

Bacterial pattern and antibiotic sensitivity in children and adolescents with infected atopic dermatitis

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Abstract. Atopic dermatitis (AD) is a pruritic and chronic inflammatory skin disease which affected approximately 20% in children. Bacterial infection is common in AD patients and correlates directly with AD severity. A cross-sectional study was conducted to evaluate the prevalence of bacterial skin infection in AD patients and its relation with severity of AD and also to study bacteria in the infected AD and its antibiotic sensitivity. Samples were 86 children and adolescents with an AD in Helvetia Community Health Center Medan from March 2016 until February 2017. Index of SCORing Atopic Dermatitis (SCORAD) was used to evaluate the severity of AD. Lesion and nonlesional skin were swabbed to take sterile cultures. All bacteria noted and tested for antibiotic sensitivity. Data were by using Chi-Square and Mann Whitney test with 95% CI and p-value < 0.05 was considered statistically significant. Fifty-six AD patients (65.1%) were bacterial infected. There was a significant relationship between severity of AD and bacterial infection ($p = 0.006$). *Staphylococcus aureus* was the leading bacteria from all degrees of AD severity. Isolated *Staphylococcus aureus* was sensitive to amoxicillin-clavulanate (93.3%), clindamycin (90%), erythromycin (90%), and gentamicin (90%), while sensitivity to tetracycline was low (20%).

1. Introduction

Atopic dermatitis (AD) is a pruritic and chronic resistive inflammatory skin disease which affected approximately 20% in children and 3% in adults¹, but the prevalence varies throughout the world. According to Study Group of Indonesian Pediatric Dermatology in five big cities in Indonesia, the AD is the leading often most common skin diseases in children (23.67%).²

One of the major medical comorbidities in the AD is the skin infection. Bacterial infection is common in AD patients. *Staphylococcus aureus* is the leading bacteria found in the infected AD. The density of bacteria in skin correlates directly with AD severity.³

This study was about to evaluate the prevalence of bacterial skin infection in children and adolescents with the AD and its relationship with severity of AD. This study also determined bacteria that found in the infected AD and its antibiotic sensitivity.

2. Methods

This cross-sectional study conducted in 86 AD patients, aged below 18 years after approval from Research Ethics Committee Faculty of Medicine University of Sumatera Utara, Medan, Indonesia. Sample size estimated using formula one proportion, with 10% margin of error that was acceptable ($d=10\%$), patients were consecutive. All children with AD who visited Helvetia Community Health Center, Medan, Indonesia from March 2016 until February 2017 were exclusion. Their parents signed



written consent after being informed about the study. The AD was diagnosed by two pediatricians by fulfilling at least three major and three minor of Hanifin Rajka criteria.⁴ Patients with malnutrition, chronic disease, or taking antibiotics for the last 14 days were excluded.

The severity of AD was graded using SCORing of Atopic Dermatitis (SCORAD), and it was mild (<15), moderate (15-50), and severe (>50).⁵ Skin cultures were performed to screen the presence of bacterial infection in the AD using sterile transport swab (Oxoid®) by rolling it twice in two areas (lesion skin and non-lesion skin). The transport swabs were taken immediately to Microbiology Laboratory, Faculty of Medicine University of Sumatera Utara, Medan, Indonesia to be cultured on blood agar and McConkey agar. Samples were incubated aerobically at a temperature of 37°C. After 24 hours, bacterial colonies were tested for gram staining and were identified using Vitek machine. All bacterial isolates tested with antibiotic sensitivity using nine antibiotics; ampicillin 10µg, amoxicillin 25µg, amoxicillin-clavulanate 30µg, chloramphenicol 30µg, clindamycin 10µg, cotrimoxazole 25µg, erythromycin 5µg, gentamicin 10µg, and tetracycline 30µg.

Data were entered and analyzed using univariate and bivariate analysis by SPSS statistical software version 22. Categorical data presented in numbers and percentages. Numerical data (age) presented in median (minimum-maximum) because the data were not normal distribution. Bacteria isolated from skin swabs then calculated to determine common etiology of bacterial infection in the AD. Antibiotic sensitivity tests were on each bacterium. Chi-Square test was performed to assess the relationship between severity of AD and presence of bacterial infection. A p-value <0.05 were considered statistically significant with 95% confidence interval.

3. Results

There were 90 AD patients during our study period, two were excluded because of antibiotic consumption, one because of HIV infection, and one refused to join this study (Figure 1).

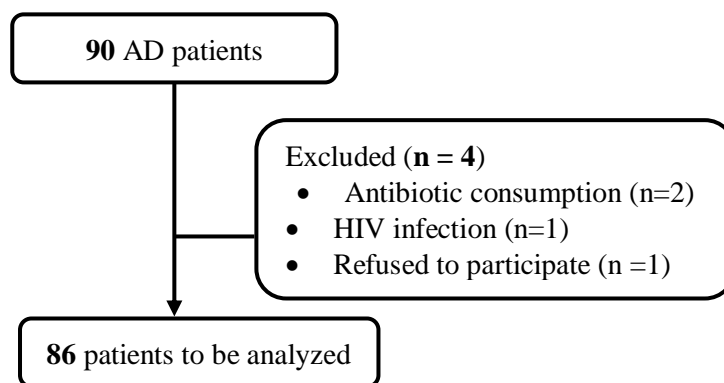


Figure 1. Study profile.

Our data from 86 AD patients, we found female preponderance with a female: male ratio 1.46:1. The age of these patients ranged from 1 month to 14 years (Table 1).

Table 1. Subject characteristics.

Parameters	n=86
Sex, n(%)	
Boys	35 (40.7%)
Girls	51 (59.3%)
Age (years), median (min – max)	5 (0.08 – 14)

Data of gender and age were not significantly different in infected and uninfected AD groups, showed that populations were homogenous. There was a significant relationship between severity of

AD and bacterial infection ($p = 0.006$), where moderate and severe AD were 1.62 times higher risk to have a bacterial infection than mild AD (Table 2).

Table 2. The relationship between sex, age, and SCORAD index with the infected AD.

	Infected AD (n=56)	Uninfected AD (n=30)	p value	PR (95% CI)
Sex, n(%)				
Boys	24 (68.6%)	11 (31.4%)	0.578 ^a	
Girls	32 (62.7%)	19 (37.3%)		
Age (years), median (min – max)	4 (0.08 – 14)	5.75 (0.16 – 14)	0.061 ^b	
Severity of AD, n(%)				
Moderate and severe	41 (75.9%)	13 (24.1%)	0.006 ^a	1.62 (1.09–2.41)
Mild	15 (46.8%)	17 (53.2%)		

^aChi-square test

^bMann-Whitney test

From this study, bacteria were significantly higher in lesion than lesion area ($p < 0.05$). Most common bacteria isolated from AD skin lesion was *Staphylococcus aureus*. It was also the leading bacteria from all degrees of AD severity. *Staphylococcus aureus* was isolated in 30 out of 86 lesional skin (34.8%), while only 12 out of 86 (13.9%) non-lesional skin in the AD ($p = 0.002$). Out of 30 *Staphylococcus aureus*, two (6.67%) were methicillin-resistant *Staphylococcus aureus* (MRSA). Four most common bacteria isolated from the infected AD are *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, and *Streptococcus haemolyticus* (Table 2).

Table 3. Bacteria isolated from atopic dermatitis based on its severity according to SCORAD index.

	Mild (n=15)	Moderate (n=33)	Severe (n=8)
<i>Staphylococcus aureus</i>	8	<i>Staphylococcus aureus</i> 17	<i>S. aureus</i> 5
<i>S. epidermidis</i>	3	<i>S. haemolyticus</i> 3	<i>Proteus penneri</i> 1
<i>Escherichia coli</i>	2	<i>S. epidermidis</i> 2	<i>Escherichia coli</i> 1
<i>Klebsiella pneumonia</i>	1	<i>Escherichia coli</i> 2	<i>S. epidermidis</i> 1
<i>S. haemolyticus</i>	1	<i>Enterobacter cloacae</i> 2	
		<i>Acinetobacter lwoffii</i> 2	
		<i>Klebsiella pneumonia</i> 1	
		<i>Citrobacter koseri</i> 1	
		<i>Burkholderia cepacia</i> 1	
		<i>Serratia ficaria</i> 1	
		<i>Kocuria Roseau</i> 1	

We evaluated antibiotic sensitivity test in these four most common bacteria. Infected AD patients with *Staphylococcus aureus* were sensitive to amoxicillin-clavulanate (93.33%), clindamycin (90%), erythromycin (90%), and gentamicin (90%), while only 20% were sensitive to tetracycline. Chloramphenicol was antibiotic with relatively low sensitivity to *Staphylococcus aureus* (Table 3).

Table 4. Antibiotic sensitivity test of four most common bacteria in the infected AD.

Antibiotics	<i>Staphylococcus aureus</i> n = 30		<i>Staphylococcus epidermidis</i> n = 6		<i>Escherichia coli</i> n = 5		<i>Streptococcus haemolyticus</i> n = 4	
	S ^a		S ^a		S ^a		S ^a	
Ampicillin 10µg	16/30	53.33%	4/6	66.67%	0/5	0%	2/4	50%

Amoxicillin 25µg	23/30	76.67%	3/6	50%	1/5	20%	3/4	75%
Amoxicillin-clavulanate 30 µg	28/30	93.33%	4/6	66.67%	2/5	40%	3/4	75%
Chloramphenicol 30 µg	13/30	43.33%	2/6	33.33%	1/5	20%	3/4	75%
Clindamycin 10 µg	27/30	90%	4/6	66.67%	2/5	40%	4/4	100%
Cotrimoxazole 25 µg	16/30	53.33%	5/6	83.33%	3/5	60%	2/4	50%
Erythromycin 5µg	27/30	90%	2/6	33.33%	2/5	40%	2/4	50%
Gentamicin 10 µg	27/30	90%	5/6	83.33%	4/5	80%	3/4	75%
Tetracycline 30 µg	6/30	20%	3/6	50%	2/5	40%	2/4	50%

^aSensitive

4. Discussion

Bacterial infection is a factor aggravating skin lesion in the AD, as there was a significant relationship between severity of AD and bacterial infection in this study. Similar results of the other reports were higher density of bacteria correlated with higher SCORAD.^{3,6}

Etiology of bacterial infection in the AD were similar in many studies, with gram-positive as the leading bacteria isolated (71.4%). Farajzadeh et al reported *Staphylococcus aureus*, *Streptococcus beta-hemolytic* group A and B, *Streptococcus viridans*, and *Enterobacter* as most common bacteria isolated from the infected AD. Study in China by Gong et al reported *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus hemolytic*, *Staphylococcus lugdunensis*, *Staphylococcus capitis*, *Escherichia coli*, *Micrococcus tetragenus*, *Enterobacter cloacae*, and *Proteus*.^{6,7}

Staphylococcus aureus was tended to colonized in AD skin rather than normal skin. Out of 86 AD patients, 56 were a bacterial infection (65.1%). In our study, *Staphylococcus aureus* isolated in 30 (34.8%) AD lesion skin, in contrast to 12 (13.9%) from the non-lesion skin. These isolation rates varied, ranging from 42.5% by Pezesk Pour et al, 48.5% by Hon et al, to higher rates 86% by Gilani et al.⁸⁻¹⁰ This variation in prevalence of *Staphylococcus aureus* in AD patients might be ascribed to the fact that *Staphylococcus aureus* colonized intermittently. Therefore it is not always detected at the time of examination. Variation in clinical severity of AD in each study might also contribute to this discrepancy.¹¹

According to Study Group of Indonesian Pediatric Dermatology, first line antibiotics in treating AD with infection are amoxicillin-clavulanate, cephalexin or erythromycin if allergic to penicillin. As second-line antibiotics, we can use erythromycin or second generation of cephalosporin (cefuroxime), azithromycin, clarithromycin, and clindamycin.²

The rate of *Staphylococcus aureus* sensitivity to amoxicillin-clavulanate remains high in this study (93.3%). This result was similar to some previous studies done in the UK by Hoeger et al and Niebuhr et al in Germany where the sensitivities were 100% and 97%, respectively.¹²⁻¹³ Amoxicillin-clavulanate is highly active against not only *Staphylococcus aureus* but also *Streptococcus* sp., which is a second most common etiology of bacteria infected AD.¹² So that, it can be as first-line treatment of the bacterial infection of the AD.

Many previous studies showed high resistance to erythromycin. In 1990s erythromycin had already been used as first-line treatment of bacterial infected AD.¹⁴ Its use decreased after many reports of high resistance in *Staphylococcus aureus*. Farajzadeh et al reported 66.7% resistance rates for erythromycin against *Staphylococcus aureus*,⁶ while Niebuhr et al in Germany found resistance rate was 46%.¹³ But in an earlier study in 2015 done in Korea by Jung et al susceptibility to erythromycin was higher (85.7%).¹⁵ In our study, also showed the high sensitivity of erythromycin (90%).

Clindamycin showed high sensitivity in Hoeger et al study, reported a sensitivity of 99%.¹² In our study, we also found high clindamycin sensitivity (90%). But it seems to be a growing resistance rate of *Staphylococcus aureus* against clindamycin. Paul-Ehrlich Society¹⁶ and Niebuhr et al¹³ found 15% and 21% resistance rate, respectively. Its sensitivity in the AD should have an evaluation in the further clinical trial.

Gentamicin is the most common aminoglycoside and conventionally used an antibiotic in skin infections.¹⁷ A study done by Alenizi showed sensitivity rate of gentamicin against *Staphylococcus*

aureus was 74.36%.¹⁷ In our study sensitivity rate remains high (90%). This discrepancy might be due to the variation of population setting and sample size.

We found that *Staphylococcus aureus* isolates had low sensitivity to tetracycline (20%) and 43.3% to chloramphenicol. Drugs containing tetracycline and chloramphenicol are cheap and highly popular in Indonesia, widely used as self-prescription medication. It can explain the resistance to those antibiotics. Similar results showed in other studies, Goh et al reported tetracycline resistance was 67%¹⁸ while Niebuhr et al¹³ reported 83% susceptibility to tetracycline. Chloramphenicol ointment was FDA-approved for conjunctivitis, and its usage for skin infection remains low. No significant difference in preventing skin infection on suturing wound between chloramphenicol use and not.¹⁹

From this result, we suggested amoxicillin-clavulanate as the first line and clindamycin or erythromycin as second-line treatment in the infected AD, which is narrow spectrum antibiotics with higher sensitivity rates, rather than broad-spectrum antibiotics such as tetracycline or chloramphenicol. A broader coverage antibiotic is not required in the AD, as *S. aureus* is the most frequent bacterial causing skin infections.

Antibiotic resistance is increasing around the world and has been as an important issue in *Staphylococcus aureus* treatment especially methicillin-resistant *Staphylococcus aureus* (MRSA). We found two MRSA (6.7%) in this study. A study in Korea by Jung et al reported 12.9% MRSA among 583 *Staphylococcus aureus* isolates.¹⁵ Jagadeesan et al in India had reported 30.5% MRSA out of 96 *Staphylococcus aureus*.²⁰ According to a study in India, MRSA associated with AD disease severity.²⁰ We could not perform the association because of a limited number of MRSA isolated, but two MRSA in this study were isolated from thesevere AD. MRSA strain was eradicated with clindamycin, cotrimoxazole, and vancomycin.² Two MRSA in this study were sensitive to clindamycin.

Limitation of this study was the sensitivity of usual antibiotics used in skin infections, such as mupirocin and fusidic acid was not tested. Further studies about giving antibiotics to moderate and severe AD patients can be considered.

5. Conclusion

Bacterial skin infection was common in children and adolescents with the AD, with *Staphylococcus aureus* as the most common isolates. It was related to severity of AD, more severe AD was 1.62 times higher risk of bacterial infection than a milder AD. *Staphylococcus aureus* isolates were sensitive to amoxicillin-clavulanate, clindamycin, erythromycin, and gentamicin, and likely to be effective as treatment in the infected AD.

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