

## Evaluation of Faecal Calprotectin Level in Psoriatic and Hidradenitis Suppurativa Patients as A Model of An Autoimmune and Auto-Inflammatory Disease Retrospectively

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### ABSTRACT

**Background:** Psoriasis represents an example of an autoimmune disease where adaptive immune system activation, T helper 17 secretory cytokines secretion such as IL 17 and IL 21, and self-antigen intolerance are the hallmarks of its pathology. Hidradenitis suppurativa on the contrary, could be described as a neutrophilic dermatosis disease while recurrent abscess formation and skin fibrosis compose the clinical features. Inflammatory bowel diseases association with diverse dermatological diseases is well known. **Objectives:** To evaluate the role of the diagnostic application of fecal calprotectin (FCP) in patients with either hidradenitis suppurativa or psoriasis.

**Patients and Methods:** A sectional-cross study was done on 20 patients with varying severity of plaque psoriasis and 10 patients with hidradenitis suppurativa (HS). Demographic data, duration of illness, area extent affected, gastrointestinal symptoms, and severity scores were taken as Psoriasis Assessment and Severity Index (PASI) score and Hurley staging for psoriasis and HS retrospectively. A fecal calprotectin (FCP) assay was also tested.

**Results:** While the psoriasis group demonstrated significantly higher age (median = 51 vs. 25 years,  $P < 0.001$ ) than the HS group, hidradenitis suppurativa showed significantly higher FCP levels (median = 215 vs. 83, respectively,  $P = 0.013$ ). Significant strong positive correlations between FCP and severity were observed in the hidradenitis suppurativa group ( $r = 0.921$ ,  $P < 0.001$ ).

**Conclusion:** To our knowledge, our study could be the first comparative study between hidradenitis suppurativa and psoriasis in relation to fecal calprotectin.

**Keywords:** Hidradenitis suppurativa, Psoriasis, Fecal calprotectin.

### INTRODUCTION

Many dermatological diseases could be classified according to their etiology into autoimmune or autoinflammatory diseases. Adaptive immune system activation and self-antigen intolerance are the hallmark of autoimmune disease pathology. However, the innate immune system and inflammasome play a fundamental role in autoinflammatory disease that is usually related to genetic links<sup>(1)</sup>.

Psoriasis pathogenesis is linked predominately to T helper 17 secretory cytokines such as IL 17 and IL 21 that could perpetuate the inflammatory cascade leading to keratinocyte proliferation and subsequently neovascularization development<sup>(2,3)</sup>.

Psoriasis encompasses a heterogenous spectrum of many subtypes that begin from mild localized plaque to the more severe pustular form. Extracutaneous features such as psoriatic arthritis sometimes precede the primary skin lesions. Also, another autoimmune disease like inflammatory bowel disease may accompany its presence<sup>(4)</sup>.

Many severity scores were utilized to standardize a stratification of psoriasis intensity that can be used clinically and in treatment modalities applications trials. It usually depends on lesion extent, desquamation, and erythema overlying. Psoriasis Assessment and Severity Index (PASI) score is the most validated and studied psoriasis score in clinical practice<sup>(5)</sup>.

Hidradenitis suppurativa (HS) is a chronic debilitating inflammatory disorder that consists of

recurrent abscess formation, sinus tracking, and skin fibrosis mostly affecting apocrine glands areas like the axilla and groin<sup>(6)</sup>. HS may go through a severe course over intertriginous areas leading to extensive skin scarring and mutilation. HS is led mostly by an autoinflammatory immune response with multifactorial elements sharing its pathogenesis like genetic, bacterial, and environmental factors<sup>(7,8)</sup>. Hurley classification is mostly used to describe the HS severity for clinical follow-up and surgical decisions in a single area affection<sup>(9)</sup>. HS might associate inflammatory bowel disease with an odd ratio of 2.12 and 1.51 for Chron's disease and ulcerative colitis respectively. Also, more than ten percent of IBD cases could develop an extraintestinal cutaneous manifestation, especially perianal fistula, pyoderma gangrenosum, and hidradenitis suppurativa<sup>(10,11)</sup>.

Fecal calprotectin (FCP) is a predominant neutrophilic component representing most of the cytosolic protein in the granulocytes. It is more abundant in the stool than other body fluids. It increases in many intestinal pathologies such as inflammatory bowel disease, non-steroidal anti-inflammatory drugs (NSAID) regular use, and even colorectal cancers<sup>(12)</sup>.

Many studies tried to explore the prevalence of increased FCP levels and subsequently provisional diagnosis of IBD association with many dermatological diseases<sup>(13)</sup>.

Our study aimed to evaluate the role of the diagnostic application of FCP in patients with either

hidradenitis suppurativa or psoriasis as an example of auto-inflammatory and autoimmune disease respectively.

## PATIENTS AND METHODS

A sectional-cross study was done at Dermatological and Internal Medicine outpatients' clinics and admission wards at Benha University Hospitals, Egypt from March 2023 to July 2023.

Thirty patients were recruited: 20 patients with varying severity of plaque psoriasis and 10 hidradenitis suppurativa (HS) patients.

While inclusion criteria included patients aged over 14 years old with psoriasis vulgaris or hidradenitis suppurativa, exclusion criteria included patients with known malignancy, active autoimmune disease, or other causes that may affect fecal calprotectin assays such as acute gastroenteritis or recent NSAID use.

For each patient, the following variables were collected: Demographic data such as age and gender, duration of illness, area extent affected, intensity, gastrointestinal symptoms, and detailed medical examination.

PASI Severity score and Hurley Staging were applied for psoriasis vulgaris or hidradenitis suppurativa respectively. PASI score ranges from 0 to 72. Mild disease is defined when the PASI score is less than 10. Moderate to severe is considered when the PASI score reaches over 10. For more stratification, moderate and severe psoriasis differentiation could be defined by Dermatology Life Quality Index in PASI Score ranges from 10 to 15, and over 15 respectively. Fecal calprotectin with EILSA immunoassay was tested for every patient in the studied groups <sup>(14)</sup>.

### Ethical approval:

**Informed consent was obtained from every adult patient or the caregiver of every child patient and our study was approved by the Benha Medical Ethical Committee, Benha Faculty of Medicine, Egypt. (RC.5.4.2023). The Helsinki Declaration was upheld throughout the course of the investigation.**

### Statistical methods:

SPSS version 28 was used for data management and statistical analysis. The Shapiro-Wilk test was used to determine the normality of quantitative data. Medians and ranges were used to summarise quantitative data. Numbers and percentages were used to represent a categorical set of data. The Mann-Whitney U test was used to compare quantitative data between the study groups. The Chi-square test was used to compare categorical data. Spearman's correlation was used to perform the correlations. To forecast fecal calprotectin, multivariate linear regression analysis

was conducted. Each and every statistical test has two sides. P-values of 0.05 or less were regarded as significant.

## RESULTS

### General and clinical characteristics

Psoriasis group demonstrated significantly higher age and disease duration than the hidradenitis suppurativa group. Hidradenitis suppurativa showed significantly higher fecal calprotectin (FCP) levels than the psoriasis group. Females predominated in psoriasis (60%) and hidradenitis suppurativa groups (80%), with no statistical significance. Also, no statistically significant difference was observed regarding gut symptoms. Regarding severity, severe psoriasis was the most common. For hidradenitis suppurativa, Hurley staging demonstrated that half of the patients 5 (50%) were in stage I (Table 1).

**Table (1): General and clinical characteristics of the studied groups**

	<b>Psoriasis (n = 20)</b>	<b>Hidradenitis suppurativa (n = 10)</b>	<b>P-value</b>
<b>Age (years) median (range)</b>	51 (15 - 71)	25 (14 - 42)	<b>&lt;0.001*</b>
<b>Gender</b>			
Males n. (%)	8 (40)	2 (20)	0.273
Females n. (%)	12 (60)	8 (80)	
<b>Disease duration (years) median (range)</b>	4 (1 - 7)	1 (1 - 2)	<b>&lt;0.001*</b>
<b>Psoriasis score (PASI)</b>			
Mild n (%)	5 (25)	-	-
Moderate n (%)	6 (30)	-	
Severe n (%)	9 (45)	-	
<b>Hurley staging</b>			
Stage I n. (%)	-	5 (50)	-
Stage II n. (%)	-	2 (20)	
Stage III n. (%)	-	3 (30)	
<b>FCP median (range)</b>	83(10 - 210)	215 (67 - 410)	<b>0.013*</b>
<b>Gut symptoms n (%)</b>	11 (55)	5 (50)	0.796

\*Significant P-value; FCP: Fecal calprotectin.

### Correlation between FCP and severity

Significant positive correlations between fecal calprotectin (FCP) and severity were observed in psoriasis and hidradenitis suppurativa groups, with the correlation being moderate in the psoriasis group and strong in the hidradenitis suppurativa group (Figure 1).

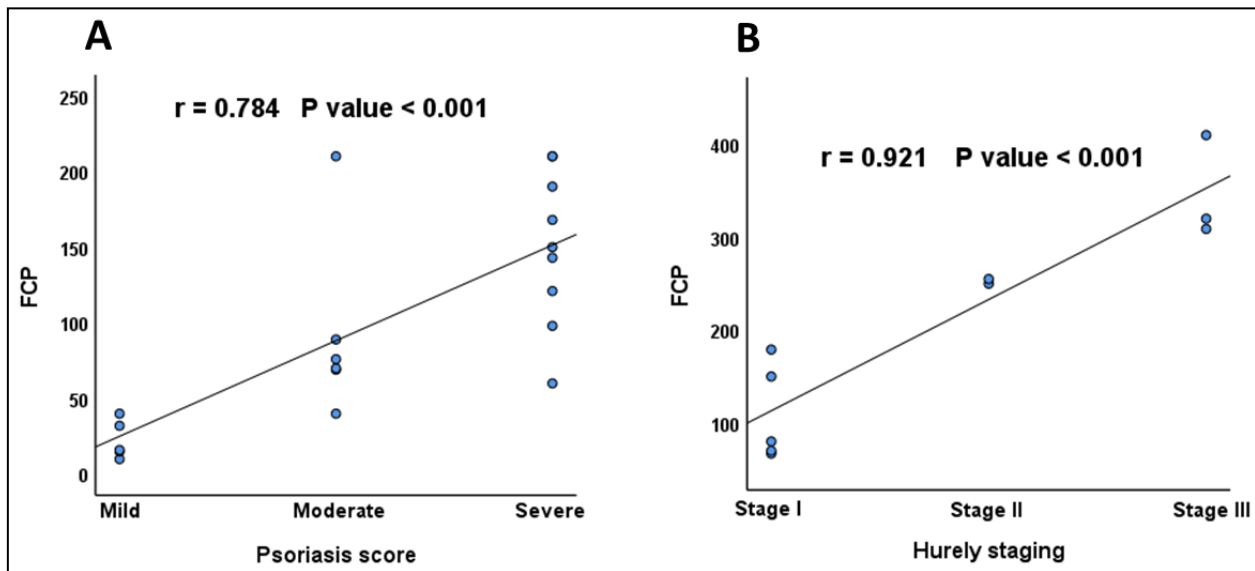


Figure (1): Correlation between FCP and A) psoriasis severity and B) Hurley score.

**Fecal calprotectin according to gut symptoms**

Fecal calprotectin (FCP) did not significantly differ according to the presence of gut symptoms in the psoriasis group and the hidradenitis suppurativa group (Table 2).

**Table (2): Fecal calprotectin according to gut symptoms in psoriasis and hidradenitis suppurativa groups**

Psoriasis			Hidradenitis suppurativa		
Gut symptom	No gut symptoms	P-value	Gut symptom	No gut symptoms	P-value
76 (16 - 210)	89 (10 - 210)	0.94	250 (70 - 410)	179 (67 - 320)	0.69

FCP: Fecal calprotectin

**Prediction of fecal calprotectin**

Multivariate linear regression analysis was done to predict fecal calprotectin (FCP). It revealed that age and hidradenitis suppurativa were significant predictors for FCP (Table 3).

**Table (3): Multivariate linear regression analysis to predict fecal calprotectin**

	B (95% CI)	P-value
Age (years)	2.7 (0.2 - 5.2)	<b>0.033*</b>
Female gender	43.2 (-27.9 - 114.2)	0.222
Disease duration (years)	15.7 (-5.9 - 37.2)	0.146
Hidradenitis suppurativa	200.0 (100.5 - 299.6)	<b>&lt;0.001*</b>

\*Significant P-value; B: Regression coefficient; 95% CI: 95% confidence interval

**DISCUSSION**

Inflammatory bowel disease is more prevalent than in the past and has greater morbidity and lower quality of life when it is in severe degrees at diagnosis (15). Many recent studies explored that IBD is related to many allergic and immunological diseases like atopic dermatitis, which is linked with close causal associations (16), and even primary immunodeficiency disease (17,18).

Skin disorders related to inflammatory bowel disease are extensive and some of them are related either to activity or irrelevant to the disease stage as pyoderma gangrenosum, erythema nodosum, Sweet’s syndrome, and psoriasis (19). Hidradenitis suppurativa is one of the dermatological diseases recently associated with inflammatory bowel disease. Neutrophilic dermatoses are one of the innate cell-mediated skin diseases, HS could be considered in that disorder’s spectrum that could be labeled an autoinflammatory disease example (20).

In our study, psoriatic patients showed higher age than hidradenitis suppurativa, which could be explained. While hidradenitis suppurativa is a disease of adolescents and young adults, psoriasis had 2 age peaks, the first in young adulthood and the other in the fifties and sixties (21).

Hidradenitis suppurativa-studied patients showed a higher mean fecal calprotectin (FCP) level that was correlated with many other recent studies (10,22). Our study is unique in that research area because, to our knowledge, there is no comparative study with psoriasis in relation to inflammatory bowel disease.

In our study, while only 3 (30 %) hidradenitis suppurativa patients had a severe degree of dermatological disease, a more significant positive correlation with fecal calprotectin level could be explored (r = 0.921, P < 0.001).

One of our explanations of that strong association might be explained as hidradenitis suppurativa is an example of an autoinflammatory disease with the same

pathogenic mechanisms, cytokines, and innate cells involvement which could be a distant extraintestinal regions feature of an inflammatory bowel disease. Also, hidradenitis suppurativa prevalence rises with one of the inflammatory bowel diseases age peaks. Many authors explored the companion of both diseases, they suggested genetic loci associations in some proven cases or microbiota dysregulation theory in both disorders<sup>(23,24)</sup>.

Hidradenitis suppurativa is a risk factor for developing inflammatory bowel disease nine times more than healthy controls<sup>(25)</sup>. Contrary to our results, **Kluger et al.**<sup>(26)</sup> found no relation between both disorders bearing in mind the small sample size and retrospective nature of their methodology.

Fecal calprotectin should not be thought of as a unique and only way to diagnose inflammatory bowel disease because many false positive and false negative results are known to be a minor limitation for its use. This could be obviously seen in our results as there is no relation between gut symptoms and fecal calprotectin positivity either for psoriasis or hidradenitis suppurativa. Subclinical colitis or enteritis may be the cause of elevated fecal calprotectin in such cases that can not be established or refuted unless a colonoscopy is done for these patients.

Although the psoriasis association with other autoimmune disorders mostly occurs in older patients, we found a lesser correlation between psoriatic patients and fecal calprotectin levels in our psoriatic group with higher median age compared to hidradenitis suppurativa patients.

## CONCLUSION

Elevated fecal calprotectin had a strong correlation with hidradenitis suppurativa disease compared to psoriasis patients and that might be used in the clinical screening of these patients as a surrogate biomarker for colonoscopy evaluation.

To our knowledge, our study could be the first comparative article between hidradenitis suppurativa and psoriasis in relation to fecal calprotectin. Shared etiopathogenesis might be the leading factor that clarifies the stronger correlation with hidradenitis suppurativa.

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**Competing interests:** Nil.

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