Original Research Article

Assessment of Nutritional Status of Locally Advanced Head and Neck Carcinoma Patients Treated With Concomitant Chemo-radiation, using Body Mass Index (BMI)

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Abstract
Background: The aim of present study was to assess the change in nutritional status of locally advanced head and neck carcinoma patients (LAHNC), who were treated by concomitant chemo-radiation, using Body Mass Index (BMI) and the nutritional status was correlated with local control of disease and the side effects of treatment.

Methods: The present study was conducted in 60 previously untreated, histopathologically proven locally advanced head and neck cancer patients who received conventional radical external beam radiation therapy (66Gy / 33 fractions over 6.3 weeks / 2 Gy per fraction) concomitant with Inj.Cisplatin 75mg/m², 3 weekly. Nutritional status of patients was performed at time of presentation, at the end of treatment and three months after completion of treatment by using Body Mass Index (BMI).

Result: Thirty five percent patients were mild/moderate underweight and none were severely underweight (BMI 16) before starting treatment. At the end of treatment, 28.33% of patients were mild/moderate underweight (BMI 16.0-18.49) and 33.33% were severely underweight (BMI <16). Approximately forty one percent of patients were mild/moderate underweight and 21.67% of patients were severely underweight at third month of follow up. Grade 3 acute skin radiation reactions were seen in 38.10% mild/moderate underweight patients and 42.87% of obese patients (p value-0.001). Grade 3 acute mucosal radiation reactions were seen in 42.86% mild/moderate underweight patients and 57.14% of patients of obese patients. Complete response was seen in 85.71% mild/moderate underweight patients and 57.14% of patients of obese patients. No evidence of disease was seen in 80.96% mild/moderate underweight patients at third month of follow up.

Conclusion: The current study concludes that prevalence of underweight patients increases shortly after concomitant chemo-radiation in locally advanced head and neck cancer patients. Subsequently, prevalence of underweight patients substantially decreases during the first three months after treatment.

Keywords: Cancer, head and neck, concomitant chemo-radiation, body mass index, nutrition assessment.

Introduction
Head and neck cancers such as carcinomas involving oral cavity, Pharynx, Larynx and paranasal sinuses are very common in India. Among head and neck cancer patients at time of diagnosis, approximately 35% to 60% patients are...
malnourished\textsuperscript{[1]}. This malnutrition seems to increase to 44-88% due to chemoradiation induced toxicity such as dysphagia, mucositis, dryness of mouth and nausea/vomiting\textsuperscript{[2]}. Prevalence of malnutrition was significantly higher during first three months following treatment than in comparison to prevalence of malnutrition before the start of treatment then it gradually decline in the period>3 months following treatment\textsuperscript{[3]}. Malnutrition greatly affects treatment outcome in cancer patients so it has become essential to take nutritional status into account in the patient’s management\textsuperscript{[4]}. Nutrition status of cancer patients can be assessed by objective and subjective methods. Objective nutrition methods includes anthropometric [BMI], biochemical and immunological. Body mass index (BMI) is informative for nutritional assessment of a cancer patient in clinical practice as an indicator of malnutrition\textsuperscript{[5]}. Body mass index (BMI) is an independent prognostic factor for overall survival in patients receiving Radiotherapy or Concomitant chemo-radiotherapy\textsuperscript{[1]}. At the time of diagnosis in head and neck cancer patients, body mass index was independent predictors for malnutrition\textsuperscript{[6]}. The present study was planned to assesses the nutritional status of locally advanced head and neck carcinoma patients (LAHNC) treated with concomitant chemo-radiation by using Body Mass Index (BMI) and then nutritional status of patients is correlated with local control of disease and side effect of treatment.

Material and Methods
The study was conducted on 60 previously untreated, histopathologically proven squamous cell carcinoma of head and neck patients. The patients were staged according to American Joint Committee on Cancer 2010 staging system. Sixty patients of locally advanced head and neck carcinoma received conventional radical external beam radiation therapy (66 Gy / 33 fractions over 6.3 weeks / 2 Gy per fraction) concomitant with Inj. Cisplatin 75mg/m\textsuperscript{2}, 3 weekly. The patients were assessed for nutritional status at time of presentation, at the end of treatment and three months after completion of treatment. The nutritional status of patients were assessed using Body Mass Index (BMI).

Anthropometric assessment was done by Body mass index of the subjects by dividing body weight(in kg) by square of height(in meter) (weight/height\textsuperscript{2}). Based on Indian guidelines patients were classified as underweight (BMI<18.5), mild/moderately underweight (BMI 16.0-18.49), severely underweight (BMI <16), normal weight (BMI between 18.5 - 22.9), overweight (BMI between 23-24.9), obese (BMI more than 25).

Statistical analysis
Data was entered in Microsoft excel spread sheet and checked for errors. Data was analysed using SPSS for Windows version 16.0. Z-test for proportions was used to evaluate difference in 2 proportions. Chi-square test was used to see association of qualitative data. Point of statistical significance was taken when p<0.05.

Results and Discussion
Patient’s Characteristics
In this study most of the patients were males (95%), approximately 68.33% of the patients were in the age group of 41-60 years who were mainly from the rural areas (85%) and most of them were smokers (96.67%) and alcoholics (73.33%). Most of the patients were presented with chief complaints of pain throat and difficulty in swallowing. Ulcero-proliferative growth was more common (86.67%) and moderately differentiated squamous cell carcinomas (95%) was the most common histology. Oropharynx (66.67%) including base of tongue, tonsils, soft palate was the most common site in all patients with majority of patients having T3 tumour status (88.33%). Sixty five percent of patients have stage III disease.
Nutritional Status by Body Mass Index before Start of Treatment

Figure-1 shows pre-treatment BMI of all 60 patients. Based on Indian guideline of BMI, out of sixty patients, 35% were mild/moderate underweight (BMI 16.0-18.49), 41.66% were normal weight (BMI 18.5-22.9), 11.67% were overweight (BMI 23-24.9) & 11.67% were obese (BMI more than 25).

Similar pattern was observed in study by Singh et al whereas Chatterjee et al observed that as many as sixty percent of patients were under weight in head and neck cancer patients[7,8].

Correlation between Body Mass Index and Acute Skin Radiation Toxicity

Figure-2 shows correlation between Body Mass Index (BMI) with acute skin toxicity noted during 6th week of treatment. Grade 2 acute skin reactions were seen in 61.9% patients with BMI 16-18.49, 76% patients with BMI 18.5-22.9, 100% patients with BMI 23-24.9 and 57.14% patients with BMI >25. The difference was statistically significant (P value - 0.001). Grade 3 acute skin reactions were seen in 38.10% patients with BMI 16-18.49, 24% patients with BMI 18.5-22.9 and 42.87% patients with BMI>25. The difference was statistically significant (P value - 0.001).

Meyer et al in their study observed that 27.3% grade 3 and grade 4 acute radiation toxicity in head and neck cancer patients with BMI>25 and 17.5% in patients with BMI≤25[9].

Correlation between BMI and Acute Mucosal Radiation Toxicity

Figure – 3 shows correlation between Body Mass Index (BMI) and acute mucosal toxicity noted during 6th week of treatment. Grade 2 acute mucosal reactions were seen in 57.14% patients with BMI 16-18.49, 80% patients with BMI 18.5-22.9, 57.14% patients with BMI 23-24.9 and 42.86% patients with BMI >25. The difference is not statistically significant (p value-0.240).

Grade 3 acute mucosal reactions were seen in 42.86% patients with BMI 16-18.49, 20% patients with BMI 18.5-22.9, 42.86% patients with BMI 23-24.9 and 57.14% patients with BMI >25. The difference is not statistically significant (p value-0.240).

Gorence et al in their study observed that malnutrition was more frequently associated with severe RT induced toxicities in head and neck cancer patient[2].

Jain et al in their study reported that overweight (BMI ≥25) patients had significantly lower rates mucositis in head and neck cancer patients during concomitant chemoradiation[10].

Egestad et al observed in their study that head and neck cancer patients with BMI ≥ 25 had less mucosal changes after 2 weeks of radiation treatment than patients with BMI < 25[11].

Nutritional Status by Body Mass Index at End of Treatment

Based on Indian guideline of BMI, out of sixty patients, 28.33% were mild/moderate underweight (BMI 16.0-18.49), 33.33% were severely underweight (BMI <16), 28.33% were normal weight (BMI between18.5-22.9), 8.33% were overweight (BMI between 23-24.9) & 1.67% were obese (BMI more than 25) at end of treatment. BMI of all 60 patients is detailed in figure -4.

Similar pattern of nutrition post treatment was observed in studies by Singh et al and Chatterjee et al [7,8].

Correlation between Body Mass Index and Disease Control at the end of treatment

Figure-5 shows Correlation between Body Mass Index(BMI) with local control of disease at the end of treatment. Complete response was seen in 85.8% of patients with mild/moderate underweight (BMI 16-18.49), 76% of patients of normal weight patients (BMI 18.5-22.9), 85.7% patients with overweight (BMI 23-24.9) and 100% of patients who were obese (BMI >25). The difference are statistically not significant.

Jain et al in their study observed that pre-treatment BMI > 25 have a significantly better prognosis than patients with BMI < 25 in head and neck cancer cases treated by concomitant chemoradiation[10].
Huang et al in their study found that BMI was not associated with locoregional failure free survival (LR-FFS) in head and neck cancer patients\[12\].

**Nutritional Status by Body Mass Index (BMI) At 3rd Month of Follow Up**

Figure-6 shows BMI of all 60 patients at 3rd month of follow up. Based on Indian guideline of BMI, out of sixty patients, 41.67% were mild/moderate underweight (BMI 16.0-18.49), 21.66% were severely underweight (BMI <16), 28.34% were normal weight (BMI between18.5-22.9) & 8.33% were overweight (BMI between23-24.9).

Similar trend was observed by Jager-Wittenaar et al\[3\].

**Correlation between Body Mass Index and Disease Control at 3rd Month of Follow Up**

Figure – 7 show correlation between Body Mass Index (BMI) with local control of disease at 3rd month follow up. No evidence of disease was seen in 80.95% of patients with mild/moderate underweight (BMI 16-18.49), 72% of patients of normal weight (BMI 18.5-22.9), 85.7% patients with overweight (BMI 23-24.9) and 100% of patients who were obese (BMI >25). The difference is not statistically significant.

Jain et al in their study observed that patients with BMI > 25 had significantly better overall survival outcomes than patients with BMI<25 head and neck cancer cases who received concomitant chemoradiation\[10\].

Takenaka et al in their study observed that 5year overall survival of head and neck cancer patients receiving Concurrent chemo-radiation were 67.2% for the overweight group, 59.9% for the normal weight group, and 27.1% for the underweight group\[13\].

Hu et al in their study found that overweight and obese head and neck cancer patients had a significantly higher overall Survival rate than normal weight patients\[14\].

Huang et al in their study reported that obese patients had a worse overall survival than overweight patients\[12\].

Arthur et al in their study found that overweight and obese HNSCC patients had a significantly better overall survival than patients in lower BMI categories\[15\].
Figure 2-Correlation between BMI and Acute skin toxicity

| Body Mass Index(BMI)               | % of patients | Grade 1 | Grade 2 | Grade 3 |
|------------------------------------|--------------|---------|---------|---------|
| Severe underweight (<16)           | 61.9         | 38.1    | 24      | 0       |
| Mild/moderate underweight (16-18.49) | 76           | 42.86   | 20      | 0       |
| Normal weight (18.5-22.9)          | 100          | 57.14   | 42.86   | 0       |
| Overweight (23-24.9)               | 100          |         |         |         |
| Obese (>25)                        | 57.14        |         |         |         |

Figure 3-Correlation between BMI and Acute mucosal toxicity

| Body Mass Index(BMI)               | % of patients | Grade 1 | Grade 2 | Grade 3 |
|------------------------------------|--------------|---------|---------|---------|
| Severe underweight (<16)           | 57.14        | 42.86   | 20      | 0       |
| Mild/moderate underweight (16-18.49) | 57.14        | 42.86   | 20      | 0       |
| Normal weight (18.5-22.9)          | 80           | 42.86   | 20      | 0       |
| Overweight (23-24.9)               | 57.14        | 42.86   | 20      | 0       |
| Obese (>25)                        | 57.14        | 42.86   | 20      | 0       |
Figure 4 - BMI at end of treatment

Figure 5 - Correlation between BMI and disease control at end of treatment

Body Mass Index (BMI)

% of patients

| BMI Category       | % of Patients |
|--------------------|--------------|
| Severely underweight | (<16)        |
| Mild/moderate underweight | (16-18.49)  |
| Normal weight      | (18.5-22.9)  |
| Overweight         | (23-24.9)    |
| Obese              | (>25)        |

% of patients

| BMI Category       | % of Patients |
|--------------------|--------------|
| Severely underweight | (<16)        |
| Mild/moderate underweight | (16-18.49)  |
| Normal weight      | (18.5-22.9)  |
| Overweight         | (23-24.9)    |
| Obese              | (>25)        |

% of patients

| Disease Control          | % of Patients |
|--------------------------|--------------|
| Complete response        | 85.8         |
| Partial response         | 76           |
| No response              | 16           |
| Progressive disease      | 0            |

% of patients

| Disease Control          | % of Patients |
|--------------------------|--------------|
| Complete response        | 85.7         |
| Partial response         | 14.3         |
| No response              | 0            |
| Progressive disease      | 0            |

% of patients

| BMI Category       | % of Patients |
|--------------------|--------------|
| Severely underweight | (<16)        |
| Mild/moderate underweight | (16-18.49)  |
| Normal weight      | (18.5-22.9)  |
| Overweight         | (23-24.9)    |
| Obese              | (>25)        |
Conclusion
The current study concludes that prevalence of underweight patients increases shortly after concomitant chemo-radiation in locally advanced head and neck cancer patients. Subsequently, prevalence of underweight patients substantially decreases during the first three months after treatment.

Acknowledgement
There was no source of financial grant or other funding. The contribution of colleagues or institutions is highly acknowledged.
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