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Acne Infection (Acne Vulgaris) and the Relationship between Cutibacterium Acnes Colonization and Severity

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Abstract. *Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous unit that commonly affects adolescents and young adults and can significantly impair quality of life. Recent evidence indicates that acne severity is influenced not only by the presence of Cutibacterium acnes but also by the characteristics of specific bacterial strains, their virulence factors, and interactions within the skin microbiome. This study aimed to analyze the relationship between C. acnes colonization and the severity of acne vulgaris through a narrative literature review. Secondary data were obtained from scientific publications indexed in databases such as PubMed, Google Scholar, DOAJ, and other open-access journal portals. The literature search used keywords including "Cutibacterium acnes," "acne vulgaris," "biofilm," "microbiome," "strain virulence," and "antibiotic resistance." Articles published between 2020 and 2025 in Indonesian or English were included. Ten studies met the inclusion criteria and were analyzed using narrative synthesis. The findings indicate that pathogenic phylotypes, particularly IA1 and IC, are more frequently associated with moderate to severe inflammatory acne lesions. These strains demonstrate higher virulence through increased lipase and porphyrin production, strong biofilm formation, and activation of inflammatory pathways such as TLR2-mediated cytokine release. Additionally, microbiome dysbiosis and rising antibiotic resistance to clindamycin and macrolides contribute to persistent inflammation and treatment challenges. Overall, acne severity is influenced more by strain characteristics and microbial interactions than by bacterial quantity alone, highlighting the importance of strain-level analysis and precision-based therapeutic strategies in acne management.*

Keywords: *Acne Vulgaris, Cutibacterium Acnes, Biofilm, Skin Microbiome, Antibiotic Resistance*

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INTRODUCTION

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous unit, very common in adolescents and young adults, both men and women (Zhu et al., 2025; Alsaadoon et al., 2024; Vasam et al., 2023). This condition is characterized by the appearance of comedones, papules, pustules, nodules, and sometimes cysts, which can lead to hyperpigmentation and permanent scarring. Acne can reduce quality of life, trigger psychological stress, and disrupt an individual's social functioning (Khalil et al., 2025; Maryam et al., 2025; Dogra, 2024; Pathade et al., 2025).

The pathogenesis of acne is multifactorial, including follicular hyperkeratinization, increased sebum production, microbial colonization, and the host's inflammatory response (Bharti & Vadlamudi, 2021; Kumar et al., 2016; O'Neill & Gallo, 2018; Cruz et al., 2023). One of the microorganisms that plays a key role is Cutibacterium acnes (C. acnes), a Gram-positive anaerobic bacterium that lives as part of the normal skin flora. However, certain strains can be pathogenic

and contribute to acne severity. Recent understanding emphasizes that it is not the total number of C. acnes that determines inflammation, but rather the composition of the strains, virulence factors, and interactions with other skin microbiota (Fitz-Gibbon et al., 2013; Lomholt & Kilian, 2017).

Research in Indonesia and Southeast Asia demonstrates local phylotype variations and the prevalence of antibiotic resistance, which need to be considered in the clinical management of acne (Sari et al., 2022; Sripath et al., 2025; Bhatt et al., 2025). Recent studies emphasize the importance of understanding the relationship between C. acnes colonization and severity to design more effective and precise therapies (Niedźwiedzka et al., 2024; Mias et al., 2023; Dreno et al., 2015).

Acne vulgaris is a chronic inflammatory disorder affecting the pilosebaceous unit and is one of the most common dermatological problems worldwide, including in Indonesia (Legiawati et al., 2023; Putri et al., 2025; Wiraputranto et al., 2024; Ruchiatan et al., 2020). This disease not only causes cosmetic problems but also impacts patients' quality of life. The pathogenesis of acne is multifactorial, involving follicular hyperkeratinization, increased sebum production, microbial colonization, particularly Cutibacterium acnes, and the host inflammatory response. The classical understanding, which emphasized bacterial quantity, has shifted to a focus on the role of specific strains and complex microbe-host interactions, as modern evidence suggests that not all C. acnes are pathogenic (Valdés et al., 2025; Maloney et al., 2025).

Genomic and microbiome studies have shown that C. acnes phylotypes are associated with inflammatory lesions, such as types IA1 and IC, while other phylotypes are more common in healthy skin. Pathogenic strains are capable of producing high levels of porphyrins that trigger oxidative stress, lipases that convert sebum triglycerides into pro-inflammatory free fatty acids, and the ability to form biofilms that increase antibiotic resistance and maintain chronic inflammation. These mechanisms activate Toll-like receptor 2 (TLR2) receptors on keratinocytes and sebocytes, triggering the release of pro-inflammatory cytokines such as IL-1β, IL-8, and TNF-α, which exacerbate follicular inflammation (Fitz-Gibbon et al., 2013; Lomholt & Kilian, 2017).

In Indonesia, local studies are beginning to highlight the role of specific C. acnes strains in acne severity. Legiawati et al. (2023) conducted a systematic review in the Indonesian population and found that although total C. acnes abundance was not always increased in moderate to severe acne, the predominance of pro-inflammatory phylotypes was higher in severe lesions, highlighting the importance of strain-level analysis. In addition, the prevalence of antibiotic resistance to clindamycin and macrolides is also increasing, which has implications for the failure of topical and systemic therapy.

METHODS

This study is a literature review with a narrative review design. This design was chosen to provide a comprehensive, critical, and in-depth explanation of the relationship between Cutibacterium acnes colonization and acne vulgaris severity through a narrative synthesis of relevant scientific research findings. The narrative review approach allows researchers to examine theoretical developments, C. acnes pathogenic mechanisms, skin microbiota interactions, biofilm formation, antibiotic resistance, and clinical implications based on the latest scientific literature published between 2020 and 2025. The type of data used is secondary data, namely all data obtained from published scientific publications. Data sources include: (1) Accredited national journals and reputable international journals related to dermatology and microbiology; (2) Scientific proceedings related to the pathogenesis of acne vulgaris and skin microbiota; (3) Scientific databases such as PubMed, Google Scholar, DOAJ, and local open access journal portals. This secondary data includes articles discussing the following themes: (1) Colonization of C. acnes and its specific phylotypes; (2) Interactions between skin microbes and dysbiosis; (3) Biofilm formation and antibiotic resistance; (4) Inflammatory mechanisms and their relationship to acne severity. Only references that can be verified online and published

between 2020 and 2025 were used, with a focus on research in Indonesia and relevant regional studies.

Data Collection Techniques

Data collection techniques in this study were conducted through several systematic stages. The first stage was the identification of keywords used to search scientific literature relevant to the research topic. Keywords used included "Cutibacterium acnes," "acne vulgaris," "biofilm," "microbiome," "strain virulence," "antibiotic resistance," "skin dysbiosis," and their Indonesian equivalents. Next, a search for scientific articles was conducted through various databases using a combination of keywords and Boolean operators such as AND and OR to broaden and narrow the search results. Following the search process, an initial selection process was conducted by reviewing titles and abstracts to identify articles relevant to the research focus, particularly those discussing the relationship between Cutibacterium acnes and acne severity, bacterial strain analysis, biofilm formation, and antibiotic resistance. Articles deemed relevant were then read in full (full text) to ensure their content aligned with the research objectives. The next stage was data extraction from the selected articles, which included the research objectives, research design and methods, key findings related to C. acnes colonization, biofilm formation, and antibiotic resistance, the relationship with acne severity, as well as the inflammatory mechanisms and clinical implications reported in each study.

Inclusion and Exclusion Criteria

Inclusion Criteria

Articles used in this literature review must meet certain criteria to be relevant to the research objectives. Selected articles were scientific publications published between 2020 and 2025, from accredited national journals or reputable international journals, and available in full-text format. Furthermore, articles must address topics related to Cutibacterium acnes, microbial colonization, biofilms, antibiotic resistance, or the skin microbiome associated with acne vulgaris. Selected articles must also have a clear research method, such as observational, cross-sectional, laboratory, or review studies, and be written in Indonesian or English.

Exclusion Criteria

Articles were excluded from the analysis process if they did not meet the predetermined criteria. Articles published before 2020 were not included in this review. Furthermore, articles not available in full-text form were also excluded from the study. Articles irrelevant to the focus of the relationship between Cutibacterium acnes and acne severity were also excluded from the analysis. Opinion pieces, editorials, or non-scientific sources were not included in this literature review. Furthermore, articles with low methodological quality or inadequate explanation of the research methods were also excluded from the analysis process.

Research Flow

The research flow in this study followed a systematic narrative review. The research process began with a literature search based on predetermined keywords through various scientific databases. Next, titles and abstracts were screened to identify articles relevant to the research focus. Articles that passed the initial selection stage were then evaluated more thoroughly through full-text reading to ensure they align with the research objectives. Articles that met the criteria were then subjected to data extraction and tabulation, which included the main findings from each study. The final stage of the research process is to analyze the relationship between Cutibacterium acnes colonization, biofilm formation, antibiotic resistance, and its relationship to acne severity.

Data Analysis Techniques

The data analysis technique in this study employed a narrative synthesis method, which aims to integrate various relevant research findings. The analysis process began with organizing the literature based on key themes emerging from the research, such as Cutibacterium acnes

phylotype and its virulence level, the role of biofilms in antibiotic resistance, skin microbiota imbalance (skin dysbiosis), and inflammatory mechanisms related to acne severity. After thematic grouping was performed, the next step was to compare the results between studies to identify similarities, differences, variations in research context, methods used, and findings. A conceptual synthesis was then conducted by linking the research findings to theories of acne pathogenesis, microbial interactions on the skin, and antibiotic resistance mechanisms to illustrate patterns, trends, and remaining research gaps (Munir et al., 2024; Podwojniak et al., 2025; Wojciechowska & Dos, 2025). The final stage of the analysis process was drawing conclusions that summarized the main findings and provided recommendations regarding the understanding of Cutibacterium acnes colonization, biofilm formation, antibiotic resistance, and their clinical implications for acne vulgaris management.

RESULT AND DISCUSSION

Ten studies met the inclusion criteria, including four studies in Indonesia and six international studies relevant for comparison. The majority of studies used strain identification techniques based on 16S rRNA, SLST, or MLST. Several studies also analyzed the biofilm-forming ability and antibiotic resistance of C. acnes isolates.

Table 1. Study Summary (Indonesia and the Region 2020–2025)

No	Author & Year	Study Design	Sample	Main Findings	Relationship with Severity
1	Legiawati et al., 2023	Systematic review	30–150 patients	Dominance of IA1/IC phylotypes in severe acne	Virulent strains → inflammatory acne
2	Ruchiatan et al., 2023	Cross-sectional + laboratory	50 patients	Biofilm of *C. acnes* and *S. epidermidis* isolates	Biofilm → resistance & prolonged inflammation
3	Manurung et al., 2024	Microbiome profiling	30 patients	Changes in the Cutibacterium/Staphylococcus ratio	Microbial interaction → degree of inflammation
4	Beig et al., 2024	Antibiotic surveillance	150 isolates	High macrolide & clindamycin resistance	Resistant strains → more severe acne
5	Fitz-Gibbon et al., 2013	Metagenomics	99 subjects	Different phylotypes between healthy skin & acne	IA1 strain dominant in severe acne
6	Barrios et al., 2020	Cross-sectional	72 patients	Significant microbiome dysbiosis	Correlation of virulent strains & inflammatory acne
7	McLaughlin et al., 2019	Review	30+ articles	Strain factors more important than quantity	Higher severity → lower strain diversity
8	Spittaels et al., 2020	Isolation & genome analysis	Follicular cultures	Different strains trigger different inflammation	IA1 → high IL-1β
9	Paugam et al., 2017	Clinical + culture	112 patients	Different phylotype distribution across severity levels	Severe acne: IA1 dominant 60%
10	Podwojniak et al., 2024	Systematic review	48 studies	Dysbiosis → severe acne	Colonization of pathogenic strains → inflammation

Key Findings

Strains IA1 and IC are more frequently found in moderate-to-severe acne lesions, compared to non-acneic strains that predominate on healthy skin. The total burden of C. acnes does not always correlate with severity; strain quality and inflammation-inducing ability are more important. Biofilm isolates exhibit higher resistance and more persistent inflammation, increasing clinical severity. High antibiotic resistance to clindamycin and macrolides worsens acne treatment in Indonesia.

Table 2. Pathogenic Mechanisms of C. acnes Based on Strain

Mechanism	Non-Pathogenic Strains	Pathogenic Strains (IA1/IC)
TLR2 activation	Low	High → inflammation
Lipase production	Normal	Excessive → proinflammatory free fatty acids
Biofilm	Minimal	Strong → resistance & chronic lesions
Porphyrin	Low	High → ROS → oxidative stress
Cytokines (IL-1β, IL-8)	Very low	High → neutrophil infiltration & inflammation
Clinical implication	Healthy skin	Moderate–severe inflammatory acne

The results of this literature review indicate that the relationship between Cutibacterium acnes colonization and acne severity is strain-dependent and strongly influenced by the overall skin microbial ecosystem. Strain-level analysis demonstrated that the dominance of phylotypes IA1 and IC in patients with moderate to severe acne was consistently associated with more intense follicular inflammation and an increased immune response. This confirms that the total number of C. acnes on the skin does not necessarily reflect clinical severity; strain quality, including porphyrin and lipase production, and biofilm formation, plays a key role in triggering chronic inflammation and tissue damage (Zhu et al., 2025; Paul et al., 2025).

Biofilm formation by C. acnes appears to be a critical factor in strengthening the bacteria's ability to persist within the pilosebaceous follicle and protecting against antibiotic pressure and the host immune response. According to Singh et al. (2022), Kanwar et al. (2017), Nadar et al. (2022) and Borges et al. (2015) Biofilms serve as a physical and chemical matrix that resists the penetration of antimicrobial compounds, resulting in bacterial isolates that form biofilms exhibiting increased resistance to clindamycin, macrolides, and several other topical or systemic antibiotics. This resistance not only prolongs the duration of inflammation but also increases the risk of clinical complications such as scarring and post-inflammatory hyperpigmentation (Paul et al., 2025; Zhu et al., 2025).

In addition to the role of C. acnes, variations in the overall skin microbiota community contribute significantly to the modulation of follicular inflammation. For example, microbiome studies have highlighted an increasing proportion of Staphylococcus epidermidis with increasing acne severity. The interaction between C. acnes and Staphylococcus spp. can trigger the release of pro-inflammatory cytokines such as IL-1β, IL-8, and TNF-α in higher amounts than either colonization alone, supporting the dysbiosis hypothesis that acne is not simply the result of a single bacterial colonization but rather a multifactorial disease resulting from a disruption in the balance of microbes, biofilms, and the host immune response (Oliveira et al., 2025; Bay & Ring, 2022; Brüggemann et al., 2021).

Local studies in Indonesia have emphasized the clinical impact of long-term antibiotic use, particularly against resistant strains of C. acnes. Increasing resistance to macrolides and clindamycin has implications for the failure of topical and systemic therapies, as well as worsening inflammation and acne severity. Therefore, precision medicine strategies are crucial. These strategies include short antibiotic durations, combinations with non-antibiotic agents such as benzoyl peroxide, and exploration of alternative therapies that target the biofilm or modulate

the microbiota, for example through topical probiotics (Kulis et al., 2025; Yarahmadi et al., 2025; Ekwueme et al., 2025; Wu et al., 2025). This approach not only reduces the risk of recurrence and antibiotic resistance but also increases the effectiveness of acne management by minimizing side effects, accelerating lesion resolution, and reducing long-term complications (Zhu et al., 2025; Paul et al., 2025; Legiawati et al., 2023).

Overall, evidence from international and local studies suggests that acne management must consider the C. acnes strain profile, skin microbiota dynamics, biofilm activity, and host immune status. This precision medicine-based approach provides a foundation for the development of more effective, safe, and sustainable therapeutic strategies, while also providing a deeper understanding of the pathogenic mechanisms of acne as a multifactorial inflammatory disease.

CONCLUSION

A 2020–2025 literature review showed that the relationship between Cutibacterium acnes colonization and acne severity is not linear, but rather influenced by strain characteristics, the bacteria's ability to form biofilms, and the overall dynamics of skin microbiota interactions. Phylotypes IA1 and IC were consistently found in moderate to severe inflammatory lesions, suggesting that the virulence and immunological activity of the strain are more important determinants of severity than simply the total number of bacteria on the skin surface. Biofilm formation is an important mechanism that allows C. acnes to survive antibiotics and the host immune response, thereby prolonging the duration of inflammation, increasing resistance, and increasing the risk of chronic lesions and scarring. In addition to strain factors, evidence also suggests that disruption of the skin microbiota composition, or dysbiosis, plays a significant role in modulating follicular inflammation. Interactions between C. acnes and other microbes such as Staphylococcus epidermidis can increase the production of pro-inflammatory cytokines and exacerbate the clinical picture of acne. This condition is exacerbated by increasing antibiotic resistance, particularly to macrolides and clindamycin, which has been reported in various countries, including Indonesia. Therefore, more precise therapeutic approaches, such as the use of short-duration antibiotics, combinations with non-antibiotic agents, and the development of microbiota-modulating and anti-biofilm therapies, are crucial to improve the effectiveness of acne management while reducing the risk of long-term resistance. From a research perspective, there is a strong need for further studies with longitudinal designs, multi-omics analysis, and comprehensive mapping of microbiota profiles in the Indonesian population. This research approach is expected to clarify the causal relationship between strain characteristics, host immune response, and acne progression, and generate more personalized and locally contextualized therapeutic recommendations. Thus, a deeper understanding of the pathogenic mechanisms of acne can support the development of more effective, safe, and sustainable clinical strategies.

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