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Assessment of Serum Dermcidin Level in Patients with Rosacea: A Comprehensive Review

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Abstract
Background: Rosacea is a common chronic skin condition characterized by facial erythema, flushing, papules, and telangiectasia. Understanding the underlying mechanisms and identifying reliable biomarkers are essential for effective diagnosis and management. Dermcidin, an antimicrobial peptide secreted by eccrine sweat glands, has been implicated in various skin disorders due to its role in the innate immune system. **Objectives:** This review aims to assess the current evidence regarding the assessment of serum dermcidin levels in patients with rosacea. It aims to provide an overview of the association between dermcidin and rosacea, discuss the methodologies used for dermcidin assessment, summarize the clinical findings, and explore the potential implications and limitations of utilizing dermcidin as a biomarker in rosacea. **Conclusions:** The assessment of serum dermcidin levels in rosacea patients holds promise as a potential diagnostic and monitoring tool. Clinical studies have reported elevated dermcidin levels, altered peptide profiles, or genetic variations in rosacea patients compared to healthy controls. Correlations between dermcidin levels and disease severity, subtypes, or treatment response have been observed.

Keywords: Rosacea, Dermcidin, Biomarker, Serum Levels, Assessment.

1. Introduction

Rosacea is a chronic inflammatory skin condition characterized by facial erythema (redness), flushing, papules, pustules, and telangiectasia (visible blood vessels). It primarily affects the central facial area, including the cheeks, nose, chin, and forehead. Rosacea commonly occurs in adults and is more prevalent in fair-skinned individuals. While the exact cause of rosacea remains unclear, various factors such as genetic predisposition, abnormal immune response, vascular dysfunction, and environmental triggers are believed to contribute to its development [1].

Table (1) the different subtypes of rosacea and their characteristics

Subtype	Symptoms/Characteristics
Erythemato-telangiectatic	- Flushing and persistent redness of the central face - Visible blood vessels - Very sensitive skin - Possible stinging or burning sensation
Papulopustular	- Papules and/or pustules on the central face - Transient or persistent facial redness - Burning and stinging - Small visible blood vessels (telangiectasia) - Raised, scaly red patches (plaques)
Rhinophyma	- Thickening and irregular surface nodularities, especially on the nose (rhinophyma) - Telangiectasia - Fibrosis and increased volume of sebaceous glands - Histopathological signs: dilated infundibulum and dense inflammatory infiltrate
Ocular	- Irritation, foreign body sensation, dryness, and blurry vision - Blepharitis and conjunctivitis - Lid margin and conjunctival telangiectasias - Eyelid thickening, crusts, and scales - Corneal complications: infiltrates, ulcers, scars, vascularization, but sight-threatening disease is rare with rosacea

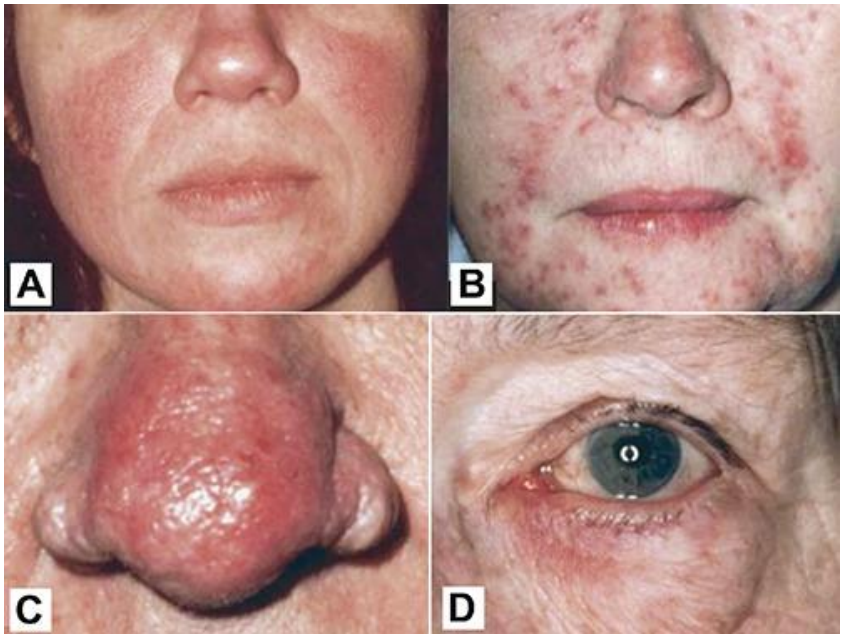

Fig. (1) The 4 different types of rosacea examined: A) erythematotelangiectatic rosacea; B) papulopustular rosacea; C) rhinophyma (phymatous rosacea) and D) ocular rosacea. (Van Zuuren, 2017)

Understanding the underlying mechanisms and identifying reliable biomarkers are essential for advancing our knowledge of rosacea and improving its diagnosis and treatment. Biomarkers are measurable indicators that can provide information about the presence, severity, or progression of a disease. By identifying specific biomarkers associated with rosacea, clinicians and researchers can enhance diagnostic accuracy, monitor disease activity, and develop targeted therapies [2].[3]

Dermcidin, an antimicrobial peptide primarily secreted by eccrine sweat glands, has emerged as a potential biomarker in the context of rosacea. It plays a crucial role in the innate immune system by protecting the skin against pathogens. Dermcidin's antimicrobial properties, along with its involvement in inflammatory processes, make it an intriguing candidate for exploring its relevance to rosacea. It is hypothesized that alterations in dermcidin levels or expression may contribute to the dysregulation of immune responses and contribute to the development or severity of rosacea symptoms [4, 5].

Investigating dermcidin as a potential biomarker in rosacea holds promise for several reasons. Firstly, dermcidin is readily accessible through non-invasive methods, such as assessing its levels in serum samples. This makes it a feasible candidate for routine clinical use. Secondly, dermcidin's association with the immune system and inflammation aligns with the underlying pathophysiology of rosacea. Therefore, understanding its role and potential alterations in rosacea patients may provide valuable insights into disease mechanisms. Lastly, identifying dermcidin as a biomarker may aid in subtyping rosacea patients, as well as predicting disease severity and treatment response, enabling more personalized approaches to patient care [6, 7].

This review article will evaluate the existing literature on the assessment of serum dermcidin levels in patients with rosacea, shedding light on its relevance and potential implications for this complex dermatological condition.

1. **Dermcidin:**

Dermcidin is an antimicrobial peptide that is primarily secreted by eccrine sweat glands, which are found throughout the body. It belongs to the family of cathelicidin peptides and plays a crucial role in the innate immune system's defense mechanisms against pathogens [5, 8].

As an antimicrobial peptide, dermcidin exhibits broad-spectrum antimicrobial activity, meaning it can effectively target a wide range of microorganisms, including bacteria, fungi, and viruses. It acts by disrupting the cell membrane of these pathogens, leading to their destruction. By combating harmful microorganisms, dermcidin helps protect the skin from infections [9].

In addition to its antimicrobial properties, dermcidin is also involved in modulating the immune response and promoting inflammation. It can interact with immune cells, such as neutrophils and monocytes, to regulate their functions and promote the release of inflammatory mediators. This suggests that dermcidin may have a broader role in immune regulation beyond its direct antimicrobial activity [8].

Due to its involvement in the immune system and inflammation, dermcidin has attracted attention in the context of various skin disorders. Previous research has explored dermcidin's association with conditions such as atopic dermatitis, psoriasis, acne, and wound healing. In these studies, alterations in dermcidin levels, expression, or genetic variations have been observed in patients with these skin disorders [10].

For instance, in atopic dermatitis, a chronic inflammatory skin condition characterized by intense itching and eczematous lesions, dermcidin expression has been found to be reduced compared to healthy

individuals. This suggests that decreased dermcidin levels may contribute to the impaired skin barrier function and increased susceptibility to infections seen in atopic dermatitis patients [11, 12].

Similarly, studies investigating psoriasis, a chronic autoimmune disease characterized by skin inflammation and rapid cell turnover, have shown altered dermcidin expression in affected skin lesions. Dermcidin may play a role in modulating the inflammatory response and immune dysregulation observed in psoriasis [13, 14].

Moreover, dermcidin has been implicated in acne pathogenesis. Acne is a common skin disorder characterized by inflammation, excess sebum production, and the colonization of the skin by Propionibacterium acnes. Studies have reported variations in dermcidin levels in acne patients, suggesting its potential involvement in the regulation of sebum production and immune responses in the context of acne [15, 16].

Furthermore, dermcidin has been investigated in the context of wound healing. It has been shown to promote angiogenesis (formation of new blood vessels) and enhance the migration of keratinocytes and fibroblasts, which are crucial for wound closure and tissue regeneration [17, 18].

2. The Relationship Between Dermcidin and Rosacea:

Rationale for investigating dermcidin levels in patients with rosacea:

The investigation of dermcidin levels in patients with rosacea stems from the need to better understand the underlying mechanisms and identify potential biomarkers for this complex skin condition. Rosacea is characterized by chronic inflammation, and identifying specific biomarkers associated with the disease could aid in its diagnosis, classification, and management [19, 20].

Studies exploring the association between dermcidin and rosacea:

Several studies have investigated the potential relationship between dermcidin and rosacea. These studies have utilized various methods to assess dermcidin expression, levels, or genetic variations in rosacea patients [19].

Findings regarding dermcidin expression, levels, or genetic variations in rosacea patients:

The findings from these studies have provided valuable insights into the potential involvement of dermcidin in rosacea. However, it is important to note that the results have been somewhat inconsistent, potentially due to variations in sample sizes, assessment techniques, and patient characteristics [21].

Some studies have reported alterations in dermcidin expression or levels in rosacea patients compared to healthy individuals. For instance, a study found increased dermcidin mRNA expression in the skin of rosacea patients, particularly in areas with visible blood vessels and inflammation. This suggests that dermcidin may play a role in the vascular and inflammatory aspects of rosacea [10].

Other studies have explored dermcidin levels in the serum of rosacea patients. One study reported significantly higher dermcidin levels in the serum of patients with erythematotelangiectatic rosacea (ETR) compared to healthy controls. Another study found increased dermcidin levels in the serum of patients with papulopustular rosacea (PPR) compared to healthy individuals. These findings suggest a potential association between dermcidin levels and specific rosacea subtypes [22].

In addition to dermcidin expression and levels, genetic variations in the dermcidin gene have also been investigated in relation to rosacea. A study identified genetic polymorphisms in the dermcidin gene that were associated with an increased risk of rosacea development [23].

2. Assessment Methods:

Several techniques and assays have been employed to assess serum dermcidin levels in studies exploring its association with rosacea. These methods vary in their complexity, sensitivity, and specificity.

Assessment Method	Advantages	Limitations	Reliability
Enzyme-Linked Immunosorbent Assay (ELISA)	Precise and quantitative measurement	Cross-reactivity with similar peptides	High with proper standardization
	Commercially available kits	Requires specialized equipment	
		and trained personnel	
Mass Spectrometry	High sensitivity and specificity	Technically demanding	High with proper standardization
	Simultaneous analysis of multiple	Time-consuming and expensive	
	peptide variants		
Western Blotting	Identification of specific protein bands	Semi-quantitative results	Moderate, requires careful optimization

a) Enzyme-Linked Immunosorbent Assay (ELISA):

ELISA is a widely used technique that utilizes specific antibodies to detect and quantify dermcidin levels in serum samples. It involves immobilizing dermcidin-specific antibodies on a solid surface, followed by the addition of the serum sample. The bound dermcidin is then detected using a secondary antibody conjugated with an enzyme, which produces a measurable signal. Advantages: ELISA allows for precise and quantitative measurement of dermcidin levels. It is a well-established technique with high sensitivity and specificity. ELISA kits are commercially available, making it relatively easy to implement. Limitations: ELISA may be susceptible to cross-reactivity with other structurally similar peptides. Standardization of assays and antibody specificity is crucial to ensure accurate and reproducible results. Additionally, ELISA typically requires specialized laboratory equipment and trained personnel [24].

b) Mass Spectrometry:

Mass spectrometry is a technique used to analyze the mass and composition of molecules. It has been utilized to identify and quantify dermcidin peptides in serum samples. Mass spectrometry-based methods involve sample preparation, peptide separation, and detection of dermcidin peptides using mass spectrometry instruments. Advantages: Mass spectrometry provides high sensitivity and specificity for identifying and quantifying dermcidin peptides. It offers the advantage of simultaneously analyzing multiple peptide variants, which can provide more comprehensive information. Limitations: Mass spectrometry techniques are technically demanding and require specialized equipment and expertise. The analysis can be time-consuming and expensive. Standardization and quality control are crucial to ensure reliable results [25].

c) Western Blotting:

Western blotting is a widely used technique for protein analysis. It involves separating proteins based on their molecular weight using gel electrophoresis and transferring them onto a membrane. The membrane is then probed with specific antibodies to detect and quantify dermcidin. Advantages: Western blotting allows for the identification of specific dermcidin protein bands and their relative abundance. It provides qualitative and semi-quantitative information about dermcidin expression levels. Limitations: Western blotting is a semi-quantitative technique and may not provide precise quantification of dermcidin levels. It requires careful sample preparation and optimization to ensure accurate results. It may also have limitations in detecting low-abundance dermcidin isoforms [26].

Comparing findings from different assessment techniques:

The use of different assessment techniques has led to variations in the reported findings regarding dermcidin levels in rosacea patients. Some studies utilizing ELISA have reported elevated dermcidin levels in the serum of rosacea patients compared to controls, suggesting its potential association with the disease. However, other studies employing mass spectrometry or Western blotting have not consistently observed significant differences in dermcidin levels between rosacea patients and healthy individuals.

These discrepancies may be attributed to several factors, including variations in sample sizes, patient characteristics, and assay specificity. Differences in assay sensitivity and the ability to detect specific dermcidin isoforms may also contribute to the discrepancies. It is worth noting that the interpretation of dermcidin levels in rosacea is complex due to the heterogeneity of the disease and variations in its clinical manifestations.

2. Potential Implications and Future Directions:

- **Dermcidin assessment in diagnosing or monitoring rosacea:**

The assessment of dermcidin levels holds potential implications in the diagnosis and monitoring of rosacea. If dermcidin is established as a reliable biomarker, it could aid in the accurate and early diagnosis of the disease. Currently, the diagnosis of rosacea relies primarily on clinical presentation and exclusion of other conditions. Having a specific biomarker like dermcidin could provide an objective and quantitative measure to support the diagnostic process [27, 28].

Furthermore, dermcidin assessment may have value in monitoring disease activity and treatment response. If dermcidin levels correlate with disease severity or specific clinical features, monitoring changes in dermcidin levels over time could help gauge disease progression and response to therapy. This information could guide treatment decisions and allow for personalized management strategies for rosacea patients.

- **Limitations and challenges in utilizing dermcidin as a biomarker:**

While dermcidin shows promise as a potential biomarker for rosacea, several limitations and challenges need to be considered. First, the current body of evidence regarding dermcidin in rosacea is still limited, with relatively small sample sizes and variations in assessment techniques. Replication of findings and standardization of methods across larger cohorts are necessary to establish the reliability and validity of dermcidin as a biomarker [29].

Additionally, the complexity and heterogeneity of rosacea pose challenges in utilizing dermcidin as a standalone biomarker. Rosacea encompasses various subtypes with distinct clinical features and underlying pathophysiological mechanisms. Dermcidin levels may differ among these subtypes, and additional biomarkers or clinical parameters may be needed to capture the full spectrum of the disease [30].

Another challenge is the potential influence of confounding factors on dermcidin levels. Factors such as age, sex, ethnicity, comorbidities, and medications may impact dermcidin expression or metabolism. Future studies should account for these factors and perform subgroup analyses to better understand their influence on dermcidin levels in rosacea patients.

- **Areas for future research:**

To further advance the understanding of dermcidin in rosacea, several areas warrant future investigation. Firstly, larger-scale studies involving diverse patient populations

are needed to validate the findings and establish the consistency of dermcidin as a biomarker across different cohorts.

Longitudinal assessments are also crucial to evaluate the dynamic changes in dermcidin levels over time. Tracking dermcidin levels in individual patients throughout the course of the disease, including during flare-ups and remission, can provide insights into the utility of dermcidin as a monitoring tool and its potential for predicting disease progression.

Moreover, investigating the functional role of dermcidin in rosacea pathogenesis is essential. Understanding how dermcidin contributes to the inflammatory processes, immune dysregulation, and vascular abnormalities observed in rosacea can provide mechanistic insights and potentially lead to targeted therapeutic approaches.

Furthermore, exploring the interplay between dermcidin and other biomarkers or clinical parameters may enhance the diagnostic and prognostic value of dermcidin assessment. Combining dermcidin with other established markers or genetic factors associated with rosacea may improve the accuracy and specificity of diagnostic algorithms.

2. Conclusion

In conclusion, this review article has explored the assessment of serum dermcidin levels in patients with rosacea and its potential implications in understanding the pathogenesis, diagnosis, and monitoring of the disease. The findings from various clinical studies suggest a potential association between dermcidin and rosacea, although further research is warranted to validate these findings and overcome the limitations and challenges associated with its utilization as a biomarker.

The evidence indicates that dermcidin, an antimicrobial peptide secreted by eccrine sweat glands, may play a role in the innate immune system and have relevance to skin disorders. Studies investigating dermcidin in rosacea patients have reported elevated dermcidin levels, altered peptide profiles, or genetic variations compared to healthy controls. Furthermore, correlations between dermcidin levels and rosacea severity, subtypes, or treatment response have been observed in some studies.

However, it is important to acknowledge the limitations and challenges in utilizing dermcidin as a standalone biomarker for rosacea. These include the need for larger-scale studies, standardization of assessment methods, consideration of confounding factors, and accounting for the heterogeneity of rosacea. Additionally, the functional role of dermcidin in rosacea pathogenesis and its interplay with other biomarkers warrant further investigation.

Despite these challenges, the assessment of dermcidin levels holds potential implications for diagnosing and monitoring rosacea. It could provide an objective and quantitative measure to support the diagnostic process, monitor disease activity, and guide treatment decisions. However, more research is needed to establish the reliability, validity, and clinical utility of dermcidin assessment in rosacea.

In conclusion, the assessment of serum dermcidin levels in patients with rosacea represents an exciting area of research that may enhance our understanding of the disease and improve patient care. Future studies should aim to replicate and validate the findings, investigate the functional role of dermcidin, and explore its combination with other biomarkers to advance the field of rosacea diagnostics and personalized management strategies.

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