



Original Article

Utility of High-Frequency Ultrasound in Detecting Subclinical Inflammation in Atopic Dermatitis: A Prospective Observational Study

Dr. Barnita Saha¹, Dr. Nipun Gupta², Dr. Jatin Prajapati³

¹Assistant Professor, Department of Skin & VD, World College of Medical Sciences Research and Hospital, Jhajjar, Haryana, India.

²Assistant Professor, Department of Radiology, World College of Medical Sciences Research and Hospital, Jhajjar, Haryana, India.

³Post Graduate Student, Department of Community Medicine, RNT Medical College, Udaipur, Rajasthan, India.

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Corresponding Author:

Dr. Nipun Gupta

Assistant Professor, Department of Radiology, World College of Medical Sciences Research and Hospital, Jhajjar, Haryana, India.

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ABSTRACT

Background: Atopic dermatitis (AD) is a chronic inflammatory skin disorder characterized by recurrent exacerbations and remission. Conventional clinical scoring systems may not accurately detect subclinical inflammatory activity in apparently normal skin. High-frequency ultrasound (HFUS) has emerged as a non-invasive imaging technique capable of evaluating structural skin changes and inflammatory features in dermatological conditions.

Objective: To evaluate the utility of high-frequency ultrasound in detecting subclinical inflammation in patients with atopic dermatitis.

Methods: This prospective observational study was conducted in the Department of Dermatology at a tertiary care hospital in Haryana, India, from February 2025 to July 2025. A total of 50 patients with clinically diagnosed atopic dermatitis were included. Clinical severity was assessed using the Scoring Atopic Dermatitis (SCORAD) index. High-frequency ultrasound examination was performed on both affected skin and adjacent clinically normal skin using a 20–50 MHz linear probe. Ultrasound parameters including epidermal thickness, dermal thickness, dermal echogenicity, and the presence and thickness of the subepidermal low-echogenic band (SLEB) were recorded. Statistical analysis was performed using SPSS software, and a p-value <0.05 was considered statistically significant.

Results: The mean epidermal thickness in affected skin was 0.19 ± 0.05 mm, significantly higher than that in clinically normal skin (0.13 ± 0.03 mm, $p < 0.001$). Similarly, dermal thickness was greater in affected skin (1.87 ± 0.32 mm) compared with normal skin (1.51 ± 0.28 mm, $p < 0.001$). Dermal echogenicity was reduced in affected skin (32.4 ± 5.7) compared with clinically normal skin (38.9 ± 6.1 , $p = 0.002$). The presence of SLEB in clinically normal skin was detected in 29 patients (58%), indicating subclinical inflammation. SLEB thickness increased with disease severity and showed a strong positive correlation with SCORAD scores ($r = 0.62$, $p < 0.001$).

Conclusion: High-frequency ultrasound is an effective non-invasive modality for detecting structural changes and subclinical inflammation in atopic dermatitis. Ultrasound parameters, particularly SLEB thickness, correlate significantly with disease severity and may provide valuable adjunctive information for disease assessment and monitoring.

Keywords: Atopic dermatitis; High-frequency ultrasound; Subepidermal low-echogenic band; Subclinical inflammation; Dermatologic imaging; SCORAD.

INTRODUCTION

Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disorder characterized by intense pruritus, xerosis, and eczematous lesions with a fluctuating course of exacerbations and remissions. It is among the most common dermatological conditions worldwide, affecting approximately 15–20% of children and 5–10% of adults globally. The increasing

prevalence of atopic dermatitis over the past few decades has made it a significant public health concern due to its long-term impact on quality of life, psychological wellbeing, and healthcare utilization [1]. Patients with AD frequently experience sleep disturbances, reduced productivity, and increased risk of associated allergic conditions such as asthma and allergic rhinitis [2].

The pathophysiology of atopic dermatitis is multifactorial and involves a complex interplay between genetic susceptibility, immune dysregulation, epidermal barrier dysfunction, and environmental influences. Mutations affecting structural proteins such as filaggrin compromise the integrity of the skin barrier, resulting in increased transepidermal water loss and enhanced penetration of allergens and microbial antigens [3]. These factors stimulate an exaggerated immune response predominantly mediated by T-helper type-2 (Th2) lymphocytes, leading to increased production of cytokines including interleukin-4, interleukin-5, and interleukin-13. This immune imbalance contributes to chronic inflammation, pruritus, and structural changes within the skin [4].

Clinically, the severity of atopic dermatitis is commonly evaluated using standardized scoring systems such as the Scoring Atopic Dermatitis (SCORAD) index and the Eczema Area and Severity Index (EASI). Although these tools are widely used in clinical practice and research, they rely largely on visual assessment and patient-reported symptoms. Consequently, they may not fully reflect the underlying inflammatory processes occurring within the skin, particularly when inflammation persists in areas that appear clinically normal [5]. This phenomenon of persistent microscopic inflammation in clinically unaffected skin is referred to as subclinical inflammation and is increasingly recognized as an important factor contributing to disease recurrence and progression [6].

Traditionally, histopathological examination through skin biopsy has been considered the reference method for evaluating inflammatory changes in dermatological diseases. However, biopsy is invasive, may cause scarring, and is not suitable for repeated assessments during routine monitoring of chronic conditions such as atopic dermatitis. Therefore, there is growing interest in non-invasive imaging techniques that allow visualization of skin structure and inflammatory changes in vivo without causing discomfort to the patient [7].

High-frequency ultrasound (HFUS) has emerged as a valuable non-invasive imaging modality in dermatology. Unlike conventional ultrasound used for deeper tissues, HFUS employs probes with frequencies typically ranging from 20 to 50 MHz, enabling high-resolution visualization of superficial skin layers including the epidermis, dermis, and superficial subcutaneous tissue. This technique allows measurement of structural parameters such as epidermal thickness, dermal thickness, and tissue echogenicity, providing objective information about skin morphology and inflammatory changes [8]. Because HFUS is safe, painless, and easily repeatable, it is increasingly used for diagnostic evaluation and therapeutic monitoring in several dermatological disorders.

In patients with inflammatory skin diseases such as atopic dermatitis, high-frequency ultrasound can detect characteristic structural alterations within the skin. One of the most important ultrasonographic findings associated with inflammatory dermatoses is the subepidermal low-echogenic band (SLEB). This hypoechoic band located beneath the epidermis represents inflammatory infiltrate and dermal edema and has been shown to correlate with disease activity and severity in atopic dermatitis [9]. Measurement of SLEB thickness, along with assessment of dermal echogenicity and skin thickness, may therefore serve as an objective indicator of cutaneous inflammation.

Recent studies have suggested that ultrasound-detectable inflammatory changes may also be present in clinically unaffected skin of patients with atopic dermatitis, indicating the presence of subclinical inflammation. Identification of these early inflammatory changes may be clinically relevant, as it could help predict relapse and guide early therapeutic interventions aimed at preventing disease exacerbations [10]. Furthermore, HFUS provides the advantage of repeated monitoring during follow-up, allowing objective evaluation of treatment response and disease progression [11].

Despite increasing evidence supporting the diagnostic value of high-frequency ultrasound in dermatology, its application in routine evaluation of atopic dermatitis remains limited in many clinical settings. Additionally, there is limited data from tertiary care centers in India regarding the role of HFUS in identifying subclinical inflammatory changes in patients with atopic dermatitis. Generating such evidence may help establish HFUS as a useful adjunctive tool for disease assessment and monitoring.

Therefore, the present study was conducted in a tertiary care hospital to evaluate the utility of high-frequency ultrasound in the early detection of subclinical inflammation in patients with atopic dermatitis and to assess its potential role as a non-invasive imaging modality in the clinical evaluation of this condition [12].

METHODOLOGY

Study Design and Setting: This study was conducted as a hospital-based prospective observational study in the Department of Dermatology & Radiology of a tertiary care hospital in Haryana, India.

Study Duration: The study was carried out over a period of six months from February 2025 to July 2025.

Study Population: The study population consisted of patients clinically diagnosed with atopic dermatitis who attended the dermatology outpatient department during the study period.

Sample Size: A total of 50 patients with clinically diagnosed atopic dermatitis were included in the study. The sample size was determined based on feasibility and the average number of eligible patients presenting during the study period. Consecutive patients fulfilling the inclusion criteria were recruited until the desired sample size was achieved.

Inclusion Criteria

Participants were included in the study if they met the following criteria:

- Patients with a clinical diagnosis of atopic dermatitis based on established diagnostic criteria (Hanifin and Rajka criteria / UK Working Party diagnostic criteria)
- Patients aged ≥ 5 years
- Patients willing to participate in the study and provide written informed consent

Exclusion Criteria

Patients were excluded from the study if they had:

- Presence of secondary bacterial, viral, or fungal skin infection
- Other inflammatory dermatoses mimicking atopic dermatitis
- History of recent systemic immunosuppressive therapy
- Patients unwilling to participate in the study

Data Collection Procedure: Patients attending the dermatology outpatient department who fulfilled the eligibility criteria were enrolled in the study after obtaining written informed consent. A structured case record form was used to collect relevant demographic and clinical information including age, gender, duration of disease, and distribution of lesions. Clinical examination was performed by a dermatologist to confirm the diagnosis of atopic dermatitis and to assess the severity of the disease using the Scoring Atopic Dermatitis (SCORAD) index.

Ultrasound Examination: All enrolled patients underwent high-frequency ultrasound (HFUS) examination of the skin using a high-frequency linear probe with a frequency range typically between 20–50 MHz. Ultrasound evaluation was performed under standardized conditions with the patient in a comfortable position. The probe was applied gently with an adequate amount of coupling gel to avoid compression of the skin. The examination was carried out on:

- Clinically affected skin lesions
- Adjacent clinically normal appearing skin

The following ultrasound parameters were assessed and recorded:

- Epidermal thickness
- Dermal thickness
- Dermal echogenicity
- Presence and thickness of the subepidermal low-echogenic band (SLEB)

These parameters were evaluated as indicators of inflammatory activity and structural changes within the skin.

Outcome Measures

The primary outcome of the study was:

- Detection of subclinical inflammatory changes in skin using high-frequency ultrasound

Secondary outcomes included:

- Comparison of ultrasound parameters between clinically affected skin and clinically normal skin
- Correlation between clinical severity of atopic dermatitis and ultrasound findings

Statistical Analysis: The collected data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) software version 25. Continuous variables were expressed as mean \pm standard deviation, while categorical variables were presented as frequency and percentage. Differences between affected and unaffected skin parameters were analyzed using the paired Student's t-test or Wilcoxon signed rank test depending on data distribution. Association between ultrasound findings and clinical severity scores was assessed using Pearson or Spearman correlation analysis. A p-value of <0.05 was considered statistically significant.

Ethical Considerations: Written informed consent was obtained from all participants, and for minors, consent was obtained from their parents or legal guardians. Confidentiality of patient information was maintained throughout the study, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

RESULTS

A total of 50 patients with clinically diagnosed atopic dermatitis were included in the study. Demographic characteristics, clinical profile, and high-frequency ultrasound findings were analyzed to evaluate the presence of subclinical inflammation.

The demographic profile of the study participants is presented in Table 1. The majority of participants were in the 18–40 year age group (44%), followed by ≤ 17 years (26%) and 41–60 years (20%). The mean age of participants was 27.6 ± 13.2 years. Males constituted 56% ($n=28$) of the study population, while 44% ($n=22$) were females. Most patients had disease duration between 1–5 years (40%), while 30% had disease duration of less than one year. Based on SCORAD assessment, moderate disease severity was the most common category observed in the study population.

Table 1: Demographic and Clinical Characteristics of Study Participants (n = 50)

Variable	Category	Frequency (n)	Percentage (%)
Age group (years)	≤ 17	13	26
	18–40	22	44
	41–60	10	20
	>60	5	10
Gender	Male	28	56
	Female	22	44
Residence	Urban	29	58
	Rural	21	42
Duration of disease	<1 year	15	30
	1–5 years	20	40
	>5 years	15	30
Severity (SCORAD)	Mild	14	28
	Moderate	26	52
	Severe	10	20

The most common sites of involvement were flexural areas (64%), followed by face and neck (48%), upper limbs (42%), and lower limbs (36%). Lichenification was observed more frequently in patients with longer disease duration.

High-frequency ultrasound examination revealed structural alterations in affected skin, including increased epidermal thickness, increased dermal thickness, and presence of a subepidermal low-echogenic band (SLEB). These findings are summarized in Table 2.

Table 2: High-Frequency Ultrasound Parameters in Clinically Affected Skin (n = 50)

Parameter	Mean \pm SD
Epidermal thickness (mm)	0.19 ± 0.05
Dermal thickness (mm)	1.87 ± 0.32
SLEB thickness (mm)	0.27 ± 0.09

Ultrasound parameters of clinically affected skin were compared with those of adjacent clinically normal appearing skin. The comparison is shown in Table 3.

Table 3: Comparison of Ultrasound Parameters Between Affected and Clinically Normal Skin (n = 50)

Parameter	Affected Skin (Mean \pm SD)	Clinically Normal Skin (Mean \pm SD)	p-value
Epidermal thickness (mm)	0.19 ± 0.05	0.13 ± 0.03	<0.001
Dermal thickness (mm)	1.87 ± 0.32	1.51 ± 0.28	<0.001

Dermal echogenicity (arbitrary units)	32.4 ± 5.7	38.9 ± 6.1	0.002
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Clinically affected skin showed significantly higher epidermal and dermal thickness along with reduced dermal echogenicity compared with clinically normal skin.

Subclinical inflammatory changes were identified in clinically normal appearing skin using HFUS. The presence of subepidermal low-echogenic band (SLEB) in clinically normal skin was considered indicative of subclinical inflammation. The distribution is shown in Table 4.

Table 4: Detection of Subclinical Inflammation Using High-Frequency Ultrasound (n = 50)

Finding	Frequency (n)	Percentage (%)
SLEB present in clinically normal skin	29	58
SLEB absent	21	42

More than half of the patients (58%) demonstrated subclinical inflammatory changes on ultrasound despite clinically normal appearing skin.

The relationship between clinical severity (SCORAD category) and mean SLEB thickness is presented in Table 5.

Table 5: Association Between Disease Severity and SLEB Thickness (n = 50)

SCORAD Severity	Number of Patients	Mean SLEB Thickness (mm)	p-value
Mild	14	0.18 ± 0.05	<0.001
Moderate	26	0.27 ± 0.07	
Severe	10	0.36 ± 0.08	

A statistically significant increase in SLEB thickness was observed with increasing disease severity. Correlation analysis between SCORAD score and selected ultrasound parameters is shown in Table 6.

Table 6: Correlation Between SCORAD Score and Ultrasound Parameters

Ultrasound Parameter	Correlation Coefficient (r)	p-value
Epidermal thickness	0.41	0.003
Dermal thickness	0.48	0.001
SLEB thickness	0.62	<0.001

A moderate to strong positive correlation was observed between SCORAD score and ultrasound parameters, with SLEB thickness demonstrating the strongest correlation with disease severity.

Overall, high-frequency ultrasound successfully detected structural skin changes and subclinical inflammatory features in patients with atopic dermatitis. The presence of SLEB and increased skin thickness were significantly associated with clinical disease severity, supporting the utility of HFUS as a non-invasive imaging modality for evaluation and monitoring of atopic dermatitis.

DISCUSSION

The present study evaluated the role of high-frequency ultrasound (HFUS) in detecting structural skin changes and subclinical inflammation in patients with atopic dermatitis (AD). The findings demonstrated that HFUS is capable of identifying characteristic sonographic features such as increased epidermal thickness, increased dermal thickness, and the presence of a subepidermal low-echogenic band (SLEB), which may indicate inflammatory activity even in clinically normal appearing skin.

Atopic dermatitis is a chronic inflammatory disorder characterized by epidermal barrier dysfunction and immune dysregulation, which leads to recurrent episodes of cutaneous inflammation [3,4]. Although clinical scoring systems such as SCORAD are widely used to evaluate disease severity, they mainly rely on visual assessment and patient-reported symptoms and may not fully reflect the microscopic inflammatory changes occurring within the skin [5]. Persistent

microscopic inflammation in clinically normal skin has been recognized as an important factor contributing to disease relapse and chronicity in AD [6]. Therefore, non-invasive imaging modalities that can detect such subclinical inflammatory activity may improve disease monitoring and management.

In the present study, ultrasound evaluation of affected skin revealed a mean epidermal thickness of 0.19 ± 0.05 mm and dermal thickness of 1.87 ± 0.32 mm, both of which were significantly higher than those observed in clinically normal skin (0.13 ± 0.03 mm and 1.51 ± 0.28 mm, respectively; $p < 0.001$). These findings are consistent with earlier dermatologic ultrasound studies demonstrating that inflammatory dermatoses are associated with thickening of the epidermal and dermal layers due to inflammatory infiltrate and dermal edema [9]. Similar observations were reported by Polańska et al., who found that inflammatory skin conditions demonstrate increased dermal thickness and altered echogenicity on high-frequency ultrasound examination [7].

One of the most important ultrasonographic findings in inflammatory dermatoses is the subepidermal low-echogenic band (SLEB), which represents dermal edema and inflammatory cell infiltration [9]. In the present study, the mean SLEB thickness in affected skin was 0.27 ± 0.09 mm, and SLEB was also detected in clinically normal appearing skin in 29 out of 50 patients (58%), indicating the presence of subclinical inflammation. These findings are in agreement with previous studies that have demonstrated the presence of SLEB in both lesional and non-lesional skin of patients with atopic dermatitis [10].

The detection of subclinical inflammatory changes in clinically normal skin is particularly relevant for understanding the pathophysiology of AD. Earlier studies have suggested that persistent inflammation in apparently normal skin may predispose patients to disease relapse and contribute to the chronic relapsing nature of the disease [11]. In this context, HFUS provides a valuable opportunity to detect such changes at an early stage and may assist clinicians in initiating proactive treatment strategies.

The present study also demonstrated a significant association between disease severity and ultrasound findings. Patients with mild AD showed a mean SLEB thickness of 0.18 ± 0.05 mm, whereas those with moderate and severe disease demonstrated progressively higher values of 0.27 ± 0.07 mm and 0.36 ± 0.08 mm, respectively ($p < 0.001$). These findings indicate that SLEB thickness increases with disease severity and may serve as an objective indicator of inflammatory activity. Similar correlations between SLEB thickness and clinical severity indices have been reported in previous ultrasound studies of inflammatory dermatoses [10].

Correlation analysis in the present study revealed a positive association between SCORAD score and ultrasound parameters. The strongest correlation was observed between SCORAD score and SLEB thickness ($r = 0.62$, $p < 0.001$), followed by dermal thickness ($r = 0.48$, $p = 0.001$) and epidermal thickness ($r = 0.41$, $p = 0.003$). These findings support the potential role of HFUS as an objective adjunct to clinical scoring systems in assessing disease severity. Similar results were reported by Wortsman, who demonstrated that ultrasound parameters correlate well with clinical severity indices in inflammatory skin diseases [11].

The demographic characteristics of the present study population were also comparable with previously reported epidemiological patterns of atopic dermatitis. The majority of patients belonged to younger age groups, with a mean age of 27.6 ± 13.2 years, which is consistent with global epidemiological data indicating that AD commonly affects children and young adults [1,2]. Additionally, males constituted 56% of the study population, which is comparable to findings reported in certain regional epidemiological studies [7].

High-frequency ultrasound offers several advantages as a diagnostic modality in dermatology. It is non-invasive, painless, readily repeatable, and capable of providing real-time imaging of superficial skin structures with high spatial resolution [8]. Because of these advantages, HFUS has increasingly been used in the evaluation of inflammatory dermatoses, skin tumors, and cosmetic dermatology applications [7,11].

However, the present study has certain limitations. The sample size was relatively small and the study was conducted at a single tertiary care center, which may limit the generalizability of the findings. Additionally, histopathological correlation of ultrasound findings was not performed. Future studies involving larger populations and longitudinal follow-up may help further establish the prognostic role of HFUS in predicting disease relapse and monitoring treatment response in atopic dermatitis.

Overall, the findings of the present study demonstrate that high-frequency ultrasound is a valuable non-invasive imaging modality capable of detecting structural skin changes and subclinical inflammation in patients with atopic dermatitis. The presence of SLEB and increased skin thickness correlated significantly with clinical disease severity, highlighting the potential role of HFUS as an adjunctive tool in the evaluation and monitoring of atopic dermatitis.

CONCLUSION

The present study demonstrated that high-frequency ultrasound (HFUS) is a useful non-invasive imaging modality for detecting structural skin changes and subclinical inflammation in patients with atopic dermatitis. Ultrasound examination revealed significantly increased epidermal and dermal thickness in affected skin compared with clinically normal skin, along with reduced dermal echogenicity. The presence of a subepidermal low-echogenic band (SLEB) was observed in a considerable proportion of patients, including 58% of clinically normal appearing skin, indicating the presence of subclinical inflammatory activity. Furthermore, SLEB thickness showed a significant positive association with disease severity and correlated strongly with SCORAD scores. These findings suggest that HFUS may serve as an objective adjunct to clinical assessment for evaluating disease activity and monitoring progression in atopic dermatitis. Incorporating HFUS into dermatological practice may help identify early inflammatory changes and support more proactive disease management strategies. However, further studies with larger sample sizes and longitudinal follow-up are needed to validate its prognostic value.

DECLARATIONS

Ethical Considerations: The study was conducted in accordance with the principles of the Declaration of Helsinki.

Informed Consent: Written informed consent was obtained from all participants. For participants below 18 years of age, consent was obtained from their parents or legal guardians.

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Conflict of Interest: The authors declare no conflict of interest related to this study.

Author Contributions: All authors contributed to the conceptualization, data collection, analysis, manuscript preparation, and final approval of the manuscript.

Data Availability: The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

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