

Serum Albumin Levels Pre-Operatively and Post-Operatively as Predications of Wound Healing In Head and Neck Cancer

Wazir Fairoze Ahmad, Faisal Manzoor, Shahzaib Shoukat, Rao Tahir, Rahat Kalsoom, Hareem Azhar

Department of ENT, Combined Military Hospital Rawalpindi/National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To determine the serum albumin levels, pre-operatively and post-operatively as predictors of wound healing in head and neck cancer.

Study Design: Prospective analytical study

Place and Duration of Study: Department of ENT, CMH Rawalpindi, Pakistan from Apr 2023 to Sep 2023.

Methodology: Sixty-seven individuals, diagnosed with head and neck squamous cell carcinoma (HNSCC) were included. A week before surgery, blood work including serum albumin levels, and body mass index (BMI, kg/m²) were all assessed. Both males and females between 40-70 years who were diagnosed with carcinoma of the oral cavity and underwent surgical resection, were included, while individuals with chronic liver diseases were excluded from this study.

Results: Of 67 patients 58(86%) were males while 9(14%) were females. The study found a significant association between preoperative and postoperative albumin levels ($p<0.001$) and wound infection, which shows that patients with serum albumin levels <28 exhibit a higher rate of wound infection compared to those with levels ≥ 28 . Other factors such as diabetes mellitus ($p=0.379$), cancer stage (0.367), recurrence ($p=0.65$), and did not show significant associations with postoperative wound infection

Conclusion: Preoperative and postoperative hypoalbuminemia are effective markers representing the onset of severe complications following surgery in head and neck cancer patients.

Keywords: Hypoalbuminemia; Head and Neck Neoplasms; Serum Albumin, Wound Healing.

How to Cite This Article: Ahmad WF, Manzoor F, Shoukat S, Tahir R, Kalsoom R, Azhar H. Serum Albumin Levels Pre-Operatively and Post-Operatively as Predications of Wound Healing in Head and Neck Cancer. Pak Armed Forces Med J 2026; 76(Suppl-8): S1335-S1339. DOI: <https://doi.org/10.51253/pafmj.v76i2.12042>

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Cancer in the head and neck comprise a diverse range of cancer types, often linked to heavy tobacco and alcohol use or human papillomavirus (HPV) infection.¹ The majority of these cancers are squamous cell carcinomas. Despite advancements in diagnosis and treatment, head and neck squamous cell carcinomas (HNSCCs) have a poor prognosis.² The measurement of serum albumin level has developed significantly in both medical practice and as a biochemical indicator for assessing the risk before surgery.³ In humans, albumin is the primary protein found in plasma, making up roughly half of the total protein present. Albumin is essential for maintaining overall health through various physiological functions. For adults, the standard range of albumin in the bloodstream is considered to be between 35 and 50 g/L, with concentrations below 35 g/L referred to as hypoalbuminemia. Over the years, hypoalbuminemia has been linked to adverse clinical outcomes across a

variety of clinical specialties.⁴ Meyer et al.⁵ demonstrated a link between low albumin levels and several negative outcomes. Based on their findings, they concluded that it is crucial to evaluate preoperative albumin levels and address nutritional status appropriately.

Patients diagnosed with head and neck squamous cell carcinoma (HNSCC) frequently experience malnutrition, which can impact the progression and results of the disease.⁶ Malnutrition is prevalent at the time of diagnosis, as well as during and after treatment. Dysphagia, odynophagia, anorexia, and fatigue are common symptoms related to the tumor and its treatment, increasing the risk of malnutrition among HNSCC patients.⁷ It is essential to closely monitor the nutritional status of patients, especially those with HNSCC who experience considerable weight loss or swallowing difficulties before treatment.⁸

This monitoring should extend to all cancer patients, focusing on providing dietary guidance, especially for those who have undergone radiation therapy. The indicators of weight loss and body

Correspondence: Dr Wazir Fairoze Ahmad, Department of ENT, Combined Military Hospital Rawalpindi Pakistan

Received: 15 Jul 2024; revision received: 22 Jul 2024; accepted: 24 Jul 2024

composition indicate patients' nutritional well-being and play a crucial role in determining the prognosis of HNSCC. Serum albumin levels could be connected to weight reduction in cancer patients because of alterations in body cell mass and systemic inflammatory responses.⁹ Continuous decrease in essential proteins and the existence of a persistent inflammatory response element may ultimately result in the demise of cancer patients. Furthermore, systemic hematological indicators (e.g., complete blood counts) have been linked to the prognosis of HNSCC.¹⁰

This study aims to determine the serum albumin levels pre-operatively and post-operatively as predictors of wound healing in head and neck cancer.

METHODOLOGY

This prospective analytical study was carried out at the Department of ENT, Combined Military Hospital (CMH), Rawalpindi, April 2023 to September 2023. It was authorized by the Institutional Review Board (IRB), Department of ENT, CMH Rawalpindi, vide reference number 580.

A total of 67 individuals who were diagnosed with head and neck squamous cell carcinoma and underwent surgical tumor excision and microvascular free flap reconstruction were employed in this study. The sample size was calculated using the WHO calculator by keeping a confidence interval of 95%, a margin of error of 5%, 4.5% prevalence of head and neck squamous cell carcinoma among all cancers, and it came out to be 67.¹¹ After providing a thorough explanation of the research, written and verbal informed consent was taken from every patient for their participation in the study. A non-probability consecutive sampling technique was used for data collection.

Inclusion Criteria: This study enrolled both male and female patients of age 40-70 years. All the participants who were diagnosed with carcinoma of the oral cavity and who underwent surgical excision were included in this study.

Exclusion Criteria: All the patients with chronic liver diseases were excluded from this study.

After the informed consent was obtained all the participants had routine assessments of their body weight and laboratory investigations. The eighth edition of the American Joint Committee on Cancer Staging (AJCC) was used to stage the tumors. The American National Comprehensive Cancer Network

(NCCN) recommendations served as the main basis for treatment.

The clinical features of age, gender, cancer stage, primary tumor site, and follow-up data regarding residual and survival following therapy were taken into consideration while enrolling patients. A week prior to the surgery, blood work including serum albumin levels, and body mass index (BMI, kg/m²) were all routinely assessed. Postoperative serum albumin level is characterized as the serum albumin measured the morning after surgery. Serum albumin levels less than 2.8 g/dL are referred to as hypoalbuminemia. Any recipient-site wound state following surgery that requires wound debridement in the operating theater is referred to as a major postoperative wound infection.

Statistical Package for Social Sciences (SPSS) version 23.0 was used for data analysis. Descriptive statistics including the mean and standard deviation were determined for continuous variables like age, preoperative and postoperative albumin levels. Frequencies and percentages were calculated for categorical variables like gender etc. Chi square test was applied to find the association between preoperative and postoperative albumin level and wound healing. The *p* value of ≤ 0.05 was considered significance.

RESULTS

A total of 67 patients diagnosed with head or neck cancer were included in this study, Out of the total patients, 58(86%) were males with a mean age of 48.05 ± 4.751 , and 9(14%) were females with a mean age of 55.11 ± 7.219 . The mean and standard deviation of quantitative variables were measured as seen in Table-I. Patients were categorized into different groups according to their Gender, Diabetes Mellitus, Cancer Stage, Recurrence, Preoperative albumin levels, Postoperative Albumin levels, and Postoperative wound Infection as seen in Table-II.

Table-I: Mean of Quantitative Variables (n=67)

Parameters	Mean $\pm$ SD
Age (year)	49.00 ± 5.63
Preoperative Albumin Level (g/L)	31.46 ± 5.36
Postoperative Albumin Level (g/L)	25.43 ± 4.69

The study found a significant association between pre and post-operative albumin levels ($p < 0.001$) and wound infection in head and neck cancer patients that elaborated that patients with postoperative albumin levels < 28 exhibits a higher rate

of wound infection compared to those with levels ≥ 28 . Other factors such as diabetes mellitus ($p=0.379$), cancer stage ($p=0.367$), and recurrence ($p=0.65$) did not show significant associations with postoperative wound infection in this analysis as seen in Table-III.

Table-II: Demographic and Clinical Characteristics of Head and Neck Cancer Patients (n=67)

Variables		n (%)
Gender	Male	58(86.6%)
	Female	9(13.4%)
Diabetes Mellitus	Yes	19(28.4%)
	No	48(71.6%)
Cancer Stages	III	22(32.8%)
	IV	45(67.2%)
Recurrence	Yes	24(35.8%)
	No	43(64.2%)
Preoperative Albumin	<28	20(29.9%)
	≥ 28	47(70.1%)
Postoperative Albumin	<28	54(80.6%)
	≥ 28	13(19.4%)
Postoperative wound Infection	Yes	35(52.2%)
	No	32(47.8%)

Table-III: Association of Various Variables with Postoperative Wound Infection in Head and Neck Cancer Patients (n=67)

Variables		Postoperative Wound Infection		p-value
		Yes	No	
Diabetes Mellitus	Yes	11(16.4%)	8(11.9%)	0.379
	No	24(35.8%)	24(35.8%)	
Cancer Stage	III	14(20.9%)	8(11.9%)	0.148
	IV	21(31.3%)	24(35.8%)	
Recurrence	Yes	16(23.9%)	8(11.9%)	0.65
	No	19(28.4%)	24(35.8%)	
Preoperative albumin	<28	17(25.4%)	2(4.5%)	<0.001
	≥ 28	18(26.9%)	29(43.3%)	
Postoperative Albumin	<28	34(50.7%)	20(30.0%)	<0.001
	≥ 28	1(1.5%)	12(17.9%)	

DISCUSSION

Albumin is a common metric for assessing the nutritional status. Its serum concentration has a half-life of about 20 days, and it provides a long-term indicator of a patient's nutritional state. Numerous studies have shown that hypoalbuminemia more accurately represents protein-energy deficiency than other anthropometric markers.¹² There is strong evidence that the risk of postoperative complications and mortality increases when the blood albumin levels are lower than normal.¹³ In prior research, malnutrition was identified by preoperative hypoalbuminemia as a risk factor for surgical site infections (SSIs). This increased risk was attributed to many causes, such as compromised immune system function, prolonged inflammation, and impaired

wound healing. However, after surgery, low serum albumin levels, even hypoalbuminemia, are frequently observed. These can be brought on by a number of factors, such as high consumption, dilution of the serum, decreased albumin synthesis, and an excess of exudates. Most patients will recover from surgical hypoalbuminemia within days, regardless of albumin therapy.¹⁴ Malnutrition usually affects 20-67% of individuals with head and neck cancer.¹⁵ Currently, following tumor removal, microsurgical free flap transfer is the cornerstone of reconstruction for significant deformities in the head and neck region.¹⁶ In cancer patients, appropriate and successful head and neck reconstruction is essential since delayed wound healing can negatively impact these patients' oncologic prognosis and extend their hospital stays. Similar to the current study, multiple other researches have investigated the role of blood serum albumin levels in pre and postoperative wound healing in individuals that had free tissue transfer and head and neck cancer resection.

Lo et al,¹⁷ conducted a similar research to the current study and included 158 patients of HNSCC, 13 females and 145 males. The microvascular surgery has a 95.6% success rate. 6.3% of serious complications and 27.8% of mild complications were reported in this study. Moreover, this investigation revealed that in 61 individuals who went through head and neck surgery along with the free tissue transfer, decreased albumin levels are indicative of a higher risk of developing postoperative complications.¹⁷ The current study suggested the same outcomes that patients with postoperative albumin levels less than 28 show a higher rate of wound infection compared to those with albumin levels greater than or equal to 28. Additionally, a report by Hoppe et al,¹⁸ also came up with the results that supported the current research and concluded that postoperative low albumin levels have been attributed to complications following free flap transfer.¹⁸

A study by Danan *et al*,¹⁹ also suggested similar results to the present study. However, this investigation included 604 patients of all cancer types, while the present study only included 67 patients with head and neck squamous cell carcinoma. It was demonstrated that serum albumin had a statistically significant inverse relationship with postoperative wound infection ($p = .001$, HR = 0.455) and overall survival (OS) ($p = .001$, HR = 0.685). This concludes that reduced preoperative serum albumin levels are linked

to poorer overall survival (OS) and higher risks of wound infection in patients of head and neck cancer. The current study also suggested that preoperative serum albumin levels show significant associations with postoperative wound infection.¹⁹

Results of the current research support prior studies by presenting that postoperative hypoalbuminemia was associated with an increased risk of severe wound infection following surgery. This is because the decreased levels of serum albumin correspond to a decline in critical immune system proteins, which are vital for controlling tumor growth and infection.²⁰ The preoperative and postoperative serum albumin levels proved to be the key factor influencing wound infection in participants of the current study.

Another research by Lim WS et al,²¹ showed similar results to the present study's results. In this study, preoperative levels of serum albumin were found to be a reliable indicator of overall survival, disease-free survival, and cancer-specific mortality. Individuals with head and neck squamous cell carcinoma presenting with hypoalbuminemia before surgery had almost six times higher chances of cancer-specific death, tumor progression, and general mortality.²²

The current research findings on the clinical implications of hypoalbuminemia in the surgical management of head and neck squamous cell carcinoma suggest that medical professionals should be cautious while treating such conditions.

LIMITATION OF STUDY

The main limitation is that this was a single-centered study and only included 67 patients with head and neck squamous cell carcinoma (HNSCC). Future studies should consider conducting multi-center investigations that encompass all types of head and neck malignancies. It is important to ensure a relatively large sample size to enhance the generalizability of the findings.

ACKNOWLEDGEMENT

We would like to acknowledge all the efforts and thank all the individuals who participated directly or indirectly and helped us complete this research.

CONCLUSION

Preoperative and postoperative hypoalbuminemia in HNSCC patients are effective markers representing the onset of severe complications following surgery in patients of HNSCC.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

WFA & FM: Data acquisition, data analysis, critical review, approval of the final version to be published.

SS & RT: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

RK & HA: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Chow LQ. Head and neck cancer. *New Eng J Med* 2020; 382(1): 60-72.
2. Konings H, Stappers S, Geens M, De Winter BY, Lamote K, Van Meerbeeck JP et al. A literature review of the potential diagnostic biomarkers of head and neck neoplasms. *Front Oncol* 2020; 10: 1020. <https://doi.org/10.3389/fonc.2020.01020>
3. Loftus TJ, Brown MP, Slish JH, Rosenthal MD. Serum levels of prealbumin and albumin for preoperative risk stratification. *Nutr Clin Pract* 2019; 34(3): 340-348. <https://doi.org/10.1002/ncp.10271>
4. Almasaudi AS, Dolan RD, Edwards CA, McMillan DC. Hypoalbuminemia reflects nutritional risk, body composition and systemic inflammation and is independently associated with survival in patients with colorectal cancer. *Cancers* 2020; 12(7): 1986. <https://doi.org/10.3390/cancers12071986>
5. Meyer CP, Rios-Diaz AJ, Dalela D, Ravi P, Sood A, Hanske J et al. The association of hypoalbuminemia with early perioperative outcomes—a comprehensive assessment across 16 major procedures. *Am J Surg* 2017; 214(5): 871-883. <https://doi.org/10.1016/j.amjsurg.2016.11.023>
6. Zheng Z, Zhao X, Zhao Q, Zhang Y, Liu S, Liu Z et al. The effects of early nutritional intervention on oral mucositis and nutritional status of patients with head and neck cancer treated with radiotherapy. *Front Oncol* 2021; 10: 595632. <https://doi.org/10.3389/fonc.2020.595632>
7. Brewczyński A, Jabłońska B, Mrowiec S, Skłodowski K, Rutkowski T. Nutritional support in head and neck radiotherapy patients considering HPV status. *Nutrients* 2020; 13(1): 57. <https://doi.org/10.3390/nu13010057>
8. Machiels JP, Leemans CR, Golusinski W, Grau C, Licita L, Gregoire V. Squamous cell carcinoma of the oral cavity, larynx, oropharynx and hypopharynx: EHS-ESMO-ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2020; 31(11): 1462-1475. <https://doi.org/10.1016/j.annonc.2020.07.011>
9. Cordeiro LD, Silva TH, de Oliveira LC, Neto JF. Systemic inflammation and nutritional status in patients on palliative cancer care: a systematic review of observational studies. *Am J Hosp Palliat Med* 2020; 37(7): 565-571. <https://doi.org/10.1177/1049909119886833>
10. Budach V, Tinhofer I. Novel prognostic clinical factors and biomarkers for outcome prediction in head and neck cancer: a systematic review. *Lancet Oncol* 2019; 20(6): e313-e326. [https://doi.org/10.1016/S1470-2045\(19\)30177-9](https://doi.org/10.1016/S1470-2045(19)30177-9)
11. Barsouk A, Aluru JS, Rawla P, Saginala K, Barsouk A. Epidemiology, Risk Factors, and Prevention of Head and Neck Squamous Cell Carcinoma. *Med Sci* 2023; 11(2): 42. <https://doi.org/10.3390/medsci11020042>
12. Kuzu MA, Terzioğlu H, Genç V, Erkek AB, Özban M, Sonyürek P et al. Preoperative nutritional risk assessment in predicting postoperative outcome in patients undergoing major surgery. *World J Surg* 2006; 30: 378-390. <https://doi.org/10.1007/s00268-005-0163-1>
13. Gibbs J, Cull W, Henderson W, Daley J, Hur K, Khuri SF. Preoperative serum albumin level as a predictor of operative mortality and morbidity: results from the National VA Surgical Risk Study. *Arch Surg* 1999; 134(1): 36-42.
14. Donaldson M, Bradley PJ. Current management of the nutritional needs of the head and neck cancer patient. *Curr Opin Otolaryngol Head Neck Surg* 2000; 8(2): 107-112.
15. Cross MB, Yi PH, Thomas CF, Garcia J, Della Valle CJ. Evaluation of malnutrition in orthopaedic surgery. *J Am Acad Orthop Surg* 2014; 22(3): 193-199.

Wound Healing in Head and Neck Cancer

16. Grammatica A, Piazza C, Paderno A, Taglietti V, Marengoni A, Nicolai P. Free flaps in head and neck reconstruction after oncologic surgery: expected outcomes in the elderly. *Otolaryngol Head Neck Surg* 2015; 152(5): 796-802. <https://doi.org/10.1177/0194599815576905>
 17. Lo SL, Yen YH, Lee PJ, Liu CH, Pu CM. Factors influencing postoperative complications in reconstructive microsurgery for head and neck cancer. *J Maxillofac Surg* 2017; 75(4): 867-873. <https://doi.org/10.1016/j.joms.2016.09.025>
 18. Hoppe IC, Abernathie BL, Datiashvili RO. Examination of possible predictors of complications after free tissue transfer to the head and neck for oncologic defects. *Ann Plast Surg* 2012; 69(4): 368-370.
 19. Danan D, Shonka Jr DC, Selman Y, Chow Z, Smolkin ME, Jameson MJ. Prognostic value of albumin in patients with head and neck cancer. *Laryngoscope* 2016; 126(7): 1567-1571. <https://doi.org/10.1002/lary.25877>
 20. Zhang F, Liu X, Tan Z, Li J, Fu D, Zhu L. Effect of postoperative hypoalbuminemia and supplement of human serum albumin on the development of surgical site infection following spinal fusion surgery: a retrospective study. *Eur Spine J* 2020; 29: 1483-1489. <https://doi.org/10.1007/s00586-020-06306-w>
 21. Lim WS, Roh JL, Kim SB, Choi SH, Nam SY, Kim SY. Pretreatment albumin level predicts survival in head and neck squamous cell carcinoma. *Laryngoscope*. 2017; 127(12): E437-E442.
-