RESEARCH LETTER

Decreased glomerular function is associated with disease severity in patients with hidradenitis suppurativa

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1 | INTRODUCTION

Chronic, systemic inflammation is associated with chronic kidney disease (CKD).[1] With the growing literature on hidradenitis suppurativa (HS) as a systemic disease with a long-standing inflammatory burden and multiple disease trajectories, HS was recently associated with renal dysfunction expressed by glomerular hyperfiltration.[2] Glomerular hyperfiltration is a condition characterized by increased glomerular pressure that occurs in patients with impaired kidney function and/or reduced nephron numbers, reflecting increased filtration per nephron. The condition is caused by afferent arteriolar vasodilation and/or by efferent arteriolar vasoconstriction, and might be a precursor of renal injury in various kidney diseases associated with increased mortality.[3] Therefore, early signs of impaired renal function are important to recognize to prevent irreversible kidney damage in patients with HS. On this background, the aim of this study was to examine the association between disease severity, systemic inflammatory load, and renal function; and explore patient-specific risk factors for impaired renal function in patients with HS.

2 | METHODS

We included a total of 490 newly-referred outpatients with HS from January 2016 to January 2021, from the Department of Dermatology, Bispebjerg Hospital, Copenhagen, Denmark. Patients aged >18 years and a hidradenitis suppurativa score (HSS) >0 were eligible to participate in the study after written consent was obtained. HSS is a clinical assessment instrument of disease severity based on a number of involved anatomical regions, lesions (nodules, abscesses, fistulas, other), and distance between relevant lesions. Patients with missing data on glomerular function were excluded. Information on age, sex, smoking, ethnicity, body mass index, disease duration, and a number of boils in the last month was noted. Furthermore, the presence of systemic comorbidities and severity of HS was obtained through interview and clinical examination and confirmed from diagnoses in patient files. All patients were assessed using the Hurley system as well, which is a measurement of three distinct clinical stages of severity from 1 to 3. Blood was drawn to determine lipid levels (cholesterol, high-density lipoprotein, low-density lipoprotein, triglycerides), inflammatory markers (erythrocyte sedimentation rate [ESR], C-reactive protein, neutrophil–lymphocyte ratio), and creatinine.

TABLE 1 Demographic factors and disease characteristics of patients with hidradenitis suppurativa according to renal function

	Renal function (eGFR, ml/min per 1.73 m^2)				Renal function, continuous			
	Decreased (<90) N = 120 (24.5%)	Normal (≥90) N = 370 (75.5%)	Total N = 490	p value	Mean	SD	B value	p value
Age, years, median (IQR)	50 (19.5)	35.5 (19)	39 (23)	<0.001			−8.05	<0.001
Sex, n (%)				0.027				0.131
Female	87 (72.5)	227 (61.4)	314 (64)		99.4	18.5		
Male	33 (27.5)	143 (38.6)	176 (36)		102.1	18.7		
Ethnicity				0.026				<0.001
White	107 (89.2)	297 (80.3)	404 (82.4)		98.9	18.3		
Non-White	13 (10.8)	73 (19.7)	86 (17.6)		107.2	18.3		
Disease severity, n (%)				0.728				0.035
Hurley I	37 (30.8)	125 (33.8)	161 (32.8)		101.9	17.4		
Hurley II	64 (53.3)	197 (53.2)	261 (53.3)		100.7	18.4		
Hurley III	19 (15.8)	49 (13.2)	68 (13.9)		95.1	21.3		
Disease duration, years, median (IQR)	19 (25)	10 (15)	11 (17)	<0.001			−0.483	<0.001
HSS, median (IQR)	12.5 (15.7)	12 (17)	12 (16)	0.836			−0.059	0.227
Total boils, median (IQR)	1 (3)	1 (3)	1 (3)	0.198			0.534	0.027
Boils last month, mean (IQR)	1 (3)	2 (3)	2 (3)	0.228			0.434	0.106
BMI, median (IQR), kg/m^2	28.7 (7.3)	27.8 (9.8)	28.07 (9.2)	0.766			−0.022	0.858
Smoking, n (%)				0.327				0.27
Yes	93 (77.5)	301 (81.6)	394 (80.6)		99.9	18.7		
No	27 (22.5)	68 (18.4)	95 (19.4)		102.3	18.1		
Comorbidities, n (%)								
Dyslipidemia	18 (15)	25 (6.8)	43 (8.8)	0.006	88.6	20.8		<0.001
No	102 (85)	345 (93.2)	447		101.5	18		
Hypertension	76 (63.3)	181 (48.9)	257 (52.3)	0.006	97.2	18.9		<0.001
No	44 (36.7)	189 (51.1)	233		103.8	17.6		
Diabetes	14 (11.7)	28 (7.6)	42 (8.6)	0.163	92.7	25.8		0.005
No	106 (88.3)	342 (92.4)	448		101.1	17.6		
Mean arterial pressure, mmHg (SD)	104.8 (13.1)	101.4 (12.6)	102.2 (12.8)	0.011			−0.197	0.003
Lipid levels, median (IQR), mmol/L								
Total cholesterol	4.8 (1.3)	4.5 (1.3)	4.6 (1.2)	0.102			−0.117	0.59
HDL-C	1.3 (0.5)	1.3 (0.6)	1.3 (0.5)	0.047			−4.474	0.012
LDL-C	2.8 (1.3)	2.4 (1.2)	2.5 (1.2)	0.676			−0.928	0.356
Triglycerides	1.5 (1)	1.2 (1.1)	1.3 (1.1)	0.003			−2.69	0.001
Inflammatory markers, median (IQR)								
ESR, mm/h	11 (16)	10 (13)	10 (13)	0.118			−0.167	<0.001
CRP, mg/L	3 (7)	3 (7)	3 (7)	0.89			−0.056	0.221
NLR	2.4 (1.5)	2.2 (1.3)	2.23 (1.3)	0.237			−0.809	0.254

Note: Boils are a total number of boils at clinical examination. eGFR was estimated from creatinine levels at clinical examination and calculated using the age and sex-specific CKD-EPI equation. Hypertension: systole >140 mmHg, diastole >90 mmHg. Smoking data missing on one patient in those with normal renal function.

Abbreviations: BMI, body mass index; CKD, chronic kidney disease; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; ESR, erythrocyte sedimentation rate; HDL, high-density lipoprotein; HSS, hidradenitis suppurativa score; IQR, interquartile range; LDL, low-density lipoprotein; NLR, neutrophils–lymphocytes ratio.

Estimated glomerular filtration rate (eGFR) was calculated from creatinine levels, as defined by Chronic Kidney Disease Epidemiology Collaboration.[4] Patients were then divided into three groups with normal, mildly, and severely decreased eGFR, respectively, with an eGFR of ≥90, 60–89, and <60 ml/min per 1.73 m^2.

2.1 | Statistical analysis

We analyzed the data using a crude model and a model adjusted for age, sex, and smoking, and with eGFR as a continuous variable. All tests were considered statistically significant at a $p < 0.05$ and 95% confidence interval.

3 | RESULTS

The median age was 39 years (interquartile range: 23) and the majority were female (64%) and smokers (80.6%) (Table 1). A total of 370 (75.5%), 107 (21.8%), and 13 (2.7%) patients had normal, mildly, and severely decreased eGFR. We formed two groups with an eGFR <90 ($n = 120$) or ≥90 ($n = 370$), to examine differences between patients with decreased and normal glomerular filtration.

We found a statistically significant difference in eGFR level as a continuous variable between the Hurley stages, with a mean eGFR of 101.9, 100.7, and 95.1 for Hurley stage I, II, and III, respectively ($p = 0.035$). HSS did not correlate to eGFR in the crude model ($r = 0.33$, $p = 0.963$). Erythrocyte sedimentation rate correlated negatively with eGFR, $r = -0.167$ ($p < 0.001$), indicating that systemic inflammatory burden associates with decreased GFR, however, not after adjustment ($p = 0.712$).

A significant number of HS patients with decreased eGFR had dyslipidemia and hypertension (both $p = 0.006$) and an increase in triglyceride levels ($p = 0.003$), indicating cardiovascular risk factors commonly associated with HS. The mean arterial pressure was significantly higher in those with decreased eGFR at 104.8 mmHg, compared to 101.4 mmHg in those with normal eGFR ($p = 0.011$), but not after adjustment ($p = 0.78$).

Moreover, a total of 237 patients were currently or previously treated with tetracycline. Although long-term treatment with antibiotics is known to possibly affect renal function, tetracycline use had no statistically significant impact on their eGFR ($p = 0.161$).

We formed two groups of patients aged ≥50 years ($n = 135$), defined by eGFR above the 75 percentile sex- and age-specific values by Wetzels et al.[5] to explore the presence of hyperfiltration. Patients with hyperfiltration ($n = 104$, 77%) had more often hypertension, $n = 80/104$ (76.9%) ($p = 0.039$), however, we did not find a higher HSS or Hurley stage in this group, ($p = 0.659$) and ($p = 0.695$), respectively.

4 | DISCUSSION

Patients with HS have chronic systemic inflammation, characterized by persistent, elevated levels of circulating inflammation markers.[6] Abnormal cytokine expression of interleukin-1 (IL-1) has been demonstrated in both lesional and uninvolved skin, supporting the increased systemic inflammatory load in patients with HS.[7]

The role of inflammation in CKD pathogenesis and progression has been recognized for several years, expressed as upregulated monocyte release of IL-1 causing vascular dysfunction in patients with CKD.[8] Our study found a significant decrease in eGFR in more severe diseases, possibly due to the long-standing inflammatory burden in patients presenting with Hurley stage III, supported by the inverse relationship between elevated ESR and decreased eGFR.

Chronic inflammatory disorders have been associated with multiple comorbidities, including cardiovascular disease and metabolic syndrome.[9] We found that the presence of dyslipidemia and hypertension was significantly higher in patients with decreased eGFR, which are frequently associated as both a cause and effect of renal dysfunction.[10]

Although renal dysfunction traditionally has been attributed to reduced renal flow and low eGFR, an increased GFR can be an expression of early manifestations of renal dysfunction. While glomerular hyperfiltration may act as a marker of early renal damage in prediabetes and prehypertension, patients are often misclassified with normal renal function, even though both low and high eGFR is associated with a significantly higher risk of death and cardiovascular disease, presenting as an upside-down U curve.[11] The pathogenesis is not completely understood but is attributed to an increase in glomerular capillary pressure, which increases tensile stress applied to the capillary wall structures.[3] However, different methods are used to determine glomerular hyperfiltration and the definition has not been agreed upon. A previous study by Miller et al. has shown elevated eGFR in HS patients when compared to controls.[2] We found that among patients >50 years, the presence of hypertension was significantly higher in those with glomerular hyperfiltration. Although we did not find an association with disease severity, this indicates that hypertensive stress on the capillary walls increases the glomerular filtration.

Our study is limited by the lack of urine samples to measure proteinuria, lack of a control group, and the confounding of age. Furthermore, the study is a single-center hospital-based study, which might be biased by demographic differences and disease severity, as patients attending a hospital typically have more severe disease.

5 | CONCLUSION

We found that patients with severe HS disease had a significantly decreased eGFR. This may be due to an increased systemic inflammatory load and excessive stress on the nephron in more severe disease, supported by the negative correlation between ESR and eGFR. In addition, patients with decreased renal function had a worsened cardiometabolic profile, expressed by an increased presence of hypertension and dyslipidemia. In patients above 50 years of age, we found a high proportion of hypertension and glomerular hyperfiltration. This calls for more awareness in both patients with decreased eGFR and patients presenting with abnormally elevated eGFR.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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