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Original Article

Biochemistry Section

HALP Score as a Composite Immunonutritional Marker in Chronic Kidney Disease: A Cross-sectional Analysis Across Albuminuria Stages

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ABSTRACT

Introduction: Chronic Kidney Disease (CKD) contributes to inflammation and malnutrition thereby increasing the risk of mortality. The Haemoglobin, Albumin, Lymphocyte, and Platelet (HALP) score is a novel and comprehensive immunonutritional marker offering complete picture on both inflammation and nutrition. The HALP score is explored in various malignancies, but its novelty in CKD is least assessed.

Aim: The present study was aimed to evaluate HALP scores across albuminuria-based CKD groups and assess its correlations with established inflammatory markers like Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR), thereby assessing the disease severity and guide therapeutic interventions.

Materials and Methods: The present cross-sectional study was conducted between June 2024 to June 2025 at the Adichunchanagiri Hospital and research centre, a tertiary care teaching hospital in Karnataka, India. Study included 150 CKD subjects in three Urine Albumin-Creatinine Ratio (UACR)-based groups (n=50 each): G1 (<30 mg/g), G2 (30-300 mg/g), G3 (>300 mg/g). HALP score was calculated using haemoglobin, albumin, lymphocyte and platelet counts. eGFR was calculated using Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) 2021 equation. Data was analysed using Analysis of Variance (ANOVA), Pearsons's correlation and Receiver Operating Characteristic (ROC) curve analysis. The p-value of <0.05 was considered statistically significant.

Results: The present study subjects showed a mean age of 44.44±16.82 years in group 1, 43.65±12.51 years in group 2 and 55.46±16.96 years in group 3 which was significant at p-value 0.000353. The gender distribution was 27 (54%) males and 23 (46%) females in group 1, 31 (62%) males and 19 (38%) females in group 2, and 39 (78%) males and 11 (22%) females in group 3. HALP correlated negatively with NLR (G1 r=- 0.6125, p<0.00001), G2 (r=- 0.5277, p=0.000084), and G3 (r=- 0.5898, p<0.00001) and PLR in G1 (r=- 0.770, p<0.00001), G2 (r=- 0.7221, p<0.00001) and G3 (r=- 0.3119, p=0.0279). ROC of HALP showed AUC=0.816, cut-off=28.79, sensitivity=86.7%, specificity=67.6%.

Conclusion: The immunonutritional status of CKD patients decreases as the stage advances. HALP score being a straightforward and composite marker can be incorporated in routine clinical practice for early risk assessment, monitoring and also for therapeutic and nutritional interventions.

Keywords: Haemoglobin albumin lymphocyte platelet score, Neutrophil-to-Lymphocyte ratio, Platelet-to-lymphocyte ratio, Renal impairment, Systemic inflammation

INTRODUCTION

The CKD is characterised by a gradual decline in the renal function [1] accompanied by metabolic derangements that often lead to malnutrition and a heightened inflammatory state. These disturbances weaken immune function and increase susceptibility to infections and long-term complications [2]. To evaluate the inflammatory status, indices like ratio of NLR, PLR [3], and the systemic immune-inflammation index are being used. Likewise, parameters including haemoglobin, serum albumin and Body Mass Index (BMI) provide insight into nutritional reserve. Although each parameter offers partial information, none alone gives a comprehensive picture of immunonutritional health [4].

Although Estimated Glomerular Filtration Rate (eGFR) is commonly used for staging CKD, albuminuria is considered as an important indicator of renal damage and disease progression. It is also associated with systemic inflammation and nutritional status [5]. Hence, categorisation based on albuminuria stages was considered more appropriate to evaluate the relation between immunonutritional status and severity of renal injury in CKD patients. The HALP score [6] is recently introduced as a composite score that incorporates key haematological and nutritional variables into single measure proving it as a reliable prognostic indicator which provides the overall picture of inflammation and nutritional status of the patients [4]. Initially, explored in oncology for its prognostic value, HALP score has subsequently demonstrated its relevance in chronic and acute conditions also. Emerging research suggests that low HALP scores are associated with higher morbidity, poorer outcomes, greater mortality risk in various populations, including those on haemodialysis [7].

Although, HALP score has gained relevance as a prognostic biomarker in several malignant and acute conditions [8], its significance in CKD, other than End-Stage Renal Disease (ESRD) is not well established [9]. There is a paucity of data regarding its relevance across earlier stages of CKD. Therefore, the present study aimed to evaluate HALP scores across different CKD stages and also to assess its correlation with inflammatory markers (NLR, PLR). To the best of the authors' knowledge, this was one of the first studies to evaluate HALP across albuminuria-based CKD groups and also correlate with inflammatory indices like NLR and PLR.

MATERIALS AND METHODS

The present cross-sectional study was conducted between June 2024 to June 2025 at the Adichunchanagiri Hospital and research centre, a tertiary care teaching hospital in Karnataka, India. Ethical

clearance was obtained by the institutional ethical committee (No. AIMS/IEC/024/2022). The purpose and aim of the study were explained clearly to all participants before being included in the present study.

Inclusion criteria: After obtaining written informed consent, a total of 150 adult patients (≥18 years), diagnosed with CKD were enrolled. The diagnosis of CKD was confirmed according to the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, defined as an eGFR <60 mL/min/1.73 m^2 for ≥ three months and/or markers of kidney damage such as albuminuria [10,11].

Exclusion criteria: Subjects with acute infections, recent hospitalisation, chronic inflammation, autoimmune diseases, malignancies, pregnancy, recent blood transfusions (within 3 months), active bleeding, haematological disorders, alcoholics, unwillingness to participate in the present study were excluded.

Sample size calculation: The sample size was calculated based on feasibility and availability of eligible participants during the present study period. Participants were recruited using consecutive sampling. Each group consisted of 50 participants (n=50 per group).

Study Procedure

Based on eGFR, the CKD stages are classified into five stages and based on albuminuria it is categorised into three stages [Table/Fig-1] [10,11]. The present study had grouped the participants based on albuminuria criteria.

Category	24h Albuminuria mg/24 hrs	A/C Ratio mg/g	Classification
A1	<30	<30	Normal
A2	30-300	30-300	Moderate
A3	>300	>300	Severe

[Table/Fig-1]: CKD Stages/Category based on albuminuria; A/C ratio-albumin/creatinine ratio in a urine sample.

A1 (Group 1), A2 (Group 2), and A3 (Group 3)

- **Group 1:** Participants with normal to mild albuminuria.
- **Group 2:** Participants with moderate albuminuria.
- **Group 3:** Participants with severe albuminuria.

Although albuminuria criteria were used for grouping, eGFR values were recorded for all participants to assess renal function status.

The demographic data like age, gender, body weight, height and clinical history were documented using a standardised proforma. A 3 mL of random blood sample was collected in an Ethylenediaminetetraacetic acid (EDTA) tube under aseptic conditions for analysis of haematological parameters. Additionally, 3 mL of random blood was collected in clot activator tube for the analysis of biochemical parameters. All the parameters were analysed at the Central Diagnostic Laboratory of Adichunchanagiri Hospital following the standard operating procedures and quality assurance.

The following parameter was assessed:

- Complete Blood Count (CBC) parameters including haemoglobin, total leukocyte count, platelet count and lymphocyte count were measured using an automated haematology analyser based on the electrical impedance and flow cytometry principle. The reference ranges of haemoglobin for female is 120-160 g/L and males is 130-170 g/L, total leukocyte counts is 4,000-11000 cells/ µL, platelet count is 1.5-4.5 x 105/µL, and lymphocyte is 20-40% [12].
- Serum albumin was estimated by bromocresol green method which is a colorimetric end-point assay using a fully auto analyser - Meril Auto quant 400. The reference range for serum albumin is 3.5-5.0 g/dL [13].
- Serum C-Reactive Protein (CRP) was estimated using nephelometry method on a Vitros fully auto analyser. The reference range being <1 mg/L [13].

Calculations:

1. HALP Score was calculated using the formula, "HALP={Haemoglobin (g/L)×Albumin (g/L) × Lymphocytes (/L)} divided by Platelets (/L)" [14].
2. eGFR was calculated using CKD-EPI 2021 formula, eGFR=142×min (standardised Scr/K, 1)α×max (standardised Scr/K, 1) $^{-1.200}$×0.9938^{Age}×1.012 (if female) , where, Scr (Serum creatinine) =mg/dL, K=0.7 (females) or 0.9 (males) , α=-0.241 (females) or -0.302 (males), min=minimum of Scr/K or 1, max=indicates the maximum of Scr/K or 1 [15].
3. NLR ratio=Absolute neutrophil count/Absolute lymphocyte count [16] cut-off=3.52
4. PLR=Absolute platelet count/Absolute lymphocyte count [16] cut-off=133.64
5. BMI=weight (kilograms) divided by height squared (meters) [17].

STATISTICAL ANALYSIS

To analyse the data, Statistical Package for the Social Sciences (SPSS) version 31.0 software for Windows was used. Continuous variables were expressed as mean and Standard Deviation (SD). ANOVA was used to compare the variables among the three groups, with p-value <0.05 considered significant. The relationship between HALP, NLR and PLR was assessed using Pearson's correlation coefficient within each group. ROC curves were plotted for HALP, NLR and PLR using the combined cohort of 150 subjects across all albuminuria-based groups. Stage wise ROC was not performed as the primary objective was to evaluate the overall discriminative ability of these markers and sub group sample size would have been insufficient to yield the values of sensitivity, specificity and optimal cut-offs.

RESULTS

In present study, males constituted a higher proportion in all three groups when compared to females. The prevalence of diabetes was n=15 (30%) in group 1, n=19 (38%) in group 2 and n=18 (36%) in group 3. Whereas the prevalence of hypertension increased progressively from group 1 to group 3, with highest in group 3, n=34 (68%) [Table/Fig-2].

Parameters	Group 1	Group 2	Group 3
Male N (%)	27 (54 %)	31 (62 %)	39 (78 %)
Female N (%)	23 (46 %)	19(38 %)	11 (22 %)
Diabetes N (%)	15 (30%)	19 (38%)	18 (36%)
Hypertension N (%)	10 (20%)	18 (36%)	34 (68%)

[Table/Fig-2]: Gender distribution and prevalence of diabetes and hypertension among three groups.

[Table/Fig-3] shows the comparison of biochemical and haematological parameters between three groups. Subjects of age in group 3 were older compared to group 1 and 2. Renal parameters like blood urea, serum creatinine and 24 hours urinary protein were markedly elevated in group 3 (p<0.001). In contrast, parameters such as serum albumin, haemoglobin, BMI, and HALP score significantly reduced in group 3. Inflammatory markers including CRP and NLR showed a progressive increase across the groups, while random plasma glucose and PLR did not show a statistically significant difference. ANOVA showed a statistically significant difference in all the above parameters except for Random plasma glucose and PLR.

[Table/Fig-4] shows Tukey's post-hoc analysis which was done only for NLR, PLR and HALP as these were the main variables of interest. As shown in [Table/Fig-4], NLR and HALP scores showed a significant difference across groups (p<0.001), with post-hoc

Parameters	Group 1	Group 2	Group 3	p-value
	Mean±SD			
Age (years)	44.44±16.82	43.65±12.51	55.46±16.96	<0.001*
Random plasma glucose (mg/dL)	173.16±52.11	161.34±36.96	176.94±47.59	0.21
Blood Urea (mg/dL)	26.59±6.70	26.75±6.76	97.89±40.75	<0.001*
Serum Creatinine (mg/dL)	0.83±0.10	1.14±0.18	7.72±3.75	<0.001*
Serum Albumin(g/L)	39.84±3.18	37.02±2.59	33.34±7.15	<0.001*
Haemoglobin (g/L)	137±17.47	144.60±22.85	99.72±15.21	<0.001*
Lymphocytes × 10^9/L	2.55±1.03	2.09±0.54	1.89±0.72	<0.001*
Neutrophils× 10^9/L	4.83±1.94	5.38±1.87	6.38±1.11	<0.001*
Platelets(/L)	293.62±95.61	249.92±51.09	245.84±96.96	<0.001*
C-Reactive Protein (CRP) (mg/L)	0.91± 0.33	3.44±0.78	10.70±3.68	<0.001*
HALP score	52.52±27.58	46.54±17.74	30.37±19.15	<0.001*
NLR	2.19±1.16	2.85±1.55	4.04±2.21	<0.001*
PLR	138.06±85.60	127.90±47.47	171.69±175.60	0.14
BMI	20.66±2.98	19.64±3.25	18.04±2.85	0.001*
24 h urine protein (mg/24 h)	17.20±6.51	162.00±81.15	450.94±101.93	<0.001*

[Table/Fig-3]: Comparison of age, biochemical and haematological parameters among CKD groups.
Continuous variables were analysed using One-way ANOVA; Data expressed as mean±SD; *Statistically significant
Significant ANOVA observed for blood urea was primarily attributable to the difference between Group 3 and Groups 1 and 2, whereas no statistically significant difference was observed between Groups 1 and 2

Parameter	f-ratio	p-value	Post-Hoc Tukey HSD (beta)
NLR ratio	15.28074	<0.00001*	G1:G2, Q=2.75 (p = 0.13008) G1:G3, Q=7.71 (p <0.001) G2:G3, Q=4.96 (p =0 .00172)
PLR ratio	1.99943	0.139078	G1:G2, Q=1.19 (p = 0.68002) G1:G3, Q=2.82 (p = 0.11790) G2:G3, Q=1.63 (p = 0.48300)
HALP score	13.66076	<0.00001*	G1:G2, Q=1.93 (p =0 .36258) G1:G3, Q=7.14 (p <0.001) G2:G3, Q=5.22 (p = 0.00092)

[Table/Fig-4]: Comparison of group means ANOVA followed by post-hoc Tukey's test.
One-way ANOVA with Tukey's post-hoc test; *Statistically significant; G1= Group 1, G2= Group 2, G3= Group 3.

analysis indicating significant difference involving group 3. PLR did not differ significantly between groups (p=0.139).

[Table/Fig-5] shows that HALP score had a statistically significant negative correlation with both NLR and PLR across all three groups. The correlation between HALP and NLR was moderately negative in group 1 (r=-0.6125, p =<0.00001), group 2 (r=-0.5277, p=0.000084) and group 3 (r=-0.5898, p =<0.00001). HALP showed a strong negative correlation with PLR in group 1 (r=-0.770, p =<0.00001) and group 2 (r=-0.7221, p =<0.00001), while weaker but statistically significant negative correlation was observed in group 3 (r=-0.3119, p=0.027927). These findings indicate that lower HALP scores are associated with higher levels of systemic inflammation.

The ROC analysis in [Table/Fig-6,7], showed good predictive value for HALP with AUC 0.816, with better sensitivity (86.7%) and specificity (67.6%) with a cut-off value of 28.79. PLR showed AUC of 0.542 and AUC of NLR was 0.305 indicating inverse discriminatory ability.

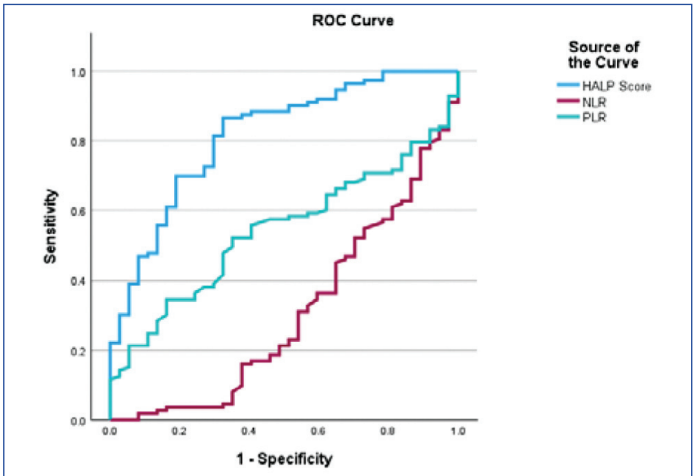
[Table/Fig-7] illustrates the ROC curves of HALP, NLR and PLR. Among these, HALP showed better predictive performance with larger AUC than NLR and PLR.

Parameters	Group 1		Group 2		Group 3	
	R value	p-value	R value	p-value	R value	p-value
NLR	-0.6125	<0.00001*	-0.5277*	0.000084*	-0.5898*	<0.00001*
PLR	-0.770	<0.00001*	-0.7221*	<0.00001*	-0.3119*	0.027927*

[Table/Fig-5]: Pearson's correlation analysis of HALP with NLR and PLR.
Correlation analysis was performed using Pearson's correlation coefficient test.
*Statistically significant.

Marker	AUC (95% CI)	p-value	Optimum cut-off	Sensitivity (%)	Specificity (%)
PLR	0.542	0.381	133.64	34.5	83.8
NLR	0.305	<0 .001	3.52	77.0	54.1
HALP score	0.816	< 0.001	28.79	86.7	67.6

[Table/Fig-6]: ROC analysis.
ROC curve analysis was used to determine the optimal cut-off.



[Table/Fig-7]: ROC analysis of HALP, NLR, and PLR.

DISCUSSION

The present study highlights that with declining renal function, there is increase in systemic inflammation with decrease in the nutritional reserves, as reflected by progressive decline in HALP with advancing CKD stage indicating worsening immunonutritional status.

It was observed that there was a significant difference in the inflammatory markers such as NLR, PLR as well as HALP. The present study also supports the evidence that albuminuria is not just a sign of glomerular damage but also indicates underlying pro-inflammatory and decreased nutritional state [18]. Pearson's correlation analysis revealed that HALP showed a negative correlation with NLR and PLR suggesting that it integrates systemic inflammation (reflected by NLR and PLR) with nutritional status reflected by Albumin and haemoglobin) [16].

The ROC analysis of HALP in the combined cohort revealed an optimum cut-off value of 28.79 with AUC of 0.816 making it a good predictor. In contrast, a study which included patients with IgA nephropathy showed a cut-off of 36.54 with AUC of 0.69 for HALP suggesting its moderate utility [19]. Yuan Y et al., in their study showed lower HALP was an indicator of poor renal outcomes in Immunoglobulin A (IgA) nephropathy patients [7].

Xing L et al., study on individuals with Diabetic Kidney Disease (DKD), showed an inverse relationship of HALP with incidence and death [4]. This finding align with our findings that lower HALP was associated with advancing stage of CKD. Zhang F et al., revealed that HALP is a prognostic indicator of morbidity and mortality in haemodialysis patients [9]. Another study by Babovic B et al., reported that patients undergoing haemodialysis had a lower HALP (28.56±20.27) compared to those not on dialysis indicating a poor immunonutritional status [1]. Antar R et al., also reported that individuals undergoing dialysis had a lower HALP of 33.5 compared to general population [2]. These findings align with the present

study, where the group 3 subjects showed a lower HALP score of 30.37±19.15.

HALP has been shown as a prognostic marker in various studies conducted on patient population with different underlying diseases, suggesting its potential use in risk stratification beyond traditional used inflammatory ratios like NLR and PLR. These ratios reflect only single status either inflammation or immune [20], whereas HALP score serves as a composite marker reflecting both inflammation and nutrition by mirroring multidimensional disturbances in CKD thereby eliminating the need to calculate these ratios [21].

Altogether, HALP may be incorporated in routine clinical practice as it uses readily available parameters in laboratory testing of CKD patients. By monitoring HALP, the clinicians may be able to recognise high risk patients early and implement dietary and therapeutic intervention.

Limitation(s)

There are some limitations in the present study. As the current study was cross-sectional type, it limits making any inferences about causality. The findings cannot be generalised as the sample size was inadequate within each albuminuria-based group. The findings have to be validated with bigger, multi-centre population. Confounding factors like comorbidities and medications were not fully adjusted.

CONCLUSION(S)

The HALP scores decrease considerably with increased albuminuria. Its strong correlation with inflammatory markers like NLR and PLR highlights its integrative relevance in assessing the inflammation and nutrition status in CKD patients. Hence, incorporating HALP into routine clinical examination helps in risk classification and guide in complete patient care. However, future multicentre longitudinal studies with larger sample sizes are required to validate HALP as a prognostic tool in nephrology practice. Longitudinal studies are also needed to evaluate its potential disease progression.

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