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Staphylococcus aureus and Atopic Dermatitis: A Complex and Evolving Association

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REVIEW ARTICLE

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ABSTRACT

Atopic dermatitis (AD) is a chronic inflammatory skin disease associated with pruritus and epidermal barrier dysfunction. A key contributor to AD pathogenesis is *Staphylococcus aureus* (S. aureus), which colonizes the skin of affected individuals, exacerbating disease severity through toxin production and immune dysregulation. The microbiota of AD patients is significantly altered, with a reduction in microbial diversity and antimicrobial peptides, leading to an imbalance favoring *S. aureus*. The bacterium disrupts epidermal integrity, induces inflammasome activation, and promotes apoptosis, further worsening the inflammatory response. Methicillin-resistant *S. aureus* (MRSA) colonization poses a significant challenge in managing AD due to antibiotic resistance.
Multiple factors contribute to *S. aureus* dominance in AD skin, including genetic predisposition, altered immune responses, and environmental triggers. Th2/Th17 cytokine profiles are elevated in AD patients, leading to increased susceptibility to microbial invasion and inflammation. Filaggrin mutations, a common genetic trait in AD, further compromise the skin barrier, facilitating bacterial colonization. Treatment strategies include topical and systemic antibiotics, monoclonal antibodies, microbiome transplantation, and bacteriophage therapy. However, antibiotic resistance necessitates novel therapeutic approaches, such as targeting virulence factors, modulating immune responses, and restoring microbiome balance.
Recent studies emphasize the role of commensal *Staphylococcus* species in protecting against *S. aureus* colonization, highlighting the potential of microbiome-based interventions. Future research should focus on developing targeted therapies that restore skin homeostasis while minimizing antibiotic resistance. Understanding the intricate relationship between *S. aureus* and AD will aid in refining treatment strategies and improving patient outcomes.

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Introduction

Atopic dermatitis is commonly discerned problem of skin, depending on many factors especially interactions of many genes. This chronic infection is delineated by the bacteria named as *Staphylococcus aureus* [1]. Flare features confirmed the genetic expression as this infectious disease leads to dysfunction. In prospered countries, it causes infection in children with 20% frequency. Infections in some infants resolve earlier but, in other conditions it has estimated that it becomes fatal. It leads to respiratory infections until juvenescence. The severity of this infection depends on some ecological factors like inhaling of allergens or pollutants and some climatic factors [2]. It has been determined that the infectious bacteria colonize on the epidermis as 60 to 100% patients shows symptoms. However, the contrivance behind this is unknown but according to some facts, it has been demonstrated that it is assembled through direct mechanism of bacteria or through

immunologic reactions evoked by host fortification system of the infected person. Patients manifest methicillin resistant *staphylococcus aureus*. Its provocation endorsed by some facts like rate of bacteria in carrier, number of bacteria at specific skin area which shows relatively high manifest, immunologic reactions observations, host fortification system abnormalities, observations after oral treatment or direct therapy [3].

Staphylococcus aureus: The 'opportunist'

In 1880, inductive character of microorganism in infection was observed. Later, Louis Pasteur and his coworkers noticed pus from blister of 88 patients under microscope. They observed some gram-positive round "micrococci". He termed these microorganisms as Staphylococcus as they seemed as bunch of grapes. It shows golden shade in culturing so named as *Staphylococcus aureus* in 1961 [4].

It is common aerobic microbe and facultative anaerobe which is 0.8 to 1micro meter. It is non motile and peptidoglycan, protein and ribitol teichoic acid are present in its cell wall. It can show better growth at 30 degree centigrade to 37 degree centigrade. The pH which is optimum for this microbe is about 7 to 7.5 but it can multiply at 4.5 to 9 also. It shows resistant to dehydration as it can survive in dry condition [5]. Coagulase synthesize by this bacterium, stiffen the plasma. It is the major manifest for scientist to recognize the bacteria. It produces alpha, beta and sigma hemolysins. Due to some factors like environmental and host fortification factor, it alters its structure. It makes proteins that metabolize microbial elements and destroy the immune system during blood poisoning [6].

It causes many infections like SSTIs that abbreviated as skin soft tissue infections, life threatening inflammations and devastating fasciitis. This capability of clinical manifestation is allocated to the production of many exotoxins [7]. It is commonly known as extra cellular microorganisms. It can interiorize by a number of different host cells in a fibronectin binding protein. In epidermis that produces keratin, there are strains dependent and FnBP independent mechanism is revealed. It has also been estimated the discharging of endosome and persuade programmed cell death in epithelial cells of intracellular *Staphylococcus aureus*. In short, this microbe is not only general skin flora but also dominant on contributed and un-contributed skin sites of patients infected [8].

Atopic Dermatitis (AD)

Atopic dermatitis is a long-term irritant skin condition as it is pervaded clinically by interval flares of dry, itchiness, rashes, redness and pathogenically by deformed skin barrier, perennial infections. Infection is generally common in infants and relatively less in adults. There is a high pervasiveness in progressed countries of about 20% in infants. Prevalence is rising especially in citified regions [9]. Increased hygiene in a comprehensive way may result in a decrease in accurate immune provocation that may bestow not for dermatitis only but also for infectious disease like asthma, coryza and contention of the prevalence data. Other factors linked with citified living like subjection to pollutants (fumes, endotoxin, infectious particle, washing means, and other factors). So, these are major facts about prevalence of infection [10].

Atopic dermatitis is considered as the most convoluted disease that can activate in persons from variety of genetic histories [11]. Genomic research and studies have declared that polymorphism in different genes regulates skin barrier stability which is connected with atopic dermatitis. It involves filaggrin alternative functional loss. Filaggrin is a protein that is essential for the growth of outer layer of epidermis [12]. The skin of infected person strikes the virtue of barrier that increased the possibility of irritants pervasive the epidermis and increasing the infection forming cruel cycle. The microbiota of dermis is necessary as it perpetuates immune stability and avoids the growth of microorganisms like *S. aureus* [13].

Susceptibility to irritant

The susceptibility of many irritants was estimated due to provoking the role of the barrier function of the epidermis layer, desiccation of skin and in case of a background of atopic dermatitis was an aspect. According to study on susceptibility, the trans-epidermal water loss was considered by evaporimeter and dermal drench by Corneometer. So, results concluded as that the dry skin was much susceptible to irritant as after investigation, it was observed that there is no difference in the pre denunciation barrier activity clinically. The enhanced susceptibility and sensitivity to irritants in those with a previous background of atopic dermatitis was due to disabled barrier activity or the existence of a dry skin [7].

Time period	Infected children	Country	Incidence per 100,000 person-years for all *S. aureus* isolates	Severity of clinical manifestation			References
(year)	(age)			Mild	Moderate	Severe	
1971-2000	Children with ≤20 year of age	Denmark	4.5-8.4	✓			[14]
2000-2006	Children with ≤18 year of age	Calgary	6.5		✓		[15]
1998-2002	Children with <5 year of age	Kenya	27			✓	[16]
2001-2006	Children with <15 year of age	Mozambique	48		✓		[17]
2007-2009	Children with <5 year of age	Ghana	630	✓			[18]
2005-2006	Children with <13 year of age	South Africa	26			✓	[19]

Epidemiology

The past years have witnessed that *S. aureus* cause infections in not only Asia, but also has affected other countries as well. Inappropriate therapy is the major reason to this infectious disease. Some regions have the highest prevalence rate. Many hospitals were endemic and two pandemics were also disseminated. Staphylococcal skin colonization is considered as a common feature of AD and many studies have documented its prevalence. Many infected people were observed during diagnosis and treatment during past years. Signs and symptoms were observed in that patients and then, *S. aureus* was isolated from these patients [6][9].

Children and adult patients have also taken to be observed that estimated highest prevalence in children. It is due to because of self-contamination and transmission by direct contact. Incidence of this infection per 100,000 person per years in different countries are documented. Children with different ages were taken from different sub-populations within different time periods of years. Then, incidence per 100,000 person- years for all *Staphylococcus aureus* was estimated in given table [13].

First line of defense: 'The skin'

Against infection of bacteria, skin is the foremost line of vindication. Bacteria are not present under the skin layer but in clinical infections, they are found. Function of barrier relies on intact skin layer. Bacteria are present on either upper or lower side of skin layer and also esteemed on the hair follicles, mainly in between the hair and concentric layers. The morphology inclination of *S. aureus* at normal skin of infected person has not been interpreted yet. However, at disordered skin, gram positive cocci are frequent in the stratum corneum as it has infectious particles [20].

Antimicrobial properties of skin

According to dermatological studies, skin has some antibiotic possessions as it exfoliates bacteria. Flora, hidrosis, superficial integrant and other kinds of microbes alter the pH of skin that leads to hinder the growth of bacteria and indulge the other bacterial growth. The site where two skin touches, is supreme antimicrobial factor as dehydration is normal in the genus of bacteria. Number and kind of microbes can be altered by the deformity of skin as *S. aureus* is much recurrent at irritating surface than on normal skin [21].

The normal skin layer of infected person with atopic dermatitis can be irregularly amenable to *S. aureus* infection in accordance with imperative nutrient factors or insane normal flora. If skin eroded with ether, there will more growth of *S. aureus* than normal skin. The attachment of this bacterium to skin can be attained either through normal skin or the nasal mucosa of persons infected with this infectious atopic dermatitis. There is another postulate that is for describing the high conveyance rate of these bacteria on normal skin. Fact is that wound provoke and summon the colonization of *Staphylococcus aureus*. Patients generally scratch the layers abrade the skin layer. Plasma ingredients are

linked with slow discharge from wound of injured skin. Actually, peeling away the skin gives nutrient broth to that surface layer. It perhaps obliges colonization of microbes like *S. aureus* and relates to environmental factors of microbiology. Clinically, normal skin surface is related to infectious from adjacent skin abrasions [1].

Role of Staphylococcus aureus in the AD skin

Iwamoto et al (2019) reported that *Staphylococcus* is normally observed in those persons who are infected with atopic dermatitis. Meta- analysis of about 95 cases intimated that almost 70% cases showed these bacteria in their lesions but 39% cases showed no lesions. However, it is less likely to observe in healthy persons. Using DNA sequencing methods, it was estimated for detecting micro-biome that these microbes were present in AD patients and its number increased by increasing flares. It was estimated and declared by epidemiologist that *S. aureus* are the reason behind contagious superficial pyoderma observed in that patient. Density is collated with the ferocity of infection. Colonization occurs on the skin is differ in their sizes that relate to dispensation of disease. The colonization in patients with no abscess due to microbial imbalance causes inflammation of epidermis that ultimately promotes the colonization of microbes [22]. In comparison to voluminous colonization of *Staphylococcus aureus*, *S. epidermidis* is frequently present in healthy person's skin. Many cases concentrate on comparison of these bacteria and immune feedback. IL-10 emanation and actuation of T cells was persuaded by monocyte- drived neuron cells. These are accelerated by *S. epidermidis* but the consequence has not been was analyzed for *S. aureus*. Anti-inflammatory cytokines synthesis was also determined. The studies on their comparison persuade immune sympathy with surmised to contribute to the servicing of skin stability [23].

Pathogenesis of infection: There are some phases of pathogenesis like colonization, localized infection, infection in entire body, cancerous cells infection and toxinosis. Colonization is found at every place as it has been observed the lesion around vagina and perianal area. It may don't show symptoms for many days but it is only momentary carried on unblemished skin. It is presumed that it leads to infection. Localized inflammation occurs when organism is introduced from an area of posture and get approach to enter into blood. In blood, it goes to peripheral areas and spread. Transience rate is high if no therapy is being received. Propagation results many infections like inflammation of heart valves, infection of bone marrow, renal carbuncle and blood poisoning. If it doesn't get approach to blood then it leads to many syndromes like food borne syndrome (fever, vomiting, nausea, hypotension and skin rash). According to some investigations regarding cases, it can also cause diabetes mellitus, injecting chemicals and drugs via hypodermic vein and AIDS [24].

Colonization by S. aureus

AD patients are affiliated to impetuous hospitalization as they use recent calcineurin inhibitors coalition with recent steroids [25]. It has been estimated that initially colonization can give rise to clinical manifestation and cause malignant cycles between infection and provocation by influencing TSLP abbreviated as thymic stromal lymphopoietin along with Th2 or Th 17 type tenderness. DNA sequencing methods like pyrosequencing have been increasing our understanding regarding alternation in organization of microbe. In comparison to diversified group of mutualistic bacteria in normal skin, tempestuous AD skin is prominently colonized by *Staphylococcus aureus* [3]. Nakatsuji et al. has been reported that coagulase negative *Staphylococcus* secures from *S. aureus* so deficiency of safeguard bacteria can lead to increased colonization of S. aureus as they displayed CoNS strains impeded *S. aureus* [12]. Kennedy et al. had also reported and studied that bacterial community organization and variety relocates over time period. Initial colonization with it at 2 months minimized the chances of appearing atopic dermatitis at about 11 to 12 months [11].

Why is in AD skin infection dominant in clinical practice? There has been raising authentication that *Staphylococcus aureus* play vital contribution in the provocation of disease along with impediments like contagious skin infection, swelling bacterial infection and many other transmissible infections. Density always depends on the severity and reduced variety of microbiota present on healthy skin was noticed. However, MRSA colonization is remarkably linked with dissipate of antibiotics as well as initially at hospital medical care [4]. The interaction is because, it synthesizes toxins, peptidases and signaling molecules cytokines. It is also connected with dysfunctioning of coalition of SC, penetrability and water content on skin on normal skin. Patients infected with this disease manifest higher trans-epidermal water loss rather than normal persons. There is difference in clonal complex types excluded from patients of atopic dermatitis and

patients with no manifestations. pH is also higher in skin of patients infected with this infection. It has linked with allergens, tissue damage and food allergens (eggs white, milk) that contribute to atopic march [26].

Immune dysregulation in Atopic Dermatitis

AD originates from genetic predilection for disruption in the epidermal impediment of the skin. The acute stage may start when any irritant enters the barrier. It is then rectified by skin antigen displaying cells [9]. Keratinocytes are activated to release TSLP along with IL-25 AND IL-23 that extend skin connective tissues. The trait or feature order of IL-3, IL-4, IL-5, IL-13, IL-31 are synthesized that provokes the immunoglobulin E reaction along with antibiotics that retaliate with irritants and self-antigens [4]. Fc area is detected by the amount of IgE linked with autoreactive receptors. Dendritic cells attach with IgE are enduring so that's why it stayed prepared to react with irritants. It influences corneocyte activity along with skin barrier strength. Skin is infected causing itching so its extent gets more mutilate due to scratching [27].

Skin defense mechanism and TH2 environment

Normal skin has direct association with surroundings and many microorganisms. Commensal microbes are appropriate for growth of microbes linked with low pH and calefaction made the surrounding that impede the growth of bacteria. Outer surface of the skin produces a variety of armaments like AMPs [28]. AMPs is actually the antimicrobial proteins that decimate or inhibit the growth of microbes and the most known antimicrobial protein is ribonuclease, human beta defensin-1, human beta defensin-2, human beta defensin-3, and cathelicidin IL-37. These are produced by the human keratinocytes and combine with lipids portion to increase the protective activity [29]. Moreover, Th2 cytokines impede lamellar body creation important for making barrier on outer layer of skin and transfer acid sphingomyelinase. It may minimize the quantity of ceramides. Alpha toxin is most dominant one that host expresses on the outer layer of skin. Th2 cytokine display cells that are susceptible to alpha toxin instigate cell death so it linked with enhanced vulnerability to Th2 cytokines. Another enzyme sphingomyelinase produced by protein FLG and quantity of sphingomyelinase lessen in the patient skin infected with atopic dermatitis but keratinocytes level is raised. TSLP impede production of T cells that is constant natural killer so it is major factor between the skin and the surroundings as a relating response of immune [30].

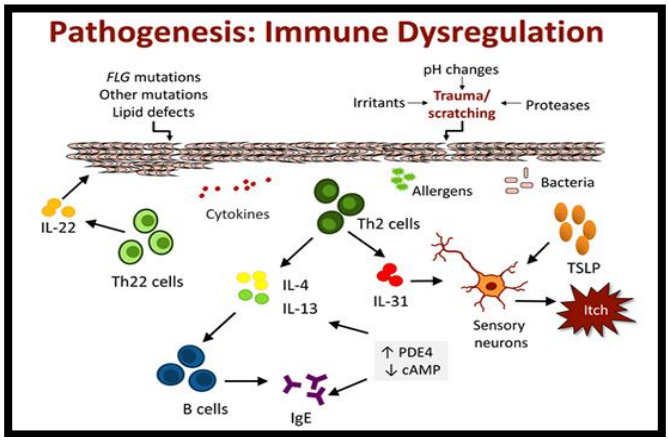

Figure 1: Immune Dysregulations in AD patients.

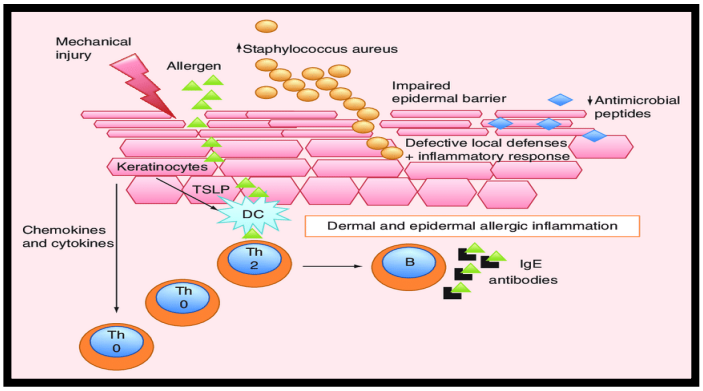

Figure 2: Lesions of atopic dermatitis due to allergens

Specific S. aureus strains

Genetic history of patients infected with atopic dermatitis revealed that on the skin, there are strains which can stimulate the particular surrounding of atopic dermatitis. Some cases of severe infections, strains were isolated in order to analyze. Th1 and Th2 which is alterable, immune reaction is induced through strain of Atopic dermatitis. It was also determined that aggregation of strains of atopic dermatitis in the lysosomes persuades the IL-1 alpha generation through the Toll like receptor and stimulation of complement in keratinocytes introducing *Staphylococcus aureus* regulates balance of tissue [26]. Patients of Atopic dermatitis have skin that always has particular strain according to recent researches on it. By using DNA sequencing methods, CC type has been detected in the protein A of bacteria. CC 30 is illustrated that has link

with the endocarditis but some factors at clinical level are unclear and studies on it are limited. CC1 is considered most common among the patients of severe infected with atopic dermatitis [31].

Association of S. aureus with Atopic Dermatitis

As explored the reviews and researches, it is now clear that atopic dermatitis patients have the bacteria-*Staphylococcus aureus*. Stance rate can be from 30 to 100% as it depends on the severity of infection in the patient [32]. Cultured based studies illustrate the major observations that frequency of carriage was compared in between the 70% patients of lesional skin with 39% of non-lesional skin. Secondly, as the disease severity increased, prevalence and pervasiveness rate increased [33].

Many researches on strains that a patient carry from various positions have revealed that community formation is relied on the multi-locus sequencing. Strains obtained from the infected children skin was CC30 after researches and CC1 was over exhibited if comparison occurs with normal persons. Researchers investigates that the patients who have CC1 strain are much infected and has severity of disease [34].

Lesions of Atopic Dermatitis

Leyden et al. reported a review in which he studied and observed lesions in the patients of AD and contain *Staphylococcus aureus*. He and his coworkers illustrate that AD patients also have chances to have disease of herpes simplex and vaccine viruses but manifestations of bacterial infection are not shown generally. Pus formation, heat, excess fluid in the tissues of the body and hard outer layer formation are the common manifestations that occur as initially. In his report, he demonstrated that patients who don't show clinical manifestations, they have shown major sign of eczema. So out of 106 patients, 44 were manifesting this infection. Lesions were observed in many patients that have *S. aureus* after investigation [35].

Filaggrin in AD

Mutation in the structural protein "filaggrin" is extensive risk factor in this infectious disease. Mutation in filaggrin gene gives a postulate that skin defense procedure to irritants along with microorganisms imitated by polarized TH2 lymphocyte reactions in severe infection. Research on genes illustrate that FLG exposes flustered barrier function as an important player in the transmission of pathogen in many patients. The endowment of FLG to disease and its characteristics alter the expression along with its role to stay specify [35].

S. aureus molecules that contribute to Atopic Dermatitis

Some molecules and products are the reason that leads to Atopic dermatitis. It is detected by AD skin factors [36]. The major factors are superantigens that generate IE response, phenol soluble modulins that activate cytokines expression of proinflammation, alpha toxin which is pore forming cytolysin virulence factor, protein A that recognize tumor necrosis, lipoprotein or lipoteichoic acid manifesting proinflammation, proteases that provokes the penetration of bacteria and bacterial allergens provoking colonization [37].

Impairment of epidermal barriers by infection

Staphylococcus aureus is the reason behind peripheral and invasive inflammation that spread itself throughout on the body causing life threatening condition and bacteremia. It colonizes and synthesizes acrimony factors like some enzymes that lead to infection and cause skin barrier functionally abnormal [38]. It enters into skin that only relies on its activity of protease. Searches on it illustrate that it is linked with increased expression of some factors. These factors may include IL-4, IL-13, IL-22, IL-17 along with TSLP. Its linkage is also associated with decreased expressions of IL-37. Some strains of this bacteria intimates superantigens like Staphylococcus enterotoxin A, SED. In some cases, other strains show SEB and SEC. About 80% patient manifest complicated pattern as strains promotes polyclonal T cells [39]. Actually, this expression cause keratinocytes inhibition especially IL-31 that is the reason. Superantigens are actually irritants suppressing filaggrin assertion. It promotes the immunoglobulin E and amphipathic peptides are separated so named as phenol soluble modulins (PSM) that is released by transporter Pmt. It causes alpha hemolysis as it is more sensitive for alpha toxin. Protein A along with other lipoproteins persuades reactions of proinflammation. It aggravates infection on the skin by secretion of superantigens and damage keratinocytes along with immune cells [40].

Molecular diagnostic characterization

Mostly, AD patients manifest high total serum IgE in laboratory test. It shows positive against mite- specific IgE antibody and *Pityrosporum*- specific IgE antibody because of high incidence of *Staphylococcus aureus*. Increasing of peripheral blood eosinophil has been observed during molecular diagnosis. On the other hand, patients with higher entity of AD show high serum of LDH values. Many intracutaneous tests are performed in laboratory in this

way. In some cases, Atopic dermatitis and seborrheic dermatitis differentiation is difficult. So, diagnosis of this disease has to done with very carefully. PCR is performed during molecular diagnosis to determine the expressions of genes involved. Samples were isolated from the lesions of patients and then plated on the blood agar, Mannitol agar, MRSA ChromID-BioMerieux, France media. After then, it is incubated for about 24 to 48 hours at 37°C. Through diagnostic system, antimicrobial susceptibility has been observed and drugs recommended according to resistance to oxacillin. Penicillin-Binding Protein latex agglutination test is also the concern while recommending treatments. In some cases, immunoassay technique is performed for detection of staphylococcal enterotoxins and toxic shock syndrome toxic-1. In this way, isolates have to be incubated in tryptone soya broth and brain heart infusions. PFGE (pulsed- field gel electrophoresis) analysis is considered as another confirmatory test. It is basically used to determine the genotyping of the isolated *S. aureus* strains. It is performed at a voltage of 6V/cm at 14°C. It is placed for 23 hours and stained with ethidium bromide solution [41].

Treatment of AD

In atopic dermatitis pathogenesis, bacterial antigens are involved then it can be treated or may reduce the severity of disease. This kind of research is complex because it is impossible for us to clear the epidermal layers of all bacteria. Immunologic reactions are not dependent on the medicines. Remaining other bacteria can lead to dermatitis through process of immunologie. After sterilization, the dead microorganisms act as antigens. When the patient is medicated with topical antimicrobial agents, the disease atopic dermatitis refines almost. However, the skin ameliorates with treatments and therapies are not fully restrained [42].

Abating of disease severity

Colonization is main issue that has to manage. Topical mupirocin or topical retapamulin is the common treatment given to the patients with skin infection. It reduces the severity of disease and patients recover steadily [43]. Some antibiotics are orally taken like anti-staphylococcal penicillin for a week. Another antibiotic named as cephalosporins that are taken orally. Doxycycline and sulfamethoxazole trimethoprim are used for tissue inflammation as well as for MRSA infection. These have less effect because production of antibiotic resistant strains so other medicines may include vancomycin, glycopeptides or tigecycline. Recent researches suggested that bleach bathing can result in better improvement but it might possible that it can have effect on commensal bacteria and pathogenic bacteria [44].

Future perspective

Infections caused by *S. aureus* are difficult to treat. Some important efforts have been made regarding the research and development of certain strategies that include vaccines, therapeutic monoclonal antibodies (mAbs), and the phage lysins of *S. aureus*. However, in clinical testing the approaches to monoclonal antibodies and vaccines that can target surface antigens of *S. aureus* species remains unsuccessful [45]. In this way, the advancements of new antitoxins and multiple antigen vaccine are made and further approaches are yet to be proceed. To reduce the severity of disease, high neutralizing anti-a-toxin IgG and mAb therapy can be provided to AD patients. More researches are needed to validate the colonization by dependent bacteria (commensal) can amend immunity and secure the skin. MEDI4893 is an mAb that can be used in preventing *S. aureus* pneumonia. This should also be used in clinical testing as it protects from skin infection of *S. aureus* in mice [46].

Conclusions

S. aureus is commonly an infectious microbe that usually colonizes on the skin of patients infected with Atopic dermatitis. It leads to aggravation of Atopic dermatitis due to deficiency of AMPs, low presence of filaggrin and microbial imbalance. It just not only damage skin but maintains proinflammatory cytokines. It causes Th2 or Th17 alternations and infection. Some major treatments have been introduced to control this disease. Efforts of researches regarding balancing the dysbiosis have been attempted and advancement to increase our knowledge of its role in pathophysiology has been tried. It seems that new advancements and technologies will help to treat this infectious disease effectively like immunotherapy.

Authors' contributions

ICMJE criteria	Details	Author(s)
1. Substantial contributions	Conception, OR Design of the work, OR Data acquisition, analysis, or interpretation	1 1,2 3,4,5
2. Drafting or reviewing	Draft the work, OR Review critically for important intellectual content	1,2 3,4,5
3. Final approval	Approve the version to be published	1,2,3,4,5
4. Accountable	Agree to be accountable for all aspects of the work	1,2,3,4,5

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations
Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

References
[1]. Dahl MV. Atopic dermatitis: the concept of flare factors. South Med J. 1977;70(4):453-5.
[2]. Leung DY. The microbiome and allergic diseases: A struggle between good and bad microbes. Ann Aller Asth Immunol. 2019;122(3):231-2.
[3]. Kim J, Kim BE, Ahn K, Leung DY. Interactions between atopic dermatitis and Staphylococcus aureus infection: clinical implications. Aller Asth Immunol Res. 2019;11(5):593-603.
[4]. Salimi M, Barlow JL, Saunders SP, Xue L, Gutowska-Owsiak D, Wang X, et al. A role for IL-25 and IL-33–driven type-2 innate lymphoid cells in atopic dermatitis. J Exper Med. 2013;210(13):2939-50.
[5]. Silva V, Capelo JL, Igrejas G, Poeta P. Molecular epidemiology of Staphylococcus aureus lineages in wild animals in Europe: a review. Antibiotics. 2020;9(3):122.
[6]. Dahlman D, Jalalvand F, Blomé MA, Håkansson A, Janson H, Quick S. High perineal and overall frequency of Staphylococcus aureus in people who inject drugs, compared to non-injectors. Cur Microbiol. 2017;74:159-67.
[7]. Burian M, Rautenberg M, Kohler T, Fritz M, Krismer B, Unger C, et al. Temporal expression of adhesion factors and activity of global regulators during establishment of Staphylococcus aureus nasal colonization. J Infect Dis. 2010;201(9):1414-21.
[8]. Dekio S, Onimura K. Coagulase types of coagulase-positive Staphylococci from bacterial skin infections. J Dermatol. 1981;8(3):223-8.
[9]. Manz J, Rodríguez E, ElSharawy A, Oesau EM, Petersen BS, Baurecht H, et al. Targeted resequencing and functional testing identifies low-frequency missense variants in the gene encoding GARP as significant contributors to atopic dermatitis risk. J Invest Dermatol. 2016;136(12):2380-6.
[10]. Boguniewicz M, Leung DY. Atopic dermatitis: a disease of altered skin barrier and immune dysregulation. Immunol Rev. 2011;242(1):233-46.
[11]. Flohr C, Mann J. New approaches to the prevention of childhood atopic dermatitis. Allergy. 2014;69(1):56-61.
[12]. Kennedy EA, Connolly J, Hourihane JO, Fallon PG, McLean WI, Murray D, et al. Skin microbiome before development of atopic dermatitis: early colonization with commensal staphylococci at 2 months is associated with a lower risk of atopic dermatitis at 1 year. Journal of Aller Clin Immunol. 2017;139(1):166-72.
[13]. Nakatsuji T, Chen TH, Narala S, Chun KA, Two AM, Yun T, et al. Antimicrobials from human skin commensal bacteria protect against Staphylococcus aureus and are deficient in atopic dermatitis. Sci Trans Med. 2017;9(378):eaah4680.
[14]. Howden BP, Davies JK, Johnson PD, Stinear TP, Grayson ML. Reduced vancomycin susceptibility in Staphylococcus aureus, including vancomycin-intermediate and heterogeneous vancomycin-intermediate strains: resistance mechanisms, laboratory detection, and clinical implications. Clin Microbiol Rev. 2010;23(1):99-139.
[15]. Frederiksen MS, Espersen F, Frimodt-Møller N, Jensen AG, Larsen AR, Pallesen LV, et al. Changing epidemiology of pediatric Staphylococcus aureus bacteremia in Denmark from 1971 through 2000. Pediatr Infect Dis J. 2007 May 1;26(5):398-405.
[16]. Asgeirsson H, Thalme A, Weiland O. Staphylococcus aureus bacteraemia and endocarditis–epidemiology and outcome: a review. Infect Dis. 2018;50(3):175-92.
[17]. Berkley JA, Lowe BS, Mwangi I, Williams T, Bauni E, Mwarumba S, et al. Bacteremia among children admitted to a rural hospital in Kenya. New Eng J Med. 2005;352(1):39-47.
[18]. Sigaúque B, Roca A, Mandomando I, Morais L, Quintó L, Sacarlal J, et al. Community-acquired bacteremia among children admitted to a rural hospital in Mozambique. Pediatr Infect Dis J. 2009;28(2):108-13.
[19]. Nielsen MV, Sarpong N, Krumkamp R, Dekker D, Loag W, Amemasor S, et al. Incidence and characteristics of bacteremia among children in rural Ghana. PLOS One. 2012;7(9): e44063.
[20]. Groome MJ, Albrich WC, Wadula J, Khoosal M, Madhi SA. Community-onset Staphylococcus aureus bacteraemia in hospitalised African children: high incidence in HIV-infected children and high prevalence of multidrug resistance. Paediatr Int Child Health. 2012;32(3):140-6.
[21]. Davies RR, Noble WC. Dispersal of bacteria on desquamated skin. I962;p.1295-7.
[22]. Aly R, Maibach HI, Shinefield HR, Strauss WG. Survival of pathogenic microorganisms on human skin. J Invest Dermatol. 1972;58(4):205-10.
[23]. Iwamoto K, Moriwaki M, Miyake R, Hide M. Staphylococcus aureus in atopic dermatitis: Strain-specific cell

wall proteins and skin immunity. Allergol Int. 2019;68(3):309-15.
[24]. Volz T, Kaesler S, Draing C, Hartung T, Röcken M, Skabytska Y. Induction of IL-10-balanced immune profiles following exposure to LTA from Staphylococcus epidermidis. Exper Dermatol. 2018;27(4):318-26.
[25]. O'Callaghan RJ. The pathogenesis of Staphylococcus aureus eye infections. Pathogens. 2018;7(1):9.
[26]. Ong PY, Leung DY. Bacterial and viral infections in atopic dermatitis: a comprehensive review. Clin Rev Aller Immunol. 2016;51:329-37.
[27]. Byrd AL, Deming C, Cassidy SK, Harrison OJ, Ng WI, Conlan S, et al. *Staphylococcus aureus* and Staphylococcus epidermidis strain diversity underlying pediatric atopic dermatitis. Sci Transla Med. 2017;9(397):eaal4651.
[28]. Furue M, Chiba T, Tsuji G, Ulzii D, Kido-Nakahara M, Nakahara T. Atopic dermatitis: immune deviation, barrier dysfunction, IgE autoreactivity and new therapies. Allergol Int. 2017;66(3):398-403.
[29]. Schlievert PM, Case LC, Strandberg KL, Abrams BB, Leung DY. Superantigen profile of Staphylococcus aureus isolates from patients with steroid-resistant atopic dermatitis. Clin Infect Dis. 2008;46(10):1562-7.
[30]. Howell MD, Gallo RL, Boguniewicz M, Jones JF, Wong C, Streib JE. Cytokine milieu of atopic dermatitis skin subverts the innate immune response to vaccinia virus. Immunity. 2006;24(3):341-8.
[31]. Breuer K, Wittmann M, Bösche B, Kapp A, Werfel T. Severe atopic dermatitis is associated with sensitization to staphylococcal enterotoxin B (SEB). Allergy. 2000;55(6):551-5.
[32]. Josse J, Laurent F, Diot A. Staphylococcal adhesion and host cell invasion: fibronectin-binding and other mechanisms. Front Microbiol. 2017;8:2433.
[33]. Totté JE, Van Der Feltz WT, Hennekam M, van Belkum A, Van Zuuren EJ, Pasmans SG. Prevalence and odds of S taphylococcus aureus carriage in atopic dermatitis: a systematic review and meta-analysis. Br J Dermatol. 2016;175(4):687-95.
[34]. Weidenmaier C, Goerke C, Wolz C. Staphylococcus aureus determinants for nasal colonization. Trends Microbiol. 2012;20(5):243-50.
[35]. Yeung M, Balma-Mena A, Shear N, Simor A, Pope E, Walsh S. Identification of major clonal complexes and toxin producing strains among Staphylococcus aureus associated with atopic dermatitis. Microb Infect. 2011;13(2):189-97.
[36]. Leyden JJ, Marples RR, Kligman AM. Staphylococcus aureus in the lesions of atopic dermatitis. Br J Dermatol. 1974;90(5):525.
[37]. Arad G, Levy R, Nasie I, Hillman D, Rotfogel Z, Barash U, et al. Binding of superantigen toxins into the CD28 homodimer interface is essential for induction of cytokine genes that mediate lethal shock. PLoS Biol. 2011;9(9):e1001149.
[38]. Geoghegan JA, Irvine AD, Foster TJ. Staphylococcus aureus and atopic dermatitis: a complex and evolving relationship. Trends Microbiol. 2018;26(6):484-97.
[39]. Benenson S, Zimhony O, Dahan D, Solomon M, Raveh D, Schlesinger Y. Atopic dermatitis—a risk factor for invasive Staphylococcus aureus infections: two cases and review. Am J Med. 2005;118(9):1048-51.
[40]. Spaulding AR, Salgado-Pabón W, Kohler PL, Horswill AR, Leung DY, Schlievert PM. Staphylococcal and streptococcal superantigen exotoxins. Clin Microbiol Rev. 2013;26(3):422-47.
[41]. Vu AT, Baba T, Chen X, Le TA, Kinoshita H, Xie Y, et al. Staphylococcus aureus membrane and diacylated lipopeptide induce thymic stromal lymphopoietin in keratinocytes through the Toll-like receptor 2–Toll-like receptor 6 pathway. J Aller Clin Immunol. 2010;126(5):985-93.
[42]. Cafiso V, Bertuccio T, Spina D, Purrello S, Stefani S. Tigecycline inhibition of a mature biofilm in clinical isolates of Staphylococcus aureus: comparison with other drugs. FEMS Immunol Med Microbiol. 2010;59(3):466-9.
[43]. Puar N, Chovatiya R, Paller AS. New treatments in atopic dermatitis. Ann Aller Asth Immunol. 2021;126(1):21-31.
[44]. Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJ, Gorbach SL, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis. 2014;59(2):e10-52.
[45]. Maarouf M, Shi VY. Bleach for atopic dermatitis. Dermatitis. 2018;29(3):120-6.
[46]. Dayan GH, Mohamed N, Scully IL, Cooper D, Begier E, Eiden J, et al. Staphylococcus aureus: the current state of disease, pathophysiology and strategies for prevention. Expert Rev Vac. 2016;15(11):1373-92.
[47]. Hua L, Hilliard JJ, Shi Y, Tkaczyk C, Cheng LI, Yu X, Datta V, et al. Assessment of an anti-alpha-toxin monoclonal antibody for prevention and treatment of Staphylococcus aureus-induced pneumonia. Antimicrob Agent Chemother. 2014;58(2):1108-17.