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Effects of chemotherapy and disease burden on the nutritional status of patients undergoing treatment for burkitt's lymphoma

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ABSTRACT

Burkitt's lymphoma is a malignant tumour of the B cellsand a major form of childhood cancer in sub-Saharan Africa. Treatment is through intensive cycles of cyclophosphamide and other chemotherapeutic agents. This study was aimedat determining the impact of disease burden and chemotherapy on the nutritional status of children suffering from the disease at the KATH, Kumasi, Ghana. Anthropometric measurements of BMI, TS), and MUAC of the patients were compared with normal healthy age – matched children. A total of 104 children were recruited for the study with 47 having the Burkitt's lymphoma and 57 control children. Male children (72.3%) were the most affected and the rest (27.7%) were females. Age block < 5 yrs TSF showed a significant difference between test and control (p=0.0340). BMI was significantly different for the age block 10-14 yrs (p=0.0014) so was MUAC for the age block 5-9 yrs and 10-14 yrs (p=0.0002 and < 0.0001 respectively). A negative correlation (-0.385 and -0.230) was found between stage of disease as well as stage of treatment and BMI (p=0.008 and p=0.005) respectively. The study showed that there was significant difference between test and control subjects for at least one age block.However BMI proved to be the strongest anthropometric indicator for nutritional status.Chemotherapy and disease burden were found to have significant effect on the nutritional status of patients undergoing treatment for Burkitt'slymphoma and thus nutritional intervention may be necessary during chemotherapy.

Keywords: Burkitt's lymphoma, Malignanttumour, lymphoid tissues, Tricep skin fold, BMI.

INTRODUCTION

Burkitt's lymphoma is one of the most prevalent cancers that affect children in sub-Saharan Africa and it accounts for about 74% of all malignant child disorders. It also known to affects adults and young adults of the temperate regions (Thorley-Lawson and Allday, 2008) and thought to be one of the fastest growing cancers. It is more common in damp and sultry regions and absent in dry places, hence its popularity in the tropics of Africa and South America (Van den Bosch, 2004). ThusBurkitt's lymphoma was originally referred to as the African lymphoma and then, endemic Burkitt lymphoma (Thorley-Lawson and Allday, 2008). There are three subtypes of the disease: endemic, sporadic and HIV – associated or immunodeficiency – related BL (Rochford*et al.*, 2005). There is no known cause for the disease, but studies have shown a close relationship of the disease with the Epstein-Barr virus (EBV) and malaria (Rochford*et al.*, 2005). According to Shapira and Peylan-Ramu(1998),malaria patients show incidences of an increase in the number of cells carrying the Epstein-Barr virus which suggests the possible relationship between the malaria parasite and the virus (EBV) - a hypothesis based, for the most part, on the similarity in the geographical distribution of malaria incidences, EBV and Burkitt's lymphoma.

Treatment for Burkitt's lymphoma is based on the stage of the disease and the main type of treatment given is chemotherapy. According toShapira and Peylan-Ramu (1998),it is one of the first human cancers believed to be cured by chemotherapy alone though in more severe cases, surgery and radiotherapy are used when disease is not responding to chemotherapy.

The chemotherapy drugs commonly used include cyclophosphamide, vincristine, methotextrate and doxorubicin. Rituximab, a monoclonal anti – CD20 antibody is sometimes also used (Orem*et al.*, 2007). These chemotherapeutic drugs function by targeting rapidly dividing cells and this adversely affect normal body cells of similar character such as the cells of the gastrointestinal tract, mouth, hair follicles and blood cells. Thedrugs also have side effects that directly or indirectly affect the nutritional status of the children by inducing nausea, vomiting, diarrhoea and weakness (Capra*et al.*, 2001). The malignant cells of the tumour compete with the normal body cells for nutrients and because they replicate faster than normal body cells, they use up more nutrients than the normal cells. When the nutritional status of children is affected, their tolerance to treatment is impaired and this leads to poor prognosis (Capra *et al.*, 2001; Donaldson andLenon, 1979).

Cogill (2003) describes anthropometric measurements as widely accepted non – invasive methods for determining the nutritional status of individuals. The measurements include weight-for-age which is an indication for underweight, length-for-age (Height for age) for stunting, weight-for-length (weight-for-height) for wasting, BMI-for-age, Mid-upper arm circumference and tricep skin fold.

The aim of this study was thus to investigate the effects chemotherapy and disease burden on the nutritional status of children suffering from Burkitt's lymphoma by determining the nutritional status of patients using anthropometric methods against patients with normal healthy age – matched children.

PATIENTS AND METHODS

The study was conducted between February 2011 and March 2012 and a total of 104 children were enrolled, out of which 47 were Burkitt's patients visiting the PaediatricOncology Unit (POU) of the Komfo-Anokye Teaching Hospital, Kumasi-Ghana while the remaining 57 controls were healthy age-matched pupils of Weweso M/A Primary School Kentikrono, Kumasi. Informed consent was sought from parents as well the children and from the school's management before study was begun. Inclusioncriteria for the test samples were children who hadclinical/ histological diagnosis of endemic Burkitt's lymphoma by a physician and aged between 1 and 15year(s) and have undergone at least one chemotherapy cycle of treatment.Ethical approval for the study was obtained from the Committee on Human Research, Publications andEthics of KNUST and KATH (CHRPE/ KNUST/ KATH/ 17/11).Questionnaires were administered while the age, height, weight,tricep skinfold and mid-upper arm circumferences as well as the stages of chemotherapy and cancer were recorded. The BMI was then calculated.

DATA COLLECTION AND STATISTICAL ANALYSES

Anthropometric indices of weight, height, mid-upper arm circumference andtricep skin fold were measured for each of the children using an electronic scale (Seca 767, Birmingham, UK), a height board (stadiometer), a TR 16 tape measure (Perfect Measuring Tape Company, Toledo, Ohio) and a set of 160-125 vernier calipers (Tide Machine Tool Supply Co. Ltd., China). Data obtained was subjected to statistical analysis using Graph Pad Prism version 5 for Windows (Graph Pad Software, San Diego California, USA) where a two-tailed, unpaired t-test was performed on data to compare BMI, triceps skin fold (TSF) and mid-upper arm circumference (MUAC) of cancer patients with that of the healthy age-matchedchildren (control). $P<0.05$ was considered statistically significant for any measure of difference. The data was further subjected to Pearson correlation analysis to determine the relation between stage of disease and stage of chemotherapy with the various anthropometric measurement.

RESULTS AND DISCUSSION

Table 1 gives the general characteristics of the study population with the test group constituting 47 (45.2%) and control group (non-cancer children) representing 57 (54.8%) of the study population. Majority of the males had cancer contributing (72.3%). Majority of the children with cancer fell within the 5-9 age block (42.6%).

Table 1: General characteristics of the study population stratified by gender, sex, age stage of disease and cycle of chemotherapy

CHARACTERISTIC	TEST N = 47	CONTROL N = 57	TOTAL
GENDER			
M	34 (72.3)	28 (49.1)	62
F	13 (27.7)	29 (50.9)	42
AGE (Years)			
< 5	12 (25.5)	6 (10.5)	18
5-9	20 (42.6)	27 (47.4)	47
10-14	15 (31.9)	24 (42.1)	39
STAGE OF DISEASES			
STAGE 1	25 (53.18)	-	25
STAGE 2	10 (21.28)	-	10
STAGE 3	10 (21.28)	-	10
STAGE 4	2 (4.26)	-	2
CYCLE OF CHEMOTHERAPY			
Prephase - Cycle 4	40 (85.11)	-	40
Cycle 5 - cycle 8	7 (14.89)	-	7

Table 1 confirms the predominance of males with BL compared to females, similar to observations by Owusu*et al.* (2009). The study reported an age range of 4-8yrs for endemic Burkitt's lymphoma which is consistent with this study. It was also observed that most of the diseases were in their early stages (n=25, 53.19%) and this is probably due to subsidized cost of treatment at the hospital motivating parents to report early.

Nitenberg andRaynard (2000)reported that malnutrition can result from the parasitic metabolism of the tumour at the expense of the host and from increasingly aggressive chemotherapy, leading to increased risk of complications and death. Thus even without chemotherapy, the disease itself affects the nutritional status of the patients.

Cronk*et al.* (1982) described TSF as the best clinical indicator of body fat on statistical grounds. However, it appears this very important nutritional marker is not in common use because reference values are not readily available. For this reason, we compared this indicator for patients with healthy children age for age. The results in Table 2 showed that for patients < 5 yrs, the mean TSF was statistically different from that of the control subjects while others were not. This could be due to the fact that children under 5 are still actively growing and require a lot of nutrients. Thus any condition that reduces the amount of nutrients available to the body adversely results in a loss of body fat as the body quickly turns to the fat reserves for energy needs and thus leads to reduction in the total fat reserves in the body.

Table 2. Anthropometric measurement for Cancer and Non-cancer children

AGE RANGE (Yrs)	TEST Mean±SD	CONTROL Mean±SD	p-value
BMI (kg/m^2)			
<5	16.15± 2.883	16.62± 1.074	0.7114
5 -10	15.59± 2.735	15.6± 1.406	0.9795
10-14	14.22± 3.366	17.03± 1.298	0.0014
TSF (cm)			
<5	5.464± 4.676	10.01± 1.003	0.034
5-10	8.67± 3.978	8.885± 1.584	0.7955
10-14	12.49± 3.796	10.07± 3.268	0.0793
MUAC (mm)			
<5	146.2± 19.11	152.3± 8.959	0.475
5 -10	141.4± 30.62	166.9± 10.16	0.0002
10-14	142.4± 50.23	199.4± 18.56	< 0.0001

Results for BMI showed a significant differences between patients and control subjects and their mean values (Table 2) for the 10 to 14 age block. Dintiman and Greenberg (1983)described BMI as a guideline that compares an individual's weight to height to determine the individual's risk of health – related weight problems. Barr(2002) also stated that BMI may not be the best way to ascertain the nutritional status in paediatric oncology as some children have very large tumours especially abdominal tumours that contribute appreciably to overall body weight. Although it was not possible to measure how significant the size and weight of the tumours contributed to the weight of the individual, the fact that the test subjects in the 10 to 14 age block still showed a significant difference from the control group implies that in spite of the weight of the tumor, the test subjects were significantly underweight for that particular age block.It was expected that BMI of BL patients would be significantly lower than those of control subjects for all age blocks. However, this was not observed (Table 2). In a similar report, Barr (2002) observed that

about 50% of all children in developing countries are malnourished. This can be seen from the results of mean BMI (Table 2) where even the control subjects recorded mean BMI values less than 18.5 kg/ m^2 which is the cut off point for underweight according to WHO (2006).

Cogill (2003) reports that MUAC is a good predictor of immediate risk of death and is relatively easier to measure. It is also used as a quick screening method of assessing acute malnutrition. Thus for MUAC, which takes into account muscle as well as fat stores, the 5 – 9 and 10 – 14 age blocks showed significant differences ($p=0.0002$ and $p<0.0001$ respectively) in mean values between test and the control groups (Table 2). This implies that for those age blocks the patients suffered from acute malnutrition due to the effect of the disease burden as well as the chemotherapy on the test subjects. However, the below 5 age block were found to be statistically insignificant and this may be due to the fact that children below age 5 has special nutritional needs because of their extensive growth and development compared to their older counterparts hence no need to store body fats in the upper arm (Bishnoi*et al.,* 2004).

Table 3: Relation between Stage of Disease and stage of Treatment with BMI, TSF and MUAC

Parameter (p-value)	Stage of Treatment	BMI	MUAC	TSF
Stage of Disease		-0.385(**0.008**)	0.040	-0.011
BMI	-0.230(**0.005**)		0.193	-0.110
MUAC	-0.168	0.193		0.027
TSF	-0.048	-0.110	0.027	

Table 3 showsthe Pearson analysis to determine the association between the stage of the diseases and how it relates with the various anthropometric variables. BMI showed a negative correlation which was statistically significant ($p=0.008$). The correlation was also significant between stage of treatment and BMI ($p=0.005$). All the parameters showed negative correlation because as disease and chemotherapy progressed, body fat and muscle mass as well as weight decreased and thus all three parameters of TSF, MUAC and BMI reduced. TSF is a measure of body fat whiles MUAC measure both fats and muscle. From Table 3 it was clear that in cancer and non-cancer cases, the anthropometries decrease as disease and chemotherapy progress. It implies that when the values for patients at different stages of the disease and different stages of chemotherapy were compared, there should be some differences but these differences were not expected to be significant unless diseases was at a far advanced stage, such as stage four before the onset of the treatment. For BMI, however, weight is directly proportional whereas height is inversely proportional. This means that as weight begins to decrease and height remains the same, due to both disease burden and chemotherapy, the BMI will reduce drastically and because patients have different ages between two and fourteen, their heights will vary greatly and thus their BMI's will also vary significantly.

CONCLUSION

From this study, it is clear that disease burden and chemotherapy do have an effect on nutritional status as shown bythe BMI and TSF of Burkitt's lymphoma patients and the effect is statistically significant for patients within the under 5 and 10 to 14 age block respectively. Chemotherapy and disease burden had a statistically significant effect on the MUAC of patients in the 5 to 9 age blocks and the 10 to 14 age blocks but not on the below 5 age block. BMI is also a better anthropometry indicator for nutritional status in children undergoing chemotherapy.

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