promote research and best practices between treating hospital.

REFERENCE

1. Ribeiro RC, Steliarova-Foucher E, Magrath I, Lemerle J, Eden T, Forget C, et al. Baseline status of paediatric oncology care in ten low-income or mid-income countries receiving My Child Matters support: a descriptive study. The lancet oncology. 2008;9(8):721-9.
2. Hadley LG, Rouma BS, Saad-Eldin Y, editors. Challenge of pediatric oncology in Africa. Seminars in pediatric surgery; 2012: Elsevier.
3. Central Statstical Agency of Ethiopia AA. Population census commission,Statstical reports of the census for Amhara region. 2007.
4. Teka T. Childhood malignancies in an Ethiopian teaching hospital. Ethiopian medical journal. 1992;30(3):159-62.
5. Gordon DM, Frenning S, Draper HR, Kokeb M. Prevalence and burden of diseases presenting to a general pediatrics ward in Gondar, Ethiopia. Journal of tropical pediatrics. 2013;59(5):350-7.

6. Moges T. ETHIOPIAN JOURNAL OF ETHIOPIAN JOURNAL OF PEDIATRICS AND CHILD PEDIATRICS AND CHILD HEALTH.
7. Ekanem IA, Asindi AA, Ekwere PD, Ikpatt NW, Khalil MI. Malignant childhood tumours in Calabar, Nigeria. African journal of medicine and medical sciences. 1992;21(2):63-9.
8. Pearce MS, Parker L. Childhood cancer registrations in the developing world: still more boys than girls. International journal of cancer Journal international du cancer. 2001;91 (3):402-6.
9. Ocheni S, Okafor CO, Emodi IJ, Ibegbulam OG, Olusina DB, Ikefuna AN, et al. Spectrum of childhood malignancies in Enugu, Nigeria (1999-2004). African journal of medicine and medical sciences. 2005;34(4):371-5.
10. Yaris N, Mandiracioglu A, Buyukpamukcu M. Childhood cancer in developing countries. Pediatric hematology and oncology. 2004;21(3):237-53.
11. Baade P, Youlden D, Valery P, Hassall T, Ward L, Green A, et al. Trends in incidence of childhood cancer in Australia, 1983–2006. British journal of cancer. 2010;102(3):620-6.
12. Agugua NE, Okeahialam T. Malignant diseases of childhood seen at the University of Nigeria Teaching Hospital (UNTH), Enugu, Nigeria. East African medical journal. 1986;63 (11):717-23.
13. Swaminathan R, Rama R, Shanta V. Childhood cancers in Chennai, India, 1990-2001: incidence and survival. International journal of cancer Journal international du cancer. 2008;122 (11):2607-11.
14. Reilly JJ, Odame I, McColl JH, McAllister PJ, Gibson BE, Wharton BA. Does weight for height have prognostic significance in children with acute lymphoblastic leukemia? The American journal of pediatric hematology/oncology. 1994;16(3):225-30.
15. Good RA, Lorenz E. Nutrition and cellular immunity. International journal of immunopharmacology. 1992;14(3):361-6.
16. Wessels G, Hesseling PB. Incidence and frequency rates of childhood cancer in Namibia. 1997.
17. Agboola AO, Adekanmbi FA, Musa AA, Sotimehin AS, Deji-Agboola AM, Shonubi AM, et al. Pattern of childhood malignant tumours in a teaching hospital in south-western Nigeria. Medical Journal of Australia. 2009;190(1):12.
18. Haroun HM, Mahfouz MS, Elhaj AM. Patterns of childhood cancer in children admitted to the institute of nuclear medicine, molecular biology and oncology (INMO), Wad Medani, Gezira state. Journal of family & community medicine. 2006;13(2):71.

19. Kebudi R. Pediatric oncology in Turkey. Journal of pediatric hematology/oncology. 2012;34 Suppl 1:S12-4.
20. Li J, Thompson TD, Miller JW, Pollack LA, Stewart SL. Cancer incidence among children and adolescents in the United States, 2001–2003. Pediatrics. 2008;121(6):e1470-e7.
21. de Camargo B, de Oliveira Santos M, Rebelo MS, de Souza Reis R, Ferman S, Noronha CP, et al. Cancer incidence among children and adolescents in Brazil: First report of 14 population-based cancer registries. International Journal of Cancer. 2010;126(3):715-20.
22. Ross JA, Olshan AF. Pediatric cancer in the United States: The children's oncology group epidemiology research program. Cancer Epidemiology Biomarkers & Prevention. 2004;13 (10):1552-4.
23. Michel G, Von Der Weid N, Zwahlen M, Redmond S, Strippoli MP, Kuehni C. Incidence of childhood cancer in Switzerland: the Swiss childhood cancer registry. Pediatric blood & cancer. 2008;50(1):46-51.
24. Shehu U, Adegoke S, Abdulsalam U, Ibrahim M, Oyelami O, Adeodu O. Pattern of childhood malignant tumours in two tertiary teaching hospitals in Nigeria: comparative study. Nigerian Journal of Paediatrics. 2013;40(2):175-8.