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Biomarkers and Clinical Disease Severity in Hidradenitis Suppurativa: A Linear Mixed-Effects Modeling Study

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To the Editor,

Hidradenitis suppurativa (HS) is a systemic inflammatory disorder with a multifactorial pathophysiology that remains incompletely understood. Previous research has demonstrated that specific inflammatory markers, including leukocytes, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and interleukin-6 (IL-6) are significantly associated with severe disease as defined by HS-Physician Global Assessment (HS-PGA) score.[1] Importantly, however, no studies have validated the sensitivity of these markers with fluctuations in disease activity over time. Herein, we investigate the utility of various biomarkers in continuous outcome monitoring for patients with HS and assess their sensitivity in a real-world setting.

A retrospective chart review was conducted to identify patients seen at Montefiore Medical Center between September 1, 2017, and May 1, 2025. Patients were included if they had clinical and laboratory markers of disease severity at baseline and at ≥4 follow-up visits. Collected data included patient demographics, comorbid medical conditions, HS-PGA score, numerical rating scale for pain (NRS-pain) score, hemoglobin (Hgb), hematocrit (Hct), mean corpuscular volume (MCV), leukocyte count, ESR, CRP, and IL-6 across repeat patient visits.

Linear mixed-effects models with patient identifier (MRN) as a random intercept were employed to examine associations between disease severity and laboratory markers over time. Disease severity was modeled continuously using the HS-PGA score. Analyses were conducted using R (version 4.2.1).

The cohort was predominantly female (66%) and Black (49%). The average age at intake was 35.5 years (SD 13.52); consistent with the epidemiological profile of HS in the US population at large.[2] Patients had a median of eight visits (IQR 6) where primary outcome measures were recorded, with a median interval between visits and a median follow-up duration of 70 days (IQR 84) and 878 days (IQR 695), respectively. A detailed summary of visit characteristics, demographic information, and comorbid medical conditions can be found in Table 1.

Longitudinal analysis of laboratory markers revealed positive associations between HS-PGA and leukocyte count (β=0.03, $P<0.001$), CRP (β = 0.14, $P<0.001$), ESR (β = 0.012, $P<0.001$), and IL-6 (β =0.005, $P<0.001$) indicating that higher inflammatory marker levels correlated with greater disease severity. Conversely, significant negative associations were observed between HS-PGA and hemoglobin (β=-0.16, $P<0.001$), hematocrit (β=-0.05, P<0.001), and mean corpuscular volume (β=-0.02, $P<0.001$). A detailed summary of associations between clinical disease severity and the various inflammatory markers studied can be found in Table 2.

Extending beyond previous work, we demonstrate statistically significant longitudinal associations between clinical disease severity and serum biomarkers known to be associated with HS.[1,3] Establishing the sensitivity of specific biomarkers to changes in disease state over time supports their use as validated primary endpoints for HS clinical trials and prospective studies, which largely rely on subjective outcome measures to evaluate drug efficacy at present.[4,5] Moreover, the effect size estimates derived from longitudinal analyses that quantifiably assess relationships between specific biomarkers and clinical measures of disease severity may ultimately help inform power calculations and dose-response modeling during early-phase trial design. Taken together, these findings suggest a role for specific serum biomarkers across multiple stages of the clinical research process.

This study is limited by its retrospective nature and small sample-size; larger prospective studies must validate our findings before they can be applied in clinical research settings more broadly. Nevertheless, this study provides a strong foundation for integrating objective biomarkers into the broader framework of HS research and, pending further validation, may ultimately support more rigorous and reproducible approaches to disease monitoring and treatment evaluation moving forward.

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TABLE 1.

Baseline Demographic and Clinical Characteristics of Patients With Hidradenitis Suppurativa (HS)

Patient Characteristics	
Age at Diagnosis (N = 128)	35.46 (13.52)
BMI (N = 123)	33.76 (7.86)
Sex (N = 128)	
Male	42 (33.81)
Female	85 (66.41)
Other	1 (0.78)
Race (N = 128)	
White	15 (11.72)
Black	63 (49.22)
Asian	2 (1.56)
Other/Unknown	48 (37.5)
Ethnicity (N = 128)	
Not Hispanic/Latino	67 (52.34)
Hispanic/Latino	46 (36.72)
Unknown	14 (10.94)
FST (N = 73)	
II	5 (6.85)
III	11 (15.07)
IV	17 (23.29)
V	31 (42.47)
VI	9 (12.33)
Insurance (N = 128)	
Medicare/Medicaid	60 (46.88)
Commericial	65 (50.78)
Uninsured	3 (2.34)
Language (N = 128)	
English	122 (95.31)
Spanish	6 (4.69)
Smoking History (N = 128)	
Never	81 (63.28)
Active	17 (13.28)
Former	30 (23.44)
Comorbidities	
T2DM (N = 128)	27 (21.09)
Metabolic Syndrome (N = 128)	13 (10.16)
PCOS (N = 128)	13 (10.16)
IBD (N = 128)	2 (1.56)
Iron Supplementation (N = 128)	10 (7.87)
Disease Severity	
HS-PGA (1-6) (N = 128)	3.27 (1.33)
NRS-Pain (0-10) (N = 127)	3.90 (3.45)
Laboratory Markers	
Leukocytes (k/uL) (N = 128)	10.0 (3.65)
HGB (g/dL) (N = 128)	12.16 (1.93)
HCT (N = 128)	38.79 (5.23)
MCV (fL) (N = 128)	85.41 (7.66)
CRP (mg/dL) (N = 128)	3.03 (3.50)
ESR (mm/h) (N = 127)	60.32 (37.04)
IL-6 (pg/mL) (N = 68)	33.30 (115.73)
Visit Characteristics (N = 1259)	Median (IQR)
Visits Per Patient	8 (6)
Time Between Visits (days)	70 (84)
Follow-Up Duration (days)	878 (695)

Continuous variables are presented as mean (standard deviation), and categorical variables as counts (percentages), unless otherwise specified. Reported averages for clinical and laboratory markers include data from intake visit only to represent baseline disease severity of the cohort. Reported averages for longitudinal measures (visits per patient, time between visits, follow-up duration) include data from all visits. BMI, body mass index; FST, Fitzpatrick skin type; T2DM, type II diabetes mellitus; PCOS, polycystic ovarian syndrome; HS-PGA, Hidradenitis Suppurativa-Physician Global Assessment; NRS-pain, Numerical Rating Scale for pain; HGB, hemoglobin; HCT, hematocrit; MCV, mean corpuscular volume; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IL-6, interleukin-6; STD, standard deviation.

TABLE 2.

Longitudinal Associations Between Inflammatory Markers and Clinical Disease Severity in a Cohort of patients With Hidradenitis Suppurativa.

Predictor	β	Standard Error	t-value	*P*-value
Leukocytes	0.029	0.006	4.556	<0.001
HGB	-0.161	0.017	-9.659	<0.001
HCT	-0.053	0.007	-7.775	<0.001
MCV	-0.018	0.004	-4.684	<0.001
CRP	0.144	0.012	12.425	<0.001
ESR	0.012	0.001	12.228	<0.001
IL-6	0.005	0.001	5.933	<0.001

Results of a linear mixed-effects model evaluating the association between clinical and laboratory predictors and HS-PGA score (n=128 patients). Subject was included as a random intercept to account for multiple visits per patient. Reported are standardized regression coefficients (β), standard errors, t-values, and *P*-values. HGB, hemoglobin; HCT, hematocrit; MCV, mean corpuscular volume; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IL-6, interleukin-6.

DISCLOSURES

The authors have no conflict of interest to declare.

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