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Research Article

Assessing the Prognostic Utility of the HALP Score in Breast Cancer and Its Association with Axillary Lymph Node Involvement

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Abstract

Background: The Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) score has recently gained fame as a novel prognostic marker for predicting clinical outcomes in different cancers. Data regarding its applicability in breast cancer is rare. This study aimed to evaluate the prognostic utility of the HALP score in breast cancer, specifically its correlation with clinicopathological features and its effectiveness in predicting axillary lymph node involvement.

Methods: This cross-sectional study was performed in the Breast Surgery Unit, Liaquat National Hospital, Pakistan during Jan-Sep 2023. HALP score was calculated in patients who planned to undergo surgery for breast cancer. Included in the study were 180 patients who underwent surgical treatment for breast cancer. HALP values were obtained by taking the product of hemoglobin, albumin, and lymphocytes and dividing it by the platelet count. The Area Under the Curve (AUC) was calculated to determine the predictive ability of the HALP score. The young index was computed. Two groups were formed using the threshold value and compared using the Chi-square of the Fisher exact test.

Results: 180 patients were studied with a median age of 53.5 (IQR=22-85) years. Lymph node involvement was seen in 32.2% of patients. Median HALP score was 5.7 (IQR=4-7.2). The receiver operative characteristic curve showed an AUC of 0.544 (p=0.338). Youden index showed 5.95 to be the cut-off value. 53.3% of patients had a HALP score of <5.95. None of the patients' features were found to be significantly different between those with HALP scores of <5.95 and ≥5.95.

Conclusion: The study did not find a link between the HALP score and the clinicopathological characteristics of breast cancer. However, younger patients and those with positive lymph nodes tend to have higher HALP scores.

Keywords: HALP: Hemoglobin, Albumin, Lymphocytes, Platelets; Axillary Lymph Node Involvement; Predictive Tool

Introduction

Breast cancer is the most common cancer in women worldwide. It has now overtaken lung cancer as the leading cause of cancer-related deaths in women [1]. Developing countries, particularly those in Asia, are experiencing a significant increase in breast cancer incidence and mortality, often attributed to lifestyle changes [2,3]. In Pakistan, the situation is alarming, with one in nine women at risk of developing breast cancer. Alarmingly, 178,388 new cases were reported in 2020 alone [4].

Prognostic factors in breast cancer are crucial for individualized treatment planning and predicting outcomes. Factors such as molecular subtypes, hormone receptor status, tumor size, and histological grade play a significant role in guiding therapy. Axillary Lymph Node (ALN) status is a critical determinant, with metastasis significantly reducing five-year survival rates. Although several imaging modalities (ultrasound, MRI, and PET scan and biopsy techniques (image-guided and sentinel node biopsy) are used for ALN assessment, several studies have been conducted to determine the presence of metastasis in the axilla using preoperative data in breast cancer [7-11]. But, they often lack sensitivity or are prohibitively expensive.

The Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) score is a novel composite biomarker that integrates nutritional and immune status. Initially introduced by Chen in 2015, the HALP score has been correlated with cancer prognosis in various malignancies [12-14]. Hemoglobin and albumin levels reflect nutritional status, while lymphocyte and platelet counts are markers of immune function. This study investigates the correlation between the HALP score and clinicopathological features in breast cancer and explores its potential in predicting axillary lymph node involvement.

This study aimed to evaluate the prognostic utility of the HALP score in breast cancer, specifically its correlation with clinicopathological features and its effectiveness in predicting axillary lymph node involvement.

Ethical Statement

The project did not meet the definition of human subject research under the purview of the IRB according to federal regulations and therefore was exempt.

Material and Methods

This cross-sectional study was performed in the Breast Surgery Department at Liaquat National Hospital and Medical College, Karachi, Pakistan from January 2023 to September 2023. First, a pilot study was performed on thirty patients to estimate the sample size in which AUC was 0.417. Thus at 95% confidence interval and 8% margin of error, the sample size came out to be 180. Sample size estimation was performed using the formula given by Karim M, et al., Those enrolled in the study were breast cancer patients who had undergone surgery [15]. Patients' data was obtained from the medical records and hospital files. Those with missing data and male patients were excluded from the study.

Patients' blood samples were taken for HALP score parameters before surgery. HALP values were obtained by taking the product of hemoglobin, albumin, and lymphocytes and dividing it by platelet count. Staging of breast cancer was done using TNM Staging AJCC 8th edition [16]. A multidisciplinary team of breast cancer specialists, comprising surgeons, oncologists, and radiation oncologists, made treatment decisions. Neoadjuvant therapy was administered to patients with locally advanced tumors and those with unfavorable biology of tumors. The expression of Estrogen Receptor (ER) and Progesterone Receptor (PR) was determined using immunohistochemistry. Human Epidermal Growth Factor Receptor 2 (HER2) expression was determined using immunohistochemistry or Fluorescent *In-Situ* Hybridization (FISH). Lymph node involvement was confirmed when doing the staging of the axilla either by sentinel lymph node biopsy or axillary dissection.

The predictive ability of HALP was determined through the receiver operating characteristic curve and its area under the curve. The Youden index was determined. Two groups were formed using the threshold value. Patient's demographic characteristics: pathological diagnosis, neoadjuvant treatment status, sentinel lymph node sampling, T stage, number of metastatic and total lymph nodes, ER (%), PR (%), c-erbB2, Ki-67 (%), menopausal status, number of children, breastfeeding status, family history of cancer, and the surgical and oncological treatment administered to the patients in the postoperative period. Furthermore, the HALP score at the established cut-off value for axillary positive lymph node prediction was analyzed and all these details were entered into a proforma that is shown in Fig. 1,2.

Data was entered into SPSS version 26 to perform statistical analysis. Categorical variables were computed as frequencies and percentages. Numerical variables were summarized as median with inter-quartile range as they were non-normal. The normality assumption was assessed using the Shapiro-Wilk test. Patients' features were compared among the two groups using the Chi-square of the Fisher-exact test. The sensitivity and specificity of the HALP score were calculated based on the axillary lymph node positivity of the patients. The cut-off value was determined from the area under the ROC curve. A Spearman correlation test was used to determine the relationship between lymph node count and HALP score. P-value ≤ 0.05 was considered as statistically significant.

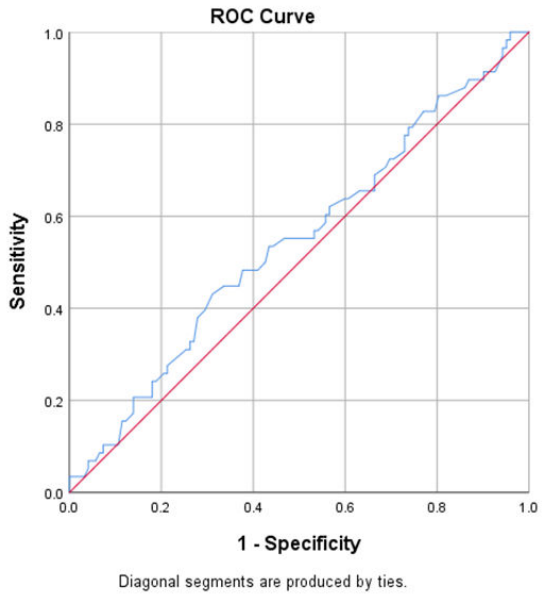
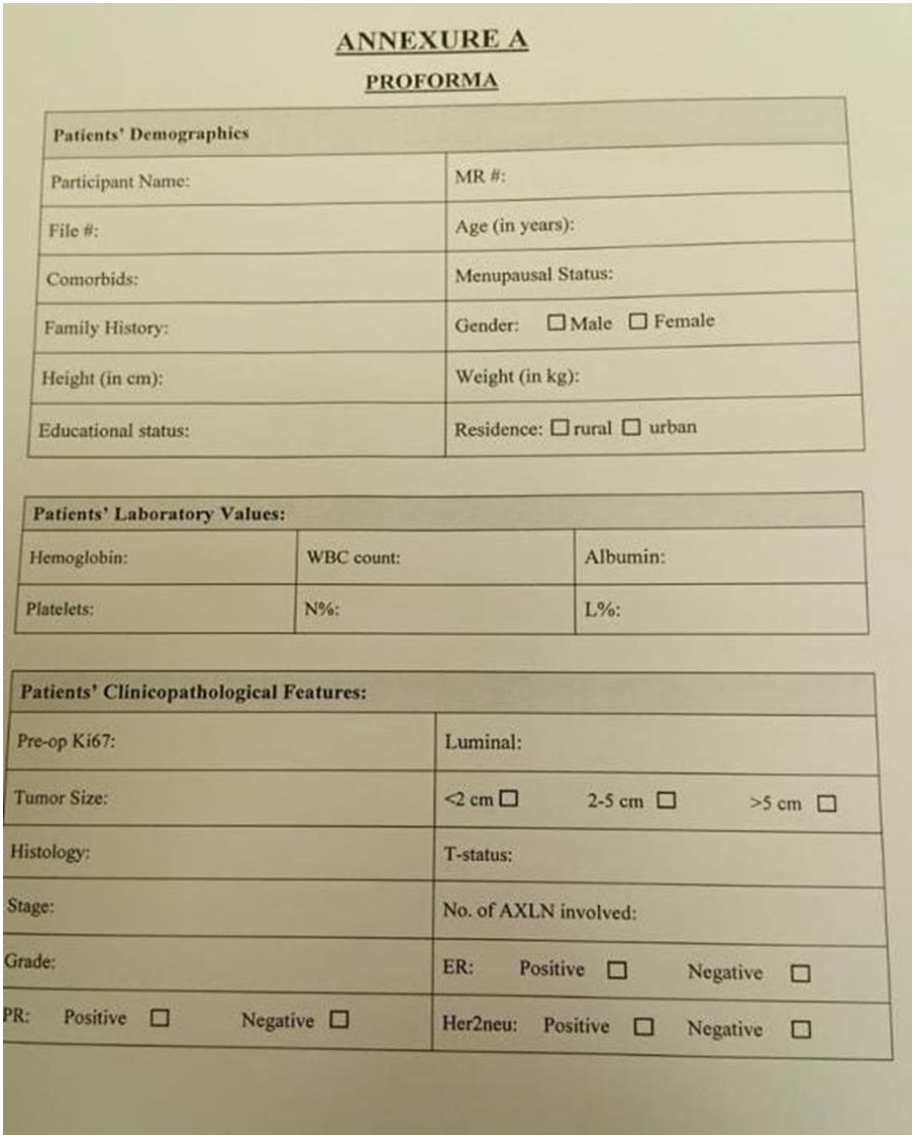


Figure 1: Receiver operating characteristic curve for HALP score predicting axillary lymph node metastasis.



ANNEXURE A

PROFORMA

Patients' Demographics	
Participant Name:	MR #:
File #:	Age (in years):
Comorbids:	Menupausal Status:
Family History:	Gender: ☐ Male ☐ Female
Height (in cm):	Weight (in kg):
Educational status:	Residence: ☐ rural ☐ urban

Patients' Laboratory Values:		
Hemoglobin:	WBC count:	Albumin:
Platelets:	N%:	L%:

Patients' Clinicopathological Features:	
Pre-op Ki67:	Luminal:
Tumor Size:	<2 cm ☐ 2-5 cm ☐ >5 cm ☐
Histology:	T-status:
Stage:	No. of AXLN involved:
Grade:	ER: Positive ☐ Negative ☐
PR: Positive ☐ Negative ☐	Her2neu: Positive ☐ Negative ☐

Figure 2: Proforma for HALP score.

Results

A total of 180 patients were included in this study. The median age was 53.5 years, ranging from 22 to 85 years. The median values for hemoglobin, albumin, lymphocyte count, and platelet count were 12.3, 4.4, 29, and 271.5, respectively. Table 1 summarizes the patients' clinical features. Lymph node metastasis was observed in 32.2% of patients, with a median of four lymph nodes involved. The median HALP score was 5.7. The receiver operating characteristic curve showed an Area Under the Curve (AUC) of 0.544, indicating limited predictive ability (p=0.338). The Youden index suggested a HALP cut-off value of 5.95. Among these patients, 46.7% had a HALP score of ≥5.95. There was no significant difference in lymph node involvement between those with HALP scores below and above 5.95 (Table 2). The sensitivity and specificity of the HALP score for predicting axillary lymph node involvement were 36.9% and 71.8%, respectively. No significant differences were observed in clinicopathological features between those with HALP score of <5.95 and ≥5.95 (Table 3). Younger patients and those with positive lymph nodes tended to have higher HALP scores, but these associations were not statistically significant.

Variables	Groups	Frequency	Percentage
Age groups	<30 years	11	6.1
	30-39 years	21	11.7
	40-49 years	35	19.4
	50-59 years	54	30.0
	60 years and above	59	32.8
Lymph node-positive	yes	58	32.2
	no	122	67.8
Tumor grade	To	18	10.0
	T1	108	60.0
	T2	40	22.2
	T3	14	7.8
Tumor histopathology	DCIS	4	2.2
	DCIS II	3	1.7
	IDC I	6	3.3
	IDC II	93	51.7
	IDC III	56	31.1
	Mucinous ca	5	2.8
	ILC II	13	7.2
Estrogen Receptor	Positive	138	76.7
	Negative	42	23.3
Progesterone Receptor	Positive	129	71.7
	Negative	51	28.3
Tumor stage	0	7	3.9
	I	1	0.6
	II	4	2.2
	III	8	4.4
Her2 neu status	Positive	144	80.0
	Negative	4	2.2
Molecular classification	Luminal A	1	0.6
	Luminal B	39	21.7
	Her2 Positive	78	43.3
	TRIPLE - VE	1	0.6

Table 1: Summary of patient's clinical features.

Lymph Node Involvement	HALP Score		p-value
	<5.95	≥5.95	
Yes	27(46.6)	31(53.4)	0.209
No	69(56.6)	53(43.4)	

Table 2: Comparison of lymph node involvement and HALP score of <5.95 and ≥5.95).

Variables	Groups	HALP Score		p-value
		<5.95	≥5.95	
Age groups	<30	3(27.3)	8(72.7)	0.084
	30-39	16(76.2)	5(23.8)	
	40-49	18(51.4)	17(48.6)	
	50-59	26(48.1)	28(51.9)	
	60+	33(55.9)	26(44.1)	
Tumor grade	To	9(50)	9(50)	0.728
	T1	61(56.5)	47(43.5)	
	T2	20(50)	20(50)	
	T3	6(42.9)	8(57.1)	
Tumor stage	0	5(71.4)	2(28.6)	0.537
	I	7(53.8)	6(46.2)	
	II	67(54.9)	55(45.1)	
	III	17(44.7)	21(55.3)	
Molecular classification	Luminal A	21(52.5)	19(47.5)	0.953
	Luminal B	50(52.6)	45(47.4)	
	Non-luminal Her2+	13(39.1)	9(40.9)	
	TRIPLE - VE	12(52.2)	11(47.8)	

Table 3: Comparison of patients 'clinicopathological features' among those with HALP scores <5.95 and ≥5.95.

Discussion

The prognostic ability of the HALP score has been evaluated in several types of malignancies [17]. This study explored the value of the HALP score in breast cancer in predicting lymph node involvement and other clinicopathological features in breast cancer. Patients' immune and nutritional status can be evaluated using simple and reproducible blood tests including neutrophil/lymphocyte ratio, serum albumin, and tumor-infiltrating lymphocytes [18]. However, The HALP score's predictive power is insufficient, but it does provide a rationale for the composite index in the current study which examines the role of the immune system and nutritional status in cancer prognosis.

These results are consistent with previous studies that questioned the HALP score's efficacy in breast cancer, contrasting with its demonstrated utility in gastric and colorectal cancer [19]. In these malignancies, the HALP score has been linked to tumor stage and lymph node status. In our study, the stage of the disease, grade of the tumor, and aggressive histology had no association, and the lack of significant association between HALP score and aggressive tumor characteristics suggests the need for a deeper understanding of breast cancer's biological context and its immune-nutritional profile.

Prognostic significance of the HALP score was also evaluated in early-stage triple-negative breast cancer in one study, but no significant finding was reported [20,21]. To determine whether the HALP score could be used to predict the presence of axillary lymph node involvement in breast cancer patients, Duran, et al., conducted a study in 2022 in which HALP's predictive ability was assessed. The threshold of 29.01 was determined using the Receiver operative characteristic curve. The score demonstrated high sensitivity (84.3%) in detecting positive lymph nodes but its low specificity (26.1%) in identifying negative ones was observed, indicating its limitations for reliable prediction.

In the current study, axillary lymph node involvement was found to be higher in the high HALP score group, but the findings were not statistically significant. In retrospective studies on breast cancers, the HALP score had a cutoff range of 24.14-29.01, which is higher than the cutoff obtained in our study i.e., 5.95 and in these studies, node positivity was found to be higher in the low HALP score group, contrary to our results.

Dagmura, et al., study showed on survival analysis in patients undergoing colorectal surgery, patients with a high HALP score had a statistically significantly longer overall survival than patients with low scores. They also determined that HALP scores were higher for older patients compared to younger patients. In our study, younger patients exhibited higher HALP scores, but without statistical significance. However, in our study the proportion of young patients (<30 years) having HALP score of ≥5.95 was higher (72.7%) than other age groups, but it did not achieve statistical significance. Our results also highlight the variability in optimal HALP cut-off values across different cancers, complicating its clinical application in breast cancer.

Overall, while the HALP score remains a cost-effective measure of immune and nutritional status, its role as a standalone predictive marker for breast cancer appears insufficient. Further research is required to refine the cut-off values and investigate the HALP score's performance alongside other biomarkers.

Limitations and Future Directions

Sample Size

The study's small sample size limits the generalizability of the findings.

Biological Insights

Further studies should investigate the biological link between HALP components and breast cancer progression.

Comprehensive Evaluation

Future research should assess the HALP score's utility in combination with other prognostic markers for a more robust assessment.

Conclusion

This study found no significant correlation between the HALP score and clinicopathological features of breast cancer or its predictive value for axillary lymph node involvement. Although younger age and lymph node positivity were associated with higher HALP scores, these were not statistically significant. Future research should involve larger sample sizes and explore combining the HALP score with other established prognostic markers.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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Consent to Participate

Informed consent was obtained from each participant prior to specimen collection.

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Data Availability

Data is available for the journal. Informed consents were not necessary for this paper.

Author's Contribution

The authors contributed equally.

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