

Online Resource 1

Article title: Seborrheic Dermatitis Exhibits Only a Modest Systemic Inflammatory Signature: A Retrospective Case-Control Study

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Contents

- **Table S1** Blood counts, acute-phase reactants, and blood count-derived indices in patients with seborrheic dermatitis and healthy controls
- **Table S2** Receiver operating characteristic analysis for discriminating patients with seborrheic dermatitis from healthy controls
- **Table S3** Multivariable linear regression of the Seborrheic Dermatitis Area and Severity Index score on each marker
- **Table S4** False discovery rate-adjusted q values for the association of each marker with each outcome
- **Table S5** Sensitivity analysis with chronic disease defined as duration of at least 120 months
- **Table S6** Sensitivity analysis excluding patients with comorbidity
- **Table S7** Exploratory sex-stratified comparisons of hemoglobin- and platelet-containing markers
- **Fig. S1** Receiver operating characteristic curves for 7 blood count-derived indices
- **Fig. S2** Forest plot of adjusted odds ratios for each marker and outcome
- **Fig. S3** Scatter plots of Seborrheic Dermatitis Area and Severity Index score against selected markers
- **Fig. S4** Exploratory sex-stratified receiver operating characteristic curves for HPR and PIV
- **Code availability**

Table S1 Blood counts, acute-phase reactants, and blood count-derived indices in patients with seborrheic dermatitis and healthy controls

Parameter	Patients (n = 142), median (IQR)	Healthy controls (n = 72), median (IQR)	Cliff δ^a	P value ^b
Blood counts				
White blood cells, $\times 10^9/L$	7.43 (6.37-8.56)	6.97 (5.82-7.83)	0.16	.05
Neutrophils, $\times 10^9/L$	4.15 (3.17-5.31)	3.90 (3.08-4.75)	0.13	.13
Lymphocytes, $\times 10^9/L$	2.39 (2.02-2.85)	2.20 (1.90-2.69)	0.15	.08
Monocytes, $\times 10^9/L$	0.57 (0.46-0.72)	0.50 (0.40-0.60)	0.23	.006
Platelets, $\times 10^9/L$	276 (228-320)	249 (215-288)	0.19	.02
Hemoglobin, g/dL	13.6 (12.7-15.2)	14.3 (13.2-15.8)	-0.19	.03
Mean platelet volume, fL	10.1 (9.4-10.9)	10.1 (9.5-11.0)	-0.01	.95
Acute-phase reactants				
C-reactive protein, mg/L	2.1 (0.9-5.0)	0.9 (0.4-1.3)	0.45	<.001
Erythrocyte sedimentation rate, mm/h	10 (6-18)	4 (2-6)	0.59	<.001
Blood count-derived indices				
NLR	1.67 (1.33-2.37)	1.79 (1.39-2.15)	0.01	.92
PLR	111.1 (89.2-152.1)	114.2 (98.6-139.1)	-0.01	.92
MLR	0.24 (0.19-0.30)	0.23 (0.19-0.28)	0.04	.66
SII	467 (327-669)	438 (288-585)	0.10	.24
SIRI	1.03 (0.68-1.50)	0.90 (0.64-1.18)	0.14	.11
PIV	276 (174-424)	208 (164-322)	0.20	.02
dNLR	1.29 (1.00-1.75)	1.31 (1.00-1.55)	0.03	.69
Neutrophil-to-platelet ratio ($\times 100$)	1.51 (1.18-1.98)	1.49 (1.23-2.00)	-0.02	.84
HPR ($\times 100$)	5.03 (4.09-6.34)	5.56 (4.73-6.79)	-0.23	.007

Abbreviations: dNLR, derived neutrophil-to-lymphocyte ratio; HPR, hemoglobin-to-platelet ratio; IQR, interquartile range; MLR, monocyte-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; PIV, pan-immune-inflammation value; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index; SIRI, systemic inflammation response index.

^aNonparametric effect size; positive values indicate higher values in patients.

^bMann-Whitney U test, unadjusted.

Index formulas: NLR = neutrophils/lymphocytes; PLR = platelets/lymphocytes; MLR = monocytes/lymphocytes; SII = platelets $\times$ neutrophils/lymphocytes; SIRI = neutrophils $\times$ monocytes/lymphocytes; PIV = neutrophils $\times$ platelets $\times$ monocytes/lymphocytes; dNLR = neutrophils/(white blood cells - neutrophils); neutrophil-to-platelet ratio = neutrophils $\times$ 100/platelets; HPR = hemoglobin $\times$ 100/platelets (cell counts in $\times 10^9/L$; hemoglobin in g/dL).

Table S2 Receiver operating characteristic analysis for discriminating patients with seborrheic dermatitis from healthy controls

Marker	AUC (95% CI)	Optimal cutoff	Sensitivity, %	Specificity, %
NLR	0.504 (0.420-0.581)	≥2.06	38.0	70.8
PLR	0.496 (0.412-0.577)	≥162.68	21.1	88.9
MLR	0.519 (0.436-0.595)	≥0.40	10.6	98.6
SII	0.549 (0.464-0.627)	≥618.38	31.7	80.6
SIRI	0.568 (0.487-0.643)	≥1.04	50.0	68.1
PIV	0.599 (0.515-0.673)	≥258.56	54.2	65.3
dNLR	0.517 (0.434-0.594)	≥1.56	35.2	76.4
Neutrophil-to-platelet ratio	0.491 (0.413-0.570)	≥1.30	67.6	37.5
HPR	0.613 (0.535-0.687)	≤4.88	48.6	73.6
C-reactive protein	0.725 (0.658-0.791)	≥1.5 mg/L	57.7	81.9
Erythrocyte sedimentation rate	0.795 (0.734-0.852)	≥7.0 mm/h	71.8	79.2

Abbreviations as in Table S1. AUC, area under the receiver operating characteristic curve.

Cutoffs were derived by maximizing the Youden J statistic; 95% CIs are from 1000 bootstrap resamples. The AUCs were calculated with higher values indicating seborrheic dermatitis, except for HPR, for which lower values were taken to indicate seborrheic dermatitis (hence the ≤ cutoff). Values below 0.50 (PLR and neutrophil-to-platelet ratio) indicate no discrimination. In Fig. S1, the PLR curve is plotted in the opposite orientation (AUC, 0.504).

Table S3 Multivariable linear regression of the Seborrheic Dermatitis Area and Severity Index (SDASI) score on each marker within the seborrheic dermatitis cohort (n = 142)

Marker (per 1-SD increase)	β coefficient (95% CI)	P value	q value ^a
NLR	-0.51 (-0.94 to -0.07)	.02	.10
PLR	-0.31 (-0.74 to 0.12)	.16	.36
MLR	-0.34 (-0.78 to 0.10)	.13	.36
SII	-0.45 (-0.88 to -0.01)	.05	.16
SIRI	-0.62 (-1.06 to -0.18)	.005	.06
PIV	-0.65 (-1.10 to -0.21)	.005	.06
dNLR	-0.40 (-0.83 to 0.04)	.07	.20
Neutrophil-to-platelet ratio	-0.38 (-0.81 to 0.05)	.08	.20
HPR	0.42 (-0.02 to 0.86)	.06	.20
C-reactive protein	-0.10 (-0.54 to 0.34)	.66	.85
Erythrocyte sedimentation rate	-0.14 (-0.58 to 0.30)	.53	.85

Abbreviations as in Table S1.

β is the change in SDASI score per 1-SD increase in the marker; negative values indicate lower SDASI scores at higher marker values. Each marker was entered separately. Models were adjusted for age, sex, body mass index, pack-years of smoking, and comorbidity.

^aP value adjusted for the false discovery rate (Benjamini-Hochberg procedure) across the 11 markers shown. Four markers (NLR, SII, SIRI, and PIV) had P ≤ .05 before correction for multiple testing, but none had q < .05.

Table S4 False discovery rate-adjusted q values for the association of each marker with each outcome

Outcome	NLR	PLR	MLR	SII	SIRI	PIV	HPR	CRP	ESR	MPV
Case-control: patients vs healthy controls	.993	.993	.418	.418	.189	.045	.006	<.001	<.001	.571
Moderate-to-severe vs mild disease	.505	.833	.833	.505	.505	.505	.763	.833	.505	.833
Extra-scalp involvement	.895	.895	.915	.915	.895	.915	.895	.895	.895	.933
Chronic disease (duration ≥60 mo)	.908	.908	.908	.968	.908	.908	.908	.908	.908	.908
Treatment refractoriness	.721	.746	.746	.721	.721	.721	.746	.746	.721	.746
Pruritus	.643	.643	.790	.554	.790	.643	.790	.790	.554	.684

Abbreviations as in Table S1. CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; MPV, mean platelet volume.

Values are q values adjusted for the false discovery rate (Benjamini-Hochberg procedure) from separate models for each marker, as displayed in Fig. 3 in the main text; bold indicates $q < .05$. Case-control models were adjusted for age, sex, body mass index, and pack-years of smoking; models within the seborrheic dermatitis cohort were additionally adjusted for comorbidity. Across the 5 within-disease outcomes (50 marker-by-outcome comparisons), q values ranged from .505 to .968. Treatment refractoriness was defined as moderate or higher severity despite a documented prescription for topical antifungal or corticosteroid therapy in the preceding month. This table and Fig. 3 in the main text show 10 markers (including MPV). Table 2 in the main text and Tables S3, S5, and S6 show 11 markers (including dNLR and the neutrophil-to-platelet ratio), so q values differ slightly between them.

Table S5 Sensitivity analysis with chronic disease defined as duration of at least 120 months (23 patients)

Marker (per 1-SD increase)	aOR (95% CI)	P value	q value ^a
NLR	0.95 (0.59-1.51)	.81	.96
PLR	1.00 (0.62-1.61)	.99	.99
MLR	1.07 (0.68-1.69)	.77	.96
SII	0.84 (0.50-1.41)	.51	.96
SIRI	0.99 (0.59-1.66)	.96	.99
PIV	0.89 (0.53-1.50)	.66	.96
dNLR	0.99 (0.62-1.60)	.98	.99
Neutrophil-to-platelet ratio	0.92 (0.58-1.46)	.72	.96
HPR	1.16 (0.71-1.91)	.55	.96
C-reactive protein	0.96 (0.55-1.66)	.87	.96
Erythrocyte sedimentation rate	0.94 (0.55-1.62)	.84	.96

Abbreviations as in Table S1. aOR, adjusted odds ratio.

Models were adjusted for age, sex, body mass index, pack-years of smoking, and comorbidity. No marker was associated with chronic disease at the threshold of 120 months (all $q \geq .96$) or at the primary threshold of 60 months (Table S4).

^aBenjamini-Hochberg false discovery rate-adjusted P value across the 11 markers shown.

Table S6 Sensitivity analysis excluding patients with comorbidity (88 patients with seborrheic dermatitis vs 72 controls)

Marker (per 1-SD increase)	aOR (95% CI)	P value	q value ^a
NLR	0.95 (0.69-1.32)	.78	.86
PLR	0.91 (0.65-1.27)	.59	.81
MLR	1.11 (0.78-1.59)	.55	.81
SII	1.07 (0.75-1.51)	.71	.86
SIRI	1.36 (0.81-2.27)	.24	.45
PIV	1.59 (0.98-2.58)	.06	.17
dNLR	1.06 (0.74-1.51)	.76	.86
Neutrophil-to-platelet ratio	1.01 (0.74-1.39)	.94	.94
HPR	0.61 (0.42-0.89)	.01	.06
C-reactive protein	24.61 (4.51-134.18)	<.001	<.001
Erythrocyte sedimentation rate	11.85 (4.86-28.91)	<.001	<.001

Abbreviations as in Table S1. aOR, adjusted odds ratio.

Models were adjusted for age, sex, body mass index, and pack-years of smoking. The aORs for PIV (1.59) and HPR (0.61) were similar to those in the primary analysis (1.75 and 0.56; Table 2 in the main text) but less precise, and both fell short of the false discovery rate threshold ($q = .17$ and $.06$). C-reactive protein and erythrocyte sedimentation rate remained strongly associated with seborrheic dermatitis (both $q < .001$).

^aBenjamini-Hochberg false discovery rate-adjusted P value across the 11 markers shown.

Table S7 Exploratory sex-stratified comparisons of hemoglobin- and platelet-containing markers

Parameter, median (IQR)	Men			Women		
	Patients (n = 64)	Controls (n = 31)	P value ^a	Patients (n = 78)	Controls (n = 41)	P value ^a
HPR ($\times 100$)	6.09 (5.36-7.02)	6.08 (5.41-7.49)	.50	4.36 (3.74-5.04)	5.22 (4.37-6.12)	<.001
PIV	276 (182-411)	184 (155-302)	.03	281 (161-424)	234 (173-334)	.24
Hemoglobin, g/dL	15.2 (14.1-15.8)	15.9 (15.5-16.5)	.001	13.0 (11.9-13.6)	13.2 (12.5-13.9)	.13
Platelets, $\times 10^9/L$	253 (215-289)	248 (223-286)	.86	290 (255-346)	251 (213-288)	.002
Monocytes, $\times 10^9/L$	0.62 (0.50-0.73)	0.56 (0.46-0.61)	.10	0.53 (0.45-0.70)	0.48 (0.39-0.60)	.03
Neutrophils, $\times 10^9/L$	4.38 (3.36-5.35)	3.80 (2.97-4.62)	.05	3.73 (3.08-5.13)	3.94 (3.13-4.95)	.82

Abbreviations as in Table S1.

These analyses were exploratory. Formal tests for interaction by sex were not significant (all $P > .10$), the strata were small, and a difference in statistical significance between strata does not establish that effects differ. Sex-stratified areas under the curve are shown in Fig. S4.

^aMann-Whitney U test, unadjusted.

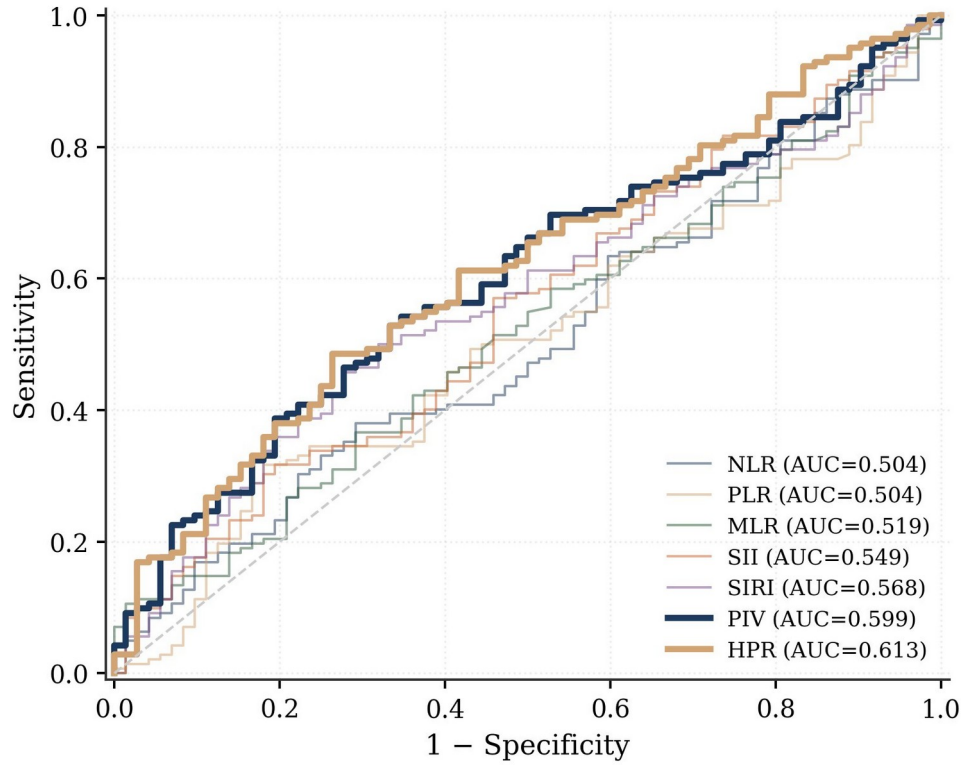


Fig. S1 Receiver operating characteristic curves for 7 blood count-derived indices. Curves for discriminating patients with seborrheic dermatitis ($n = 142$) from healthy controls ($n = 72$). Areas under the curve: NLR, 0.504; PLR, 0.504; MLR, 0.519; SII, 0.549; SIRI, 0.568; PIV, 0.599; HPR, 0.613. PIV and HPR had the highest areas under the curve among the indices but discriminated poorly. The PLR curve is plotted in the opposite orientation to that used in Table S2 (area under the curve, 0.496; $1 - 0.496 = 0.504$). The dashed diagonal line indicates chance performance. Abbreviations are defined in Table S1.

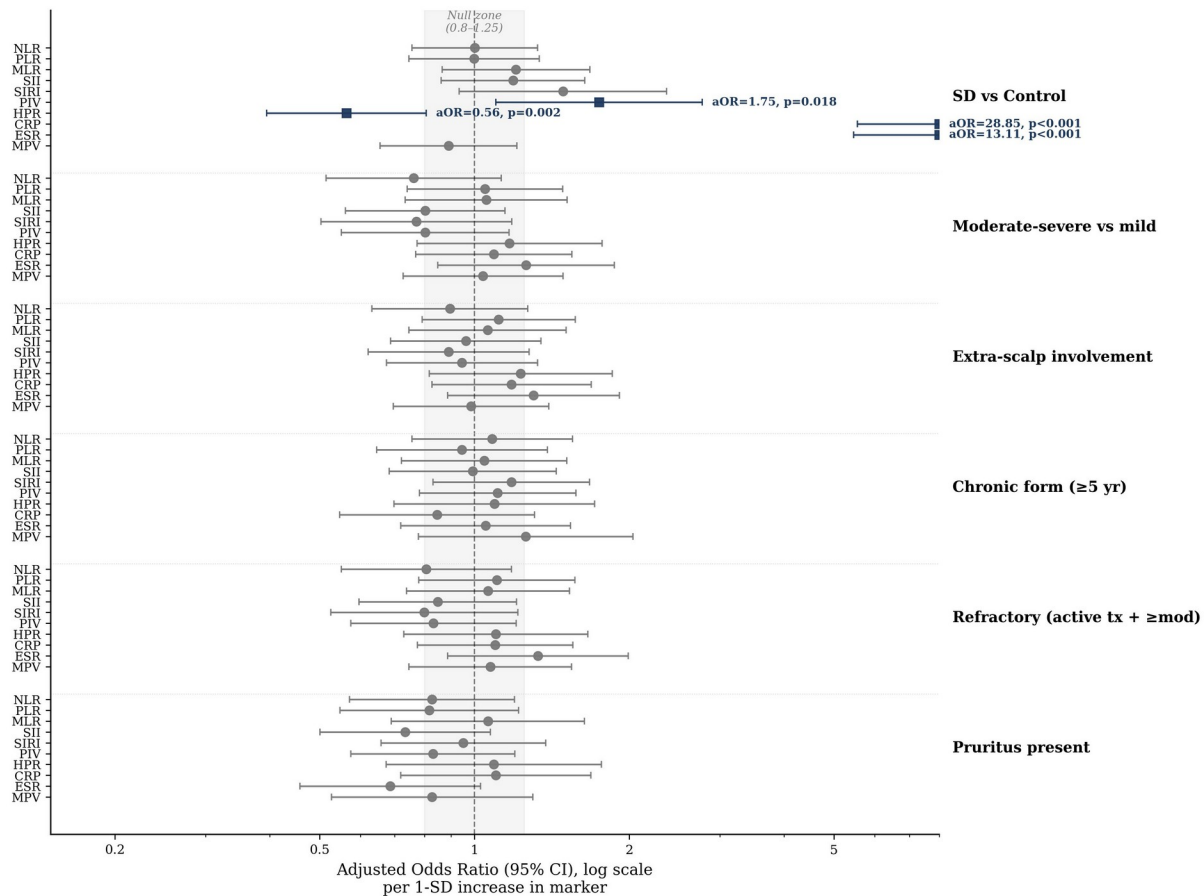


Fig. S2 Forest plot of adjusted odds ratios for each marker and outcome. Adjusted odds ratios (points) and 95% CIs (horizontal lines) per 1-SD increase in each of 10 markers (NLR, PLR, MLR, SII, SIRI, PIV, HPR, CRP, ESR, and MPV) for the case-control comparison (patients vs controls) and 5 within-disease outcomes: moderate-to-severe vs mild disease, extra-scalp involvement, chronic disease (duration ≥ 5 years), treatment refractoriness (moderate or higher severity despite active topical treatment), and pruritus. The horizontal axis is logarithmic; the shaded band marks odds ratios of 0.8 to 1.25, and the dashed line marks an odds ratio of 1. Markers highlighted in blue (PIV, HPR, CRP, and ESR) had $q < .05$ in the case-control comparison; the point estimates and upper confidence limits for CRP and ESR exceed the range of the axis. No marker was associated with any within-disease outcome. Case-control models were adjusted for age, sex, body mass index, and pack-years of smoking; within-disease models were additionally adjusted for comorbidity. In the figure, “SD vs Control” denotes patients with seborrheic dermatitis vs healthy controls, and “1-SD” in the axis label denotes 1 standard deviation. aOR indicates adjusted odds ratio; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; MPV, mean platelet volume; other abbreviations are defined in Table S1.

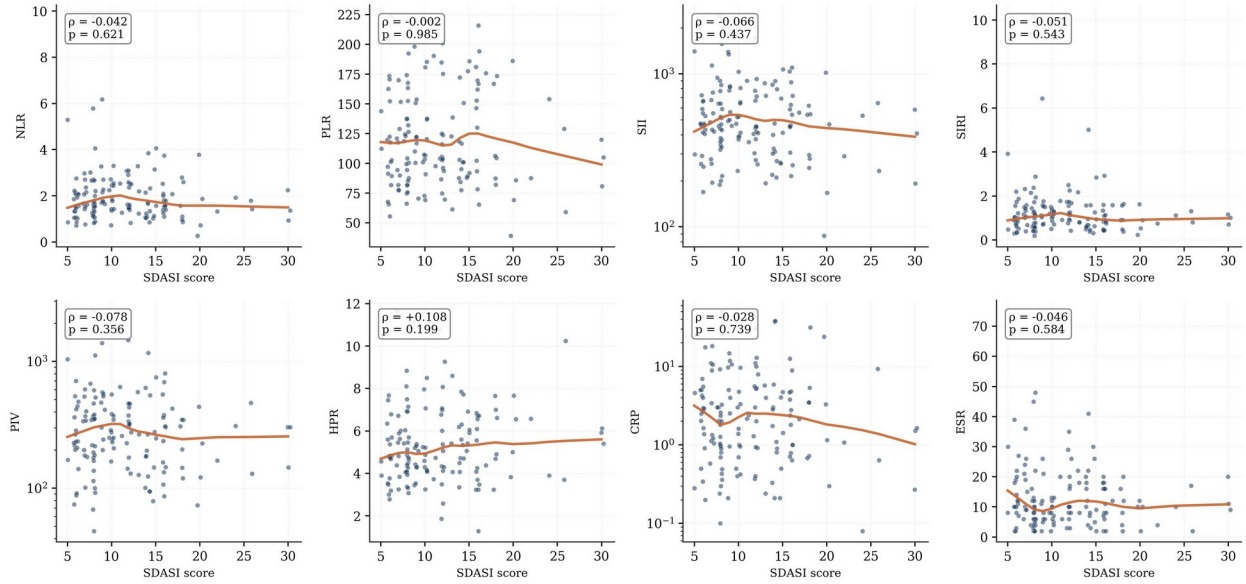


Fig. S3 Scatter plots of Seborrheic Dermatitis Area and Severity Index (SDASI) score against selected markers. Scatter plots of SDASI score against 8 markers (NLR, PLR, SII, SIRI, PIV, HPR, CRP, and ESR) among 142 patients with seborrheic dermatitis. Each point is a patient, and the curve is a smoothed trend line. Spearman ρ and unadjusted P values shown in each panel: NLR, -0.042 (P = .62); PLR, -0.002 (P = .99); SII, -0.066 (P = .44); SIRI, -0.051 (P = .54); PIV, -0.078 (P = .36); HPR, 0.108 (P = .20); CRP, -0.028 (P = .74); ESR, -0.046 (P = .58). Correlations were weak, and none was statistically significant. The other markers are not plotted. The vertical axes for SII, PIV, and CRP are logarithmic. CRP indicates C-reactive protein; ESR, erythrocyte sedimentation rate; other abbreviations are defined in Table S1.

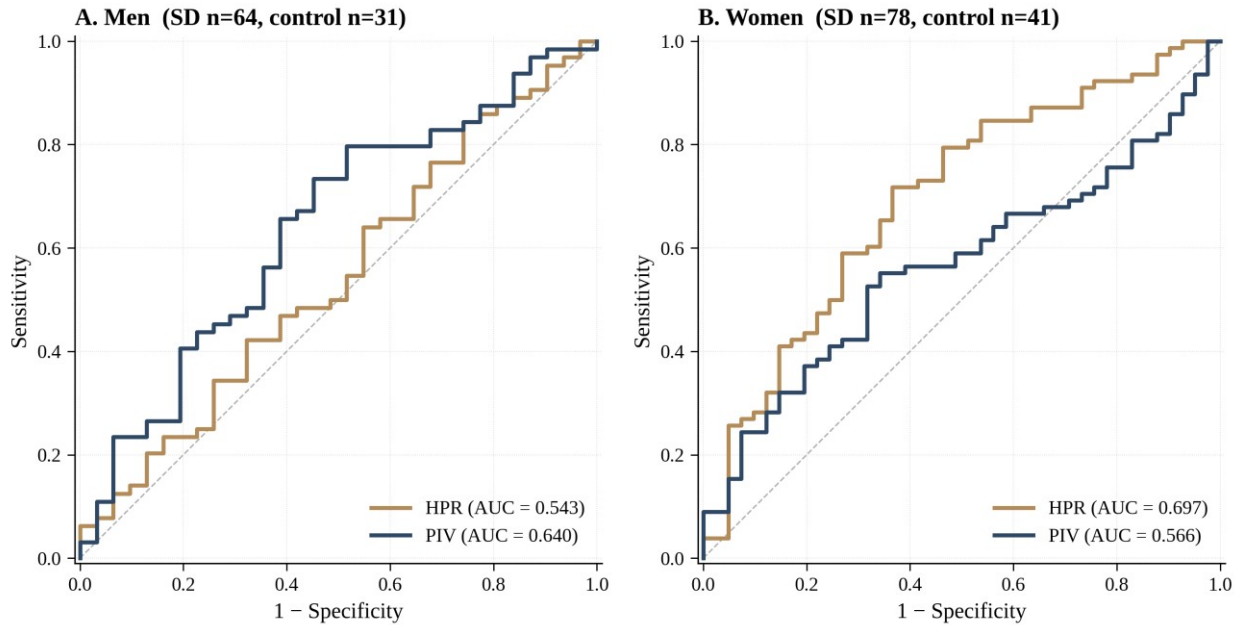


Fig. S4 Exploratory sex-stratified receiver operating characteristic curves for HPR and PIV. Receiver operating characteristic curves for discriminating patients with seborrheic dermatitis from healthy controls among men (panel A; 64 patients and 31 controls) and women (panel B; 78 patients and 41 controls). Areas under the curve: men, PIV 0.640 and HPR 0.543; women, HPR 0.697 and PIV 0.566. These analyses were exploratory. Formal tests for interaction by sex were not significant, the strata were small, and the curves should not be interpreted as evidence of sex-specific biology. The dashed diagonal line indicates chance performance. In the panel titles, SD denotes seborrheic dermatitis; other abbreviations are defined in Table S1.

Code Availability

All statistical analyses were performed in Python, version 3.12, with statsmodels 0.14, scikit-learn 1.4, scipy 1.13, numpy 1.26, and pandas 2.2. The random seed was fixed at 42 for all bootstrap procedures. Analytic code is available from the corresponding author on reasonable request.