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Factors associated with malnutrition among head and neck cancer in-patients before radiotherapy in National Cancer Institute, Putrajaya

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ABSTRACT

Introduction: Head and neck cancer (HNC) patients are often malnourished during diagnosis and before treatment. This study determined the prevalence of malnutrition and factors associated with malnutrition among HNC patients. **Methods:** A cross-sectional study among HNC in-patients before radiotherapy was conducted. Malnutrition status of the patients was determined using scored Patient Generated-Subjective Global Assessment (PG-SGA). Nutritional parameters of muscle mass, fat mass, albumin, energy and protein intakes were collected. Nutrition impact symptoms (NIS) of the patients were assessed using a validated Head and Neck Symptoms Checklist© (HNSC©). **Results:** Fifty HNC patients were recruited in this study and the age range of patients was 21 to 78 years old, with gender distribution of 78% males and 22% females. More than half of the patients were malnourished, with 20% severely malnourished before radiotherapy. The lack of dietitian referral before treatment was found to significantly affect nutritional status (p=0.027). There was a significant negative relationship between energy intake (r=0.342, p=0.015) and protein intake (r=0.386, p=0.006) with PG-SGA, indicating lower energy and protein intakes related with poor nutritional status. The result showed a significant positive relationship between NIS score (r=0.731, p<0.001) and PG-SGA, indicating the lower the NIS, the better the nutritional status among HNC patients. More than half of the HNC patients had difficulty chewing. **Conclusion:** A strong association between nutritional status and NIS showed the importance of dietary management in HNC patients. Early identification of the nutritional status of HNC patients can ensure optimal nutritional status to improve treatment outcomes.

Keywords: Head and neck cancer, nutritional status, nutrition impact symptoms, energy intake, protein intake

INTRODUCTION

Head and neck cancers (HNC) are malignancies in the head and neck region, which includes the oral and nasal cavities, sinuses, salivary glands, pharynx, larynx and lymph nodes in the neck (Stewart & Wild, 2014). It is the sixth most common cancer worldwide.

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The incidence of oral cavity and pharyngeal cancers has been the highest in Southeast Asia, Western and Central Europe, and South America (Chaturvedi *et al.*, 2013). A total of 103,507 new cancer cases were diagnosed among Malaysians from 2007 to 2011, and the report indicated that HNC contributed 10% (10,608) of the cases (Azizah *et al.*, 2015). Nasopharynx cancer is one of the HNC and is the third most common cancer among Malaysian men (Azizah *et al.*, 2015).

The current treatment of advanced HNC requires multimodal therapy. Surgery, radiotherapy (RT), concurrent chemotherapy and radiotherapy (CCRT) have become standards of care for HNC patients. Prior to RT or CCRT treatment, HNC patients undergo either surgery or neoadjuvant chemotherapy to shrink the size of their tumour, depending on patients' clinical conditions. According to Prevost's review study, optimal nutritional status before treatment is able to improve the effectiveness of treatment and treatment outcomes (Prevost *et al.*, 2014).

However, HNC patients are often malnourished at the time of diagnosis, before treatment or during treatment due to the catabolic state induced by the malignancy and the potential for dysphagia caused by an obstructing tumour (Bower & Martin, 2009). In individuals with HNC, their weight may be affected by the tumour location and related symptoms that interfere with dietary intake. These symptoms are referred to as nutritional impact symptoms (NIS), which include loss of appetite (LOA), nausea, vomiting, taste change, anxiety, depression, difficulty swallowing, pain, dry/sore mouth, difficulty chewing, dental problems, thick saliva, and constipation (Kubrak *et al.*, 2010).

Various studies that have been done previously have shown the prevalence of weight loss before HNC treatment to be between 19% and 45%, which is an indicator of subacute malnutrition (Jager-Wittenaar *et al.*, 2007; Lees, 1999; van den Berg *et al.*, 2006). Malnutrition before treatment due to insufficient food intake is mostly related to mechanical obstruction of food or pain caused by the tumour (Luis, Izaola & Aller, 2007). Cachexia that is associated with muscle wasting with or without the loss of fat mass has contributed to malnutrition as well (Evans *et al.*, 2008). Swallowing problems and pain in the mouth are identified as main risk factors for malnutrition in HNC patients before treatment (Jager-Wittenaar *et al.*, 2007; Kubrak *et al.*, 2010; Righini *et al.*, 2013). Jager-Wittenaar *et al.* (2007) has suggested that total nutrition impact symptoms score could be assessed and addressed as part of a comprehensive care plan in order to optimise the nutritional status of patients before commencing treatment.

Nutrition is a significant aspect in HNC patient management. It determines a patient's functional status, tolerance towards treatment, and overall prognosis. A survey conducted by Spiro *et al.* (2006) demonstrated insufficient detection of malnutrition among 334 oncologists, with only one third having assessed weight loss during consultation, and 65% indicated the importance of malnutrition. Currently, HNC patients in the National Cancer Institute (NCI), Putrajaya are seldom referred to dietitians at diagnosis, instead, they are only referred when having inadequate dietary intake during RT. Dietitian referral is important to identify those who have malnutrition problems in order to optimise nutritional status before treatment. Therefore, nutritional assessments including dietary assessment and nutrition impact symptoms before treatment are important for early nutrition intervention to improve the effectiveness of treatment (Righini *et al.*, 2013).

There is a lack of study in Malaysia to evaluate the prevalence of malnutrition among patients with HNC at the time of initial management (pre-treatment). The purpose of the present study is to determine the prevalence of malnutrition among HNC patients before RT and to examine the associations between pre-treatment weight loss, laboratory parameters, dietary intake, protein intake, and NIS score with malnutrition.

MATERIALS AND METHODS

Study design and setting

This study was part of a prospective study about the changes in nutritional status among HNC patients during RT. Consecutive sampling was used to enrol every HNC patient who was admitted to receive RT or CCRT at NCI, Putrajaya, from March until December 2018, based on inclusion criteria and their informed consents, until the desired sample size was achieved. RT patients received a RT dosage between 60Gy to 70Gy in daily factions of 2.0Gy within seven weeks, while CCRT patients received additional weekly cisplatin or carboplatin during the seven weeks of RT. The inclusion criteria were HNC patients who were admitted into the ward for undergoing RT for seven weeks with or without chemotherapy for curative treatment intentions and aged ≥18 years. Besides that, patients were also on 100% oral intake at the time of the study, and without any forms of enteral tube feeding or total parenteral nutrition. Patients were excluded from this study if they were involved in another research project and ongoing artificial nutrition (enteral/ parenteral) before RT or CCRT.

Ethical approval

This study was registered with The National Medical Research Registry (NMRR ID 17-2647-37667). Ethical approval for the study was obtained from the Medical Research Ethics Committee (MREC), Ministry of Health Malaysia and the Medical Research Ethics Committee of the Faculty of Medicine & Health Sciences, Universiti Putra Malaysia. Permission to conduct the study was obtained from the Director, NCI, Putrajaya, Malaysia.

Socio-demographic and clinical characteristics

Socio-demographic data collected included age, gender, ethnicity, marital status, occupation, and education level. For clinical characteristics, they included tumour location and stage, type of treatment, duration and dosage of RT. These were obtained from the computerised Hospital Information System (HIS). Co-morbidities, smoking status, alcohol consumption and family history before RT were collected.

Nutritional status

Malnutrition status

The malnutrition status of patients was determined by using the Patient-Generated Subjective Global Assessment (PG-SGA). The PG-SGA is a global rating and scoring nutritional assessment tool specialised for cancer patients (Bauer, Capra & Ferguson, 2002). This instrument is a subjective questionnaire with closed-ended structure. The first part of the questionnaire included weight loss history, dietary intake, activities and functions, while the second part was about the patient's disease and its relation to nutrition requirements. The metabolic demand (stress) and physical examination were filled out by a physician, trained nurse or dietitian who assessed the patient's metabolic and physical demands (Ottery, McCallum & Polisena, 2000). Patients were subjectively categorised as well-nourished (PG-SGA category A), moderately or suspected of being malnourished (PGSGA category B) or severely malnourished (PG-SGA category C) upon the completion of the assessment. The scored PG-SGA is a further development of the subjective

global assessment (SGA) concept that incorporates a numerical score. A score ranging from 0 to 4 was given for each domain, depending on the impact on nutritional status. A high score indicated a lower nutritional status of the patient, thus requiring nutrition intervention. Scores with 0 to 1 point requires no intervention, health education for those with 2 to 3 points, dietetic intervention for those with 4 to 8 points, and nutrition support for those with >9 points.

Anthropometric measurements

Anthropometric measurements used in this study included body weight, height, and body composition. Body height was measured using a stadiometer (Seca 222, medical scales & measuring systems Seca, United Kingdom). Measurements of body weight and body composition were assessed with a calibrated TANITA total body composition analyser (model SC-300, bioelectrical impedance analysis scales, Japan), which can provide body weight in kg (up to 0.1 kg), fat percentage (up to 0.1 %), and total muscle mass (up to 0.1 kg). The patients were required to be bare footed and to stand upright and front facing during measurement. The patients were requested to have minimal clothing, emptied their pockets, and stand upright while barefooted on the metal plate of the scale.

Body mass index (BMI) was calculated as actual body weight/height^2 in (kg/m^2). BMI was then classified as either underweight (BMI <18.5 kg/m^2), normal (BMI 18.5–24.9 kg/m^2), overweight (BMI 25 – 29.9 kg/m^2) or obese (BMI >30 kg/m^2) (WHO, 2004). Percentage weight loss was calculated as (normal body weight – actual body weight)/ (normal body weight) x 100. Normal body weight was defined as the body weight one month before treatment and was retrieved from medical records. Actual body weight was assessed at the beginning of treatment.

Laboratory parameters

Data on serum albumin, haemoglobin (Hb) and white blood cells (WBC) count at the beginning of treatment were extracted from the patient's medical record. This is a standard routine procedure for blood sampling to monitor the patient's clinical condition.

Dietary intake (energy and protein intakes)

Dietary intake was measured through a one day 24-hour dietary recall. Foods and beverages consumed in the last 24 hours, starting from the last midnight and finishing at midnight, were identified by 24-hour dietary recall. This questionnaire consisted of six meals including breakfast, lunch, dinner and three snacks. Intakes of foods in household servings, and subsequently in grams, were collected for every meal to estimate energy and macronutrient intakes. Household measurements were used to calculate the grams of foods consumed. For this purpose, a set of household measurement tools (glass, soup bowl, plate, cup, teaspoon and tablespoon) and food models were used to guide patients in estimating portion sizes. Then, the intakes of energy and macronutrients were determined. The Nutritionist Pro software was used to analyse information on the amount of macronutrient intakes (in gram) and total energy intake (kcal) by entering the meals' recipes with the exact gram intake of all food items. The software calculated the nutrition facts of all the foods taken in a day from recall. Data on total energy and protein intakes were recorded to compare with the energy requirement of patients.

Functional status

Functional status was measured by handgrip strength using the Jamar hand dynamometer (Fred Sammons Inc, Burr Ridge, Illinois, USA). Patients sat with their shoulder adducted and neutrally rotated, elbow flexed at 90°, forearm in neutral position. Standard verbal instructions were given to the

patients to squeeze the dynamometer as hard as possible for three times after an interval of five seconds in between grips. The average of three successive attempts on the non-dominant hand was used as the final result. The handgrip strength results were then descriptively compared with reference values from the other two studies among cancer patients, whereby low hand-grip strength was defined as grip strength <25 kg (Chen *et al.*, 2011). High strength was defined as above 19.84 kg in women and 34.39 kg in men; while intermediate strength was considered between 14.68 kg and 19.84 kg in women and between 25.00 kg and 34.39 kg in men (Mendes, Alves & Amaral, 2014).

Nutrition impact symptoms (NIS)

The NIS were measured with the Head and Neck Symptoms Checklist© (HNSC©). This validated instrument aids in the early identification of symptoms that place HNC patients at risk of reductions in dietary intake, weight, and functional performance (Schmidt *et al.*, 2013). This checklist had 12 of the symptoms included in the PG-SGA (pain, dry mouth, LOA, constipation, feeling full, diarrhoea, sore mouth, nausea, altered smell, vomiting, difficulty swallowing, and taste change) plus five additional symptoms (lack of energy, depression, difficulty chewing, thick saliva, and anxiety) which were not included in the PG-SGA but reported in the literature as being associated with reduced dietary intake (Schmidt *et al.*, 2013). The HNSC© also provided space for patients to record any additional NIS interfering with eating. Patients were asked to rate the severity of each symptom and the degree to which it interfered with eating (dietary intake) using a five-point Likert scale ranging from "1=not at all" to "5=a lot". A symptom was considered "present" if the severity score was at least 2 (Kubrak, Olson & Baracos, 2013). All 17 symptom scores in the checklist were added together to make the total NIS score, which varied from 17 (no symptoms) to 85 (highest score of 5 for every symptom in the list) (Farhangfar *et al.*, 2014).

Statistical analysis

All statistical analyses were performed using the IBM SPSS for Windows, version 23 (SPSS Inc, Chicago, USA). Data were checked for normality via Shapiro-Wilk analysis. All data were normally distributed as indicated by $p>0.05$, unless otherwise stated. If the data was not normally distributed, analysis was carried out on natural logarithm of the values to improve the symmetry and homoscedasticity of the distribution.

Descriptive statistics including percentages, means and standard deviation were used to describe demographic data, clinical characteristics, nutritional status, anthropometric data, biochemical data, NIS, energy and protein intakes. The mean values from both groups were compared by using an independent *t*-test. For ordinal data or data that were not normally distributed, Mann-Whitney U-test was carried out to test the differences between groups. Spearmen's rho was performed to evaluate the association between two numerical variables. Chi-square test was used to test the significant differences between groups for categorical data. A statistical probability of $p<0.05$ was considered as significant.

RESULTS

Fifty-four patients consented to participate in this study. A total of four patients were excluded as they did not meet the study's criteria. The recruitment for this study showed that there were more male than female patients with HNC (78% versus 22%) and the median age of the population was 60 years with a range of 21-78 years old. More than half of the HNC patients in this study had nasopharynx ca ncer and 84% were in an advanced stage of the tumour. In

Table 1. Patient socio-demographic and clinical characteristics

Characteristics	*Overall (n=50)*	*Well nourished (n=22)*	*Malnourished (n=28)*	*p-value*
Age (years)†, median (IQR)	60 (49-67)	54 (44-67)	61 (52-66)	0.163
Gender§, n (%)				
Male	39 (78.0)	16 (72.7)	23 (82.1)	0.425
Female	11 (22.0)	6 (27.3)	5 (17.9)	
Ethnicity§, n (%)				
Malay	21 (42.0)	9 (40.9)	12 (42.9)	0.501
Chinese	19 (38.0)	10 (45.5)	9 (32.1)	
Indian	10 (20.0)	3 (13.6)	7 (25.0)	
Education level§, n (%)				
Primary or below	20 (40.0)	8 (36.4)	12 (42.9)	0.642
Secondary or above	30 (60.0)	14 (63.6)	16 (57.1)	
Marital status§, n (%)				
Single	13 (26.0)	4 (18.2)	9 (32.1)	0.264
Married	37 (74.0)	18 (81.8)	19 (67.9)	
Working status§, n (%)				
Yes	14 (28.0)	6 (27.3)	8 (28.6)	0.919
No	36 (72.0)	16 (72.7)	20 (71.4)	
Co-morbidities§, n (%)				
Yes	29 (58.0)	12 (54.5)	17 (60.7)	0.661
No	21 (42.0)	10 (45.5)	11 (39.3)	
Smoking history§, n (%)				
Active smoker	7 (14.0)	3 (13.6)	4 (14.3)	0.164
Non-smoker	25 (50.0)	14 (63.6)	11 (39.3)	
Ex-smoker	18 (36.0)	5 (22.7)	13 (46.4)	
Alcohol history§, n (%)				
Yes	12 (24.0)	6 (27.3)	6 (21.4)	0.631
No	38 (76.0)	16 (72.7)	22 (78.6)	
Family history§, n (%)				
Yes	14 (28.0)	7 (31.8)	7 (25.0)	0.753
No	36 (72.0)	15 (68.2)	21 (75.0)	
Tumour location¶, n (%)				
Tongue	7 (14.0)	3 (13.6)	4 (14.3)	0.623
Mouth	6 (12.0)	2 (9.1)	4 (14.3)	
Salivary gland	3 (6.0)	1 (4.5)	2 (7.1)	
Tonsil	2 (4.0)	0 (0.0)	2 (7.1)	
Oropharynx	2 (2.0)	0 (0.0)	2 (7.1)	
Nasopharynx	26 (52.0)	15 (68.2)	11 (39.3)	
Sinuses	1 (2.0)	0 (0.0)	1 (3.6)	
Larynx	3 (6.0)	1 (4.5)	2 (7.1)	
Stage of tumour§, n (%)				
1-2	8 (16.0)	5 (22.7)	3 (10.7)	0.277
3-4	42 (84.0)	17 (77.3)	25 (89.3)	
Type of treatment§, n (%)				
Radiotherapy	17 (34.0)	7 (31.8)	10 (35.7)	0.773
Chemoradiotherapy	33 (66.0)	15 (68.2)	18 (64.3)	

Table 1. Patient socio-demographic and clinical characteristics (cont'd)

Characteristics	*Overall (n=50)*	*Well nourished (n=22)*	*Malnourished (n=28)*	*p-value*
PG-SGA global rating				
A (well-nourished)	22 (44.0)			
B (moderately malnourished)	18 (36.0)			
C (severely malnourished)	10 (20.0)			
Triage intervention				
No intervention (Score of 0–1)	4 (8.0)			
Health education (Score of 2–3)	13 (26.0)			
Dietetic intervention (Score of 4–8)	10 (20.0)			
Critical interventions (≥ 9)	23 (46.0)			
BMI category ¶				
Underweight (<18.5 kg/m2)	12 (24.0)	3 (13.6)	9 (32.1)	0.224
Normal weight (18.5-24.9 kg/m2)	25 (50.0)	13 (59.1)	12 (42.9)	
Overweight (25-29.9 kg/m2)	5 (10.0)	1 (4.5)	4 (14.3)	
Obese (>30 kg/m2)	8 (16.0)	5 (22.7)	3 (10.7)	
Pre-treatment weight loss ¶				
None	14 (28.0)	12 (54.4)	2 (7.1)	<0.001
<5% in 1 month or <10% in 6 months	30 (60.0)	10 (45.5)	20 (71.4)	
≥5% in 1 month or ≥10% in 6 months	6 (12.0)	0 (0.0)	6 (21.4)	
Nutrition Impact Symptoms (NIS) §				
Yes	40(80.0)	14 (63.6)	26 (92.9)	0.014
No	10 (20.0)	8 (36.4)	2 (7.1)	
Dietitian referral §				
Yes	23 (46.0)	14 (63.6)	9 (32.1)	0.045
No	27 (54.0)	8 (36.4)	19 (67.9)	

Note: NA: not applicable
† Mann-Whitney U test
§Chi-square test for proportions
¶Fisher's exact test.
$p<0.05$ shows the significant difference between well-nourished (PG-SGA category A) and malnourished patients (PG-SGA category B/ PG-SGA category C)

addition, 33 (66%) received CCRT while 17 (34%) received RT only. All patients received a total of 60Gy and above 30 fractions radiation dosage (Table 1).

The prevalence of pre-treatment malnutrition was 56% (PG-SGA category B and PG-SGA category C), with 20% severely malnourished (PG-SGA category C) (Table 1). The median score for PGSGA was 7, indicating a requirement for dietetic intervention. More than 50% of the malnourished HNC patients were in advanced stage. There were no significant differences between malnutrition status with gender and ethnic groups.

Mean body weight was 60.24±14.73 kg with 43.03±8.12 kg muscle mass. Half of the HNC patients had a normal BMI before treatment, followed by 24% underweight, 16% obese and 10% overweight (Table 1). About 72% HNC patients had weight loss before treatment,

Table 2. Anthropometric measurements, laboratory parameters, handgrip strength, dietary intake, PG-SGA score, NIS score of well-nourished and malnourished patients

Measurements	*Overall (n=50)*	*Well nourished (n=22)*	*Malnourished (n=28)*	*p-value*
Mean±SD†				
Body weight (kg)	60.24±14.73	62.69±12.30	58.32±16.36	0.303
Muscle Mass (kg)	43.03±8.12	43.32±6.90	42.79±9.11	0.823
Albumin (g/L)	40.68±2.65	41.86±1.93	39.75±2.80	0.003
WBC (10^9/L)	7.29±2.51	7.53±2.33	7.11±2.68	0.566
Hb (g/dL)	12.86±1.61	13.16±1.46	12.62±1.70	0.539
Handgrip strength (kg) Male Female	25.17±7.46 27.50±6.67 16.88±2.62	26.20±8.20	24.35±6.86	0.390
Energy intake (kcal/kg BW/day)	24±9	27±9	21±8	0.032
Protein intake (g/kg BW/day)	1.03 ± 0.43	1.13±0.33	0.95±0.49	0.115
Median (IQR)‡				
Pre-treatment weight loss (%)	1.85 (0.00-3.42)	0 (-2.35-1.33)	3.23 (1.84- 4.43)	<0.001
BMI (kg/m2)	21.58 (18.60-25.00)	23.68 (19.90-28.87)	20.0 (17.32- 24.95)	0.118
Fat Mass (kg)	13.3 (9.3-18.5)	14.1 (9.7-15.2)	13.2 (7.8-15.2)	0.301
PGSGA score	7 (2.75-14)	2 (2-3.25)	14 (10-18)	<0.001
NIS score	20 (18-25)	18 (17-20)	23 (20.25-27)	<0.001

†Independent T-test
‡Mann Whitney U-test
$p<0.05$ shows the significant difference between well-nourished (PG-SGA category A) and malnourished patients (PG-SGA category B/ PG-SGA category C). Abbreviations: WBC: White blood cells, Hb: Hemoglobin, PG-SGA: patient-generated subjective global assessment, BMI: body mass index, NIS: nutrition impact symptoms

Table 3. Nutrition Impact Symptoms (NIS) interference scores from the Head and Neck Symptoms Checklist (HNSC©) of the patients (*n*=50)

NIS interference score (1-5)	*Prevalence n (%)*	*Median (IQR)*	*Well nourished (n=22)*	*Malnourished (n=28)*	*p-value*
Taste change	5 (10)	1 (1-1)	1 (1-1)	1 (1-1)	0.039
Difficulty swallowing	9 (18)	1 (1-1)	1 (1-1)	1 (1-2)	0.004
Difficulty chewing	26 (52)	2 (1-3.25)	1 (1-2)	2.50 (1-4)	0.017
Constipation	8 (16)	1 (1-1)	1 (1-1)	1 (1-1.75)	0.048
Loss of appetite	19 (38)	1 (1-2)	1 (1-1)	2 (1-3)	0.001
Dry mouth	19 (38)	1 (1-2)	1 (1-1)	2 (1-2)	0.011
Pain	11 (22)	1 (1-1)	1 (1-1)	1 (1-2.75)	0.007
Anxious	9 (18)	1 (1-1)	1 (1-1)	1 (1-1)	0.455
Nausea	4 (8)	1 (1-1)	1 (1-1)	1 (1-1)	0.197
Lack of Energy	14 (28)	1 (1-2)	1 (1-1)	1 (1-2)	0.057
Sore mouth	6 (12)	1 (1-1)	1 (1-1)	1 (1-1)	0.155
Diarrhoea	0 (0)	1 (1-1)	1 (1-1)	1 (1-1)	1.000
Thick saliva	12 (24)	1 (1-1.25)	1 (1-1)	1 (1-2)	0.107
Depressed	2 (4)	1 (1-1)	1 (1-1)	1 (1-1)	0.863
Fullness	4 (8)	1 (1-1)	1 (1-1)	1 (1-1)	0.455
Vomiting	3 (6)	1 (1-1)	1 (1-1)	1 (1-1)	0.704
Smell bothersome	6 (12)	1 (1-1)	1 (1-1)	1 (1-1)	0.716

Note: Prevalence of NIS when severity scores ≥2; Mann-Whitney U test for skewed data
$p<0.05$ shows the significant difference between well-nourished (PG-SGA category A) and malnourished patients (PG-SGA category B/PG-SGA category C)

with 12% having critical weight loss of ≥5%. The median percentage of weight loss at the beginning of treatment from all 50 patients was 1.85%, with a range of 0% to 3.42% (Table 2). There was a significant difference in pre-treatment weight loss between well-nourished and malnourished patients. There was a weak positive relationship between pre-treatment weight loss and NIS (r=0.332, p=0.019), which indicated that those with higher NIS scores experienced higher pre-treatment weight loss (Table 5). However, there were no significant associations between pre-treatment weight loss with albumin, energy intake, and protein intake (Table 5).

About 80% HNC patients had NIS before the start of treatment, with only 20% of patients experiencing none of the 17 symptoms listed (Table 2). Almost all malnourished HNC patients had NIS symptoms compared to 63.6% among those well-nourished. Well-nourished patients had a statistically better total NIS score compared to malnourished patients. There were seven significant differences in NIS between well-nourished and malnourished patients including taste change, constipation, difficulty chewing, difficulty swallowing, dry mouth, LOA and pain around tumour (Table 3). More than half of the HNC patients had the symptom of difficulty in chewing before treatment (Table 3).

The energy intake and protein intakes of HNC patients in this study were 24±9 kcal/day and 1.03±0.43 g/day, respectively. About 72% HNC patients were on normal diet, 10% on soft diet,

Table 4. Correlation between independent variables and PG-SGA total score (*n*=50)

Independent variables	*Relationship (r)*	*Significance (p)*
NIS score	0.731	<0.001
Albumin (g/L)	-0.278	0.05
Energy intake (kcal/kg BW/d)	-0.342	0.015
Protein intake (g/kg BW/d)	-0.386	0.006

Spearmen's rho $p<0.05$ shows significant association
Abbreviations: PG-SGA: patient-generated subjective global assessment, NIS: nutrition impact symptoms

Table 5. Correlation between independent variables and pre-treatment weight loss (*n*=50)

Independent variables	*Relationship (r)*	*Significance (p)*
NIS score	0.332	0.019
Albumin (g/L)	-0.245	0.087
Energy intake (kcal/kg BW/d)	0.20	0.892
Protein intake (g/kg BW/d)	0.068	0.638

Spearmen's rho $p<0.05$ shows significant association
Abbreviations: PG-SGA: patient-generated subjective global assessment, NIS: nutrition impact symptoms

6% on minced diet, 10% on blended diet and 2% on full liquid diet. The energy and protein intakes for well-nourished and malnourished patients were 27±9 kcal/kg BW/day and 1.13±0.33 g/kg BW/day, and 21±8 kcal/kg BW/day and 0.95±0.49 g/kg BW/day (Table 2). Significant difference was found in energy intake between well-nourished and malnourished patients ($p<0.05$). A majority of HNC patients (90%) were not on any oral nutritional supplement (ONS) support at the beginning of treatment. There were only 14.2% malnourished HNC patients on ONS before treatment.

All HNC patients had normal albumin with a mean±standard deviation (*SD*) of 40.7±0.4 g/L. Furthermore, mean Hb value for both male (13.1±0.3 g/L) and female (12.0±0.4 g/L) patients were at normal values as well. WBC was within the normal range with means of 7.3±0.4 10^9/L. There were no significant differences between WBC and Hb of patients who were well-nourished ($p=0.566$) and malnourished ($p=0.539$), according to PG-SGA. Based on gender, the overall reading for males was better than females, which were 27.50±6.67 kg and 16.88±2.62 kg, respectively.

Out of 50 HNC patients, only 23 patients (46%) had been referred to a dietitian before the start of treatment (Table 1). However, around 70% malnourished patients had no dietitian referral. There was a significant difference in dietitian referral between well-nourished and malnourished patients, $p=0.045$.

Table 4 shows there were significant negative relationships between energy intake ($r=0.492$, $p<0.001$) and protein intake ($r=0.478$; $p<0.001$) with PG-SGA; which indicated lower energy and protein intakes related with poor nutritional status (lower mean score of PG-SGA). A significant strong association with PG-SGA was observed for NIS score ($r=0.731$, $p<0.001$), indicating the better the nutritional status, the lower the NIS of the HNC patients.

DISCUSSION

The prevalence of malnutrition in this study was high (56%). Similar findings were obtained from other studies using PG-SGA on patients with cancer, which also reported 42% to 76% patients either being malnourished or at risk of being malnourished (Bauer *et al.*, 2002; Luis *et al.*, 2007). It is a concern that >50% HNC patients had malnutrition problems before starting RT or CCRT, which can further worsen their nutritional status with treatment-related symptoms. Untreated malnutrition has been associated with reduced response towards treatment, poor survival and a diminished quality of life (Santarpia, Contaldo & Pasanisi, 2011). Therefore, it is crucial to maintain an optimal nutritional status for patients before treatment for better outcomes and reduce complications such as treatment interruption (Lin *et al.*, 2005).

Weight loss remains a clinically relevant, simple, and reliable marker of malnutrition. Our study reported that 12% HNC patients had a critical weight loss ≥5% in one month. Langius *et al.* (2016) revealed a similar result in a study of HNC patients where 16% of the patients had critical weight loss (>5%) before treatment. Another study reported that at the time of diagnosis, 34% of patients with oral/oropharyngeal cancer had already lost ≥10% of body weight in six months or ≥5% in one month (Jager-Wittenaar *et al.*, 2007). Weight loss of ≥10% in six months or ≥5% in one month has been shown to increase complication rates, such as impaired wound healing, reduced immune function and decreased tolerance towards surgery, RT and chemotherapy. The outcomes may lead to higher mortality and reduced quality of life (van Bokhorst-de van der Schueren *et al.*, 1997).

Although there was no significant difference for handgrip strength among well-nourished and malnourished groups, the handgrip strength of HNC patients in this study was categorised as intermediate strength when compared to a previous study on cancer patients (Mendes *et al.*, 2014). This indicated that cancer patients may experience some muscle wasting due to diminished synthesis of muscle protein and increased degradation of proteins (Kilgour *et al.*, 2013; Chen *et al.*, 2011).

There was a significant difference in NIS (taste change, difficulty swallowing, difficulty chewing, constipation, LOA, dry mouth and pain) between well-nourished and malnourished patients. Neoadjuvant chemotherapy prior to RT is one of the reasons HNC patients experience LOA, dry mouth, lack of energy, thick saliva, and pain. Farhangfar *et al.* (2014)'s study reported that LOA, difficulty chewing, dry mouth and pain were symptoms associated with reduced dietary intake. Most of the malnourished patients experienced reduced dietary intake due to these symptoms. This study found that the malnourished group had a lower dietary intake compared to the well-nourished group. The average daily energy and protein intakes in this study were below the European Society for Clinical Nutrition and Metabolism (ESPEN) recommended guidelines of 30 – 35 kcal/kg of body weight and 1.2 – 1.6 g/kg body weight. Advanced staging showed a significant association with decreased energy and protein intakes, and nutritional depletion, according to Ravasco *et al.* (2003)'s study on HNC patients. In our study, majority of HNC patients were in advanced stage and were found to have a higher tendency of nutritional depletion with inadequate energy and protein intakes, which marked the same nutrition intake deficits with the earlier mentioned study.

In our study, there was a significant relationship between pre-treatment weight loss with NIS score. Multiple NIS are more likely to reduce dietary intake and induce weight loss. Half of the HNC patients had the symptom of difficulty in

chewing. Most patients with oral cancer are edentulous or partially dentate, which adversely affects their masticatory function (Farhangfar *et al.*, 2014). Post-dental extraction before treatment might expose patients to difficulty in chewing hard solid foods and thus lead to pre-treatment weight loss. Patients having chewing problems have been seen changing their diet into a soft, mashed or liquid diet. As nutritional density of a mashed or liquid diet is lower than that of a solid diet, these patients are at a high risk of malnutrition too. For those patients who have received early nutrition management before treatment where they are advised to use energy and protein enriched liquid dietary supplements, the use of these supplements increases energy and protein intakes and in turn decreases the risk for malnutrition (Nejatinamini *et al.*, 2018). For a patient who is having NIS prior to RT, especially one who is malnourished, ONS initiation should be implemented as soon as at the beginning of RT.

The timing of nutritional intervention is fairly important. This study revealed that malnutrition could happen before RT commencement and perhaps at the time of diagnosis. Jager-Wittenaar *et al.* (2017)'s exploratory study suggested a high prevalence of cachexia (42%) in patients with newly diagnosed HNC. There was about 54% HNC patients in this study who have had no dietitian referral prior to RT and this remains a concern in clinical oncology. Majority of malnourished patients in this study were unable to start their treatment in optimal nutritional status due to the lack of dietitian referral, with only 32.1% receiving nutrition management. This result is similar to other studies that reported only 30% to 60% of cancer patients at risk of malnutrition having received nutritional treatment, and even patients diagnosed with severe malnutrition failed to receive an appropriate nutritional intervention (Attar *et al.*, 2012; Segura *et al.*, 2005). A significant number of cancer patients at risk of malnutrition remain undetected due to the lack of nutrition screening during diagnosis and absence of nutritional evaluation as part of routine practice in the clinical setting (Koom, Ahn & Song, 2012). According to the Clinical Oncology Society of Australia, malnutrition screening should be undertaken by all patients at diagnosis to identify those at nutritional risk, and then repeated at intervals through each stage of treatment.

The factors associated with malnutrition in this study included high pre-treatment weight loss, high NIS score, reduced energy and protein intakes. Our study is consistent with another HNC patients study which found that malnutrition was significantly associated with multiple NIS, reduced dietary intake, and involuntary weight loss (Schmidt *et al.*, 2013). Patients with HNC should be nutritionally screened using a validated screening tool (PG-SGA or SGA) and NIS checklist at diagnosis.

The strength of the current study was the rich data of nasopharynx patients among all other categories of HNC such as laryngeal, tonsil and tongue. The results serve as a reference and benchmark for further research on particular types of nasopharynx cancer. At the same time, NIS of HNC patients were observed clearly with a validated HNSC© that allowed us to design a more effective nutrition intervention in future. To the best of our knowledge, our study was the first in Malaysia to examine the association between nutritional status with energy intake, protein intake and NIS in HNC patients at the beginning of RT.

Limitations of this study were the inherently limited single-institution design with only HNC in-patients as opposed to having data on outpatients across multiple institutions, thus making it difficult to draw stronger conclusions. This study has only observed the

nutritional status of HNC patients at the beginning of RT, therefore, it is suggested that a further observational study at diagnosis could be done in order to generate a more comprehensive data on the nutritional status among HNC patients. Long-term follow-up is proposed to enable an investigation of any associations between pre-treatment nutritional status with treatment outcomes.

CONCLUSION

In summary, 56% of patients from this study were malnourished and 20% were severely malnourished at the beginning of RT. However, the lack of dietary counselling has led to higher risks of malnutrition among HNC patients before RT. In addition, this study showed that malnourished HNC patients experienced higher NIS scores, and reduced energy and protein intakes at the beginning of RT. More than half of the HNC patients had the symptom of chewing difficulty. Our study provided important preliminary data suggesting that early identification of malnutrition and dietitian referral before treatment commencement are warranted. Our results have presented the need for active nutritional status screening including NIS assessment at cancer diagnosis apart from at the beginning of treatment. Early identification of the nutritional status of patients at presentation ensures optimal nutritional status to improve overall treatment outcomes.

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Authors' contributions

NMK, principal investigator, conceptualised and designed the study, prepared the draft of the manuscript and reviewed the manuscript; ZAR, NJ, advised on the data analysis and interpretation, and reviewed the manuscript; SNAS, AA, HCY, BSHL, NWH, AMM, led the data collection and reviewed the manuscript; ZAZ, advised on data analysis and interpretation, assisted in drafting of the manuscript, reviewed the manuscript; NBMY, ZI, ZAMD reviewed the manuscript.

Conflict of interest

All authors declare that they have no conflict of interest with any party in relation to this manuscript.

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