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# Cutaneous Clues to Gut Disease: The Prevalence of Subclinical IBD in Neutrophilic Dermatoses

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**Abstract**

**Background and Aims:** Chronic neutrophilic dermatoses (CNDs), including Sweet's syndrome and pyoderma gangrenosum, are inflammatory skin conditions often associated with systemic inflammatory disorders such as inflammatory bowel disease (IBD). These dermatoses frequently present without overt gastrointestinal symptoms, complicating the diagnosis of co-existing IBD, which may remain subclinical in many cases. This review investigates the prevalence and characteristics of subclinical Crohn's disease and ulcerative colitis in patients with CNDs, focusing on clinical, pathophysiological, and diagnostic challenges.

**Methods:** A systematic approach was employed to collect data from databases such as PubMed and Scopus using relevant keywords. Studies were included based on their investigation of the link between CNDs and subclinical IBD. The review explored the utility of non-invasive diagnostic tools, such as fecal calprotectin measurements and imaging techniques (abdominal ultrasound, MRI), in detecting IBD in asymptomatic patients. A quality assessment of selected studies ensured reliability of findings.

**Results:** CNDs and IBD share common immune-mediated inflammatory mechanisms, including neutrophil-driven pathology and dysregulated immune responses. Patients with CNDs appear to have an increased risk of subclinical IBD, even without gastrointestinal symptoms. Non-invasive diagnostic tools, such as fecal calprotectin and advanced imaging techniques, show promise in identifying subclinical IBD in asymptomatic individuals. However, diagnostic challenges persist due to the lack of specific biomarkers for subclinical IBD and difficulty justifying comprehensive gastrointestinal evaluations without symptoms.

**Conclusions:** Clinicians should maintain a high index of suspicion for subclinical IBD in patients with CNDs, even without classic gastrointestinal symptoms. Early detection and intervention could improve outcomes and prevent long-term complications associated with undiagnosed IBD. A multidisciplinary approach, integrating dermatology and gastroenterology, is essential for effective patient care. Future research should refine diagnostic criteria, deepen the understanding of molecular mechanisms, and develop objective biomarkers to improve management and outcomes for this patient population.

**Keywords**

Chronic neutrophilic dermatoses; Sweet's syndrome; Pyoderma gangrenosum; Inflammatory bowel disease; Crohn's disease; Ulcerative colitis; Subclinical IBD; Fecal calprotectin; Diagnostic challenges; Immune-mediated inflammation.

## Introduction

### Background and Context

Chronic neutrophilic dermatoses (CNDs) are a heterogeneous group of cutaneous diseases characterized by neutrophilic infiltration without evidence of bacterial infection or vasculitis [1]. These diseases manifest with various clinical features, including vesicles, pustules, plaques, nodules, or ulcerations, and some patients may experience extracutaneous involvement. The underlying pathophysiology of CNDs remains incompletely understood, but current evidence suggests that abnormal activation of the innate immune system plays a central role [2]. In some cases, elevated levels of neutrophil-activating cytokines, such as interleukin-1 and tumor necrosis factor-α, have been implicated in excessive neutrophil recruitment. Overexpression of these molecules can lead to excessive and unnecessary neutrophil recruitment. While neutrophilic dermatoses can be triggered by infections or medications, they are frequently idiopathic. Treatments typically include systemic and topical steroids, along with management of known triggers when applicable.

Two of the most common CNDs are Sweet's syndrome and pyoderma gangrenosum. Sweet's syndrome, or acute febrile neutrophilic dermatosis, is characterized by the sudden onset of painful erythematous plaques or nodules, often with systemic symptoms such as fever [3]. Diagnosis is established by a skin biopsy demonstrating an infiltrate of neutrophils in the dermis. Sweet's syndrome is relatively uncommon in the general population and accounts for an estimated three of every 10,000 dermatology office visits [4]. However, this condition affects a disproportionate number of patients with inflammatory bowel disease (IBD) with a prevalence ranging from 0.07% to 0.21%,

depending on the patient group studied [5,6]. Neutrophilic dermatoses like Sweet's syndrome and pyoderma gangrenosum can be categorized as extraintestinal manifestations (EIMs) of IBD.

Pyoderma gangrenosum is a neutrophilic dermatoses that presents as rapidly progressive, painful ulcerating lesions [7]. These ulcers often have a necrotic center and irregular borders. To diagnose pyoderma gangrenosum, skin infection must be ruled out, and a biopsy must be taken. A biopsy of pyoderma gangrenosum demonstrates a neutrophilic infiltrate in the dermis without any infection. Like Sweet's syndrome, pyoderma gangrenosum affects patients with IBD to a greater degree than the general population. Approximately 1-3% of patients with IBD suffer from pyoderma gangrenosum at some point in their disease [7,8]. This association highlights the importance of considering pyoderma gangrenosum as a potential extraintestinal manifestation in patients with IBD, necessitating careful clinical evaluation and management.

IBD includes two major disorders: Crohn's disease and ulcerative colitis, both characterized by autoimmune-driven inflammation of the gastrointestinal tract. The mechanisms underlying the abnormal immune response and neutrophil activation in IBD parallel those seen in chronic neutrophilic dermatoses. Although IBD primarily affects the gastrointestinal system, extraintestinal manifestations such as pyoderma gangrenosum and Sweet's syndrome are common. These conditions can precede or follow the onset of gastrointestinal symptoms, complicating diagnosis. Patients without gastrointestinal complaints may be reluctant to undergo a diagnostic workup, believing their condition is unrelated to IBD. Typically, IBD is diagnosed based on persistent gastrointestinal symptoms such as abdominal pain, diarrhea, and hematochezia. In the absence of these symptoms, clinical suspicion for active IBD is low, even in patients with known CNDs. Additionally, screening biomarkers such as C-reactive protein and fecal calprotectin have limited sensitivity and specificity for IBD [9,10]. Despite these challenges, investigating CNDs patients for underlying IBD is critical, as some may have subclinical disease that could be identified through a thorough evaluation.

Currently, the prevalence of subclinical IBD in patients with CNDs is largely unknown. While Sweet's syndrome and pyoderma gangrenosum are more common in individuals with IBD compared to the general population, limited data exist on how many patients with these conditions eventually develop IBD. Understanding the prevalence of subclinical IBD in patients with CNDs could inform more targeted recommendations for IBD screening, even in the absence of gastrointestinal symptoms. Early detection of IBD allows for timely intervention, potentially altering the disease's natural course. By diagnosing IBD before significant symptoms arise, patients with CNDs could achieve better disease control and improved quality of life compared to cases where IBD remains undetected until severe gastrointestinal symptoms develop.

## Research Objectives

The primary objective of this research is to determine the prevalence of subclinical IBD, including Crohn's disease (CD) and ulcerative colitis (UC), in patients with CNDs such as Sweet's syndrome and pyoderma gangrenosum. Subclinical IBD refers to a preclinical phase characterized by underlying inflammatory processes and the presence of endoscopic lesions before the clinical diagnosis of IBD, often triggered by various factors [11]. Although the exact prevalence remains unclear, IBD is known to cause extraintestinal symptoms, including skin conditions, in 36% of patients [12]. Cutaneous manifestations of IBD include erythema nodosum, pyoderma gangrenosum, and aphthous ulcers. However, diagnosing subclinical IBD in patients with CNDs is challenging, especially in the absence of gastrointestinal symptoms, which can lead physicians to overlook underlying conditions [13]. Additionally, IBD-related extraintestinal manifestations, such as skin lesions, and other functional gastrointestinal disorders, such as irritable bowel syndrome (IBS), often present similarly. These conditions require invasive, costly, and time-consuming procedures, such as endoscopy or biopsy [10]. This research aims to identify non-invasive diagnostic methods, such as fecal biomarkers, serological markers, and advanced imaging techniques, to address these diagnostic challenges.

This research aims to explore non-invasive diagnostic methods such as fecal biomarkers, serological markers, and advanced imaging techniques to improve detection. The findings could influence dermatology and gastroenterology practices by facilitating earlier recognition of subclinical IBD in CNDs patients. Noninvasive diagnostic tools, such as fecal biomarkers (e.g., calprotectin and lactoferrin), serological markers (e.g., anti-Saccharomyces cerevisiae antibodies and perinuclear antineutrophil cytoplasmic antibodies), and advanced imaging techniques, are valuable for minimizing patient discomfort, reducing healthcare costs, and decreasing the need for invasive procedures [14]. The outcomes of this research may lead to the creation of a multidisciplinary, patient-centered care model that optimizes clinical care, enhances patients' quality of life, and advances the diagnosis and management of subclinical IBD in patients with chronic neutrophilic dermatoses.

## Methods

A systematic approach was employed to collect data from databases such as PubMed and Scopus using relevant keywords. Studies were included based on their investigation of the link between CNDs and subclinical IBD. Multiple database searches examined the utility of non-invasive diagnostic tools, such as fecal calprotectin measurements and imaging techniques (e.g., abdominal ultrasound and MRI), in detecting IBD in asymptomatic patients, as well as investigating the prevalence of subclinical IBD in patients with pyoderma gangrenosum or Sweet's syndrome. A quality assessment of the selected studies ensured the reliability of the findings.

### Fecal Calprotectin

The utility of fecal calprotectin in diagnosing subclinical IBD was investigated through a literature search in PubMed and Scopus using the terms "fecal calprotectin" AND "IBD" AND ("asymptomatic" OR "screening" OR "subclinical"). Studies published between 2000 and 2024 that addressed the utility of fecal calprotectin as a screening measure for IBD in asymptomatic patients were included. Studies outside this time frame or not available in English were excluded. Additionally, studies that focused on disease severity in known IBD patients and calprotectin, but not on screening, were excluded.

### Imaging Techniques

Current guidelines for imaging in the diagnosis of IBD were sought from professional American organizations through PubMed and Scopus.

### Prevalence and Characteristics of Subclinical IBD in Patients with Sweet's Syndrome or Pyoderma Gangrenosum

The prevalence and characteristics of subclinical IBD in patients with Sweet's syndrome or pyoderma gangrenosum were assessed through a search in PubMed and Scopus using the terms "IBD" AND "Sweet's syndrome" OR "pyoderma gangrenosum." Inclusion criteria were studies published between 2014 and 2024 that assessed patients with Sweet's syndrome or pyoderma gangrenosum and potential underlying IBD. Studies outside this time frame, those not available in English, and studies that did not discuss potential underlying asymptomatic IBD in these conditions were excluded.

## Results

### Fecal Calprotectin

In analyzing fecal calprotectin (FC) as a diagnostic tool for detecting subclinical IBD in asymptomatic patients, multiple studies have highlighted its potential for both diagnosis and disease activity monitoring. A systematic review by Heida et al. evaluated FC's effectiveness in predicting flares in asymptomatic IBD patients [15]. The review found that elevated FC levels strongly correlated with the likelihood of relapse, with consecutive measurements indicating a 53-83% probability of relapse within 2-4 months. In contrast, normal FC levels were associated with a 67-94% probability of sustained remission. These findings underscore FC's prognostic value in monitoring disease activity and detecting subclinical IBD in asymptomatic individuals. Additionally, Margo et al. compared FC with neutrophil gelatinase-associated lipocalin (NGAL) in ulcerative colitis patients, using endoscopy and histology as gold standards [16]. FC showed strong correlations with both histological and endoscopic activity, with optimal cutoff values of 150 µg/g and 250 µg/g yielding negative predictive values (NPV) of up to 92%. These results further establish FC's utility in identifying inflammation in IBD and emphasize its potential role in detecting subclinical disease in asymptomatic patients.

Bello et al. validated the practicality of FC testing by comparing home-based kits to laboratory-based enzyme-linked immunosorbent assays (ELISA) [17]. The study demonstrated a high level of agreement between the two methods, indicating that non-invasive home testing could serve as a reliable alternative for monitoring intestinal inflammation, even in asymptomatic individuals. Kapel et al. expanded on FC's diagnostic value, showing that FC levels correlated strongly with subclinical IBD, with a sensitivity of 80-98% and specificity of 68-96% [18]. Elevated FC levels prompted the need for further diagnostic evaluations, such as colonoscopy. These findings confirmed that FC plays a critical role in the early detection and assessment of disease severity in asymptomatic patients and can differentiate IBD from irritable bowel syndrome (IBS), as IBS patients typically do not exhibit elevated FC levels.

A consensus report by Reenaers et al. established FC thresholds for diagnosing and monitoring IBD, with levels exceeding 250 µg/g indicating active inflammation [19]. This further supports FC's utility in identifying early signs of IBD, particularly in asymptomatic individuals at risk. Rodriguez-Lago et al. highlighted FC's potential to detect subclinical inflammation, identifying patterns months to years before a clinical IBD diagnosis [11]. Elevated FC levels were found to correlate with early histological abnormalities and immune dysregulation in asymptomatic patients. Combined with anti-Saccharomyces cerevisiae antibodies (ASCA) and perinuclear antineutrophil cytoplasmic antibodies (pANCA), FC demonstrated significant relevance in early intervention strategies. Finally, Sakurai and Saruta solidified FC's position as a crucial biomarker, emphasizing its ability to distinguish IBD from non-IBD conditions such as IBS and colorectal cancer [20]. Their study confirmed that FC's sensitivity and specificity were highest for ulcerative colitis, further reaffirming its diagnostic utility.

The reviewed studies collectively confirm that FC is a highly valuable biomarker for diagnosing and monitoring IBD, particularly in asymptomatic individuals. Elevated FC levels strongly correlate with subclinical IBD, making it an effective tool for distinguishing IBD from other conditions, such as IBS. Given its high sensitivity and specificity, FC presents a promising screening tool for identifying at-risk individuals before clinical symptoms emerge, facilitating early intervention and improved disease management.

### Imaging Techniques

Although a definitive diagnosis of IBD requires histopathology, non-invasive imaging techniques such as ultrasound and magnetic resonance imaging (MRI) can aid in the assessment of a patient who may have IBD. The American Gastroenterological Association currently recommends intestinal ultrasound for diagnosing and monitoring IBD, especially Crohn's disease [21]. The American College of Radiology currently recommends magnetic resonance enterography (MRE) as the preferred imaging modality for evaluating suspected or established IBD due to its high accuracy and lack of radiation exposure, which is particularly important for younger patients or pregnant individuals [22]. Both of these modalities provide valuable insight into the extent of the disease and can detect complications such as abscesses, fistulas, and strictures [23]. Despite the established role of these imaging techniques in diagnosing and monitoring IBD, their utility in screening asymptomatic patients with CNDs remains unclear. There are currently no specific guidelines regarding which imaging modalities, if any, should be used to screen for IBD in patients with Sweet's syndrome or pyoderma gangrenosum who are not experiencing gastrointestinal symptoms.

### Prevalence and Characteristics of Subclinical IBD in Patients with Sweet's Syndrome or Pyoderma Gangrenosum

Several studies examined the prevalence of subclinical IBD in patients with Sweet's syndrome (SS). Sleiman et al. reviewed studies involving SS and IBD, finding that SS was diagnosed before IBD in 5.3% of cases, highlighting the possibility of undiagnosed subclinical IBD in these patients [3]. SS was diagnosed after IBD in 64.2% of cases, with 29.5% experiencing concurrent diagnoses. These findings suggest that SS may serve as an early dermatologic manifestation of IBD, warranting further evaluation in affected patients. Amouri et al. reported that 4.4% of SS patients had actively progressing or flaring IBD, further supporting the idea that SS may occasionally be associated with subclinical IBD (2016). Though this prevalence is low, it underscores the need for clinicians to monitor for IBD in SS patients.

The prevalence of subclinical IBD in pyoderma gangrenosum (PG) was more significant. Vacas et al. found that 32% of PG patients had an associated diagnosis of IBD [24]. Notably, PG often preceded IBD diagnosis in 26% of cases, suggesting that PG might act as an early indicator of IBD. Kridin et al. confirmed this finding, reporting a 17.6% prevalence of IBD in PG patients, with a higher prevalence in ulcerative colitis (11.5%) [25]. Ashchyan et al. further highlighted the importance of screening for IBD in PG patients, particularly younger individuals, where IBD was present in 47.7% of patients under 65 [26]. This underscores the necessity for tailored diagnostic approaches for PG patients, particularly in younger cohorts, as they may have a higher risk for undiagnosed IBD.

In terms of prevalence, while Sweet's syndrome (SS) and pyoderma gangrenosum (PG) both have associations with IBD, the data suggests that PG shows a stronger link to subclinical IBD, with a more substantial proportion of patients exhibiting IBD as a comorbidity. SS, on the other hand, shows a lower prevalence of associated IBD, but it remains important to consider in SS patients, especially if IBD is diagnosed after or concurrently with SS. The studies also illustrate that while the prevalence of subclinical IBD in SS is rare, its presence in PG is more pronounced, with PG potentially serving as an early marker for IBD. FC, along with other diagnostic tools, could enhance early detection and intervention, particularly in these patient populations.

## Discussion

### Fecal Calprotectin

Fecal calprotectin (FC) has emerged as a promising non-invasive biomarker for detecting subclinical IBD in asymptomatic individuals. FC is well-established as a tool for monitoring active IBD, but its application in identifying subclinical disease in patients without gastrointestinal symptoms represents a relatively novel concept. Several studies have demonstrated that elevated FC levels correlate strongly with IBD inflammation and can identify subclinical disease, offering an opportunity for early intervention before clinical symptoms manifest. This insight suggests that FC could serve as an effective screening tool, especially in patients with chronic dermatologic conditions like Sweet's syndrome (SS) and pyoderma gangrenosum (PG), where subclinical IBD may otherwise go unnoticed. Incorporating FC into routine clinical practice in patients with CNDs could enable earlier detection of IBD in these patients, ultimately improving long-term outcomes by facilitating timely intervention. Overall, FC holds significant potential for identifying asymptomatic IBD in CNDs patients and could be an integral part of proactive screening strategies.

### Prevalence and Characteristics of Subclinical IBD in Sweet's Syndrome and Pyoderma Gangrenosum

The link between CNDs, particularly pyoderma gangrenosum (PG), and IBD is well-documented, with studies reporting a higher prevalence of IBD among PG patients compared to the general population, with rates ranging from 17.6% to 41%. In contrast, Sweet's syndrome (SS) has a less robust association with IBD, with fewer cases diagnosed before or concurrently with SS. The overall prevalence of subclinical IBD in CNDs patients remains largely unexplored, highlighting a significant gap in the current literature. Despite this, studies suggest that both PG and SS may be associated with undiagnosed IBD, with PG demonstrating a stronger correlation and sometimes serving as an early indicator of underlying IBD. However, current guidelines for screening IBD in CNDs patients are limited, as most clinicians rely on the presence of gastrointestinal symptoms or established IBD associations to guide diagnostic workups. There is potential for proactive screening, particularly in patients with persistent or severe CNDs, to facilitate earlier detection of subclinical IBD. Integrating tools such as fecal calprotectin testing and advanced imaging into routine care could aid in identifying IBD before symptoms develop, ultimately improving patient outcomes through timely intervention. Further research is needed to quantify the prevalence of subclinical IBD in SS and PG patients and to refine screening protocols for enhanced early detection and management.

### Clinical or Practical Implications

Utilizing noninvasive screening modalities with high sensitivity and specificity, such as fecal calprotectin or magnetic resonance enterography (MRE), to detect subclinical IBD could significantly influence current treatment guidelines for patients with coexisting CNDs. Due to the lack of unified data on treatment strategies for CNDs, definitive guidelines for therapy are not yet established. Instead, management primarily focuses on controlling inflammation during acute flares with immunosuppressants [27]. For localized lesions, topical glucocorticoids are used for Sweet's syndrome (SS), while corticosteroids or tacrolimus are employed for pyoderma gangrenosum (PG). In cases of diffuse disease, treatment regimens vary depending on the type of CNDs, with systemic glucocorticoids serving as the mainstay for acute flares of both SS and PG. However, in severe cases, higher doses of glucocorticoids are often required, which can impose a significant burden due to the adverse effects of chronic steroid use. Consequently, immune modulators and anti-inflammatory agents commonly used in IBD therapy are also employed to manage acute CNDs flares [28]. Notably, a review by Ben Abdallah et al. demonstrated that TNF-α inhibitors achieved promising results in treating refractory PG, with an 87% response rate and a 67% remission rate in a cohort of 356 patients [29]. This finding not only underscores the efficacy of IBD-directed therapies in controlling refractory CNDs progression but also highlights the shared pathogenesis between IBD and CNDs. Implementing early screening protocols in CNDs patients could facilitate a multidisciplinary approach between dermatologists and gastroenterologists, allowing for the integration of established IBD therapies as both maintenance and potentially prophylactic treatment for CNDs patients.

Early identification of subclinical IBD can lead to better patient outcomes, including fewer complications and earlier interventions. Notably, delays in the presentation and diagnosis of both Crohn's disease (CD) and ulcerative colitis (UC) are well-documented, with CD being more frequently associated with delayed recognition. Many individuals are diagnosed only when their condition reaches an emergent state [30]. Walker et al. conducted a study identifying factors contributing to diagnostic delays in IBD, with the primary issue being the vagueness of subclinical IBD symptoms, which are often mistaken for IBS. This misclassification further postpones diagnosis and treatment initiation [31]. Avoiding unnecessary delays is crucial, as late diagnosis increases the risk of complications. Early diagnosis and treatment, in turn, can lead to improved clinical outcomes. For instance, Jayasooriya et al. analyzed 2,645 patients diagnosed with IBD three years after their first symptom onset and found that early intervention

significantly reduced the risk of surgery, chronic steroid use, and adverse clinical outcomes [32]. These findings emphasize the critical role of proactive screening in identifying IBD at an earlier stage, allowing for timely treatment and improved patient outcomes.

Moreover, untreated or undiagnosed IBD patients have been shown to experience worse clinical outcomes, a higher risk of surgery, and an increased likelihood of chronic steroid dependence, particularly in UC. For example, Safroneeva et al. examined 292 patients with CD who began therapy within two years of diagnosis, categorizing them as the "early treatment" group. These patients, treated with TNF-α inhibitors (n=55), immunomodulators (n=188), or a combination of both (n=49), were compared to a "late treatment" group of 248 patients who initiated therapy more than two years after diagnosis. The study revealed that early treatment with immunomodulators or TNF-α inhibitors significantly reduced the risk of bowel strictures, while combination therapy further decreased the likelihood of future complications [33]. Similarly, Oh et al. demonstrated that early initiation of anti-TNFα therapy or immunomodulators in Asian patients with poor prognostic factors for CD was associated with better long-term outcomes. In contrast, late treatment initiation was linked to higher risks of surgery, disease progression, and complications from strictures [34]. While numerous studies support the benefits of early treatment in CD, evidence remains insufficient to confirm whether early treatment improves outcomes in UC [35]. However, with more frequent early detection of UC, larger sample sizes could be studied to better evaluate the impact of early treatment in both forms of IBD.

**Public Health Considerations**

Expanding screening and diagnostic protocols for IBD in patients with CNDs would encourage healthcare providers to adopt a broader inflammatory perspective rather than treating each disease in isolation. Incorporating fecal calprotectin screening into routine care for CNDs patients offers a cost-effective, time-efficient approach that could significantly reduce the delay in IBD diagnosis. As discussed, subclinical IBD may go undetected during comprehensive physical exams or be misdiagnosed as IBS, further prolonging the time to diagnosis. However, recognizing that CNDs patients frequently present with dermatologic symptoms as extraintestinal manifestations of IBD supports the integration of fecal calprotectin testing to identify inflammatory activity. A positive result would warrant further evaluation with advanced imaging such as MRE or colonoscopy. Implementing this screening strategy could streamline care by facilitating earlier gastroenterology referrals, expediting definitive workups, and ultimately enabling prompt initiation of appropriate treatment.

Further research is needed to identify specific biomarkers that link subclinical IBD and CNDs. While inflammatory markers such as IL-17, TNF-α, and IL-23 are associated with both conditions [27], there remains a significant gap in studies exploring novel biomarkers in subclinical IBD patients who present with CNDs. Additionally, research should focus on optimizing imaging techniques, particularly the role of MRE as a preliminary diagnostic tool in CND patients. More investigations are also warranted to clarify the relationship between UC and CNDs, as most dermatologic manifestations are observed in CD rather than UC patients. Currently, there is a wealth of data supporting the benefits of early diagnosis and treatment in CD, yet limited research exists on similar outcomes in UC patients [35]. Implementing early diagnostic strategies in all CNDs patients, even those without gastrointestinal symptoms, maybe a crucial step in enhancing patient care and improving long-term outcomes for those with subclinical IBD.

**Future Directions**

While ongoing investigations explore the prevalence of subclinical IBD in patients with CNDs, there remains a lack of large-scale, multicenter studies. Existing research is limited by small sample sizes, making it difficult to establish a broader understanding of the proposed link between CNDs and subclinical IBD. Current systematic reviews of Sweet's syndrome associated with IBD have sample sizes of fewer than 100 patients [3], while case reports are often documented on an individual patient basis [36]. Similarly, reviews examining the correlation between pyoderma gangrenosum and IBD are also constrained by small sample sizes [37]. Larger, multicenter studies are needed to better define the potential association.

Additionally, non-invasive biomarkers like fecal calprotectin (FC) may strengthen the investigation of the link between CNDs and subclinical IBD by improving early detection. As FC is both non-invasive and highly sensitive to intestinal inflammation, it appears to be an ideal tool for the early identification of nonspecific IBD [38]. Further research should explore the role of FC in the early manifestation of IBD to help establish standardized protocols for earlier detection. Regarding imaging for early screening, MRI enterography is the preferred modality; therefore, continued research is necessary to validate the efficacy of advanced imaging in subclinical IBD patients who first present with extraintestinal dermatologic manifestations. Establishing a combined FC and MRE protocol may also facilitate more widespread screening of patients with inflammatory dermatoses. Future studies could further investigate potential links between other inflammatory dermatologic conditions, such as psoriasis and eczema, and IBD.

Determining potential genetic or environmental factors linking CNDs to IBD may be an insightful path for future research. Understanding possible predispositions for both CNDs and IBD could provide valuable insights into shared pathogenesis. Additionally, more studies should focus on the effectiveness of early interventions based on non-invasive, earlier diagnoses through FC testing and MRI enterography. It appears that IBD patients who begin treatment earlier, with first-line treatments such as biological agents or aminosalicylates, experience improved outcomes [39]. To further enrich the study of this topic, it would be beneficial to examine the role of non-invasive diagnostic tools in early IBD detection. Potential methodologies for this could include longitudinal cohort studies, where patients with CNDs are monitored over time for the development of subclinical IBD. This would involve regular surveillance of FC levels and routine imaging to assess the predictive value of non-invasive techniques. Clinical trials could then be conducted to evaluate the efficacy of early therapeutic interventions following disease detection. Addressing the gaps between non-invasive diagnostic tools and early intervention could lead to a better understanding of the link between extraintestinal inflammatory manifestations and early intestinal disease, ultimately improving detection strategies.

## Conclusion

This review underscores the link between chronic neutrophilic dermatoses (CNDs) and subclinical inflammatory bowel disease (IBD), with pyoderma gangrenosum showing a particularly strong association. Fecal calprotectin has emerged as a reliable non-invasive biomarker for detecting subclinical IBD, offering a promising option for screening asymptomatic individuals. Advanced imaging techniques such as magnetic resonance enterography (MRE) further complement FC testing by providing detailed insights into intestinal inflammation. Integrating these diagnostic modalities into routine screening for CND patients could facilitate earlier intervention, improving disease management and patient outcomes. A multidisciplinary approach involving dermatologists and gastroenterologists is essential to optimize care for these patients. Early identification of subclinical IBD enables timely therapeutic interventions, potentially mitigating the long-term consequences of delayed diagnosis. Targeted therapies, including TNF-α inhibitors and immunomodulators, could address both the intestinal and dermatologic manifestations of IBD, improving patient outcomes.

Future research should focus on large-scale, multicenter studies to validate the prevalence and clinical characteristics of subclinical IBD in CND populations. Longitudinal cohort studies would be particularly valuable in assessing the predictive value of fecal calprotectin and advanced imaging for early diagnosis. Additionally, investigating the genetic and environmental links between CND and IBD may reveal new therapeutic targets and enhance understanding of shared pathophysiological mechanisms. These efforts could lead to more precise diagnostic tools, earlier interventions, and improved disease management strategies for patients with chronic neutrophilic dermatoses and subclinical IBD.

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