

Skin Acidity Level in Children with Atopic Dermatitis

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Abstract

Background: Atopic dermatitis (AD) is a chronic, relapsing, and pruritic inflammatory skin disease commonly found in children. It is characterized by a complex and multifactorial pathogenesis involving genetic, immunologic, and environmental factors. One of the proposed pathomechanisms includes mutations in the filaggrin gene, which plays a crucial role in maintaining epidermal barrier integrity, skin hydration, and regulating skin surface acidity or potential of hydrogen (pH). Alterations in skin pH have been associated with barrier dysfunction, increased susceptibility to infection, and worsening of inflammation in AD patients.

Objective: To analyze and compare the skin pH in children with AD, specifically between lesional and non-lesional areas.

Methods: This was a cross-sectional analytical study conducted from January to April 2024 at the Pediatric Dermatology Division, Department of Dermatology, Venereology, and Aesthetic Medicine, and the Allergy and Immunology Division, Department of Pediatrics, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia. Skin pH was measured in both lesional and non-lesional areas. Lesional measurements were performed on areas presenting with erythema and/or lichenification.

Results: A total of 33 patients were enrolled in the study. The mean skin pH of lesional areas was 5.92 ± 0.45 , while that of non-lesional areas was 5.38 ± 0.42 . Statistical analysis showed a significant difference in pH values between lesional and non-lesional skin ($p = 0.001$). A subgroup analysis comparing erythema and lichenified/hyperpigmented lesions revealed no significant difference in pH values ($p = 0.102$).

Conclusion: In children with AD, the skin pH of lesional areas is significantly higher than that of non-lesional areas.

Keywords: Atopic dermatitis; children; pH level; human and disease.

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Introduction

Atopic dermatitis (AD), also known as atopic eczema, is a chronic, recurrent inflammatory skin disease characterized by itching and typically appears in specific predilection areas.^{1,2} According to data from the World Health Organization (WHO), the global prevalence of AD is estimated to be approximately 230 million people, or around 0.2% to 36% worldwide. In Indonesia, the

prevalence of AD is estimated to be 23.67%, based on data from the Indonesian Paediatric Dermatology Study Group.³

The skin's potential of hydrogen (pH) is a key regulator of skin barrier homeostasis and plays an important role as part of the innate immune defense system. An effective skin barrier is typically marked by good hydration levels and a slightly acidic skin pH.^{4,5} In patients with AD, the

skin's normally acidic pH tends to become alkaline. The exact factors influencing skin pH are not yet fully understood. However, several mechanisms may contribute to increased pH in AD patients, such as decreased sebum secretion, impaired maturation of stratum corneum lipids, increased filaggrin degradation, and reduced levels of transglutaminase, keratin, loricrin, involucrin, and intercellular proteins.^{4,6}

A previous study reported that skin pH levels were higher in lesional areas.⁷ Recently, skin pH has gained attention as a therapeutic target in AD management, aiming to restore the skin barrier and reduce pruritus, ultimately improving patients' quality of life (QoL). The aim of this study was to evaluate skin pH levels in children with AD, comparing lesional and non-lesional skin areas.

Methods

This was a cross-sectional analytical study conducted between January and April 2024 at the Pediatric Dermatology Division, Department of Dermatology, Venereology, and Aesthetics Outpatient Clinic, as well as the Allergy and Immunology Division, Department of Pediatrics Outpatient Clinic, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia. Ethical approval for this study was obtained from the Hospital Ethics and Research Committee of Dr. Soetomo General Academic Hospital, Surabaya (registration number: 0822/KEPK/IX/2023).

The study population consisted of children diagnosed with atopic dermatitis (AD). The study sample comprised all accessible individuals who met the inclusion and exclusion criteria. The inclusion criteria were children aged over 1 year and under 18 years who fulfilled the diagnostic criteria for AD based on the Hanifin-Rajka criteria, were in generally adequate health condition, had obtained informed consent from their parents, and were willing to participate in the study. The exclusion criteria were patients clinically diagnosed with other skin diseases such as psoriasis, seborrheic dermatitis, or contact dermatitis, which could potentially affect skin pH parameters.

Patients who met the inclusion criteria were recruited as study subjects. Basic demographic data, medical history, and physical examination findings were recorded. Clinical photographs were taken of both lesional and non-lesional skin areas. Skin pH measurements were performed in a controlled environment with a temperature of $20 \pm 4^\circ\text{C}$ and a humidity level of 40–60%. Each patient was asked to rest in the room for 20 minutes prior to the measurement. Skin pH was assessed using a Hanna Instruments HI 99181 Portable Waterproof Skin pH Meter with a flat glass electrode (probe), and all measurements were carried out by a single examiner. Measurements were taken from both lesional and non-lesional skin. Lesional skin measurements were performed on areas showing erythema and/or lichenification. Non-lesional skin measurements were conducted on the mid-volar region of the right and left forearms, approximately 2 cm below the cubital fossa. Before measurement, the selected skin area was cleansed with gauze moistened with 0.9% normal saline (sodium chloride), and allowed to dry completely.

Data analysis was performed using Microsoft Excel and the Statistical Package for the Social Sciences (SPSS) version 26. Comparative analysis was conducted using the Independent t-test for normally distributed data or the Mann-Whitney U test for non-normally distributed data. Written informed consent was obtained from the parents of all participants after a thorough explanation of the study procedures.

Results

A total of 33 patients was included in this study. There were 14 (42.4%) boys and 19 (57.6%) girls.

Table 1: Sample demographics.

Sex	n (%)
Boys	14 (42.4%)
Girls	19 (57.6%)
Age, n (%)	
>12 months - 59 months (toddlers)	10 (30.3%)
>60 months - 72 months (pre-school children)	10 (30.3%)
>6 years - <18 years (school-age children)	13 (43.0%)

Most children in this study were school-age children (>6 years) with 13 patients (43%) (Table 1). The most common clinical manifestations were xerosis (dry skin), which was present in almost all patients with 32 (96.9%), as well as erythematous macules and hyperpigmented macules which were each present in 21 patients (63.6%). Other manifestations in this study were papules, lichenification, scaling, and excoriation (Table 2).

The results of pH measurements on the skin of children with AD revealed that the median pH value of the lesion area was 5.96, and the pH of the non-lesion area was 5.41 (Table 3). Statistical test regarding the difference in pH values in the lesion and non-lesion areas was conducted using T-test because the data was normally distributed. The results of the data analysis showed that there was a significant difference in the pH values of lesion and non-lesion areas ($p = 0.001$) (Table 3 and Figure 1).

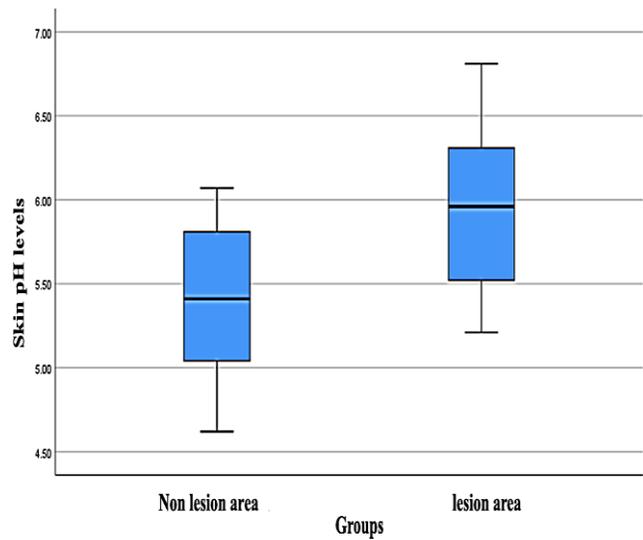


Figure 1: Boxplot graph comparing the distribution of pH levels in the lesion area and non-lesion area.

The lesion pH measurement area in this study was conducted on erythema and/or lichenification or hyperpigmentation lesions. Subgroup analysis was conducted on the lesion area, comparing erythema lesions with lichenification or hyperpigmentation lesions. The measurement results showed a median value for erythema lesions of 6.17, and for lichenification or hyperpigmentation lesions the result was 5.69. Differences in pH values in erythema and lichenification or hyperpigmentation lesions showed no significant difference between the two areas ($p=0.102$) (Table 4 and Figure 2).

Table 2: Clinical manifestations.

Clinical manifestations*	n (%)
Xerosis	32 (96.9%)
Erythematous macules	21 (63.6%)
Hyperpigmented macules	21 (63.6%)
Papules	17 (51.5%)
Excoriation	16 (48.4%)
Scaling	9 (27.2%)
Lichenification	8 (24.2%)

*1 subject may have more than 1 clinical manifestation

Table 3: Results of skin pH measurements in lesion and non-lesion areas.

	Minimum	Maximum	Median	Mean + SD	p-value
Lesion area pH	5.21	6.81	5.96	5.92 ± 0.45	0.001*
Non-lesion area pH	4.62	6.07	5.41	5.38 ± 0.42	

*significant <0,05

Table 4: Results of skin pH measurements in erythema lesions and lichenification/hyperpigmentation lesions.

Minimum	Maximum	Median	Mean ± SD	p-value	
Erythema Lesion	5.21	6.81	6.17	6.06 ± 0.45	0.102
Lichenification/hyperpigmentation lesion	5.14	6.84	5.69	5.84 ± 0.46	

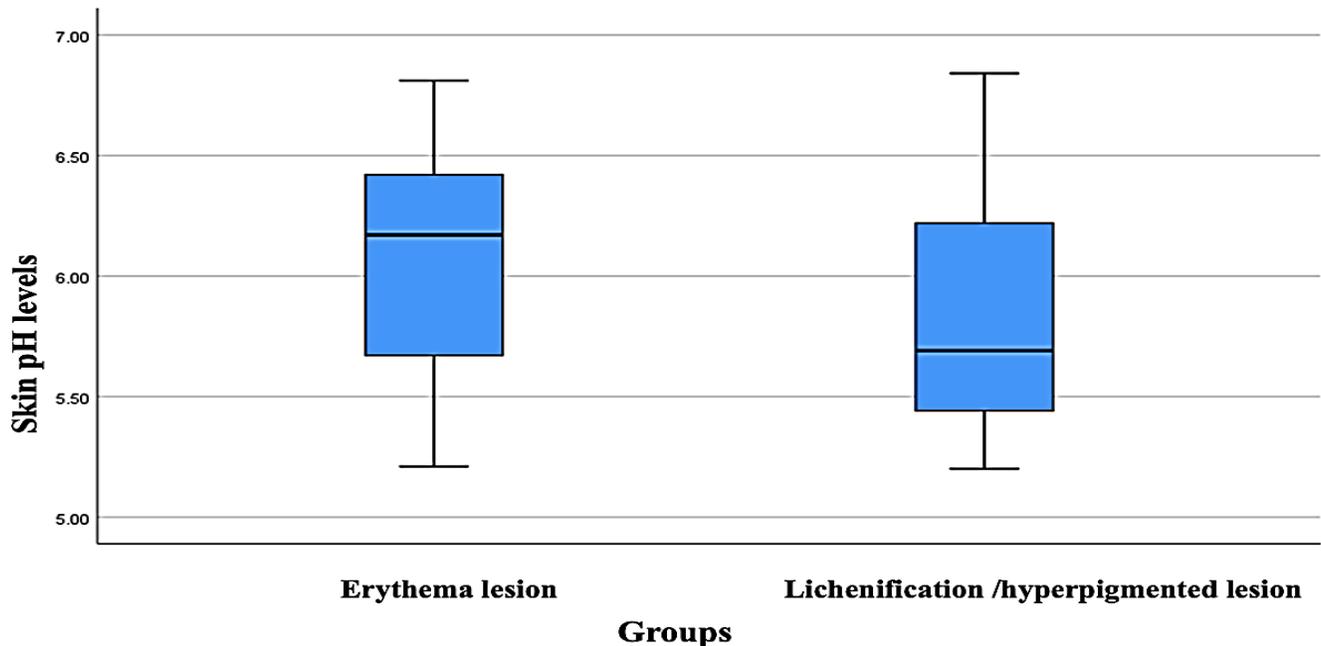


Figure 2: Boxplot graph comparing the distribution of pH levels in erythema lesions and lichenification/hyperpigmentation lesions.

Discussion

This study had 33 samples. The number of girl patients was greater than boys, with the ratio of 1.3:1. This result had the same with previous study conducted by Sihaloho and Indramaya in 2015. The study showed that the number of boys with AD was greater than girls, it was 53.4% and 46.6% respectively.⁸ The incidence ratio of these sex differences varies, and was also seen in different countries. The reason for this difference is not yet known for sure, but it is likely due to the influence of sex hormones in men and women.⁹

In this study, age was grouped from toddler to children, based on Minister of health regulation number 25 of 2014. The age range of AD patients were 2 to 16 years, with the most frequent was in school-age children aged >6 years, as many as 13 patients. This is line with research conducted by Narla and Silverbergh in 2021, which stated that prevalence of AD in the age group 6 months - <6 years was 12.1%, age >6 years - <12 years was 13% and age >12 years was 14.8%.¹⁰ Also, Aisyah et al, in 2019 stated that 65% of AD patients in children were aged >6 years.¹¹ This may be due to the high activity of children at that age who are more susceptible to triggering factors in the sur-

rounding environment, thus triggering a recurrence of AD.¹²

The most frequent clinical manifestation found in this study was xerosis or dry skin, which was present in almost all patients with 32 patients (96.9%), followed by complaints of erythematous macules and hyperpigmented macules, which was present in 21 patients (63.6%), respectively. These results were similar to a previous study by Aisyah et al, which stated that all patients in the study had clinical manifestations in the form of xerosis cutis and erythema.¹¹ These results were also in accordance with the literature which stated that AD lesions vary and are grouped based on the patient's age. In infants and children, the lesions commonly found are acute lesions in the form of erythematous lesions, papules, vesicles, erosions, and crusts. Subacute lesions might include erythematous plaque, scale, crusting and excoriation.^{13,14}

The results of skin pH measurement in this AD children showed that the pH in the lesion area was 5.92 ± 0.45 and in the non-lesion area the value was 5.38 ± 0.42 . The results of data analysis showed that there was a significant difference in

the pH value between lesion and non-lesion areas ($p = 0.001$). Primadiarti et al, conducted a study by measuring the skin pH of healthy children and children with AD aged 1-12 years. The results obtained were that the pH value of healthy children's skin was 4.89 ± 0.46 , then further study was conducted by measuring the skin pH level in children with AD aged 0-14 years. The results of the follow-up research showed that the pH of non-lesional skin in AD patients was 5.2 ± 0.46 , and the pH of skin lesions in AD patients was 5.86 ± 0.56 .⁴ A study from Zainal et al, in 2019 reported similar findings, that skin pH in the lesion area of AD patients was higher than in non-lesion areas. The pH in lesion area was 5.40 ± 0.13 , and the pH in non-lesion area was 5.27 ± 0.14 ($p=0.01$).¹⁵ In this study, skin pH results were also compared between the erythema and lichenification / hyperpigmentation lesion areas. The skin pH result in the erythema lesion area was 6.06 ± 0.45 , and lichenification or hyperpigmentation lesions were 5.84 ± 0.46 ($p=0.102$), which shows that there was no significant difference between the two groups. Previous study by Sparavigna et al, compared the pH of acute, subacute, and chronic lesions. Acute lesion in this study was described as itchy lesions, and erythema due to scratching. Subacute lesion was defined as erythematous lesions but already appear hyperkeratosis, and chronic lesion was described as itchy lesion with lichenification. This study stated that the pH level of acute lesions had a slightly higher value compared to subacute and chronic lesions.¹⁶

The skin pH is the main regulator of skin barrier homeostasis and an important innate defense mechanism for the skin.⁵ Normal skin pH level is naturally acidic or it is known as acid mantle. Skin pH level varies according to exogenous and endogenous factors. Endogenous factors that influence skin pH include age, gender, anatomical location, sebum levels, and sweat levels, while exogenous factors that influence skin pH include the use of topical products such as cosmetics, lotions, frequency of cleaning the skin area with soap, weather, and environmental temperature.^{7,17}

Skin pH level in AD patients tends to shift towards alkaline in both lesion and non-lesion areas when compared with normal patients. This is because in AD there is a mutation in the gene that codes for filaggrin, which is one of the most frequent causes of skin barrier dysfunction.¹⁸ Filaggrin is a protein involved in the formation of natural moisturizing factor (NMF) by aggregating keratin filaments. Filaggrin also plays a role in hydration and pH regulation in the stratum corneum, hence if there is a defect in function or a decrease in the amount of filaggrin, there will be disturbances in hydration and skin pH regulation. The skin of AD patients also shows lipid composition disorders and changes in sphingomyelin metabolism which cause a decrease in ceramide concentration and impaired skin barrier function.¹

The increase pH levels in AD patients causes an increase in serine protease and kallikrein activity. This result could initiate itching and chronic inflammation. In the acute phase, lymphoid cells secrete chemokines such as thymus and activation-regulated chemokine (TARC) (also known as CCL17) as well as other cytokines including interleukin (IL)-25, IL-33 and thymic stromal lymphopoietin (TSLP). Upon activation by these mediators, T-helper (Th)2 cells secrete IL-4, IL-5, IL-13, and IL-31 and trigger the accumulation of IL-5 and increased Immunoglobulin (Ig)E, which causes inflammation and damage to the skin barrier.¹ The phase progression from acute AD to chronic AD is characterized by an increase in Th2 and Th17 as well as an increase in Th1 activation such as interferon gamma ($\text{IFN-}\gamma$) and IL-12. Apart from that, there is IL-17 released by Th17, which contributes to epidermal hyperplasia. Th1 cytokines stimulate macrophages, lymphocytes and polymorphonuclear neutrophils (PMN) in the destruction of pathogenic bacteria. These cytokines also help promote the development of cytotoxic lymphocytes (CTL & natural killer cells), which are responsible for cell-mediated immune responses against viruses and tumor cells.^{19, 20}

The results of this study showed that the skin pH level in the lesion area was higher than in the

non-lesion area. This was in accordance with the theory which explains that the increase in Th2 cytokines dominates the lesion area. This increase in Th2 cytokines reduces filaggrin expression which causes a decrease in NMF, impaired hydration, and regulation of skin pH, hence pH level in the lesion area will be higher than the pH level in the non-lesional area.²¹ The pH levels between erythema lesions and lichenification/hyperpigmentation lesions in this study showed that the pH of erythema lesions had a higher value than the pH of lichenification/hyperpigmentation lesions, however there was no statistically significant difference between the two groups. This was in accordance with the pathomechanism of AD disease, where in the acute phase there is an increase in Th2 which secretes IL-4, IL-5, IL-13 and IL-31. This leads to an increased inflammation and damage to the skin barrier, while in the chronic phase there is a predominance of Th1, an increase Th2, Th22, Th17 that affects the thickening of the epidermis and the skin barrier repair mechanism occurs. The results of this study showed that there was no statistically significant difference between the pH levels of erythema lesions and lichenification/hyperpigmentation lesions. This could be due to differences in the location of skin pH level measurement in erythema and lichenification/hyperpigmentation lesions, which could affect the pH level value.^{20,22}

Conclusion

There is a significant difference between the skin pH value of the children with AD in the lesion area and the non-lesion area. However, there is no significant difference between the skin pH value between erythema lesions and hyperpigmentation/lichenification lesions.

Skin pH measurement is an important parameter in assessing epidermal barrier dysfunction in pediatric patients with AD. It plays a key role in guiding hydration therapy and the selection of appropriate topical agents, such as cera-mide-containing moisturizers and pH-balanced cleansers, which are essential for restoring and maintaining the skin barrier. The regular use of moisturizers, applied two to three times daily, has been

shown to be effective in improving skin condition and reducing disease severity in children with AD.

Ethical Approval: Ethical approval for this study was obtained from the Hospital Ethics and Research Committee of Dr. Soetomo General Academic Hospital, Surabaya (registration number: 0822/KEPK/IX/2023).

Conflict of Interest: There was no conflict of interest to be declared by any author.

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Author's Contribution:

S: Substantial contributions to concept, study design, acquisition of data, analysis and interpretation of data, manuscript writing and critical review, has given final approval of the version to be published.

PHS: Substantial contributions to concept, study design, Critical review, manuscript writing, has given final approval of the version to be publish.

D: Substantial contributions to concept, study design, acquisition of data, analysis and interpretation of data, manuscript writing and critical review, has given final approval of the version to be published.

EE: Substantial contributions to acquisition of data, manuscript writing, has given final approval of the version to be published.

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