

Development of a Nutritional Screening Tool for Pediatric Cancer Patients in Uganda and
Tanzania: An Exploratory Analysis

by

Abdoulie Ceesay

Duke Global Health Institute
Duke University

Date: _____

Approved:

Tamara Fitzgerald, Advisor

Amy Herring

Kristin Schroeder

Thesis submitted in partial fulfillment of
the requirements for the degree of
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ABSTRACT

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Abstract

Background: Nutrition is a key determinant of pediatric cancer patient outcomes in sub-Saharan Africa. Accurately identifying pediatric cancer patients at risk of malnutrition remains a challenge. There is a need for a standardized nutritional screening tool, developed and validated in sub-Saharan Africa. Study aims: The aims of this study were to: 1) select candidate variables in the development of a nutritional screening from predictors associated with malnutrition in pediatric cancer patients and, 2) conduct a secondary data analysis estimating the prevalence of pediatric cancer in Uganda from cases presented at the Uganda Cancer Institute between January 1, 2017 and December 31, 2019. Methods: This study is a longitudinal hospital-based study, carried out at the Bugando Medical Center in Tanzania and Uganda Cancer Institute in Uganda. The study enrolled clinically confirmed pediatric cancer patients (<18 years) at the study sites. Measures of interest include: nutritional status, symptom duration, abdominal distention, anthropometric measures such as height, weight, mid-upper arm circumference, abdominal circumference, triceps skinfold thickness, and clinical characteristics such as serum albumin, mean corpuscular volume, and protein. Logistic regression models examined predictors of nutritional status in pediatric cancer patients. Lastly, geospatial analysis estimated the prevalence and examined the country-wide distribution of the pediatric cancers presented at the Uganda Cancer Institute between 2017 and 2019. Results: The sample of 77 pediatric cancer patients enrolled at the two study sites ranged from 1 to 17 years old. Solid tumor malignancies like Wilms tumor comprise of 40% of all diagnoses. 60% of cancer patients were malnourished at baseline. The strongest

predictors of nutritional status were mid-upper arm circumference (AOR 0.52, 95% CI: 0.31 – 0.87), abdominal circumference (AOR 1.38, 95% CI: 1.16 – 1.65) and serum albumin (AOR 0.73, 95% CI: 0.62 - 0.86). Secondary analysis of the Uganda Cancer Institute registry shows 11607 patients with confirmed cancer diagnosis between 2017 and 2019. Acute lymphoblastic leukemia (31.4%) is the most common cancer diagnosis, followed by Wilms tumor (19.1%), rhabdomyosarcoma (9.4%) and Burkitt's lymphoma (6.9%). Blood cancers are most common cancer types, of them the most frequent cases being leukemia (37%). 2018 saw the highest number of cancer presentations within the study timeframe. Conclusions: The results show abdominal circumference, serum albumin, and muac are candidate variables in developing a nutritional screening tool for pediatric cancer patients in SSA. Blood and solid cancers are prevalent in Uganda; thus, a customized nutritional screening tool is much needed.

Dedication

This thesis is dedicated to my three siblings who tragically lost their lives in a boat accident on December 4, 2019. Here's to you Mariama Ceesay (Maaya), Sulayman Ceesay (Daad), and Lamin Ceesay. Till we meet again!

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1. Introduction

Pediatric cancer remains a leading cause of death for children globally, often undiagnosed but related to severe morbidity and mortality.¹ Every year, approximately 220,000 children are diagnosed with cancer, with 85% of these new cases arising in low- and middle-income countries (LMIC).² Although survival of pediatric cancer has steadily increased over the years and exceeds 85% in high-income countries (HIC), survival in many LMICs is below 25%.³ This disparity in survival rates is multifactorial, including presenting stage and comorbidities, but nutrition plays a key role.^{4,5} Malnutrition effectively reduces the tolerance and efficacy of chemotherapy treatments.⁶ It is also associated with increased infection rates, poor clinical outcomes and an influential factor on mortality.⁶ Studies have estimated that 20-30% of deaths in cancer patients globally are suspected to be associated with malnutrition rather than solely the cancer.^{7,8} Treatments that cancer patients undergo are associated with various side effects, ranging from loss of appetite, change in taste, dry mouth, nausea, diarrhea, constipation, and fatigue.⁷ These side effects can negatively affect dietary intake, causing patients undergoing cancer treatment to lose weight as result of chemotherapy treatment.⁶ This weight loss deteriorates a patient's nutritional status and places them at higher risk for complications such as mortality. Evidence from several recent studies shows that poor nutritional status is strongly correlated with decreased chemotherapy tolerance and lower effectiveness of anticancer drugs by means of suboptimal tolerated dose intensity.^{1,5,9,10}

Studies have also indicated stark differences in survival rates between malnourished and well-nourished pediatric patients. Loeffen et al. (2015) showed that

malnourished patients fared worse than well-nourished patients. The study showed worse survival for malnourished patients than well-nourished patients (hazard ratio (HR)=3.65, 95% confidence interval (CI)=1.52-8.70, p=0.004).¹ A 5% weight loss in such pediatric patients in their first three months after diagnosis is also significantly related to occurrences of complications as a result of low neutrophil granulocytes in the blood.¹

1.1 Child malnutrition in sub-Saharan Africa

Sub-Saharan Africa (SSA) has the greatest burden of child malnutrition,¹¹ accounting for about a third of all undernourished children globally.¹² Child malnutrition remains a major health challenge for SSA nations, resulting in suboptimal child brain development which leads to impaired cognitive development, educational achievement and economic performance in adulthood.¹¹ Globally, undernutrition specifically is the underlying cause in about 45% of all under-5 years of age deaths, majority of which are in SSA.^{11,12} Globally in 2015, 7.7% of children are wasted, 24.5% stunted and 15% underweight. Of these estimates, SSA accounts for 39.4% of the stunted, 24.9% of the underweight and 10.3% of the wasted children.¹¹⁻¹³ These numbers highlight not only how malnutrition can hamper national development but also impact health outcomes, signaling a need for urgent nutritional interventions in SSA.

1.2 Pediatric cancer in sub-Saharan Africa

By 2050, an estimated 70% of annual cancer diagnosis will be in LMICs.^{14,15} Within these countries, the vast majority of the burden of pediatric oncology is in SSA. The incidence of mortality in pediatric oncology patients in SSA is more than 15 times that of

the developed world, mainly due to high infection rates and prevalence of malnutrition.¹⁶ Within the continent of Africa, there is variable disparity in the survival rates for pediatric cancer. North African nations have seen high overall survival rates of pediatric cancer owing to improvement in diagnostic capabilities, decreased infection rates and metabolic disturbances.¹⁶ By contrast, SSA continues to struggle with meagre overall pediatric oncology survival rates owing to lack of different competences and multidisciplinary approach, diagnostic delays, high infection rates and metabolic disturbances.¹⁶

Estimating the true incidence rates of pediatric cancer in SSA is difficult due to frequent misdiagnosis or underdiagnoses. In many SSA countries, inadequate infrastructure in terms of diagnostic ability and treatment facilities contributes to immense misdiagnosis and under-estimation of certain childhood cancers, notably brain tumors and leukemias.¹⁷ Despite these inadequacies, an analysis of 16 population based cancer registries from SSA by Stefan et al. (2017) revealed the obvious: for several pediatric cancers, SSA has higher incidence rates than the developed world.¹⁷

Sub-Saharan Africa continues to lead in incidence rates of infection-related and embryonal cancers. Burkitt's lymphoma, Kaposi sarcoma, Hodgkin's lymphoma and hepatocellular carcinoma are among leading infection-related pediatric cancer malignancies in SSA whereas Wilms tumor and retinoblastoma constitute the greatest incidence rates of embryonal cancers.¹⁷ Wilms tumor continues to present treatment challenges due to inadequacies in imaging, surgery, and pathology competences in many SSA countries compared to Northern Africa or HIC.¹⁶ A 2 year event free survival in 32

patients from SSA was 46.7% whereas it was 86.6% in 101 patients from North Africa.^{16,18,19} In addition to the difference in competences, radiotherapy also contributes to this difference in 2-year event free survival rates between North Africa and SSA.

1.3 Need for nutritional screening tool in pediatric oncology

Simple nutritional interventions can diminish the burden of under-nourishment in children with malignant diseases in LMICs in a cost-effective manner, contributing to enhanced likelihood of survival.²⁰ Identifying children at severe risk of malnutrition early on remains a challenge in SSA. This is due to the absence of a gold standard nutritional assessment tool for identifying malnutrition in pediatric patients in SSA. A variety of nutritional risk assessment tools are available, such as World Health Organization (WHO) reference and standards (2007), Nutritional Risk Screening Tool, Malnutrition Universal Screening Tool, Malnutrition Screening Tool (MST), Short Nutritional Assessment Questionnaire and the Subjective Global Assessment (SGA).⁶ However, these screening tools were developed for general patients and validated mostly in HIC.⁷ Thus, they might not be suitable for use in LMIC due to the severity of disease and large tumor burden often seen in SSA.²¹

Poor nutritional status is strongly correlated with decreased chemotherapy tolerance and altered metabolism of antineoplastic drugs and is associated with increased infection rates and poor clinical outcomes.^{9,10,20} To allow for improved clinical outcomes, the first step is to identify the nutritional status of patients at risk so that a more thorough evaluation can be carried out.⁶ This can be accomplished by the implementation of a screening tool. A simple and accurate nutritional screening tool would identify those at

nutritional risk early and refer for nutritional supplementation and intervention, allowing for an efficient diagnostic tool for nutritional professionals without unduly increasing workload.⁶ This early detection of nutritional risk can avert the progression of the disease, thereby improving outcomes.

An ideal nutritional screening tool is simple, can be completed without needing a specialist, reproducible and reliable in identifying individuals at risk of malnutrition, and can facilitate referral for appropriate nutritional assessment.²² Current methods of assessing nutritional status in children rely on anthropometric, dietary, biochemical, and immunologic measures; and although these measurements are useful, no single construct has the sensitivity and specificity to be a reliable index predictive of nutrition-related complications.²³ Indices such as serum albumin and body mass index (BMI) have been included in nutritional assessment for clinical trials in the United States but have not been consistently correlated with outcomes.⁹ Weight as an acute parameter of nutritional status is frequently unreliable in patients with a large tumor mass, as is common in SSA.²⁰ Thus, indicators for developing a nutritional screening tool must be chosen based on their association and significance with the dependent variable of nutritional status. Therefore, a novel simple nutritional assessment tool developed in SSA from candidate variables, tailored to SSA would more accurately identify pediatric patients at nutritional risk than internationally developed nutritional assessment tools used in HIC. If shown to have high predictive value, this tool could be evaluated and become a standard of measurement for pediatric nutritional risk assessment in SSA, and potentially LMICs generally.

1.3 Study aims and objectives

The main aim of this study is to evaluate factors associated with nutritional status in pediatric cancer patients and how these factors can be used to develop an efficient and valid nutritional screening tool for pediatric cancer patients in Uganda and Tanzania. The secondary aim of the study is a) to determine the prevalence of the different types and forms of pediatric cancer in Uganda, estimated from cases presented at the out-patient department of the Uganda Cancer Institute (UCI) between January 1, 2017 and December 31, 2019, and b) provide a geospatial representation of pediatric cancer prevalence in the districts and regions of Uganda. This study completes its aims as part of the larger study: *“A Pilot Study to Measure Nutrition Status and Treatment Outcomes in Paediatric Oncology Patients at Uganda Cancer Institute and Bugando Medical Center.”*

For the main objective, the study was carried out in a hospital setting, prospectively enrolling patients and monitoring outcomes longitudinally. Key variables collected during the study were assessed by logistic regression for association with nutritional status in pediatric cancer patients. For the secondary objective, a secondary analysis is conducted on the UCI cancer registry (2017 - 2019). This registry contains all patients presenting at the out-patient department of UCI over the 3-year time period, their demographic information, place of residence, and type of diagnosis. Prevalence of the different types and forms of pediatric cancers in Uganda are estimated from this registry.

2. Methods

2.1 Setting

The study was conducted at the UCI at Mulago National Referral Hospital in Kampala, Uganda and Bugando Medical Center (BMC) in Mwanza, Tanzania. Both hospitals are the main referral pediatric cancer hospitals in their region. BMC has a 60-bed inpatient ward that provides care to children. The center offers services in cancer screening, early diagnosis, staging, chemotherapy, radiation therapy, and surgery. Mulago National Referral Hospital in Kampala Uganda attends to approximately 830,000 outpatients, 800,000 inpatients, 62,000 emergency visits, 40,000 births, and 12,000 postnatal visits per year. There is an operating room dedicated to pediatric surgery within the main hospital, with access to basic radiology services including plain radiographs, ultrasound, and CT scanners for oncologic cases. The pediatric surgery team cares for approximately 1000 children per year, 650 of which are major surgery cases. The hospital receives referrals from all over the country and neighboring areas, such as Democratic Republic of Congo, Burundi, and South Sudan. The UCI is a tertiary, specialized, teaching and research center affiliated with Makerere University School of Medicine and Mulago National Referral Hospital. The institute has an 80-bed inpatient capacity and attends to an average of 200 patients daily. The institute offers free cancer screening, education and awareness as part of the broader Comprehensive Cancer Control Program in Uganda.

2.2 Participants

2.2.1 Aim 1: Factors associated with nutritional status in pediatric cancer patients

In Tanzania, participants were recruited out of patients presenting at BMC. Pediatric patients (<18 years) with clinically confirmed case of cancer were enrolled in the study. Consent was obtained from parents, guardians, or caretakers. Assent was obtained from patients older than 12 years of age. Patients older than 18 years at the time of enrollment and those with non-cancer cases were automatically excluded from the study.

In Uganda, participants were recruited out of patients presenting at the outpatient department of the UCI. Patients aged 0-15 years with a clinical confirmed case of a solid tumor malignancy destined for surgery were enrolled in the study. Patients who received previous chemotherapy treatment were excluded from the study. Patients with other forms of cancer not eligible for surgery or those deemed too ill or hemodynamically unstable were also excluded from the study. Consent was obtained from parents, guardians, or caretakers. Assent was obtained from patients older than 8 years of age.

When patients present to the outpatient department at UCI and BMC, they are assessed and once clinically confirmed to have cancer, parents, guardians, or caretakers are approached for consent to enroll the child in study. Parents, guardians or caretakers are informed of the study in a private consultation room with a witness in presence. Parents, guardians or caretakers are asked to confirm understanding of the study and

procedures that will be performed in the study. Once approval is given, the intake process is executed by the research assistant.

2.2.2 Aim 2: Prevalence estimates of pediatric cancers in Uganda

This is a secondary data analysis of pediatric cancer cases presented at the UCI between January 1, 2017 and December 31, 2019. The registry contains patient demographics, residence, and diagnosis. Patients in the registry range from 3 months old to 18 years. Patient information is prospectively entered into the database during presentation at the hospital. Diagnosis information is entered into the database once confirmed. The registry contains cancer and non-cancer cases, confirmed and unconfirmed diagnoses.

2.3 Procedures

2.3.1 Aim 1: Factors associated with nutritional status in pediatric cancer patients

During the intake process, parents, guardians or caretakers of patients with a clinical confirmed case of cancer are approached for enrolling their child in the study. Consent is read to parents, guardians, or caretakers in English, Kiswahili or Luganda with a translator/witness in presence in a private room. During the consenting process, parents, guardians, or caretakers were also asked to ascertain they understand the study, its procedures and their rights in the study. After answering in the affirmative, final consent was obtained by the signing or thumb printing of the consent documents by the parent, guardian or caretaker, research assistant and the witness in presence. Child assent was obtained in the presence of the parent, guardian, or caretaker following the consenting

process. When parents, guardians or caretakers are unable to read, verbal consenting is performed in the presence of a witness.

Following, the first-contact-with-patient questionnaire is completed. During this, patient identifiers and demographic information are collected. Anthropometric measurements of height, weight, mid upper arm circumference (MUAC), triceps skinfold thickness (TSFT) and head circumference (if less than 1 year old) are collected. Height is collected using a stadiometer, weight is collected using a weighing scale, muac is collected using a muac tape, tsft is collected using a skin caliper and head circumference is collected using a tape measure. Further, abdominal circumference of the patient is measured using a tape measure if abdominal distention is present. Tumor size is either measured using a tape measure or measurement is obtained electronically from the latest patient ultrasound or computerized tomography (CT) scans. Laboratory information such as serum albumin, hemoglobin, mean corpuscular volume (MCV) and protein level are extracted from patient's chart. This laboratory blood work information is completed as part of the routine standard of care at the hospital. The nutritional status of the patient is determined by the nutritionist. At the end of the intake process, parents, guardians, or caretakers are compensated a one-time fee of 20,000 Ugandan Shillings.

Subsequently, the surgical patients are clinically followed between intake and surgery. During this time, patients are assessed, and the clinic-follow-up questionnaire is completed at each follow up. Anthropometric measurements described above are collected. Tumor size is measured, and further laboratory blood work information is collected. The patient's nutritional status is also categorized during this follow up.

Prior to surgery, the peri-operative questionnaire is completed. During this process, standard anthropometric measurements are taken, laboratory blood work information is collected, tumor size is measured and assessed for rupture, and the patient is assessed for blood loss. The type of operative procedure to be performed is also recorded. Finally, 48 hours after surgery, a postoperative follow up in the form of a survey questionnaire is completed. This questionnaire is also completed 30 days post operation. During this assessment, surgical outcomes in the form of complications that occurred 48 hours and 30 days post-surgery are recorded.

2.3.2 Ethical approval

Ethical approval for the project was granted as part of the larger project by the Catholic University of Health and Allied Sciences (CUHAS) and the National Institute for Medical Research (NIMR) in Tanzania; Duke University Institutional Review Board in the United States; and in Uganda by UCI and the Uganda National Council for Science and Technology (UNCST).

2.3.2 Data Management

Survey data was collected on paper-based questionnaires. The paper forms were stored in binders in secure filing cabinets in both locations. Study data were collected and managed using REDCap electronic data capture tools hosted at Duke University.^{24,25} REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies, providing an intuitive interface for validated data capture; audit trails for tracking data manipulation and export procedures; automated export procedures for seamless data downloads to common statistical

packages; and procedures for data integration and interoperability with external sources. Access to REDCap was role-based, with access only granted to study investigators by the system administrators.

As a multi-site study, data was shared between collaborators at UCI, Kampala, BMC, Mwanza, and Duke University, United States. Data collected at UCI belongs to UCI and data collected BMC belongs to BMC. Data transfer agreement between the two study sites and Duke University was submitted to NIMR.

2.4 Measures

The primary outcome/dependent variable for aim 1 is nutritional status. Nutritional status was determined and categorized by the nutritionist as severely malnourished, moderately malnourished or normal. For this analysis, nutritional status is dichotomized as either malnourished, consisting of severely and moderately malnourished patients or well nourished, consisting of the normal patients.

Independent/predictor variables are treated as continuous or categorical dependent on their nature. Predictors identified and included in the analysis are anthropometric measurements (muac, tsft, height, weight), serum albumin, protein, mcv, symptom duration, abdominal distention, visible mass and abdominal circumference. Symptom duration was recorded in months. For this analysis, it was treated as a continuous numerical variable. Abdominal circumference is recorded in centimeters and treated as a continuous numerical predictor. Serum albumin is recorded in g/L and treated as continuous. Studies have shown that factoring in serum albumin measurements, the proportion of severe malnutrition identification rose from 45% to 59%, highlight the

importance of serum albumin as an indicator in identifying severe malnutrition.²⁰ Tsft and muac are recorded in millimeters and centimeters, respectively. Both variables are treated as a continuous numerical variable. Abdominal distention and visible mass are dichotomized as yes or no.

2.4 Analysis

Data analysis and visualizations were performed using Stata 16.0 (StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LP) and RStudio, version 1.1.463 (RStudio, Inc. 2009-2018). Geospatial analysis was performed through QGIS version 3.12.0 București (released February 21, 2020) and GeoDa™ version 1.14.0.4 (Spatial Analysis Laboratory, University of Illinois, Urbana Champaign, IL, USA).

Descriptive analysis was performed for each dataset. For aim 1, Kruskal-Wallis tests were performed to compare the three nutritional status groups for each of the continuous predictor variables presented in Table 3. Missing data analysis was performed for the predictor variables, and the missing data were imputed 10 times by means of predictive mean matching using the Multivariate Imputation by Chained Equations (MICE) package in R, with Rubin's rules used to combine analyses of individual imputed datasets. Multicollinearity between predictor variables was assessed through correlational analysis and variance inflation factors (vif). Predictors with a vif greater than 4 are assessed for inflationary properties and not included in the final logistic regression. Multiple logistic regression was performed to identify predictors associated with nutritional status, with the referent group set to normal nutritional status. Wald's test was

performed for the logistic models to assess significance of the explanatory predictor variables. Youden's index (sensitivity + specificity – 1) was assessed by a receiver operator (ROC) curve and optimal cutoffs were determined from this graph. Statistical significance was set at p-values less than 0.05. Odds ratios and 95 percent confidence intervals are reported for all predictors.

For aim 2, a secondary data analysis was performed on cancer cases presented at UCI between January 1, 2017 and December 31, 2019. Only confirmed diagnoses are included in the analysis. Prevalence estimates are calculated for each major type and form of cancer. The types and forms of cancer diagnoses are geospatially represented on a Geographic Information System (GIS) map of Uganda, showing prevalence estimates in the different districts and regions of the country.

3. Results

3.1 Aim 1: Factors associated with nutritional status in pediatric cancer patients

3.1.1 Characteristics of the study sample

The study enrolled 85 patients in the two study sites: 80 patients at BMC and 5 patients at UCI. Only 77 of these patients have a confirmed case of cancer and 45% of these patients are female and 55% are male. 59 patients presented with abdominal distention, 25 of which had visible mass, an indication of presence and the gravity of the malignant tumor. At intake, there is a statistically significant difference in nutritional status between those with abdominal distention and those without ($p=0.0296$) and those with visible mass in comparison to those without ($p=0.0296$). Most of the patients have abdominal tumors, but there are also few cases of tumors in locations such as the neck, face, jaw, and arm. Overall, the most common form of cancer diagnosis is Wilms tumor, which is approximately 40% of all diagnoses. There are 8 cases of Burkitt's lymphoma and 5 cases of retinoblastoma. Together, the top five most common cancers constitute approximately 80% of all diagnoses in the study. Society of Pediatric Oncology Wilms Tumor (SIOP-WT) is the most common treatment protocol, which is expected since most diagnoses in the study are Wilms tumor. The intake nutritional status of the patients comprises about 60% of patients with malnourishment, i.e. severe or moderate, and 40% with normal nutritional status. There is no evidence of a statistically significant difference in nutritional status at intake between male and female patients ($p=0.1961$) in the study.

Table 1: Demographic and clinical characteristics of the pediatric cancer patients

<i>Variable</i>	<i>N (%)</i>	<i>p-value</i>
<i>Sex</i>		
Female	35 (45.45)	0.1961
Male	42 (54.55)	
<i>Abdominal Distention</i>		
Yes	59 (76.62)	0.0296
No	18 (23.38)	
<i>Visible Mass</i>		
Yes	25 (32.5)	0.0296
No	51 (66.2)	

Table 2: Baseline clinical characteristics

<i>Variable</i>	<i>N</i>	<i>%</i>
<i>Nutritional Status</i>		
Normal	31	40.3
Moderately Malnourished	17	22.1
Severely Malnourished	29	37.7
<i>Diagnosis</i>		
Wilms Tumor	31	40.3
Burkitt's Lymphoma	8	10.4
Retinoblastoma	5	6.5
Hepatomegaly	3	3.9
Hodgkin's Lymphoma	3	3.9
Rhabdomyosarcoma	3	3.9
Acute Lymphoblastic Leukemia	1	1.3
Acute Myeloid Leukemia	1	1.7
Germ Cell Tumor	2	2.6
Hepatoblastoma	1	1.3
Nasopharyngeal carcinoma	1	1.3
Osteosarcoma	1	1.3
<i>Treatment protocol</i>		
SIOP-WT	18	60.0

CEB	1	10.0
CHOP	3	3.3
ABVD	1	3.3
Other	7	23.3
<i>Primary tumor location</i>		
Abdominal	22	78.6
Other	6	21.4

There is evidence of a statistically significant difference between normal, moderately malnourished and severe malnourished patients in terms of muac ($p < 0.001$), tsft ($p = 0.0436$), hemoglobin ($p = 0.0295$), and serum albumin ($p = 0.0031$) at intake. Pediatric patients with normal nutritional status have higher mean muac (14.51 cm) compared to moderate malnourished (13.62 cm) or severely malnourished (12.13 cm). Mean serum albumin levels are higher in patients with normal nutritional status (41.27 g/L) and lower in moderately (32.51 g/L) and severely (29.37 g/L) malnourished patients. Mean tsft results are higher for moderately malnourished (14.07 cm) than normal (12.01 cm) or severely malnourished (12.24 cm) patients. This trend in tsft results is inconsistent and counterintuitive in that normal patients are expected to have higher mean tsft than malnourished patients. Moderately malnourished patients have higher mean abdominal circumference (61.97 cm) compared to normal (55.29 cm) and severely malnourished (60.59 cm). All other predictors presented in Table 3 show no evidence of a statistically significant difference between the different categories of nutritional status. Mean symptom duration is higher for the normal patients (5.95 months) compared to moderately malnourished (2.67 months) or severely malnourished (3.20 months).

Except for age, height and weight, all variables presented in Table 3 have some missing data. Missing data analysis was performed for these variables. To understand the influence of these missing values on inference, a multinomial regression including all predictors with missing values was fitted to the pattern of missingness of these predictors. Based on the results of this regression, the t-statistics (estimate/standard error) is below 1.96 for all predictors of interest. Therefore, there was no evidence to suggest non-random missingness to these predictors. As a result, imputing the data to replace the missing values before analysis is an appropriate step. The data was imputed 10 times using the MICE package in R, missing values replaced by the predictive mean matching method, and with results combined after analysis using Rubin's rules.

Table 3: Baseline anthropometric and clinical characteristics

Variable	Overall N (mean, sd)	Nutritional Status			P value*
		Normal n (mean, sd)	MAM n (mean, sd)	SAM n (mean, sd)	
Age (years)	77 (5.42,4.07)	31 (4.70, 3.66)	17 (6.11,3.78)	29 (5.80,4.63)	0.2734
Height (cm)	71 (105.25, 23.13)	31 (103.15,23.23)	17 (107.15, 19.50)	29(106.38, 25.46)	0.7518
Weight (Kg)	71 (18.42, 13.41)	31 (16.86,8.11)	17 (18.41, 7.37)	29 (20.08, 19.52)	0.5498
Symptom duration (months)	63 (4.21, 8.96)	26 (5.95, 13.8)	15 (2.67, 1.18)	22 (3.20, 1.72)	0.7553
MUAC (cm)	75 (13.39, 2.21)	29 (14.51, 2.02)	17 (13.62, 1.15)	29 (12.13, 2.26)	0.0001
Tsft (cm)	75 (12.57, 10.74)	29 (12.01, 7.98)	17 (14.07, 11.88)	29 (12.24, 12.59)	0.0436
Abdominal circumference (cm)	68 (59.05, 8.69)	24 (55.29, 7.19)	16 (61.97, 9.56)	28 (60.59, 8.52)	0.0566
Hemoglobin (g/dL)	63 (8.97, 2.50)	27 (9.55, 2.53)	14 (9.42, 2.75)	22 (7.98, 2.05)	0.0295
Protein (g/L)	31 (63.88, 12.81)	10 (67.27, 7.70)	7 (59.37, 19.53)	14 (63.72, 11.91)	0.6213
Serum albumin(g/L)	31 (33.92, 9.31)	10 (41.27, 4.44)	7 (32.51, 10.52)	14 (29.37, 8.38)	0.0031
MCV	63 (67.47, 11.24)	27 (70.21, 9.20)	14 (65.93, 16.65)	22 (65.09, 8.90)	0.0843

*p-value from the Kruskal-Wallis test (non-parametric)

MAM=moderately malnourished

SAM=severely malnourished

3.1.2 Multicollinearity: Variance inflation factors (vif) and correlational analysis

Correlational analysis was performed for the imputed dataset to assess how predictors correlate with one another (see appendix A). Age has a strongly positive correlation with height ($r = 0.94$) but moderate positive correlation with weight ($r = 0.48$) and muac ($r = 0.57$). Height has a moderate positive correlation with muac ($r = 0.6$). Weight has a moderate positive correlation with symptom duration ($r=0.66$). Serum albumin is negatively correlated with nutritional status ($r = -0.51$). The potential effect of the correlation between age, weight, height and muac on the regression models was examined with vif analysis. In the linear model, height and age had a vif value greater than 4 (see Appendix B). Including both age and height in the model does lead to some variance inflation; thus, age and height have been excluded from the logistic regression analysis. Consequently, all other predictors have a vif value below the conservative estimate of 4.

3.1.3 Predictors of nutritional status in pediatric cancer patients

Multiple logistic regression was conducted to explore the association of predictors with nutritional status. The full model included all predictor variables listed in Table 3 with the exception of age and height. Wald's test conducted assessed the significance of each predictor to the model. The results of the test showed that weight, mcv, symptom duration and hemoglobin are not significant in the model. In other words, these predictors bring no meaningful addition to the model. Thus, excluding them from the model does not affect the validity of the model. The final logistic regression model included abdominal circumference, muac, tsft, protein, and serum albumin. Categorical variables

abdominal distention and visible mass were also excluded due to the small sample size and the effect that has on whether such variables are significant or not.

Univariate analysis indicates that abdominal circumference (COR 1.09, 95% CI: 1.02 – 1.16) serum albumin (COR 0.86, 95% CI: 0.80 – 0.93) and muac (COR 0.65, 95% CI: 0.50 – 0.86) are significantly associated with nutritional status. Adjusting the model for all predictor variables, odds ratios from multivariate analysis indicate that a one-unit cm increase in muac is associated with a decreased odd of 0.52 (95% CI: 0.31 – 0.87) of being malnourished in comparison to patients with normal nutritional status. In contrast, increase in the size of the abdominal circumference is associated with increased odds of 1.38 (95% CI: 1.16 – 1.65) of being malnourished in comparison to a patient with normal nutritional status. Increase in a patient’s serum albumin level is associated with decreased odds of 0.73 (95% CI: 0.62 - 0.86) of being malnourished compared to a patient with a normal nutritional status.

Table 4: Predictors of nutritional status in pediatric cancer patients

Variable	Crude OR (95% CI)	p- value*	Adjusted OR (95% CI)	p- value*
Abdominal circumference	1.09 (1.02 – 1.16)	0.007	1.38 (1.16 – 1.65)	<0.001
MUAC	0.65 (0.50 – 0.86)	0.002	0.52 (0.31 – 0.87)	0.012
TSFT	1.01 (0.96 – 1.06)	0.678	1.13 (1.01 – 1.27)	0.034
Serum albumin	0.86 (0.80 – 0.93)	<0.01	0.73 (0.62 - 0.86)	<0.001
Protein	0.99 (0.96 - 1.03)	0.734	1.08 (1.01 - 1.16)	0.018
Symptom duration	0.94 (0.81 – 1.09)	0.410	-	-
Hemoglobin	0.83 (0.68 - 1.02)	0.084	-	-
MCV	0.97 (0.93 - 1.01)	0.177	-	-
Weight	1.01 (0.97 - 1.06)	0.420	-	-

* Significance level at p<0.05

3.1.3 ROC curve analysis

Increase in abdominal circumference is associated with increased odds of being malnourished. According to the Wald test, abdominal circumference improves the fit of the logistic model. A ROC analysis of abdominal circumference in predicting nutritional status shows an area under the curve (AUC) of 0.6725. Optimal cutoffs for sensitivity and specificity for abdominal circumference was determined at 61.4%, indicating the potential importance of such a predictor in differentiating between those patients who are malnourished and those patients who are not malnourished. Other associated predictor variables lack the sensitivity to identify truly those that are malnourished, while other predictor variables lack both the sensitivity and specificity to differentiate between malnourished and well-nourished patients.

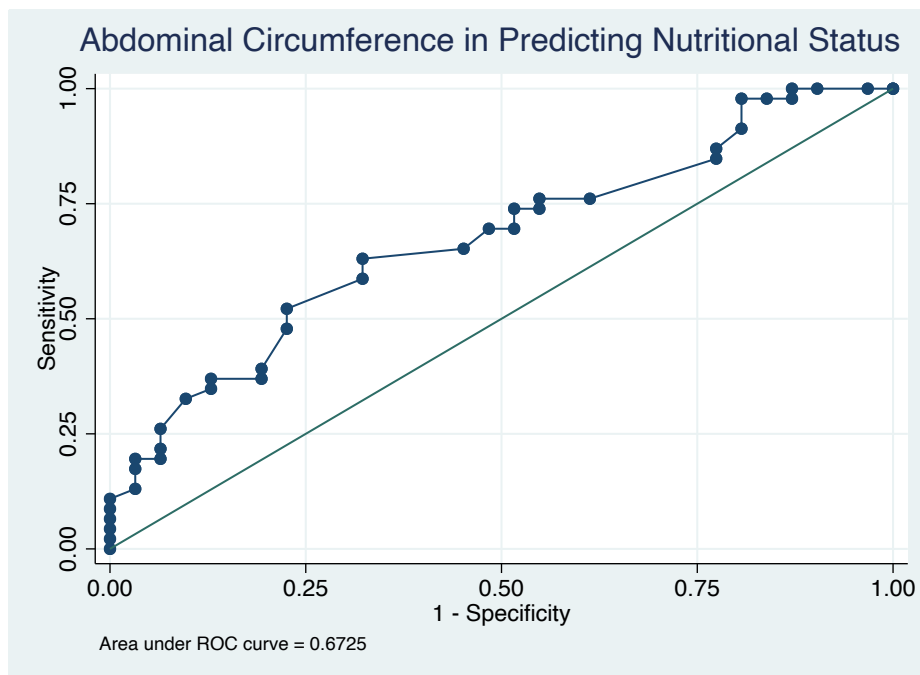


Figure 1: ROC curve of abdominal circumference predicting nutritional status in pediatric cancer patients

3.2 Aim 2: Prevalence of pediatric cancers in Uganda

3.2.1 Patient characteristics and diagnosis

The cancer registry at the out-patient department at the UCI has 16906 patients, seen between January 1, 2017 and December 31, 2019. Of these 14084 have either a confirmed or unconfirmed/suspected diagnosis and 2828 are missing diagnosis completely. Out of the 14084 patients, 11607 have complete confirmed diagnosis. 42.9% of these patients are female while 4.1% are missing sex designation in the registry. In terms of presentation, 2018 has the greatest number of cancer cases.

Table 5: Patient characteristics

Variable	N	(%)
Sex		
Female	5810	42.9
Male	7175	53.0
Missing	555	4.1
<i>Confirmed Cases (Year)</i>		
2017	3,743	32.3
2018	4,564	39.3
2019	3,300	28.4
<i>Age (years)</i>	mean	sd
Female	7.52	4.21
Male	7.81	4.32

The most common cancer cases presented between 2017 and 2019 are acute myeloid leukemia, acute lymphoblastic leukemia, Burkitt's lymphoma, Hodgkin's lymphoma, germ cell tumor, Kaposi sarcoma, lymphoblastic lymphoma, oro-facial Kaposi sarcoma, osteosarcoma, retinoblastoma, rhabdomyosarcoma and Wilms tumor. Acute lymphoblastic leukemia is the top most common cancer, having 3632 cases presented within the 3-year period. The second most common cancer cases are Wilms tumor with 2217 confirmed cases, and rhabdomyosarcoma with 1097 confirmed cases.

Table 6: Cancer diagnosis at UCI between 2017 and 2019

Diagnosis	Year			Total
	2017	2018	2019	
Abdominal Tumor	6	10	4	20
Acute Myeloid Leukemia	24	159	83	266
Acute Lymphoblastic Leukemia	998	1353	1281	3632
Acute Promyelocytic Leukemia	11	46	5	62
B-cell Lymphoma	0	21	12	33
Bladder Carcinoma	5	3	12	20
Brain Tumor	28	30	31	89
Burkitt's Lymphoma	334	262	207	803
Chronic Myeloid Leukemia	25	35	26	86
Desmoplastic Small Round Cell Tumor	6	3	0	9
Diffused Large B-cell Lymphoma	2	17	9	28
Dysgerminoma	0	4	3	7
Embryonal Rhabdomyosarcoma	2	3	25	30
Ewing's sarcoma	12	22	2	36
Fibrosarcoma	4	4	2	10
Germ cell tumor	10	58	81	149
Hemangioma	0	8	5	13
Hepatoblastoma	36	18	2	56
Hodgkin's lymphoma	291	209	116	616
Kaposi sarcoma	166	93	48	307
Leukemia	76	2	1	79
Lymphoblastic lymphoma	103	137	63	303
Lymphoma	4	5	25	34
Medulloblastoma	7	19	5	31
Nasopharyngeal cancer	13	9	19	41
Neuroblastoma	40	89	39	168
Non-Hodgkin's lymphoma	3	20	37	60
Oro-facial Kaposi sarcoma	51	82	27	160
Osteosarcoma	128	131	53	312
Pineoblastoma	5	18	3	26
Retinoblastoma	46	176	345	567
Rhabdomyosarcoma	548	442	97	1087
Sacroccygeal teratoma	1	17	2	20
Squamous cell carcinoma	7	10	8	25
Teratoma	1	8	4	13
Wilms tumor	712	990	515	2217
Yolk sac tumor	1	12	0	13

3.2.2 Cancer types

Leukemias are the most commonly presented cancer category at the UCI between 2017 and 2019. A total of 4129 leukemia confirmed cases have been presented to the institute. This is seconded by blastomas, with 3077 confirmed cases. 2018 saw the most presented cancer cases, with each major cancer category registering a spike in the number of presented cases. Overall, 11130 presented cancer cases were categorized into the five major cancer categories, as presented in Table 7.

Table 7: Types of cancer diagnosis at UCI between 2017 and 2019

Year	Type of Cancer					Total
	Blastoma	Carcinoma	Leukemia	Lymphoma	Sarcoma	
2017	846	14	1135	738	924	3657
2018	1311	14	1595	671	794	4385
2019	920	21	1399	477	271	3088
Total	3077	49	4129	1886	1989	11130

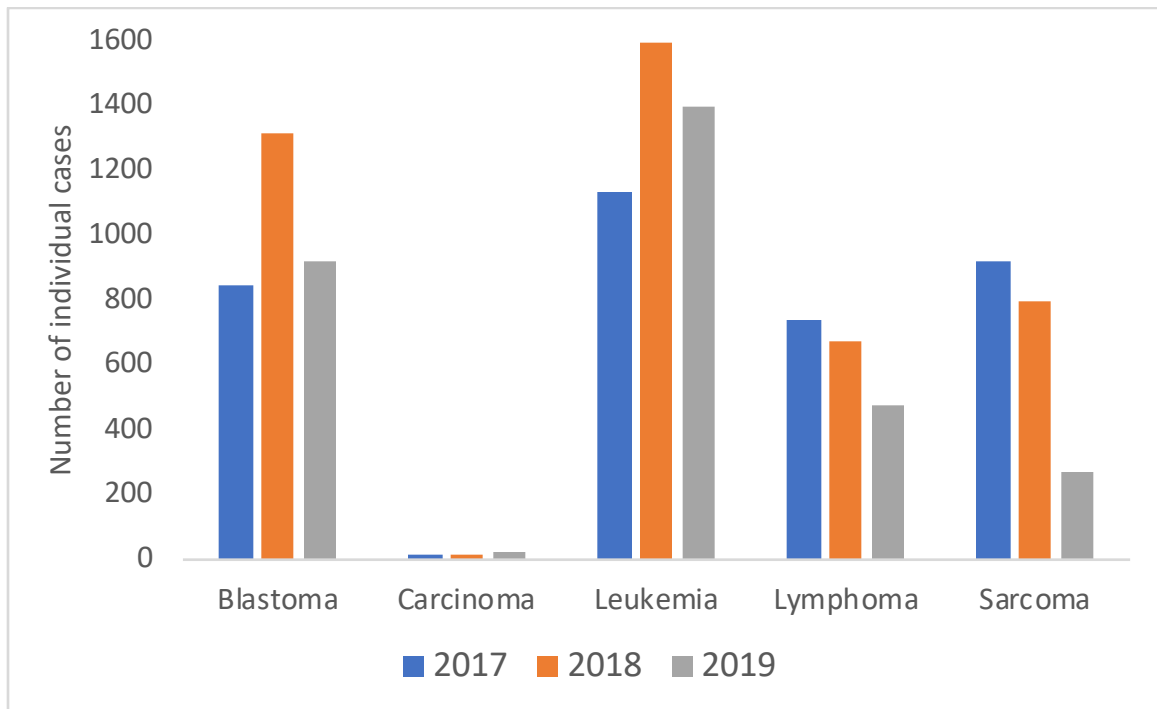


Figure 2: Types of cancer diagnosis at UCI (2017-2019)

3.2.3 Diagnosis by administrative region

Uganda is divided in four main administrative regions: Eastern, Western, Northern and Central. These regions are further divided into 111 districts and the capital city Kampala. Acute lymphoblastic leukemia remains the most common form of pediatric cancer diagnosis within these regions, the majority of the cases are from the central region of the country. The central region includes districts such as Kampala, Wakiso, Mukono, etc. which are highly populated areas compared to other parts of the country. The central region has the highest prevalence of all presented cancer diagnoses in the country. In total, this region has 10958 confirmed cancer cases between 2017 and 2019, as presented in Table 8.

Table 8: Pediatric cancer diagnoses by administrative region in Uganda

Diagnosis	Administrative Region				Total
	Central	Eastern	Northern	Western	
Acute Myeloid Leukemia	278	1	0	0	279
Acute Lymphoblastic Leukemia	3,820	20	3	7	3,850
Burkitt's Lymphoma	814	22	1	4	841
Germ cell tumor	173	0	0	2	175
Hodgkin's lymphoma	614	5	1	12	632
Kaposi sarcoma	302	4	1	2	309
Lymphoblastic lymphoma	303	2	0	2	307
Neuroblastoma	168	1	0	0	169
Non-Hodgkin's lymphoma	66	0	0	0	66
Oro-facial Kaposi sarcoma	161	2	0	0	163
Osteosarcoma	310	1	0	7	318
Retinoblastoma	633	5	0	1	639
Rhabdomyosarcoma	1,083	23	1	8	1,115
Wilms tumor	2,233	21	2	26	2,282
Total	10,958	107	9	71	11,145

Overall, there is no specific pattern to the distribution of the different cancer cases within the country. Most districts in the northern and eastern regions of the country are

missing data. Acute myeloid leukemia remains the most prevalent cancer diagnoses in the capital area of Uganda.

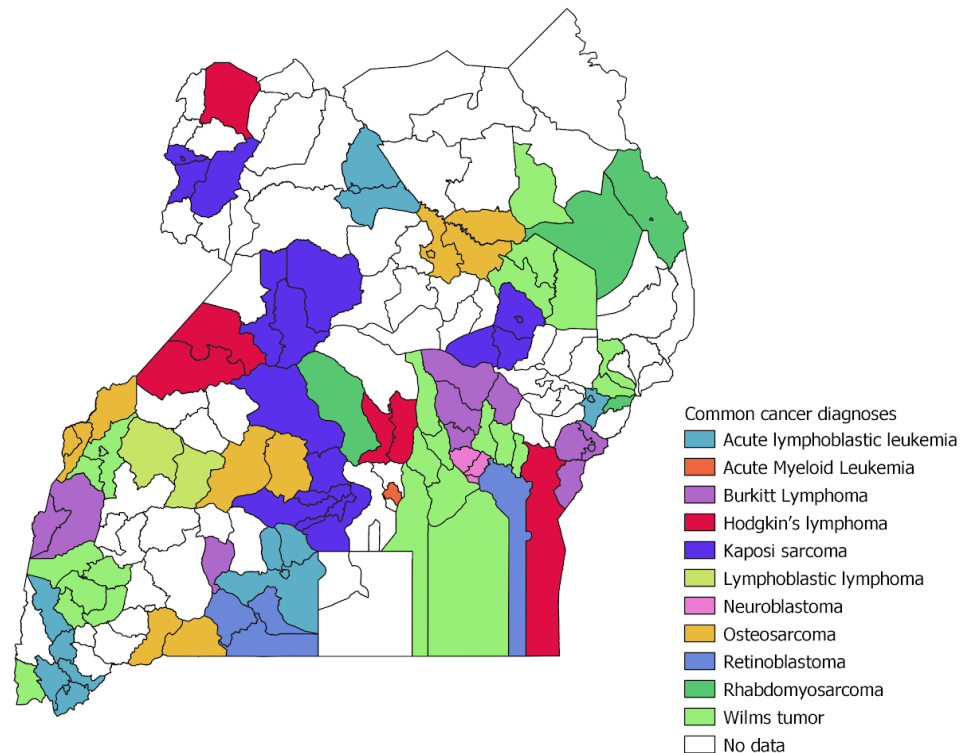


Figure 3: Geospatial distribution of common cancer diagnoses at UCI in Uganda between January 2017 and December 2019

As Figure 4 shows, the general distribution of the cancer types shows sarcomas as the most common cancer type in the districts. This is not consistent with the results presented in Table 7 where leukemias are the most common cancer type. Majority of leukemia cases come from mainly the central region of the country including Kampala, which may explain the concentration of the cases around that region. Out in other parts of the country, lymphomas appear to mainly come from the eastern, central and western regions of the country. Only one district in the northern region of the country shows

lymphomas to be the most common cancer type. East of the capital region, blastomas are the most common cancer type, with the western region also contributing other cases. Carcinomas have not been represented on the GIS map because patients with such diagnosis have residence information missing. Despite this, the prevalence of carcinomas is very low as shown in Table 7.

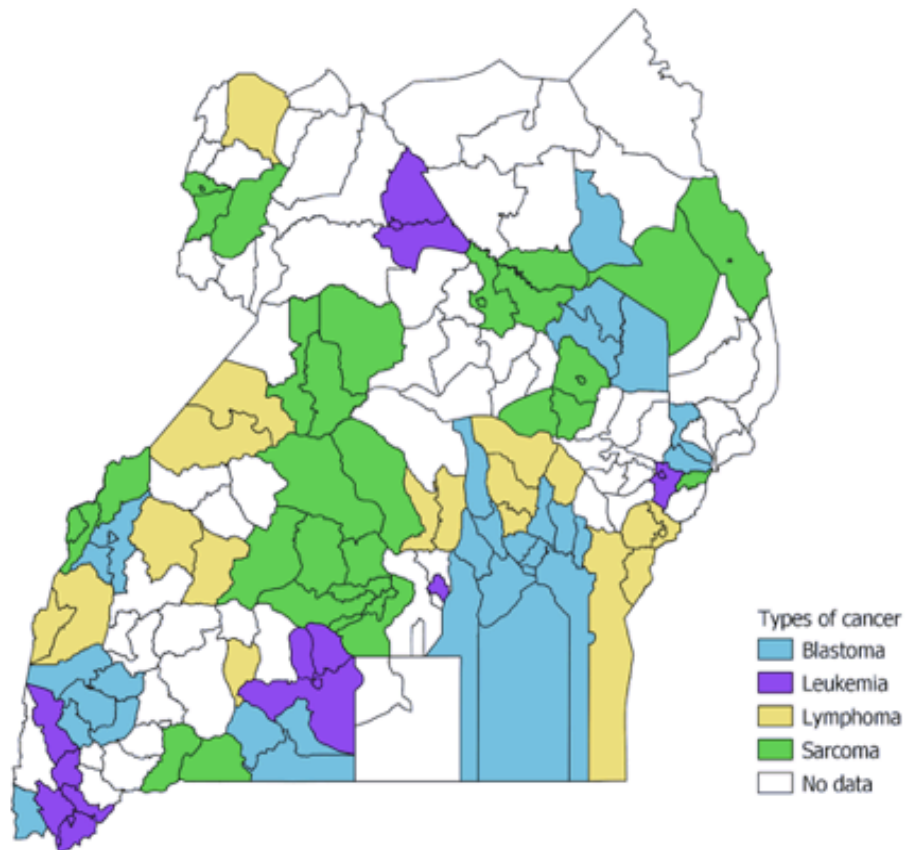


Figure 4: Uganda country-wide geospatial distribution of type of cancers presented at UCI between January 2017 and December 2019

3.2.3 Prevalence estimates of pediatric cancers at UCI

A total of 11607 patients have a confirmed cancer diagnosis. Of these, acute lymphoblastic leukemia is the most common, with a 3-year prevalence of 31.4%. Wilms tumor has a 19.1% 3-year prevalence, followed by rhabdomyosarcoma (9.4%), Burkitt's

lymphoma (6.9%), Hodgkin's lymphoma (5.3%) and retinoblastoma (4.9%). Other less common cancer diagnoses including Kaposi sarcoma, osteosarcoma, lymphoblastic lymphoma and others have less than 3% 3-year prevalence (see Appendix D). Quintile maps (Figure 5) show that most cases for all major cancer types come from the central region of Uganda, which is consistent with earlier results. For sarcomas, the majority of the districts have low numbers of diagnosis. However, districts north of the central capital region also show higher prevalence than most northern districts. Leukemia shows similar trends; however, a greater proportion of the diagnoses are from the central region. A greater proportion of blastoma cases come from different parts of the country, but the most concentration of cases also come from the central region of the capital city and surrounding areas.

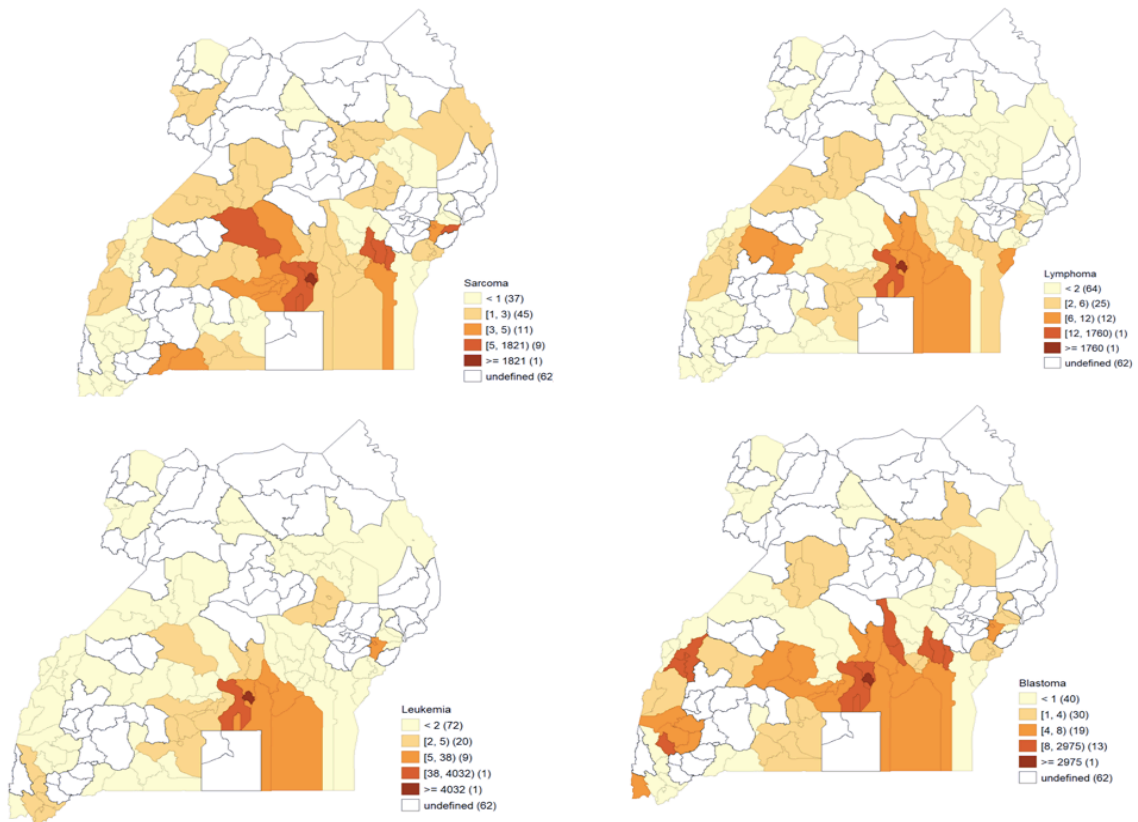


Figure 5: Geospatial distribution by quintile of cancer cases at UCI from districts in Uganda

A GIS percentile map (Figure 6) shows similar trends in proportion of cases originating from the different districts in Uganda. 57 districts fall between the 50th to 90th percentile of sarcoma cases in the country, however, only Kampala district falls in the >99th percentile of sarcoma cases. 95 districts fall in the 50th to 90th percentile for lymphoma, and similar to sarcoma, only Kampala falls in the greater than 99th percentile of lymphoma cases. For leukemia, 96 districts fall within the 50th to 90th percentile of cases, whereas for blastoma, the number of districts is 53. Anywhere from 6 to 9 districts fall in the 90th to 99th percentile of cancer cases for all cancer types in the study.

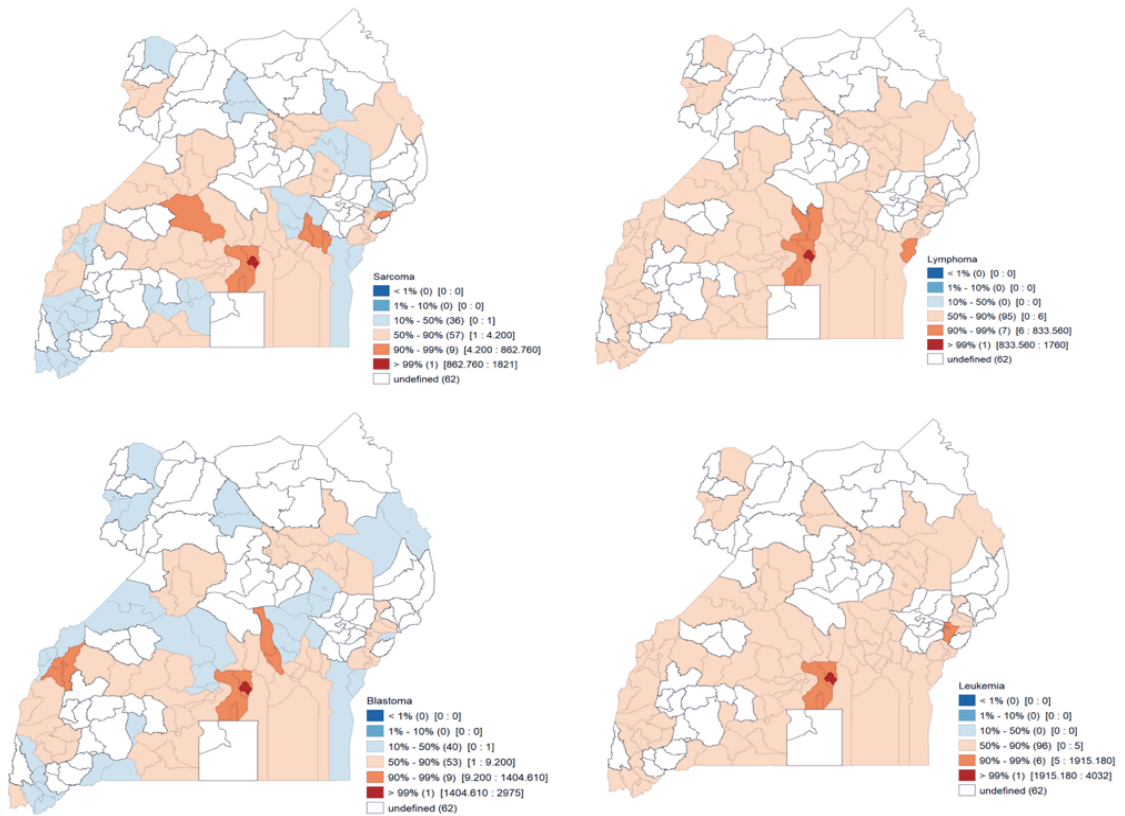


Figure 6: Geospatial distribution by percentage of cancer cases at UCI from districts in Uganda

4. Discussion

4.1 Aim 1: Factors associated with nutritional status in pediatric cancer patients

This study provides insight into factors associated with nutritional deficiencies in pediatric cancer patients in Tanzania and Uganda; and a 3-year detailed view of the prevalence, types, and forms of pediatric cancers presented at the out-patient department of UCI. Overall, abdominal circumference (AOR 1.38, 95% CI: 1.16 -1.65; $p<0.001$), serum albumin (AOR 0.73, 95% CI: 0.62 - 0.86; $p<0.001$) and muac (AOR 0.52, 95% CI: 0.31 - 0.87; $p=0.012$) are significantly associated with nutritional status in the study.

These predictors of nutritional status should be factored into nutritional screening tool development. Other factors explored in the study such as tsft (AOR 1.13, 95% CI: 1.01 - 1.27; $p=0.034$) and protein (AOR 1.08, 95% CI: 1.01 - 1.16; $p=0.018$) may also have potential as indicators in a nutritional screening tool. Although these variables were found to be significant, the confidence interval indicates a smaller effect on risk of nutritional status within the context of this study. This might explain why tsft and protein are associated with increased odds of being malnourished as the values increase, which is counterintuitive in reality but may be due to the lack of robust data for these indicators.

Collinearity has a big impact on the relevance of predictors of nutritional status. Weight, height and age variables negatively impact the accuracy and validity of a nutritional screening tool. This low accuracy and validity are the result of the unreliability of weight and age in SSA. These variables make it more difficult to estimate the correct partial effect of predictor variables on nutritional status because of the large standard error of the estimated coefficients.² Excluding such unreliable and collinear variables in a

logistic regression model helps prevent low sensitivity and specificity of the predictive model.

Weight is often unreliable in SSA, for several reasons.²⁰ In acutely ill patients, it is often confounded by fluid status and active metabolic tumors.^{26,27} Furthermore, active metabolic tumors can rapidly cause weight shifts as metabolic demands increases.²⁶ Fluctuating body fluid status renders BMI, weight-for-height, and weight-for-age not useful as indicators of nutritional status. Nutritional assessment tools reliant on unreliable or unvalidated anthropometric measures will potentially result in misdiagnosis or under-diagnosis, missing potential patients in need of critical nutritional intervention. As such, in surgical patients postoperative outcomes may not be correlated with nutritional status. Perioperative nutritional status is associated with significant postoperative complications including mortality.²⁶ Duration of postsurgical hospital stay is also shown to be longer in malnourished patients.²⁶ This finding is consistent with results in other studies examining the effect of perioperative malnutrition on postsurgical outcomes.²⁷⁻²⁹

Perioperative low levels of serum albumin are associated with adverse postsurgical outcomes.²⁶ Just like malnutrition, low serum albumin levels can act as good predictors of postoperative outcomes, however, serum albumin have poor correlation with nutritional status.^{30,31} Alone, serum albumin does not predict nutritional status well due to its multifactorial influence.³¹ However, when combined with peripheral blood lymphocyte count, termed prognostic nutritional index (PNI), calculated as $10 \times \text{serum albumin (g/dl)} \times 0.005 \times \text{total lymphocyte count (per mm}^3\text{)}$, PNI can assess nutritional status and predicts postoperative complications.^{32,33} PNI, easily measurable before surgery, can also predict long term survival after surgery.³² Patients with low PNI values

are at an increased odds of having adverse outcomes, thus, it is recommended physicians pay attention to this value in care for cancer patients. In this study however, PNI has not been assessed for its association with nutritional status due to the lack of total lymphocyte count data.

Furthermore, many studies use logistic regression to select indicators in the development of nutritional screening tools.² In this analysis, logistic regression estimated the probability of events with nutritional status. Increased abdominal circumference is associated with increased odds of being malnourished compared to patients with normal nutritional status. This is logical given that about 40% of patients in the study have Wilms tumor, a solid tumor malignancy often visible with large tumor mass. Often, these metabolic solid tumors may cause distention. In the case of Wilms tumor, distention results in an increase in abdominal circumference. The association between increased abdominal circumference and higher odds of malnourishment in this study is consistent with the notion that active metabolic solid tumors deteriorate the nutritional status of pediatric cancer patients.^{34,35}

Unlike abdominal circumference, muac is independent of the weight of a patient, ensuring reliability and fewer errors in measurement of nutritional status.¹⁰ The major determinants of muac are arm muscle and subcutaneous fat, both of which are important predictors of survival in adverse conditions such as starvation.³⁶ Patients with increasing muac have decreased odds of being malnourished in comparison to patients with normal nutritional status. This finding is consistent with the fact that muac is more sensitive and a better indicator of mortality risk associated with malnutrition than weight-for-height (WFH).⁹ Muac is independent of height and weight based indices such as WFH, body

shape and BMI, and is more indicative of tissue atrophy than low body weight.³⁶ Tsft is also independent of the weight of a patient. However, tsft is subjective in terms of measurement and thus lacks precision and accuracy. The variability in its measurement could account for why it may not be a reliable indicator of nutritional status in pediatric cancer patients. Similarly, symptom duration is also an unreliable indicator and subject to recall bias since it is often reported by patients or caretakers. Estimating when symptoms first occurred can be affected by other confounders or comorbidities.

4.2 Prevalence of pediatric cancer in Uganda

Data on cancer presentation and outcomes is often lacking in many SSA countries,³⁷ Uganda being no exception. This study describes cancer presentations at the UCI. Blood cancers such as leukemia (32.7%) are the most commonly presented cancer types at UCI, acute myeloid leukemia (2.3%) and acute lymphoblastic leukemia (31.4%) being top diagnoses among blood cancers. This high prevalence of blood cancers in an LMIC like Uganda burdens the system and poses several challenges. Information on the availability of all 22 chemotherapeutic drugs on the WHO essential medicines list in Uganda is scarce, however, most of the drugs imported within the region are generics, and not all of the drugs are in stock at all times.³⁸ This shortage of essential drugs results into diagnostic and treatment delays, which can cause immense physical and emotional suffering, disrupting family lives.³⁹ In addition, health expenditures of countries in SSA are dismal compared to HIC. It can range from \$17.00 per person in places like Congo to \$819.00 per person in South Africa.²¹ SSA government expenditure focuses on health priorities like malaria, HIV/AIDS, and tuberculosis.²¹ Thus, childhood cancer, among other NCDs, is perceived as low priority. Coupled with high poverty rates, dismal

government health expenditure challenges cancer treatment of presented cases, presentation stage at hospitals, and low presentation rates overall. Moreover, financial burden on families is exacerbated by a cancer diagnosis within the family. Low income families have an increased likelihood of non-compliance and defaulting on treatment.³⁹⁻⁴³ The estimated cost of burden on the poor could be between 30-50% of their monthly income, thus increasing their risk of impoverishment due to these catastrophic health expenditures.^{39,44} This increased financial distress causes treatment-seeking delays, late presentation to hospitals, and ultimately undermines help-seeking efforts.⁴⁴

B-cell lymphomas have been described in literature as the commonest childhood malignancies in SSA, followed by Wilms tumor, retinoblastoma, non-Hodgkin's lymphoma, rhabdomyosarcoma, and germ cell tumors.²¹ At the UCI, lymphomas (14.9%) are one of commonest presented blood malignancies, majority of which are Burkitt's lymphoma (6.9%) and Hodgkin's lymphoma (5.3%). The trend of presentation at UCI echoes similar childhood malignancies found in other SSA countries. Solid tumors sarcomas (15.8%) and blastomas (24.4%) are common diagnoses, but carcinomas are rare with only 49 confirmed cases over the 3-year period.

Wilms tumor is prevalent in SSA, ranked the second or third most common childhood malignancy.^{21,45} This claim in literature is supported by presentations at UCI, where Wilms tumor (19.1%) is the second commonest solid tumor malignancy, followed by rhabdomyosarcoma (9.4%) and retinoblastoma (4.9%). In the developed world, Wilms tumors treatment registered tremendous success, cure rates often exceeding 90%.²¹ Similar success rates are not mirrored in SSA, largely due to anesthetic, unresectability and tumor rupture problems.^{21,46} In addition, there is a scarcity of general surgeons and

pediatric surgeons in particular, with similar paucity in anesthetic and support staff in SSA.^{21,47–49} These lack of clinicians and support staff delegates Wilms tumor surgery to general surgeons, and given the lack of formal oncology structures in many SSA countries, treatment results are usually disappointing.²¹

Cancer cases at UCI come from many districts within Uganda. The number of cases presented at UCI represents the strain put on by the overwhelming number of new cases of cancer on the few centers of excellence for pediatric care in Africa. However, about 97% of all diagnoses at UCI within the 3-year timeframe come from the Kampala region. This result could be due to proximity and selection bias. But more importantly, the disparity in representation across the country could be the result of the strain seeking and receiving care from UCI places on families traveling from far. Certain out-of-pocket costs such as laboratory tests, imaging studies, and chemotherapy leave financially insecure families in dilemmas, thus they may have to choose the alternative of refusing treatment.²¹ In addition, family economic situations hinders regular follow-up especially from regions where travel is challenging and expensive.²¹

4.3 Implications for further research

Accurately identifying malnourished pediatric patients will allow for targeted, cost-effective nutritional interventions to be implemented during care for pediatric patients, thus, improving outcomes and survivability. To my knowledge, no prior study has engaged in this area in Uganda and Tanzania to date. This research paves the way for tailoring nutritional screening tools for pediatric cancer patients in SSA. Therefore, future researchers should aim to understand on a larger scale factors associated with nutritional status in pediatric cancer patients in SSA. The research should go beyond the hospital

setting to understand the influence of socio-economic status, family dynamics, etc., on nutritional status of pediatric patients. In addition, future studies should evaluate the effect diet and nutritional interventions have on cancer treatment as well as peri and postoperative surgical outcomes.

4.4 Limitations

This is a longitudinal hospital-based study. As such, data is acquired by means of convenience sampling. The results of this study are therefore not generalizable to other settings in SSA, or LMICs in general. In addition, the sample size for aim 1 of the study is relatively small for establishing association between predictors and dependent variables in the study. A larger sample size for a study like this would allow for better determination of factors associated with nutritional status in pediatric cancer patients. Mis-diagnosis of nutritional status is also a possibility, which will undoubtedly bias study estimates. Anthropometric measurements are also subjected to random errors, especially in measurements taken only once. Wilms tumor is overrepresented in the sample; thus, this factor may influence or force associations between predictors such as abdominal circumference and nutritional status in the study.

5. Conclusion

This study sought to understand factors that are associated with nutritional status in pediatric cancer patients and cancer prevalence in an LMIC setting. The study has shown that certain predictors that other developed nutritional screening tools from HIC use are not reliable in SSA setting. Predictors identified in this study are tailored to SSA, therefore, will more accurately identify nutritional deficiencies in pediatric cancer patients. Overall, the results show association of predictors with nutritional status, however, due to sample size and other limitations in the study, further studies must explore nutritional deficiencies in pediatric cancer patients on a larger scale. Both solid and blood cancers are prevalent in Uganda. Thus, further studies must also explore association of blood and solid cancers individually with pediatric nutritional status.

Appendix A: Correlational analysis of predictors with one another

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	<i>Nutritional Status</i>	<i>Age</i>	<i>Symptom Duration</i>	<i>Height</i>	<i>Weight</i>	<i>MUAC</i>	<i>TSFT</i>	<i>Abdominal Circumference</i>	<i>Serum Albumin</i>	<i>Protein</i>	<i>Hemoglobin</i>	<i>MCV</i>
Nutritional Status	1											
Age	0.1468	1										
Symptom Duration	-0.0405	0.0947	1									
Height	0.0751	0.9374	0.0331	1								
Weight	0.096	0.4837	0.6561	0.4388	1							
MUAC	-0.3862	0.5694	0.1204	0.5988	0.2774	1						
TSFT	0.0478	0.2324	-0.0821	0.2735	0.1458	0.312	1					
Abdominal Circumference	0.3244	0.2924	-0.0935	0.2888	0.2533	-0.0319	-	1				
Serum Albumin	-0.5132	0.0274	-0.2618	0.0544	-	0.3306	0.0395	0.0257	1			
Protein	-0.0388	-	-0.2	-	-	0.0186	-	-0.1578	0.3545	1		
Hemoglobin	-0.1549	-	0.1453	-	-0.121	0.1268	-	-0.1212	-0.0282	0.1542	1	
MCV	-0.3142	0.1042	0.1244	0.1114	0.1513	0.3513	-	-0.1466	0.0978	-	0.0767	1
							0.0586			0.2128		

Appendix B: Variance inflation factor analysis

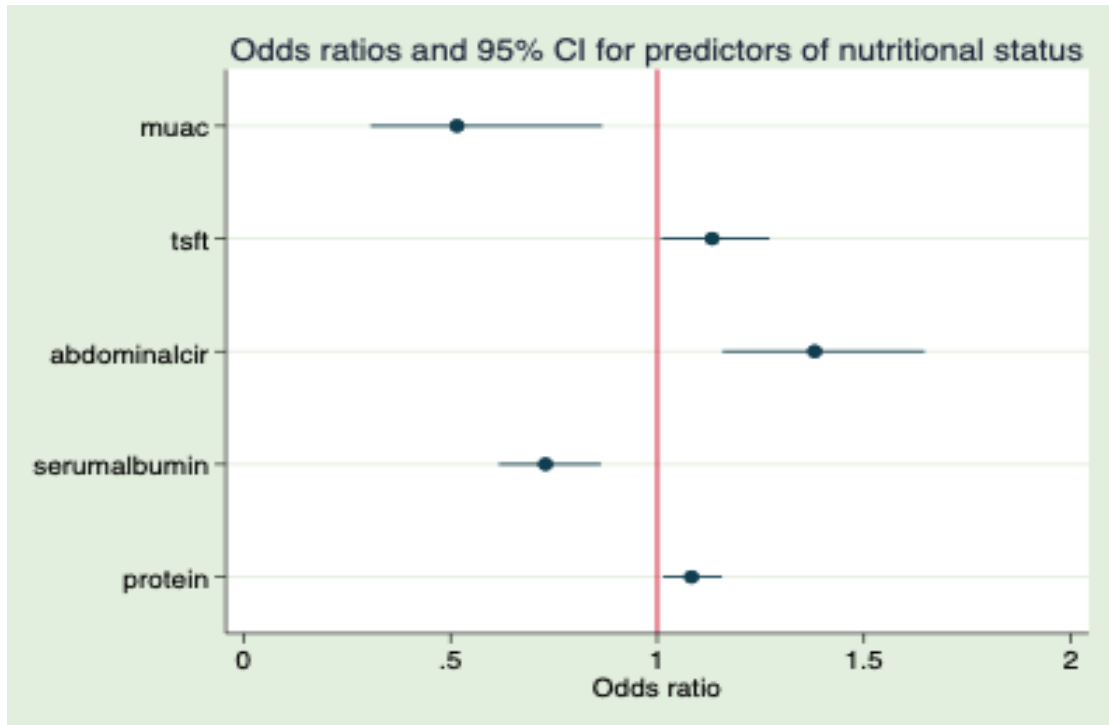
A: Variance inflation factor for all predictors in the regression model

Variable	VIF	1/VIF
Height	9.60	0.1042
Age	9.44	0.1060
Weight	3.50	0.2860
Symptom Duration	2.81	0.3558
MUAC	2.55	0.3917
Abdominal Circumference	1.62	0.6174
Serum Albumin	1.51	0.6643
Protein	1.47	0.6781
TSFT	1.46	0.6839
MCV	1.40	0.7143
Hemoglobin	1.22	0.8163
Mean VIF	3.33	

B: Variance inflation factors for the remaining predictors in the regression model after dropping age, weight, and height.

Variable	VIF	1/VIF
Weight	3.11	0.3217
Symptom duration	2.58	0.3870
MUAC	1.68	0.5954
Abdominal Circumference	1.56	0.6422
Serum Albumin	1.47	0.6802
TSFT	1.45	0.6919
Protein	1.40	0.7133
MCV	1.36	0.7337
Hemoglobin	1.2	0.83078
Mean VIF	1.76	

Appendix C: Odds ratios and 95% CI for predictors of nutritional status



Appendix D: 3-year pediatric cancer prevalence estimates at UCI (2017 - 2019)

Diagnosis	<i>Regional prevalence (%)</i>				
	Country	Central	Eastern	Northern	Western
Acute Myeloid Leukemia	2.3	2.4	<1.0	<1.0	<1.0
Acute Lymphoblastic Leukemia	31.4	32.9	<1.0	<1.0	<1.0
Burkitt's Lymphoma	6.9	7.0	<1.0	<1.0	<1.0
Germ cell tumor	1.3	1.5	<1.0	<1.0	<1.0
Hodgkin's lymphoma	5.3	<1.0	<1.0	<1.0	<1.0
Kaposi sarcoma	2.6	5.3	<1.0	<1.0	<1.0
Lymphoblastic lymphoma	2.6	2.6	<1.0	<1.0	<1.0
Neuroblastoma	1.5	2.6	<1.0	<1.0	<1.0
Non-Hodgkin's lymphoma	0.5	1.4	<1.0	<1.0	<1.0
Oro-facial Kaposi sarcoma	1.4	0.6	<1.0	<1.0	<1.0
Osteosarcoma	2.7	1.4	<1.0	<1.0	<1.0
Retinoblastoma	4.9	2.7	<1.0	<1.0	<1.0
Rhabdomyosarcoma	9.4	5.5	<1.0	<1.0	<1.0
Wilms tumor	19.1	9.3	<1.0	<1.0	<1.0

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