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Prevalence of Staphylococcus Epidermidis and Biofilm-Associated Genes (icaA and icaD) in Children with Otitis Media: A Cross-Sectional Study in Al-Diwaniyah City, Iraq

Zainab Abdul Kareem Ataia[1]*

[1]Department of Microbiology, College of Education, University of Al-Qadisiyah, Iraq

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***Corresponding author:** Zainab Abdul Kareem Ataia
Department of Microbiology, College of Education, University of Al-Qadisiyah, Iraq

Abstract

Background: Ear infections rank among the most common health presentations in children attending clinics in Iraq and their microbiology continues to evolve. Staphylococcus epidermidis has transitioned from being disregarded as an innocuous commensal organism to a creeping opportunist drug-resistant pathogen, primarily due to its prolific biofilm-forming ability enabling the establishment of chronic and recurrent otitis media that are significantly more resistant to eradication. ***Objectives:*** The aim of this study was to identify the prevalence of S. epidermidis, evaluate biofilm genes carriage (icaA/icaD) and their associated factors among children with otitis media in Al-Diwaniyah. ***Methods:*** A total of 120 afresh suffering children age between 5-10 years with clinically diagnosed otitis media were enrolled in hospitals through the period between January and May 2024 in Al Diwaniyah City. Swab from the ear were cultured on blood agar and mannitol salt agar. Identification of isolates was performed by standard methods and confirmed with API Staph. Tubes were tested by PCR for icaA and icaD, and disk diffusion was performed to determine antibiotic susceptibility according to CLSI 2024. ***Results:*** Staphylococcus epidermidis was isolated from 76 out of the 120 children (63.3%). The predominant risk factor was poor nail hygiene; children with dirty nails had a much higher culture positivity (82.1% vs. 45.5%; OR = 5.42, 95% CI: 2.38–12.35, p <0·001). Bilateral ear involvement was also positively associated (p = 0.012). ***Conclusion:*** Staphylococcus epidermidis is an important pathogen in the pediatric otitis media in Al Diwaniyah and must be more than a contaminant. The close link with the bad hygiene of nails gives a very inexpensive and educable form of prevention for the ones who care for it. In addition, our antimicrobial data show that empirical penicillin therapy would otherwise be futile. Thus, it will be recommended that either ciprofloxacin or gentamicin is preferred concerning to the empirical therapy while waiting for definitive culture products.

Keywords: Staphylococcus epidermidis; otitis media; icaA; icaD; biofilm; antibiotic resistance; pediatric infection; Iraq.

1. INTRODUCTION

Otitis media (OM), noted as one of the most prevalent bacterial infections in children globally, is a major driver for antibiotic prescribing and has long been responsible for surgical intervention on more severe occasions [1]. It includes a range in ear diseases: acute otitis media (AOM), otitis media with effusion (OME) and chronic suppurative otitis media (CSOM). Similar to many developing countries, children 5–10 years in Iraq are particularly heavily affected by this [2].

Your typical microbiology class still teaches the well-worn list of bacterial offenders Streptococcus pneumoniae, Hemophilus influenzae, Moraxella catarrhalis and rightly so. But it is increasingly incomplete. For nearly two decades, coagulase-negative staphylococci - particularly Staphylococcus epidermidis - have appeared in culture reports from children with chronic and healthcare-associated otitis media [3, 4]. The organism that was once dismissed as a contaminant is now acknowledged as a true, albeit opportunistic, pathogen [5]. The ultimate reason *Staphylococcus epidermidis* has become clinically relevant comes from a single word: biofilm. Once this organism colonizes a mucosal surface and secretes its polysaccharide matrix, it will be much more resistant to both drug- and immune-associated attacks. This process is regulated by the ica operon. E.g. rickettsia surface proteins/adhesins ecoetyolate and ecotype which is the genomic basis for

biofilm of *Staphylococcus aureus* [6]. As the alleles (icaB, icaC) are genes that encode polysaccharide intercellular adhesin (PIA) synthases respectively from clumping and adhesion of bacterial cells itself will glue them together to become a "coated" full aggregate where anchored in place. Thus, strains harboring both genes are typically believed to have phenotypically full biofilm-forming ability with in vivo associations with persistent and antibiotic-resistant infections

Two other factors deserve mention. [7] For those involved in skin particularly, young children's nail hygiene our new data suggest that it should be taken much more seriously as a factor. Staphylococcus epidermidis colonises the subungual space effortlessly, and children are more than capable of independently inoculating their ear canals by touching their ears with dirty hands [8]. In contrast, that rural versus urban setting may drive both what type of exposures are present and the overall access to preventive health services [9].

The next layer of complication is antibiotic resistance. The strains of the methicillin-resistant Staphylococcus epidermidis (MRSE), usually carrying the mecA gene, are described all over the world, and it seems to arise in the community [10]. In Al-Diwaniyah City we had no local data regarding any of this; not the prevalence, or biofilm gene carriage and not the resistance patterns. This study was designed to close that gap.

2. MATERIALS AND METHODS

2.1 Study Design and Population

The sample size was determined a priori to ensure sufficient statistical power. Based on an expected prevalence of S. epidermidis of approximately 60% (p = 0.60) in pediatric otitis media cases, a desired precision of ±10% (d = 0.10), and a 95% confidence level (Z = 1.96), the minimum required sample size was calculated using the formula: n=Z 2 P(1−P)/d 2. This yielded a requirement of approximately 92 participants. To account for potential dropouts or incomplete clinical records, the target enrollment was increased to 120 children.

2.2 Data Collection

A structured questionnaire recorded age, sex, urban or rural residence, which ear(s) were affected, and nail hygiene. Nail hygiene was assessed visually by nursing staff and called clean or dirty a simple binary classification. To minimize potential observer bias, nursing staff were provided with a standardized visual definition of 'dirty' (defined as the presence of visible debris or dark staining under the subungual space) prior to the study. However, we acknowledge this assessment remains subjective.

2.3 Sample Collection

Ear swabs were taken aseptically under direct otoscope visualization by clinicians. Samples reached the microbiology laboratory within two hours and were processed immediately. Delays beyond this window were not accepted.

2.4 Isolation and Identification

Swabs were plated on blood agar (Oxoid, UK) and mannitol salt agar, then incubated aerobically at 37°C for 24 to 48 hours. Suspect colonies white to opaque, non-hemolytic, Gram-positive cocci in clusters, catalase-positive, coagulase-negative were taken forward as coagulase negative staphylococci. Final identification as S. epidermidis required novobiocin susceptibility plus confirmation by API Staph (bioMérieux, France).

2.5 DNA Extraction

Genomic DNA was extracted using the QIAamp DNA Mini Kit (Qiagen, Germany). We added a lysozyme step before column lysis to handle the staphylococcal cell wall. Purity was checked by Nano Drop 2000; samples outside an A260/A280 ratio of 1.8–2.0 were re-extracted.

2.6 PCR Detection of icaA and icaD

Each gene was amplified separately. Primer sequences (GenBank accession U43366):

Table 1: Primer sequences and physicochemical characteristics used for PCR amplification of biofilm-associated genes

Gene	Primer Direction	Primer Sequence (5′–3′)	Amplicon Size (bp)	Tm (°C)	GCContent (%)	Reference
icaA	Forward	ACAGTCGCTACGAAAAGAAA	103	58	45	Arciola *et al.,* 2006
	Reverse	GGAAATGCCATAATGACAAC		57	45	
icaD	Forward	ATGGTCAAGCCCAGACAGAG	198	60	55	Arciola *et al.,* 2006
	Reverse	CGTGTTTTCAACATTTAATGCAA		58	43	

Reaction mix (25 µL): 2 µL template, 1 µL each primer at 10 pmol/µL, 12.5 µL 2× PCR Master Mix (Thermo Scientific), water to volume. Cycling on Applied Biosystems Veriti: 95°C × 5 min; 35 cycles of 95°C × 30 s / 55°C × 30 s / 72°C × 45 s; final 72°C × 7 min. Products were run on 1.5% agarose-EtBr gel at appropriate voltage and sized against a 100 bp ladder under UV.

2.7 Antimicrobial Susceptibility Testing

Medium: Disk diffusion on Mueller–Hinton agar (Oxoid, UK) according to CLSI 2024 Inoculum: 0.5

McFarland. Carried out the disk diffusion for penicillin (10 U), oxacillin (1 µg), erythromycin (15 µg), gentamicin (10 µg), ciprofloxacin (5 µg) and vancomycin [30 ug]. The zone diameters were read at 18–24 hours at 35 °C and interpreted as susceptible (S), intermediate (I) or resistant (R) according to CLSI breakpoints.

2.8 Ethical Considerations

The study was carried out in accordance with the Declaration of Helsinki. IRB approval was obtained from Al Qadisiya University, IRB/2025. All participants (parents or guardians of participants) gave informed consent. All patient information was treated confidentially and anonymized prior to analysis.

2.9 Statistical Analysis

We used SPSS v26 (IBM Corp, Armonk, NY). We performed Chi-square tests to assess the association between *Staphylococcus epidermidis* isolation and demographic or clinical variables, with Fisher's exact test applied where cell counts were less than 5. Statistical significance was defined as $P < 0.05$ throughout.

3. RESULTS

3.1 Patient Demographics and S. epidermidis Prevalence

Ear swab samples was collected (120). *Staphylococcus epidermidis* is isolat from 76 of them a prevalence rate of 63.3%. This is summarized in Table 2 by patient characteristics. It didn't matter the age group or sex. Rural residence emerged as significant (71.7% versus 56.9% urban, $p = 0.047$). Unilateral involvement was also associated (84.7% vs. 63.8% bilateral, $p = 0.035$). However, the most remarkable discovery turned out to be nail hygiene: children with dirty nails had an isolation rate of 82.1%, compared with 45.5% in those with clean ones ($p < 0.001$). That gap is hard to ignore.

Table 2: Demographic and clinical characteristics of study participants and *Staphylococcus epidermidis* prevalence (N = 120)

Variable	Category	Total N (%)	S. epi + N (%)	S. epi − N (%)	χ^2	p-value
Age (years)	5–7	65 (54.2)	40 (52.6)	25 (56.8)	0.178	0.673
	8–10	55 (45.8)	36 (47.4)	19 (43.2)		
Gender	Male	67 (55.8)	43 (56.6)	24 (54.5)	0.099	0.753
	Female	53 (44.2)	33 (43.4)	20 (45.5)		
Residence	Urban	72 (60.0)	41 (53.9)	31 (70.5)	3.946	**0.047***
	Rural	48 (40.0)	35 (46.1)	13 (29.5)		
Affected ear(s)	Unilateral	77 (64.2)	42 (55.3)	35 (79.5)	6.287	**0.012***
	Bilateral	43 (35.8)	34 (44.7)	9 (20.5)		
Nail hygiene	Clean	64 (53.3)	29 (38.2)	35 (79.5)	18.023	**<0.001***
	Dirty	56 (46.7)	47 (61.8)	9 (20.5)		

**** p < 0.05 (statistically significant). Staphylococcus epidermidis.***

3.2 PCR Detection of icaA and icaD Genes

PCR was performed on preserved isolates for all 76 confirmed cases. As depicted in Figure 1, icaA and icaD produced clean bands as expected (103 bp and 198 bp respectively). Gene distribution is summarized in table 3. The presence of icaA was detected in 52 isolates (68.4%) and icaD in 54 (71.1%). Strains that had both genes present simultaneously accounted for sixty three percent of the isolates, suggesting that a complete PIA-synthesis pathway was intact in most strains. Only 6 isolates (7.9%) were negative for both.

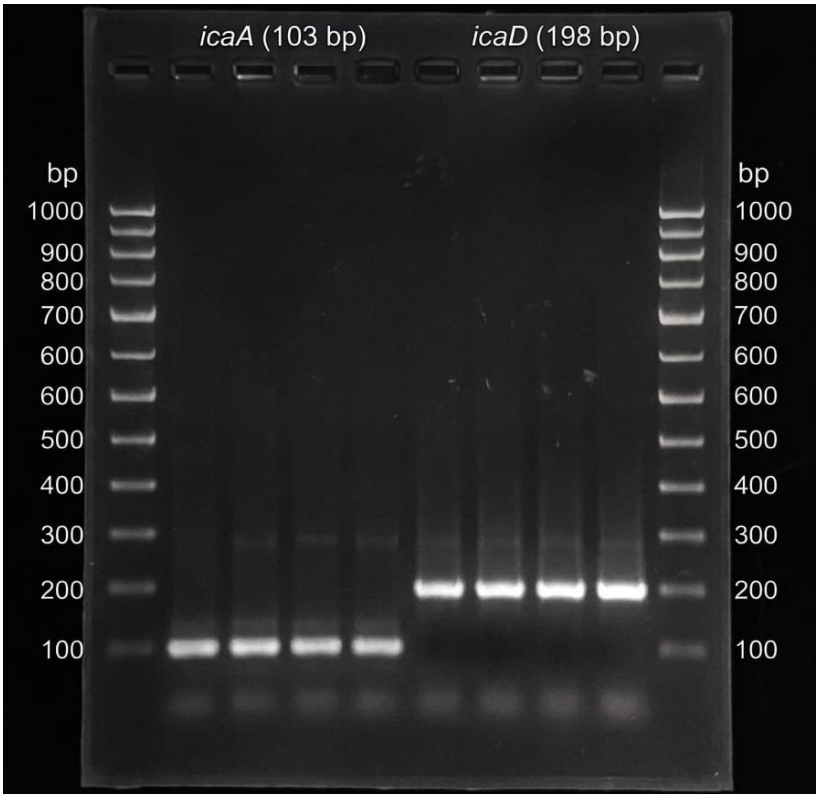

Figure 1: Agarose gel electrophoresis of PCR products for icaA (103 bp) and icaD (198 bp) from representative S. epidermidis clinical isolates. Lanes include 100 bp DNA ladder (leftmost and rightmost) and positive samples.

Table 3: Distribution of icaA and icaD genes among *S. epidermidis* isolates (N = 76)

Gene Status	Number of Isolates	Percentage (%)
icaA positive only	4	5.3
icaD positive only	6	7.9
Both icaA and icaD positive	48	63.2
Both genes negative	6	7.9
Total icaA positive	**52**	**68.4**
Total icaD positive	**54**	**71.1**

PCR product sizes: icaA = 103 bp; icaD = 198 bp. Confirmed by gel with 100 bp ladder.

3.3 Antimicrobial Susceptibility Profiles

We can see the complete view of resistance in Table 4. Inevitably a few numbers catch the eye. Near-total penicillin resistance, (85.5%) Oxacillin resistance at 55.3% therefore, indicates that more than half of the isolates were MRSE [19]. Between ~ 69% of the callers requested amoxicillin and it also found, Erythromycin, was almost as bad at 71.1%. Gentamicin (44.7%) and ciprofloxacin (36.8%) conferred greater activity, but neither are usable as empirics without further dissection. Vancomycin: all 76 isolates susceptible that lasted. Carriage of both ica genes and multi-drug resistance was significantly associated with p = 0.018.

Table 4: Antimicrobial susceptibility patterns of S. epidermidis isolates (N = 76)

Antibiotic (disk load)	Susceptible N (%)	Intermediate N (%)	Resistant N (%)	Resistance Rate (%)
Penicillin (10 U)	8 (10.5)	3 (3.9)	65 (85.5)	**85.5**
Oxacillin (1 µg)	32 (42.1)	2 (2.6)	42 (55.3)	**55.3**
Erythromycin (15 µg)	18 (23.7)	4 (5.3)	54 (71.1)	**71.1**
Gentamicin (10 µg)	37 (48.7)	5 (6.6)	34 (44.7)	**44.7**
Ciprofloxacin (5 µg)	41 (53.9)	7 (9.2)	28 (36.8)	**36.8**
Vancomycin (30 µg)	76 (100.0)	0 (0.0)	0 (0.0)	0.0

CLSI 2024 breakpoints applied throughout. MRSE = methicillin-resistant, defined by oxacillin resistance. ica+/MDR association: p = 0.018.

4. DISCUSSION

We have reinforced the comparative context in the Discussion section (Section 4.0) by providing actual prevalence estimates from regional studies. In this paper, we present data to specifically benchmark our 63.3% isolation rate in comparison with other findings from Al-Hillah [12]. and the current available literature from Egypt to allow the better interpretation of our results in a regional epidemiological context. [13]

4.1 The Nail Hygiene Signal

We found the nail hygiene finding to be the most alarming. The 82.1% isolation rate when children were with dirty nails compared to a 45.5% rate for clean nails is an enormous difference (p-value <0.001 coin toss doubtful). The biology is simple: ***S. epidermidis*** colonizes the subungual space, children constantly insert their fingers into and around their ears, and self-inoculation of the canal ensues [14]. Going into the study this was not a new hypothesis, but nice to have local evidence. This result is actually quite promising from a public health perspective. Even trimming nails and hand washing cost no money or medical infrastructure. If hygiene education delivered in schools and in the context of well-child visits moves even a small percentage of children from the dirty nail column to the clean-nail column, some cases of S. epidermidis–associated otitis media would presumably be prevented as well.

4.2 Rural Residence and Bilateral Involvement

In our sample, a larger proportion of rural children were culture-positive (71.7% vs 56.9%, p = 0.047). We can only guess at these things - lack of sanitation access, household crowding, delayed care seeking, higher stage disease at presentation ,but cannot disentangle from our data.

This is a trend we plan to continue tracking with more detailed exposure data [15]. Interestingly, isolation was higher for bilateral ear involvement tracking with (78.9% vs 54.5%).

All that is, unless you are infected with a biofilm-forming strain of this bacteria-biofilm strains seem to be less likely to focus on sealed up infections in locations where they belong. It remains debatable whether bilateral disease in those children appears to be due to more virulent strains, wider initial colonization or merely delay treatment that we cannot elucidate with this design.

4.3 What the ica Genes Mean Clinically

Detection of icaA in 68.4%, icaD in 71.1%, both together in the same isolate was present at the rate of only 63.2%. These figures imply that virtually all strains now extant have functional machinery capable of PIA synthesis [6, 7, 15]. If grown as a biofilm, which is the way many infections occur in the body biofilm-positive strains can better tolerate antibiotics than should be predicted from their planktonic counterparts; penetration of most drugs is reduced by the matrix they produce, metabolic activity decreases and slow-growing cells are known to be much harder to kill. This explains partly why children with chronic otitis media sometimes do not respond to one course of antibiotics after another [16].

That includes carrying ica genes in addition with multidrug resistance (p = 0.018). Biofilms are an ecosystem that promotes horizontal gene transfer bacteria are close together, membranes connect, plasmids move. In this context, resistance genes can disseminate easily [20]. We are not saying that biofilm genes lead to resistance this is a cross-sectional snapshot and therefore no inference can be made about causation. But the correlation exists, and is worth making note of.

4.4 The Resistance Figures and Their Practical Consequences

So, lets set the record straight on that 55.3% MRSE rate. Thus, if a clinician in Al-Diwaniyah decides to treat empirically with amoxicillin or ampicillin for a child that has uncomplicated otitis media: there is almost 50% chance the drug will work. Beta-lactam therapy as first-line treatment is nearly ineffective (85.5% already have penicillin resistance) due to these strains [17]. This threshold of 71.1% resistance to erythromycin negates the historic rescue of macrolides for penicillin-allergic patients [18]. We believe gentamicin and ciprofloxacin are effective against the bulk of strains, but should never be used empirically in pediatric outpatient ear infections due to resistance being at levels higher than would usually be localized in this population. Agar dilution results: Vancomycin (fully active against all (76) isolates; but collection not a suitable community drug and kept for life threatening systemic infection without alternative [19]. Local prescribers are reminded that empirical therapy should always be guided by local susceptibility data rather than treated with cookie-cutter treatment guidelines written for other settings.

4.5 Limitations

So, we would like to be clear about what this study cannot tell us. Cross-sectional designs portray a snapshot, not an ongoing process; hence we do not know about illness duration or treatment response in children with *S. epidermidis*. A main limitation is the global subjective binary classification of nail hygiene. Observer bias cannot be completely ruled out without interrater reliability data (a Kappa coefficient). Future work should use well-validated hygiene scoring tools to increase specificity. Moreover, selection bias is a possibility since hospital cases are likely to have greater severity of symptoms than community cases (prevalence figures may be inflated). In addition, the sampling period (January–May) may not include seasonal effects depending on the otitis media season for the full year.

5. CONCLUSION

Staphylococcus epidermidis is a significant and frequently isolated pathogen in pediatric otitis media in Al-Diwaniyah City, present in 63.3% of cases. The high frequency of icaA and icaD in these clinical isolates confirms genuine virulence potential. Poor nail hygiene was the strongest risk factor we found, and unlike resistance genes or biofilm machinery it is directly modifiable through simple hygiene education targeting children and caregivers.

The antimicrobial resistance data carry a clear clinical message: empirical beta-lactam prescribing for pediatric otitis media in this setting will often miss the mark. Local susceptibility data should guide treatment. Vancomycin remains active but is not appropriate for outpatient use. There should be an emphasis in future research on evaluating the phenotypic expression of biofilms using the crystal violet method with the current S. epidermidis isolates. This would be an inexpensive, practical way to establish the presence of biofilm expression and phenotype with respect to the gene positive strains that have been identified in this study. A retrospective clinical evaluation of the enrolled child will help to evaluate the patterns of recurrence and long-term clinical outcome associated with infection. Finally, given the strong correlation seen between nail hygiene and bacterial isolation in this study, it would likely be most beneficial to conduct a clustered randomized intervention study in the Al-Diwaniyah primary school population that assesses nail hygiene education for public health impact.

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Conflict of Interest

The author declares no conflict of interest

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