

A Study on Clinical Characteristics of Locally Advanced HNSCC Patients

Dr. Rumana Afroz Majumder^{1*}, Dr. Khandaker Md. Rezwan Bayzid², Dr. Afsana Sharmin Anika³

¹Associate Consultant, Clinical Oncology, Labaid Cancer Hospital & Super Specialty Centre, Dhaka, Bangladesh

²MD, Clinical Oncology, Specialist Clinical and Radiation Oncology, Labaid Cancer Hospital and Super Specialty Center, Dhaka, Bangladesh

³Specialist, Labaid Cancer Hospital and Super Specialty Center, Dhaka, Bangladesh

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*Corresponding author: Dr. Rumana Afroz Majumder

Associate Consultant, Clinical Oncology, Labaid Cancer Hospital & Super Specialty Centre, Dhaka, Bangladesh

Abstract

Background: Head and Neck Squamous Cell Carcinoma (HNSCC) is a heterogeneous group of malignancies arising from the mucosal linings of the oral cavity, pharynx, and larynx. Locally advanced HNSCC (LA-HNSCC), encompassing stages III and IV, involves large tumors and regional lymph node metastases without distant spread, contributing to high morbidity and mortality. Understanding the clinical features of LA-HNSCC is crucial for improving treatment strategies and patient outcomes. **Objective:** To evaluate the clinical characteristics of patients with LA-HNSCC and their impact on treatment outcomes, specifically comparing the TPLF and LFP regimens. **Methods:** An experimental study was conducted at Khwaja Yunus Ali Medical College & Hospital from January to December 2015, involving 60 patients with LA-HNSCC. Patients were treated with neoadjuvant chemotherapy (TPLF or LFP regimens) followed by concurrent chemoradiation. Data was collected through patient interviews, clinical evaluations, and laboratory tests. The primary outcome measures were tumor regression, clinical response, and acute toxicities. Statistical analysis was performed using SPSS, with significance set at $p < 0.05$. **Results:** The majority of patients were male (80% in Arm A and 77% in Arm B) and over 50 years old. Smoking prevalence was high (83.3% in Arm A and 80% in Arm B). The most common primary tumor sites were the oral cavity (Arm A: 30%, Arm B: 33.3%) and oropharynx (Arm A: 23.3%, Arm B: 26.7%). Neck node swelling, pain, dysphagia, and weight loss were the most frequent clinical complaints. No statistically significant differences were found between the two treatment arms in terms of age, smoking, occupation, ECOG performance status, or histological grading. **Conclusion:** Both TPLF and LFP regimens provided similar outcomes in terms of clinical characteristics and treatment response in patients with LA-HNSCC. These results suggest that the choice between TPLF and LFP regimens may not significantly influence treatment outcomes. Further research is needed to explore additional factors affecting treatment efficacy and refine therapeutic strategies for LA-HNSCC.

Keywords: Locally advanced head and neck squamous cell carcinoma, TPLF regimen, LFP regimen.

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INTRODUCTION

Head and Neck Squamous Cell Carcinoma (HNSCC) is a heterogeneous group of malignancies that arise in the mucosal linings of the oral cavity, pharynx, and larynx. Locally advanced HNSCC (LA-HNSCC) refers to stages III and IV disease, which often involve large primary tumors, regional lymph node metastases, or both, without distant metastasis. These tumors represent a significant proportion of HNSCC cases and are associated with considerable morbidity and mortality [1-3].

Understanding the clinical characteristics of LA-HNSCC is crucial for tailoring treatment approaches

and improving patient outcomes. These characteristics include demographic factors such as age, gender, and geographic distribution, as well as risk factors like tobacco and alcohol use, human papillomavirus (HPV) infection, and betel nut chewing in specific populations. Clinically, LA-HNSCC is marked by aggressive local invasion, frequent lymphatic spread, and a high likelihood of treatment-related complications [4-7].

The prognosis of LA-HNSCC remains challenging despite advancements in multimodal therapies, including surgery, radiation therapy, and systemic treatments such as chemotherapy and immunotherapy. Therefore, identifying and analyzing the clinical features of patients with LA-HNSCC can

provide valuable insights into disease progression, treatment response, and survival outcomes. This understanding is essential to optimize therapeutic strategies and enhance the quality of life for affected individuals.

Objective

To evaluate the clinical characteristics and their impact on treatment outcomes in patients with locally advanced head and neck squamous cell carcinoma (LA-HNSCC).

METHODOLOGY

Study Design and Duration: This was an experimental study conducted from January 2015 to December 2015 at Khwaja Yunus Ali Medical College & Hospital, Enayetpur, Sirajgonj.

Study Population: The study involved patients diagnosed with locally advanced squamous cell carcinoma of the head and neck, who were treated with either neoadjuvant chemotherapy (TPLF or LFP) followed by concurrent chemoradiation.

Sample Size Calculation: The sample size was determined using the following formula:

$p1 = 50\%$ (proportion of patients developing the outcome in one arm),

$p2 = 80\%$ (proportion of patients developing the outcome in another arm),

$z\alpha = 1.96$ (Z value for 5% significance level),

$z\beta = 1.64$ (Z value for 95% power).

Taking a 10% allowance for loss to follow-up, the final sample size was calculated to be 66. A total of 60 patients were ultimately selected, with 30 patients in each arm.

Selection Criteria:

Inclusion criteria were as follows:

- Patients with locally advanced head and neck carcinoma (stage III or IV without distant metastasis),
- Age between 18 to 70 years,
- ECOG performance status up to grade 2,
- Adequate laboratory values, including hemoglobin >10 gm/dl, WBC count ≥ 4000 cells/cmm, platelet count $\geq 100,000$ cells/cmm, and other criteria as detailed.

Exclusion criteria included:

- Distant metastasis,
- Other cancer types,
- History of prior chemotherapy or radiotherapy to the head and neck region,
- Serious medical illnesses, pregnancy or lactation, and uncontrolled infections.

Sampling Method: Purposive sampling was used to select patients who met the inclusion and exclusion

criteria, with informed written consent obtained from each participant.

Data Collection Instruments and Procedures: Data was collected over the course of one year using a semi-structured questionnaire, patient interviews, and hospital records. The data collection involved detailed histories, clinical examinations, and laboratory tests.

Main Outcome Variables: The study focused on tumor regression, short-term clinical response, and acute toxicities in patients diagnosed with locally advanced head and neck squamous cell carcinoma.

Pretreatment Evaluation: Patients underwent complete history-taking, physical examination, and laboratory tests, including complete blood count, liver and kidney function tests, ECG, and imaging studies (X-ray, CT scan, MRI, USG). Biopsy and fine needle aspiration cytology were also performed for diagnosis.

Treatment Plan: Neoadjuvant chemotherapy was administered with a TPLF regimen (Arm A) or LFP regimen (Arm B), followed by concurrent chemoradiation. The chemotherapy regimen involved docetaxel, cisplatin, leucovorin, and 5-FU, with cycles repeated every three weeks for a total of three cycles. Radiotherapy was administered using 3D CRT with a total dose of 66 Gy in 33 fractions. Concurrent chemoradiation involved weekly cisplatin injections.

Follow-up and Assessment: Patients were monitored regularly during and after treatment for tumor response, toxicities, and clinical evaluation. Treatment response was assessed using RECIST 1.0 criteria, while toxicities were recorded according to RTOG and CTCAE guidelines.

Ethical Considerations: Ethical approval was obtained from the institutional review board. Informed consent was obtained from each patient after explaining the study procedures, risks, and benefits in the local language.

Data Analysis: data were compared using Chi-square and Fisher's Exact tests. A p-value of <0.05 was considered statistically significant.

RESULTS

The cross-tabulation of patients by age group is shown in the above table. The majority of patients in both arms were over 50 years old (Arm A: 50%; Arm B: 56.7%). In the 41–50 age group, there were seven patients (23.3%) in Arm A and eight patients (26.7%) in Arm B. The smallest number of patients in both arms were aged ≤ 40 years. However, these differences were not statistically significant ($p > 0.05$).

Table 1: Age group distribution of the patients (n=60)

Age group (years)	Category of treatment		Fisher's Exact Test	p-value
	TPLF regimen (Arm A)	LFP regimen (Arm B)		
30-40	02 (6.7)	01 (3.3)	0.814	0.541
41-50	07 (23.3)	08 (26.7)		
51-60	15 (50.0)	17 (56.7)		
61-70	06 (20.0)	04 (13.3)		
Total	30 (100.0)	30 (100.0)		

Thirty patients with locally advanced head and neck squamous cell carcinoma were included in Arm A of the study, representing the TPLF regimen group.

These patients were categorized by gender, with 24 (80%) being male and 6 (20%) being female.

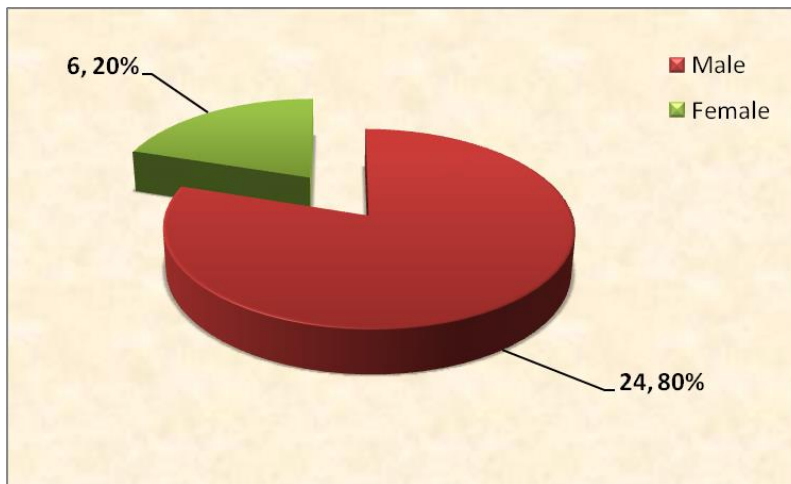


Figure 1: Pie chart showing sex distribution of Arm A (TPLF regimen)

Thirty patients with locally advanced head and neck squamous cell carcinoma were included in Arm B of the study, representing the LFP regimen group.

Among them, 23 (77%) were male, while 7 (23%) were female.

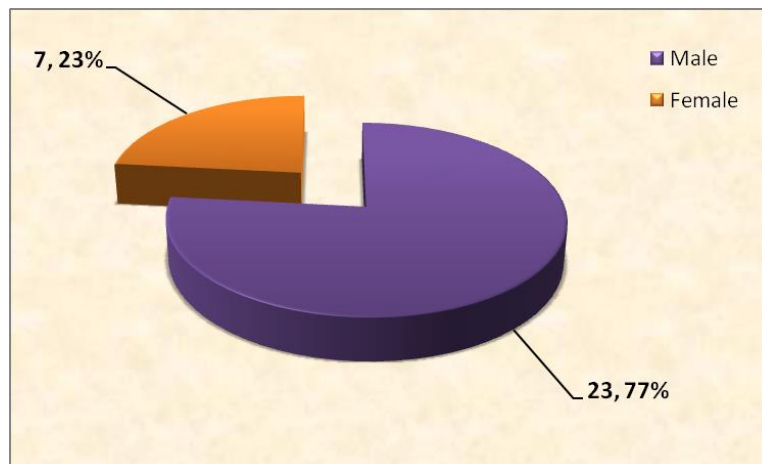


Figure 2: Pie chart showing sex distribution of Arm B (LFP regimen)

The majority of patients in both arms were farmers (36.7% in Arm A (TPLF regimen) and 33.3% in Arm B (LFP regimen)), followed by service holders (23.3% in Arm A and 26.7% in Arm B). Additionally,

six patients (20%) in Arm A and seven patients (23.3%) in Arm B were engaged in business. No statistically significant differences in occupation were observed between the two groups ($p = 1.00$).

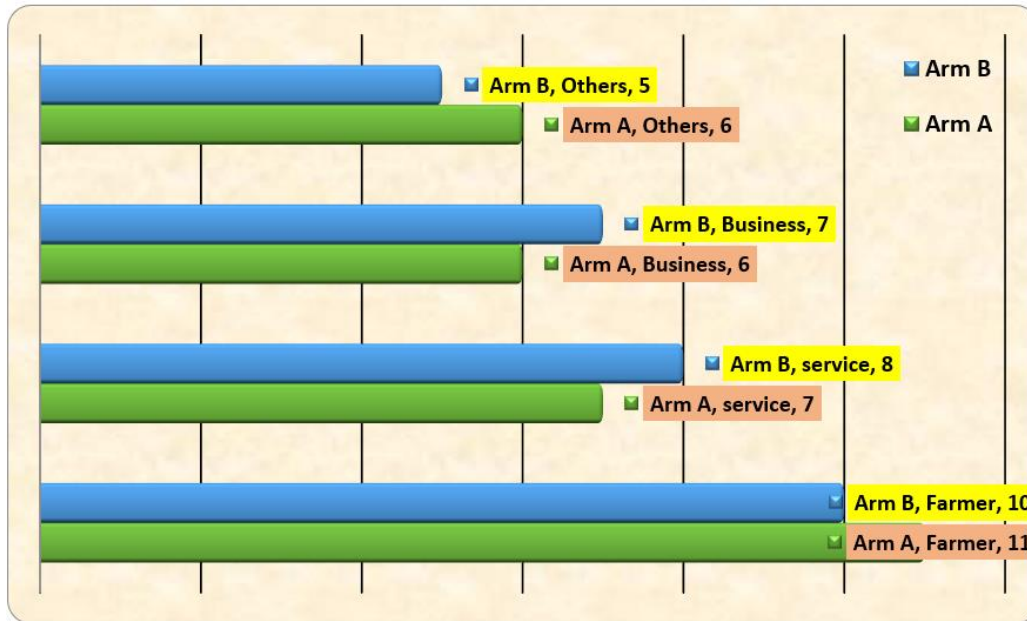


Figure 3: Distribution of the patients by occupation

Out of 60 patients, 49 were smokers. In Arm A, 83.3% of the patients were smokers, compared to 80% in

Arm B. There was no statistically significant difference between the two groups ($p > 0.05$).

Table 2: Distribution of the patients by smoking habit

Smoking	Category of treatment		Fisher's Exact Test	p-value
	TPLF regimen (Arm A)	LFP regimen (Arm B)		
Yes	25 (83.3)	24 (80.0)	0.475	0.457
No	5 (16.7)	6 (20.0)		
Total	30 (100.0)	30 (100.0)		

* Fisher's Exact Test

The majority of patients in both arms had an ECOG score of 1 (53.3% in Arm A and 43.3% in Arm B). Eight patients in Arm A and ten patients in Arm B had an ECOG score of 0. Additionally, six patients

(20%) in Arm A and seven patients (23.3%) in Arm B had an ECOG score of 2. These differences were not statistically significant ($p > 0.05$).

Table 3: Distribution of the patients by ECOG performance status

ECOG performance status	Category of treatment		Chi-square test	p-value
	TPLF regimen (Arm A)	LFP regimen (Arm B)		
0	8 (26.7)	10 (33.3)	0.609	0.737
1	16 (53.3)	13 (43.3)		
2	6 (20.0)	7 (23.4)		
Total	30 (100.0)	30 (100.0)		

The oral cavity was the most common primary site in both arms (9 patients in Arm A and 10 in Arm B). In 15 patients (25%), the primary tumor was located in the oropharynx (7 in Arm A and 8 in Arm B), while the

larynx was the primary site in 14 patients (23.3%) (8 in Arm A and 6 in Arm B). No significant differences were observed between the groups.

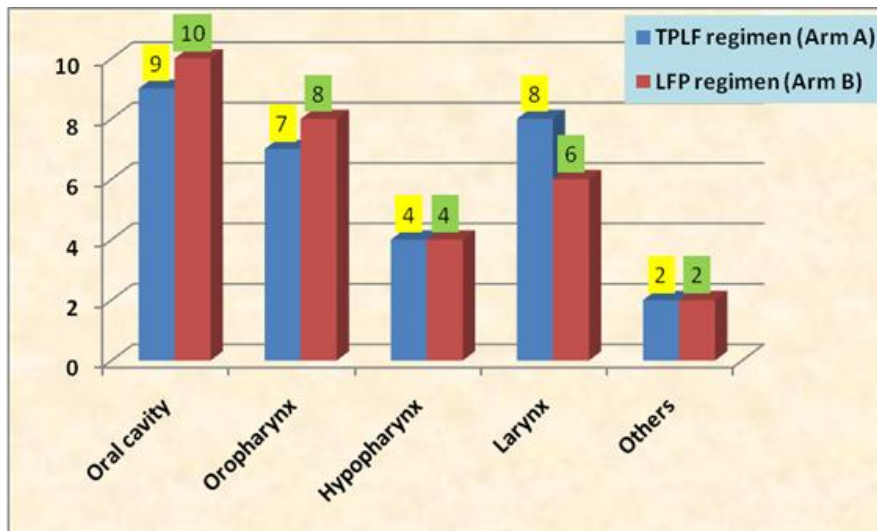


Figure 4: Distribution of the patients by site of primary tumor

Table 4 presents the distribution of patients by their chief complaints. Neck node swelling was reported by all patients in both arms. Pain was a common complaint, reported by 20 patients in Arm A and 22 patients in Arm B. Dysphagia or odynophagia was noted

in 39 patients, while weight loss was reported by 21 patients across both arms. Altered phonation or hoarseness of voice and ulceration were each reported by 30 and 21 patients, respectively.

Table 4: Distribution of the patients by complaints (n=60)

Site	TPLF regimen (Arm A)		LFP regimen (Arm B)		Total (n=60)	
	n	%	n	%	n	%
Swelling of neck node	30	100.0	30	100.0	60	100.0
Pain in affected site	20	66.7	22	73.3	42	70.0
Dysphagia/ odynophagia	18	60.0	21	70.0	39	65.0
Weight loss	17	56.7	18	60.0	35	58.3
Altered phonation/ hoarseness of voice	16	53.3	14	46.7	30	50.0
Ulceration	10	33.3	11	36.7	21	35.0
Dyspnoea	9	30.0	11	36.7	20	33.3
Hemoptysis	4	13.3	6	20.0	10	16.7
Trismus	2	6.7	1	3.3	3	5.0
Altered hearing/ otalgia	1	3.3	0	0.0	1	1.7

The distribution of patients by histological grading is shown in the above table. In Arm A, three patients (10%) had grade I disease, 19 patients (63.3%) had grade II, and eight patients (26.7%) had grade III

disease. In Arm B, four patients (13.3%) had grade I, 17 patients (56.7%) had grade II, and nine patients (30%) had grade III disease. However, no statistically significant differences were observed ($p > 0.05$).

Table 5: Distribution of the patients by histological grading

Grading	Category of treatment		χ^2	p-value
	TPLF regimen (Arm A)	LFP regimen (Arm B)		
Grade I	03 (10.0)	04 (13.3)	1.144	0.571
Grade II	19 (63.3)	17 (56.7)		
Grade III	08 (26.7)	09 (30.0)		
Total	30 (100.0)	30 (100.0)		

* Fisher's Exact Test

DISCUSSION

In this study, we analyzed the clinical characteristics of patients with locally advanced head and neck squamous cell carcinoma (LA-HNSCC) treated

with either the TPLF (Arm A) or LFP (Arm B) regimens. A key finding was the distribution of patients by age group. The majority of patients in both arms were over 50 years old, which is consistent with the findings of

other studies that report a higher incidence of head and neck cancers in older populations [8]. However, unlike some studies that have observed a higher proportion of younger patients, especially in HPV-related cancers, our study found that fewer patients were aged ≤ 40 years in both arms [9]. This discrepancy may be attributed to regional variations in risk factors, such as tobacco and alcohol use, which are more prevalent in older age groups.

Regarding gender distribution, a clear male predominance was observed in both arms (80% in Arm A and 77% in Arm B), which is consistent with the findings of several other studies. Male patients are generally more susceptible to head and neck cancers due to higher exposure to risk factors such as smoking and alcohol consumption. However, the role of HPV in the rising incidence of head and neck cancers in younger, non-smoking women may not have been evident in our sample, as the gender distribution remained largely male.

In terms of occupation, the majority of patients in both arms were farmers, followed by service holders, which aligns with studies that have shown a correlation between certain occupations and an increased risk of head and neck cancers. Farmers may be at increased risk due to prolonged exposure to environmental carcinogens, such as pesticides and tobacco cultivation. However, there were no statistically significant differences between the two arms with regard to occupation, which is consistent with previous studies that have not found a strong association between occupation and treatment outcomes in HNSCC [10-11].

Smoking was highly prevalent in both arms, with 83.3% of patients in Arm A and 80% in Arm B being smokers. This is similar to other studies which report smoking as a major risk factor for LA-HNSCC. Despite this high prevalence, no statistically significant difference was observed between the two arms, suggesting that smoking status alone may not significantly impact the outcomes of the treatment regimens in this study.

Regarding the Eastern Cooperative Oncology Group (ECOG) performance status, most patients in both arms had an ECOG score of 1, indicating that they were able to carry out light work or perform normal activities. This finding is consistent with other studies, where patients with locally advanced HNSCC typically present with an ECOG score of 1 or 2. Again, no significant differences between the two arms were noted in terms of ECOG score, which suggests that the performance status may not be a distinguishing factor in treatment response between the TPLF and LFP regimens.

The primary site of the tumor in our study was predominantly the oral cavity, followed by the oropharynx and larynx. This distribution is consistent with the general patterns observed in HNSCC, where the

oral cavity is often the most common primary site, particularly in regions with high rates of smoking and alcohol use. No significant differences between the two arms were observed in terms of primary tumor site, which may indicate that the treatment regimens studied were similarly effective across different tumor locations.

When analyzing patients' chief complaints, neck node swelling was the most common symptom, followed by pain, dysphagia, and weight loss. These complaints are typical for patients with LA-HNSCC and reflect the locally advanced nature of the disease. Altered phonation and hoarseness of voice were also common, particularly in patients with laryngeal involvement, which correlates with findings in other studies [12-14]. However, no significant differences were found between the two treatment arms in terms of these complaints, indicating similar symptom profiles regardless of the treatment regimen.

Finally, the histological grading of tumors in our study revealed a higher proportion of grade II disease in both arms, which is consistent with other studies reporting that the majority of head and neck cancers are moderately differentiated (grade II). The lack of significant differences between the two arms in terms of histological grading suggests that tumor grade alone did not influence the response to the TPLF or LFP regimens in our cohort.

CONCLUSION

In conclusion, our study on locally advanced head and neck squamous cell carcinoma (LA-HNSCC) patients treated with TPLF and LFP regimens revealed that the majority of patients were male, over 50 years of age, and predominantly smokers, with neck node swelling being the most common complaint. No significant differences were observed between the two treatment arms in terms of age, occupation, smoking status, ECOG performance status, primary tumor site, clinical complaints, or histological grading. These results suggest that both treatment regimens may offer similar outcomes across various patient characteristics, although further studies are needed to better understand the factors influencing treatment response in LA-HNSCC.

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