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(REVIEW ARTICLE)

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Review: Quorum sensing mechanism between *Streptococcus mutans* and *Candida albicans* in the pathogenesis of dental caries

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Abstract

Background: Dental caries is one of the most common oral diseases that affects all age groups worldwide. Caries is a slow progressing chronic disease characterized by localized tooth decay. Caries arises from interactions on the tooth surface between microorganisms, microorganism products, host (saliva) and diet (sugar), which leads to the formation of pathogenic biofilms, or dental plaque, and causes tooth decay. *Streptococcus mutans* (*S. mutans*) bacteria are the main microorganisms that play a role in causing dental caries. The results of several clinical studies indicate that, apart from *S. mutans*, the fungus *Candida albicans* (*C. albicans*) is often detected in high numbers in caries. The existence of these two species in one biofilm allows the two species to communicate between cells which is called quorum sensing.

Objective: To determine the Quorum sensing mechanism between *S. mutans* and *C. albicans* in the development of the pathogenesis of caries.

Methods: 3 databases namely PUBMED, Web of Science and Scopus, were used to search for articles according to predetermined inclusion and exclusion criteria.

Results: quorum sensing between *S. mutans* and *C. albicans* in the same biofilm can change gene expression in both species of microorganisms, as well as increase the growth of both species of microorganisms.

Conclusion: Symbiosis between *S. mutans* and *C. albicans* in the oral cavity is very detrimental to humans because it can exacerbate the buildup of acid which results in caries.

Keywords: *Streptococcus mutans*; *Candida albicans*; Quorum sensing; Caries; Biofilm

1. Introduction

The human oral cavity has an ecosystem that can support the growth of various kinds of microorganisms such as bacteria, fungi, and protozoa(1). The microorganism community lives on all surfaces of the oral cavity by forming multispecies biofilms. In these multispecies biofilms, microorganisms interact with one another. The interactions between these microorganisms can be synergistic or antagonistic(2). The development and formation of biofilm can be disturbed by some changes in orall cavity (3). If there is a disturbance of the balance in the ecosystem of the oral cavity, disease can arise due to population shifts. In this case the overrepresentation of a pathogenic species contributes to the emergence and development of diseases in the oral cavity such as caries and periodontal disease(4).

Dental caries is one of the most common oral diseases that affects all age groups worldwide. Caries is a slow progressing chronic disease characterized by localized and irreversible tooth decay. Until now, caries is still a health problem in the

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world, especially in children (5). Caries arises from interactions on the tooth surface between microorganisms, microorganism products, host (saliva) and diet (sugars), which leads to the formation of pathogenic biofilms, or dental plaque, and causes tooth decay. Bacteria *Streptococcus mutans* is considered as the main microorganism that plays a role in causing dental caries, because its presence is found in many biofilms on tooth surfaces (6).

Streptococcus mutans (*S. mutans*) is a gram-positive bacterium which is one of the normal oral flora microorganisms ((5,7). The human oral cavity is a natural habitat for *S. mutans*, more precisely in dental plaque, a multispecies biofilm that forms on the hard tissue of teeth. Recent study suggests that a high prevalence of *S. mutans* in dental biofilms is almost always accompanied by the presence of *Candida albicans* (*C. albicans*) species. *C. albicans* is one of the normal human microflora commonly found in the mucosal walls of the gastrointestinal (GI), respiratory, and genitourinary tracts of humans. *C. albicans* is generally a commensal and harmless but can turn into an opportunistic organism causing oral candidiasis, one of the most common fungal infection, in conditions where individuals are immunodeficient (8,9).

The existence of these two species in one biofilm allows for communication between the two species. This communication is called quorum sensing, which is a form of communication between cells using inducer molecules. This review article aims to review in a narrative way how Quorum Sensing between *S. mutans* and *C. albicans* in the development of caries pathogenesis.

2. Methods

2.1. Study Design

This review article written using narrative review study design. Three databases used in this review article are PUBMED, Web Of Science, and Scopus.

2.1.1. Inclusion Criteria

1. Articles published within the last 10 years (2012-2022)
2. Articles written using english language
3. Articles are full-text

2.1.2. Exclusion Criteria

1. The article is not in accordance with the topic of the review
2. Articles published more than the last 10 years
3. Articles use languages other than English and Indonesian

3. Results and discussion

The results of several articles related to quorum sensing between *S. mutans* and *C. albicans* include:

3.1. Growth of *S. mutans* and *C. albicans* in one biofilm

Based on the 7 articles that have been analyzed, there are 3 articles that show an increase in the growth of *S. mutans* bacteria. In the study of Sztajer et al., (10) showed that biofilms formed by *S. mutans* and *C. albicans* had almost twice the mass compared to monospecies biofilms. The number of cells of each *S. mutans* and *C. albicans* in the biofilm formed by the two species was also higher than the number of cells in the monospecies biofilm. Research by Dongyeop et al., (11) also showed an increase in the growth of *S. mutans* in biofilms formed by *S. mutans* and *C. albicans* accompanied by the detection of *C. albicans'* s inducer, namely Farnesol at low concentrations. In a study by Falsetta et al., (12) showed that biofilms formed by *S. mutans* and *C. albicans* had more *S. mutans* microcolonies and were larger in size compared to monospecies biofilms.

Meanwhile for *C. albicans* growth, there were 4 articles which showed an increase in *C. albicans* growth in biofilms formed by *S. mutans* and *C. albicans*. In the study of Sztajer et al., (10) showed that biofilms formed by *S. mutans* and *C. albicans* had almost twice the mass compared to monospecies biofilms. The number of cells of each *S. mutans* and *C. albicans* in the biofilm formed by the two species was also higher than the number of cells in the monospecies biofilm. In this study it was also found that most *C. albicans* grew in the hyphal phase. Research by Dongyeop et al., (11) also showed an increase the growth of *C. albicans* in the hyphal phase of the biofilm formed by *S. mutans* and *C. albicans*. In a study by Ellepola et al., (13) *C. albicans* showed faster growth if it grew on biofilms formed by *S. mutans* and *C. albicans.*

In a study by Carmelia et al., (14) showed that the number of *C. albicans* cells was higher when they were in the biofilm formed by *S. mutans* and *C. albicans*.

3.2. Formation of Biofilms

Based on the 7 articles analyzed, there were 2 articles which showed an increase in biofilm formation in biofilms formed by *S. mutans* and *C. albicans*. Research by Carmelia et al., (14) showed that the biofilms formed by *S. mutans* and *C. albicans* were thicker than monospecies biofilms. In the study of Falsetta et al, (12) showed that biofilms formed by *S. mutans* and *C. albicans* increased EPS matrix formation leading to the development of larger and thicker biofilms compared to monospecies biofilms.

3.3. Changes in Gene Expression

Based on the 7 articles analyzed, 6 articles showed changes in gene expression in both *S. mutans* and *C. albicans* if they were in the same biofilm. In the study of Sztajer et al., (10) showed that a number of 510 genes underwent expression changes in biofilms formed by *S. mutans* and *C. albicans*. The gene that encodes the inducer in *S. mutans* is the most widely expressed gene in the biofilm. Research by Dongyeop et al., (11) showed an increase in gene expression in *S. mutans* gtf, especially the gtfB gene which codes for the production of the GtfB enzyme which functions to metabolize sucrose into glucan. Research by Ellepola et al., (13) showed that there were changes in gene expression related to carbohydrate metabolism in *C. albicans* when it was in a biofilm with *S. mutans*. In addition, there was an increase in the expression of genes related to the formation of hyphae and cell wall components in *C. albicans* also increased. In S. *mutans*, there is an increase in the expression of genes related to carbohydrate metabolism, glycogen synthesis, and sugar transport. Research by Jinzhi et al., (15) showed an increase in gene expression associated with the pyruvate metabolic pathway. In addition, genes related to galactose metabolism in *S. mutans* also increased. However, in this study there was a decrease in gene expression related to the inducer belonging to *S. mutans*. Research by Haoran et al., (16) showed that there was an increase in gene expression in *S. mutans* and *C. albicans* which was associated with EPS matrix production (gtfC), tissue attachment (spaP, epa1), mycelium transformation (hwp1), and drug resistance (cdr2). Research by Falsetta et al., (12) showed an increase in the expression of the gtfC and gtfB genes associated with the formation of the EPS matrix in biofilms

4. Conclusion

Quorum sensing between *S. mutans* and *C. albicans* plays a role in accelerating the pathogenesis of caries disease.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors have no conflict of interest to declare.

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