



## Bacterial infections concomitant with skin allergy

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### Abstract

Background: Infectious agents, including bacteria, viruses, fungi, and parasites, have been highlighted by several pioneers as contributing factors to the etio-pathogenesis of allergic and non-allergic disorders, including rhinitis, asthma, and dermatitis. Objective: This study was done to show the most common bacterial infections associated with skin allergies. In addition, the levels of skin allergies were reported according to age, gender, residence, and occupation. Methods: (80) patients and (20) normal individuals were included in this study, skin swabs were taken from each patient and control individual. The study was done during the period from October 2023 to January 2024. All patients were attending dermatology units, Ramadi Teaching Hospital. A skin swab and blood specimen were taken from each individual. Each swab was processed following standard bacteriological guidelines. Results: (59) out of (80) allergic patients revealed positive skin swab cultures, while (21) patients showed negative skin swab cultures. The most dominant bacterial isolate was *S. aureus* (35%) from both genders and age groups, *Pseudomonas aeruginosa* took the second rank of isolation (18.75%), followed by *E. coli* (7.5%), *Staphylococcus epidermis* (3.75%), *Staphylococcus hominis* (2.5%), *Pantoea spp* (2.5%), *Staphylococcus haemolyticus* (1.25%), *Sphingomonas paucimobilis* (1.25%), and *Acinetobacter lwoffii* (1.25%). Swab culture from Control individuals revealed growth of normal skin flora. Conclusion: We can conclude from this study that atopic skin lesions in atopic dermatitis can be complicated with bacterial infections, particularly *Staphylococcus aureus*, *pseudomonas aeruginosa* bacteria, particularly *Staphylococcus aureus* and *pseudomonas aeruginosa*. This makes skin lesions more worse. An antimicrobial agents should be used in such cases beside antiallergic therapy. In addition, there is

no significant difference in gender, residence and occupation were found between skin allergic patients and control individuals.

**Key words:** Skin infection, Skin allergy, *staphylococcus aureus*, *Pseudomonas aeruginosa*, *E.coli*.

## Introduction:

The traditional definition of an allergy is a specific, unfavorable reaction based on the secondary immune response to exposure to an allergen. Atopy is the term used to describe the inherited predisposition to overproduce a particular kind of IgE in response to common antigen dosages [1],[2]. Urticaria and angioedema, allergic contact dermatitis, atopic dermatitis, hand dermatitis, photoallergic reactions, and phototoxic reactions are examples of allergic skin conditions [3]. Because of the constant exposure to external microorganisms, the barrier function of the skin is essential for maintaining skin homeostasis. Previous researches had demonstrated that barrier dysfunction is one of the most important risk factors for the onset of allergic skin illnesses like atopic dermatitis[4]. Regarding the causative triggering factors, skin allergy may be due to exogenous or endogenous factors or both [5].

Infectious agents, including bacteria, viruses, mycoses, and parasites, have been highlighted by several pioneers as contributing factors to the etiopathogenesis of allergic and non-allergic disorders, including rhinitis, asthma, and dermatitis [6]. Without any active infection or illness (colonization), 15-20% of healthy individuals have *Staphylococcus aureus* carriers on their skin[7]. People who frequently sustain skin injuries are more likely to get infections from *Staphylococcus aureus*, especially if their skin is dry. Eighty to one hundred percent of patients with atopic dermatitis have *S. aureus* colonization [8], and a large number of this microbe appears to eradicate the lipophilic coryneform bacteria from the skin [9]. *S. aureus* is responsible for the majority of cutaneous infections in atopic dermatitis. Additionally, patients with skin allergies may get infections due to *Streptococcus pyogenes* either alone or in conjunction with *Staphylococcus aureus*. These infections usually manifest as impetigo or pustules [10]. The two most common coagulase-negative commensal staphylococci are *Staphylococcus epidermidis* and *S. hominis*. In patients with indwelling foreign bodies, such as heart valves and intravenous catheters, these

organisms can occasionally result in nosocomial infections [11]. Non-typical resident skin microflora include Gram-negative organisms that can cause cutaneous infections, such as *Pseudomonas aeruginosa*, *Pasteurella multocida*, *Capnocytophaga canimorsus*, *Bartonella sp.*, *Klebsiella rhinoscleromatis*, and *Vibrio vulnificus* [12]. A Gram-negative rod that lives in damp conditions is called *Pseudomonas aeruginosa*. Ecthyma gangrenosum is mainly seen in patients with compromised immune systems when pseudomonas sepsis is present [13]. If left untreated, bacterial skin infections in AD can develop into systemic and result in life-threatening conditions such as sepsis, endocarditis, and infections of the bones and joints [14].

### **Patients and methods:**

**A- Patients and control individuals:** Eighty (80) patients with skin allergies and twenty (20) normal individuals were included in this study. The study was done during the period from October 2023 to January 2024 at the Department of Microbiology, College of Medicine, University of Anbar, Iraq. A questionnaire was followed to include patients in this study, inclusion criteria were (eczema, atopic dermatitis, and other skin allergies). Exclusion criteria were that patients with other allergic diseases like asthma, allergic rhinitis, sinusitis, psoriasis, cancer, parasitic infection, and other autoimmune diseases were excluded. At the same time, patients who were taking immunosuppressed drugs were excluded.

**Patients demographic and clinical data:** The patients were from both genders, their age, residence, occupation, and medication (anti-allergic and cortisone). Skin infections and complications were reported. Specimens were taken from patients who were attending dermatology clinics in Ramadi Teaching Hospital and private clinics who suffer from various types of skin allergies. All patients were attending dermatology units at Ramadi Teaching Hospital in addition to the private dermatology clinics in Ramadi City, Anbar Governorate. Each of the patients and control individuals included in this study was examined by the senior dermatologist, and investigation results were reported.

**Ethical approval:** This study was approved by the Medical Ethics Committee of the University of Al-Anbar Governorate in Ramadi, Iraq, following the Helsinki Declaration (Ref: 8 in 18/01/2024). All research participants, including patients and their parents, provided signed informed consent.

**Specimen Collection:** Skin Swabs were taken from each patients and control individuals, sterile swabs were moistened with sterile normal saline, and patients' dry skin lesions were smeared aseptically, moist skin lesions were directly smeared. .

**Bacteriological investigations:** Each skin swab was examined as soon as possible at the Bacteriological Lab, Microbiology Department, Collage of Medicine, University of Anbar. Each specimen was processed the following[15]. Skin swabs are necessary in the case of skin lesions complicated with bacterial infections, so a skin swab must be taken for bacteriological investigation to detect the causative agent(s) and identify the suitable antimicrobial therapy.

**1. Cultivation:** Each swab was cultivated on blood agar, chocolate agar and MacConkey agar. Each swab was streaked on each medium, aseptically near the flame. Cultivated plates were kept at the incubator at 37°C for 24 hours. Culture was inspected and followed for bacteriological diagnosis using the Vitek system.

**2. Morphological examination:** Bacterial colonies were inspected following guidelines bacteriological methods, and Gram-stained smears were used for each specimen and then examined under a compound light microscope.

**Biochemical investigations:** A set of biochemical tests was used to diagnose each isolate as well as confirm their diagnosis using the Vitek system [15] Results were reported and analyzed.

### **Statistical Analysis:**

Analysis of data was carried out using the available statistical package of IBM SPSS-29 (IBM Statistical Packages for Social Sciences- version 29, Chicago, IL, USA). Data were presented in simple measures of frequency, percentage, mean, standard deviation, and range (minimum-maximum values). The significance of difference of different means (quantitative data) were tested using Students-t-test for difference between two independent means or ANOVA test for difference among more than two independent means. The significance of difference of different percentages (qualitative data) were tested using Pearson Chi-square test ( $X^2$ -test) with application of Yate's correction or Fisher Exact test whenever applicable. Statistical significance was considered whenever the P value was equal or less than 0.05.

## Results:

1. **Age groups:** Higher percentage of skin allergy was found within the age group (30-39) 22.5% and (20-29) 18.8% respectively (Fig.-1).

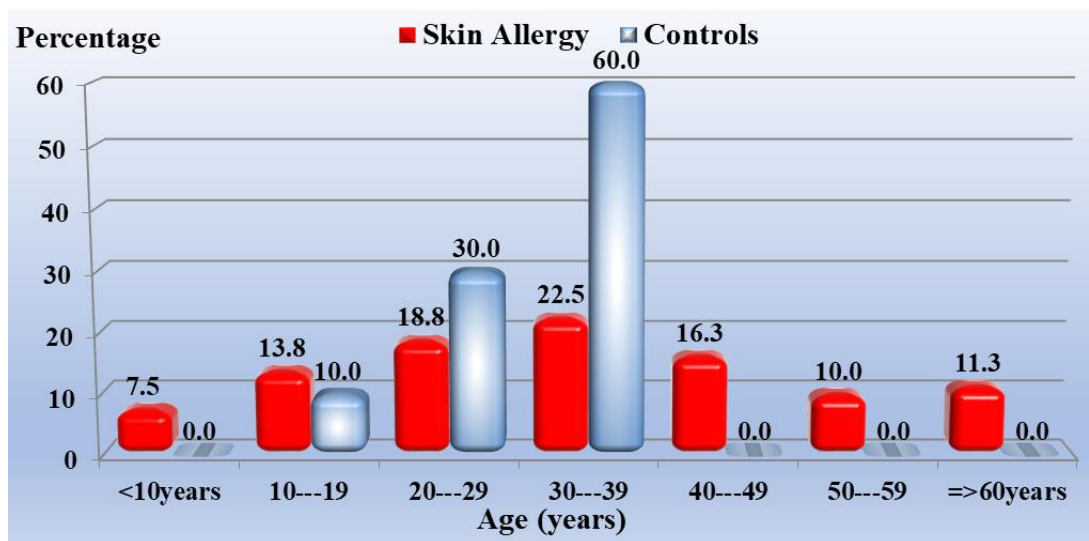


Figure (1): skin allergy distribution according to the age groups of patients and control.

2. **Gender and Residence:** Regarding gender, no-significant difference ( $P > 0.05$ ) was found between males and females. Also a no-significant difference ( $P > 0.05$ ) was found between Urban and Rural, 45 %, 55% for each respectively (Fig.-2).

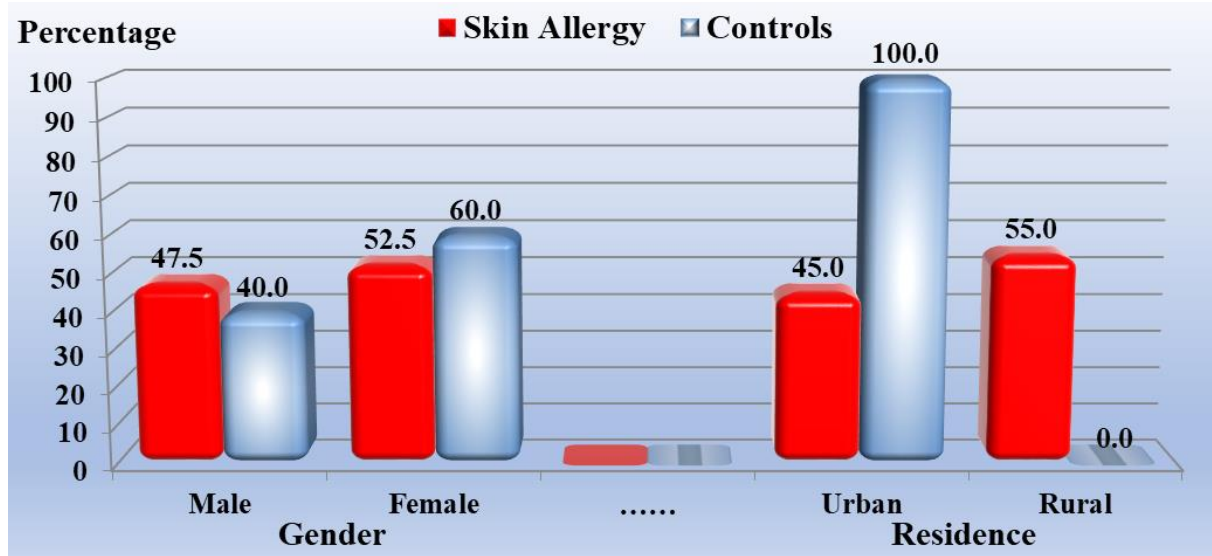


Figure (2): Distribution of patients and control individuals according to gender and residence.

**3. Occupation:** Occupational distribution of allergic cases in individuals of this study revealed the highest ratio (30%) in housewives, followed by government employees (28.7%). The lowest ratio of allergies was found in students and self - employees (7.5 %) for each, respectively (Fig.-3).

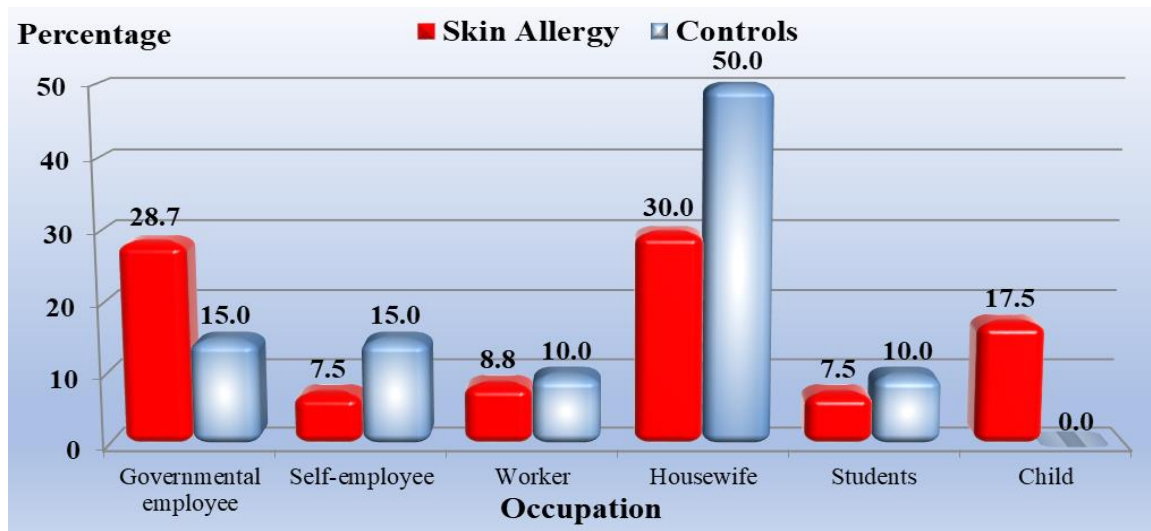


Figure (3): Distribution of patients and control individuals according to their occupations.

#### 4. Bacteriological results:

Culture results revealed that 57.6% (34 isolates) of isolates were Gram positive, whereas Gram negative bacteria resembled 42.3% (25 isolates) of isolates, while 26.25% (21 isolates) of samples revealed no growth. Among Gram positive bacteria, *Staphylococcus aureus* took the first rank of isolation 35% (28 isolates). While *Pseudomonas aeruginosa* was dominated among Gram negative bacteria 18.75% (15 isolates). Followed by *E.coli* 7.5% (6 isolates) (Table-1), (Fig.-4).

	NO	%
<b>G+</b>	<b>34</b>	<b>57.6</b>
<b>G-</b>	<b>25</b>	<b>42.3</b>
<b>Total</b>	<b>59</b>	

Table-1: Number of bacterial isolates according to Gram stain.

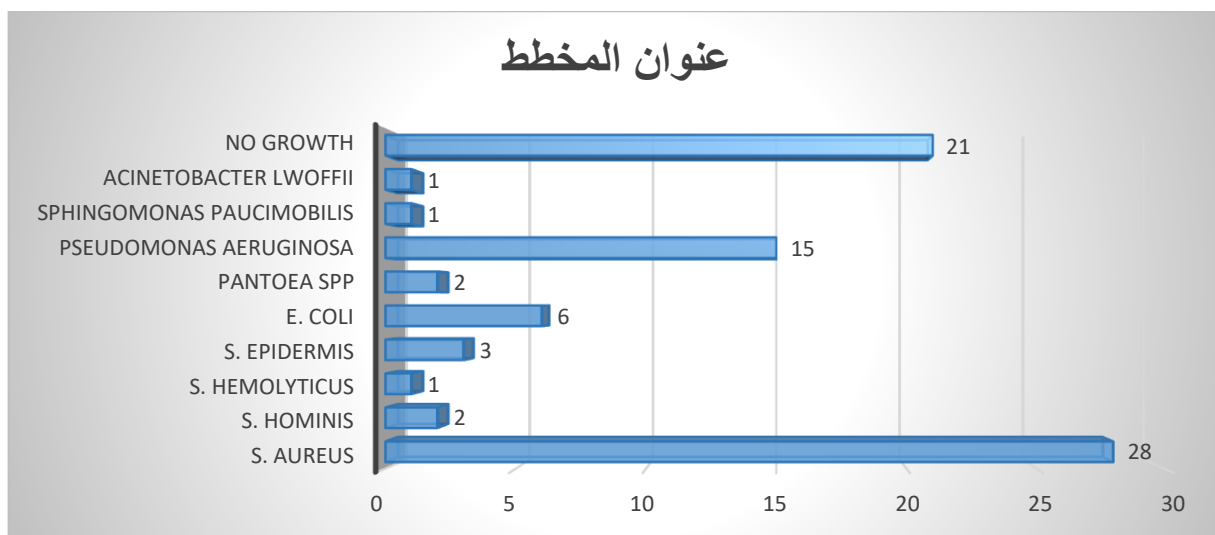


Figure (4): Types of bacterial isolates from skin swabs.

### Mixed bacterial growth:

A total of (8) growth results revealed mixed growth cultures, three (3) of them were *Staphylococcus aureus* with *Pseudomonas aeruginosa*, (3) of them were *Staphylococcus aureus* with *E.coli* and the other revealed mixed growth of *S. aureus* + *S. epidermis* (Fig.-5).

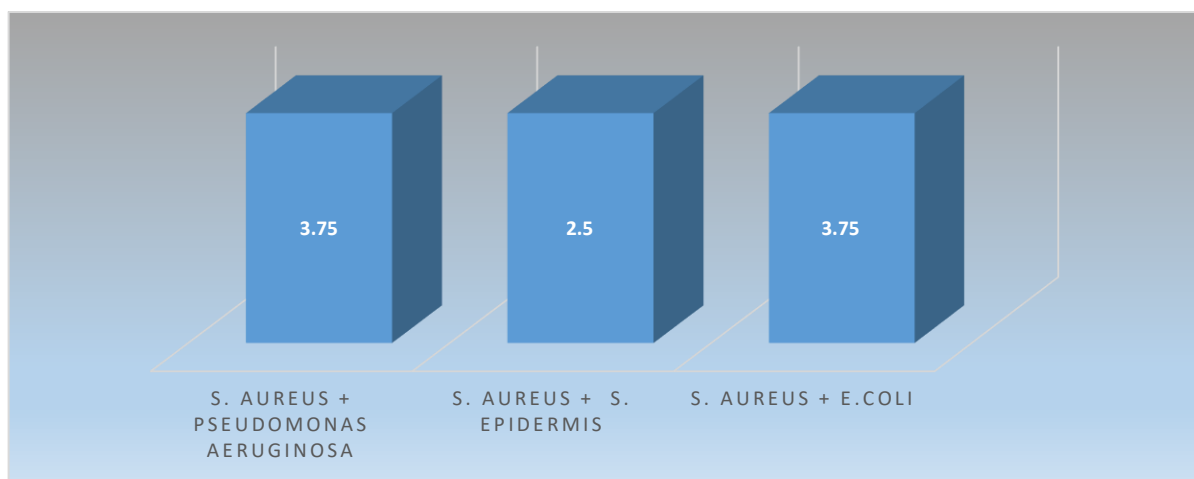


Figure (5): Mixed bacterial growth.

## Discussion:

A higher percentage of skin allergy was found within the age group (30-39) 22.5% and (20-29) 18.8% respectively. This might be attributed to the exposure of young individuals to different allergens more than other age groups through their different occupations. This result disagreed with the findings of [16] who found males 75 years of age and older had the highest frequency of atopic dermatitis, a condition that has become more common throughout adulthood. In older people, atopic dermatitis was more active and severe than in children ages 0–17 and adults ages 18–74. It is necessary to further characterize the disease's causes and mechanisms and provide tailored therapy recommendations for older adults with atopic dermatitis because the condition has become more common over time. Regarding gender, no significant difference was



found between males and females ( $p < 0.05$ ). This result disagreed with [17] who found that the allergy illness ratio varies during life and differs in genders. Sex disparities in the development and management of allergy diseases are influenced by genes, hormones, environmental, and immunological factors.

It is less common to examine and report these differences in relation to social, psychological, cultural, economic, and employment aspects. While no significant difference ( $P < 0.05$ ) was found between urban and rural, 45% and 55% for each, respectively. Occupational distribution of allergic cases in individuals of this study revealed the highest ratio (30%) in housewives, followed by Government employees (28.7%). The lowest ratio of allergies was found in students and self-employees (7.5%) for each, respectively. This result agreed with the findings of [18] who found that farmers had the lowest frequency of allergies (22.9%), whereas indoor workers had the highest prevalence (32.7%;  $p < 0.001$ ). Among other outdoor workers (8.2%), interior workers (11.6%), and other occupations (12.5%), pollen allergy was the most frequent type of allergy. Pollen allergy was less common than contact allergies (5.3%) and medication allergies (5.0%) only among farmers. This can be explained by the high exposure of housewives to allergens like detergents, cooking materials, house dust, and house dust mites during cleaning at homes. On the other hand, Government workers may be exposed to allergens during their jobs. Culture results revealed that 57.6% (34 isolates) of isolates were Gram positive, whereas Gram negative bacteria resembled 42.3 % (25 isolates) of isolates, while 26.25% (21 isolates) of samples revealed no growth. Among Gram-positive bacteria, *Staphylococcus aureus* took the first rank of isolation 35% (28 isolates). While *Pseudomonas aeruginosa* was dominated among Gram-negative bacteria 18.75% (15 isolates). Followed by *E. coli* 7.5% (6 isolates). These results were in accordance with [5] who found that out of 80 individuals with eczema, fifty (50) had positive skin swab cultures, with *S. aureus* accounting for the majority of the samples from both adults and children (58%) while *Corynebacterium* and diphtheroid species took the second and third place in isolation (22%, 16% and 10% respectively). This can be explained by the ability of *Staphylococcus* and *Pseudomonas* to cause infection due to their own virulence factors [19]. Skin microbiota plays a critical role in immunological homeostasis and inhibits the growth of pathogens like *S. aureus*. The diversity of the normal microflora is reduced during an eczema flare, which facilitates the growth of *S. aureus*, partly due to a decrease in bacteria that exhibit anti-*S. aureus* activity. Multiple chemicals that have the ability to trigger inflammation and encourage more

immunological dysregulation are produced by *S. aureus* [20],[21]. Staphylococci can cause disease because of their capacity to proliferate and spread broadly throughout tissues, as well as because they generate a variety of extracellular materials. While certain compounds are classified as toxins (hemolysins, exfoliative toxins, toxic shock syndrome toxin, enterotoxins) even though they may also serve as enzymes, others are classified as enzymes (catalase, coagulase, hyaluronidase, lipase, etc.) [19]. *Pseudomonas aeruginosa* is widely distributed in nature and is commonly present in moist environments in hospitals. While not a part of the normal human microbiome. Multiple virulence factors, including adhesins, enzymes, and poisons, are produced by *Pseudomonas aeruginosa*. To facilitate adhesion to host epithelial cells, fimbriae, or pili, protrude from the cell surface. Many of the organism's endotoxic characteristics are caused by lipo-polysaccharide, which is present in different immunotypes. Two hemolysins (a heat-labile phospholipase C and a heat-stable glycolipid) and elastases are among the extracellular enzymes produced by the majority of *Pseudomonas aeruginosa* isolates from clinical infections. Furthermore, *Pseudomonas aeruginosa* produces pyocyanin, which triggers the release of interleukin-8 (IL-8) and produces superoxide and hydrogen peroxide. The neutrophils are drawn in by the elevated production of IL-8. Pyoverdine, the other pigment, binds iron by acting as a siderophore. Also, some strains of *Pseudomonas aeruginosa* produce exotoxin A, which causes tissue necrosis [22]. The isolation of *E. coli* from atopic patients may be due to fecal contamination, especially in children and the elderly [23]. Otherwise, the negative growth result of some specimens was attributed to the following causes:

1. Actual negative findings (no bacterial type was found in the lesion).
2. No growth of organisms which cannot grow on ordinary used culture medium or cultivation condition
3. It could be an infection with non-cultivable organisms which cannot grow on synthetic culture medium like *Nanobacter* spp. , *Chlamydia trachomatis* or viruses .

## Conclusion:

We can conclude from this study that atopic skin lesions in atopic dermatitis can be complicated with bacterial infections, particularly *Staphylococcus aureus* for Gram-positive

bacteria and *Pseudomonas aeruginosa* for Gram-negative bacteria. In addition, results revealed that there is a mixed bacterial growth of *S. aureus* + *Pseudomonas aeruginosa*, *S. aureus* + *E.coli*, and *S. aureus* + *S. epidermis*. This makes skin lesions more worse. An antimicrobial agents should be used in such cases beside antiallergic therapy. No significant difference in gender, residence and occupation were found between skin allergic patients and control individuals, the highest ratio of skin allergies was in the housewives due to the high exposure of housewives to allergens like detergents, cooking materials, house dust during cleaning at homes.

#### **Declarations:**

**Conflicts of Interest:** The authors declare that there is no conflict of interest.

**Authors Contributions:** I hereby verify that all authors mentioned on the title page have made substantial contributions to the conception and design of the study, have thoroughly reviewed the manuscript, confirm the accuracy and authenticity of the data and its interpretation, and consent to its submission.

**Funding:** No funding was received.

**Availability of data and Materials:** All datasets analyzed and described during the present study are available from the corresponding author upon reasonable request.

**Acknowledgements:** The Authors thank patients and control individuals for their acceptance to be included in this study. Also we thank Staff workers in Dermatology Divisions and Central laboratory in Ramadi Teaching Hospital for their support.

#### **References:**

- [1] S. F. Thomsen, "Epidemiology and natural history of atopic diseases," *Eur. Clin. Respir. J.*, vol. 2, no. 1, p. 24642, 2015.
- [2] M. Pinart *et al.*, "Systematic review on the definition of allergic diseases in children: the MeDALL study," *Int. Arch. Allergy Immunol.*, vol. 168, no. 2, pp. 110–121, 2016.
- [3] H. M. Motswaledi, "Allergic skin conditions-causes, clinical features and treatment," *South African Fam. Pract.*, vol. 60, no. 6, pp. 34–37, 2018.

- [4] G. Egawa and K. Kabashima, "Multifactorial skin barrier deficiency and atopic dermatitis: Essential topics to prevent the atopic march," *J. Allergy Clin. Immunol.*, vol. 138, no. 2, pp. 350–358, 2016.
- [5] K. Zaynab and A. Shehab, "INFLUENCES OF BACTERIA ON ECZEMA: BACTERIAL AND IMMUNE ASPECTS," *J. Univ. Anbar Pure Sci.*, vol. 2, no. 2, 2008.
- [6] S. B. DeVore, T. Gonzalez, M. G. Sherenian, A. B. Herr, and G. K. K. Hershey, "On the surface: Skin microbial exposure contributes to allergic disease," *Ann. Allergy, Asthma Immunol.*, vol. 125, no. 6, pp. 628–638, 2020.
- [7] J.-M. Leyva-Castillo, A. McGurk, and M. D. R. Geha, "Allergic skin inflammation and *S. aureus* skin colonization are mutually reinforcing," *Clin. Immunol.*, vol. 218, p. 108511, 2020.
- [8] K. Breuer, A. Kapp, and T. Werfel, "Bacterial infections and atopic dermatitis," *Allergy*, vol. 56, no. 11, pp. 1034–1041, 2001.
- [9] J. A. Geoghegan, A. D. Irvine, and T. J. Foster, "Staphylococcus aureus and atopic dermatitis: a complex and evolving relationship," *Trends Microbiol.*, vol. 26, no. 6, pp. 484–497, 2018.
- [10] V. Wang, J. Boguniewicz, M. Boguniewicz, and P. Y. Ong, "The infectious complications of atopic dermatitis," *Ann. Allergy, Asthma Immunol.*, vol. 126, no. 1, pp. 3–12, 2021.
- [11] K. Becker, C. Heilmann, and G. Peters, "Coagulase-negative staphylococci," *Clin. Microbiol. Rev.*, vol. 27, no. 4, pp. 870–926, 2014.
- [12] K. Chiller, B. A. Selkin, and G. J. Murakawa, "Skin microflora and bacterial infections of the skin," in *Journal of Investigative dermatology Symposium proceedings*, Elsevier, 2001, pp. 170–174.
- [13] A. Russo, E. M. Trecarichi, and C. Torti, "The role of Gram-negative bacteria in skin and soft tissue infections," *Curr. Opin. Infect. Dis.*, vol. 35, no. 2, pp. 95–102, 2022.
- [14] H. Alexander *et al.*, "The role of bacterial skin infections in atopic dermatitis: expert statement and review from the International Eczema Council Skin Infection Group," *Br. J. Dermatol.*, vol. 182, no. 6, pp. 1331–1342, 2020.
- [15] P. Tille, *Bailey & Scott's diagnostic microbiology-E-Book*. Elsevier Health Sciences, 2015.
- [16] L. N. Chan *et al.*, "The epidemiology of atopic dermatitis in older adults: A population-based study in the United Kingdom," *PLoS One*, vol. 16, no. 10, p. e0258219, 2021.
- [17] M. De Martinis, M. M. Sirufo, M. Suppa, D. Di Silvestre, and L. Ginaldi, "Sex and gender aspects for patient stratification in allergy prevention and treatment," *Int. J. Mol. Sci.*, vol. 21, no. 4, p. 1535, 2020.
- [18] L. Tizek, E. Redlinger, J. Ring, K. Eyerich, T. Biedermann, and A. Zink, "Urban vs rural—Prevalence of self-reported allergies in various occupational and regional settings," *World Allergy Organ. J.*, vol. 15, no. 1, p. 100625, 2022.
- [19] M. F. Al-Kobaisi, "Jawetz, Melnick & Adelberg's Medical Microbiology 24th Edition,"

- Sultan Qaboos Univ. Med. J.*, vol. 7, no. 3, pp. 273–275, 2007.
- [20] C. E. Powers, D. B. McShane, P. H. Gilligan, C. N. Burkhart, and D. S. Morrell, “Microbiome and pediatric atopic dermatitis,” *J. Dermatol.*, vol. 42, no. 12, pp. 1137–1142, 2015.
- [21] T. Nakatsuji *et al.*, “Antimicrobials from human skin commensal bacteria protect against *Staphylococcus aureus* and are deficient in atopic dermatitis,” *Sci. Transl. Med.*, vol. 9, no. 378, p. eaah4680, 2017.
- [22] N. Spervovasilis, M. Psychogiou, and G. Poulakou, “Skin manifestations of *Pseudomonas aeruginosa* infections,” *Curr. Opin. Infect. Dis.*, vol. 34, no. 2, pp. 72–79, 2021.
- [23] S. A. Lafi, S. O. AL-Mawala, A. A.-L. AL-Ani, and A. S. AL-Dulaym, “Bacterial infections associated with cutaneous leishmaniasis,” *AL-Kindy Coll. Med. J.*, vol. 4, no. 1, pp. 23–26, 2007.