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Original Research Article

Role of HALP (Hemoglobin, Albumin, Lymphocyte, Platelet) Score for Prediction of Prognosis of Patients with Hepatocellular Carcinomas

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Abstract: ***Background:*** Hepatocellular carcinoma (HCC) is one of the main causes of cancer-associated death on the global scale, and the prognosis is determined by the tumor burden, liver performance, and inflammatory system conditioning. Studies indicate the value of composite biomarkers like Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) score in the determination of cancer outcomes. Aim: To determine the predictive accuracy of the HALP score in assessing survival among patients with hepatocellular carcinoma. ***Methods***: The cross-sectional analysis study was carried out at the Department of Gastroenterology, Jinnah Hospital, Lahore, between 1st June 2025 and 30th October 2025. Non-probability consecutive purposive sampling was employed to use 217 patients aged 1865 years with confirmed hepatocellular carcinoma. Demographic, clinical, and laboratory data were gathered and the HALP scores were computed. Follow-up of the patients was done after 3 months and mortality was taken as the main outcome. The SPSS version 25.0 was used to make statistical analysis, including ROC curve analysis and correlation test. ***Results:*** The mean age of patients was 52.4 ± 9.8 years, with 63.6% males. The mean HALP score was 35.6 ± 14.7. Mortality was observed in 33.2% of patients. A significantly higher mortality rate was found in patients with HALP <30 (70.8%) compared to those with HALP ≥30 (15.9%) ($p < 0.001$). The HALP score showed significant negative correlations with tumor grade ($r = -0.31$, $p < 0.001$) and disease duration ($r = -0.26$, $p < 0.001$), and positive correlations with hemoglobin ($r = 0.48$, $p < 0.001$) and albumin ($r = 0.52$, $p < 0.001$). ***Conclusion:*** The HALP is a valid and affordable prognostic biomarker to predict survival in patients with hepatocellular carcinoma. A reduction in the HALP scores is strongly linked to the higher mortality rates, which points to its possible application in the clinical risk stratification and management.

Keywords: Hepatocellular carcinoma, HALP score, prognosis, survival, inflammation, biomarkers.

INTRODUCTION

Hepatocellular carcinoma (HCC) is the most prevalent primary malignancy of the liver and the leading health issue that poses the highest significant worldwide health burden because of its elevated rates of incidence and mortality (Giri and Singh, 2024). It is the sixth most prevalent cancer and the third cause of cancer-related deaths in the world because it is the cause of more than 800,000 new cases each year (Singh et al., 2025). HCC distribution is strongly geographical, and its prevalence is the highest in East Asia and sub-Saharan Africa, which is mainly attributable to chronic infection with hepatitis B and C (Singal et al., 2023). Regardless of the development of diagnostic and treatment interventions, the overall five-year survival rate of HCC is less than 20% because of its late presentation and heterogeneity of the tumor (Serraino et al., 2022). The prediction of prognosis in HCC is complicated by the fact that it is determined not only by the peculiarities of the tumor but also by the functioning of the liver and the inflammatory situation in the body in general (Hwang et al., 2024). The traditional staging systems like the Barcelona Clinic Liver Cancer (BCLC) or those that use the tumor burden and liver functions tend to overlook the host-related prognostic variables. This has led to an emerging interest in finding reliable, readily

measurable biomarkers that indicate tumor biology as well as overall condition (Serraino et al., 2022).

Systemic inflammation and nutritional status have become known to be the key factors of cancer progression and patient survival in HCC (Argenziano et al., 2024). Chronic hepatitis or cirrhosis can lead to chronic inflammation, which is a contributor to hepatocarcinogenesis by involving oxidative stress, genomic instability, and tumor promoting effects of cytokines (Tuemen et al., 2022). Hematologic parameters (lymphocytes, platelets, hemoglobin, and serum albumin) indicate the interaction of immune competence, coagulation pathways, and nutritional reserves (Gabbia and De Martin, 2024). It has been linked to lymphopenia that leads to the inability of antitumor immunity, and thrombocytes to proliferate and spread the tumor due to platelet-derived growth factors. Hypoalbuminemia indicates low nutritional and hepatic synthetic capacity and is associated with adverse clinical outcomes in liver cancer patients (Choi and Thung, 2023). On the same note, anemia can be a sign of chronic disease burden and low oxygen carrying capacity, which leads to tumor hypoxia and aggressiveness. Nevertheless, their joint predictive ability might provide a more detailed evaluation of patient prognosis (Renne and Di Tommaso, 2022).

The Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) score is a new composite biomarker that puts these four parameters in one index that captures both the inflammatory and the nutritional status (Bati et al., 2025). The HALP score was first studied to evaluate the prognosis of gastrointestinal malignancies, but it has demonstrated a high level of prognostic significance in various types of cancers (Qian et al., 2025). Increased HALP has a tendency to represent improved immune-nutritional health and has been linked with the increased overall survival and disease-free survival (Wang et al., 2025). The progress made by the patients with HCC is that the HALP score could be an independent predictor of the prognosis, which is better than some of the classic markers. It has the following advantages: it is simple, cost-effective, and accessible via routine laboratory tests; thus, it is especially useful in resource-limited settings (Zhou and Yang, 2023). Further, the HALP score is multidimensional, as it identifies the development of cancer in the body, such as the presence of systemic inflammation, immune system, and nutritional state (Leetanaporn and Hanprasertpong, 2023). Irrespective of such encouraging discoveries, the clinical value of HALP in HCC is not fully researched in contrast with the other indices like neutrophil-to-lymphocyte ratio (NLR). Thus, its prognostic relevance needs to be confirmed by further research and standardized cutoff values in a variety of populations need to be developed (Farag et al., 2023).

HCC is an emerging public health issue in Pakistan, with the prevalence of infection of hepatitis B and C being among the critical etiological agents of liver cancer (Aftab et al., 2024). According to a recent research, Pakistan is considered one of the countries with intermediate and high levels of HCC and a high percentage of patients arrive at an advanced stage (Siddiqui et al., 2023). The lack of early screening and diagnostic services also increases the burden and outcomes of survival become poor (Akram et al., 2024). Prognostic markers such as the HALP score are cost-effective and readily available in such resource-constrained settings and may be important in clinical decision-making (Toshida et al., 2023). Nevertheless, a lack of local data on the evaluation of prognostic value of HALP among Pakistani patients with HCC is observed (Zhai et al., 2021). Considering the specific demographic, etiological and healthcare characteristics of Pakistan, the issue of applicability and predictive precision of HALP in this population should be evaluated (Butt et al., 2013). Potential uses of such research include risk stratification, therapeutic planning, and better patient outcomes in the standard clinical practice. Consequently, the research problem of this research is to establish whether the HALP score is a predictive tool of whether a patient with hepatocellular carcinoma will survive or not in Pakistan.

Methodology

Study Design and Setting

This research was done as a cross-sectional analytical study at the Department of Gastroenterology, Jinnah Hospital, Lahore. The period of the study was changed to 10th July 2025 until 30th January 2026.

Sampling Population and Sample Size

Non-probability consecutive purposive sampling was used to recruit participants in the study. Consecutive enrollment of all the patients who presented themselves within the study period and met the eligibility criteria was done. The number of patients used in the study is 217. This sampling method was chosen as it would enable the inclusion of all the available and eligible cases in the specified time. The study included patients between the ages of 18 and 65 years of either sex with diagnosed hepatocellular carcinoma. The patients who did not have at least 15 lymph nodes were not included, regardless of the presence or the absence of the lymph nodes that were removed surgically. Other exclusion criteria were active infection and bleeding disorders or other hematological disorders especially with a long PT (PT >20 seconds). Patients that underwent a gastrectomy previously, autoimmune diseases, or people who had hematological disorders recorded in their medical history were also excluded in order to eliminate the confounding effects on the hematological parameters.

Data Collection

A structured data collection proforma was used to collect demographic and clinical data after an informed consent was obtained. Age, gender, history of hepatitis B or C infection, length of hepatocellular carcinoma, smoking habits, over 20 ml/day alcohol use, and comorbid (hypertension blood pressure over 140/90 mmHg), diabetes mellitus (random blood sugar over 200mg/dl) and anemia (hemoglobin less than 10 g/dl) were recorded as variables. Aseptic venous blood samples were taken and were forwarded to the hospital laboratory to be analyzed in terms of hemoglobin levels, serum albumin, lymphocytes count, and platelet count. The standard formula was used to compute the HALP score of each patient with the help of the following laboratory parameters.

Follow-up and Outcome Measures

The Liver Clinic followed up all the enrolled patients monthly to monitor the progress of the disease. Clinical outcomes like the development of complications, including hematemesis, ascites, and hepatic encephalopathy were noted. The data about treatment modalities used in the treatment of hepatocellular carcinoma was also recorded. Completion of a three months follow-up period or death, whichever came first, was set as the main outcome measure.

Data Analysis

Statistical Package of social Sciences (SPSS) version 25.0 was used to enter and analyze all data collected. Quantitative variables were tested on the normality through the Shapiro-Wilk test. The continuous variables including age, duration of carcinoma, and HALP score were used in mean and standard deviation. The categorical variables such as gender, hepatitis status, tumor grade, smoking status, alcohol use, hypertension, diabetes, anemia, and mortality were in the form of frequencies and percentages. As part of the receiver operating characteristic (ROC) curve analysis, the analysis was done to identify the best cutoff value of the HALP score to predict survival. The 2x2 contingency table was used to calculate Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy. The age, gender, duration of carcinoma, hepatitis, tumor grade, smoking, alcohol consumptions, hypertension, diabetes, and anemia were stratified. The analysis of the sensitivity and specificity of a positive result, PPV, NPV, and diagnostic accuracy of the HALP score were estimated in each stratum with the primary outcome as the reference standard.

Ethical Considerations

The study was conducted with an ethical approval of the institutional review board of Jinnah Hospital, Lahore. All the participants provided informed consent in writing prior to being included in the study. Patient information confidentiality was also taken seriously and any data were anonymized before analysis. The research work was carried out in line with the ethics of the Declaration of Helsinki.

RESULTS

Demographic and Clinical Characteristics

The mean age of patients was 52.4 years old with a standard deviation of 9.8, which showed that most of the patients were in middle age. A larger percentage of males (63.6%), was noted than females (36.4%). The most prevalent etiological agent was hepatitis C infection (57.1% of patients), and then hepatitis B (28.1%). Most patients were grade II carcinoma (47.5%), but there was a significant percentage of advanced Grade III (29.9%). Comorbidity was also very common, including hypertension (47.0%), diabetes (41.0%), and anemia (51.2%), thus indicating a significant systemic illness load to the study group (Table 1).

Table 1: Demographic and Clinical Characteristics of Study Participants (n = 217)

Variable	Category	Frequency (n)	Percentage (%)
Age (years)	Mean ± SD	52.4 ± 9.8	—
Gender	Male	138	63.6
	Female	79	36.4
Duration of Carcinoma (months)	Mean ± SD	7.6 ± 3.2	—
Hepatitis Status	Hepatitis B	61	28.1
	Hepatitis C	124	57.1
	None	32	14.7
Grade of Carcinoma	Grade I	49	22.6
	Grade II	103	47.5
	Grade III	65	29.9
Smoking (>5 pack-years)	Yes	96	44.2
	No	121	55.8
Alcohol Intake (>20 ml/day)	Yes	68	31.3
	No	149	68.7

Hypertension	Yes	102	47.0
	No	115	53.0
Diabetes Mellitus	Yes	89	41.0
	No	128	59.0
Anemia (Hb <10 g/dl)	Yes	111	51.2
	No	106	48.8

Laboratory Findings and Mortality Outcomes

The mean hemoglobin level was 10.8 ± 1.9 g/dL, consistent with the high prevalence of anemia observed clinically. Serum albumin levels were relatively low (3.2 ± 0.6 g/dL), indicating compromised nutritional and hepatic synthetic function. The mean HALP score was calculated as 35.6 ± 14.7, demonstrating substantial variability among patients, which reflects heterogeneity in inflammatory and nutritional status (Table 2).

Table 2: Laboratory Findings Including HALP Score (n = 217)

Variable	Mean ± SD
Hemoglobin (g/dL)	10.8 ± 1.9
Albumin (g/dL)	3.2 ± 0.6
Lymphocyte Count ($\times 10^9$/L)	1.4 ± 0.5
Platelet Count ($\times 10^9$/L)	210.5 ± 64.3
HALP Score	35.6 ± 14.7

The mortality was observed in 33.2% of patients during the follow-up period and 66.8% of patients were alive up to three months of the follow-up. This shows that there was a significant short-term mortality cost in this cohort of patients with hepatocellular carcinoma (Table 3).

Table 3: Mortality Outcomes (n = 217)

Outcome	Frequency (n)	Percentage (%)
Mortality (Yes)	72	33.2
Mortality (No)	145	66.8

The age ($p = 0.002$), duration of carcinoma ($p = 0.001$), and HALP score ($p < 0.001$) were non-normally distributed. Thus, the use of non-parametric statistical methods was deemed suitable in making additional inferential statements (Table 4).

Table 4: Normality Testing Using Shapiro–Wilk Test

Variable	W Statistic	p-value
Age	0.972	0.002
Duration of Carcinoma	0.964	0.001
HALP Score	0.951	<0.001

The HALP score was statistically significantly correlated with age ($r = -0.21$, $p = 0.002$), carcinoma duration ($r = -0.26$, $p < 0.001$) and tumor grade ($r = -0.31$, $p < 0.001$), which indicated that the higher the HALP scores, the less advanced the disease in the characterized state. On the other hand, positive correlations were high with hemoglobin ($r = 0.48$, $p < 0.001$) and albumin ($r = 0.52$, $p < 0.001$), which supports the idea that HALP is a variety of nutritional and physiological outcomes (Table 5).

Table 5: Correlation of HALP Score with Clinical Variables

Variable	Correlation Coefficient (r)	p-value
Age	-0.21	0.002
Duration of Carcinoma	-0.26	<0.001
Grade of Carcinoma	-0.31	<0.001
Hemoglobin	0.48	<0.001
Albumin	0.52	<0.001

ROC and Contingency Analysis Outcomes

Analysis of ROC curves showed that a HALP cutoff value of 30 is the most appropriate in predicting mortality with an area under the curve (AUC) of 0.781 (95% CI: 0.719-0.842, $p < 0.001$), which represents good predictive ability. The sensitivity identified by the HALP score at this threshold was 70.8% (95% CI: 59.0-80.9) which indicates that it is able to correctly identify the dead. The specificity was 76.6% (95% CI: 68.8-83.2), which indicated a good ability to classify correctly survivors. The positive predictive value (PPV) of 60.0% indicates that there is a moderate accuracy of predicting mortality among patients whose HALP scores are low and the negative predictive value (NPV) of 84.1% is a high chance of survival in patients whose HALP is 30 or above. The total diagnostic accuracy amounted to 74.2% (95% CI: 67.9-79.8), which proves the strength of HALP as a prognostic

predictor. As shown by the contingency analysis, a statistically significant correlation between the category of the HALP and mortality was observed ($p < 0.001$) with 60.0% of patients suffering mortality where the HALP was less than 30, and 15.9% where the HALP was 30 or above (Table 6-7).

Table 6: Association Between HALP Score Categories and Mortality

HALP Score Category	Mortality (Yes) n (%)	Mortality (No) n (%)	Total (n)	p-value
Low HALP (<30)	51 (60.0%)	34 (40.0%)	85	<0.001
High HALP (≥30)	21 (15.9%)	111 (84.1%)	132	—
Total	72 (33.2%)	145 (66.8%)	217	—

Table 7: Diagnostic Performance of HALP Score for Predicting Mortality Using ROC Curve Analysis (Cutoff = 30)

Diagnostic Indicator	Estimate (%)	95% Confidence Interval
Sensitivity	70.8	59.0 – 80.9
Specificity	76.6	68.8 – 83.2
Positive Predictive Value (PPV)	60.0	48.7 – 70.4
Negative Predictive Value (NPV)	84.1	76.9 – 89.5
Overall Diagnostic Accuracy	74.2	67.9 – 79.8
Area Under Curve (AUC)	0.781	0.719 – 0.842
p-value (ROC)	<0.001	—

DISCUSSION

The major objective of the research was to establish the predictive value of the HALP score in predicting survival in patients with hepatocellular carcinoma. The results showed that the mean HALP score was 35.6 ±14.7 with a mortality rate of 33.2% at three months, shows a significant variability in prognostic outcomes among the cohort. An important inverse correlation was established between HALP score and mortality whereby patients whose HALP 30 below had significantly higher death rates (70.8%) than patients whose HALP 30 above had significantly lower death rates (15.9%). These results are also in line with those of Liu et al., (2024), who indicated a hazard ratio of 2.3 to mortality of low HALP groups in a cohort of 808 patients with HCC (Liu et al., 2024). In the same way, Hashimoto et al., (2024) noted that lower scores on HALP led to poor survival in hepatocellular carcinoma among 685 patients when compared to higher scores ($p < 0.001$). The existing research supports the idea according to which HALP is a combined biomarker of both systemic inflammation and nutritional reserve (Hashimoto et al., 2024). Statistical power that is evident in predictive capacity of ROC also contributes to its clinical usefulness. Hence, HALP could be an effective, yet affordable, prognostic factor in the management of HCC.

The demographic characteristics of the study population indicated that the mean age of the population was 52.4 ± 9.8 years, and the population was mostly male (63.6%), which is in line with the epidemiological patterns of HCC distribution across the globe. Hepatitis C was detected in 57.1% of the patients, which is very high as compared to hepatitis B (28.1), which reflects the patterns of the disease in the region, South Asia. This can be compared to the results of Jiang et al., (2024), who found that HCV was prevalent in HCC patients in Pakistan (60%). Comorbidities like hypertension (47.0%), diabetes (41.0%), and others, also highlighted the metabolic load that was causing the development of the disease. It is interesting to note that 51.2% of patients had anemia, which was associated with low HALP scores and outcomes. Past research has shown that anemia is associated with a significant effect on tumor hypoxia and survival, where Toshida et al., (2023) reported a 65% higher risk of death in 542 Japanese patients of hepatocellular carcinoma. The association of these risk factors highlights the multifactorial HCC prognosis (Toshida et al., 2023). These results highlight the need to incorporate clinical and laboratory parameters in prognostic studies.

The lab results showed the mean hemoglobin level at 10.8 ± 1.9 g/dL and the mean of albumin at 3.2 ± 0.6 g/dL, which indicated impaired physiological conditions. The HALP score had a strong positive correlation with hemoglobin ($r = 0.48$, $p < 0.001$) and albumin ($r = 0.52$, $p < 0.001$) which supports its biological plausibility. Zhang et al., (2023) also proved that the correlation coefficients of HALP and nutritional markers are greater than 0.45 in a cohort of 339 patients of tongue squamous cell carcinoma (Zhang et al., 2023). Also, lymphocyte counts (1.4 ± 0.5 $\times 10^9$/L) indicated immune competence, which is important in the surveillance of tumor. A low level of lymphocytes has been linked to poor cytotoxic response, as indicated by Templeton et al. (2014) in a meta-analysis study carried out on 209 patients of colorectal liver metastases. Platelet counts (210.5 ± 64.3 $\times 10^9$/L) also were used as part of the HALP

score, and high levels were associated with tumor angiogenesis (Okazaki et al., 2025). The combination of all these variables in HALP has given a multidimensional evaluation of the patient status. Therefore, the laboratory results confirm that HALP is an overall prognostic index.

The study also found that HALP score had significant negative correlations with clinical severity indicators, such as tumor grade ($r = -0.31$, $p < 0.001$) and duration of carcinoma ($r = -0.26$, $p < 0.001$). Grade III patients had significantly lower ratings in HALP than Grade I and II. The trend follows the data provided by Zhai et al., (2021), who also found the values of HALP were significantly lower in cancers at an advanced stage ($p < 0.001$) among 238 patients of lung cancer. The negative correlation implies that the decreasing scores in HALP can indicate an increasing tumor burden and the general deterioration of the system (Zhai et al., 2021). Moreover, the correlation with age is negatively correlated ($r = -0.21$, $p = 0.002$), which suggests that older patients have lower physiological reserve. These outcomes are in line with Jiang et al., (2024) who stressed the importance of host factors in the prognosis of HCC. The significant statistical values of the multiple variables indicate the strength of HALP as an integrative marker. As a result, HALP can be used as an alternative predictor of disease severity (Jiang et al., 2024).

The mortality analysis showed that of the 217 patients, 72 patients (33.2%) died within the follow-up period with a disproportional distribution in low HALP scores. In particular, the number of deaths in the HALP <30 group amounted to 51 as opposed to 21 in the ≥30 group, which also produced a very significant association ($p < 0.001$). This observation is similar to that of Ustaoglu et al., (2024) who observed that low HALP patients experienced a 2.5 times higher mortality in a cohort of 204 subjects. The predictive accuracy of HALP was further proved by the sensitivity and specificity obtained during the ROC analysis (Ustaoglu et al., 2024). The significant difference in survival emphasizes the clinical importance of the timely risk stratification. Moreover, the results are consistent with Li et al., (2024), who emphasized that HALP is a better predictor, in contrast to the traditional indices like NLR. The discrimination between clinical outcomes of survival makes the HALP useful in clinical decision making. As such, HALP shows better prognostic performance in HCC (Li et al., 2024).

In spite of the strengths, this research has a few limitations, which must be admitted. The cross-sectional design prevents laying down causal relationships between long-term survival outcomes and HALP score. The follow-up period of three months might not comprehensively represent the prognostic course of hepatocellular carcinoma, which in most cases takes a long period in terms of observation. Moreover, non-probability purposive sampling can introduce elements of selection bias, which can be a problem as far as the generalizability of the results is concerned. As a single-center study, using a tertiary care hospital, the findings may not be applicable to the general population. Some of the possible confounders, including treatment heterogeneity, and the severity of underlying liver function scores, were not controlled in detail. Moreover, no external validation undermines the generalizability of the retrieved values of HALP cutoffs. These findings should be followed up by multicenter, longitudinal studies including large sample sizes in the future to validate them.

Conclusion

This research found that the HALP score is a substantial and clinically useful prognostic biomarker of predicting short-term survival in patients with hepatocellular carcinoma. The mortality rate of patients in the low HALP group was significantly higher with 70.8% of patients dying whereas only 15.9% of the patients with high scores had their mortality rate. The HALP score demonstrated strong associations with the important clinical and laboratory parameters, such as tumor grade ($r = -0.31$, $p = 0.001$) and albumin levels ($r = 0.52$, $p = 0.001$), which supports its multidimensional prognostic usefulness. Considering the simplicity of the tool, its cost-efficiency, and the need to be based on readily-obtained laboratory parameters, HALP can be a viable resource in risk stratification in resource-constrained environments. Its application in regular clinical examination is supported by the findings to inform therapeutic decision-making and prognostic analysis. Altogether, HALP is an effective predictor of the interaction between systemic inflammation, nutritional status, and tumor evolution in hepatocellular carcinoma.

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