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Halp Score (Hemoglobin Albumin Lymphocyte Platelet Score) As Predictive Indicator For Treatment Response In Patients With Stage Iv Colorectal Cancer On First Line Palliative Chemotherapy

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Abstract:
Background*: Colorectal cancer is one of the most common malignancies and the fourth leading cause of cancer mortality in the world. HALP score is a comprehensive index that reflects components of the nutritional and immune status of patients, which had been shown to have a prognostic role in gastrointestinal cancers, including gastric cancer, esophageal cancer, colorectal cancer, and genitourinary cancers, including bladder cancer, and renal cell carcinoma. It is calculated according to the following formula: [hemoglobin (g/L) × albumin (g/L) × lymphocytes (/L)] / platelets (/L). The purpose of this evaluation is to assess the predictive significance of HALP score in metastatic colorectal cancer patients receiving first line palliative chemotherapy in an Indian population.*
Materials and Methods*: We retrospectively analyzed data from patients diagnosed with metastatic colorectal cancer from January 1, 2021 to December 31, 2023 for baseline CBC with differentials, serum albumin, CT abdomen and pelvis. Follow up imaging was assessed post 6 months of first line palliative chemotherapy with FOLFOX/ CAPEOX for response. Response evaluation was done using RECIST1.1. The radiological responses were then compared with baseline HALP scores. HALP score cutoff was determined based on ROC curve analysis. The radiological responses were then correlated with the baseline HALP score. HALP score at baseline was correlated with basic clinico-pathological factors like age, sex, and tumor histology. The progression-free survival was defined as time from randomization to disease progression or death during first line treatment.*
Results*: 52 patients with metastatic colorectal cancer were evaluable for response analysis according to RECIST 1.1. A HALP score of >34.65 (ROC) was determined as cutoff. The Overall Response Rate (ORR) of palliative therapy was 34.6% and the Disease Control Rate (DCR) 80.7%. Patients with a HALP > 34.65 (N=23, ORR 56.5%) had a significantly higher ORR to palliative chemotherapy as compared to patients with a lower HALP < 34.65 (N=29, ORR 17.2%) (P=0.0077). 18 patients with a HALP > 34.65 (N=23) had a PFS > 9 months compared to 7 patients with a HALP ≤ 34.65 (N=29) (P=0.00032).*
Conclusion: *Overall, our findings suggest that the HALP index is a viable independent predictor of response to palliative chemotherapy in metastatic colorectal cancer. Our study results give us reason to believe that the HALP index reflects the traditionally unaccounted nutritional and inflammatory factors that play a significant role in treatment response and its adoption in clinical practice feasible. To date, HALP has only shown theoretic prognostic ability, and has not yet been used in clinical practice to tailor treatment for those at risk for immunonutritional deficiencies.*
Keyword*: Metastatic colorectal Cancer, HALP score, CAPEOX, FOLFOX, Palliative chemotherapy, Progression free survival, Overall Response Rate.*

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I. Introduction

Colorectal cancer is one of the most common malignancies and the fourth leading cause of cancer mortality in the world.[1] Colorectal cancers frequently progress to the metastatic stage even after loco-regional treatments. Systemic therapy is one of the main therapies administered to colorectal cancer patients through 5-fluorouracil based chemotherapy, such as the FOLFOX (leucovorin, fluorouracil and oxaliplatin) regimen and CAPEOX (Capecitabine, Oxaliplatin) regimen.

HALP score is a comprehensive index that reflects components of the nutritional and immune status of patients, which had been shown to have a prognostic role in gastrointestinal cancers, including gastric cancer, esophageal cancer, colorectal cancer, and genitourinary cancers, including bladder cancer, and renal cell

carcinoma. It is calculated according to the following formula: [hemoglobin (g/L) × albumin (g/L) × lymphocytes (/L)] / platelets (/L). [2]

It is widely accepted that an inflammatory response and an overall nutritional status correlate with the survival rates for cancer patients. Hemoglobin levels have been reported to be significantly related to the survival and progression of tumors. Serum albumin levels were also significantly correlated with the survival of cancer. Lymphocytes, which can release some cytokines, such as interferon-γ and tumor necrosis factor-alpha (TNF-α), can inhibit tumor growth and improve the prognosis for cancer patients. Some studies indicated that, through mediation by TNF-α, platelets inhibited tumor necrosis. From these findings, it is observed that hemoglobin, albumin, lymphocytes, and platelets may be risk factors, where if levels are good, can highlight a good prognosis. [3] [4] [5] [6] [7] [8]

In a study published by Chen et al. in 2015, assessing the prognostic significance of HALP score in gastric carcinoma, it was seen that HALP score >56.8 was an independent prognostic factor in patients with gastric carcinoma. [9]

The purpose of this evaluation is to assess the predictive significance of HALP score in metastatic colorectal cancer patients receiving first line palliative chemotherapy in an Indian population.

II. Material And Methods

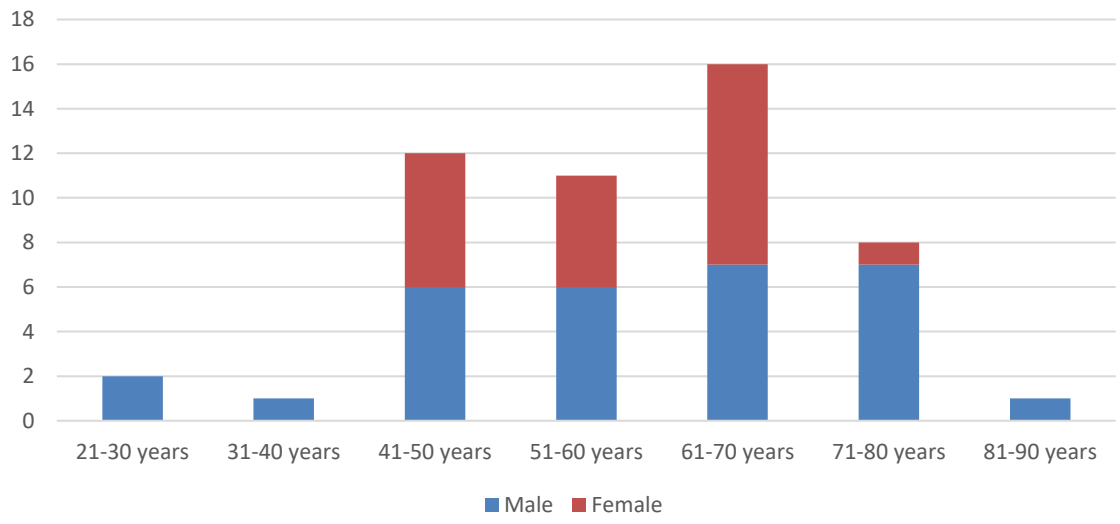
We retrospectively analyzed data from patients diagnosed with metastatic colorectal cancer who have attended the Department of Medical Oncology, Government Kilpauk Medical College, Chennai from January 1, 2021 to December 31, 2023 after obtaining approval from the Institutional Ethics Committee. The records of metastatic colorectal cancer patients were analyzed for reports of complete blood counts with differentials, serum albumin, CT abdomen and pelvis and basic clinico-pathological factors like age, sex, tumor histology and chemotherapy regimen administered. Further routine imaging studies done after first line palliative chemotherapy or at symptomatic progression to document the response were analyzed. Response evaluation was done using Response Evaluation Criteria in Solid tumors (RECIST1.1)

HALP score was calculated according to the following formula: [hemoglobin (g/L) ×albumin (g/L) ×lymphocytes (/L)] / platelets (/L). It will be calculated at baseline before administration of first cycle. The optimal cut-off value of HALP score was determined using receiver operator characteristic (ROC) curve. The radiological responses were then correlated with the baseline HALP score. HALP score at baseline was correlated with basic clinico-pathological factors like age, sex, and tumor histology. The progression-free survival was defined as time from randomization to disease progression or death during first line treatment.

III. Result

We included 52 patients diagnosed with metastatic colorectal cancer in the study. The median age of patients included in the study was 60.5, ranging from 21 to 82 years [Figure 1]. The sex distribution was skewed with 30 males (57.6%) and 22 females (42.4%) [Figure 2]. The tumor histology was predominantly Adenocarcinoma for 51 patients and one patient had signet ring cell carcinoma [Figure 3]. Palliative chemotherapy was administered as follows: 32 patients with CAPEOX regimen, 20 patients with FOLFOX regimen. [Figure 4].

Figure no 1: Age and sexwise distribution of the patients included in the study.



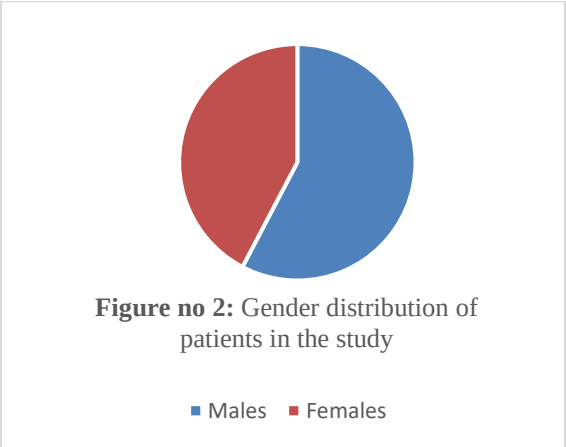


Figure no 2: Gender distribution of patients in the study

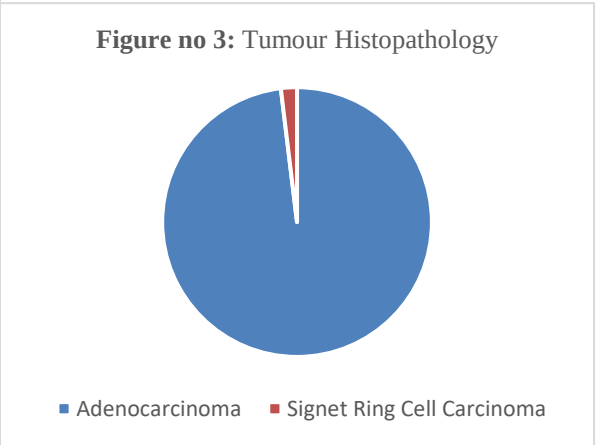


Figure no 3: Tumour Histopathology

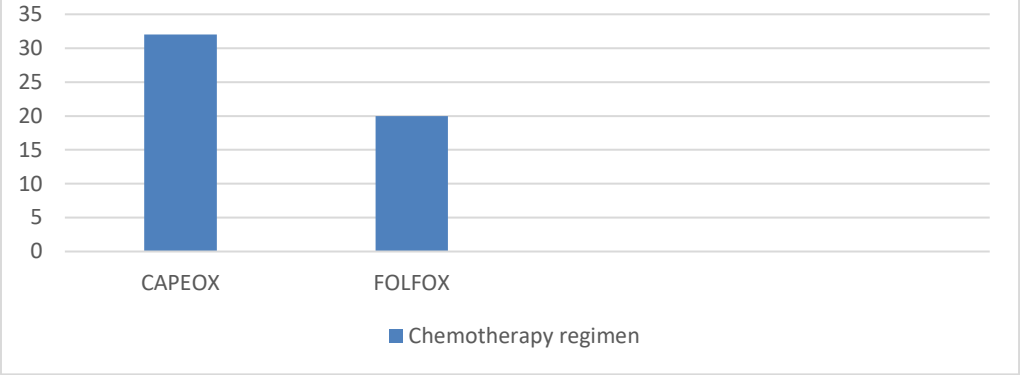
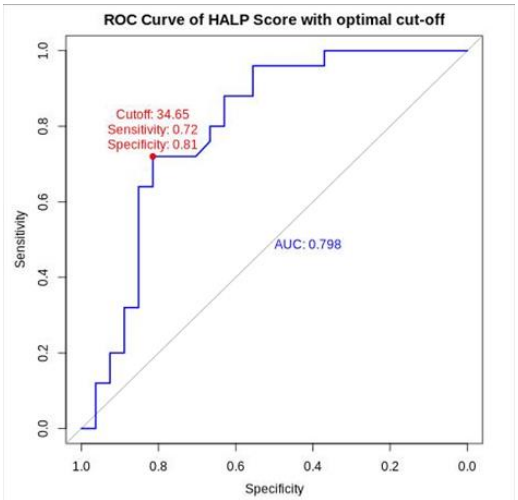


Figure no 4: Chemotherapy regimen used

A HALP score of >34.65 (ROC) was determined as cutoff and patients were divided into low HALP group (≤34.65) and high HALP group (>34.65).



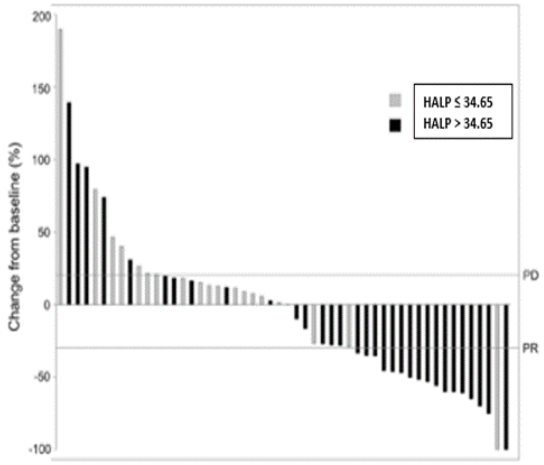


Figure no 5: ROC Curve of HALP Score with optimal cut-off

Figure no 6: Waterfall plot showing the response rate to palliative chemotherapy with respect to HALP score

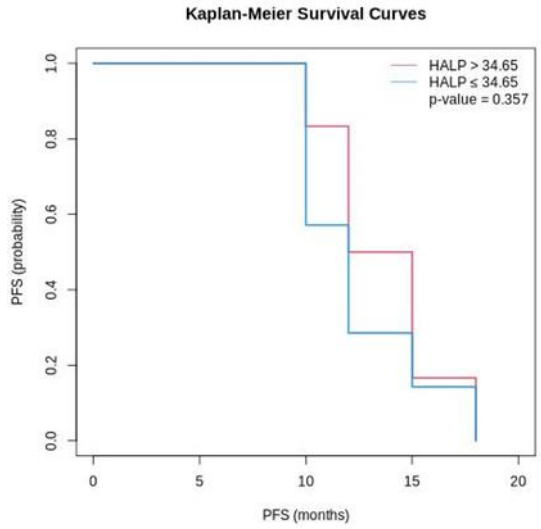


Figure no 7: Kaplan-Meier Survival Curves for progression free survival in 52 patients according to the HALP score.

Table no 1: Clinical characteristics of 52 patients with metastatic colorectal cancer		
Gender	Cases	%
Male	30	57.6
Female	22	42.4
Age		
≤60	26	50
>60	26	50
CEA		
≤2.5	8	15.4
>2.5	44	84.6
Chemotherapy regimen		
CAPEOX	32	61.4
FOLFOX	20	38.6
First evaluation results		
ORR (CR+PR)	18	34.6
SD+PD	34	65.4
Progression Free Survival		
≤9 months	27	51.9
>9 months	25	48.1

Table no 2: Association between clinical features and the HALP score in metastatic colorectal cancer.				
Clinical Features	HALP Score			Remarks
	≤ 34.65	> 34.65	p-value	
Gender				
Male	18	12	0.664	Chi-squared test
Female	11	11		
Age				
≤60	16	10	0.5767	Chi-squared test
>60	13	13		
CEA				
≤2.5	2	6	0.118	Fischer's Exact test
>2.5	27	17		
Chemotherapy regimen				
CAPEOX	16	16	0.44	Chi-squared test
FOLFOX	13	7		
First evaluation results				
ORR (CR+PR)	5	13	0.0077	Chi-squared test
SD + PD	24	10		
Progression Free Survival				
≤9 months	22	5	0.00032	Chi-squared test
>9 months	7	18		

Table no 3: Univariate and multivariate analysis of PFS in 52 patients with metastatic colorectal cancer.			
Variable	Univariate Analysis	Multivariate Analysis	
	p-value	HR (95% CI)	p-value

Gender			
Male	0.189	Reference	0.278
Female		1.690 (0.654 - 4.365)	
Age			
≤60	0.164	Reference	0.272
>60		1.682 (0.665 - 4.252)	
CEA			
≤2.5	0.049	Reference	0.02
>2.5		3.564 (1.220 - 10.414)	
Chemotherapy regimen			
CAPEOX	0.629	Reference	0.867
FOLFOX		0.917 (0.333 - 2.526)	
HALP Score			
≤ 34.65	0.48	Reference	0.097
> 34.65		0.419 (0.150 - 1.172)	

IV. Discussion

The HALP score (Derived from Hemoglobin, Albumin, Lymphocyte, and Platelet count) has emerged as a promising predictive indicator for treatment response in various cancers. This score offers a simple, inexpensive, and readily available tool for clinicians to assess patient outcomes and tailor treatment strategies.

The HALP score is calculated based on four easily measurable parameters:

1. Hemoglobin (Hb) levels
2. Albumin levels
3. Lymphocyte count
4. Platelet count

The HALP index efficiently compiles the aforementioned marker values into a joint score, to bolster their independent prognostic and predictive value. HALP score has already been shown to have a prognostic role in gastric cancer, esophageal cancer, non-metastatic colorectal cancer, bladder cancer and renal cell carcinoma. [9][11][12][13][14] Studies have demonstrated that a lower HALP score is associated with poor treatment response to chemotherapy, reduced progression-free survival, shorter overall survival. Conversely, a higher HALP score is linked to better treatment response, improved PFS and OS.

The HALP score's predictive power stems from its ability to reflect the tumor's systemic inflammatory impact, nutritional status, and hematological parameters. A higher score indicates a more favorable host-tumor interaction, which correlates with improved treatment outcomes.

Hemoglobin has been widely validated as a prognostic factor for disease progression and survival cancer. Anemia generated hypoxia in the tumor microenvironment increases the tumor's proliferative and metastatic potential. Albumin, a known Acute phase reactant, is known to stabilize cell growth, promote DNA repair and have antioxidant properties. In vitro, albumin has been shown to suppress tumor proliferation. Lymphocytes play an important role in the immune response toward malignant cells. Platelets can release a variety of cytokines, growth factors, and proangiogenic molecules which directly induce tumorigenesis, cancer proliferation, and metastasis.

In our study, a high HALP score was found to be independently associated with improved Overall Response Rate and Progression-free survival. The results were statistically significant and suggests that HALP score is able to predict Overall Response Rate and Progression-free survival after administering palliative chemotherapy to patients with metastatic colorectal cancer.

The optimal HALP score in our study was determined as 34.65 using the ROC curve while previous study cut-off points ranged from 22.2 to 56.8. [9][13] Most of the previous studies were conducted on an Asian population and in our study which was conducted in a south Indian population also had a similar cut-off score.

Previous studies have reported female gender and older age to be associated with lower HALP score. Female patients tend to have a lower Hemoglobin level compared to male patients whereas the elderly usually have both anemia and lower albumin compared to younger patients. However, we did not find any such association in our study population.

To our knowledge, there are no previously reported studies on the predictive and prognostic significance of HALP score in metastatic colorectal cancer. In our study, we confirmed higher overall response rates as well as improved progression free survival to palliative chemotherapy in metastatic colorectal cancer patients with high HALP score > 34.65.

This study has several limitations. HALP score is not specific to metastatic colorectal cancer and may apply to other cancer types. The cut-off value for the HALP score was determined by ROC curve from the baseline blood parameters of 52 patients included in this study. Also, this was a retrospective study conducted at a single

centre, and further prospective studies from multiple centres are required to validate the findings of this study. It should be used in conjunction with other established prognostic factors and biomarkers.

V. Conclusion

Overall, our findings suggest that the HALP index is a viable independent predictor of response and progression free survival to palliative chemotherapy in metastatic colorectal cancer. Our study results give us reason to believe that the HALP index reflects the traditionally unaccounted nutritional and inflammatory factors that play a significant role in treatment response. The wide availability of the routine lab values needed to compute this score, along with the very practical nature of its implementation, make its adoption in clinical practice feasible. To date, HALP has only shown theoretic prognostic ability, and has not yet been used in clinical practice to tailor treatment for those at risk for immunonutritional deficiencies.

Further research will help refine the HALP score's application and explore it's potential in personalizing treatment approaches for metastatic colorectal cancer patients.

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