International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 13, No. 11, November 2024 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_13.11.2024.154

ORIGINAL RESEARCH

Evaluation of Role of Pre-Radiotherapy Haemoglobin Levels as a Prognostic Indicator in Advanced Head and Neck Carcinoma Patients on Concurrent Chemoradiation

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Received: 22September 2024 Accepted: 10November 2024

ABSTRACT

Background: Head and neck cancers (HNCs) represent a diverse group of tumors that encompass various anatomical sites, including theoropharynx, hypopharynx, larynx, and additional subregions. Anemia has shown considerable contribution in hypoxia in tumor and so making it radiation resistant but still exact co-relation needs to be investigated. Hence the present study was conducted to evaluate the role of pre-radiotherapy haemoglobin levels as a prognostic indicator in advanced head and neck carcinoma patients on concurrent chemoradiation.

Materials &Methods: A total of 50 patients with presence of LAHNC undergoing treatment with concurrent chemoradiation were enrolled. Patients were categorized into two groups: Anaemic and non-Anaemic, based on a pre-radiotherapy hemoglobin (Hb) level of ≤ 12 g/dl. A comprehensive assessment was conducted for each patient, which included detailed medical history, physical examination, clinical and endoscopic evaluations, as well as blood and radiological tests. The methodology focused solely on the hemoglobin levels recorded prior to the initiation of radiation therapy. The radiation therapy approach was tailored to the individual needs of each patient. The outcomes were subsequently evaluated and correlated with the pre-radiotherapy hemoglobin levels. All the results were recorded in Microsoft excel sheet and were subjected to statistical analysis using SPSS software.

Results: A total of 50 patients were evaluated. Mean age of the patients was 55.3 years. 66 percent of the patients were males while the remaining were females. 38 percent of the patients were of rural residence while the remaining were of urban residence. Complete response was seen in 58 percent of the patients while incomplete response was seen in 42 percent of the patients. Among patients with complete response, Pre-RT Hb levels were more than or equal to 12 g/dL, noted in 22 patients (75.86 percent) while among patients with incomplete response, Pre-RT Hb levels were more than or equal to 12 g/dL was noted in 5 patients (23.81 percent). Significant correlation of Pre-RT Hb with outcome was seen establishing its role as prognostic factor.

Conclusion: Reduced hemoglobin levels significantly contribute to the delayed healing of normal tissues, the severity of mucositis, and the experience of fatigue. A decrease in pre-treatment hemoglobin may result from inadequate nutritional status, the interplay between pro-apoptotic and anti-apoptotic factors, or inherent differences in tumor biology.

Key words: Head and neck cancer, Chemoradiation, Haemoglobin.

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INTRODUCTION

Head and neck cancers (HNCs) represent a diverse group of tumors that encompass various anatomical sites, including the oral cavity, oropharynx, hypopharynx, larynx, and additional subregions. Globally, there are approximately 750,000 new cases and 360,000 fatalities attributed to these cancers each year. Among these, head and neck squamous cell carcinoma (HNSCC) is the predominant variant, constituting about 3% of all new cancer diagnoses and corresponding deaths worldwide. Notably, around 30% to 40% of patients with HNSCC present with early-stage disease (stages I and II) at the time of diagnosis, and these individuals are often successfully treated with either surgical intervention or radiotherapy (RT) alone. Conversely, more than 60% of HNSCC patients are diagnosed with locally advanced (LA) disease. According to the 8th edition of the American Joint Committee on Cancer (AJCC) staging system (2017), LA-HNSCC is classified as T3-4 or N1-3. This category of HNSCC is associated with a significant risk of local recurrence and a poor prognosis, typically necessitating a multimodal treatment approach that includes surgery, RT, and systemic therapies.[1-3]

A discourse on induction chemotherapy (IC) within the head and neck oncology community invariably incites vigorous debate and contention. The standard treatment for locally advanced head and neck cancer (LAHNC) is concurrent chemoradiotherapy (CRT), which typically involves the administration of cisplatin, three weeklyat a dosage of 100 mg/m^2. Incorporating chemotherapy alongside radiation therapy has been shown to enhance both survival rates and locoregional control compared to radiation therapy administered in isolation.[3-5] Anemia has shown considerable contribution in hypoxia in tumor and so making it radiation resistant but still exact co-relation needs to be investigated Hence; the present study was conducted to evaluate the role of pre-radiotherapy haemoglobin levels as a prognostic indicator in advanced head and neck carcinoma patients on concurrent chemoradiation.

MATERIALS & METHODS

A total of 50 patients with presence of LAHNC undergoing treatment with concurrent chemoradiation were enrolled. Patients were categorized into two groups: Anaemic and non-Anaemic, based on a pre-radiotherapy hemoglobin (Hb) level of ≤ 12 g/dl. A comprehensive assessment was conducted for each patient, which included detailed medical history, physical examination, clinical and endoscopic evaluations, as well as blood and radiological tests. Those with a pre-radiotherapy Hb level of <10 g/dl received haematinic therapy and/or blood transfusions. The pre-radiotherapy assessments, encompassing both laboratory and radiological investigations, adhered to the American Joint Committee on Cancer (AJCC) Staging Criteria, 8th Edition, published in 2017.[7] The methodology focused solely on the hemoglobin levels recorded prior to the initiation of radiation therapy. The radiation therapy approach was tailored to the individual needs of each patient, and treatment was administered concurrently with weekly Cisplatin at a dosage of 30 mg/m² during the radiation course. The outcomes were subsequently evaluated and correlated with the pre-radiotherapy hemoglobin levels. All the results were recorded in Microsoft excel sheet and were subjected to statistical analysis using SPSS software.

Complete Response (CR) is defined as the disappearance of all target lesions. Partial Response (PR) is defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Progressive Disease (PD) is defined as at least a 20% increase in the sum of diameters of target lesions taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study). Stable Disease (SD) is defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD.

RESULTS

A total of 50 patients were evaluated. The mean age of the patients was 55.3 years. 66 percent of the patients were males while the remaining were females. 38 percent of the patients were of rural residence while the remaining were of urban residence. Complete response was seen in 58 percent of the patients while incomplete response was seen in 42 percent of the patients. Among patients with complete response, Pre-RT Hb levels were more than or equal to g/dL in 22 patients (75.86 percent) while among patients with incomplete response, Pre-RT Hb levels were more than or equal to g/dL in 22 patients (23.81 percent). Significant correlation of Pre-RT Hb with outcome was seen establishing its role as prognostic factor.

Table 1: Demographic data

Demographic data	Number	Percentage
Mean age (years)	55.3	
Males	33	66
Females	17	34
Rural residence	19	38
Urban residence	31	62

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Table 2: Distribution of patients according to tumor size

TNM	Number	Percentage
T3	22	44
T4a/b	28	56
Total	50	100

Table 3: Distribution of patients according to nodal status

TNM	Number	Percentage
N2a/b	19	38
N2c	21	42
N3a	10	20
Total	50	100

Table 4: Distribution of patients according to response at the end of therapy

End of therapy	Number	Percentage
Complete response	29	58
Incomplete response	21	42
Total	50	100

Table 5: Comparison of pre-RT Hb levels among patients divided on the basis of outcome

Pre-RT Hb levels	Complete response [n (%)]	Incomplete response [n (%)]
<12	7 (24.14 %)	16 (76.19 %)
≥12	22 (75.86 %)	5 (23.81 %)
Total	29 (100 %)	21 (100 %)
p-value	0.0012 (Significant)	

DISCUSSION

Head and neck squamous cell carcinoma (HNSCC) and its various subtypes arise from several anatomical regions, including the oral cavity, oropharynx, hypopharynx, and larynx. The diverse biological characteristics of HNSCC across these subsites' complicate treatment strategies. Typically, the management of HNSCC is informed by factors such as the primary tumor site, tumor stage, lymph node involvement, and pathological features, which collectively influence the selection of specialized interventions, including surgical options, radiotherapy, and/or systemic chemotherapy.[8,9] Approximately 40% of individuals diagnosed with HNSCC present with localized or early-stage disease, for which treatment is usually limited to a single modality, either surgical intervention or radiotherapy. The remaining 60% of patients are classified as having locally advanced (LA) HNSCC, for whom a multidisciplinary therapeutic approach is generally advocated. This may involve surgery followed by adjuvant radiotherapy or chemoradiotherapy (CCRT), or definitive CCRT. Despite extensive research over the years into the treatment of LA-HNSCC, the role of induction chemotherapy (IC) remains uncertain. In terms of multimodal treatment strategies for HNSCC, the implementation of therapeutic approaches in clinical settings relies heavily on a collaborative effort from a multidisciplinary team at each healthcare facility. The optimal treatment modality has yet to be definitively determined.[10-12]Anemia has shown considerable contribution in hypoxia in tumor and so making it radiation resistant but still exact co-relation needs to be investigated

Only a few reports could be identified in the literature that prospectively evaluated prognostic factors of chemoradiation in HNSCC patients.[13-19]

Danish Head and Neck Cancer (DAHANCA) Group Trial: DAHANCA 5 randomized HNSCC patients treated with the hypoxic radiosensitizer nimorazole or placebo, and in addition, patients with "low" pre-irradiation Hb values (females<13 g/dL; males<14.5 g/dL) were sub-randomized to plus or minus transfusion and found that, patients with high Hb levels had a significantly better probability of LRC, disease-specific survival (DSS) and overall survival (OS) compared to 'low Hb no transfusion' patients.[20]

Melo-Alvim C et al evaluated pretreatment hemoglobin values as a prognostic factor in patients with locally advanced head and neck squamous cell carcinoma treated with concurrent chemoradiotherapy.Retrospective evaluation of patients with HNSCC treated with cCRT. Primary and secondary endpoint was to evaluate the correlation of Hb levels (≥12.5 g/dL or <12.5 g/dL) at the beginning of cCRT with overall survival (OS) and progression-free survival (PFS), respectively.A total of 108 patients were identified. With a median follow-up of 16.10

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months median OS was 59.70 months for Hb ≥12.5 g/dL vs. 14.13 months for Hb <12.5 g/dL (p = 0.004). PFS was 12.29 months for Hb ≥12.5 g/dL and 1.68 months for Hb <12.5 g/dL (p = 0.016).Hb ≥12.5 g/dL correlated with significantly better OS and PFS.[21]

In the present study, significant correlation of Pre-RT Hb with outcome was seen establishing its role as prognostic factor. Ma SJ et al defined the optimal threshold for anemia in head and neck cancer patients and evaluate its role as a prognostic biomarker. A total of 496 patients were identified. Threshold for Hgb was determined to be 11.4 for both overall survival (OS) and progression-free survival (PFS). Low Hgb was associated with worse OS. Similar findings were observed among 39 matched pairs for OS and PFS. Among those with HPV-negative tumors, low Hgb was associated with worse OS and PFS. However, among those with HPV-positive tumors, low Hgb was not associated with both OS and PFS. Low Hgb below 11.4 was an independent adverse prognostic factor for worse survival. It was also prognostic among patients with HPV-negative tumors, but not for HPV-positive tumors.[22] Narayanaswamy RK et al analysed the Pre-Radiotherapy haemoglobin level and early response of treatment in stage III/IVA HNSCC.Ninety-one patients enrolled had mean age of 55.63, a median of 56 and mode of 60. Seventy-one were males (78%) and 20 females (22%) with a performance status of ECOG 1 in 43 (47%) patients and ECOG 2 in 48 (53%); Pre-RT Hb level of <10.7 g/dl in 38 (42%) patients and ≥10.7 in 53 (58%) patients; Pre-RT Hb level was <12 g/dl in 67 (74%) patients and ≥12 in 24 (26%) patients. Tumour sites were - Nasopharynx 7 (8 %), Oral Cavity 18 (20 %), Oropharynx 32 (35 %), Hypopharynx 23 (25 %) and Larynx 11 (12 %). Twenty-five (27%) had Grade 2 mucositis and 66 (73%) had Grade 3 mucositis. Fifty-eight (64%) patients completed treatment with NO breaks and 33 (36%) with treatment breaks for ≥5 days. Pre-radiotherapy haemoglobin ≥ 10.7 g/dl, ECOG performance status, Treatment interruptions for > 5 days, Mucositis reaction showed statistical significance with outcome of response.[23]

CONCLUSION

Reduced hemoglobin levels significantly contribute to the delayed healing of normal tissues, the severity of mucositis, and the experience of fatigue. A decrease in pre-treatment hemoglobin may result from inadequate nutritional status, the interplay between pro-apoptotic and anti-apoptotic factors, or inherent differences in tumor biology. Crucially, it is essential to determine whether the tumor biology varies among patients with lower pre-treatment hemoglobin levels.

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