DISSERTATION

TITLE OF STUDY

THE NUTRITIONAL STATUS OF PATIENTS PRESENTING WITH NASOPHARYNGEAL CARCINOMA AT KENYATTA NATIONAL HOSPITAL

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DECLARATION

This dissertation is my original work and has not, to the best of my knowledge been presented for a degree in any university.

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TABLE OF CONTENTS

1.1 LIST OF TABLES AND FIGURES

1.2 ACRONYMS & ABBREVIATIONS

NPC	Nasopharyngeal carcinoma
WHO	World Health Organization
ENT-HNS	Ear, Nose, Throat, Head and Neck Surgery
KNH	Kenyatta National Hospital
EBNA1	Epstein Barr Nuclear Protein1
LMP	Latent infection Membrane associated Protein
HNSCC	Head and Neck Squamous Cell Carcinoma
BMI	Body mass index
IBW	Ideal Body Weight
OR	Odds ratio
EORTC-QLQ	European Organization for Research and Treatment of Cancer- Quality of Life Core Questionnaire
ECOG	Eastern cooperative oncology group
NPY	Neuropeptide Y
IL-1	Interleukin-1
IL-2	Interleukin-2
IL-6	Interleukin-6
TNFα	Tumor necrosis factor α
MCH	Melanin-concentrating hormone
AGRP	Agouti-related peptide
CRF	Corticotropin-releasing factor

2.0. ABSTRACT

Background: Nasopharyngeal carcinoma is a common malignancy in the Kenyan population. Kenyan patients tend to present in advanced disease increasing their risk of malnutrition. This affects their prognosis and quality of life.

Objectives: To determine the nutritional status of patients presenting with Nasopharyngeal Carcinoma at the KNH and the effect of the stage of disease and the histology on the nutritional status in Nasopharyngeal Carcinoma patients.

Design: A case-control study.

Methodology: 60 patients with Nasopharyngeal carcinoma were recruited into the study. The patients' bio-data, history, anthropometric measurements and serum albumin levels were recorded in a customized questionnaire. 123 patients matched for age and gender were recruited into the control group all of whom had a negative history of weight change in the preceding six months.

Study setting: The Kenyatta National Hospital

Results: 35% of patients with Nasopharyngeal carcinoma were found to be malnourished *(P value <0.0001)*. Anorexia, dysphagia and odynophagia were the most common problems affecting food intake. The probability of being underweight in patients with nasopharyngeal carcinoma was increased (OR 9.3 [95% CI] 3.4 – 25.3 *P value <0.001*). Patients with BMI <18.5 were more likely to have low albumin levels compared to those with normal BMI values (OR 8.0 [1.6-39.5] CI 95% *P value 0.013*). Advanced disease was associated with a decrease in BMI (*P value 0.019*) and serum albumin levels (*P value 0.002*). The patients with BMI <18.5, serum albumin levels <30 g/L and percentage IBW <90% were found to have a lower mean caloric intake (*P value <0.001*). Patients with metastatic disease had hypoalbuminemia (mean 29.0g/L SD 5.0*P value 0.002*)

Conclusions and recommendations: Nutritional status is adversely affected by Nasopharyngeal carcinoma. Nasopharyngeal carcinoma is associated with lower BMI, lower percentage IBW and reduced caloric intake compared to controls. Advanced disease and metastatic disease is associated with underweight and hypoalbuminemia. Nutritional intervention is therefore necessary for all patients presenting with Nasopharyngeal carcinoma.

3. INTRODUCTION

Nutrition is a significant aspect of cancer management given that it determines the patient's functional status, tolerance to therapeutic interventions and thus the overall prognosis of the disease. Mutation of normal eukaryotic cells to cancerous state and their continuation to establish a successful progeny tends to alter the metabolism of the whole organism to support the malignancy's metabolic interests. These alterations push the organism to a catabolic mode, and cause dysgeusia and anorexia thereby causing malnutrition[1]. Furthermore, the patient's metabolic and immunologic response to cancer also tends to encourage malnutrition. Clinical nutrition is the management of nutritional status in a patient with established disease. This requires striking a balance between the caloric intake and the energy expenditure by the individual. The physiological changes in the body's metabolic functions that occur in cancer cause a change in nutritional requirement. In sub-Saharan African adult population, an elevated baseline malnutrition has been documented with Eastern Africa burdened with the highest rates of poor nutrition and stunting in Africa with rates as high as 32% in some regions.[3] The prevalence of undernutrition in Kenya stands at 33%[4].

Nasopharyngeal carcinoma is an epitheloid tumor arising from the cells that line the surface of the nasopharynx. Nasopharyngeal carcinoma (NPC) accounts for 0.7% of all cancers and is the 23rd most prevalent cancer globally [5]. However among the East and South East Asian populations it is the most prevalent cancer[5]. In North Africa and Middle East, especially in Turkey, Tunisia and Iran, nasopharyngeal cancer is among the most common head and neck cancers but is not as frequent as in Asia[6]. In sub-Saharan Africa, it is estimated to be among the most prevalent head and neck cancer[7]. The dearth of accurate and current national cancer registries in sub-Saharan Africa makes its precise incidence and prevalence rates uncertain at the least. For this reason it is important that the prevalence of malnutrition and its effects on the management of such a high profile cancer like NPC is documented in order to alleviate the morbidity and improve the quality of life of these patients.

3.1. BACKGROUND

The nasopharynx is located posterior to the choanae of the nasal cavity above the level of the soft palate. Further laterally in the anterior limit are the pterygoid plates from which the masticatory muscles attach. Its posterior and superior boundaries are formed by the body of the sphenoid, the clivus of the occipital bone and the upper two cervical vertebrae. Its lateral wall is formed by the medial end of the cartilaginous Eustachian tube, the torus tobarius, the Eustachian tube opening and the lateral pharyngeal recess otherwise known as the fossa of Rossenmuller. Lateral to the fossa of Rosenmuller is the parapharyngeal space in which the cranial nerves IX through XII are located. The most common site of origin of nasopharyngeal carcinoma is around the nasopharyngeal opening of the Eustachian tube in the fossa of Rosenmuller. However, this tumour can arise from any part of the nasopharynx. Wherever the origin, this tumour rapidly spreads anteriorly to the nasal cavity, laterally through the pharyngobasilar fascia into the parapharyngeal spaces, inferiorly to the oropharynx and along the foramin lacerum, foramen ovale or via bony erosion intracranially . Such spread has direct effect of deglutition by causing obstructive effects and infiltrating nerves that coordinate swallowing mechanism.

The V, VII, IX, X and XII cranial nerves are crucial in the process of mastication and swallowing. The oral preparatory phase is a mechanical voluntary phase in which food is chewed into smaller pieces and tasted. It is mixed with saliva whose secretion is under the control of cranial nerve IV and forms a food bolus. Tongue motion and a labial seal as well as tension in the buccal muscles ensures the food is well mixed and prevents pocketing. The oral transport stage is voluntary and food is moved to the back of the mouth by the tongue via an anterior to posterior rolling motion. When the bolus comes into contact with the posterior wall of the pharynx the pharyngeal stage, which is involuntary, begins. The cranial nerves VII, IX and X sends afferent information to the medullary swallowing centre and the posterior pillars contract and the bolum passes down the pharynx. At the same time the soft palate closes off the nasopharynx by the action of the levator and tensor veli palatini muscles. The tongue retracts preventing return of the bolus into the mouth. Simultaneously the larynx and the hyoid are pulled both upward and forward, enlarging the pharynx and encouraging relaxation of the cricopharyngeous muscle. Closure of the larynx

begins as the true vocal folds and progresses up to the false vocal folds and then to the aryepiglottic folds. The epiglottis covers the laryngeal inlet and in so doing diverts the bolus into the pyriform sinuses protecting the airway. The bolus passes the upper oesophageal sphincter into the oesophagus thereby heralding the oesophageal phase which is involuntary. The bolus moves down via peristalsis and gravity. The larynx returns to its normal position and the cricopharyngeus contracts to prevent reflux.[36]

Despite the fact that most nasopharyngeal carcinomas are of the undifferentiated type, the cells show microscopic evidence of squamous differentiation. Undifferentiated carcinoma has a higher mitotic rate hence the overall catabolic effect on the host is inevitable higher than in the Western set up where the majority of cancers are of well differentiated variety and are more common in the very elderly population. In 1978 the WHO proposed a histological classification of nasopharyngeal carcinoma, categorizing the tumour into three groups namely; type I which is a keratinizing squamous-cell carcinomas, type II which is a non-keratinizing squamous carcinomas and type III which is an undifferentiated carcinoma. The histological distribution in southern Chinese patients is 95% have type III carcinoma compared to 63% in North America. Type II and III variety of cancers are linked to Epstein Barr Virus (EBV) in suitably genetically oriented subjects in the right environmental atmosphere. Patients with keratinising squamous-cell carcinomas (WHO type I) have been found to have a lower EBV titre compared to those with nonkeratinizing carcinomas (WHO type II and III). Type II and type III tumors are associated to EBV in the present WHO classification. This defines nasopharyngeal carcinoma as keratinizing squamous-cell carcinomas or non-keratinising carcinomas. The non-keratinizing carcinomas are then further subdivided into differentiated and undifferentiated carcinomas. [44] The TNM classification of the American Joint Committee on Cancer considers the sites involved, the extent of the primary tumor, the size and number of cervical lymph nodes involved and presence of metastasis when determining the tumor stage. This employs the prognostic value of nodal disease especially extending into the lower cervical and supraclavicular areas.

STAGE GROUPING			
Stage 0	**Tis**	**No**	**Mo**
Stage 1	T1	No	Mo
Stage IIA	T2a	No	Mo
Stage IIB	T1, T2	N1	Mo
Stage III	T1-T3	N2	Mo
Stage IVA	T4	No-N2	Mo
Stage IVB	Any T	N3	Mo
Stage IVC	Any T	Any N	M1

In Kenya Nasopharyngeal carcinoma is the second most prevalent head and neck cancer seen at the Kenyatta National Hospital (KNH). Muchiri M in 2003 did a hospital based study at the KNH on the demographic pattern and clinical characteristics of nasopharyngeal carcinoma[8]. There was a male preponderance of 2.2:1. Majority (83%) of patients presented in late disease (stage III and IV). Today head and neck cancers occupy 40% of in-patient beds at the Ear Nose and Throat Surgical ward at the KNH and in the year 2010, of the total head and neck cancer patients admitted into the unit, 15% had nasopharyngeal carcinoma[9].

Nasopharyngeal carcinoma causes poor nutrition through both local, neurological and physiological alteration of the body's normal homeostatic state. This is via dysphagia, odynophagia, anorexia, advanced age of patients, protein loss via tumour necrosis, ulceration, infection and haemorrhage and the cancer cachexia syndrome. Anorexia, dysphagia, oral sores are significant predictors of reduced dietary intake and weight loss which affects overall survival[10]. Patients with NPC usually present with enlarged cervical nodes but direct questioning frequently reveals that they have had complaints of headaches, facial pain and unilateral deafness before the appearance of the node. Consequently most patients present late with stage III and IV disease with profound consequences on their nutritional status.

Nasopharyngeal carcinoma is a highly radiosensitive tumor and the mainstay of treatment of the primary tumor is radiotherapy. Chemotherapy is used in controlling cervical spread and distant metastasis. Stage I and IIa disease which has no regional node involvement is treated by radiotherapy. Stage IIb and advanced stages of the disease are treated via combined chemotherapy and radiotherapy. Currently the NPC-2003-GPOH protocol is considered the optimum treatment practice in children and adolescents with nasopharyngeal carcinoma. In this protocol immunotherapy with interferon-beta after chemotherapy and radiotherapy is shown to improve the outcomes of the patients.[40] Stage I and II tumors receive radiotherapy only followed by adjuvant interferon beta (IFN- β) three times a week for 6 months. Stage IIb and above receive three courses of chemotherapy (cisplatinum and 5-fluorouracil) every 3 weeks or on full blood count recovery. This is followed by irradiation and IFN-β as adjuvant therapy. If clinical remission does not occur after three courses of chemotherapy, concomitant cisplatinum with radiotherapy is given for two courses. Mucositis, anorexia, odynophagia and dysphagia commonly occur on patients on treatment. Malnutrition, severe anaemia and leucopenia from chemoradiation place the patient at higher risk of toxicity from further treatment. A recent study of the use of the NPC-2003-GPOH protocol in adults has shown promising results.[49]

3.2. METABOLISM IN HEALTH

Metabolism is defined as the sum of the physical and chemical processes in an organism by which its material substance is produced, maintained and destroyed and by which energy is made available[11]. Catabolism is the phase of metabolism in which nutrient molecules such as carbohydrates, fats and proteins are converted into simpler end products with the release of energy. Anabolism is a biosynthetic process in which simple precursors are built up into more complex molecules requiring input of energy. In the average diet the daily energy intake is derived 45% from carbohydrates, 40% from fats, and 15% from proteins. Energy output is used for performing essential metabolic functions of the body known as the basal metabolic rate. Also the energy is consumed when digesting, absorbing, and processing food, maintaining body temperature and performing various physical activities;.

Carbohydrates absorbed from the gastrointestinal system are converted into glycogen for storage and released into the bloodstream as glucose when necessary. Glucose undergoes aerobic respiration via three stages namely glycolysis, Kreb's cycle and the Electron Transport Chain to produce energy.[12] The energy requirement in an individual is determined by a variety of factors such as his age, weight, physical activity level and health status. It can range from 20 – 30 kilocalories per kilogram of ideal body weight under normal circumstances and with additional stress factors it may increase upto 50kcal/kg of the ideal body weight.

Proteins are essential for cell growth and production of various body chemicals. Of the body proteins 20-30g of the body proteins are degraded. An average person can maintain normal stores of protein, provided the daily intake is above 30-50g. Some partial proteins have inadequate quantities of certain essential amino acids and therefore cannot be used to replace the degraded proteins. When they are present in large quantities in the diet, the daily protein requirement is much greater than normal. When the diet contains an abundance of carbohydrates and fats, almost all the body's energy is derived from these two substances, and little is derived from proteins. Therefore, both carbohydrates and fats are said to be protein sparers. Conversely, in starvation, after the carbohydrates and fats have been depleted, the body's protein stores are consumed rapidly for energy. Healthy individuals require a kilocalorie to nitrogen ratio of 300:1 for protein sparing. This reduced to 150:1 in protein depleted individuals. Nourished individual thus require 0.8 – 1.0g of protein per kilogram of ideal body weight and this amount increases to upto 2.0g /kg of ideal body weight in patients in catabolic mode.

In most eukaryotic cells, triglycerides serve as depots of metabolic fuel in adipocytes. Adipocytes contain lipases that catalyze the hydrolysis of stored triglycerides, releasing fatty acids for export to sites where they are required as fuel. Oxidation of lipids yields more than twice as much energy, gram for gram, as the oxidation of carbohydrates. In addition, as triglycerides are hydrophobic, the organism that carries fat as fuel does not have to carry the extra weight of water of hydration that is associated with stored polysaccharides (2 g per gram of polysaccharide). Normal fat dietary requirements is 20-30% of kilocalories should be derived from them.

3.3. METABOLISM IN CANCER

Malignant cell have impaired metabolic pathways as a primary feature. Malignant cells usually show self-sufficiency in growth signals, avoidance of apoptosis, insensitivity to growth-inhibitory signals, limitless replicative potential, unremitting angiogenesis, tissue invasion and metastasis. [13] Malnutrition increases the risk of infections, treatment toxicity and health-care costs and decreases response to treatment, quality of life and life expectancy[14, 15, 16]. Quality of life issues are based on among others, pain issues, functional aspects and nutritional and swallowing problems.

Energy production in cells primarily depends on oxidative phosphorylation within mitochondria to produce the energy necessary for normal cell functions. Malignant cells on the other hand rely on glycolysis even in the presence of oxygen, a phenomenon termed "the Warburg effect." Glycolysis is a highly inefficient way to generate adenosine 5'-triphosphate (ATP) the primary energy molecule within the cell. Mitochondrial uncoupling plays a role in this process. This effect is also noted to infer chemoresistance in certain cancers such as leukemia and further research is being done on the role it plays in other malignancies[17]. Particular mutations in the mitochondrial DNA have been shown to affect the normal respiratory function.

The malignant cells demonstrate increases rates of glycolysis and gluconeogenesis. There is also a shift toward the Cori cycle to replenish the glucose and as a result there are high levels of lactic acid produced. When the glucose stores in the body are depleted then an alteration in lipid metabolism occurs with a shift to gluconeogenesis. Depletion of the fat stores then occurs with is decreased lipogenesis resulting an elevation of the levels of free fatty acid. The tumors cells also produce lipolytic factors decreasing the lipoprotein lipase activity. Muscle catabolism also occurs with substrates for gluconeogenesis produced and also due to increased tumor protein synthesis. There is high protein turnover and the secretory liver proteins are reduced in production.[17]

Anorexia can be defined as a reduction in food intake caused primarily by diminished appetite. This definition emphasizes the important role of central neural mechanisms in the pathophysiology of anorexia in diseases such as cancer. Other common problems, such as pain

and nausea, may also cause a person to consume less food.[18] The anorexia of malignancy is defined as food intake inadequate to meet the combined needs of malignancy and the host significantly contributes to increased weight loss and mortality in cancer patients [26, 27].

3.3.1 MALNUTRITION IN CANCER

Malnutrition and wasting in cancer is a prevalent condition and the incidence ranges from 40 to 80% as shown by Bruera et al[34] and Ollenschlager et al.[33] It frequently occurs in patients with cancer of the head and neck area. The risk of infections, treatment toxicity and costs of health-care is increased and the response to treatment, quality of life and life expectancy are decreased.[19, 20, 21, 25]

Cancer cachexia is a metabolic syndrome associated with underlying illness and typified by loss of muscle with or without loss of fat mass. The prominent clinical feature of cachexia is weight loss in adults (corrected for fluid retention) or growth failure in children (excluding endocrine disorders) [23]. There is increased energy expenditure leading to weight loss greater than that caused by reduced food intake alone. Anorexia and cachexia often occur together in many types of cancer or in the "wasting syndrome" observed in patients with Acquired Immunodeficiency Syndrome (AIDS) and chronic inflammatory disorders. Cancer cachexia is characterized by anorexia, early satiety, malaise, immunocompromise, loss of muscle and fat stores, anaemia and unintentional weight loss. Prolonged malnutrition can decrease the basal metabolic rate by 20 – 30%. This marked decrease in the metabolic rate may result in the body temperature falling several degrees shortly before death.

Cytokines play a crucial role in the pathophysiology of anorexia-cachexia syndrome. Cytokines alter central nervous system efferent signals that mediate hunger and satiety. Interleukin I (IL-I), Interleukin 6 (IL-6), tumor necrosis factor- alpha (TNFα) and Interferon gamma (IFNγ) have been implicated[21]. IL-I blocks neuropeptide-Y induced feeding and together with TNF-a increase the levels of the corticotrophin releasing hormone resulting in inhibition of the stimulus to feed and also causes the firing of glucose sensitive neurons that also reduce the urge to feed. A proteolysis-

inducing factor has also been shown to cause anorexia and cachexia. Interleukin- 6 and Interferon – gamma also result in cachexia via causing anorexia in patients with malignancy. These cytokines also induce a hypermetabolic state that together with the decreased food intake results in weight loss. [14, 15, 18] Most of these inflammatory cytokines appear to mediate anorexia by activation of the melanocortin system in the hypothalamus. The precise mechanisms by which cytokines or tumor products interact with the melanocortin pathway to decrease food intake are still unclear, but blockade of the hypothalamic melanocortin receptors appears to almost completely prevent their anorexic and cachectic effects in experimental animals.

Leptin is a protein hormone produced by adipocytes that mediates energy homeostasis in relation to adiposity. Increase in leptin levels is associated with increased adiposity and this initiates a negative feedback mechanism that reduces feeding and increased energy consumption. The orexigenic neuropeptides stimulate feeding while anorexigenic neuropeptides decrease feeding. Neuropeptide Y (NPY) is the most potent orexigenic peptide activated by the fall of leptin and influences the actions of galanin, opioid peptides, MCH, orexin, and AGRP[46]. Anorexigenic neuropeptides such as CRF, melanocortin, GLP-I, neurotensin, and CART expression is augmented. The anorexigenic neuropeptides increase sympathetic nervous activity, which regulates energy expenditure by activating thermogenesis in brown adipose tissue and possibly in other sites such as white adipose tissue and muscle, through induction of the mitochondrial uncoupling protein UCP-1, UCP-2 and UCP-3[47]. Cytokines produced in malignancy simulate the negative feeback effect of leptin on the hypothalamus resulting in prolonged anorexia and weight loss. IL-1 and TNF-α increase serum leptin levels by increase the expression of mRNA for leptin in adipose tissue in cachectic patients instead of the normal suppression that ought to occur.

Hsu et al in a case control study showed an increased level of IL-2 and TNFα levels in patients with nasopharyngeal carcinoma in comparison to the normal controls. Although the increase in TNFα did not correlate to the tumor stage and bulk the levels of IL-2 did.[48]

Active screening and early closely controlled nutritional care improves the recognition of malnourished patients and enables treatment to begin at an early stage of hospitalization[30]. Malnutrition impairs immune functions, performance status, muscle function, and quality of life. In addition the responses to chemotherapy are decreased, chemotherapy-induced toxicity and

complications are more frequent and severe, and survival times are shortened. Depression, fatigue and malaise also significantly impact on patient well-being. Nutritional support, addressing the specific needs of each patient individually, helps improve prognosis.[31]

3.4 NUTRITIONAL ASSESSMENT

Nutritional assessment is an in-depth evaluation of objective and subjective data related to a person's nutrient intake, lifestyle and medical history. This is the first step in the management of malnutrition. It provides an objective measure for the detection of premorbid states allowing early intervention[28]. Nutritional assessment serves to identify patients at risk who could benefit from an intervention, prognosticate and to evaluate the intervention. The nutritional status is a gauge used to measure the outcome of a nutritional assessment. It is categorized as either nourished if there is absence of weight loss of more than 5% of the usual body weight in the last 30 days, at risk of malnutrition if the weight loss is 5–10% of body weight within the last 30 days or malnourished if weight loss is more than 10% within the last 30 days. Nutritional assessment involves four basic categories of information namely; anthropometric indices, biochemical values, clinical data and dietary information.

1. **Anthropometric indices.**

   The body mass index is defined as the individual's body mass (weight) divided by the square of one's height with a unit of measure of kg/m^2. It is a simple, inexpensive and easily reproducible index of weight-for-height that is commonly used to classify underweight, normal weight and overweight adults. BMI values are age-independent and the same for both genders. The WHO Expert Committee on Physical Growth defines underweight as a BMI of less than 18.49 kg/m^2, normal weight as a BMI ranging from 18.5 kg/m^2 to 24.99 kg/m^2 and overweight as a BMI greater than 25 kg/m^2. While the problem of obesity is prevalent in the Western population, the more prevalent problem in sub-Saharan Africa is undernutrition and underweight. Mild underweight is defined as a BMI of 17.00-18.49 kg/m^2, moderate underweight as BMI of 16.00-16.99 kg/m^2 and severe underweight as BMI

less than 16.00 kg/m.$^{2(24)}$ Underweight patients are chronically energy deficient and this decreases their productivity.

Ideal body weight (IBW) is a calculated weight that is determined to be the weight for a specific age or height that is statistically determined to be associated with lowest mortality for an individual and optimum nutrition status. It is also referred to as the desirable body weight and is often taken as a standard. There are various formulas that have been derived for calculating ideal body weight. Alternatively this can be retrieved from available height-and-weight charts.

The estimated energy requirement is the average energy intake level predicted to maintain the body weight of an individual for specified age, weight, height, gender and physical activity level harmonious with good health. The unit of measure is the kilocalorie. There are various methods both direct and indirect calorimetry that allow for the evaluation of the energy requirements of an individual. The WHO/FAO/UNU equations (1985) were developed from Schofield's data of young men and women.[45]

2. **Biochemical values** are measures in the blood or in the urine and include albumin levels, prealbumin levels, creatinine, blood sugar, lipid levels e.t.c.
3. **Clinical data** involves exploring any comorbid conditions that may impact on the nutritional status such as diseases and medication.
4. **Dietary information** includes a history of the food intake, allergies, intolerance, restrictions, physical activity levels, oral health.

4.0. LITERATURE REVIEW

A review of literature on the nutritional consequences of malignancy and nasopharyngeal carcinoma was performed using Google Scholar and Pubmed.

Chan et al[22] randomized three hundred and fifty patients with nasopharyngeal carcinoma into a combined chemotherapy and radiotherapy are and radiotherapy alone arm. Those on combined treatment were found to have significantly more severe mucositis and weight loss. In the combined treatment group 74% of patients lost more than 10% of their body weight and 11% of patients lost more than 20% of their body weight. This finding was also found to be statistically more significant than in those receiving radiotherapy alone. This study was sizeable and serves to show that significant weight loss occurs during treatment and thus assessment of the nutritional status prior to treatment is important to enable active management of the same.[22]

Qiu et al studied one hundred and fifty nine newly diagnosed patients with nasopharyngeal carcinoma in China. Their weight was taken at the intial visit and at the end of radiotherapy. 56% of the patients were found to have weight loss of 5% in the last three months at baseline. The median weight loss at the end of treatment was 6.9kg. multivariate linear regression analysis found that body mass index, stage of disease, treatment protocol were independent prognostic factors for significant weight loss in the patients.[50]

Nixon and colleagues studied the nutritional status of hospitalized cancer patients at a clinical research facility[27]. The protein-calorie nutrition was evaluated in 54 ward patients by anthropometric measurement, creatinine excretion and serum albumin. Cancer patients (30 patients) found to have protein-calorie undernutrition were found to have advanced cancer. The degree of malnutrition significantly correlated with survival with patients with serum albumin levels of <35 g/L died within 70 days. Though the patients in the study have varied types of cancer the study underlined the importance of evaluation of nutritional status in patients with cancer and the active management of any deficiency early and appropriately.

Oates et al followed a cohort of 14 patients with nasopharyngeal carcinoma managed with concurrent chemoradiation for 7 weeks using the European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire and Head and Neck Module before and at 3, 6, 12, and 24 months after treatment. In the two years of follow up they reported significant

appetite loss, swallowing difficulties, trismus, difficulty with social eating. A median weight loss of 7 kg was found with most loss occurring during treatment despite nutritional support. This shows the need for nutritional intervention before treatment as the consequences of treatment remain for a substantial period. The study size was small but this is due to the relative rarity of the malignancy in the population studied. [29]

Brookes GB et al conducted a case control study to evaluate the nutritional status of patients with cancer of the head and neck[35]. Of 84 patients (347 controls) with untreated primary squamous cell carcinoma majority of the patients had advanced disease and advanced age. A statistically highly significant positive correlation between serum albumin and all the measured anthropometric indices was found *(P<O.OOl)*. Undernutrition in the patient population stood at nearly 40% and 2.4% had severe malnutrition. Though the patients had different cancers this study demonstrates cancer patients usually have poor nutrition at presentation.

Kubrak et al in 2010 prospectively screened 341 cancer patients with the patient-generated subjective global assessment tool before treatment[37]. Anorexia, dysphagia, pain and mouth sores were found to be significant predictors of reduced dietary intake and weight. The presence of these symptoms increased the probability of weight loss. Body mass index ≤18.5 related to overall survival. Nutritional screening for new patients with head and neck cancer facilitates clinicians evaluation of all potentially treatable nutritional impact symptoms detrimental to dietary intake before the onset of any treatment.

Petruson et al monitored 49 patients assessed longitudinally with the weight and Health-related Quality of Life (HRQL), EORTC QLQ-C30, the EORTC Head and Neck Cancer module (QLQ-H&N35), and the Hospital Anxiety and Depression Scale (HADS).[39] At the time of diagnosis patients who had a weight loss of greater than 10% after treatment scored significantly worse on 15 of 28 HRQL variables than did patients who lost less. The largest difference was found for role functioning, fatigue, loss of appetite, global quality of life, sticky saliva, and swallowing. Differences in HRQL

persisted even after 3 years. The fatigue scale was the only significant predictor of weight loss at diagnosis. Head and neck cancer patients at risk of severe wasting during cancer therapy should be screened at diagnosis.

No studies have been conducted specifically investigating the nutritional status of patients with nasopharyngeal carcinoma at diagnosis and the effect of the stage of the disease and the histological subtypes on the same. It is expected that while some of the factors affecting the outcomes in the studies above are typified in nasopharyngeal carcinoma the location and molecular behavior of nasopharyngeal carcinoma and the therapeutic measures employed may play a role in patients nutritional outcomes.

5.0. STUDY JUSTIFICATION

Nasopharyngeal carcinoma is the 2nd most common HNSCC seen at the Kenyatta National Hospital and patients tend present at later stages. These patients are thus at risk of malnutrition due reduced dietary intake secondary to anorexia, malaise, dysphagia, odynophagia and pain as well as increased metabolism secondary to the metabolic derangements of malignancy. Malnutrition results in immunocompromise, anaemia, depression all of which negatively impact on the patient's prognosis. Screening and early intervention in these patients prevents delays in commencing their treatment, interruption of treatment and improves their survival. This study served to determine the magnitude of the problem at help identify factors that affect the nutritional status of these patients. This will enable health professionals to improve the primary and supportive care of patients with NPC and to intervene in a timely manner.

6.0. RESEARCH QUESTION

What is the nutritional status of patients presenting with nasopharyngeal carcinoma at the Kenyatta National Hospital and how does the histological type and stage of the disease affect it?

6.1 HYPOTHESES

NULL HYPOTHESIS

Nasopharyngeal carcinoma does not affect the nutritional status of patients and there is a no difference in the nutritional status of patients with different stages of disease and histological types.

ALTERNATE HYPOTHESIS

Nasopharyngeal carcinoma affects the nutritional status of patients and there is a difference in the nutritional status of patients with different stages of disease and histological types.

7.0. OBJECTIVES

MAIN OBJECTIVE

To determine the nutritional status of patients presenting with nasopharyngeal carcinoma

SPECIFIC OBJECTIVES

i. To determine the nutritional status of patients presenting with nasopharyngeal carcinoma
ii. To determine the BMI of patients presenting with nasopharyngeal carcinoma and compare with normal controls.
iii. To determine the serum albumin levels of patients presenting with nasopharyngeal carcinoma and compare with normal controls
iv. To determine the caloric intake of patients presenting with nasopharyngeal carcinoma and compare with normal controls
v. To determine the effect of stage of disease on the BMI, albumin levels and caloric intake
vi. To determine the effect of histological type on the BMI, albumin levels and caloric intake

8.0. METHODOLOGY

8.1. STUDY DESIGN

This was a hospital based case control study.

8.2. STUDY SETTING

This study was carried out at Kenyatta National Hospital (KNH) ENT department, Radiotherapy department and the Dental unit.

8.3. SAMPLE SIZE

The following formula was be used to estimate the desired sample size.[31, 32, 33]

$$n=[(z^2*p*q)+ME^2]/[ME^2*(z^2*p*q)/N]$$

Where;

z is the critical z score at 95% confidence level = 1.96
p is the estimated population proportion of persons with poor nutrition among NPC ~=40%
q = 1-p = 60% the proportion of persons without poor nutrition among NPC
ME is the margin of error set at 5%
N is the population size

This means that at least 56 patients (cases) and 112 controls would be recruited.

66 cases were recruited but 6 were excluded due to HIV positive status. Thus 60 cases and 123 controls met the inclusion criteria. The cases and controls were matched for age and gender at a ratio of 1:2. All controls were patients without any comorbid states that would affect their metabolic activity and had no history of weight change in the six months preceeding the study.

8.4 SAMPLING PROCEDURE

A consecutive sampling method was used to select the cases.

Inclusion criteria for the Cases

a) All patients aged 12 years and above with histological diagnosis of Nasopharyngeal Carcinoma

b) Presence of a CT scan, MRI and chest Xray

c) Patients below the age of eighteen whose parent or guardian consented.

Inclusion criteria for the Controls

a) All patients aged 12 years and above attending the Dental clinic at the KNH.

b) Subjects below the age of eighteen whose parent or guardian consented

Exclusion criteria for the Cases

a) Children below the age of 12 years

b) Patients who do not consent to the study or whose guardians did not consent.

c) Patients who were HIV positive.

Exclusion criteria for the Controls

a) Children below the age of 12 years

b) Patients who have knowingly lost weight during the preceding 6 months

c) Patients with oral or pharyngeal pathology, neoplastic disease or from conditions known to be associated with either weight loss or obesity.

STUDY DURATION

The study was conducted between March- April 2012 after approval by the KNH/UON Ethics and Research Committee (P455/11/2011)

8.5. CONFOUNDING FACTORS

There are many factors which contribute to the nutritional status (independent variable) of an individual and consequently it might be difficult to wholly attribute the results to nasopharyngeal carcinoma (dependant variable). Case-control studies by their design assign confounders equally between the two groups such as age, gender and physical activity level.

8.6 PROCEDURE

All the cases and controls who met the inclusion criteria were inducted into the study after an informed consent has been signed by the patient or their guardian. Appropriate confidentiality was maintained during the study period.

Investigators

The customized questionnaire was filled in by the principal investigator. All measurements and laboratory samples were obtained by the principle investigator. A nutritional assessment based on the history, clinical examination and laboratory values was performed in conjunction with the nutritionist.

All samples were processed in the same lab by the same technician to minimize errors and for standardization.

All cases were patients presenting at the ENT department or the Radiotherapy department with a diagnosis of nasopharyngeal carcinoma with a histological diagnosis, a CT scan and a chest Xray for staging. They also had a HIV test done if none had been performed within 3 months of the diagnosis. The controls were also matched for age with age stratified into decades (12-20 years, 20-30years and so on) and gender.

A study number was assigned to each patient and their bio-data was entered into the questionnaire (Appendix II).

A thorough nutritional history was obtained using the Nutritional Assessment form (Appendix II). This included weight history, caloric intake and the problems affecting food intake. The kilocalorie intake was calculated using the KNH Food exchange list (Appendix III) that is adapted to the average Kenyan diet. The weight history, the problems taking food and the activity level was also recorded.

Anthropometric measurements were then assessed. The weight was taken using a conventional weighing scale (Ashton Myers Mechanical weighing scale Model number 7756) and recorded in kilograms in the Nutrition assessment form. Height was taken using a heightmeter for all patients and recorded in metres.

Two (2) ml of blood was drawn from each patient by the principle investigator and processed at the Kenyatta National Hospital Biochemistry lab. The samples were analyzed using the Olympus AU640 Chemistry Analyzer Automated System. Serum albumin levels were recorded in the data sheet. The lab normal values were 30-54g/dl.

A nutritional assessment was then made in conjunction with the nutritionist and this information was entered into the data sheets and classified as shown below.

1. **Problems affecting food intake:** The presence or absence of anorexia, presence or absence of odynophagia and presence and grade of dysphagia. The dysphagia is graded as grade I if the patient reported no clinical signs or symptoms of dysphagia; Grade 2 if the patient was able to take semisolids; Grade 3 if the patient was able to take liquid feeds and Grade 4 if the patient complained of inability to swallow even saliva, aspiration or had dysphagia necessitating non-oral feeding.
2. **Nutritional status:** Percent weight loss was used to assess the nutritional status. Patients with <5% weight loss in the preceding month were considered to be nourished, those with 5-10% weight loss in the preceding month were considered to be at risk of malnutrition and those with weight loss of >10% in the preceding month were considered malnourished.
3. **Body mass index:** Subjects with a BMI <18.5kg/m^2 were considered underweight, 18.5-24.9kg/m^2 were considered to have normal weight and anything above 25kg/m^2 was considered overweight.
4. **Percent of ideal body weight:** Patients with percent of ideal body weight ranging from 90% to 110% were considered to have acceptable weight, those with below 90% were considered underweight and those with weights above 110% were considered overweight.
5. **Serum albumin level:** The accepted serum albumin level was 30-54g/L. Any patient with levels below 30g/L was considered to have hypoalbuminemia.

6. **Caloric intake:** The dietary history was used to calculate the caloric intake by use of the food exchange list (Appendix III). A caloric intake of 35-40k/cal per kilogram body weight and a protein intake of 1.0g/kg body weight were considered acceptable. The estimated energy requirements were calculated using the WHO formulas shown below and this was compared to the intake.

Estimated Energy Requirement = Resting metabolic rate x Physical activity level

Male	
Age (years)	**Formula for RMR**
15-18	17.6 x weight + 656
18-30	15.3 X weight + 679
31-60	11.6 X weight + 879
>60	
Female	13.5 X weight + 487
15-18	13.3 x weight + 690
18-30	14.7 X weight + 496
31-60	8.7 X weight + 829
>60	10.5 X weight + 596

Physical activity level	**Male**	**Female**
Sedentary	1	1
Low active	1.11	1.12
Active	1.25	1.27
Very active	1.48	1.45

9.0. QUALITY CONTROL

The nutritional assessment form was pretested before commencement of data collection and appropriate modifications made. The nutrition assessment form was be filled by the principal investigator to reduce interpersonal bias. All laboratory investigations was be done at the KNH Biochemistry laboratory. The nutritional status assessment determination was be made by the principle investigator in conjunction with the same clinical nutritionist to ensure uniformity.

10.0. ETHICAL CONSIDERATIONS

The study was carried out only after approval by the Kenyatta Ethics and Research Committee. Informed consent was obtained from all subjects included in the study. All patients incurred no extra costs and those who declined were not penalized. Confidentiality was maintained at all times. There was no financial gain by the primary investigator from the study. All patients found to be at risk of malnutrition or malnourished had appropriate nutritional interventions instituted. Results will be published for the benefit of other health practitioners.

11.0. DATA MANAGEMENT

DATA ENTRY

The biodata for the cases and the controls, medical and nutritional history, clinical and laboratory findings were be recorded in the nutrition assessment form and then recorded in Microsoft Excels data sheet. The data was then sorted into;

- Clinical data (stage of disease, histology, problems affecting food intake)
- Dietary information, food intake, energy requirement
- Anthropometric measures
- Laboratory Findings: Serum albumin levels and HIV test

DATA ANALYSIS

All data was checked for completeness, consistency and accuracy. Descriptive statistics on demographic characteristics (age, gender) were analyzed and presented using percentages, frequencies, tables, pie charts and graphs. Data recorded was analyzed using Microsoft Excel, Microsoft access and the Statistical Package for Social Sciences (SPSS) 17.0. Quantitative data such as body mass index, ideal body weight, percentage of ideal body weight, kilocalorie intake and serum albumin was analyzed and presented by use of measures of central tendency (mean), range, and standard deviation.

Then Student t- test was used for comparison of means in the dependent variables among the cases and the controls. With regards to the parameters for nutritional status, these were found to

be higher in the control group. Pearson's Chi Square Test and the Fischer's Exact test were used to compare the variables used in determining the nutritional status of the patients (age, gender, BMI, albumin levels, ideal body weight and the caloric intakes and requirements in the study groups).

Logistic regression analysis was used for multivariate data e.g. stage of disease and serum albumin levels. All statistical tests were performed at 5% significance level and 95% confidence interval.

12.0. RESULTS

A total of 60 cases and 123 controls were recruited for the study.

Of the cases (patients with nasopharyngeal carcinoma) there were 20 females and 40 males and of the controls there were 42 females and 81 males. The cases had an age range of 15 - 79 years. The controls had an age range of 15 - 79 years.

The mean age of the cases was 47.2 years with (standard deviation [SD] 16.5) and that of the controls was 46.3 years with (SD 16.6).

FIGURE 1: Gender Distribution

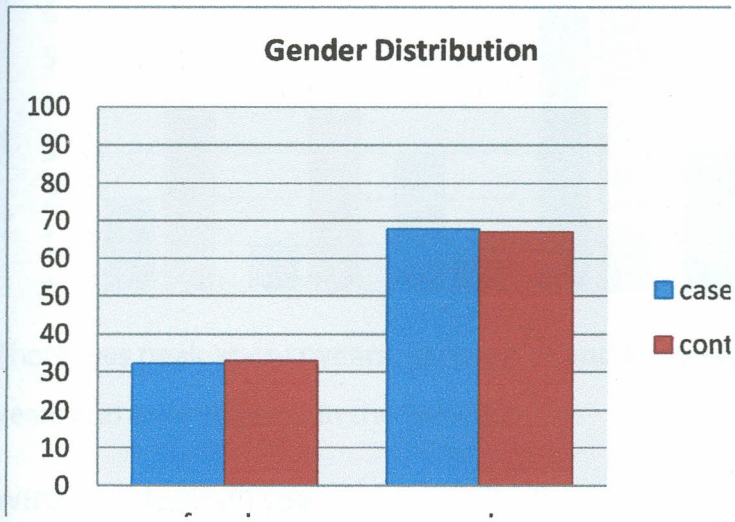
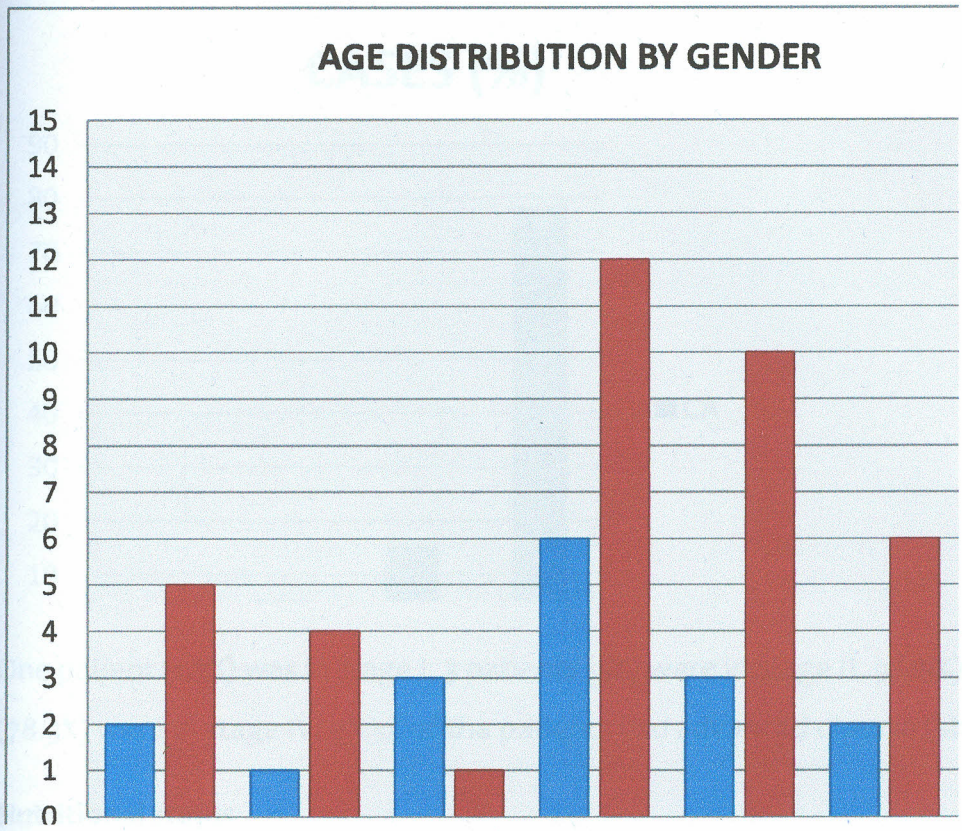


FIGURE 2: Age distribution graph



There was peak at 41-50years, 51-60 years and 61-70 years in the males and at 41-50years, 51-60 years and over 70 years in the females.

WHO Histological Type

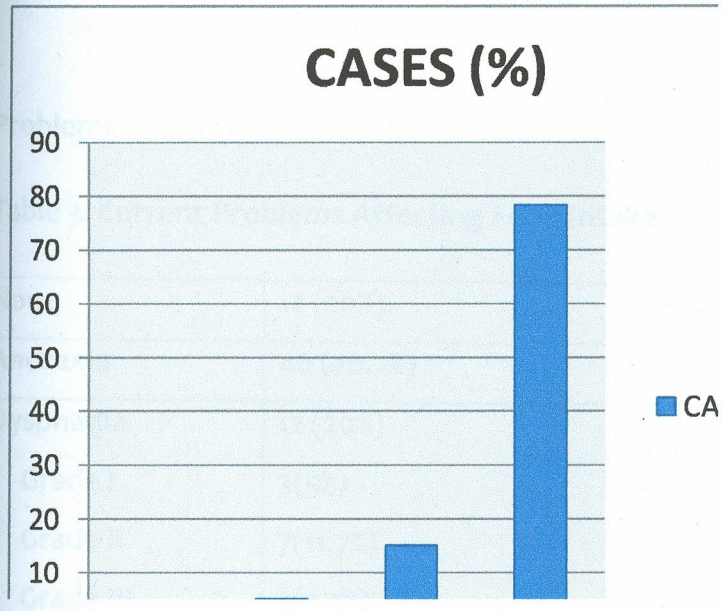
Majority of the patients had WHO type III histology (73.3%) as shown below;

Table 1: WHO histological grading

WHO Type I	10 (16.7%)
WHO Type II	6 (10%)
WHO Type III	44 (73.3%)

Nasopharyngeal Carcinoma Staging

Figure 3: Stage of disease



One patient (1.7%) was in stage I, 3 patients (5%) were in stage II, 9 (15%) were in stage three and 47 (78.3%) were in stage IV. 93.3% of the patients had advanced disease (stage III/ IV)

Nutritional status

Table 2: Nutritional status

NUTRITIONAL STATUS	CASES	CONTROLS	P VALUE
Nourished[a]	39 (65%)	123 (100%)	<0.0001
At risk of malnutrition[b]	17 (28.3%)	0	
Malnourished[c]	4 (6.7%)	0	

[a]Weight loss of <5% of the usual body weight in the last 30 days [b]Weight loss of 5–10% of body weight within the last 30 days [c]Weight loss of more than 10% within the last 30 days

35% of the patients were found to be undernourished with 6.7% reporting weight loss of >10% in the preceding month. Of the cases 39 (65%) patients reported weight loss of <5% of the usual body weight in the last 30 days, 17 (28.3%) reported weight loss of 5–10% of body weight within the last

30 days and 4 (6.7%) reported weight loss of more than 10% within the last 30 days. Among the controls none reported any history of weight loss as this was an exclusion criteria.

Problems affecting food intake

Table 3: Current Problems Affecting Food Intake

None	12 (20%)
Anorexia	46 (76.7%)
Dysphagia	12 (20%)
Grade I	3(5%)
Grade II	7(11.7%)
Grade III	2(3.3%)
Grade IV	0
Odynophagia	2 (3.3%)
Pain and depressed mood	6 (10%)

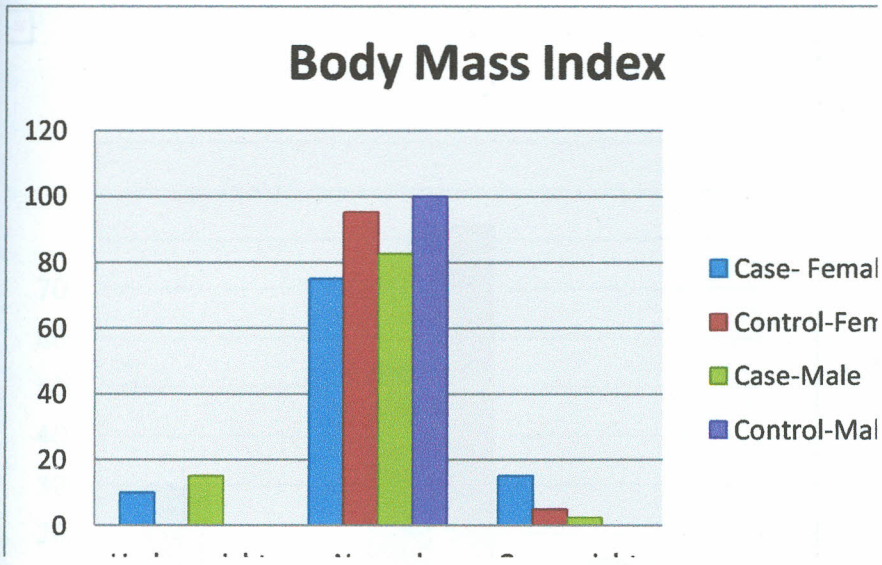
The current problems affecting food intake were recorded as none, anorexia, dysphagia, odynophagia and other problems reported as pain and depressed mood. The patients with dysphagia reported it to be grade I, grade II and grade III. No patient had dysphagia grade IV.

Body mass index

The mean body mass index (BMI) for the cases was 21.2 with SD2.7 and of the cases was 22.6 with SD1.6. This difference was found to be statistically significant (P value <0.001).

When divided into gender mean BMI for male cases was 20.8 (SD2.5) and for the male controls was 22.6 (SD1.4. The mean BMI for the female cases was 22.0 (SD2.9) and for the female control group was 22.7 (SD1.9).

Figure 4: BMI distribution in males and females in the cases



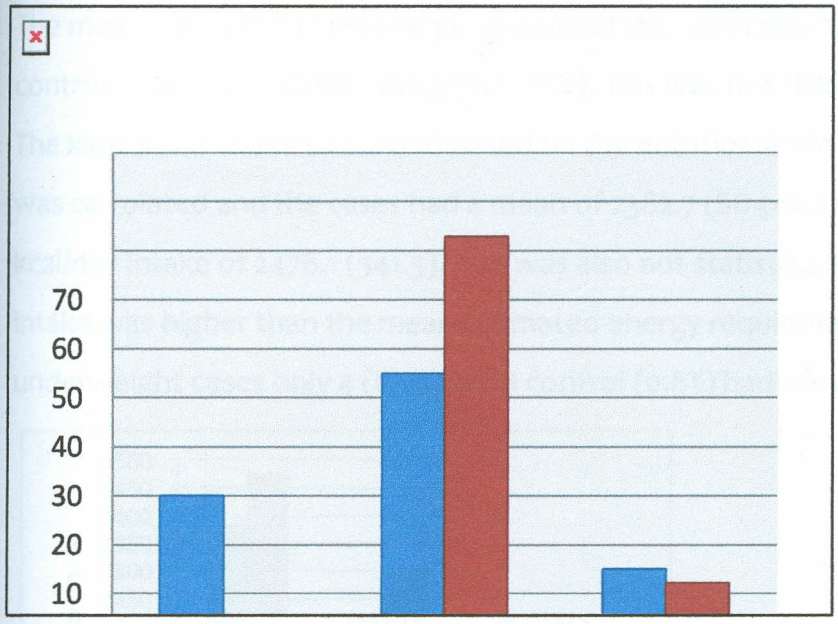
Of the cases 8 (13.3%) were underweight, 48 (80%) were of normal weight and 4 (6.7%) were overweight. Of the controls none were underweight, 121 (98.4%) were of normal weight and 2 (1.6%) were overweight. There was a statistically significant increased likelihood of being underweight P value <0.001.

Percentage of Ideal body weight

The percentage of the ideal body weight was found to have a mean of 97% (SD0.13) in the cases and 103% (SD0.08) in the controls. This was considered acceptable weight.

Of the cases 33 (55%) had acceptable weight as compared to 102 (82.9%) of the controls. These weights are adjusted for height, weight and gender. 18 cases (30%) were underweight as compared to 6 (4.9% of the controls). Of the cases who were underweight 8 (13.3%) had mild malnutrition, 6 (10%) had moderated malnutrition, 4 (6.7%) had severe malnutrition. All 6 (4.9%) controls who were underweight were at risk mild malnutrition. This was found to be statistically significant (P value <0.001) with an Odds ratio of 9.3 (3.4 – 25.3) with a 95% confidence interval. This showed that patients with nasopharyngeal carcinoma were 9 times more likely to be malnourished than their normal counterparts. Nine cases (15%) were found to be overweight whereas 15 (12.2%) of the controls were overweight.

Figure 5: Graph showing percentage of ideal body weight



Albumin levels

The serum albumin levels had a range of 24 – 54g/dl in the cases and 30 – 61g/dl in the controls. The mean was 36.7g/L with SD7.9 in the cases and of 43 g/L with SD8.0 in the controls. This was found to statistically significant with a P value of <0.001.

Table 4: Comparison between serum albumin level and percentage body weight

	CASES		
Variable (ALBUMIN)	**% IBW**		**P Value**
	< 90%	**> 90%**	
<30g/L	11	3	<0.0001
>30g/L	7	39	
	CONTROLS		
<30g/L	1	1	0.0948
>30g/L	5	117	

The percentage ideal body weight and serum albumin levels were comparable in the cases P value <0.0001.

Nutritional intake

The mean estimated energy requirements of the cases was 2222.7 kcal/day (SD339.6) and of the controls was found to be 2304.3 (SD287.4). This was not statistically significant (P value 0.092). The kilocalorie intake calculated based on the nutritional history obtained via the questionnaire was calculated and the cases had a mean of 2382.7 (SD444.2) while the controls had a mean kcal/day intake of 2476.1 (341.5). This was also not statistically significant. The mean kilocalorie intake was higher than the mean estimated energy requirements in the two groups. Of the underweight cases only 4 (6.7%) and 1 control (0.8%) had a lower intake than was required.

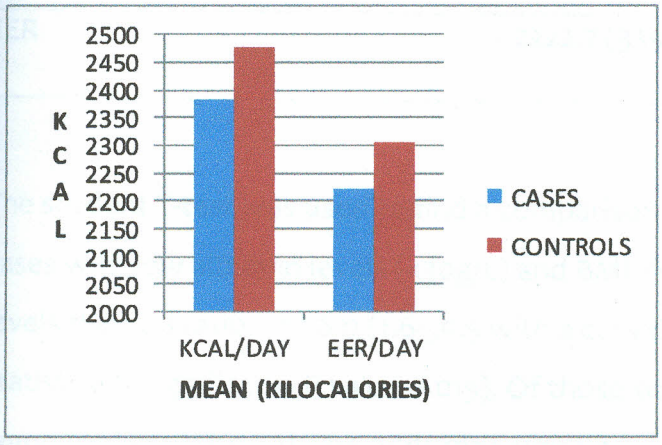


Figure 6: Kilocalorie intake compared to estimated energy requirements

Table 5: Protein intake table

	Variable	Protein intake <1.0	Protein intake >1.0	P value
Cases	Low Albumin	7	11	0.0312
	Normal Albumin	5	37	
Controls	Low Albumin	13	9	<0.0001
	Normal Albumin	5	96	

Table 6: Nutritional status parameters in the cases and controls

Variable mean (standard deviation)	Cases	Control	P value
Albumin	36.7 (7.9)	43.0 (8.0)	<0.001
BMI	21.2 (2.7)	22.6 (1.6)	<0.001
% IBW	97 (13)	103 (8)	<0.001
KCAL	2382.7 (444.2)	2476.1 (341.5)	0.118
EER	2222.7 (339.6)	2304.3 (287.4)	0.092

The student T-test was used to find a comparison between albumin levels and the BMI. Of the cases with low albumin levels (<30g/L) and BMI <18.50 compared with those with normal albumin levels the odd ratio was 8.0 (1.6-39.5 with a confidence interval of 95%) and this was found to be statistically significant (P value 0.013). Of those with normal albumin levels (>30g/L) when compared with the BMI the odds ratio was 1.0.

ANOVA was used to find out what the effect of the stage of the disease had on the parameters used in analyzing the nutritional status

Table 7: The effect of the stage of the disease on nutritional parameters

Variable	Stage of disease			P value
	Stage III and below	Stage IVA and IVB	Stage IVC	
BMI mean (SD)	22.7 (1.7)	21.1 (2.8)	19.3 (3.2)	**0.019**
Albumin mean (SD)	41.8 (7.2)	36.4 (7.5)	29.0 (5.0)	**0.002**
Kcal mean (SD)	2508.5 (405.3)	2369.3 (473.6)	2225.7 (298.8)	0.383

The BMI of the cases consistently decreased with increase in the stage of the disease as did the albumin and this was statistically significant (P value 0.019 and 0.002 respectively). The Kcal intake was also noted to reduced with increase in the stage of the disease but this was not found to be statistically significant.

Student T- test was used to compare means to see if there was an association between the caloric intake and the BMI, the albumin level and the percentage of the ideal body weight. This is shown in the table 7 below;

Table 8: Association between caloric intake and nutritional parameters

Variable	Caloric intake	P value		Caloric intake	P value
BMI			**% IBW**		
<18.50	1750 (530.2)	**<0.001**	**<90%**	2048.9 (458.3)	**<0.001**
>18.50	2480 (342.3)		**>90%**	2525.7 (356.3)	
Albumin					
<30g/L	2001.0 (482.1)		**>30g/L**	2498.5 (364.3)	**<0.001**

Association between BMI and stage of disease

The BMI of the patients was compared to the stage of the disease. BMI of <18.50 was found in 8 cases (13.3%) and none of the controls. BMI of >18.5 was found in 52 cases (86.7%).

As the stage increased the likelihood of a low BMI increased and this was found to be statistically significant (P value 0.004).

The BMI of the cases consistently decreased with increase in the stage of the disease as did the albumin and this was statistically significant (P value 0.019 and 0.002 respectively). The Kcal intake was also noted to reduced with increase in the stage of the disease but this was not found to be statistically significant.

Student T- test was used to compare means to see if there was an association between the caloric intake and the BMI, the albumin level and the percentage of the ideal body weight. This is shown in the table 7 below;

Table 9: Association between BMI and the stage of the disease

Variable	BMI		P Value
	<18.50	>18.50	
Stage			
I	0	1	0.004
II	0	3	
III	0	9	
<III	0	13 (25%)	
IV	8 (100%)	39 (75%)	

Association between the albumin levels and the stage of the disease

8 cases (13.3%) were found to have low albumin levels (<30g/L) while 52 cases (86.7%) were found to have albumin levels within normal.

Table 10: Association between the albumin levels and the stage of the disease

Variable	Albumin levels		P value
Stage	<30g/L	>30g/L	
I – III	0	13 (28.3%)	0.002
IV	8 (100%)	39 (71.7)	

Association between BMI and WHO histological type

There was no correlation found between the BMI of the patients and the histological type of the tumor.

Table 11: Association between BMI and WHO histological type

Variable	BMI		P value
Stage	<18.50	>18.50	
WHO TYPE I	2 (25%)	8 (15.4%)	0.561
WHO TYPE II	1 (12.5%)	5 (9.6%)	
WHO TYPE III	5 (62.5%)	39 (75%)	

There was no significant association between the BMI in the patients and the histological type.

Table 12: Association between metastatic disease (Stage IVC)and nutritional parameters

Variable	Stage of disease			P value
	III and below	IVA & B	IVC	
BMI	22.7 (1.7)	21.1 (2.8)	**19.3 (2.2)**	0.019
Albumin	41.8 (7.2)	36.4 (7.5)	**29.0 (5.0)**	0.002

The patients with metastatic disease had a mean BMI of 19.3 (SD 2.2) and a mean serum albumin levels of 29.0 (SD 5.0). When these variables were compared with those in earlier stages of disease the correlation was significant (BMI P value 0.019; Serum albumin P value 0.002)

Logistic regression found that serum albumin levels most significantly correlated with the stage of nasopharyngeal carcinoma (P <0.002). The stage of the disease and nutritional intake were also found to be most significant in causing weight loss, low BMI and low serum albumin. (P <0.001)

13.0 DISCUSSION

Nasopharyngeal carcinoma impacts on the nutritional status of the patient and a finding of malnutrition was found in 35% of the patients with 6.7% reporting severe weight loss. None of the controls reported any history of weight loss as this was an exclusion criteria. McWhirther et al in a review of 500 cancer patients found an incidence of 40% which was similar to the findings of Bruera et al and Mcdonald et al (40%). Pretreatment weight loss is a significant factor in determining the weight loss during treatment and those with severe pretreatment weight loss are at a higher likelihood of hospitalization[51].

The patients were aged between 15 years and 76 years. The male to female ratio was 2:1 for the cases comparable to a hospital based study by Muchiri et al[8] in a tertiary hospital and the global statistics on cancer. As the controls were matched to the cases the pattern repeated itself among this group. Most of the patients (73.3%) had undifferentiated carcinoma (WHO stage III) and in stage IV disease (78.3%) also similar to the global statistics on cancer.

Malnutrition is determined by reduced intake and hypermetabolism resulting in increased energy requirements. The reported problems affecting food intake were anorexia, dysphagia, odynophagia, pain and depressed mood. 20% of the patients reported no problems affecting food intake, 76.7% reported anorexia, 20% reported dysphagia, 3.3% reported odynophagia and 10% pain and depressed mood. Patients with complaints of dysphagia accounted for 20% of the cases. The dysphagia was due to the pressure effects of the primary tumor, the neck nodes and in one case of grade II dysphagia a hypoglossal nerve palsy was noted on the left. These patients were therefore on semi-solid or liquid diets and this increased the likelihood of reduced caloric intake and an unbalanced diet. Kubrak et al studied341 cancer patients prospectively using the Patient-Generated Subjective Global Assessment Tool.[37] Anorexia, dysphagia, pain and mouth sores were found to be significant predictors of reduced dietary intake and weight loss. Petruson et al followed up 49 head and neck cancer patients and found that patients with weight loss of more than 10% score significantly worse after treatment on Health Related Quality of Life variables. This persisted even after 3 years underscoring the significance of pretreatment weight loss.[39] Nourissat et al conducted a large study on 907 patients and found a strong correlation between

the quality of life of patients and pretreatment weight loss. This not only impacted on their disease status but also increased their hospital stay.[38]

Anthropometric indices used in the study were body weight, body mass index and percent ideal body weight. The means of the body mass index, percent ideal body weight were lower in the cases than the controls (P value < 0.001). The calculated percent ideal body weight was used to categorize the patients into underweight, acceptable weight and overweight. 30% of the cases were underweight as compared to 4.9% of the controls (P <0.001). Patients with nasopharyngeal carcinoma were 9.3 times more likely to be underweight compared to the controls (OR 9.3 [3.4 – 25.3] 95% CI). Of the cases who were underweight 13.3% had mild malnutrition, 10% had moderated malnutrition, 6.7% had severe malnutrition. This correlated well with reported weight loss rates in this series.

The mean serum albumin levels in the cases (36.7g/L) was significantly lower than in the controls (43g/L) (P <0.001). Patients with serum albumin levels of <30g/L were 8 times more likely to have a BMI <18.50 compared to those with serum albumin levels >30g/L (OR 8.0 [1.6-39.5] CI 95%) (P value 0.013). Patients with normal albumin levels (>30g/L) compared with a BMI >18.50 had an odds ratio of 1.0. Of the patients with metastatic disease the mean BMI of (stage IVC) was 19.3 (SD 2.2) P value 0.019 and the mean serum albumin levels were 29.0g/L (SD 5.0) P value 0.002. Brookes et al conducted a case control study (84cases : 347control) on patients with untreated primary SCC of the head and neck.[35] There was a positive correlation between serum albumin levels and all anthropometric indices measured*(P<O.OOl)*.

The percent ideal body weight and serum albumin levels were comparable in the cases with patients with percent ideal body weight of <0.9 more likely to have low serum albumin levels (P value <0.0001). McMillan et al in their study of 40 cancer patients found that serum albumin concentrations were significantly correlated with the percent ideal body weight ($p < 0.05$), reported weight loss ($p < 0.01$).[41] Comparison between the serum albumin levels and BMI found that patients serum albumin levels of <30g/L were more likely to have a BMI <18.50 OR 8.0 (1.6-39.5 CI 95%) and this was found to be statistically significant (P value 0.013). Patient with normal albumin levels (>30g/L) when compared with the BMI the odds ratio was 1.0. The patients with

metastatic disease had a mean BMI of 19.3 SD 2.2 (P value 0.019) and a mean serum albumin levels of 29.0 SD 5.0 (P value 0.002). When these variables were compared with those in earlier stages of disease the correlation was significant. Brookes et al conducted a case control study (84:347) on patients with untreated primary squamous cell carcinoma of the head and neck.[35] Statistically highly significant positive correlation between serum albumin and all the measured anthropometric indices was found *(P<0.001)*.

The stage of the disease was significantly associated with low BMI (P value 0.026) and low serum albumin levels <30g/dl (P value 0.012). Metastatic disease also increased the likelihood of a lower BMI significantly (P value 0.004).

The mean caloric intake was lower in patients with BMI <18.50, serum albumin levels <30 g/L and percentage ideal body weight of <90% *P value <0.001*. Protein intake and serum albumin levels were found to be significantly correlated among the patients in this study. Jager-Witenaar et al assessed the body weight and dietary intake of 29 patients with head and neck cancer 1 week before, and 1 and 4 months after treatment with radiotherapy, chemotherapy or surgery[40]. The body weight significantly declined during treatment. Patients with sufficient intake (>35 kcal and >1.5 grams protein/kg body weight) lost less body weight and lean mass. After treatment, only patients with sufficient intake gained body weight and lean mass. This shows a very important pattern as among the most significant variable in determining the nutritional status was the protein-calorie intake prior to treatment.

When the age and caloric intake were controlled for the stage of the disease and the serum albumin level were the most significant indicators of malnutrition. Increase in the stage of the disease resulted in the mean BMI decreasing (P value 0.019) and the serum albumin level reducing as well (P value 0.002). The mean caloric intake was also noted to reduce as the stage increased but this was not statistically significant. Ravasco and colleagues conducted a prospective, cross-sectional study on 205 patients with cancer. In stage III and IV disease all patients reported weight loss greater than 10%. Their energy and protein intake decreased significantly which was not observed in stage I and II. Advanced staging showed the most significant association with nutritional depletion. There was also significant associations for disease duration, nutritional

intake, tumour location and previous treatment. The ability to detect mild to extreme nutritional changes was better using the percentage weight loss compared to clinical variables. This study showed a correlation between the stage of the disease and the nutrient intake, the anthropometric indices and the serum albumin levels. There was no correlation with histology found.

14.0 CONCLUSIONS:

In this study 35% of the patients were found to be malnourished. Factors significantly affecting the nutritional status were stage of the disease, protein-calorie intake and percentage weight loss. There was an increased probability of being malnourished if one had nasopharyngeal carcinoma (cases) as compared to those who did (controls) OR 9.3 (95%CI) (3.4 – 25.3) P<0.001. This study shows that stage IV disease negatively impacts on the nutritional status of patients with nasopharyngeal carcinoma by lowering the caloric intake, lowering the serum albumin levels and thus the BMI. Statistically significant lower mean BMI levels in the cases compared to the controls was shown. This demonstrates a cause and effect relationship between the malignancy and the nutritional status. The BMI, percentage of ideal body weight, serum albumin levels were consistently lower in the patients with nasopharyngeal carcinoma. This study assisted in the preparation of an adequate nutritional intervention plan focusing on the primary problems in this population rather than on general concerns found in other co-morbid states. The active assessment and management of the nutritional status of patients presenting with malignancy is an important factor in ensure optimum quality of lives in these patients. This study shows that serum albumin and the anthropometric indices may serve as prognostic indices in patients with nasopharyngeal carcinoma and further study of the outcomes of the patients and correlation with these pretreatment indices is necessary.

15.0 RECOMMENDATIONS

1. During the initial assessment of patients presenting with Nasopharyngeal carcinoma a simple nutritional assessment should be performed to identify those that require intervention early.
2. Patients found to have malnutrition should be managed aggressively to ensure that they commence treatment at the right time and the complete their treatment without interruption due to anaemia, electrolyte imbalance, poor ECOG status and infections due to immunosuppression worsened by the treatment.

3. Meal plans and other measures that enable one to plan adequately balanced meals even with the morbidity associated with nasopharyngeal carcinoma should be made available to the patients as most receive treatment on an outpatient basis.
4. Future research to determine;
    a. The metabolic factors that impact directly on the nutritional status of patients with nasopharyngeal carcinoma.
    b. Effect of nutritional status on treatment choice, duration, outcomes, prognosis and survival.
5. Preparation of height-weight, height-age, weight-age chart for the local population is necessary to reduce confounding factors when a reference base is required.

16.0 LIMITATIONS OF THE STUDY

Used of direct and indirect calorimetry to measure energy requirements are less subjective and would have been preferable rather than simply estimating it based on equations.

17.0 APPENDICES

APPENDIX I: GENERAL PATIENT INFORMATION AND CONSENT FORM

Introduction : You are invited to participate in a research study on the Nutritional status of patients presenting with Nasopharyngeal carcinoma. My name is Dr. Catherine Irungu a Resident at the University of Nairobi.

Objective : We aim to find out the nutritional status of patients with nasopharyngeal carcinoma and the effect of stage of the disease on their nutritional status and on the treatment modality choice.

What is nasopharyngeal carcinoma? It is cancer of the tissues behind the nasal cavity.

What is involved in this study? Once you consent to participate, we will take a thorough history. We will then measure your weight, height and a blood sample of about 1-2ml that shall be taken to the laboratory to determine the albumin levels in your blood.

What benefits will I get if I participate? If you are at risk malnutrition or if you are found to be malnourished then appropriate management will be given. Secondly, information gotten from this study will help us understand more about this disease and help more patients in the future.

Are there any risks involved? There are no risks involved but for some discomfort when we prick you with the needle. However, this will last a short duration.

Will I be penalized for not participating? No, you will receive the same attention and treatment as those who choose to participate.

What about confidentiality? All the information we obtain from you will be kept confidential.

How much will it cost me? No extra cost will be incurred

What are my rights as a participant? Participation in the study is voluntary. Once inducted in the study, you can choose to discontinue at any time. This will not cause discrimination.

What do you do with the information you get? This information will help us understand better how nutritional status affects the treatment of patients with nasopharyngeal carcinoma. Like any other scientific information, we will seek to share our findings with other doctors in Kenya and the rest of the world.

Are you satisfied with the information given?
If yes and you are willing to participate or to allow your charge/ child to participate, please fill in and sign the consent below.

Contacts: you should feel free to ask questions now or at any time of the study. If you have any questions about this study you can contact Dr Catherine Irungu, phone no. 0722- 385710, email katywanjiru@yahoo.com. If you have any questions concerning the rights of human research participants, contact the Chairperson, the KNH Ethics and Research Committee at 020-2726300. I have read and fully understand the consent form. I sign it freely and voluntarily.

_____ _____

Signature of Participant/Next of kin Date

I certify that I have personally explained this document before requesting that the participant to sign it.

_____ _____

Signature of Researcher Date

KIBALI CHA KUSHIRIKI

Uchugunzi wa tatizo la kupunguka kwa hali ya lishe mwilini kwa wagonjwa walio na saratani ya sehemu ya nyuma ya pua katika hospitali ya Kenyatta

Utafiti: Unaalikwa kushiriki kwa utafiti wa kuchunguza tatizo la kupunguka kwa hali ya lishe mwilini kwa wagonjwa walio na saratani ya sehemu ya nyuma ya pua katika hospitali kuu ya Kenyatta. Utafiti unafanywa na Daktari Catherine Irungu.

Lengo la utafiti: Lengo la utafiti huu ni kutafuta ni wagonjwa wangapi walio na upungufu wa hali ya lishe mwilini na kama hilo lina athari gani kwa wagonjwa hao. Ili kama ni tatizo kubwa tuweze kutoa ushauri wa kutibu tatizo hilo ili kuboresha matibabu ya wagonjwa hawa.
Hakutakuwa na majeraha yoyote kwa washirika

Siri: Maelezo yako yatakuwa siri na matokeo ya utafiti yataelezwa kwa ujumla.

Kushiriki: Kushiriki kwako kwa utafiti huu ni kwa hiari yako. Una uhuru wa kukataa kushiriki, na kukataa kwako hakutatumiwa kukunyima tiba.
Damu mililita mbili itatolewa kupima protini mwilini wa mgonjwa.

Maswali: ukiwa na swali lolote kuhusu utafiti huu unaweza kumuuliza Daktari Catherine Irungu kwa nambari ya simu 0722-385710, barua pepe katywanjiru@yahoo.com. Ukiwa na swali kuhusu haki za mtafiti, unaweza kuwasiliana na Mwenyekiti, KNH ERC katika nambari 020-2726300

Nimesoma na kuelewa kibali hiki. Ninaweka sahihi kwa hiari yangu.

_____ _____

Sahihi ya mshirika/jamii ya mshirika Tarehe

Nimeeleza kwa ukamilifu lengo la utafiti kabla ya kumuomba kuweka sahihi.

_____ _____

Sahihi ya mtafiti Tarehe

APPENDIX II : NUTRITION ASSESSMENT FORM

CASE		**CONTROL**		Study Number	
Gender			Age		
APPROXIMATE TOTAL NUTRITIONAL INTAKE					
Protein					
Carbohydrates					
Fats					
Kcals					
Estimated Energy Requirement				Physical activity level	
ANTHROPOMETRIC MEASURES					
Current Weight (Kg)				Weight History	
Height (M)				BMI (Kg/M^2)	
Ideal Body Weight				% IBW	
LABORATORY VALUES					
Serum Albumin Levels					
Current problems affecting food intake					
Anorexia		Dysphagia (Grade[2])		Odynophagia		Other	
Comment (Other)					
DIAGNOSIS					
Stage Of Disease[1]			TNM		
Histological Type[3]					
Nutritional Status[4]					

[1]**stage Of Disease:** Stage I, Stage II, Stage III, Stage IV

[2]**Dysphagia** Grade I, II, III, IV

[3]**Histological Type:** WHO Type I Keratinizing Squamous Cell Carcinoma, WHO Type II Non-Keratinizing Squamous Cell Carcinoma, WHO Type III Undifferentiated Carcinoma

[4]**Nutritional Status:** Nourished*/ At Risk of Malnutrition**/ Malnourished^

*absence of weight loss of more than 5% of the usual body weight in the last 30 days. **weight loss of 5–10% of body weight within the last 30 days. ^weight loss of more than 10% within the last 30 days

APPENDIX III: KENYATTA NATIONAL HOSPITAL FOOD EXCHANGE LIST

	Carbohydrate	Protein	Fat	
STARCH	15 grams	0-3 grams	0-1 gram	80 calories
NON-STARCHY VEGETABLES	5 grams	2 grams	0	25 calories
FRUITS	15 grams	0	0	60 calories
PROTEIN-BASED FOODS				
High fat meat	0	7 grams	8 grams	100 calories
Medium fat meat	0	7 grams	4-7 grams	75 calories
Lean meat	0	7 grams	0-3 grams	45 calories
Plant-Based Proteins	~	7 grams	0	80 calories
Milk	12 grams	8 grams	0-3 grams fat	100 calories
FATS	0	0	5 gram	45 calories

APPENDIX IV: WEIGHT CHARTS

WHO EXPERT COMMITTEE ON PHYSICAL GROWTH	
CLASSIFICATION	**BMI(KG/M^2)**
Underweight	<18.50
Normal range	18.50 - 24.99
Overweight	≥25.00
Obese	≥30.00
PERCENTAGE OF IDEAL BODY WEIGHT	
Overweight	**>110%**
Acceptable	**90% – 110%**
Underweight (Risk of malnutrition)	**<89%**

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