

## Abstract

**Background:** In developing countries, HNSCC differs from Western world in terms of age at presentation, subsite of disease, etiology (more tobacco and alcohol related), higher malnutrition and molecular biology. Certain special challenges are faced by developing countries like illiteracy, poverty, lack of awareness, advanced stage of cancer, limited access to specialized health care, and limited treatment infrastructure create difficulties in management of cancer patients. To improve the survival in clinical practice, simple and low cost indices predicting a raised risk for poor clinical outcome, in terms of recurrent disease, distant metastasis or mortality, are required in HNSCC patients. There is need for a low cost model to predict prognosis in Indian patients, specially tailored to the needs of a lower-middle-income country.

### **Aims and Objectives:**

- i. To study the nutritional profile and systemic immunity in patients with HNSCC.
- ii. To study the correlation between the nutritional status and systemic immunity with outcome of treatment in patients being treated for HNSCC.
- iii. To develop a low cost model for early prognosis using nutritional status and systemic immunity marker in patients being treated for HNSCC.

**Materials and Methods:** This was a prospective cohort study, conducted at Cancer Research Institute, Swami Rama Himalayan University, Dehradun. The patients starting treatment for HNSCC were enrolled in the study after a written informed consent, they were evaluated for nutrition status (using anthropometric methods and Subjective Global Assessment score) and systemic immunity (using peripheral blood neutrophil/lymphocyte ratio), before starting, during, and at completion of planned treatment. The disease status and overall survival were assessed upto 6 months of completion of planned treatment. The primary end points of the study were Nutritional status and Systemic Immunity before and

after treatment, and disease status and overall survival at 6 months of completion of treatment.

Statistical Analysis: MS Excel 2010 was used for data entry, SPSS software version 22 was used for statistical analysis. Parametric and non-parametric tests were used for association and correlation analysis. "Cochran's and Mantel-Haenszel Statistic" were used to calculate Risk Ratio (RR). Multivariate analysis was performed using the Multi-nominal Logistic Regression model. ROCs were generated to get cut-off values and their sensitivity and specificity to predict the outcome. Survival curves were generated using Kaplan-Meier method and Cox-Regression model, and were used to calculate the Hazard Ratio (HR) for outcomes i.e., the Progression Free Survival (PFS) and Overall Survival (OS). Using the RR and ROC cut-off values of variables that were significantly associated with the outcome, novel Risk Stratification models were developed to predict outcomes- failure to complete planned treatment, disease recurrence 6months and death at 6 months.

**Results:** Malnutrition (defined as either  $\geq 10\%$  weight loss or BMI  $< 18.5$ , or SGA score  $\geq 40$ ) was found in 47.1% patients pre-treatment and this proportion increased to 87.6% patients post-treatment. The median neutrophil tolymphocyteratio (NLR) IQR was 3 (2-4) pre-treatment and increased to 5 (3.8-8.4) post-treatment. There was statistically significant moderate positive correlation between NLR and SGA score, pre-treatment percent weight loss and a moderate negative correlation between NLR, weight and BMI. Malnutrition was significantly associated with failure to complete planned treatment in node positive patients and raised NLR in node negative patients. On multivariate analysis, Cox-Regression and Survival Analysis with Kaplan-Meier curves, both poor nutritional status and raised NLR, were associated with poor six months progression free and overall survival.

**Conclusion:** The  $H_0$  hypothesis (there is no correlation between nutritional status and systemic immunity in patients with Head and Neck Squamous Cell Carcinoma) is rejected and the alternate  $H_1$  hypothesis (there is a positive correlation between nutritional status and systemic immunity in patients with Head and Neck Squamous Cell Carcinoma) is accepted.

The novel low cost risk stratification models, developed in this study using clinical parameters, nutritional status and the NLR were successfully tested for internal validation as predictive for poor clinical response (failure to complete planned treatment, early disease recurrence and mortality) in patients being treated for HNSCC.

**Clinical Recommendations:**

- i. Apart from the regular clinical and disease parameters (like PS, clinical stage, pathological features, subsite etc.) patients' baseline nutritional status and systemic immunity marker, NLR, should be taken into account while planning the oncological management for HNSCC patients.
- ii. A patient with malnutrition at the start of oncological treatment for HNSCC should be offered structured nutritional advice and regular nutritional monitoring during the ongoing active treatment to improve clinical outcomes of these patients.
- iii. Systemic immunity marker, NLR, as calculated from the peripheral blood sample, is a cost effective and easily available tool and should be utilized routinely to prognosticate HNSCC patients planned for treatment into high risk groups for poor clinical outcomes.
- iv. The novel low cost risk stratification models developed in this study were validated internally to prognosticate patients as low, medium, and high risk, for poor clinical outcomes, and now need to be validated externally on different HNSCC patient populations by other researchers.

**Keywords:**

Head and Neck Cancer, Systemic Immunity, Nutrition, SGA scale, Neutrophil/Lymphocyte ratio, Prospective study