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Research Article

Immune Imbalance Model of Classical Scabies in a Boarding School Setting: Evidence from Th17–Treg–Related Biomarkers and Clinical Severity

Septiana Widyantari[1,2], Armyta Denissafitri [1,2], Yuri Widia[1,2], Bagus Haryo Kusumaputra[1,2], Rahmadewi[1,2], Muhammad Yulianto Listiawan[1,2]*, Anang Endaryanto[3,4], Cita Rosita Sigit Prakoeswa[1,2]

[1]*Department of Dermatology, Venereology, and Aesthetics, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia;* [2]*Department of Dermatology, Venereology, and Aesthetics, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia;* [3]*Department of Child Health, Faculty of Medicine, Universitas Airlangga, Indonesia;* [4]*Department of Child Health, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia*

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Abstract

Background: Scabies remains a significant public health concern in communal living environments, where recurrence and variable lesion severity frequently occur. The imbalance between pro-inflammatory and regulatory immune responses, particularly within the Th17–Treg axis, may influence disease expression. ***Objective***: This study aimed to evaluate the association between Th17–Treg–related biomarkers (IL-17, IL-10, and FoxP3) and clinical severity indicators in adolescents with classical scabies. ***Methods***: An explanatory cross-sectional study was conducted among 24 adolescents diagnosed with classical scabies based on International Alliance for the Control of Scabies criteria. Serum IL-17, IL-10, and FoxP3 levels were measured using ELISA. Clinical severity was assessed based on lesion extent and recurrence frequency. Correlation analyses were performed to determine associations between immune biomarkers and clinical outcomes. ***Results***: IL-17 levels were significantly inversely correlated with recurrence (r= –0.483, *p*=0.017) and lesion extent (r= –0.460, *p*=0.024). Conversely, IL-10 and FoxP3 levels were positively associated with recurrence and lesion severity, with FoxP3 demonstrating the strongest correlation with lesion extent (r=0.690, *p*<0.001). No significant associations were observed between demographic variables and clinical or immunological parameters. ***Conclusions***: The findings suggest that reduced Th17 activity and enhanced regulatory immune responses contribute to recurrence and increased lesion severity in scabies within high-transmission settings.

Keywords: Foxp3; IL-17; IL-10; Immune imbalance; Lesion extent; Recurrence; Recurrence frequency; Th17–Treg axis.

نموذج عدم توازن المناعة للجرب الكلاسيكي في بيئة مدرسة داخلية: أدلة من العلامات الحيوية المرتبطة ب Th17–Treg والشدة السريرية

الخلاصة

الخلفية: لا يزال الجرب مصدر قلق صحي عام كبير في البيئات المعيشية الجماعية، حيث يحدث التكرار وتغيرات شدة الآفات بشكل متكرر. قد يؤثر عدم التوازن بين الاستجابات المناعية المؤيدة للالتهاب والتنظيم، خاصة ضمن محور Th17–Treg، على التعبير عن المرض. **الهدف**: هدفت هذه الدراسة إلى تقييم العلاقة بين المؤشرات الحيوية المرتبطة ب Th17–Treg (IL-17، IL-10، وFoxP3) ومؤشرات الشدة السريرية لدى المراهقين المصابين بالجرب الكلاسيكي. **الطرائق**: أجريت دراسة مقطعية تفسيرية بين 24 مراهقا تم تشخيصهم بالجرب الكلاسيكي بناء على معايير التحالف الدولي لمكافحة الجرب. تم قياس مستويات IL-17 وIL-10 وFoxP3 في الدم باستخدام ELISA. تم تقييم شدة الإصابة السريرية بناء على مدى الآفة وتكرارها. أجريت تحليلات الارتباط لتحديد الروابط بين المؤشرات الحيوية المناعية والنتائج السريرية. ***النتائج***: كانت مستويات IL-17 مرتبطة بشكل ملحوظ عكسيا مع التكرار (r= –0.483، p=0.017) ومدى الآفة (r= –0.460، p=0.024). وعلى العكس، كانت مستويات IL-10 وFoxP3 مرتبطة إيجابيا بالعودة وشدة الآفات، حيث أظهر FoxP3 أقوى ارتباط مع مدى الآفة (r=0.690، p<0.001). لم تلاحظ أي ارتباطات ذات دلالة إحصائية بين المتغيرات الديموغرافية والمعايير السريرية أو المناعية. **الاستنتاجات**: تشير النتائج إلى أن انخفاض نشاط Th17 وتعزيز الاستجابات المناعية التنظيمية يساهم في تكرار وزيادة شدة الآفات في الجرب في البيئات ذات العدوى العالية.

**Corresponding author*: Muhammad Y. Listiawan. Department of Dermatology, Venereology, and Aesthetics, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia; Email: m.yulianto@fk.unair.ac.id

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INTRODUCTION

Scabies is a highly transmissible ectoparasitic skin disease caused by *Sarcoptes scabiei* var. *hominis* and remains a major global public health concern. It is clinically characterized by intense nocturnal pruritus that leads to skin barrier disruption and secondary bacterial infections, most commonly caused by *Streptococcus pyogenes* and *Staphylococcus aureus*. These complications may progress to severe systemic sequelae, including acute rheumatic fever, rheumatic heart disease, and acute post-streptococcal glomerulonephritis (APGN), which is associated with an increased risk of chronic kidney disease later in life [1]. Recurrent APGN during childhood has been linked to persistent renal impairment, with approximately 10% of children with scabies in low-resource settings showing evidence of kidney damage [2]. Globally, scabies-associated impetigo is estimated to contribute to nearly 500,000 new APGN cases annually, while rheumatic fever and rheumatic heart disease together account for approximately 300,000 deaths each year [3]. Although scabies affects all age groups, its burden is disproportionately higher in low- and middle-income countries [4]. Global prevalence increased from an estimated 100 million cases in 2010 [5] to more than 206 million affected individuals worldwide in 2021, with over 622 million new cases occurring annually,

particularly in tropical and subtropical regions [6]. A systematic review reported prevalence rates ranging from 0.18% to 76.9%, highlighting substantial global heterogeneity [7]. Indonesia consistently ranks among countries with the highest scabies-related disability-adjusted life years (DALYs), particularly among individuals under 20 years of age and those living in communal environments such as boarding schools and pesantren [3,6]. Studies from Southeast Asia report scabies prevalence of 45–78% among boarding school students, emphasizing the role of crowding and environmental factors in facilitating transmission [7,8]. Recurrent infestations are common in endemic settings, as demonstrated by community-based studies documenting repeated reinfestation in pediatric populations [9]. Beyond cutaneous manifestations, scabies is associated with sleep disturbance, reduced quality of life, school absenteeism, social stigma, and increased risk of post-infectious complications [10,11]. From an immunopathological perspective, *Sarcoptes scabiei* infestation activates innate and adaptive immune responses through mite-derived molecules that stimulate keratinocytes and antigen-presenting cells, leading to T-cell–mediated inflammation [12]. Disease expression is increasingly understood as the result of immune imbalance, particularly between pro-inflammatory Th17 responses and regulatory T-cell (Treg) activity. Interleukin-17 (IL-17) promotes cutaneous inflammation and lesion expansion, whereas interleukin-10 (IL-10) and the transcription factor FoxP3 play essential roles in suppressing excessive inflammation and maintaining immune homeostasis [5,6,13]. Experimental and clinical evidence suggests that immune modulation by the mite contributes to persistent inflammation, variable lesion severity, and recurrent disease, with dysregulation of Th17–Treg responses implicated in extensive lesions and repeated infestations [12,14,15]. In addition to immunological mechanisms, host and environmental factors may further influence immune responses and clinical manifestations of scabies. Demographic and nutritional factors such as age and body mass index (BMI) have been reported to affect immune regulation and cytokine profiles in various inflammatory conditions, including modulation of Th17 and Treg pathways [16,17]. Duration of stay in communal living environments may increase cumulative exposure and reinfestation risk, thereby influencing recurrence frequency and lesion severity [8,9]. Socioeconomic indicators, including parental education, may also indirectly affect disease outcomes through hygiene practices, health literacy, and access to treatment [18]. Nevertheless, how these host-related factors interact with immune biomarkers in determining disease severity remains insufficiently explored. Despite growing interest in scabies immunopathogenesis, clinical studies simultaneously evaluating demographic characteristics together with key immunological biomarkers such as IL-10, IL-17, and FoxP3 in relation to classical indicators of severity, namely lesion extent and frequency of recurrence, remain limited. Existing evidence often focuses on single biomarkers or experimental models, with relatively few studies integrating immune profiles and clinical outcomes in real-world endemic settings, particularly among adolescents living in communal environments with high transmission risk. This gap limits the understanding of how immune regulation contributes to clinical heterogeneity and recurrent infestations in scabies. Understanding scabies solely from an epidemiological perspective is insufficient to explain why some individuals develop more extensive lesions or experience recurrent disease despite similar environmental exposure. A more integrated approach that links host characteristics, immune regulation, and clinical expression is required to provide biologically plausible explanations for disease severity and recurrence. Therefore, this study aimed to examine the associations of age, duration of stay in the dormitory, body mass index (BMI), father's education, and mother's education with IL-10, IL-17, FoxP3, lesion extent/severity, and frequency of recurrence. In addition, this study evaluated the associations of IL-10, IL-17, and FoxP3 with lesion extent/severity and frequency of recurrence. By integrating demographic factors, immune biomarkers, and clinical outcomes within a single analytical framework, this study seeks to provide a more comprehensive understanding of the immunological and clinical determinants of scabies severity in a high-risk boarding school population.

METHODS

Study design and setting

This explanatory observational study employed a cross-sectional design to examine the associations between demographic factors, Th17–Treg–related immune markers, and clinical severity of classical scabies among adolescents residing in a boarding school in Surabaya, Indonesia.

Sample collection

Clinical examinations, data collection, and blood sampling were performed by a multidisciplinary team consisting of consultant dermatologists and venereologists, assisted by certified medical laboratory technologists from Dr. Soetomo General Academic Hospital, between November 2021 and March 2022. Venous blood samples were analyzed at the Clinical Pathology Laboratory, Central Laboratory Installation, Dr. Soetomo General Academic Hospital.

Outcome measurements

Serum levels of interleukin-17 (IL-17), interleukin-10 (IL-10), and FoxP3 were measured using commercially available enzyme-linked immunosorbent assay (ELISA) kits according to the manufacturers' instructions. Scabies diagnosis was established clinically based on the International Alliance for the Control of Scabies (IACS) 2020 criteria. Clinical severity was evaluated using two indicators: recurrence frequency (number of recurrent episodes) and lesion extent/severity (proportion of affected body areas).

Immune activity related to the Th17–Treg axis was assessed through serum IL-17 as a marker of pro-inflammatory Th17 response, while IL-10 and FoxP3 were used to reflect regulatory T-cell–related immune activity. In addition, demographic and host-related variables were collected, including age, duration of stay in the dormitory, body mass index (BMI), father's education level, and mother's education level.

Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki and approved by the Health Research Ethics Committee of Dr. Soetomo General Academic Hospital (No. 0304/KEPK/XI/2021). Written informed consent was obtained from parents or legal guardians, and informed assent was obtained from all participants. Given the exploratory nature of this study, the sample size was determined pragmatically, and twenty-four participants were included in the final analysis.

Statistical analysis

Statistical analysis was conducted to evaluate: 1) associations between demographic variables and immune biomarkers (IL-10, IL-17, and FoxP3) as well as clinical severity indicators (lesion extent/severity and recurrence frequency); 2) associations between IL-10, IL-17, and FoxP3 and lesion extent/severity; and 3) associations between IL-10, IL-17, and FoxP3 and recurrence frequency. Data normality was assessed using the Shapiro–Wilk test. Depending on data distribution and variable type, Mann–Whitney U, chi-square, Pearson's, or Spearman's correlation tests were applied as appropriate. P-values were reported, and statistical significance was set at $p< 0.05$.

RESULTS

A total of 24 adolescents with clinically diagnosed classical scabies were included in the final analysis. Baseline demographic characteristics (Table 1), immune biomarker levels, and clinical severity indicators were first described to provide an overview of the study population. The analysis was subsequently performed in three sequential steps. First, associations between demographic and host-related factors—including age, duration of stay in the dormitory, body mass index (BMI), father's education, and mother's education—and immune markers (IL-10, IL-17, and FoxP3) as well as clinical severity indicators (lesion extent/severity and recurrence frequency) were evaluated. Second, the relationships between Th17–Treg–related immune markers and lesion extent/severity were analyzed to explore immunological correlates of disease severity.

Table 1: Demographic and Immune Regulatory Profile of Participants

Variable	Category	n(%)	Mean+SD Median (Range)
Age (year)	12	7(29.2)	13(12-15)
	13	11(45.8)	
	14	2(8.3)	
	15	4(16.7)	
BMI	Underweight	1(4.2)	
	Normal	20(83.3)	
	Overweight	3(12.5)	
Duration of stay in dormitory (month)	≤ 3	2(8.3)	
	> 3	22(91.7)	
Maternal Education	Elementary school	14(58.3)	
	Junior high school graduate	1(4.2)	
	Senior high school graduate	1(4.2)	
	Bachelor's degree	5(20.8)	
	Master's degree	2(8.3)	
	Doctoral degree	1(4.2)	
Paternal Education	No formal education	1(4.2)	
	Elementary school	8(33.3)	
	Senior high school graduate	3(12.5)	
	Master's degree	10(41.7)	
	Doctoral degree	2(8.3)	
Lesion Extent	Moderate (3–6 areas)	8(33.3)	
	Severe (>6 areas)	16(66.7)	
Frequency of Recurrence	Never	14(58.3)	
	1–2 times	3(12.5)	
	≥3 times	7(29.2)	
IL-17			49.3(29.2-110.6)
IL-10			155.66±44.29
Foxp3			7.1(4.9-18.5)
Frequency of recurrence			0(0-15)
Lesion extent			3(2-3)

Third, associations between immune markers and recurrence frequency were assessed to examine the potential role of immune balance in recurrent scabies manifestations. Results are presented according to these analytical domains. A total of 24 adolescents with classical scabies were included in the analysis, with ages ranging from 12 to 15 years (median age 13 years). The majority of participants were 13 years old (45.8%), reflecting a relatively homogeneous early-adolescent population. Most participants had normal

nutritional status (83.3%), while only a small proportion were underweight or overweight, indicating limited variability in BMI within the study population. Regarding environmental exposure, nearly all participants had resided in the dormitory for more than three months (91.7%), suggesting prolonged exposure to communal living conditions associated with sustained transmission risk. Parental education levels varied considerably, with most mothers having elementary-level education (58.3%), whereas a higher proportion of fathers had postgraduate educational backgrounds, indicating heterogeneous socioeconomic characteristics among participants. Clinically, severe lesion extent (>6 affected areas) was observed in two-thirds of participants (66.7%), while recurrent episodes remained common, with 29.2% reporting ≥3 recurrences. This distribution suggests a substantial burden of disease severity despite shared environmental exposure within the same boarding school setting. In terms of immune markers (Table 2), IL-17 showed a median value of 49.3 (29.2–110.6), while IL-10 was presented as a mean value of 155.66 ± 44.29. FoxP3 demonstrated a median value of 7.1 (4.9–18.5), indicating variability within the study population.

Table 2: Cross-tabulation of duration of stay in the dormitory with immune regulatory markers, recurrence frequency, and lesion extent

Dependent Variable	≤ 3 months Median (min–max) n(%)	> 3 months Median (Min–Max) n(%)
IL-17	50.15(35.3–65)	49.3(29.2-110.6)
IL-10	139.85(117.4-162.3)	144.85(90.7-302.9)
Foxp3	9.35(5.912.8)	7.10(4.90-18.5)
Frequency of Recurrence		
No recurrence	2(100)	12(54.5)
Recurrence 1–2 times	0(0.0)	3(13.6)
Recurrence ≥3 times	0(0.0)	7(31.8)
Lesion Extent		
Moderate lesion	0(0.0)	8(36.4)
Severe lesion	2(100)	14(63.6)

Frequency of recurrence was reported with a median of 0 (0–15), and lesion extent showed a median score of 3 (2–3). The simultaneous presence of pro-inflammatory (IL-17) and regulatory immune markers (IL-10 and FoxP3) at baseline suggests an active immune profile among participants, providing a biological basis for subsequent analyses exploring their associations with lesion extent and recurrence frequency. When participants were stratified by duration of stay in the dormitory, only two participants had stayed ≤3 months, whereas the majority had resided for more than three months. Median levels of immune regulatory markers were generally comparable between groups. IL-17 and IL-10 levels showed no clear differences across duration categories, while FoxP3 levels appeared slightly higher among participants with shorter duration of stay; however, this observation should be interpreted cautiously due to the limited sample size in this subgroup. Descriptive clinical patterns (Table 3) demonstrated that all participants with a shorter duration of stay presented with severe lesions, whereas participants with longer exposure displayed a broader distribution of lesion severity, including moderate and severe presentations.

Table 3: Cross-tabulation parental education with immune regulatory markers

Category	n	IL-17	IL-10	Foxp3
Maternal education				
Elementary school	14	51.41±14.44	153.5±34.04	7.32±2.12
Junior high school graduate	1	110.6	126.6	5.5
Senior high school graduate	1	50.1	131.2	5.8
Bachelor's degree	5	42.6±11.29	156.06±32.65	9.12± .28
Master's degree	2	48.1±2.97	205.35±137.96	9.80±3.11
Doctoral degree	1	53.6	138.1	8.4
Paternal education				
No formal education	1	35.3	117.4	5.9
Elementary school	8	47.5±13.25	152.69±37.28	6.90±1.66
Senior high school graduate	3	57.93±22.83	176.5±22.71	6.30±1.15
Master's degree	10	53.56±21.42	156.71±58.83	8.62±3.92
Doctoral degree	2	59.3±8.06	150.2±17.11	10.6±3.11

Values are presented as mean±SD.

In addition, recurrence episodes were observed exclusively among participants who had stayed longer than three months, with approximately one-third experiencing three or more recurrences. Descriptive analysis of immune regulatory markers across maternal and paternal education categories showed variable immune profiles, although interpretation should be made cautiously due to small sample sizes in several subgroups. For maternal education, IL-17 levels tended to be higher among participants whose mothers had lower educational attainment, particularly in the junior high school category, whereas participants with higher maternal education levels generally demonstrated lower IL-17 concentrations. In contrast, FoxP3 levels appeared relatively higher among participants whose mothers had undergraduate or postgraduate educational backgrounds, suggesting a potential tendency toward stronger regulatory immune

responses in this subgroup. IL-10 levels showed wide variability across categories without a consistent gradient. A similar descriptive pattern (Table 4) was observed for overall paternal education. While IL-17 levels did not demonstrate a clear linear association across educational categories, FoxP3 concentrations tended to increase in participants with higher parental educational levels, particularly in the master's and doctoral degree groups. These patterns may reflect socio-environmental influences on immune regulation; however, given the small number of participants in several categories, these findings should be interpreted as exploratory observations rather than definitive associations. The distribution of recurrence frequency across maternal and paternal education categories (Table 4) showed heterogeneous patterns without a clear linear gradient.

Table 4: Cross-tabulation parental education with recurrence frequency and lesion extent

Education	No recurrence	Recurrence (1–2)	Recurrence ≥3	Moderate lesion	Severe lesion
Maternal education					
Elementary school	8(57.1)	2(14.3)	4(28.6)	6(42.9)	8(57.1)
Junior high school graduate	1(100)	0(0.0)	0(0.0)	1(100)	0(0.0)
Senior high school graduate	1(100)	0(0.0)	0(0.0)	1(100)	0(0.0)
Bachelor's degree	2(40)	1(20)	2(40)	0(0.0)	5(100.)
Master's degree	1(50)	0(0.0)	1(50)	0(0.0)	2(100)
Doctoral degree	1(100)	0(0.0)	0(0.0)	0(0.0)	1(100)
Paternal education					
No formal education	1(100)	0(0.0)	0(0.0)	0(0.0)	1(100)
Elementary school	5(62.5)	0(0.0)	3(37.5)	4(50)	4(50)
Senior high school graduate	2(66.7)	1(33.3)	0(0.0)	1(33.3)	2(66.7)
Master's degree	4(40)	2(20)	4(40)	3(30)	7(70)
Doctoral degree	2(100)	0(0.0)	0(0.0)	0(0.0)	2(100)

Values are presented as frequency and percentage.

For maternal education, no recurrence was observed across most categories; however, recurrent episodes (≥3 times) were present in participants whose mothers had elementary, bachelor's, and master's educational backgrounds. Similarly, recurrence patterns varied across paternal education levels, with higher recurrence frequencies observed in participants whose fathers had elementary school and master's degree educational backgrounds. The distribution of lesion extent across maternal and paternal education categories (Table 5) demonstrated a predominance of severe lesions in most groups. Among maternal education categories, severe lesions were observed not only in participants with lower educational backgrounds but also in those whose mothers had higher educational attainment, including bachelor's, master's, and doctoral degrees.

Table 5: Demographic factors associated with immune regulatory markers, recurrence, and lesion severity

Correlation between Variable	Γ [a]	*p*-value
Age ~ IL-17	0.221	0.30
Age ~ IL-10	-0.283	0.18
Age ~ Foxp3	0.17	0.427
Age ~ Frequency of recurrence	-0.073	0.734
Age ~ Lesion extent	-0.027	0.899
BMI ~ IL-17	0.011	0.96
BMI ~ IL-10	0.141	0.511
BMI ~ Foxp3	-0.167	0.435
BMI ~ Frequency of recurrence	-0.080	0.712
BMI ~ Lesion extent	-0.069	0.749
Maternal education ~ IL-17	-0.079	0.715
Maternal education ~ IL-10	-0.024	0.912
Maternal education ~ Foxp3	0.217	0.308
Maternal education ~ Frequency of recurrence	0.042	0.845
Maternal education ~ Lesion extent	0.344	0.100
Paternal education ~ IL-17	0.344	0.10
Paternal education ~ IL-10	0.031	0.886
Paternal education ~ Foxp3	0.384	0.064
Paternal education ~ Frequency of recurrence	0.054	0.802
Paternal education ~ Lesion extent	0.196	0.358
Comparison or association		
IL-17 based, in duration of stay in dormitory		0.835[b]
IL-10 based on duration of Stay in dormitory		0.676[b]
Foxp3 based on duration of Stay in dormitory		0.565[b]
Duration of stay in dormitory ~ Frequency of recurrence		0.459[c]
Duration of Stay in Dormitory ~ Lesion extent		0.536[d]

[a] Spearman correlation; [b] Mann-Whitney; [c] Chi-square; [d] Fisher Exact test.

Similarly, moderate lesions were limited to a few categories, whereas severe lesions represented the majority of cases across the overall distribution. A comparable pattern was observed for paternal education. Severe lesions were present across nearly all educational levels, including participants whose

fathers had postgraduate educational backgrounds. Although some moderate lesions were identified, particularly among participants with elementary or senior high school parental education, no consistent gradient suggesting reduced lesion severity with increasing educational level was observed. Correlation analyses showed that most demographic variables were not significantly associated with immune regulatory markers or clinical severity indicators. Age and BMI demonstrated weak and non-significant correlations with IL-17, IL-10, FoxP3, recurrence frequency, and lesion extent, suggesting limited influence of these factors on immune profiles or disease severity within the study population. Similarly, duration of stay in the dormitory was not significantly associated with immune markers or clinical outcomes. Although prolonged exposure in communal settings is considered a risk factor for transmission, the present findings indicate that duration of residence alone did not show a measurable correlation with recurrence frequency or lesion extent. Maternal education (Table 6) showed no significant association with immune markers or recurrence frequency; however, a weak positive trend was observed with lesion extent (r= 0.344, *p*= 0.100). Likewise, paternal education demonstrated no significant correlations with most variables, although a trend toward a positive association with FoxP3 levels was observed (r= 0.384, *p*= 0.064). Correlation analysis demonstrated significant associations between Th17–Treg–related immune markers and clinical severity indicators, including recurrence frequency and lesion extent.

Table 6: Spearman correlation of immune regulation, frequency of recurrence, and lesion extent

Correlation between Variable	Γ [a]	*p*-value
IL17 ~ Frequency of scabies recurrence	-0.483	0.017
IL10 ~ Frequency of scabies recurrence	0.550	0.005
Foxp3 ~ Frequency of scabies recurrence	0.469	0.021
IL17 ~ Lesion extent	-0.460	0.024
IL10 ~ Lesion extent	-0.460	0.024
Foxp3 ~ Lesion extent	0.690	<0.0001

[a] Spearman coefficient.

Regarding recurrence frequency, IL-17 showed a moderate negative correlation (r= −0.483, *p*= 0.017), indicating that higher IL-17 levels were associated with fewer recurrent episodes. In contrast, IL-10 (r= 0.550, *p*= 0.005) and FoxP3 (r= 0.469, *p*= 0.021) demonstrated significant positive correlations with recurrence frequency, suggesting that stronger regulatory immune activity was associated with increased recurrence. For lesion extent, both IL-17 and IL-10 showed moderate negative correlations (r= −0.460, *p*= 0.024 for each marker), indicating that higher levels of these cytokines were associated with less extensive lesions. In contrast, FoxP3 displayed a strong positive correlation with lesion extent (r= 0.690, *p*< 0.001), representing the strongest association observed in this study.

DISCUSSION

The present study identifies a distinct immunoregulatory pattern associated with classical scabies severity, characterized by significant associations between IL-10, IL-17, and FoxP3 and clinical indicators, namely lesion extent and recurrence frequency. Importantly, FoxP3 demonstrated the strongest association with lesion severity, whereas IL-10 and IL-17 showed differential relationships with recurrence patterns. These findings suggest that disease progression in scabies is not merely driven by inflammatory burden but reflects a complex interaction between inflammatory and regulatory immune pathways. Rather than representing isolated cytokine effects, the observed biomarker profile indicates an immune balance shift in which regulatory immune activity coexists with persistent inflammatory signaling. This pattern supports the hypothesis that immune dysregulation, rather than excessive inflammation alone, underlies lesion persistence and recurrent disease in endemic settings. From a mechanistic perspective, IL-17 represents a central mediator of Th17-driven inflammation, promoting neutrophil recruitment, chemokine production, and amplification of local immune responses. In chronic inflammatory diseases, excessive IL-17 signaling contributes to sustained tissue inflammation and lesion expansion through induction of secondary mediators such as IL-6 and TNF-α [19–21]. Within scabies, prolonged activation of this pathway may contribute to epidermal inflammation and skin barrier disruption. In contrast, IL-10 and FoxP3 represent regulatory immune activity primarily mediated by Treg cells. IL-10 suppresses macrophage activation and pro-inflammatory cytokine production, while FoxP3 regulates T-cell suppression and maintenance of immune homeostasis. Although protective in limiting excessive tissue damage, excessive regulatory signaling may suppress effector immune responses required for complete parasite elimination. Similar mechanisms have been described in chronic inflammatory and infectious conditions; the heightened regulatory activity facilitates immune escape or persistence [22,23]. Consequently, the simultaneous presence of inflammatory and regulatory signals suggests that scabies severity may arise from ineffective immune resolution, where inflammation persists yet fails to eradicate the parasite fully, allowing continuous antigenic stimulation. The present findings align with evidence from multiple inflammatory diseases showing that IL-17 expression correlates with active lesions and disease severity, including psoriasis, alopecia areata, and lupus nephritis [19,20,24]. Similarly, studies of chronic oral and periodontal lesions demonstrate that IL-17 expression is enriched in active inflammatory sites, supporting its role as an indicator of ongoing immune activation [21,25]. The FoxP3 results in this study confirm the dual role that has been reported in the literature. Increased FoxP3 expression has been reported both in severe inflammatory lesions, likely representing a compensatory regulatory response, and in inactive lesions where effective immune regulation promotes disease stabilization [20,26]. This duality explains why higher FoxP3 levels may coexist with severe disease if regulatory activity fails to achieve effective immune

resolution. IL-10 has also been shown to work as a double-edged sword. While protective against excessive inflammation, high IL-10 expression has been associated with disease persistence or recurrence in chronic conditions, including malignancy and chronic inflammatory lesions [22]. These findings support the interpretation that excessive immune regulation may reduce pathogen clearance efficiency. Importantly, recent immunopathological studies on scabies highlight concurrent activation of Th17 and Treg pathways, reinforcing the relevance of the present findings within the broader context of scabies immunobiology [13]. Scabies pathogenesis is increasingly recognized as a dynamic interaction between Th1, Th2, Th17, and Treg pathways. Early infestation typically induces a protective Th1 response aimed at parasite clearance, whereas chronic infestation often shifts toward Th2 and regulatory dominance, contributing to persistent inflammation and hypersensitivity reactions [27,28]. The Th17 axis further amplifies local inflammation, while Treg activity attempts to limit tissue damage. Within this immunological landscape, excessive inflammatory activation may drive lesion expansion, whereas excessive regulatory signaling may impair effective mite elimination. Consequently, recurrence and severe lesion development likely arise from an imbalance where inflammatory activation and immune suppression coexist but fail to achieve effective immune resolution. This framework explains why both inflammatory (IL-17) and regulatory (IL-10/FoxP3) markers correlate with clinical severity, emphasizing that scabies progression reflects dysregulated immune equilibrium rather than a linear inflammatory continuum. The findings support a conceptual immunological model in which scabies severity emerges from instability within the Th17–Treg axis. In this model, persistent IL-17-driven inflammation sustains local tissue damage and antigen exposure, while compensatory increases in IL-10 and FoxP3 attempt to suppress inflammation but may simultaneously reduce effective parasite clearance. The resulting state of "regulatory–inflammatory coexistence" allows chronic immune activation without complete resolution, thereby promoting lesion expansion and recurrence. This dynamic equilibrium provides a biologically plausible explanation for the heterogeneous clinical manifestations of scabies and positions immune balance rather than inflammatory intensity alone as a central determinant of disease outcome. Such a framework may guide future immunologically informed risk stratification and therapeutic strategies aimed at restoring effective immune equilibrium rather than suppressing inflammation. This study did not demonstrate significant associations between BMI and immune biomarkers or clinical severity indicators. Although higher BMI has been associated with increased IL-17 and FoxP3 expression in chronic inflammatory conditions such as type 2 diabetes due to systemic low-grade inflammation [29,30], such relationships may not be directly applicable to scabies. In skin infestations, local immune responses and environmental exposure likely play more dominant roles than systemic metabolic factors [27,28]. Furthermore, limited BMI variation among participants may have reduced statistical power to detect subtle associations [31]. In this study, age, father's education, and mother's education were not significantly associated with immune biomarkers (IL-17, IL-10, FoxP3), lesion extent, or recurrence frequency. These findings suggest that, within this boarding school population, immunological and clinical variations may be driven predominantly by shared exposure intensity and local transmission dynamics rather than by demographic or socioeconomic background. The absence of an age effect may partly be explained by the relatively narrow age range of participants (early-mid adolescence). Differences in immune maturation are typically more evident across broader age spans, particularly when comparing early childhood, adulthood, and elderly populations. Within adolescent groups, T-cell–mediated immune pathways, including Th17 and Treg responses, tend to be biologically comparable, thereby limiting age-related variability in cytokine expression. In addition, institutional living environments may standardize exposure conditions, reducing the influence of small developmental differences on clinical outcomes. Similarly, the lack of association between parental education and clinical or immunological outcomes likely reflects the epidemiological characteristics of scabies transmission in communal settings. Although parental education is commonly used as a proxy for health literacy and household hygiene in community-based studies, scabies transmission is strongly influenced by environmental crowding, shared bedding, and repeated skin-to-skin contact—factors that often override household socioeconomic differences once individuals reside in institutional environments. The World Health Organization identifies high population density and communal living as major drivers of scabies transmission and recurrent infestation [32]. Studies conducted in boarding schools and similar institutional contexts have shown that overcrowding, room occupancy density, and shared hygiene practices are stronger determinants of scabies occurrence than individual background characteristics. For example, Indonesian boarding school studies demonstrated that environmental factors such as bedding hygiene and room density are key predictors of scabies incidence, whereas knowledge or personal background variables may show weaker associations [33]. Likewise, research from other boarding-school populations highlights that crowding and shared living conditions accelerate transmission and reinfestation regardless of socioeconomic status [34]. From an immunological perspective, cytokine expression patterns such as IL-17, IL-10, and FoxP3 primarily reflect host–parasite immune interactions occurring at the local skin level rather than distal socioeconomic determinants. Immune activation in scabies is largely driven by persistent antigen exposure and repeated infestations, which may be relatively homogeneous in high-transmission environments. Consequently, demographic factors such as parental education may

exert limited influence once exposure pressure becomes uniformly high. Taken together, these observations suggest that in endemic communal environments, disease expression is shaped less by demographic attributes than by the interaction between repeated exposure and host immune regulation. Within such settings, sustained transmission pressure may amplify underlying immunological responses, thereby obscuring the influence of conventional epidemiological factors. This perspective emphasizes that interpretation of scabies-related immunological findings requires careful consideration of environmental context, where transmission dynamics and immune balance jointly determine clinical presentation. The present findings suggest that immune regulatory dominance may represent a central mechanism underlying disease persistence and recurrence in scabies. Evaluation of IL-10, IL-17, and FoxP3 may therefore assist in identifying individuals at greater risk for severe lesions or recurrent infestation, particularly in high-transmission communal environments such as boarding schools. Scientifically, these results strengthen the concept that scabies severity is governed by immune balance within the Th17–Treg axis rather than by inflammation alone, providing a potential foundation for future immune-targeted strategies.

Study Limitations

Several limitations should be acknowledged. The cross-sectional design precludes causal inference, cytokine measurements were performed at a single time point, and functional immune assays were not conducted. Future longitudinal studies assessing temporal cytokine changes and functional characterization of Th17–Treg interactions are needed to clarify causal mechanisms and to determine whether immune modulation strategies could reduce recurrence and lesion progression.

Conclusion

This study demonstrates that the clinical severity of classical scabies is closely linked to immune regulatory balance rather than inflammatory activity alone. The inverse association between IL-17 and disease severity, together with the positive associations of IL-10 and FoxP3 with lesion extent and recurrence frequency, supports the concept that regulatory immune dominance may contribute to disease persistence and recurrent manifestations. Among the evaluated markers, FoxP3 showed the strongest relationship with lesion extent, highlighting the central role of Treg-mediated immune modulation in shaping clinical outcomes. These findings provide biologically plausible evidence that imbalance within the Th17–Treg axis represents a key mechanism underlying heterogeneous scabies severity in high-transmission communal settings. Importantly, the results suggest that recurrent or extensive scabies may arise not merely from repeated exposure but from dysregulated immune responses that favor persistence over effective parasite clearance. From the translational perspective, IL-10 and FoxP3 may serve as potential immunological indicators for identifying individuals at greater risk of recurrence or severe disease, supporting a shift toward immunologically informed management strategies. Overall, this study offers a novel clinical–immunological framework for understanding scabies severity and highlights the importance of integrating immune regulation into future approaches aimed at reducing recurrence and disease burden in endemic populations.

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Conflict of interests

The authors declared no conflict of interest.

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Data sharing statement

The data that supports the findings of this study are available from the corresponding author upon a reasonable request.

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