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Pre - and Post - Chemoradiotherapy Nutritional Evaluation in Head and Neck Cancer Patients: A Comprehensive Analysis of Laboratory and Anthropometric Parameters

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Abstract: ***Objective: This study aimed to assess the nutritional status of head and neck cancer patients before and after chemoradiotherapy, utilizing a comprehensive evaluation of laboratory and anthropometric parameters. Methods: A cohort of 75 patients undergoing chemoradiotherapy for head and neck cancer were included in this prospective study. Laboratory parameters including hemoglobin levels, total leukocyte count (TLC), blood urea, serum creatinine, and serum bilirubin were measured before and after treatment. Anthropometric parameters, encompassing Body Mass Index (BMI), Skin Fold Thickness (SFT), % Body Fat, Mid - arm Circumference (MAC),* Patient - generated Subjective Global Assessment *(PG - SGA) Class, and Nutritional Risk Indicator (NRI), were also evaluated. Correlations between SFT and various factors were examined. Results: Significant alterations in laboratory parameters were observed post - treatment, with notable shifts in hemoglobin levels (p = 0.001), TLC (p = 0.021), and blood urea levels (p = 0.0003). However, serum creatinine and bilirubin levels exhibited no statistically significant changes. Among the anthropometric parameters, SFT demonstrated a substantial decrease post - treatment (p = 0.0001), while other metrics such as BMI, % Body Fat, MAC, PG - SGA Class, and NRI showed no significant variations. Conclusion: This study highlights the dynamic nature of nutritional markers in head and neck cancer patients undergoing chemoradiotherapy. While laboratory parameters such as hemoglobin, TLC, and blood urea showed substantial shifts, anthropometric measures displayed more nuanced changes. The correlation analysis indicated that age, sex, patient habits, socioeconomic status, lifestyle, dietary habits, nature of complaints, stage (AJCC), and duration of treatment did not significantly impact SFT before and after treatment. These findings underscore the importance of tailored nutritional interventions to address the diverse needs of this patient population, with potential implications for treatment outcomes and overall quality of life.***

Keywords: Nutritional assessment, head and neck cancers, anthropometric measurements, chemoradiotherapy, Head and neck cancer

1. Introduction

Head - and - Neck Cancer (HNC) encompasses a wide range of malignancies affecting various anatomical sites, many of which are considered relatively uncommon compared to other cancers. While there is no unanimous agreement on which sites fall under HNC, it generally includes areas like the lip, oral cavity, salivary glands, tonsils, oropharynx, nasopharynx, hypopharynx, nasal cavity, middle ear, paranasal sinuses, larynx, and thyroid. Globally, Head & Neck cancers are a significant concern, ranking as the 6th most prevalent cancer in 2012 [1]. There are approximately 560, 000 new cases and 300, 000 deaths attributed to head and neck cancer each year worldwide [2]. Additionally, incidence rates are over twice as high in men compared to women [3].

Cancer cachexia is a major factor leading to health complications and death in patients undergoing surgery, chemotherapy, or radiation therapy, either individually or in combination [4 - 7]. Among these, head and neck cancer patients are particularly susceptible to malnutrition, with over 80% experiencing significant weight loss during their treatment [6]. The link between malnutrition and weakened immune function in cancer patients is well - established [8]. In head and neck cancer patients, there are observed functional changes in various immune cells. These alterations may contribute to a diminished immune response against tumors. It is widely acknowledged that nutritional support, when used alongside cancer treatment, plays a crucial role in reducing treatment - related complications and aiding in immune recovery [9 - 17]. The recent emphasis on enhancing immune function in cancer patients through biologic response modifiers has sparked greater interest in cellular immunity within this patient population [21 - 23].

Head and neck cancer treatment options encompass surgery, radiotherapy, chemotherapy, or combinations thereof. The chosen approach depends on factors like cancer stage, location, and the patient's overall health. Treatment decisions consider cancer stage, location, type, patient's health, and daily functioning. Studies show that during radiotherapy or chemoradiotherapy, around 55% of patients may lose an

additional 10% or more of body weight [24, 25], which can lead to increased treatment - related side effects and potentially longer treatment duration, impacting outcomes [26, 27]. Nutritional counselling with or without supplements is currently considered appropriate for patients undergoing chemoradiotherapy for head and neck cancer [28], although its precise role in managing treatment - related side effects is still being clarified.

Cancer cachexia, characterized by progressive loss of lean tissue and body fat, often exceeds that explained by anorexia. It involves metabolic changes, including anaemia and altered lipid profile [29]. Head and neck cancer patients are at high risk for malnutrition, with over 80% experiencing significant weight loss during treatment. Nutritional status affects treatment outcomes.

Malnutrition screening is vital, and providing nutrition support during treatment is crucial. However, cancer cachexia is not always present in all malnourished patients, but all cachectic patients are malnourished [30, 31]. Malnutrition and cachexia have significant impacts on patient quality of life and prognosis [32]. They are associated with metabolic changes and alterations in metabolism of carbohydrates, lipids, and proteins. Nutritional intervention, including progressive resistance training, can have positive effects. Malnutrition can lead to treatment complications and increased mortality rates [33]. It affects physical function, quality of life, and treatment schedules. Identification and assessment of malnutrition are critical for patient care. Factors like body weight, BMI, and biochemical parameters help in assessing nutritional status. Subjective Global Assessment (SGA) is a reliable predictor. Patients who stabilize their weight tend to have longer survival and improved quality of life [34].
This study emphasizes the importance of nutrition assessment and intervention in cancer therapy. It aims to reduce complications, improve tolerance to treatment, and enhance patient well - being. It's important to select affordable, readily available, palatable, non - allergenic, and non - upsetting foods. Analysing data from rural cancer institutions is anticipated to benefit both the research group and the patients, potentially alleviating cancer - related suffering.

2. Aims and Objectives

Aim

- Evaluate nutritional changes pre and post chemoradiotherapy in head and neck cancer patients.

Objectives

- Assess anthropometric and laboratory parameters.
- Determine nutritional risk indicators.
- Conduct Patient - Generated Subjective Global Assessment.
- Analyze and compare nutritional status variations pre and post chemoradiotherapy.

3. Materials and Methods

Patient Selection: The study enrolled 75 treatment - naïve head and neck cancer patients over 18 years old from the Department of Radiation Oncology, Government Medical College Srinagar.

Inclusion Criteria: Confirmed histopathological/ cytological diagnosis of head and neck cancer.

Exclusion Criteria: Lack of informed consent, unconscious or bed - confined patients, pre - existing non - oncological conditions impacting nutritional status, and those previously treated for cancer.

Data was collected through face - to - face interviews and exams at the Radiation Oncology Outpatient Department. This included measuring height, weight, BMI, skinfold thickness, and mid - arm circumference. Grip strength was assessed with a dynamometer. Blood samples were taken for serum protein and albumin. Nutritional risk was evaluated using serum albumin and recent weight loss. The PG - SGA tool was used for a comprehensive nutritional assessment. Results were documented and statistically analyzed to derive relevant parameters for the variables of interest.

4. Results

The study comprised 75 patients aged 20 to 80 (median age 52 years). Predominantly male (82%), head and neck cancers were prevalent, likely linked to higher male smoking rates, consistent with prior research. Smoking (74%) and betel - nut use (10%) was common, posing risks for adverse outcomes. Dietary habits included non - vegetarian diets (98%) and vegetarian (2%).

Median Age	52 Years
SEX	
Male	62 (82%)
Female	13 (18%)
HABITS	
Smoker	56 (74%)
Betel - Nut	8 (10%)
None	11 (16%)
DIETARY HABITS	
Non - Vegetarian	74 (98%)
Vegetarian	1 (2%)

Symptoms like hoarseness of voice (70%), pain (37%), neck swelling (32%), difficulty in swallowing (18%) and ulcer (13%) were common. Tumor distribution included laryngeal (55%), nasopharyngeal (18%), hypopharngeal (14%), and oral cavity carcinomas (13%). Staging revealed 49% at stage III, 22% at stage IV, 17% at stage III and 12% at stage I.

The results revealed notable shifts in various laboratory parameters post - treatment. Hemoglobin levels showed a significant increase in Grade II anaemia cases after treatment compared to predominantly Grade I & 0 anaemia before ($p = 0.001$). A decrease in Total Leukocyte Count (TLC) above 4000 post - treatment was also significant ($p = 0.021$). Conversely, Blood Urea levels notably increased after treatment ($p = 0.0003$). However, Serum Creatinine and

Serum Bilirubin exhibited no significant changes before and after treatment (p = 0.05 and p = 1, respectively). In terms of anthropometric parameters, although BMI and % Body Fat remained stable, Skin Fold Thickness (SFT) above 30 significantly decreased post - treatment (p = 0.0001). Mid - arm Circumference (MAC) and Nutritional Risk Indicator (NRI) didn't exhibit significant changes before and after treatment (p = 0.105 and p = 0.319, respectively). The PG - SGA Class displayed a notable shift towards malnourishment post - treatment (p = 0.0001). Correlation analyses with SFT revealed no significant associations with various factors like age, sex, habits, site or stage of disease.

Symptoms	
Hoarseness Of Voice	70%
Neck Swelling	32%
Pain	37%
Difficulty in Swallowing	18%
Ulcer	13%
SITE (n=75)	
Larynx	55%
Nasopharynx	18%
Hypopharynx	14%
Oral Cavity	13%
Stage (n=75)	
I	12%
II	17%
III	49%
IV	22%

5. Discussion

HNSCC, ranked sixth globally in cancer incidence, significantly impacts nutritional status, affecting about 50% of patients, particularly worsened by chemoradiotherapy. Cancer alters digestion, causing symptoms like anorexia, nausea, and vomiting, hindering mechanical and chemical processes. This study involved 75 confirmed HNSCC patients undergoing radiotherapy with chemotherapy at Government Medical College, Srinagar. Data collection included anthropometric measures, haematological tests, and PG - SGA assessments.

The observations with respect to each point are being discussed as under:

Haematological profile

Haemoglobin: In our study, mean haemoglobin levels were 12.68±1.47 gm/dl pre - treatment and 9.9±1.156 post - treatment. Montoya et al. found mean haemoglobin to be 11.9±1.60 gm/dl in 88 chemotherapy - treated cancer patients. Before treatment, 84% had normal haemoglobin (WHO Grade 0). After treatment, 52% showed Grade I anaemia, and 24% had Grade II. No Grade III anaemia was observed. The difference was statistically significant (P=0.001). The trend towards improvement in severe haemoglobin toxicity may be attributed to daily oral iron therapy. Anaemia is common in head and neck cancer patients, influenced by various factors including comorbidities, chemotherapy, and malignancy - related chronic disease anaemia. It's associated with increased radioresistance due to heightened tumor hypoxia. Studies suggest anaemia correlates with inferior local - regional control and survival across various treatment modalities. The optimal time and threshold to assess anaemia's prognostic impact remain debated. R. Bincy et al. found 64% subjects mildly anaemic before and after chemotherapy. Anaemia is a prevalent, often untreated issue in cancer patients, affecting their nutritional status. Kallajavi et al. (2000) noted transient decreases in haemoglobin post - chemotherapy, remaining within reference limits, with no change in albumin.

	Before Treatment	After Treatment	P - value
ANAEMIA			
Grade I or 0 Grade II	73 2	57 18	0.001
TLC			
<4000 >4000	0 75	8 67	0.02
BLOOD UREA			
<41 41 – 100	63 12	38 37	0.0003
SERUM CREATININE			
<1.4 1.4 - 1.8	73 2	64 11	0.05
SERUM BILIRUBIN			
<1.2 1.2 – 1.6	69 6	69 6	1.0

Total leucocyte count: In some studies, TLC (Total Lymphocyte Count) has been considered for nutritional assessment in cancer patients. While no consistent association was found in patients with fair performance status, a decrease in TLC was observed in those with poor nutritional status, especially in advanced cancer. Geirsdottir et al. used a cut - off of over 1800/mm³ in their study. In our study, only patients undergoing radical treatment were included, excluding terminal or palliative cases. We observed a decreasing TLC trend post chemotherapy, a well - known chemotherapy - induced effect. Though there was a significant numerical decrease compared to baseline, 90% of patients still had TLC above 4000/mm³. The decrease was statistically significant (p=0.021). This highlights the need for multiple measurements in nutritional assessment, as emphasized in our study.

Blood urea and Serum creatinine: In our study, before treatment, 84% had blood urea levels ≤40 mg/dl, while after treatment, 50% had blood urea levels between 40 - 100. The change in blood urea levels is statistically significant (p=0.0003). Before treatment, 98% had serum creatinine within normal limits. After treatment, 12% showed elevated serum creatinine levels. The change in serum creatinine levels is approaching significance (p=0.05). In a study by David G. et al., 19% exhibited abnormal kidney function tests, with 3 patients experiencing grade 1 - 2 reactions and 1 having a grade 3 reaction. This is notable as the chemotherapy employed included cisplatin, which is excreted through the kidneys.

Serum bilirubin: There was minimal variation in serum bilirubin levels before and after treatment, with no statistically significant change (p value - 1.0).

Anthropometric parameters

Skinfold thickness and Body Fat %: Body Fat % was calculated using the Durnin & Wormersley equation based on a sum of 4 - site skinfold thickness appropriate for age and sex. There was a statistically significant decrease in skinfold thickness before and after treatment (p value - 0.0001), with a median of 30.99. While we observed a decrease in Body Fat % pre - and post - treatment, the mean loss was 3.56. However, this trend did not reach statistical significance (p=0.153). The short duration of treatment may have contributed to the lack of significant change in Body Fat %.

	Before Treatment	After Treatment	P - value
BMI			
<18.5 >18.5	30 45	44 31	0.718
SFT			
<30 >30	47 28	75 0	0.001
% OF BODY FAT			
<21 >21	72 3	75 0	0.153
MAC			
<13.5 >13.5	14 61	9 66	0.105
PG - SGA			
CLASS - A CLASS - B, C	63 12	33 42	0.0001
NRI			
SEVERE MILD To MODERATE	30 45	38 37	0.319

Body Mass Index (BMI): Head and Neck Cancers (HNC) are primarily linked to tobacco and its interaction with alcohol. However, around 75% of HNC cases involve tobacco and alcohol, suggesting other factors may contribute. Obesity has been suggested as a risk factor, particularly in individuals who have never smoked. In our study, the average BMI before treatment was 20.52±4.06 kg/m2. After treatment, it decreased to 17.825±4.11 kg/m2, resulting in a mean weight loss of - 2.07 kgs. Initially, 40% of patients were underweight based on BMI, which increased to 48% after treatment. This change was not statistically significant (p=0.718). This highlights that a significant number of cancer patients were already nutritionally compromised at the start of treatment, and this worsened due to chemo - radiation. Other studies have also shown that BMI can identify both excess and deficit nutrition.

PG - SGA Score: Our study illustrated the PG - SGA scores, a tool used for personalized nutrition assessment and intervention. A score of ≥ 9 indicates a critical need for symptom management and potential parenteral nutrition. The mean PG - SGA score before treatment was 6.45±4.53, while after chemo - radiation, it increased to 8.79±5.47, signifying a sensitive decline in nutritional status, warranting critical nutritional management for almost all patients. This deterioration, assessed by PG - SGA Score, is dynamic and highly statistically significant at a 95% Confidence Interval (CI) with p=0.0002 (p<0.05). Our baseline mean PG - SGA score of 6.4±4.53 aligns closely with the observation reported by Isenring et al. (6.4±5.2).

SGA classification: Using the SGA Classification in our study, patients were categorized as well - nourished (SGA - A), moderately malnourished (SGA - B), or severely malnourished (SGA - C). Before treatment, 24% were well - nourished, 72% were moderately nourished, and 4% were malnourished. After treatment, 56% were malnourished, and 38% were moderately nourished. This change is statistically significant (p - value: 0.0001). Chemo - radiation led to a statistically significant decline in the nutritional status of cancer patients (p - value: 0.048). Bauer et al. (2002) also found a significant correlation in SGA classes, but their study included more elderly patients. Montoya et al. reported that 47.7% (40/88) of cancer patients suffered from malnutrition (SGA - B&C). The prevalence of baseline malnutrition was reported at 35% (21/60) by Isenring et al. in a study of cancer patients receiving radiotherapy to the head & neck and abdominopelvic region. Bauer et al. found a prevalence of malnutrition in 76% (54/71) cancer patients according to SGA classification. Koom et al. reported a prevalence of malnutrition of 39.2% in a radiation oncology department as assessed by SGA classification. Gupta et al. (2008) reported a prevalence of malnutrition of 50% (66/132) in cancer patients according to SGA classification. D Gupta et al. found a prevalence of malnutrition in 52% (113/217) cancer patients according to PG - SGA classification in a different study of colorectal cancers.

Nutritional risk indicator: Before treatment, 40% of patients were severely malnourished, while 44% had moderate malnourishment. After treatment, 50% were severely malnourished. However, this change was not statistically significant (p value – 0.319). The Nutritional Risk Indicator (NRI) is a valuable tool for classifying patients based on the risk of morbidity and mortality associated with malnutrition. It is considered a more reliable prognostic indicator in hospitalized patients compared to indexes that rely on albumin or BMI alone. The GNRI (Geriatric Nutritional Risk Index) is another straightforward and accurate assessment tool for nutritional status.

Mid - arm circumference: There was no significant variation in mid - arm circumference before and after treatment (p value - 1.0). In a study by R. Bincy et al., similar anthropometric measurements showed a decrease before and after chemotherapy. The mean triceps skinfold thickness (TSF) was 14.54±2.36 mm before chemotherapy and 14.41±2.38 mm after 3 weeks of chemotherapy. The mid - arm circumference (MAC) was 27.46±1.62 cm before chemotherapy and 27.27±1.61 cm after 3 weeks of chemotherapy. The't' test indicated a significant decrease in TSF and MAC measurements, with t values of 5.4 (p<0.01) and 6.86 (p<0.01) before and after 3 weeks of chemotherapy, respectively.

Changes in nutritional status after chemo - radiation

In our study, the mean PG - SGA score indicated a need for active nutritional intervention both before and after chemo - radiation, with the score approaching 9 after treatment, signifying critical nutritional management for almost all patients. Based on PG - SGA categorization, 84% of patients (63 out of 75) required active intervention at baseline, which increased to 88% (66 out of 75) after chemo - radiation. According to SGA, the prevalence of malnutrition was 84%

at baseline and 88% after treatment, showing a significant deterioration in nutritional status (SGA value = 3.92, P = 0.048). This decline was also observed in both PG - SGA Score (P < 0.001) and SGA class (P < 0.001) after 4 weeks of radiation therapy, aligning with findings from Isenring et al. However, our study reported lower rates of nutritional deterioration (15%) compared to Isenring's study (33%), despite a higher baseline malnutrition rate.

6. Conclusion

This study delves into the nutritional status of Head and Neck Cancer patients during chemoradiotherapy. Among 75 patients, mostly male and from lower income groups, smoking history was common. Laryngeal cancer was prevalent. After treatment, malnutrition increased according to various measures: PG - SGA Score (84% to 88%), SGA Class (76% to 94%), BMI (40% to 48%), skin fold thickness (62% to 100%), Body Fat % (96% to 100%), NRI (40% to 50%), and mid - arm circumference (18% to 12%). Hemoglobin and leukocyte counts also changed post - treatment. The study highlights the link between SGA Class and skin fold thickness, stressing the need for nutritional assessment during radical chemo - radiotherapy. Despite a decent starting point, many patients faced malnutrition, impacting their treatment and health. Using PG - SGA alongside other assessments is recommended for similar cases, with a call for larger studies for validation.

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