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Original research article

UTILITY OF HALP SCORE IN PREDICTING MORTALITY IN ACUTE ISCHEMIC STROKE

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Abstract: *Acute ischemic stroke (AIS) poses significant mortality and morbidity risks. The HALP score, integrating hemoglobin, albumin, lymphocytes, and platelets, has been proposed as a potential marker for predicting outcomes in AIS patients. This study evaluates the predictive utility of the HALP score for mortality and recurrence in these patients.* ***Objective:*** *To assess the predictive value of the HALP score at admission for mortality and recurrent stroke within one and six months post-admission.* ***Methods:*** *In this prospective hospital-based cohort study, 1206 patients presenting with AIS were included. Patients were stratified into tertiles based on their HALP score at admission. The study accounted for age, gender, medical history, and NIHSS scores at baseline.* ***Results:*** *The cohort's mean age was 60.55 years, with 33.8% female. Patients with lower HALP scores showed worse outcomes, with 1.5% lost to follow-up and 1.3% experiencing poor outcomes at one month. At six months, 9.2% were lost to follow-up, and 8.8% had poor outcomes. Higher HALP scores correlated with reduced risk of adverse outcomes, with adjusted hazard ratios of 0.8 (95% CI: 0.05–0.19) at one month and 0.21 (95% CI: 0.13–0.34) at six months. Sensitivity and specificity were 16.1% and 25.4%, respectively, at one month and 24.6% and 36.4% at six months.* ***Conclusion:*** *The HALP score at admission significantly predicts mortality and recurrent stroke within the first six months post-AIS, supporting its integration into initial assessment protocols.*

Keywords: Acute ischemic stroke, cerebrovascular accidents, HALP score, hypertension, stroke cognitive impairment.

Introduction

Stroke remains a leading cause of mortality and morbidity globally, manifesting primarily as either ischemic or hemorrhagic. Ischemic strokes, the more prevalent type, necessitates effective prognostic indicators for the early identification of patients at high risk of adverse outcomes, thereby enhancing secondary prevention strategies. Prognostic factors such as inflammation, abnormal coagulation, and poor nutritional status have been recognised as significant predictors of poor outcomes in these patients (1, 2).

The risk of stroke is exacerbated not only in the acute phase but also over the long term in various pro-inflammatory conditions, indicating that the association with stroke risk may stem more from a generalised inflammatory response rather than from specific conditions (3). The Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) score, which encompasses indicators of nutritional status and systemic inflammation, has been suggested as a useful composite marker. This score includes hypoalbuminemia and anaemia, which reflect nutritional deficiencies potentially leading to cerebrovascular events. At the same time, lymphocyte levels indicate post-stroke inflammatory responses, and platelets contribute to atherosclerosis, a known risk factor for stroke (4).

Significant research has underscored the importance of these components. David et al. (2010) highlighted that anaemia, defined by WHO criteria, was prevalent in stroke patients and was associated with a heightened risk of poor outcomes across different stroke types, irrespective of gender. This association persisted even when adjusting for confounding factors such as age, pre-existing disabilities, and comorbid conditions (5). Similarly, Mayda-Domac et al. (2010) identified mean platelet volume and platelet count as early and significant prognostic markers for ischemic stroke outcomes, further validating the relevance of these blood components in stroke pathology (6).

More recently, Xu et al. (2022) (7) reported that a low HALP score at admission correlates with an increased risk of recurrent strokes and early onset of post-stroke cognitive impairments, highlighting the score's potential in predicting long-term outcomes (8). Despite these advances, the direct association between HALP scores and overall mortality and stroke recurrence within critical periods such as 90 days and one year remains less understood. Therefore, our study aims to elucidate the predictive value of the HALP score concerning these outcomes in a local cohort, proposing that a low score at admission might serve as a potent indicator of heightened risk for recurrent stroke and mortality in patients with acute ischemic stroke.

Methodology

The study was designed as a prospective, hospital-based cohort investigation into the role of the HALP score in predicting the outcomes of patients presenting with acute ischemic stroke. The WHO calculator facilitated the determination of an adequate sample size to ensure statistical validity, culminating in 1206 participants, stratified into groups of 201 and 1005 for exposed and unexposed individuals, respectively. This sample size was calculated to detect a risk ratio of 5 with a 95% confidence level and 90% power, assuming a two-sided significance level of 0.05 (9).

Eligibility for the study was strictly defined. Included were patients who presented with symptoms of acute ischemic

stroke within the first 24 hours, with diagnoses confirmed based on WHO criteria (10). Excluded from the study were patients with active or chronic inflammatory diseases, neoplastic hematologic disorders, those undergoing treatment with immunosuppressant drugs, or those who had experienced major trauma or surgery within the previous three months. Additional exclusions were applied for severe hepatic or renal dysfunction or those lacking complete blood cell count data. These criteria were intended to mitigate confounding variables and ensure the integrity of the study's findings.

Data collection commenced with obtaining informed consent from the participants or their designated relatives. Continuous variables exhibiting normal distribution were expressed as means with standard deviations, while those with skewed distributions were reported as medians accompanied by interquartile ranges. Categorical variables were detailed using frequencies and percentages. Patients were subsequently categorised based on the tertiles of their baseline HALP scores.

The study utilised Kaplan–Meier curves to estimate the cumulative incidence of adverse outcomes across different levels of baseline HALP scores, with differences assessed using the log-rank test. The relationship between HALP scores and outcomes was further evaluated using multivariate Cox proportional hazards models, which calculated both unadjusted and adjusted hazard ratios and their 95% confidence intervals for higher HALP score groups and per one-standard-deviation increase in HALP score.

Receiver operating characteristic (ROC) curve analysis was employed to determine the optimal cutoff values for the HALP score, and the model's predictive capability was enhanced by including conventional risk factors identified from prior research as covariates. The utility of the HALP score in improving outcome prediction over conventional models was quantified using C statistics, net reclassification improvement (NRI), and integrated discrimination improvement (IDI). The shape of the association between HALP scores and outcomes was further explored by applying restricted cubic splines, with knots positioned at the fifth, 35th, 65th, and 95th percentiles of the HALP scores.

Statistical analyses were conducted using IBM SPSS software, version 29.0.2.0, with a two-tailed P-value of less than 0.05 set as the threshold for statistical significance. This comprehensive methodological framework was crafted to ensure robust and reliable results that could potentially inform clinical practice and improve the management of ischemic stroke patients.

Results

The average age of the 1206 patients analysed was 60.55, with 408 female participants. The study divided the population into two groups based on their HALP scores. Patients in the lower HALP score tertile tended to be older, more likely to be female, and more frequently presented with atrial fibrillation. They also exhibited lower levels of lymphocytes, hemoglobin, and albumin, higher platelet counts, more frequent occurrence of cardioembolic stroke, and elevated baseline NIHSS scores.

During the initial month of follow-up, 18 patients (1.5%) were lost, and 15 patients (1.3%) experienced poor outcomes. By the six-month mark, the number of patients lost to follow-up increased to 110 (9.2%), and 106 patients (8.8%) had suffered poor outcomes. Kaplan–Meier analysis revealed that those in the lowest tertile of the HALP score had a significantly higher cumulative incidence of poor outcomes both at one month and six months.

Multivariate analysis, controlling for factors such as age, gender, history of hypertension, diabetes, ischemic stroke, coronary heart disease, atrial fibrillation, smoking status, timing of blood sampling, IV thrombolysis treatment, and baseline NIHSS score, showed that higher HALP scores were consistently associated with a decreased risk of poor outcomes. Specifically, for the highest versus lowest tertile of HALP score, the adjusted hazard ratios for poor outcomes at one month and six months were 0.8 (95% confidence interval: 0.05–0.19) and 0.21 (95% confidence interval: 0.13–0.34), respectively. Additionally, each one-standard-deviation increase in HALP score was correlated with decreased risks of poor outcomes at both follow-up intervals.

The predictive accuracy of the HALP score for poor outcomes at one month showed a sensitivity of 16.1% and a specificity of 25.4%, with a C statistic of 0.69 (95% confidence interval: 0.66–0.71, p-value < 0.001). At six months, the sensitivity improved to 24.6% and the specificity to 36.4%, with a C statistic of 0.65 (95% confidence interval: 0.62–0.67, p-value < 0.001). These findings underscore the potential of the HALP score as a predictor of prognosis in patients with acute ischemic stroke.

variable	overall	Tertile 1 < 36.5	Tertile 2 >54.5	P value
Patients (n)	1206	1005	201	
Age year mean SD	60.55 ± 12.45	63.20 ± 12.45	58.20 ± 12.48	< 0.001
Female, n (%)	408 (30.5)	179 (40.2)	106 (23.8)	< 0.001
smoking	585 (43.8)	198 (44.5)	197 (44.2)	0.923
Hypertension	809 (60.5)	274 (61.6)	267 (59.9)	0.602
Diabetes	311 (23.3)	97 (21.8)	117 (26.2)	0.11
Coronary heart disease	159 (11.9)	61 (13.7)	50 (11.2)	0.250
Atrial fibrillation	125 (9.3)	64 (14.4)	25 (5.6)	<
Baseline NIHSS	3 (2-6)	4 (2-8)	3 (1-5)	0.001
Hemoglobin, g/l, median (IQR)	138 (128–148)	132 (120–143)	144 (134–153	0.001
Albumin, g/l, median (IQR)	40.9 (38.5–43.1)	39.6 (37.4–42.1)	41.8 (39.6–44.1)	0.001

Lymphocyte, 109 /l, median (IQR)	1.7 (1.3–2.2)	1.2 (0.94–1.5)	2.2 (1.9–2.6)	0.001
Platelet, 109 /l, median (IQR))	207 (173–250)	234 (192–279)	186 (159–218)	0.001
Large artery atherosclerosis	511 (38.2)	164	(177 (39.7)36.9	0.38
Stroke of undetermined etiology	277 (20.7)	83 (18.7)	104 (23.3)	0.086

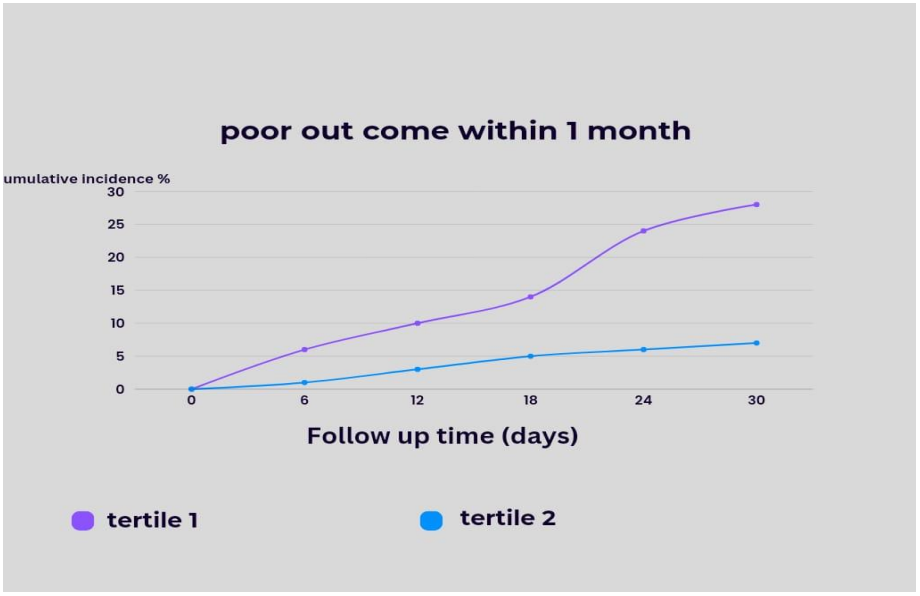

FIGURE 1: PATIENT FLOW CHART OF COHORT

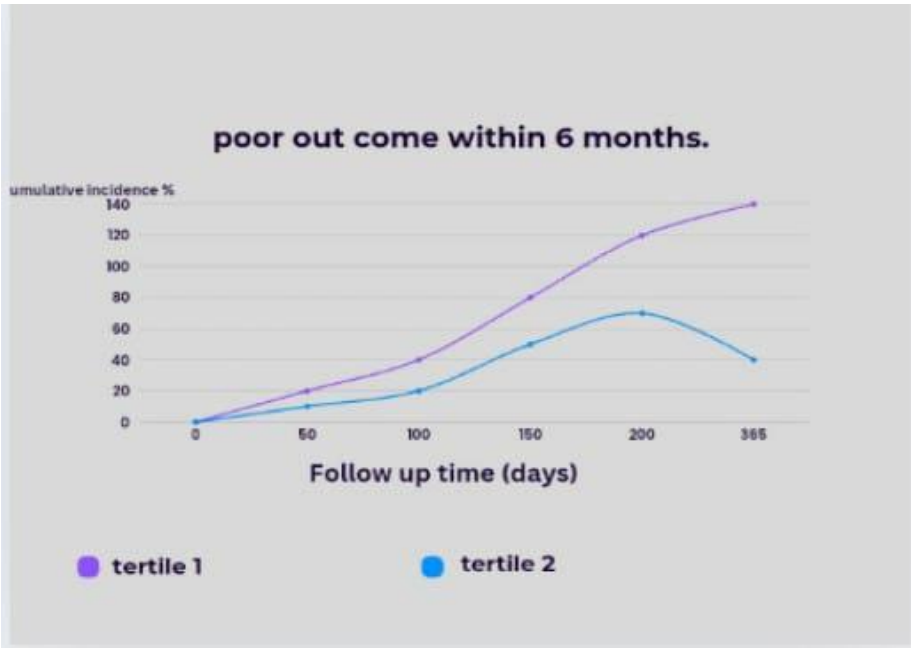

FIGURE 2: curves of cumulative incidence (%) of the poor outcome by tertiles of haemoglobin, albumin, lymphocyte, and platelet (HALP) score at 1 month and 6 months follow-up.

Discussion

In this prospective cohort study, the predictive value of the HALP score in patients with acute ischemic stroke (AIS) at admission was examined. Findings revealed that higher HALP scores are associated with a reduced risk of recurrent stroke and death within both one and six months post-admission. The HALP score incorporates measures of hemoglobin, albumin, lymphocytes, and platelets, offering a composite index that may reflect patients' inflammatory and nutritional status, which are critical factors in the progression of ischemic stroke.

AIS's pathophysiology involves cerebral ischemia and inflammation, leading to neurological deficits as ischemic brain tissue activates leukocytes and promotes migration through pro-inflammatory chemokines. The inflammatory response further triggers thrombosis, where platelets are key participants (11-13). Previous research has underscored the predictive value of individual components of the HALP score. For instance, lower lymphocyte counts have been associated with larger infarct volumes and poorer outcomes, while higher haemoglobin levels have been linked with carotid atherosclerosis, an important stroke risk factor (11-18). Moreover, serum albumin levels indicate nutritional status and correlate with the severity of inflammation and overall illness in acute settings (16, 17, 19-23).

This study contributes to understanding AIS by integrating these individual indicators into the HALP score, providing a cost-effective, straightforward parameter for assessing patients' inflammatory and nutritional status. Such an assessment can be crucial in tailoring patient-specific management strategies immediately upon admission.

Despite its insights, the study faces limitations, including its design as a single-centre cohort, which might affect the generalizability of the findings to broader populations. Additionally, while the study adjusted for several confounders, residual confounding cannot be completely ruled out. The strengths of the study include its prospective design and the robust statistical methods used to evaluate the associations between the HALP score and stroke outcomes, enhancing the reliability of the findings.

Recent studies on the HALP score in other populations, particularly in patients with multiple tumours, have shown its effectiveness as a prognostic indicator, thus supporting the validity of this study's results (10-12). Furthermore, this study's findings highlight the potential of the HALP score as a predictive tool for clinicians, helping them to assess the severity of a patient's condition quickly and efficiently and make more informed decisions regarding treatment strategies. These contributions underscore the importance of the HALP score in the clinical assessment of patients with AIS, suggesting that further research in diverse settings is warranted to confirm these findings and expand on their implications.

Conclusion

This study highlights the association between the HALP score at admission and reduced risk of recurrent stroke and death within one and six months in patients with acute ischemic stroke. Despite its insights, the study faces limitations, including potential selection bias from its single-centre design, lack of consideration for concomitant medications, and absence of longitudinal HALP score analysis. Moreover, the short duration of follow-up may obscure long-term outcomes. Further multicenter studies are needed to validate these findings and fully integrate the HALP score into clinical practice as a predictive tool.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate.

It is approved by the department concerned. (IRBEC-TCH-0394/22)

Consent for publication

Approved

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Conflict of interest

The authors declared an absence of conflict of interest.

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