Editorial

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# Biofilm Formation and Antimicrobial Resistance in *Enterococcus*

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*Enterococcus faecalis* and *Enterococcus faecium* have become particularly important etiological pathogens of nosocomial infections, as they can survive in hospital environments and colonize in patients. They cause problems such as urinary tract infections, hepatobiliary sepsis, endocarditis, surgical wound infections, bacteremia, and sepsis [1]. For *Enterococcus* spp., intrinsic resistance exists against several antimicrobial agents such as aminoglycosides and β-lactams. In fact, aminoglycosides, cephalosporins, clindamycin, and trimethoprim/sulfamethoxazole are not clinically effective in controlling *Enterococcus*. Because of the poor activity of several antimicrobial agents against enterococci due to this intrinsic resistance, a combination therapy using cell wall-active agents (β-lactams) and aminoglycosides is sometimes recommended. Vancomycin-resistant enterococci and their impacts in nosocomial settings are of considerable concern. This concern includes the emergence of acquired vancomycin resistance among clinical enterococcal isolates.

Bacterial biofilms are surface-attached communities of slow-growing or non-replicating bacteria tolerant to conventional antibiotic therapies. Biofilms also contribute to bacterial virulence in several ways. For example, adherence, an early step in biofilm formation, allows bacteria to bind to catheters (*e.g.*, urinary and intravascular catheters), biliary stents, and silicone gastrostomy devices. Additionally, biofilms contribute to bacterial resistance to antibiotics and phagocytosis, making their eradication extremely difficult [2]. Therefore, biofilm formation may be of particular importance in the development of endocarditis, endodontic or urinary infections, or implant- and other medical device-associated infections [3, 4].

The ability to form biofilms is among the prominent virulence properties of *Enterococcus*. This ability allows colonization of inert and biological surfaces while protecting against antimicrobial substances and mediating adhesion to host cells. Enterococci are known for their ability to form biofilms. These biofilms are populations of cells irreversibly attached to various biotic and abiotic surfaces and encased in a hydrated matrix of exopolymeric substances, proteins, polysaccharides, and nucleic acids [2]. The biofilm structure provides an optimal microenvironment for growth and facilitates transmission of mobile genetic elements between bacteria [5]. Enterococci frequently form biofilms on stents and other artificial devices, necessitating the long-term administration of antibiotics when removal of the device is not possible. However, the underlying

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mechanisms of biofilm formation and virulence in enterococci in the urinary tract are controversial. Biofilm-forming *E. faecalis* has been associated with oral diseases such as caries, endodontic infections, periodontitis, and peri-implantitis [6]. Therefore, biofilm eradication using antibiotic therapy is important for patients with enterococcal infection. One study has reinforced the contribution of biofilm formation to the antimicrobial resistance in enterococci [7]. Quinupristin/dalfopristin, tetracycline, and rifampin may be more effective against biofilm producers than non-producers [7]. Bacteria-forming biofilms have an antimicrobial-resistant phenotype and are difficult to eradicate. Therefore, combination therapies are recommended for the treatment of bacterial biofilm-associated infections [8]. Interestingly, vancomycin applied at sub-minimal inhibitory concentrations inhibited biofilm formation in strong-biofilm-forming isolates [2].

There are some reports regarding the relationship between biofilm-forming phenotypes and genotypes; detecting the genes associated with biofilm formation would aid in predicting which clinical isolates are likely to be problematic [1, 7, 9]. A recent study of genes involved in biofilm formation and their role in enterococcal infections has attracted considerable interest [7]. Researchers have evaluated the association between biofilm-related genes and biofilm formation in *Enterococcus* strains. Biofilm formation-associated genes included aggregation substance (*agg*), *E. faecalis* endocarditis-associated antigen A (*efaA*), *E. faecalis* adhesion of collagen (*ace*), gelatinase (*gelE*), and extracellular surface protein (*esp*) [2, 10]. Agg was significantly enriched in isolates with moderate and strong biofilm formation characteristic in Hashem's study [2]. Esp is a cell wall-associated protein that has been implicated as a significant factor contributing to the colonization and persistence of bacteria in the urinary tract and to biofilm formation [10]. GelE, a zinc metallo-protease, may be involved in the process of biofilm formation [5]. However, individual biofilm-related genes, such as *esp*, *asa1*, *ebpR*, *gelE*, and *cyl*, do not appear to be sufficient for biofilm formation in enterococci [7, 9].

In summary, biofilm formation is associated with antimicrobial resistance in *Enterococcus* isolates. In addition, bacteria that can form biofilms have an antimicrobial-resistant phenotype and are difficult to eradicate. Biofilm formation is complex and depends on various factors in *Enterococcus* strains. Further studies should explore the mechanisms underlying biofilm formation and inhibition to better treat patients with biofilm-forming bacterial infections.

## Conflicts of Interest

No conflicts of interest.

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