

# **Acute Malnutrition among Children at Time of Cancer Diagnosis at a Paediatric Oncology Centre in South West Uganda**

Jeanine Ndayisenga,MD<sup>1,2</sup>, Stella Kyoyagala,MD<sup>1,2</sup>, Daniel Atwine ,PhD<sup>3</sup>, Kevin R Schwartz, MD<sup>4</sup>; Francis Oriokot, MD<sup>1,2</sup>, Barnabas.Atwiine, MD<sup>1,2</sup>

<sup>1</sup> Department of Pediatrics and Child Health, Mbarara University of Science and Technology, P.O BOX 1410, Mbarara, Uganda

<sup>2</sup> Department of Paediatrics and Child Health, Mbarara Regional Referral Hospital, Mbarara, Uganda.

<sup>3</sup>Department of Clinical Research, SOAR Research Foundation, P.O.BOX 1596, Mbarara, Uganda

<sup>4</sup>Department of Pediatrics, Massachusetts General Hospital, Boston, MA

## **Correspondence to:**

Jeanine Ndayisenga, MD, Department of Pediatrics and Child Health, Mbarara University of Science and Technology, Mbarara Regional Referral Hospital, Mbarara, Uganda.Tel.: +257-79983952/+257-61837821,Email: jeaninendayisenga24@yahoo.fr

Text word count : 2919

Abstract word count: 249

Brief running title:Acute malnutrition and childhood cancer in Uganda

Key words: Acute malnutrition, childhood, cancer, Uganda

Tables: 2

Figures: 0

Abbreviations	
MRRH	Mbarara Regional Referral Hospital
WFL/H	weight-for-length/height
BMI	Body Mass Index
cOR	Crude odds ratio
CI	Confidence interval

## Abstract

**Background:** Acute malnutrition is a frequent comorbidity in children with cancer and is associated with poor cancer treatment outcomes. This study describes the prevalence of acute malnutrition and its predictors at time of cancer diagnosis at Mbarara Regional Referral Hospital (MRRH).

**Methods:** This was a retrospective chart review of children <15 years of age at diagnosis of cancer seen at the Children's Cancer Unit of MRRH between May 2017 and May 2019. Using a data extraction tool, information regarding demographics, anthropometry at admission and cancer diagnosis was extracted from the children's medical records. Descriptive statistics and logistic regression analysis were used to determine the prevalence and patterns of acute malnutrition among children at diagnosis of cancer and the factors associated with acute malnutrition, respectively. The study was approved by the Mbarara University of Science and Technology Research and Ethics Committee.

**Results:** One hundred and thirty-three children were included in the study with a mean age of 6.6 years (SD 3.9). 54.9% of the children were male. Overall, 46 (34.6%) of subjects had acute malnutrition at time of cancer diagnosis. Of these, 25 (54.3%) had moderate acute malnutrition and 21/46 (45.7%) had severe acute malnutrition. The factors independently associated with acute malnutrition after multivariate logistical regression analysis were age >5 years ( $p < 0.0001$ ) and reduced appetite ( $p = 0.002$ ).

**Conclusion:** Acute malnutrition is common among children with cancer at diagnosis, especially in older children and those reporting poor appetite. Nutrition assessment and care should be incorporated into routine childhood cancer care to improve cancer treatment outcomes.

**Key words:** Acute malnutrition, childhood, cancer, Uganda

## Background

Globally, about 400,000 children under 16 years of age suffer from cancer each year, the majority of whom live in the developing world, where childhood acute malnutrition is common in the general population. Consequently, acute malnutrition is a common co-morbidity among children at diagnosis of cancer. Studies in the developing world show that about one third (31%, 33% and 38%) of the children in Ghana, Casablanca and India, respectively, have severe acute malnutrition at cancer diagnosis. The causes of these high rates of acute malnutrition are multiple: delayed diagnosis, low socio-economic status, reduced food intake, the presence of other disease comorbidities and the specific cancer types.

Malnutrition has a negative effect on cancer treatment outcomes. Children with acute malnutrition tend to suffer more cancer treatment side-effects and require dose delays and/or reductions, resulting in poorer outcomes compared to their well-nourished counterparts. Our experience at Mbarara Regional Referral Hospital (MRRH) in South West Uganda is that many

children present with acute malnutrition at the time of diagnosis and yet its prevalence and associated factors have not been previously reported. This study was carried out to identify the children most likely to have acute malnutrition at diagnosis of cancer in order to inform policies and practices for improved pediatric cancer care.

## **Methods**

We conducted a retrospective chart review of all children diagnosed with cancer and admitted at a specialized paediatric cancer unit of MRRH between May 2017 and May 2019. This unit, headed by a paediatric oncologist, offers free cancer diagnosis and treatment to children from West and Central Uganda. At the time of the study, weights and heights/lengths of children after diagnosis of cancer were performed routinely at admission and subsequently at each visit by experienced nurses mainly for use to calculate dosing for chemotherapy, but not necessarily to assess and manage malnutrition. At the time, the oncology clinic did not have a specific protocol for assessing and treating acute malnutrition among children at diagnosis of cancer.

We used a structured and pre-tested data abstraction tool to collect data from medical charts of children aged below 16 years with a confirmed cancer diagnosis on record. Data collected included: age at diagnosis, body weight and length/height, presence of edema, duration of symptoms, presence of anorexia at admission, and cancer diagnosis. The socio-demographic characteristics of the children and their caregivers were also extracted.

A child was considered to have acute malnutrition if he/she had weight-for-length/height (children <5 years) or Body Mass Index-for-age (for children aged  $\geq 5$  years) Z-score  $< -2SD$  below the mean for age and gender. A child was classified with moderate acute malnutrition if his/her weight-for-length/height (WFL/H) or BMI-for-age Z-score was between  $-2SD$  and  $-3SD$  and with severe acute malnutrition if his/her weight-for-length/height or BMI-for-age Z-score was  $< -3SD$  below the mean for age and gender with or without edema. Children reported to have edema were also classified as severely malnourished regardless of their anthropometry.

The data abstracted from the medical records were entered directly into an electronic database. Descriptive statistics were used to calculate the proportions of children with acute malnutrition at diagnosis and to estimate the proportion of those with severe and moderate acute malnutrition.

A binary variable for acute malnutrition was used as the dependent variable coded 0=No and 1=yes. All factors (children, caretakers) were used as independent variables in analysis.

In univariate analysis, using Chi-square test and logistic regression, repeated analysis comparing caretaker and children characteristics with a diagnosis of acute malnutrition was performed. Unadjusted odds ratios with their corresponding 95% confidence intervals (CI) were reported. A variable was considered significant in this analysis if it had a p-value of  $< 0.05$ . All variables with  $p < 0.1$ , and those that biologically plausible were included in the multivariate model building

using a manual backward-stepwise selection method. In this method, variables that lost their association after controlling for confounding were excluded from the final model. Variables in the final model were reported together with their adjusted odds-ratios and their corresponding 95% CI. A significance level of 5% was used. All statistical analyses were performed in STATA (version 13). The research proposal was reviewed and approved by the Mbarara University of Science and Technology Review and Ethical Committee.

## **Results**

A total of 195 children were evaluated for cancer at the Children's Cancer Unit of MRRH from May 2017 to May 2019, of whom 154 (79%) were diagnosed with cancer. Five (3%) children were excluded because they were older than 16 years while 16 (10%) had incomplete anthropometry data in their medical records; leaving 133 who were enrolled into the study.

### *Children's Demographic and Clinical Characteristics*

As shown below in table 1, a majority, 73 (54.9%) of the children were male and 75 (56.4%) were aged  $\geq 5$  years with a mean age of 6.6 (SD=3.9) years. Seventy four (55.6%) children presented after an illness of  $\geq 3$  months and 93 (69.9%) had reduced appetite for food at admission. Forty-six (34.6%) children had been diagnosed with acute leukemia, 39 (29.3 %) with lymphoma and 51 (38.4) with solid tumors. Most, (74.4%) of the children lived in rural settings, 78 (58.7%) were cared for by their mothers, and the caregivers of 111 (83.5%) children were subsistence farmers.

### *Prevalence and Patterns of Acute Malnutrition.*

Out of the 133 children with cancer who were enrolled in our study, 46 (34.6%) had acute malnutrition at the time of cancer diagnosis. Of these 46 children, 25 (54.3%) had moderate and 21(45.7%) had severe acute malnutrition. Only 2 (10%) out of the 21 children with severe acute malnutrition had edema.

### *Factors associated with acute malnutrition.*

Results of bivariate analysis are shown along with the baseline characteristics in Table 1. Age over five years had a 4.4 fold unadjusted odds ratio of acute malnutrition compared to age under five. Children who reportedly had reduced appetite at diagnosis of cancer, had a 4.3 fold unadjusted odds ratio of acute malnutrition compared to those with conserved appetite (p value  $<0.001$  and  $0.003$  respectively). Female children had a positive association with acute malnutrition with 1.6 fold unadjusted odds ratio compared to male children (p value 0.235).

Children from Families with greater than or equal to 2 children had an increased risk of malnutrition 3.4 increased odds compared to families with less than two children (p=0.023) Children cared for by other caregivers other than their parents were more likely to

present with acute malnutrition at diagnosis of cancer with 2, 2 fold increased odds compared to children with their own parents.

Results of the multivariate analyses are shown in Table 2. After controlling for the effects of other variables in the multivariate analysis, only the children's age and appetite status at admission were shown to be independently associated with acute malnutrition. Older children (>5 years) and those who reported reduced appetite for food at admission were 6.4 and 5.4 more likely to be acutely malnourished than their younger (<5 years) counterparts and those reported to have had good appetite for food at admission, respectively (p-value <0.000 and 0.002 respectively).

Table 1: Results of bivariate analysis for factors associated with acute malnutrition in children at diagnosis of cancer

	Acute malnutrition		Unadjusted OR	(95% CI)	p-value
Variables	NO (n=87)	Yes (n=46)			
Age category					
≤ 5 years	48(82.76)	10(17.24)	1		
5 - 15years	39(52.00)	36(48.00)	4.4	1.95-10.04	<0.001
sex					
Male	51(69.86)	22(30.14)	1		
Female	36(60.00)	24(40.00)	1.6	0.75-3.17	0.235
Residence type					
Rural	66(66.67)	33(33.33)	1		
Urban	21(61.76)	13(38.24)	1.2	0.55-2.78	0.604
Caregiver occupation					
Trader	7(70.00)	3(30.00)	1		
Farmers	71(63.96)	40(36.04)	1.3	0.32-5.37	0.703
Civil servants	9(75.00)	3(25.00)	0.8	0.12-5.10	0.793
Caregiver relationship					
Mother	51(65.38)	27(34.62)	1		
Father	30(71.43)	12(28.57)	0.8	0.33-1.71	0.501
Others	6(46.15)	7(53.85)	2.2	0.67-7.2	0.192
Number of siblings					
0-1	29(80.56)	7 (19.44)	1		
2-3	21(55.26)	17 (44.74)	3.4	1.18-9.53	0.023
>3	37(62.71)	22(37.29)	2.5	0.92-6.56	0.071

<b>Appetite at admission</b>					
<b>Good</b>	34(85.00)	6(15.00)	1		
<b>Reduced</b>	53(56.99)	40(43.01)	4.3	1.64-11.17	<b>0.003</b>
<b>Previous hospital admissions</b>					
<b>No</b>	39(72.22)	15(27.78)	1		
<b>Yes</b>	48(60.76)	31(39.24)	1.7	0.79-3.55	0.174
<b>Duration of current illness</b>					
<b>&lt; 1 month</b>	6(75.00)	2 (25.00)	1		
<b>1-3 months</b>	44(64.71)	24(35.29)	1.6	0.31-8.74	0.565
<b>4-5 months</b>	9(64.29)	5(35.71)	1.7	0.24-11.57	0.605
<b>&gt;= 6 months</b>	28(65.12)	15(34.88)	1.6	0.29-8.96	0.588
<b>Type of cancer</b>					
<b>Leukemia</b>	29(63.0)	17(37.0)	1.2	0.55-0.68	0.676
<b>Lymphoma</b>	26(66.7)	13(33.3)	0.9	0.42-2.03	0.845
<b>Solid tumors</b>	33(64.7)	18(35.3)	1.2	0.51-2.19	0.892

cOR=Crude odds ratio.CI=Confidence interval

**Table 2: Results of multivariate analysis for factors associated with acute malnutrition among children with cancer at diagnosis**

	<b>Adjusted OR (95% CI)</b>	<b>p-value</b>
<b>Age</b>		
>5 years	6.4 (2.39-17.35)	<b>&lt;0.0001</b>
<b>Sex</b>		
<b>Male</b>	1.8 (0.73-4.22)	0.204
<b>Reduced Appetite</b>		
<b>Yes</b>	5.4 (1.90-15.28)	<b>0.002</b>
<b>Cancer Diagnosis</b>		
<b>Acute Leukemia</b>	3.8 (0.21-68.34)	0.364
<b>Lymphoma</b>	4.2 (0.27-63.36)	0.297
<b>Solid tumor</b>	5.5 (0.29-104.88)	0.225

CI=Confidence interval

## Discussion

Malnutrition is a significant pediatric health problem in developing countries. Our study examines acute malnutrition among children diagnosed with cancer in Uganda. Overall, more

than one third (34.6%) of the children studied had acute malnutrition at the time of cancer diagnosis. This is a significantly higher prevalence of acute malnutrition than the general paediatric population in Uganda which has a 4% national prevalence of acute malnutrition among children 6-59 months of age according to the Uganda Demographic and Health Survey . According to the Nigerian Demographic Health Survey (NDHS ),the national prevalence of acute malnutrition is 18%.

The rate in our study was also higher than the 14.0% malnutrition rate found among hospitalized children in a general paediatric ward in south west Uganda and the 15% rate of acute malnutrition among children aged 6 to 59 months attending Mulago hospital in Uganda's capital .A single hospital study from Malaysia, found only 11% of paediatric inpatients had acute malnutrition. Potential explanations for the increase in malnutrition among paediatric cancer patients compared to the general population include prolonged reduced food intake, increased metabolic needs, and/or recurrent infections in children with cancer. The lower rate of acute malnutrition among general paediatric patients could be explained by the fact that most of these children have been previously healthy and present with more acute illnesses as compared to many of the children with cancer who present with sub-acute and prolonged symptoms that result in prolonged periods of sub-optimal nutrition and high metabolic conditions for a relatively longer period of time.

The rate of acute malnutrition in our study is similar to the rate of malnutrition in children with cancer reported in other studies from Morocco, Ghana and India. In Morocco and Ghana, 33% and 31% of the children had acute malnutrition at time of cancer diagnosis, respectively . Similar numbers were reported in an even larger study from India that enrolled 1693 children between 2-15 years and found that 38% of the children with cancer had acute malnutrition at diagnosis . Each of these studies were conducted in a low-income country where the baseline prevalence of acute malnutrition in the general population is high and similar circumstances that cause acute malnutrition to those which exist in Uganda are at play among children with cancer .

In high income countries, where there are much lower rates of acute malnutrition in the general population, there are also lower rates among paediatric cancer patients. In Italy, for example, a study found a prevalence of acute malnutrition of 4.7% among children at diagnosis of cancer . Another retrospective cohort study in three Swiss tertiary care hospitals of 327 children diagnosed with cancer found a prevalence of acute malnutrition of 5.8%. A study done at University Medical Center Groningen in the Netherlands among 269 childhood cancer patients found a prevalence of acute malnutrition of 5.2% at diagnosis.In Brazil, a study of 1154 children with cancer found a prevalence of acute malnutrition of 11% at diagnosis.

In our study, two factors were independently associated with acute malnutrition among children at diagnosis of cancer: age older than 5 years and reduced appetite for food at admission. This

finding contradicts what is elsewhere reported in the literature that acute malnutrition is more common in a younger age group, particularly in children less than 5 years of age .

The increased prevalence of malnutrition in children above five years old may potentially be explained by greater parental attention being placed on younger children. Younger children may be monitored more closely such that their illnesses are identified earlier and they are fed more frequently during an illness resulting in less weight loss. This possibility would benefit from further study.

In our study, children who reported reduced appetite understandably had higher odds of acute malnutrition at diagnosis of cancer compared to those with a good appetite. The loss of appetite is usually caused by inflammatory processes related to cancer, which release cytokines and damage the hypothalamic center regulating appetite and/or physical pressure on the gastrointestinal tract caused by abdominal and pelvic masses that make feeding less pleasant.

The finding in our study of poor appetite as a major risk factor for malnutrition is consistent with the findings of a review of 43 studies conducted in industrialized countries regarding prevalence and possible causes of acute malnutrition among children at diagnosis of cancer. That study found that the commonest cause of acute malnutrition in children with cancer was poor appetite . It is not surprising that children with a reported reduced appetite have a higher prevalence of malnutrition because the increased energy nutrient requirements to achieve appropriate growth and development in children with cancer combined with poor intake provides two mechanisms by which acute malnutrition may occur .

The strength of our study is that it was conducted in a referral pediatric cancer unit that treats children with all cancer types from a large geographic area and all levels of socio-demographic background. Limitations of our study include its retrospective study design which makes establishing causative relationships unfeasible and available data for analysis limited.

In conclusion, we recommend that children diagnosed with cancer in low-income countries be routinely screened for acute malnutrition given its high prevalence in these settings and that treatment for acute malnutrition be administered concurrently with cancer treatment. Additional vigilance should be utilized for those in the high risk groups we identified: children above 5 years old and those reporting reduced appetite for food at admission. Future studies could prospectively identify additional risk factors for acute malnutrition and monitor effects of intervention via the cancer center to treat malnutrition in terms of nutritional outcomes as well as efficacy of cancer treatment and related toxicities.

## **ACKNOWLEDGMENTS**

The authors wish to thank the Pediatric Oncology team at Mbarara Regional Referral Hospital

## **CONFLICT OF INTEREST**

The authors declare that there is no conflict of interest

## References

1. Ward, Z.J., et al., *Estimating the total incidence of global childhood cancer: a simulation-based analysis*. The lancet oncology, 2019. **20**(4): p. 483-493.
2. Adewuyi, A.O., *Malnutrition And Its Impacts On The Rural Infants: An Example From Kuje Area Council, Federal Capital Territory-Nigeria*. Social Science Learning Education Journal, 2019. **4**(4): p. 1-5.
3. Apprey, C., et al., *The assessment and prediction of malnutrition in children suffering from cancer in Ghana*. 2014.
4. Tazi, I., et al., *Nutritional status at diagnosis of children with malignancies in Casablanca*. Pediatric blood & cancer, 2008. **51**(4): p. 495-498.
5. Shah, P., et al., *Nutritional status at presentation, comparison of assessment tools, and importance of arm anthropometry in children with cancer in India*. Indian journal of cancer, 2015. **52**(2): p. 210.
6. Sala, A., P. Pencharz, and R.D. Barr, *Children, cancer, and nutrition—a dynamic triangle in review*. Cancer, 2004. **100**(4): p. 677-687.
7. Schaible, U.E. and H. Stefan, *Malnutrition and infection: complex mechanisms and global impacts*. PLoS medicine, 2007. **4**(5).
8. Loeffen, E.A., et al., *Clinical implications of malnutrition in childhood cancer patients— infections and mortality*. Supportive Care in Cancer, 2015. **23**(1): p. 143-150.
9. Bauer, J., H. Jürgens, and M.C. Frühwald, *Important aspects of nutrition in children with cancer*. Advances in Nutrition, 2011. **2**(2): p. 67-77.
10. Sala, A., et al., *Nutritional status at diagnosis is related to clinical outcomes in children and adolescents with cancer: a perspective from Central America*. European journal of cancer, 2012. **48**(2): p. 243-252.
11. Statistics, U.B.o. and ICF, *Uganda demographic and health survey 2016: key indicators report*, 2017, UBOS, and Rockville Maryland.
12. Odong, R.J., et al., *Patterns and Factors Associated With Acute Undernutrition among Hospitalized Children Six Month to Twelve Years in Paediatric Ward of Kampala International University Teaching Hospital*. 2017.
13. Atuhairwe, M., *Prevalence of acute malnutrition and associated factors among children 6 to 59 months that present to Assessment Centre at Mulago Hospital*, 2013, Makerere University.

- 14.Lee, W.-S. and Z. Ahmad, *The prevalence of undernutrition upon hospitalization in children in a developing country: A single hospital study from Malaysia*. Pediatrics & Neonatology, 2017. **58**(5): p. 415-420.
- 15.Triarico, S., et al., *Impact of malnutrition on survival and infections among pediatric patients with cancer: A retrospective study*. Eur. Rev. Med. Pharmacol. Sci, 2019. **23**: p. 1165-1175.
- 16.Zimmermann, K., et al., *Malnutrition in pediatric patients with cancer at diagnosis and throughout therapy: a multicenter cohort study*. Pediatric blood & cancer, 2013. **60**(4): p. 642-649.
- 17.Maia-Lemos, P., F. Ceragioli-Oliveira, and E. Monteiro-Caran, *Nutritional Status at Diagnosis in Children with Cancer in Brazil*. Pediatr Ther, 2016. **6**(295): p. 2161-0665.1000295.
- 18.Badi, M.A. and I.A. Ba-Saddik, *Severe Acute Malnutrition among Hospitalized Children, Aden, Yemen*. Open Journal of Epidemiology, 2016. **6**(2): p. 121-127.
- 19.Ezeoke, C.C. and J.E. Morley, *Pathophysiology of anorexia in the cancer cachexia syndrome*. Journal of cachexia, sarcopenia and muscle, 2015. **6**(4): p. 287-302.
- 20.Brinksma, A., et al., *Malnutrition in childhood cancer patients: a review on its prevalence and possible causes*. Critical reviews in oncology/hematology, 2012. **83**(2): p. 249-275.