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ORIGINAL RESEARCH ARTICLE

Nutrition Assessment in Head and Neck Cancer Patients Pre and Post Chemoradiotherapy

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ABSTRACT

Introduction: Head and neck cancer patients are frequently malnourished at the time of diagnosis and prior to the beginning of treatment. Deterioration of the nutritional status results in an increase in chemo-radiotherapy (CRT) related toxicity, and this may increase the prolonged treatment time, which has been associated with poor clinical outcome. The present study aims to do a nutritional assessment before and after CRT in head and neck cancer patients.

Material and Methods: The present study was undertaken at the Department of Radiation Oncology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly. In this study, 50 patients of head and neck tumors were enrolled, and their nutrition was assessed before and after CRT. Nutrition assessment was done using different laboratory parameters like hemoglobin, total leukocyte count, blood urea, serum creatinine, and serum bilirubin. Anthropometric parameters used are body mass index, skinfold thickness, and mid-arm circumference. Nutritional risk indicator and patient-generated subjective global assessment (PG-SGA) score are measured before and after CRT. All the parameters were assessed and analyzed using different statistical tests – Chi-square test, Fisher exact test, and paired t-test.

Results: Hemoglobin decrease was statistically significant during treatment ($p < 0.001$), and the decrease in total leukocyte count during treatment was showing a trend towards significance (p-value -0.056). There was deterioration in other parameters like blood urea, serum creatinine, and serum bilirubin but was not statistically significant. Anthropometric parameters–body mass index (BMI), mid-arm circumference (MAC), skinfold thickness, and percent body fat showed a significant change ($p < 0.00001$).

Nutritional risk indicator and PG-SGA class have decreased for the majority of patients during treatment, and the change is statistically significant ($p < 0.00001$ and $p = 0.0251$), respectively.

Conclusion: Nutrition has an important role to play in the management of head and neck cancers by CRT. It helps to reduce the complications and improve the tolerance of CRT, thus avoiding treatment breaks, which may lead to failure of treatment.

Keywords: Nutrition assessment, Head and neck cancer, Chemo-radiotherapy (CRT).

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INTRODUCTION

Head and neck cancer patients are frequently malnourished at the time of diagnosis and prior to the beginning of treatment.[1-6] In addition, CRT causes or exacerbates symptoms, such as alteration or loss of taste, mucositis, xerostomia, fatigue, nausea, and vomiting with consequent worsening of malnutrition.[7-10] In many patients, such toxicities may be very severe and even life-threatening and may lead to treatment interruptions that are invariably associated with poorer outcome.[11-14]

Malnutrition or risk of malnutrition must be diagnosed, but the importance of this diagnosis is often underestimated. Patients with HNC have one of the highest malnutrition prevalence rates among all diagnostic groups, with 25 to 50% of these patients classified as nutritionally compromised prior to commencement of treatment.[15] Weight loss during radiation therapy to the head and neck can diminish the safety and effectiveness of the treatment. Significant amounts of weight loss can also affect the chemotherapy regimen, preventing the patient from receiving the optimal dosage.

An adequate method for assessing the nutritional status of hospitalized subjects includes dietary intake, nutritional requirements, functional status, and body composition, such as anthropometric and laboratory parameters. Certain factors may be helpful to determine nutritional status like dietary history as appetite, activity level, food habit, bowel movements, symptoms related to digestion, clinical indicators as physical signs that detect nutritional deficiencies, biochemical parameters as serum albumin and pre-albumin, anthropometric parameters as height, weight, BMI, triceps skinfold thickness (TSF),

and MAC and specific tools such as hand grip strength (HGS), subjective global assessment (SGA), and PG-SGA.

Several studies have demonstrated that patients with cancer who stabilized their weight had longer survival and improved quality of life compared with those who continued to lose weight.[16] The present study aims to do a nutritional assessment before and after chemo-radiation in head and neck cancer patients.

MATERIAL AND METHODS

The study was conducted in the Department of Radiation Oncology, Shri Ram Murti Smarak Institute of Medical Sciences (SRMS-IMS), Bhojipura, Bareilly, Rohilkhand region of Uttar Pradesh, India.

Study design: Prospective study

Study population: All the patients included in the study were histologically proven cases of head and neck cancers. Fifty patients fulfilling the inclusive criteria are taken in the study.

Inclusive Criteria

- Histopathologically/ cytologically proved head and neck cancer patients.
- Age > 18 years.

Exclusive Criteria

- Those who do not give informed consent.
- Unconscious and bed-ridden patients.
- Preceding non-oncological diseases (e.g., hypertension, COPD, etc.) that significantly affect nutritional status.
- Patients already received oncological treatment for diagnosed cancer.
- All data were collected during a face-to-face interview with the patients. General physical examination was conducted to note down the relevant clinical findings like pallor, jaundice, and edema. The socio-economic status of patients was grading using the Kuppuswamy scale.

Anthropometric Assessment

- The BMI was calculated using formula BMI = weight (kg)/height (m^2).
- Four-site (triceps, biceps, supra-iliac, and subscapular) skinfold thickness was measured using the Harpenden's caliper. The TSF, to the nearest mm, was measured at the midpoint between the acromion and olecranon processes on the non-dominant side with a Harpenden's caliper. The average of all four site skinfold thickness was calculated. % body fat is estimated from average skinfold thickness values using by Durnin Womersley formula.
- The MAC was measured to the nearest 0.1 cm with a tape at the same point as the TSF.
- Before taking measurements, the subjects will be requested to stand in a comfortable position.

All anthropometric measurements were made at least three times by the same investigator, and the reported values are the means of the repeated measurements.

Laboratory Parameters:

Blood samples were taken, and tests include the measurement of hemoglobin, total leukocyte count, serum protein, and albumin. Laboratory data were collected using standard methods.

Nutritional Risk Indicator (NRI)

The NRI was developed by the veteran's affairs total parenteral nutrition group. The NRI is a simple equation that uses serum albumin and recent weight loss:

NRI = [1.519 × serum albumin (g/L) + 0.417 × (present weight/ideal weight × 100)]

An NRI score higher than 100 indicates that the patient is not malnourished, a score of 97.5 to 100 indicates mild malnourishment, a score of 83.5 to 97.5 indicates moderate malnourishment, and score lower than 83.5 indicates severe malnourishment.

Comprehensive nutritional assessment was done using the PG-SGA tool. PG-SGA score was calculated to triage the patient for the appropriate nutritional intervention.

Data collected were analyzed using various statistical tests (Chi-square test, Fisher exact test, and paired t-test) and SPSS software. To calculate the level of significance using p-value, the level of significance (p value) has been considered as < 0.05.

RESULTS

In the present study, 50 histopathologically proven head and neck cancer patients were included, which were treated with radical intent and received CRT. The majority of patients were in the 6th decade or more. The male-female ratio was 15.7:1 (Table 1).

The common symptoms were pain (58%) and difficulty in swallowing (48%) followed by other complaints like neck swelling (30%), ulcer (16%), and increased salivation (10%). Symptoms having nutrition impact are pain, difficulty in swallowing, ulcer over the tongue, or any other area. Non-nutritional impact symptoms include increased salivation and edema. The majority of patients (86%) had symptoms with nutritional impact, and only 14% had non-nutritional impact symptoms (Table 1). Ninety four percent were taking a semi-solid diet, and the remaining six percent were on liquid diet due to dysphagia and pain.

Most of the patients (84%) were of carcinoma oral cavity and oropharynx, and the majority of the cases

(82%) were in a locally advanced stage (Table 2).

Around two-thirds of patients completed the treatment within the stipulated duration. The treatment gap of around 4–6 days was seen in 62.5% of patients, and 37.5% of patients had a gap of more than one week (Table 3).

There was no severe change in hemogram or biochemical profile (liver or kidney function tests) of the patients, pre- or post-treatment. None of the patients developed grade III or IV toxicity.

There was a decrease seen in skin fold thickness before and after treatment, with a median decrease of 9.7 mm (range 2.8–19.7 mm, $p < 0.0001$). Similarly, statistically significant decrease (p-value < 0.0001) was observed in body fat % pre- and post-treatment with mean loss 3.56% (range 0.6 to 6.0%). In nutritional assessment parameters of BMI, before treatment, 40% were underweight, which increased to 48% after treatment. Patients with normal weight (46%) decreased to 40% after treatment ($p < 0.0001$). On comparing values before and after treatment, there is an increase in PG-SGA scores, indicating increased malnourishment. Before treatment, only 4% were malnourished, which had a many-fold increase to 56% after treatment ($p = 0.02$) (Table 4).

Table 1: Demographic profile

Characteristics	*No. of patients (n = 50)*
Age (years)	
< 50	19 (38)
≥ 50	31 (62)
Gender	
Male	47 (94)
Female	3 (06)
Personal habits	
Tobacco	6 (12)
Alcohol	24 (48)
Both	20 (40)
Socio economic status	
Upper class	0 (0)
Middle class	21 (42)
Lower class	29 (58)
Lifestyle	
Sedentary	9 (18)
Moderate laborer	40 (80)
Hard laborer	1 (02)
Dietary habits	
Vegetarian	26 (52)
Non-vegetarian	24 (48)
Nature of compliance	
Nutritional impact	43 (86)
Non-nutritional impact	7 (14)

Table 2: Site and stage of tumor

Characteristics	*No. of patients (n = 50)*
Site of tumor	
Oral cavity	24 (48)
Oropharynx	18 (36)
Hypopharynx	6 (12)
Larynx	2 (04)
AJCC stage	
II	9 (18)
III	25 (50)
IV	16 (32)

DISCUSSION

Malnutrition is very common in patients with head and neck cancers, which is further exacerbated by its treatment with CRT. It is essential to take the nutritional status into account while planning the patient's management, as it determines the patient's prognosis in terms of curative treatment.

In a study by Righini *et al.*,[17] the mean age at presentation was 59 years. Nine percent of the patients were older than 75 years. Alexandra *et al*.[18] reported ages ranging between 47 and 87 years, average 63.1 ± 8.8 years, and median 63 years. Judith *et al*.[19] conducted a study on nutrition in head and neck cancer reported age of patients was in the range 11–83 years, with a median 55 years. In a study by Jeffery E *et al*.,[20] the mean age was 63 ± 13.3 years (range 34–86 years). In our study, 80% of the patients were from the 5th to 7th decades. The youngest patient was 18 years old, and the oldest was 70 years old. The mean age at presentation was 51.4 ± 12.90 years. The majority of the patients were in their sixth decade or more. Bincy R *et al*.[21] conducted a study in which the average age of patients was 52.90 ± 13.03 years, almost similar to our study.

Several studies have shown a higher incidence of head and neck cancers in males ranging from 82 to 90%.[17,20,22] In our study, patients were chosen randomly with no sex discrimination. 94% of the cases were males. This is probably attributed to males being more habituated to gutkha chewing and smoking.

In a study by Righini,[17] 80% were alcoholic, and 83% were smokers. In our study, 48% of patients were

Table 3: Treatment characteristics

Characteristics	*No. of patients (n = 50)*
Duration of treatment	
≤ 52 days	34 (68)
> 52 days	16 (32)
Treatment gap (n = 16)	
< 7 days	10 (62.5)
≥ 8 days	6 (37.5)

Table 4: Malnutrition parameters

	Before treatment	*After treatment*	
Characteristics	*Total number (n = 50)*	*Total number (n = 50)*	*P-value*
BMI (kg/m^2)			
≤18.5	20 (40)	24 (48)	< 0.0001
18.6–24.9	23 (46)	20 (40)	
25–29.9	07 (14)	05 (10)	
≥30	0 (0)	01 (02)	
PG-SGA class			
Well-nourished (class A)	12 (24)	3 (06)	0.0251
Malnourished (class B and C)	38 (76)	47 (94)	
Nutritional risk index			
<83.5 (severe malnutrition)	20 (40)	25 (50)	<0.0001
83.5–97.5 (moderate malnutrition)	22 (44)	14 (28)	
97.5–100 (mild malnutrition)	02 (04)	06 (12)	
>100 (no malnutrition)	06 (12)	05 (10)	
Mid arm circumference (cm)			
<23 (malnourished)	46 (92)	49 (98)	<0.0001
≥23 (normal)	4 (08)	01 (02)	

alcoholic, 12% were associated with tobacco intake, and 40% were both alcoholic and smokers.

Socio-economic status (SES) is an important determinant of the standard of living, nutrition, and health status of the individual/community. In the present study, the majority of patients belonged to the lower and middle-class groups. It correlates with the study by Bincy R,[21] where 40% belonged to the lower class, 43% to the middle class, and the remaining 17% were upper class. As the majority of patients were of the lower and middle class, their pre-treatment nutritional status was poor. Due to the lack of an upper-class subset, we couldn't compare nutritional status in this subgroup.

In our study, 80, 18, and 2% belonged to moderate, sedentary, and hard labor lifestyle, respectively. In a study by Righini *et al*.,[17] the employment status was reported for 68 (40%) patients, 35 were employed, 22 were unemployed, and 11 had retired. The occupation was specified for only 30 (44%) patients. The majority of patients (66%) worked or had worked in factories or in the building industry. In Bincy R[21] study, 36.3% of his patients were employed doing moderate labor. Evidence has been obtained suggesting that increasing physical activity may reduce the risk of several types of cancers like breast, colon, prostrate, and endometrium.

Nutritional impact symptoms (dysphagia, ulcer in the oral cavity, decreased appetite, etc.) are directly related to the nutritional status of patients, and these symptoms further decrease the nutritional intake. In our study, the most common complaints were pain (58%) and difficulty in swallowing (48%). 30% presented with neck swelling. 16% had complaints of ulcer, and 10% complained of increased salivation. 86% of patients had symptoms with nutritional impact, and 14% with non-nutritional impact symptoms.

Site-wise distribution of various head and neck malignancies in our study was more in terms of oral cavity compared to study by Righini *et al*.[17] (oral cavity 48 *vs.* 23.6%), and less in terms of larynx (4 *vs.* 23%) and hypopharynx (12 *vs.* 17.7%). A study by Judith[19] had more cases of the oral cavity (64 *vs.* 48%) and larynx (23 *vs.* 4%), and very less of oropharynx cases (9 *vs.* 36%) compared to our study. There is variation seen in the distribution of sites of head and neck cancers, which may be attributed to the type of tobacco consumption and various different habits of usage.

The stage of the patient is an important prognostic factor. 50% of cases belong to stage III, 32% were of stage IV, and 18% of stage II. There was no stage I case in our study group. In a study by Jeffery,[20] 12.5% patients were of stage I and II, 45.8% were of stage III and IV, and remaining 41.7% had an unknown stage. Languis[22] conducted a study in which about 50% of patients belonged to stage IV. The different stage presentation depends upon the awareness of the disease and screening programs. In our country, the majority of patients are seen on a locally advanced stage due to a lack of both issues.

Olfred *et al*.[23] assessed the importance of overall treatment time for the outcome of radiotherapy of locally advanced head and neck cancer and reported that prolongation of overall treatment time only leads to decreased locoregional control. Poor nutritional status may lead to more severe acute mucositis, which may

cause treatment breaks and prolongation of overall treatment time. In our study, 68% of patients completed treatment in < 52 days, and 32% completed in more than 52 days. Delay of 4–6 days in treatment was seen in 62.5% of patients, and 37.5 % had a gap of more than 7 days.

In the present study, the mean hemoglobin level was 12.68 ± 1.47 gm/dL before the treatment and 9.9 ± 1.156 gm/dL after treatment. Before treatment, 84% of patients had hemoglobin in their normal limits (WHO grade 0), while after treatment, 52 and 24% of patients had grade I and II anemia, respectively. The difference was statistically significant ($p < 0.001$), but none of the patients showed grade III anemia. Higher anemia grade was not seen, possibly due to the simple reason patients were on daily oral iron therapy. Similar results were observed in the study by Bincy R *et al*.,[21] where 64% of the subjects were mildly anemic before and 3 weeks after chemotherapy. The mean hemoglobin level of the patients before and after 3 weeks of chemotherapy was 10.64 ± 1.88 gm/dL and 10.41 ± 1.89 gm/dL, which showed a significant decrease ($p < 0.01$).

Anemia is the most common hematological abnormality in cancer patients, though unfortunately, it is often unrecognized and untreated, which can affect their nutritional status. Judith *et al*.[19] investigated the effect of chemotherapy on various laboratory tests and found that hemoglobin decreased transiently at 5–8 weeks but remained within the reference limits. In our study also, we did not encounter any severe hemoglobin level toxicity of grade III or IV.

In some studies, TLC has been used as a parameter for nutritional assessment in cancer patients. No consistent association could be established between the two in cancer patients with fair performance status, but a decrease in TLC was noted in cancer patients with poor nutritional status. In such patients, a cut of the value of more than 1,800/mm^3 was taken as reference by Geirsdottir *et al*. in their study.[24] In our study before treatment, all the patients had TLC within normal limits (grade 0), though a decreasing trend was seen post-chemotherapy, which is a known side effect. We did not see any grade II–IV leucopenia toxicity, which may need any intervention of using any granulocyte colony-stimulating factors.

Skinfold Thickness and Body Fat Percent

Body fat percent was derived by the sum of four site skinfold thickness as appropriate for age and sex-based on the Durnin and Womersley equation. There was a statistically significant decrease in skinfold thickness before and after treatment (p-value < 0.0001) with a median decrease of 9.7 mm skinfold thickness. Similarly, statistically significant decrease (p-value < 0.0001) in body fat percent pre- and post-treatment was observed with mean loss of 3.56%. According to Bincy R,[21] the mean TSF before and after 3 weeks of chemotherapy was 14.54 ± 2.36 mm and 14.41 ± 2.38 mm, respectively. The 't' test showed a significant decrease in TSF [$t = 5.4$ ($p < 0.01$)] similar to our study.

Body Mass Index (BMI)

In our study, pre- and post-treatment mean BMI was 20.52 ± 4.06 and 17.825 ± 4.11 kg/m^2, respectively, and the change seen was statistically significant ($p < 0.00001$). Further, it was observed that 40% of patients who were underweight before treatment increased to 48% after treatment. This shows that majority of cancer patients were already nutritionally compromised at the start of treatment, which further worsened due to chemo-radiation. In a study by Righini,[17] overweight, not malnourished, and malnourished patients were 1.2, 50.3, and 48.5%, respectively. Another study by Bincy R[21] about changes in BMI during CRT, mean weight before initiation of the first cycle of chemotherapy, and after 3 weeks of chemotherapy were 55.96 ± 9.81 and 54.36 ± 9.96, respectively. Also, the mean BMI before and 3 weeks after chemotherapy was 23.17 ± 5.33 and 22.54 ± 5.42 kg/m^2, respectively. The t-test showed significant change, i.e., a decrease in weight after 3 weeks of chemotherapy [$t = 9.002$, $p < 0.01$]. In a study by Languis J E *et al*.,[22] before CRT, 16% of patients had a weight loss of more than 5%. During CRT, 87% of patients lost weight. Mean body weight decreased with 5.1 ± 4.8%, corresponding to 3.9 ± 3.7 kg.

Patient-generated Subjective Global Assessment (PG-SGA) Score

The PG-SGA score is used for individualized nutritional triage and intervention. The score of ≥ 9 indicates a critical need for symptoms management and parenteral nutritional option. The mean PG-SGA score assessed pre-treatment was 6.45 ± 4.53, and at the end of chemo-radiation was 8.79 ± 5.47. The mean score at the presentation itself falls in active nutritional intervention category (score 4–8), whilst after chemo-radiation, there is a sensitive worsening of nutritional status with a mean score close to 9 implying critical nutritional management in almost all patients. The nutritional deterioration assessed by the PG-SGA score is dynamic and extremely statistically significant at a 95% confidence interval (CI) with $p = 0.0002$, i.e., $p < 0.05$. The mean PG-SGA score at baseline was 6.4 ± 4.53 in our study, and a similar (6.4 ± 5.2) observation was reported by Isenring *et al*.[25] In our study using SGA classification, patients were classified as well-nourished (SGA A), moderately malnourished (SGA B), or severely malnourished (SGA C). PG-SGA class before treatment, 24% were well-nourished, 72% were

moderately nourished, and 4% were malnourished, and after treatment, 56% were malnourished, 38% moderately nourished. The change is statistically significant (p-value = 0.0251). In a study by Koom WS *et al*.,[26] 60.8% were well-nourished, 34.5% were moderately nourished, and 4.7% were malnourished.

Nutritional Risk Indicator (NRI)

The NRI is a nutrition risk index that makes it possible to classify patients according to a risk of morbidity and mortality often associated with malnutrition. The NRI is a more reliable prognostic indicator of morbidity and mortality in hospitalized patients than are indexes that use albumin or BMI alone. GNRI is a simple and accurate tool. A significant change was seen in the nutritional risk indicator before and after treatment (p-value < 0.0001) in terms were severely malnourished patients (40 vs. 50%).

Mid-arm Circumference (MAC)

In our study, 92% were malnourished before treatment and 98% after treatment. The change seen is statistically significant (p-value < 0.0001). Bincy R *et al*.[21] these anthropometric measurements also showed a decrease before and after the chemotherapy. The MAC before and after 3 weeks of chemotherapy was 27.46 ± 1.62 and 27.27 ± 1.61 cm, respectively. The 't' test showed a significant decrease in MAC measurement t = 6.86 (p < 0.01) before and after 3 weeks of chemotherapy. The mean mid-arm muscle circumference 22.90 ± 1.35 and 22.76 ± 1.33 cm, respectively, before and after 3 weeks of chemotherapy. The 't' test showed a decrease in MAMC, t = 5.83 (p < 0.01) before and after 3 weeks of chemotherapy.

Despite that, a substantial number of cancer patients were found to be malnourished at the start of treatment, which was successfully assessed by the PG-SGA tool along with BMI, 4-site skinfold thickness, and NRI. The nutritional status of cancer patients deteriorated further after chemo-radiation. It shows that chemo-radiation had a negative impact on the nutritional status of cancer patients. Malnutrition is of concern as it increases the risk of infections, treatment toxicity, and health-care costs and decreases response to treatment, quality of life (QoL), and life expectancy in cancer patients. In light of these possible complications, malnutrition represents a poor prognostic factor and, as such, should be prevented or detected as early as possible.

CONCLUSION

Patients should be initiated with nutritional management on presentation, prior to treatment, to avoid nutritional depletion. Moreover, appropriate nutrition support provided during radiotherapy can help to overcome some of the nutrition impact symptoms and help patients to maintain weight compared with the standard practice where patients continued to lose weight during radiotherapy treatment. An interdisciplinary approach that includes oncologists, nutritionists, nurses, dietitians, physical therapists, psychologists, etc., is necessary for patients who are experiencing loss of physiological or biological function, fatigue, malnutrition, psychological distress, and other symptoms as a result of cancer disease or its treatment.

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