

**ORIGINAL ARTICLE**

## ***Staphylococcus aureus* as a Causative agent of Atopic Dermatitis/ Eczema Syndrome (ADES) and its Therapeutic Implications**

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### **ABSTRACT**

From 286 studied ADES cases, (94.4, 86.36) % from eczematous lesions and healthy areas gave positive bacterial cultures ( $P < 0.05$ ). *Staphylococcus aureus* recorded a highest occurrence ratio (60.84, 17.48) % from same above areas respectively than those of all of isolated bacterial agents. Antibiotic susceptibility of thirteenth antibiotics against *Staph. aureus* were carried in this study, some of these antibiotics studied at the first time such as Amoxicillin/ Clavulanic acid, Bacitracin, Doxycyclin HCl, Rifamicin, and Vancomycin. Also the results evidenced resistance of *Staph. aureus* to more of one antibiotics (three antibiotics or more) that indicate *Staph. aureus* develop a modern resistance against useful antibiotics.

**Key words:** *Staphylococcus aureus*, atopic dermatitis/ eczema syndrome.

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### **INTRODUCTION**

Atopic dermatitis/ eczema syndrome (ADES) is chronic relapsing, pruritic inflammation of the skin, affecting 10-20% of children and 1-3% adults, worldwide, with increasing prevalence in highly industrialized countries [1]. *Staphylococcus aureus* is the most important microorganism at normal skin flora [2]. The bacterial skin flora of patients with atopic dermatitis is different from that in healthy people. In addition, such patients more often suffer from microbial infections such as impetigo, folliculitis, and furunculosis [3]. The microbial flora of AD patients shows striking differences in term of the presence of *Staph. aureus*. The relative rarity (2%-25%) of colonization by *Staph. aureus* on normal skin sites [4] is in sharp contrast to the high carriage rate found in patients with ADES ranging from 76% on unaffected areas and up to 100% on acute, weeping lesions<sup>(5)</sup>. As the colonization correlates significantly with the severity of ADES, anti-staphylococcal treatment measurements are widely used [6].

The aims of the present study are to determine presence / or occurrence ratio of *Staphylococcus aureus* in eczematous lesion and healthy area of patient with ADES, and testing the antibiotic susceptibility on these bacteria.

### **MATERIAL AND METHODS**

**Patients:** A total of 286 patients (males & females) in various age groups were concluded in this study. The patients were suffered from atopic dermatitis / eczema syndrome (ADES) attending the out patients of department of dermatology of main hospitals in Basrah providence (out patients based study). ADES diagnosed under supervision of dermatologists based on criteria of Hanifin & Rajka, 1980 [7], Spengel & Schneider, 1999 [8], and Stanway, 2005 [9]. The study was carried out during a period from November 2003 to July 2005.

**Primary isolation:** Skin swabs were collected from eczematous lesions and nearly healthy areas of ADES patients saturated by Brain Heart Infusion Broth (Oxoid), and transported immediately to the laboratory<sup>(10)</sup>. And then cultured on primary isolation media: Blood Agar Base (Oxoid), MacConkey Agar, and Nutrient Agar (Himedia). And incubated at 37°C for 24-48 hrs aerobically. Samples that cultured on Chocolate Agar in addition to Nutrient Agar were incubated and CO<sub>2</sub> in candle jar at the same temperature and period mentioned above [10].

Identification technique: API technique (bioMerieux, France) as a rapid identification system was used for identification of various bacterial isolates based on enclosed instruction of supplied company. Some specialized biochemical tests and grew on Mannitol Salt Agar and Staph 110 Agar (Himedia)-that used as a selective media-were done for confirmation the diagnosis of *Staph. Aureus* [10-12].

#### Antibiotics susceptibility

Thirteen antibiotics (Himedia, India) common used with treatment of atopic dermatitis<sup>(6,13)</sup> were used to testing the antibiotics susceptibility of *Staph. aureus* :

Amoxycillin / Clavulanic acid (20/10mg) (AC), Bacitracin (10U)(B), Cephalothin (30mg)(Ch), Chloramphenicol (30mg)(C), Clindamcin (2mg)(cd), Co-trimoxazole (trimethoprim/sulphamethaxazole) (1.25/23.75mg) (Co), Doxycyclin hydrochloride 30mg) (Do), Erythromycin (15mg)(E), Gentamicin (10mg)(G), Methicillin (5mg)(M), Rifampicin (5mg) (R) Tetracyclin (30mg)(T), and Vancomycin (30mg) (Va).

#### Statistical analysis

Chi-square test and ANOVA test were carried by using computer program SPSS ver. 11, and statistical similarities were carried by using Minitab program ver. 10.

## RESULTS

Table (1) illustrates all bacterial types isolated from eczematous lesions and nearly healthy areas. The total number of positive cultures (270, 247) cases from 286 studied ADES cases in percentages (94.4, 86.36) % from eczematous and healthy areas respectively ( $P < 0.05$ ). In general, twenty bacterial types were isolated from both area separately and (959, 744) isolates with isolation ratio (3.35:1, 2.6:1) isolates: case were identified in each above area respectively. *Staph. aureus* recorded a highest occurrence ratio (60.48%, 17.48%) from above area respectively than those of all of isolated bacterial agents that recorded following percentage in eczematous lesions and healthy areas: ( $P < 0.05$ ).

Table 1: Illustrate bacterial types isolated from eczematous lesions and healthy areas of AD patients ( $P < 0.05$ ).

Bacterial types	No. of cases (%) from eczematous lesion	No. of cases (%) from healthy area
<i>Staph. aureus</i>	173(60.48)	50 (17.48)
<i>Staph. epidermidis</i>	49 (17.13)	164 (57.34)
<i>Staph. xylosus</i>	8 (2.79)	8 (2.79)
<i>Staph. saprophyticus</i>	15 (5.24)	30 (10.48)
<i>Staph. capitis</i>	8 (2.79)	8 (2.79)
<i>Staph. hominis</i>	64 (22.37)	27 (9.44)
<i>Strept.pyogenes</i>	49 (17.13)	28 (9.79)
<i>Strept. Faecalis</i>	66 (23.07)	51 (17.83)
<i>Strept. Mutans</i>	42 (14.68)	27 (9.44)
<i>E.coli</i>	73 (25.52)	95 (33.21)
<i>Enterobacter sp.</i>	16 (5.59)	51 (17.83)
<i>Klebsiella sp</i>	9 (3.14)	4 (1.39)
<i>Acinetobacter sp.</i>	16 (5.59)	10 (3.49)
<i>Proteus sp.</i>	17 (5.94)	17 (5.94)
<i>Pseudomonas aeruginosa</i>	50 (17.48)	16 (5.59)
<i>Propionibacterium acnes</i>	56 (19.58)	10 (3.49)
<i>Pr.granulosum</i>	58(20.27)	53(18.53)
<i>Haemophilus influenzae</i>	61 (21.32)	33 (11.53)
<i>Bacteroid sp.</i>	52 (18.18)	11 (3.84)
<i>Corynebacterium sp.</i>	77 (26.92)	51 (17.83)

No. of isolates	959	744
Average (isolate: case)	3.35:1	2.6:1
No. of -ve growth cultures	16 (5.59)	39 (13.63)
No. of +ve growth cultures	270 (94.4)	247 (86.36)
Total no. of cultures	286	

*Staph. epidermidis* (17.13, 57.34)%, *Staph. xylosus* (2.79)% in each, *Staph. saprophyticus* (5.24, 10.48)%, *Staph. capitis* (2.79)% in each, *Staph. hominis* (22.37, 9.44)%, *Strept. pyogenes* (17.13, 9.79)%, *Strept. Faecalis* (23.07, 17.83)%, *Strept. Mutans* (14.68, 9.44)%, *E. coli* (25.52, 33.21)%, *Enterobacter sp.* (5.59, 17.83)%, *Klebsiella sp.* (3.14, 1.39)%, *Acinetobacter sp.* (5.59, 3.49)%, *Proteus sp.* (5.94)% in each,

*Pseudomonas aeruginosa* (17.48, 5.59)%, *Probionibacterium acnes* (19.58, 3.49)%, *Pr.granulosum* (20.27, 18.53)%, *Haemophilus influenzae* (21.32, 11.53)%, *Bacteroid sp.* (18.18, 3.84)% and *Corynebacterium sp.* (26.92, 17.83)%.

Table (2) illustrate antibiotic, susceptibility pattern of *Staph. aureus* isolated from eczematous lesions and healthy areas against various antibiotics. The percentages of sensitivity modes against antibiotics in each of above areas respectively same as follows: Ac (87.28, 66.0)%, B (86.7, 72.0)%, Cd (53.75, 70.0)%, Ch (70.52, 62.0)%, Co(24.85, 46.0)%, Do (31.21, 50.0)%, C (48.55, 64.0)%, E (17.91, 10.0)%, G (73.41, 100)%, M (46.82, 72.0)%, R (74.56, 78.0)%, T (49.13, 80.0)% and Va (89.59, 100)%.

It has been found highly significant differences ( $P < 0.01$ ) between three modes of antibiotic susceptibility within the same antibiotics and between these modes of various antibiotics. Table (3) determine the percentages of antibiotics resistance modes of *Staph aureus* according the biggest percentages as follows: ( $P < 0.05$ ) (36.41, 24.27, 16.76, 13.87 and 8.67)% of resistance to three, double, single, four and five or over of antibiotics respectively for eczematous lesions. (36.0, 22.0, 20.0, 14.0, and 8.0)% of resistance to double, single, three, four, and five or over of antibiotics respectively for healthy areas of ADE patients.

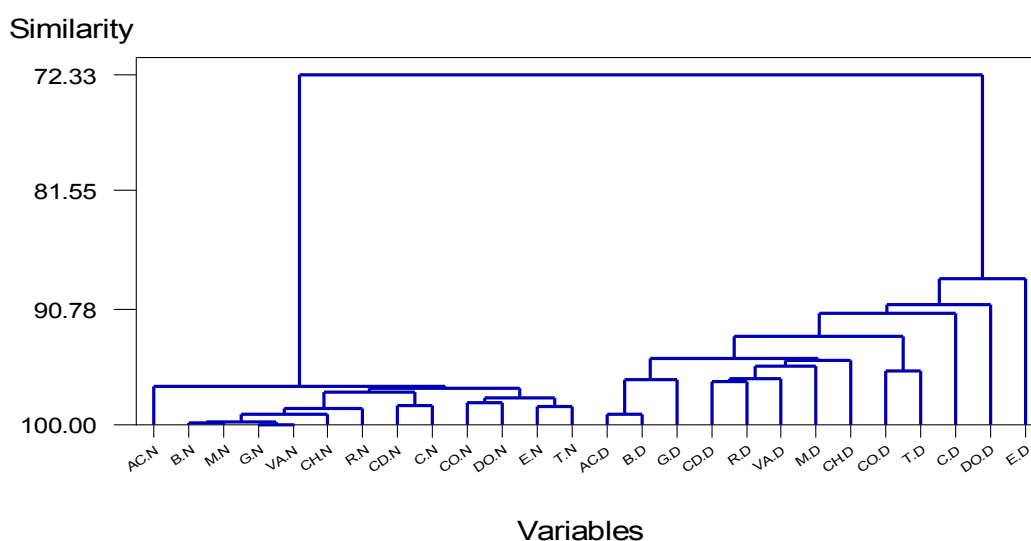
The statistical similarities between antibiotics affecting modes on *Staph aureus* showed in figure (1). It has been found that the antibiotic affecting on *Staph aureus* isolated from eczematous lesions are tightly correlated with each other in similarity ranged from 8.75-99.13)% and splitted from the same antibiotics affecting on *Staph. aureus* isolated from healthy area that also closed related with each others and have a similarity ranged from (97.0-100)%. ( $P < 0.001$ ).

**Table 2 :** Antibiotics Susceptibility Patterns Of *Staph AAureus* Isolated From Eczematous Lesions ( D ) And Healthy Area ( N ) Against Various Antibiotics . (  $P < 0.01$  )

ANTIBIOTICS	AREA	RESISTANCE	INTERMEDIATE	SENSITIVE
AC	D	13 (7.5)	9 (5.2)	151 ( 87.28 )
	N	17 (34.0)	-	33 ( 66.0 )
B	D	11 (6.35)	12 (6.9)	150 ( 86.7 )
	N	9 (18.0)	5 ( 10.0 )	36 (72.0)
CD	D	27 (15.6)	53 ( 30.63 )	93 (53.75)
	N	5 (10.0)	10 (20.0)	35 ( 70.0 )
CH	D	16 (9.24)	35 ( 20.23 )	122 ( 70.52 )
	N	8 (16.0)	11 ( 22.0 )	31 (62.0)
CO	D	104(60.11)	26 ( 15.02 )	43 ( 24.85 )
	N	15 (30.0)	12 ( 24.0 )	23 ( 46.0 )
DO	D	102 (58.9)	17 ( 9.82 )	54 ( 31.21 )
	N	21 (12.13)	4 ( 8.0 )	25 ( 50.0 )
C	D	53 (30.63)	36 ( 20.8 )	84 ( 48.55 )
	N	-	18 ( 36.0 )	32 ( 64.0 )
E	D	116 (67.05)	26 (15.02)	31 ( 17.91 )
	N	22 (44.0)	23 (46.0)	5 ( 10.0 )
G	D	-	46 (26.58)	127 ( 73.41 )
	N	-	-	50 ( 100.0 )
M	D	50 (28.9)	42 (24.27)	81 ( 46.82 )
	N	-	14 (28.0)	36 ( 72.0 )
R	D	25 (14.45)	19 (10.98)	129 ( 74.56 )
	N	4 (8.0)	7 (14.0)	39 ( 78.0 )
T	D	75 (43.35)	13 (7.51)	85 ( 49.13 )
	N	10 (20.0)	-	40 ( 80.0 )
VA	D	5 (2.89)	13 (7.51)	155 ( 89.59 )
	N	-	-	50 ( 100.0 )
TOTAL NUMBER OF CASES ( 286 )				
NO. OF POSITIVE CULTURES OF <i>STAPH AUREUS</i> FROM ECZEMATOUS LESIONS ( D ) : 173 ( 60.48 % )				
NO. OF POSITIVE CULTURES OF <i>STAPH AUREUS</i> FROM NORMAL AREA ( N ) : 50 ( 17.48 % )				
NO. OF NEGATIVE CULTURES OF <i>STAPH AUREUS</i> FROM ECZEMATOUS LESIONS ( D ) : 97 ( 33.9 % )				
NO. OF NEGATIVE CULTURES OF <i>STAPH AUREUS</i> FROM NORMAL AREA ( N ) : 197 ( 68.88 % )				
NO. OF TOTAL POSITIVE CULTURES FROM ECZEMATOUS LESIONS ( D ) : 270 ( 94.4 % )				
NO. OF TOTAL POSITIVE CULTURES FROM NORMAL AREA ( N ) : 247 ( 86.36 % )				
NO. OF TOTAL NEGATIVE CULTURES FROM ECZEMATOUS LESIONS ( D ) : 16 ( 5.59 % )				
NO. OF TOTAL NEGATIVE CULTURES FROM NORMAL AREA ( N ) : 36 ( 13.63 % )				

**Table3:** Illustrate modes of antibiotics resistance of *Staph. aureus* isolated from eczematous lesions and healthy / normal areas (  $P < 0.005$  )

Mode of antibiotics resistance	No. of isolates from eczematous lesions( % )	No. of isolates from healthy areas ( % )
Single antibiotic	29 ( 16.76 )	11 ( 22.0 )
Double antibiotics	42 ( 24.27 )	18 ( 36.0 )
Three antibiotics	63 ( 36.41 )	10 ( 20.0 )
Four antibiotics	24 ( 13.87 )	7 ( 14.0 )
Five or over antibiotics	15 ( 8.67 )	4 ( 8.0 )
No. of <i>Staph. aureus</i> isolates	173	50

**Figure 1 :** Statistical Similarities Between Antibiotics Affecting Mode On *Staph. Aureus* Isolated From Eczematous ( D ) And Healthy ( N ) Area Of Ad Patients . (  $P < 0.001$  )

## DISCUSSION

Our result revealed (94.4% and 86.36%) of positive cultures from total ADE cases (eczematous lesions and healthy areas) respectively. *Staph. aureus* was the predominant bacterial agent isolated from (60.48% and 17.48%) from same of above area respectively followed by other nineteenth bacterial types in various percentages of isolation.

Results of previous studies were evidenced our results interested on the importance of microbial factors on the pathogenesis of eczema and the therapeutical implications for the treatment of atopic dermatitis [6]. Since then, our knowledge concerning the complex interaction between microbes and skin inflammation has improved dramatically and today the Gram-positive bacterium, *Staph aureus* is recognized as an important triggering factors for the maintenance of skin inflammation and acute exacerbations of the genetically determined skin disease atopic dermatitis [14,15]. Many studies showed a heavy colonization of AD with *Staph. aureus*, this phenomenon suggests that *Staph. aureus* in Ad lesions influences the disease processes of AD [16,17]. Others evidenced that the skin of 100% of patients with ADE is colonized with *Staph. aureus*, up to 65%-90% of all *Staph. aureus* strains isolated from lesional skin have been shown to produce exotoxins with superantigenic properties [18,19].

Thirteenth antibiotics were tested against *Staph. aureus* some of these antibiotics were detailed from another studies, and others such as AC, B, Do, Co, R, and VA were not studied in any of atopic dermatitis investigations. Recent study suggest that in case of atopic dermatitis exacerbation with wide-spread weeping lesions, a systemic antibiotic treatment is warranted, with erythromycin no longer being recommended due to an increased resistance rate. In localized superinfected lesions the topical of an antibiotic-glucocorticoid preparation may offer advantages to the mere steroid

application [6]. Other study evidenced that as a significant number of *Staph. aureus* isolates are resistant to erythromycin, the antibiotics of choice are penicillin-resistant penicillins such as flucloxacillin, the oral cephalosporins such as cephalexin and fusidic acid, systemic antistaphylococcal antibiotics are particularly helpful in the treatment of acute exacerbations of AD due to diffuse *Staph. aureus* infection [20]. Due to the increased risk of bacterial resistance accompanying frequent use of antibiotics, it is important to combine antimicrobial therapy with effective skin care, since it is well established that the excoriated inflamed skin of ADE predisposes to *Staph. aureus* colonization [21]. Therefore, use of antibiotics therapy must be carried out with good skin hydration to restore skin barrier function and effective anti-inflammatory therapy to reduce overall skin inflammation and *Staph. aureus* colonization [22]. Exacerbating factors such as food allergens, inhalant allergens, irritant, and emotional triggers should be identified and eliminated because they can alter response to therapy. Since the major reservoir for *Staph. aureus* in the nose, intranasal antibiotics may be needed to reduce overall skin carriage of *Staph. aureus* [6,23].

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