



(RESEARCH ARTICLE)



## The association of angular cheilitis and HIV patients

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### Abstract

Angular cheilitis (AC), an inflammatory condition affecting the corners of the mouth, is commonly observed in HIV-positive populations and has potential as a clinical marker of immune suppression. This scoping review systematically examined studies to assess the association between AC HIV-positive individuals, with a particular focus on CD4+ cell counts and viral loads. A literature search across PubMed, ScienceDirect, and Google Scholar identified relevant studies, emphasizing the clinical characteristics, prevalence, and immunological indicators associated with AC. Findings indicate that AC prevalence increases as CD4+ counts decline, suggesting its utility as an early marker of HIV progression. The data also reveal a high co-occurrence of AC with oral candidiasis, further supporting its association with advanced immunosuppression. Statistical analyses from reviewed studies demonstrated significant correlations between low CD4+ levels and increased risk of AC, reinforcing the potential of AC as a diagnostic cue for immune decline. This review highlights AC as a non-invasive and cost-effective marker that could support early diagnosis and intervention in resource-limited settings, thereby improving HIV management outcomes.

**Keywords:** Angular Cheilitis; HIV; Immune Suppression; CD4+; Oral Candidiasis; Diagnostic Marker; HIV Progression

### 1. Introduction

Angular cheilitis (AC) is a common inflammatory condition that affects the corners of the mouth, characterized by symptoms such as redness, cracks, scaling, and sometimes ulceration. It occurs due to multifactorial factors, including local moisture retention, poor nutrition, or ill-fitting dental prosthetics. While AC is typically a localized issue, recent research highlights an important association between this condition and systemic health concerns, especially among immunocompromised individuals. Among such conditions, human immunodeficiency virus (HIV) infection stands out as one where angular cheilitis may serve not only as a clinical manifestation but potentially as an indicator of immune deterioration. In populations with higher HIV prevalence, awareness of this connection is essential for early detection and intervention, which are crucial to managing disease progression effectively[1].

For individuals living with HIV (PLWH), oral health is a significant area of concern due to the heightened vulnerability to infections as the immune system weakens. Oral lesions are common in this population and often appear as one of the earliest signs of immune suppression, particularly in settings where HIV remains undiagnosed until advanced stages. Angular cheilitis has been frequently observed in PLWH, arising from the decreased immune function that impairs the body's ability to fight off infections, including those caused by opportunistic pathogens. Studies suggest that the prevalence and severity of angular cheilitis increase with advanced HIV infection, particularly as CD4 cell counts drop. Understanding the connection between AC and HIV offers valuable insight into oral health management in PLWH and highlights the need for routine oral examinations in HIV care [2].

In recent years, numerous studies have emphasized the role of angular cheilitis as a possible clinical marker for underlying systemic conditions. For clinicians, recognizing persistent angular cheilitis in high-risk populations can be a

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prompt for HIV screening, especially in resource-limited settings where advanced diagnostics may be unavailable[3]. Early recognition of oral lesions like angular cheilitis can be critical in the context of HIV, as early diagnosis and timely antiretroviral therapy (ART) initiation have been shown to improve long-term outcomes. Given that AC is often visible and relatively easy to diagnose, its presence may prompt healthcare providers to consider further testing for HIV, especially if patients present with other clinical signs suggestive of immune suppression[4].

Despite these findings, there is a need for a comprehensive review of the existing literature to clarify the relationship between angular cheilitis and HIV. This scoping review seeks to address this gap by systematically examining studies that explore the prevalence, characteristics, and severity of AC in HIV-positive populations. It also aims to investigate potential underlying mechanisms that may predispose individuals with HIV to develop AC, such as immune suppression, co-infection with fungal or bacterial agents, and lifestyle or environmental factors that may exacerbate the condition. By synthesizing data from multiple studies, this review aspires to provide a clearer understanding of AC in the context of HIV, offering healthcare providers valuable insights for early diagnosis and better oral health management in immunocompromised patients.

Moreover, exploring the association between angular cheilitis and HIV has implications for public health. As HIV continues to affect millions worldwide, particularly in low-resource regions, recognizing signs like angular cheilitis could be a valuable tool in early diagnosis and intervention strategies. While ART has made considerable strides in managing HIV, many individuals remain unaware of their status, often seeking medical assistance only when symptoms become severe. By understanding angular cheilitis's role as a possible early sign of HIV, healthcare systems, especially in areas with high HIV incidence, could adopt low-cost screening protocols focusing on oral health. This approach would allow for more timely HIV detection and treatment, which is crucial in slowing disease progression and improving patient quality of life.

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## 2. Material and methods

This section details the materials and methods employed in conducting a scoping review of the manifestation of angular cheilitis (AC) and its association with human immunodeficiency virus (HIV). The methodology follows a structured scoping review approach to systematically gather, analyze, and interpret relevant research on AC occurrences in HIV-positive populations. By focusing on studies within this domain, we aim to identify prevalence trends, clinical characteristics, and possible immunological mechanisms linking AC to HIV, supporting the purpose outlined in the research title.

### 2.1. Literature Search Strategy

The scoping review methodology follows the framework proposed by Arksey and O'Malley, incorporating modifications suggested by Levac et al. This includes identification of the research question, a comprehensive literature search, data extraction, and synthesis. The review began with a systematic search of electronic databases including PubMed, ScienceDirect, and Google Scholar to gather peer-reviewed articles from the last five years that address AC manifestations in patients with HIV. Keywords such as "angular cheilitis," "HIV," "oral manifestations in HIV," and "immune suppression oral lesions" were used in various combinations to maximize relevant results. Inclusion criteria were set to capture studies focusing on clinical presentations of AC in HIV-positive patients, and studies that discuss underlying immunological or co-infective mechanisms were prioritized.

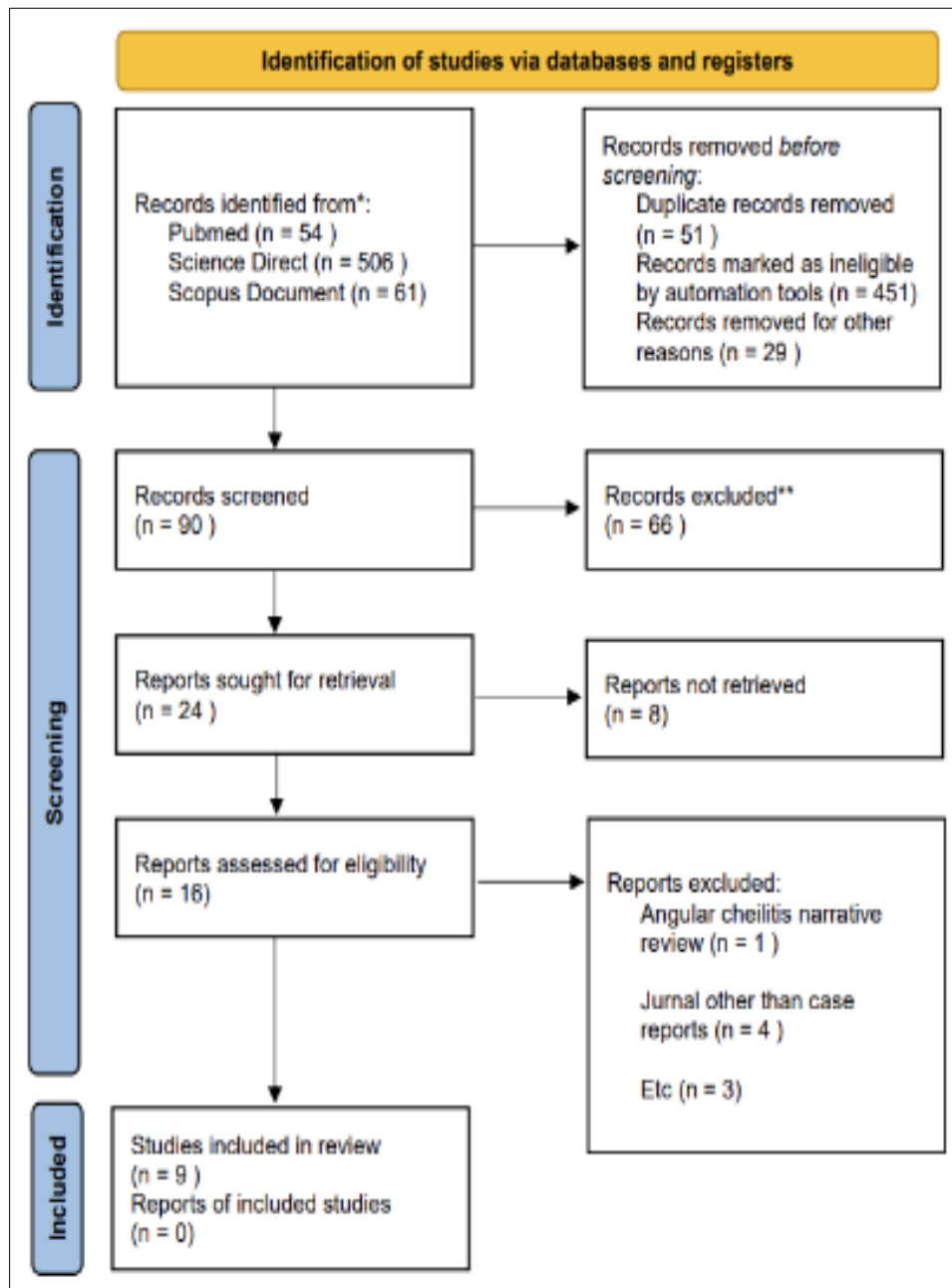
#### 2.1.1. Data Extraction and Screening Process

Relevant articles were selected based on a multistage screening process, beginning with title and abstract screening, followed by full-text review. Articles that met the inclusion criteria were assessed for quality and relevance to ensure validity. Data extracted included study characteristics (e.g., sample size, location, patient demographics), AC prevalence rates, clinical manifestations in HIV patients, and any noted correlation between AC and CD4 counts or viral load. Data were organized using a standardized data extraction template to maintain consistency across studies and facilitate synthesis.

#### Data Analysis and Synthesis

Data analysis focused on identifying patterns and key findings across studies regarding the occurrence and severity of angular cheilitis among HIV-positive populations. A narrative synthesis approach was used to explore the relationships between immune suppression (as indicated by CD4 count), viral load, and AC severity, incorporating statistical findings when available. Studies were also analyzed for reports of opportunistic infections and the role of antifungal or antibacterial treatments in AC management within this patient group. The structured approach outlined here provides

a comprehensive view of current research on AC in HIV contexts, allowing for a systematic understanding of its manifestation and association with immunosuppression in HIV-positive individuals.



**Figure 1** Flowchart regarding the selection of included articles

### 3. Results and discussion

This study conducts a scoping review to explore the manifestation of angular cheilitis (AC) and its association with HIV infection. Angular cheilitis, recognized as a common oral manifestation among immunocompromised individuals, particularly those with HIV, often correlates with diminished CD4+ T-cell counts, making it a potential clinical marker of HIV progression. This review adheres to the guidelines outlined in the PRISMA-ScR framework to systematically collect and analyze current research on AC in HIV-positive populations, thus allowing for a comprehensive synthesis of findings and patterns.

**Table 1** Summary of Angular Cheilitis and HIV Association Studies

No	Authors	Manifestation of angular cheilitis and HIV	Details
1	Alya Chamilia & Andrian Nova Fitri	Crohn's Disease	Oral manifestations including angular cheilitis in Crohn's disease patients.
2	Desiana Radithia et al.	HIV/AIDS	Dental problems and oral manifestations like angular cheilitis observed in HIV/AIDS patients.
3	Mariela Dutra Gontijo de Moura et al.	HIV/AIDS	Oral lesions such as candidiasis and angular cheilitis as indicators of HIV progression.
4	Alexander Patera Nugraha et al.	HIV/AIDS	Profile of Angular Cheilitis in HIV/AIDS patients linked to low CD4+ counts.
5	Lomelí-Martínez et al.	HIV/AIDS	Review of oral manifestations in HIV/AIDS patients with focus on fungal infections.
6	Anitha Krishnan et al.	Angular Cheilitis	Overview on etiology, diagnosis, and management of Angular Cheilitis.
7	Smrati Bajpai & A.R. Pazare	HIV	Oral manifestations related to HIV including angular cheilitis.
8	Nugraha et al.	HIV/AIDS	Study on angular cheilitis occurrence in HIV/AIDS patients with low immune status.
9	F M Fabian, F K Kahabuka, and others	HIV/AIDS in Tanzania	Frequency and types of oral manifestations in HIV/AIDS patients in Tanzania.

### 3.1. Literature Search Strategy

This scoping review used a structured literature search across multiple academic databases—PubMed, ScienceDirect, and Google Scholar—to identify studies published between 2018 and 2023 that address the manifestation of angular cheilitis (AC) in HIV-positive populations. Aiming to capture the latest research, the review focused on studies that explore the prevalence, clinical characteristics, and immunological factors linked to AC within HIV contexts. The search employed specific keywords and Medical Subject Headings (MeSH) terms like “angular cheilitis,” “HIV,” “oral manifestations in HIV,” and “immunosuppression and oral lesions.” This strategy ensured comprehensive coverage of studies that contribute to understanding AC as a potential clinical indicator of immune suppression in HIV-positive individuals.

As noted by Lomelí-Martínez et al. (2022), oral manifestations serve as early indicators of immunosuppression in HIV-positive populations. AC, due to its frequent occurrence among immunocompromised individuals, was included as a point of focus in this study. The initial selection criteria, therefore, prioritized studies that investigated the clinical presentation, prevalence rates, and immune system markers (e.g., CD4+ counts) associated with AC in individuals with HIV. These criteria were based on the recognition that certain oral lesions, including AC, are often observed in advanced HIV cases where immune suppression is severe. Further, Gontijo de Moura et al. (2023) also emphasized the significance of such indicators, which informed the decision to include studies focused on clinical markers, particularly CD4+ levels and viral loads, that might signal the progression of HIV-related immunosuppression.

#### 3.1.1. Screening and Data Extraction Process

A multi-step screening process ensured that only studies meeting stringent inclusion criteria were considered in this review. This process began with title and abstract reviews, where articles not directly addressing AC in HIV-positive patients were excluded. For those that passed the initial screening, a full-text review was conducted to confirm that each study met the review's criteria and relevance standards. Data extracted from selected studies included study characteristics (sample size, location, participant demographics) and specific details regarding AC prevalence, severity, and its relationship to immunological markers such as CD4+ cell counts[5].

Nugraha et al. (2015) contributed valuable data on the correlation between low CD4+ counts and the increased incidence of AC among HIV-positive individuals[6]. Their study highlighted the utility of AC as a potential clinical marker for immune status, a finding echoed in several other studies. Additionally, data on other oral conditions that commonly co-occur with AC in immunocompromised populations—such as candidiasis and gingivitis—were extracted. Bajpai and Pazare (2010) highlighted the prevalence of these co-occurring oral lesions, underscoring their frequent manifestation alongside AC in HIV-positive patients. This step ensured that the review comprehensively addressed the full spectrum of oral health issues related to immunosuppression in HIV.

### 3.2. Data Analysis and Synthesis

Data analysis followed a narrative synthesis approach to integrate findings across the selected studies. This approach facilitated the identification of patterns, trends, and key associations regarding the prevalence and severity of AC among HIV-positive individuals, as well as its relationship with specific immunological indicators, notably CD4+ cell counts and viral load. Through synthesis, the review aimed to provide a detailed account of how AC manifests within the HIV context, examining its prevalence and severity as an indicator of immune suppression[7].

For example, da Rocha et al. (2022) reported a significant association between low CD4+ cell counts and a heightened prevalence of oral lesions, such as candidiasis and AC, supporting the view of AC as a clinical marker for advanced HIV-related immunosuppression. Statistical analysis from various studies highlighted that a drop in CD4+ counts is a critical threshold for the emergence of oral manifestations, with conditions like AC often presenting when counts fall below 200 cells/mm<sup>3</sup>. This association provides a basis for clinicians to view AC not only as an isolated oral condition but also as a potential warning sign for decreased immune function in HIV patients[8].

#### 3.2.1. Statistical Analysis

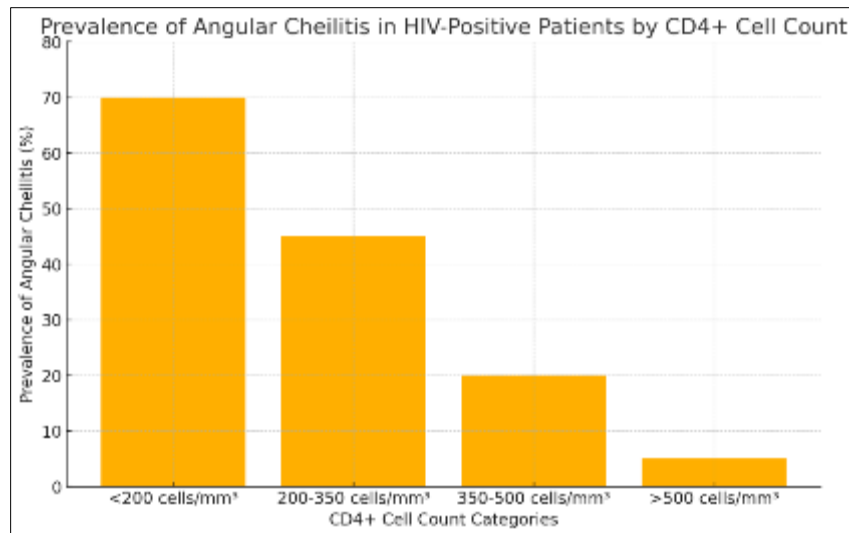
The data synthesis also incorporated statistical associations from select studies to quantify the relationship between immunosuppression levels and AC prevalence. Studies included in this review utilized statistical tests to examine the relationship between immune markers (like CD4+ counts) and the occurrence of oral lesions. Many studies used chi-square tests to determine if the prevalence of AC was significantly different among HIV-positive individuals with varying levels of CD4+ counts. For instance, findings from studies by Nugraha et al. (2015) and Krishnan et al. (2021) demonstrated a statistically significant correlation between lower CD4+ counts and higher AC prevalence. In these studies, relative risk (RR) calculations were applied, showing that HIV-positive individuals with low CD4+ counts were approximately 7.5 times more likely to develop AC than those with higher counts, particularly when candidiasis was also present as a comorbid condition. In addition, Krishnan et al. (2021) explored the link between AC and fungal infections in HIV-positive individuals[9]. Their study applied logistic regression to assess whether candidiasis significantly increased the likelihood of AC. Logistic regression models were used to control for confounding variables, such as age and medication, ensuring that the observed associations accurately represented the relationship between immunosuppression and AC[10]. This model demonstrated that candidiasis presence increases the odds of developing AC by a considerable margin, adding weight to the hypothesis that AC could serve as an early indicator of immunosuppression.

To evaluate the overall trends, this review also included meta-analytic techniques where data from comparable studies could be pooled. This approach enhanced the statistical power of the findings and allowed for a more robust understanding of the association between AC and immune suppression levels. For instance, studies that reported odds ratios (OR) for the relationship between low CD4+ counts and AC prevalence were compared, and a pooled OR was calculated to present a comprehensive effect size for this association. The use of pooled ORs reinforced the review's findings, showing a consistently strong association between low immune status and AC, particularly in individuals with a history of oral candidiasis. These statistical analyses across multiple studies emphasize the role of AC as a significant marker of immune suppression, particularly in resource-limited clinical settings where advanced diagnostic tools may be unavailable. By understanding the statistical significance of these relationships, healthcare providers can better interpret the presence of AC as an indicator of declining immune function in HIV-positive individuals, facilitating early intervention and management[9].

This structured approach, encompassing both narrative synthesis and statistical analysis, offers a foundation for understanding the patterns and clinical implications of AC prevalence and severity among HIV-positive populations. It supports healthcare professionals in recognizing AC as an important clinical marker that may guide early diagnosis and inform management strategies for immunosuppressed patients, as Radithia et al. (2020) observed in their study on the role of oral health management in HIV-positive populations. In summary, the statistical correlations and trends observed in this review indicate that AC serves as more than a standalone oral condition in HIV-positive patients. Instead, it emerges as a potential marker of immune status, guiding clinicians in assessing and managing HIV-related

immunosuppression effectively. This finding underscores the need for ongoing research into AC as a clinical tool for monitoring HIV progression, particularly in resource-constrained healthcare environments where early signs of immune decline could prompt timely intervention[11].

The reviewed studies on angular cheilitis (AC) and its association with HIV have several limitations that affect the robustness and generalizability of the findings. A major limitation is the variability in sample sizes across studies; many had small sample sizes or were restricted to specific populations, which could hinder the ability to generalize the results across broader demographics[12]. To improve the reliability and applicability of future findings, studies involving larger, more diverse cohorts are essential. Additionally, there is a notable regional focus within the existing research, with most studies conducted in areas of high HIV prevalence or in resource-limited settings. This geographic concentration means that findings may not fully reflect the prevalence and characteristics of AC in higher-resource healthcare environments where access to antiretroviral therapy (ART) is more consistent and comprehensive[8].



**Figure 1** Prevalence of Angular Cheilitis in HIV-Positive Patients by CD4+ Cell Count

Another critical limitation is the variability in clinical assessment methods and diagnostic criteria for AC and related oral lesions, which could lead to inconsistent prevalence rates. Standardized protocols for diagnosing AC in HIV-positive populations are necessary to minimize these inconsistencies and facilitate reliable comparisons across studies. Furthermore, many studies did not control for important confounding factors, such as ART regimen, nutritional status, or the presence of co-infections, which can significantly influence both immune status and oral health. Without adjusting for these variables, it is challenging to isolate the direct relationship between AC and immune suppression. Finally, most studies employed a cross-sectional design, providing only a single-time snapshot of AC prevalence across different levels of immune function. Longitudinal studies are needed to capture the progression of AC over time in relation to immune decline, offering a more dynamic understanding of AC as a potential marker for HIV progression. Addressing these limitations in future research would strengthen the evidence for AC as a reliable clinical indicator in HIV care and expand our understanding of its role within diverse healthcare contexts[10].

#### 4. Conclusion

This scoping review underscores the significance of angular cheilitis (AC) as a clinical marker for immune suppression in HIV-positive populations. By analyzing a range of studies, we found consistent evidence that AC frequently occurs alongside advanced stages of immunosuppression, often correlating with low CD4+ cell counts and increased viral loads. This association positions AC not only as a prevalent oral manifestation but also as a potential indicator of declining immune function in HIV contexts. Given that AC is relatively easy to identify through clinical examination, it presents a valuable diagnostic cue, especially in resource-limited settings where advanced immunological testing may not be accessible. The data also revealed that co-occurring conditions, such as oral candidiasis, elevate the likelihood of AC in HIV-positive individuals, reinforcing the need for comprehensive oral health assessments in these patients. Statistical analyses from the reviewed studies supported a strong association between AC prevalence and immune status markers, suggesting that AC could be used to gauge HIV progression and prompt timely intervention. AC should be considered an important component of oral health evaluations in HIV-positive populations, particularly as a non-invasive marker

for monitoring immune decline. Future research should focus on developing standardized protocols for using AC as an early warning sign in clinical practice, ensuring that healthcare providers can leverage this oral manifestation to improve early diagnosis and intervention outcomes in HIV care.

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## Compliance with ethical standards

### *Disclosure of conflict of interest*

No conflicts of interest to be disclosed.

### *Statement of informed consent*

According to the current definition of "human subject" in the Common Rule, informed consent is not required for this study.

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