

Clinical Importance of Polymicrobial Infections and Biofilms and Eradication Methods

Maria Busi*

Department of Infectious Disease Research, George Mason University, Manassas, VA 20110, USA

Abstract

Biofilms are cell populations that are growing in a controlled way and displaying tolerance to harsh surroundings. Due to the recurring nature of the infections and the rise of antibiotic resistance, biofilm-related illnesses are challenging to manage. Polymicrobial or mixed species interactions, as those seen in cystic fibrosis, otitis media, dental caries, and chronic wound infections, contribute to the majority of microbial illnesses. Based on in vitro and in vivo models, as well as various therapeutic approaches for polymicrobial biofilms, this review focuses on the polymicrobial interactions among bacterial-bacterial, fungal-fungal, and bacterial-fungal aggregations. Research on anti-microbials benefits greatly from understanding the processes of polymicrobial interactions and microbial diversity in chronic illnesses. We have talked about how metagenomic methods can be used to analyse polymicrobial biofilms. the exceptional Review of advancements in polymicrobial research, particularly the use of metagenomics and model systems for the early detection, prevention, and management of infections.

Keywords: Biofilms • Polymicrobial • Chronic infections • Metagenomics • Prevention

Introduction

A community of microorganisms called a biofilm is shielded by an extracellular matrix from the human immune system, antimicrobials, external environmental stimuli, cooperative metabolism, and community-coordinated gene expression. In biological processes, biofilms rather than planktonic forms of bacteria are frequently seen. Biofilms can develop between distinct kingdoms, with a single species, or with multiple species. The main cause of microbial infections is biofilm or polymicrobial biofilm, which includes a variety of bacteria, fungi, or viruses. Mixed biofilm communities participate in a number of environmental processes, including denitrification, biodegradation, and bioremediation. Diverse oxygen-dependent nitrifiers and anaerobic denitrifiers coexist at varying levels of biofilm in wastewater. The creation of mixed-species biofilms goes through five crucial stages [1,2].

Initial adaptable adhesion to the substrate is one of the phases of mixed-species biofilm development. stable adhesion, development of microcolonies, maturation, and dispersion. Time, microbial interactions, and environmental signals all influence how mature biofilms develop and become entangled. Microbial infections caused by biofilms are becoming a serious danger to public health [3]. This review paper investigates new updates on polymicrobial biofilm pathogens, interactions between and within microorganisms that increase biofilm formation, and model systems to study polymicrobial biofilms in light of the rising incidence of polymicrobial biofilm infections. We have also looked at recent trends in polymicrobial biofilm mitigation, such as quorum sensing inhibitors, nanoparticle- and nanoconjugate-mediated therapy, antimicrobial photodynamic therapy (aPDT), phage therapy, combinatorial probiotics, etc., as well as metagenomic approaches to the surveillance of polymicrobial biofilms [4].

***Address for Correspondence:** Maria Busi, Department of Infectious Disease Research, George Mason University, Manassas, VA 20110, USA; E-mail: Mariabusi24@gmail.com

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Antimicrobial resistance in polymicrobial biofilms

The EPS matrix's components include a support system for microbial cells' adhesion and immobilisation as well as protection from environmental stressors and antimicrobial agents. The content of EPS differs between species and also depending on the environment. According to reports, *P. aeruginosa* polysaccharide (Psl), potentially by electrostatic forces, confers resistance against colistin, polymyxin B, tobramycin, and ciprofloxacin. A similar effect is also seen in non-psl producers like *Escherichia coli* and *S. aureus* [5]. Multispecies biofilm has a different matrix composition than mono-species biofilm, which confers higher resistance. By secreting exopolysaccharide, 1,3-glucan, *Candida albicans* shields *S. aureus* from vancomycin therapy, while *Streptococcus mutans* generates glucans that shield *Candida* from fluconazole in mixed biofilms. Commensal-like interactions: One community member creates the ideal environment for the survival of another by other family members in an unfriendly setting [6].

Elias and Banin (2012) provided an example of it when they discovered that when the oxygen content is high, the presence of aerobes improves the conditions for the survival of anaerobes. Physiological modification by nearby species: According to a paper, *S. aureus* could exploit the *P. aeruginosa* compound HQNO (4-hydroxy-2-heptylquinoline-N-oxide) to become more resistant to antibiotics (vancomycin & tobramycin). The small-colony variations (SCV) of *S. aureus* become resistant after prolonged contact with HQNO or *P. aeruginosa*. bacteria that produce -lactamases: -lactamases are the enzymes that break down -lactam antibiotics (cell wall-targeting drugs). The cell itself and other cells in the polymicrobial biofilm are successfully protected by the inactivation of -lactam antibiotics. For instance, co-culturing *Streptococcus pneumoniae* (a non-producer of -lactamases) with *Haemophilus influenzae* (a producer of -lactamases) raises the MIC/MBC of amoxicillin (a -lactam antibiotic) [7].

Polymicrobial infections

One microorganism's colonisation of a host can affect how other microbes colonise it. By weakening the immune system, killing epithelial cells, and increasing the production of chemicals necessary for bacterial adherence, viruses in respiratory tract illnesses aid bacterial infection. Otitis media, a bacterial middle ear infection, is also a result of these viruses. Illustration polymicrobial biofilm infections affecting several body regions. The most prevalent oral infection, dental caries, affects between 60 and 80 percent of both children and adults. The condition film, which is composed of proteins and carbohydrates from saliva, attaches to the tooth surface to form the biofilm of

microorganisms. Studies showed that roughly 48 hours are necessary for the biofilm formation of individual cells [8].

The most frequent causative agent of dental caries, *S. mutans*, mostly attaches via glucosyltransferases and starts coaggregating other bacteria, creating a polymicrobial biofilm. Such a biofilm suppresses the host signalling pathways, preventing the host immunological response. The Eustachian tube, which is situated between the tympanic membrane and the inner ear, is impacted by otitis media or middle ear infection. It is a childhood illness that infrequently results in a person's death. Patients who suffer from a serious infection lose their capacity to hear. Commensals like *S. pneumoniae*, *H. influenzae*, and *Moraxella catarrhalis*, together with viruses like the influenza A virus, Adenovirus, Rhinovirus, and Respiratory Syncytial Virus (RSV), are what cause middle ear infections. These bacteria species can induce monomicrobial infections, which can have serious consequences, but they can also put the host at risk for polymicrobial infections [9].

Discussion

Chhibber and colleagues used phage therapy to reduce the polymicrobial biofilms of *P. aeruginosa* PAO and *K. pneumoniae* B5055. In the bacteriophage therapy, the depolymerase-encoding phage KPO1K2 damaged the *K. pneumoniae* biofilm matrix, enabling the phage Pa29 to reach *P. aeruginosa* biofilms. Since Pa29 is a phage without depolymerase activity, xylitol (a natural sugar alcohol) and other anti-biofilm agents worked together synergistically to suppress the formation of polymicrobial biofilms. The infections brought on by mixed-species biofilms were lessened by several phage-antibiotic combinations. The Pakpunavirus phage vB PaM EPA1 and various antibiotic classes, including gentamicin, kanamycin, tetracycline, chloramphenicol, erythromycin, ciprofloxacin, and meropenem, all demonstrated biofilm inhibitory action. *P. aeruginosa* and *S. aureus*' polymicrobial biofilms are frequently difficult to remove by due to their resistance to widely accessible medicines. Since of this, phages are thought to be the most effective treatment for polymicrobial illnesses because their combination can penetrate biofilms, making them more susceptible to antibiotics [10].

Conclusion

Microorganism populations known as biofilms create exopolymer compounds to defend themselves from the environment. Polymicrobial biofilms are created as a result of interactions between or within multiple kinds of bacteria. In their habitats, polymicrobial biofilms display antagonistic, cooperative, or commensal relationships. The pathogenesis of both acute and chronic infections is significantly influenced by the specialised polymicrobial interactions. Antibiotics are no longer effective against mono-species biofilms and biofilms seen in interactions between several microbes. The severity of polymicrobial infections has grown recently due to the widespread appearance of antibiotic-resistant strains in polymicrobial biofilms. Understanding microbial variety and the nature of interactions is made possible by insights into the in

vitro and in vivo biofilm models of polymicrobial illnesses. Currently, innovative and efficient anti-microbial therapies have the It is imperative to remove the polymicrobial biofilms formed by various microorganisms. We also talked about how anti-microbial research is evolving to reduce bacterial-bacterial, bacterial-fungal, and fungal-fungal interactions and the infections they cause. The authors of this review place a strong emphasis on the use of culture-independent methods, particularly metagenomics, in the detection and avoidance of polymicrobial biofilms.

Acknowledgement

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Conflict of Interest

None.

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