DENTAL CARIES AND LACTOBACILLUS: ROLE AND ECOLOGY IN THE ORAL CAVITY

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ABSTRACT: Dental caries is an infective serious transmittable bacterial disease characterized by a multi-factorial pathology. Main players in the etiology of this disease are cariogenic bacteria, fermentable carbohydrates, a susceptible tooth, the host, and the time. It is still one of the most common disease worldwide. Biological factor such as cariogenic bacteria plays an important role in dental caries initiation, progression as well as tooth decay. Previous studies suggested that the main pathogenic bacteria are Streptococcus mutans and Lactobacillus. Consequently, Lactobacillus is considered the second most cariogenic bacteria of oral flora. It is not the caries initiator but plays an important role in caries progression. Most of the previous studies were quantitative, so till now, researchers not know about the specific species of Lactobacillus which are directly associated with dental caries progression. Some species-level identification studies suggested that the most common Lactobacillus species are L. gasseri, L. fermentum, L. vaginalis and L. casei which were predominantly reported at the most of the oral sites, i.e. saliva, tongue, carious lesion, dental plaque, etc. and maybe plays the main role in caries progression. The present review spotlights the role, pathogenicity of Lactobacillus in dental caries and their ecology in the oral cavity.

INTRODUCTION: Now a day’s, the oral diseases such as dental caries and periodontal diseases are still the most prevalent diseases worldwide, and WHO considers these pathologies as one of the most important public health issues. The World Health Organization described that 60–90% of school children, and nearly 100% of adults have dental caries. Dental caries can be prevented if a constant low level of fluoride is maintained in the oral cavity.

Severe periodontal disease, which may result in tooth decay, is found in 15–20% of middle-aged (35-44 years) adults. Globally, about 30% of people aged 65–74 have no natural teeth. Cases of oral diseases in children and adults are more among poor and disadvantaged population groups. Risk factors for oral diseases include an unhealthy diet, tobacco use, abusive alcohol use, poor oral hygiene, and other social determinants .

As we know, dental caries is an infective serious transmittable bacterial disease characterized by a multi-factorial pathology. Main players in the etiology of this disease are cariogenic bacteria, fermentable carbohydrates, a susceptible tooth, the host and the time. At present, it is still one of the most common disease worldwide. If good oral hygiene is followed, chances of dental caries will
be less. When the equilibrium is compromised, and when an imbalance appears among the indigenous bacteria, pathologies such as dental caries or periodontitis could occur. However, the presence of nutrients, epithelial debris, and secretions make the mouth a favorable habitat for a great variety of bacteria. The most notorious bacteria for dental cavities are *S. mutans*, and *Lactobacilli* 10, 11, 12, among the wide range of bacteria, occurs in the mouth which produce acids from fermentable carbohydrates and cause demineralization, whereas others contribute to plaque development 13, 14, 15.

Historically, *Lactobacillus* was the first known microorganism associated with dental caries development 16. They appear during the first years of a child’s life 17 and are present in high numbers in saliva, on the dorsum of the tongue, mucous membranes, the hard palate, in dental plaque and, in fewer numbers, on tooth surfaces 18. During the past few decades, the *Lactobacillus* genus has been subjected to numerous taxonomical changes. Thus, *Lactobacillus* is the group of the bacteria which produces lactic acid after the carbohydrate fermentation. It is gram’s positive, rod shape facultative anaerobic, non-spore forming bacilli. It comprises over 150 species which are acid tolerant and characterized by a low G+C content of the genome. The percentage of GC in the DNA is 40% (by either Tm method or Bd method) 19, 20, 21. It has been abundantly present in the milk and milk production as well as also found in feces, saliva 22, 23, stomach, vagina, gastrointestinal tract, and oral cavity 24, 25.

This review aims to describe the pathogenicity and role of *Lactobacillus* in the formation of dental caries. Moreover, their ecology in the oral cavity and how to get prevent caries initiation.

**History of Lactobacillus in the Oral Cavity:** The oral cavity is the part of the mouth behind the teeth and gums that is bounded above by the hard and soft palates and below by the tongue and the mucous membrane connecting it with the inner part of the mandible. It is not a uniform atmosphere for the resident of microbes but offers numerous distinct niches for microbial growth, such as the tongue 25; teeth, gingiva, hard and soft palates 26. The history of *Lactobacillus* in the oral cavity started from over a century, a scientist name Lewkowicz (1901), was initially isolated from the oral cavity of the patients of dental caries 16.

For nearly a century, *Lactobacillus* has been generally associated with dental caries 16. However, the key ecological determinant for the sustained colonization of lactobacilli in the oral cavity seems to be the presence of caries. It is of historical note to mention that this relationship was established by Harrison and Opal (1944) 27, they isolated lactobacilli from 93% of saliva samples and 66% of fecal samples of children with dental caries but not from those who were caries free 11. The major characteristic of the genera *Lactobacillus* is acid production from fermentable sugars. Rodriguez-Vargas, (1921), had isolated three species of the lactic acid bacteria from dental caries, and he concluded that these species of *Lactobacillus* were responsible for the production of acids that cause tooth decay 28. Owen OW described that it was the first microorganism which was responsible for dental caries development 29. The oral cavity is free from microbes at the time of birth; the colonization occurs after some time 30.

*Lactobacillus* appears during the first years of a child’s life, and are present in high numbers in saliva, on the dorsum of the tongue, mucous membranes, the hard palate, in dental plaque and, in fewer numbers, on tooth surfaces 18. Although, five hundred strains of lactobacilli were isolated from fresh saliva samples of children, of which *L. salivarius* and *L. cellobiosus* are novel. Based on the above observation, Ragosa et al., concluded that not only *L. acidophilus* found in the saliva sample but also two or three species were present at a time in each sample 31. In the decade of 1950s Davis, was tried to classify *Lactobacilli* which were isolated from the human mouth, where total 473 strains were classified into five groups as *L. acidophilus*, *L. casie*, *L. plantarum*, *L. fermenti*, *L. bravis* 32.

Steinle et al., (1967) investigated the relationship between the carious lesion and dental caries; the agar-replica method was used to determine the relationship between the clinical carious lesion and the localized *Lactobacillus* growth sites. The results of the study suggested that this technique is significant in studying the relation of *Lactobacilli* to carious lesions and, further, that it can be used in
longitudinal studies of dental caries. The technique added the advantage of studying it at their actual points of growth. Their observations suggest that a direct relationship exists between the presence of Lactobacilli and the active carious lesion. Thus the concentration of Lactobacillus in the oral cavity is 1% of the entire cultivable oral flora.33,34

Lactobacillus plate count being used from 1985s for the process of caries detection,35 and shows a positive correlation in carries as carries increases the count also increase with positive carries activity.36 It is already proved that the number of DMFS and concentration of Streptococcus mutans and Lactobacillus is correlated to each other if the number of DMFS increases then S. mutans and Lactobacillus count will also be increased.37 Previous studies suggested that oral lactobacilli are directly associated with caries development.38

Modern studies suggested that the younger infants below 10 years also showed a correlation between the presence of Lactobacillus in the oral cavity and dental caries.39,40,41,22. They have regularly isolated from caries active sites and in the almost caries studies42 so that in the various private dental clinics an assay for Lactobacillus count have been used.43 In the adults, lactobacillus reported in the 100% samples and associated with dental caries.44 Most recently, three species of Lactobacillus are L. fermentum, L. gasseri, and L. salivarius were identified in the most carries active subjects and absent in caries-free subjects.45,46,47,48. The scenario in the developing countries like India is not different; their presence is reported in most of dental caries-related studies.47,49,50,51,52

**Ecology of Lactobacillus in the Oral Cavity:**

**Lactobacillus in the Saliva of Caries Active Subjects:** Saliva is a biological mixture of fluid which is secreted by salivary glands. It contains 99% of water, and the remaining 1% is electrolytes, proteins, and enzymes. Saliva establish a link between soft and hard tissues of the oral cavity.53,116,118. When oral bacteria are in the planktonic state (for instance; in saliva), they are not considered as the causative agent of dental caries. However, some bacteria in saliva mediate the transmission of pathogenic bacteria intraorally.53,54. The genus Lactobacillus represents 0.1% of the total salivary flora; however, a correlation also exists between lactic acid bacteria of dental plaque and in human saliva. The critical concentration of Lactobacillus is 10⁵ CFU/ml of saliva, which can cause oral disease such as dental caries in human.18,52. So, the total salivary count test uses for detection of dental caries. It is believed that the Lactobacillus absent in the oral cavity of newborns and colonization occurred after the few hours of birth when newborns started the breastfeeding. Various species of Lactobacillus reported in saliva Table 1: the common are L. acidophilus, L. casei, L. crispatus, L. fermentum, L. gasseri, L. oris, L. paracasei, L. plantarum, L. rhamnosus, and L. salivarius.24,26,52,56,57,58,59,120.

**TABLE 1: LACTOBACILLUS SPECIES ISOLATED FROM SALIVA OF CARRIES SUBJECTS**

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<td>L. plantarum</td>
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<td>L. fermentum</td>
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<td>L. crispatus</td>
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**Lactobacillus on Tongue:** Lactobacillus present in the all most and all sites of the oral cavity of a human. Their presence in the tongue was most studied; various species of lactic acid bacteria were reported abundantly on the soft tissues of tongue in the caries active subjects.63. Some previous studies have shown that tongue cleaning leads to a healthy oral environment, and also inhibit the growth of cariogenic bacteria as well as removed the other main etiological agents of dental caries and...
periodontal diseases. Ahumada et al. characterized lactobacilli in the children who had caries; they were identified 31 different species where 78% came from the tongue surface and rest of the gums. The other author identified two species of *Lactobacillus* on the tongue surface of periodontitis patients, but their study didn’t find any co-association between lactobacilli and periodontitis. Some previous study supported that dominant flora of tongue also associated with dental decay. Table 2, especially *L. gasseri* detected in childhood and adult caries, *L. vaginalis* reported in caries-active women, and *L. fermentum* is associated with childhood caries.

### Table 2: Lactobacillus Spp. Identified from the Surface of Tongue

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<td><em>L. acidophilus</em></td>
<td><em>L. acidophilus</em></td>
<td><em>L. fermentum</em></td>
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<td><em>L. acidi</em></td>
<td><em>L. vaginalis</em></td>
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<td><em>L. gasseri</em></td>
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<td><em>L. acidophilus</em></td>
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<td><em>L. paracasei</em></td>
<td><em>L. casei</em></td>
<td><em>L. rhamnosus</em></td>
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<td><em>L. plantarum</em></td>
<td><em>L. rhamnosus</em></td>
<td><em>L. fermentum</em></td>
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<td><em>L. fermentum</em></td>
<td><em>L. planatarum</em></td>
<td><em>L. paracasei</em></td>
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<td><em>L. rhamnosus</em></td>
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<td><em>L. reuteri</em></td>
<td><em>L. paracasei</em></td>
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<td><em>L. fermentum</em></td>
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### Lactobacillus in Dental Plaque:
Dental plaque is a very complex bacterial community which is accumulated on the hard tissue of the oral cavity. Over 500 bacterial species comprise in the plaque formation. It is difficult to give the exact idea of the relationship between *Lactobacillus* and dental plaque, but some study which is highlighted and strongly recommended that *Lactobacillus* is the part of the dental plaque and his presence plays an ideal role in caries development. Corby et al. studied on the microbial risk indicator of early childhood caries and observed that the top *Lactobacillus* species found to be overabundant in the caries-active group were *L. fermentum* and *L. gasseri* which are associated to dental plaque formation as well as caries. Some study gave interesting results because it has been quantitatively less reported in the dental plaque than in saliva. Most of the studies reported *L. fermentum*, *L. gasseri*, *L. casei* and *L. salivarius* in the dental plaque of children and young adults. Thus, these three species of *Lactobacillus* have been also reported in the childhood caries when the plaque samples had cultured anaerobically on the blood agar medium. Some recent studies conformed Table 3 that the *L. casei* and *L. gasseri* predominant in childhood caries, *L. fermentum* and *L. salivarius* are more frequently found in dental plaque samples in adults.

### Table 3: Lactobacillus Spp. Identified from Dental Plaque of Caries Subjects

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<td><em>L. gasseri</em></td>
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<td><em>L. aluunensis</em></td>
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<td><em>L. fermentum</em></td>
<td><em>L. gasseri</em></td>
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<td><em>L. gasseri</em></td>
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<td>Lactobacillus spp.</td>
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<td><em>L. salivarius</em></td>
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<td>Lactobacillus sp.</td>
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<td><em>L. rhamnosus</em></td>
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Lactobacillus in Carious Lesion: It is still not known that how many microbial species involved in dental caries, scientists have been continued to develop the new techniques for the identification of various microbial populations. Till now, over 500 bacterial species have been identified by culture-dependent and culture-independent methods in the oral cavity. Although, various microorganisms are generally recognized to be associated with disease progression, and some are associated with disease initiation. The association between lactobacilli and dental caries was reported by Goadby in 1899, and experimental evidence was established after the 1950s for the fundamental role of these bacteria in dental caries. They are now considered secondary invaders rather than initiators of the caries process.

The studies of Lactobacillus in the particular site like carious lesion in the oral cavity not much studied; various authors have only made a simple quantitative analysis of lactobacilli rates. Some site-specific studies Table 4 also suggested that Lactobacillus is the predominant oral flora of carious lesion, and it’s directly associated with deep caries and tooth decay. The most common species are L. casei, L. fermentum, L. rhamnosus, and some are L. crispatus which are abundantly present in the carious lesion of caries subjects.

Table 4: Lactobacillus spp. isolated from carious lesion of caries subjects

<table>
<thead>
<tr>
<th>Ando and Hoshino 1990</th>
<th>Becker et al., 2002</th>
<th>Byun et al., 2004</th>
<th>Munson et al., 2004</th>
<th>Chhour et al., 2005</th>
<th>Obata et al., 2014</th>
<th>Kianoush et al., 2014</th>
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<td>L. catenaformae</td>
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<td>L. crispatus</td>
<td>L. delbrueckii</td>
<td>L. fermentum</td>
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<td>L. minutes</td>
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<td>L. oris</td>
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<td>L. crispatus</td>
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Role of Lactobacillus in Dental Caries Formation: Its role in the dental caries formation is not well defined, few previous studies support that the Lactobacillus spp. play an important role in dental caries development because their nature to survive in the low pH environment. These bacteria use fermentative metabolism and according to these species, their metabolism methods are two types: homo-fermentative and hetero-fermentative. Some species produce lactic acid due to homo-fermentative metabolism, and other produce lactic acid, CO2, acetic acid or ethanol via using hetero-fermentative mechanisms 21, 81.

The Lactobacillus species whatever metabolic mechanism used, it results is only the acidification of the environment. Thus, these bacteria cause pH value decrease less than 4.5 in the oral environment, and they can survive in a pH up to 2.2. These bacteria have two cariogenic properties, such as adhesion and acid production. Although, the ability of the Lactobacillus adhere to the cells culture, and the solid surface is not noteworthy.

The species of Lactobacillus have the S-layer protein in their cell wall; the protein has a crystalline structure and responsible to the cell surface hydrophobicity. The exopolysaccharide produced by the Lactobacillus species is a key factor in the biofilm formation; numerous studies confirmed that some species of Lactobacillus produce exopolysaccharide extensively.

Cariogenic Properties and Pathogenicity of Lactobacillus: The various microorganisms play their roles in the formation of dental caries. The genera Lactobacillus also associated with the dental caries development. If microbes are in the mouth are equilibrium state, dental caries will never develop. The adherence and acid production capacity of Lactobacillus is enough for dental
The cariogenic properties of such *Lactobacillus* are discussed below:

**Acid Production:** Cariogenic activity of *Lactobacillus* is attributed to the production of lactic acid by the sugar fermentation. Based on carbohydrate metabolism *Lactobacillus* are two types homo-fermentative synthesize only lactic acid whereas hetero-fermentative synthesizes CO₂, acetic acid or ethanol apart from lactic acid. Both the metabolic pattern used by the *Lactobacilli* resulted in an acidification of the environment. It is believed that the *Lactobacillus* is the prime micro-organism in caries development because of their high numbers in carious lesions and their acidogenic and aciduric properties. Various studies have shown that *Lactobacillus* is excellent acid tolerance bacteria, and they have the ability to survive below pH 4.5. They change the pH of the oral environment neutral to acidic. In the colonization and maturation stage of dental caries formation they get attaches to dental plaque and started to dematerialize the teeth enamel.

**Cell Surface Hydrophobicity:** Attachment of *Lactobacillus* to the tissues or tooth surface is the first step for biofilm formation where the cell surface hydrophobicity greatly modulates the attachment properties of the lactic acid bacteria. In the living systems, the strongest long-range non-covalent interaction is hydrophobic interaction. The hydrophobic interactions are as a major determining factor in microbial adhesion to surfaces. Although, there are several studies concerning the cell surface hydrophobicity of the oral lactobacilli. The S-layer present at the outermost cell surface of some *Lactobacillus* species is responsible for cell surface hydrophobicity. Vadillo-Rodríguez et al., studied on the cell surface hydrophobicity of two species of *Lactobacillus*, they concluded that in a low ionic strength suspension, both *Lactobacillus* strains show higher initial deposition rates to hydrophobic glass than to hydrophilic glass, whereas in a high ionic strength suspension no clear influence of cell surface hydrophobicity on adhesion is observed.

**Exopolysaccharide Produced by Lactobacillus:** It is the extra polymorphic substances produced by some plants, fungi, and bacteria; which are long-chain, linear or branched biopolymers. It is high molecular weight biopolymers consists of repeating units of saccharide and linked by α- and β-glycoside bonds. They are sticky in nature and play an important role in the adhesion to the dental biofilm. So far, various EPS-producing *Lactobacillus* species have been identified such as *L. casei*, *L. acidophilus*, *L. brevis*, *L. curvatus*, *L. delbrueckii subsp. bulgaricus*, *L. helveticus*, *L. rhamnosus*, *L. plantarum*, and *L. johnsonii*.

**S- Layer Proteins of Lactobacillus:** The cell wall is an outer layer structural component of bacteria and essential for many aspects of their life. The S-layer proteins are the outermost cell envelope, which is made of different kinds of proteinaceous substances. Particularly, the adaptations of the microorganisms to adverse environmental conditions occur from the diverse structures of the outermost boundary layers of bacteria. The biological functions of S-layer proteins of *Lactobacillus* are not well known, but they play an important role in cell adhesion to host cell. Thus, *Lactobacillus* can adapt their surface hydrophobicity in environmental changes because they have S-layer proteins in their outer cell wall.

**Mechanisms of Dental Caries Formation:** Dental caries is commonly known as tooth decay. The mechanism of tooth decay is very complex. It is known from over 50 years that dental caries causes by the fermentation of food material, these food fermented by certain acid producing bacteria. Two types of bacteria are involved in tooth decay; which is: *mutans streptococci* and *Lactobacillus* species these both can produce acid during the metabolism of sugar fermentation. When these bacteria produced acid in the dental plaque on tooth surface they readily diffuse in all directions in the mouth. The acid, of course, also diffuses into the pores of enamel or dentine. When the acid diffuses into the tooth, it finds soluble acid mineral, and they begin to dissolve it. In the mouth, this process progresses long enough; the result is a cavity. This process usually takes several months to years for progression to cavitation, the end-point of the disease process known as dental caries.
Biofilm Formation Capability of *Lactobacillus*: The biofilm is described by Donlan and Costerton in 2002, according to them biofilm is a microbial-derived sessile community characterized by cells which are irretrievably attached to the solid surface and interface to each other. The biofilm formation and development is affected by various factors, such as bacterial population, surface properties and some environmental factors like pH, availability of nutrients and temperature of the oral environment. In the biofilm formation, so many steps are involved, but four steps are important such as adhesion, colonization, maturation, and dispersion. In the first stage, microbial cells start to attach the tooth surface. In the second step, cells start to colonize. In the third step, colonized microbial populations start to maturation, and in the last step, the mature population starts to disperse in the oral cavity. The detail description of each steps Fig. 1 of the biofilm formation describe below:

**FIG. 1: MECHANISM OF DENTAL CARIES FORMATION**

**Dental Plaque Formation:** The oral cavity is a safe place for microbial flora, where a variety of microorganisms live together. The dental plaque development occurs due to the growth of such bacteria which develops, of course on oral tissues and teeth. Thus, dental plaque is a composite microbial population which is attached on the teeth surface in the oral cavity. When the microorganism starts to adhesion on the surface of teeth is a common condition of plaque formation. Structure of dental plaque varies from the tooth to tooth and location to location, and this is not a uniform structure. When the environments of oral cavity get change, dental plaque structure also changes. Thus, we can say that dental plaque dependent on oral environment and change according to condition on oral environment and adhesion to the microbial population. The dental caries is the result of the adherent deposit of bacteria, and it is by-products. These microbial community works together and always metabolically active. The ecology of dental plaque formation changes due to some external factors such as daily diet and dental care. Normally dental plaque development takes one to two weeks for maturation. In the process of the dental plaque formation, three steps are included such as adhesion, colonization, and biofilm formation, which is described below:
**Adhesion:** Microbial adhesion to the solid surface is the first step to dental plaque formation. This process starts with the formation of the pellicle of the tooth surface, in the pellicle formation salivary glycoprotein does firstly attach to the surface of the tooth. The pellicle is the proteins-coating film which is derived from salivary glycoproteins. Some planktonic bacteria start to recognize the glycoproteins in the pellicle, and after that begin to attach. In the initial stage, attachment occurs due to electrostatic attractions and physically attractions, after some time bacterium begins to produce some extra polymorphic substances which are called exopolysaccharides. These exopolysaccharides help in the bacteria stay bound together and attach to the pellicle. The majority of microbes in pellicle are *S. mutans* and *Lactobacillus* spp. which are initially attached with the surface of naked tooth.

**Colonization:** After 4-12 hours of adhesion, colonization takes place in the dental plaque formation. Colonization is an important process in plaque formation. In this process, the microbial population attached to the tooth surface and start multiplying. The planktonic bacteria cannot directly colonize on the tooth surface; they have required some receptors site on the cell surface for early colonization and adhesion to the surface. Co-aggregation is a specific cell-to-cell interaction reaction which occurs in oral bacterial colonization and dental plaque formation. Co-aggregation is the most studies microbial interaction mechanism which occurs between distinct bacterial cells. According to the previous study, bacterial colonization starts from the bottom layer of dental biofilm. Early colonizers bind via the complementary pellicles receptors while secondary colonizer binds to previously bounded bacterial cells. *Streptococci, Lactobacilli,* and other anaerobic oral bacteria can co-aggregate with *Fusobacterium* spp, which is the primary colonizer of the tooth surface.

**Maturation:** The next phase of dental plaque formation is maturation; in this phase generates new complex architecture, channels, pores, and the redistribution of bacteria away from the solid surface. The cluster of bacteria forms the mushroom-shaped structure on the tooth surfaces; the shapes depended on the source of nutrients. For the development of mature dental plaque required 8-10 day’s period. The mature dental plaque contains numerous gram’s positive and gram’s negative bacterial species such as *Streptococcus mutans, Streptococcus mitis, Fusobacterium nucleatum, Treponema sp, Tannérella forsythensis, P. gingivalis, Aggregatibacter, Actinomycetes, Veillonella sp. and Lactobacillus sp.*

**Dispersion:** Dispersion is the last phase of dental plaque formation; during this phase biofilm of microbes will detach from the colony and quickly returns to a planktonic form, spread out in the oral cavity.

**CONCLUSION:** The present review concluded that a total of 25 species of *Lactobacillus* was reported in the various sites of the oral cavity; these vary with changing the oral sites. Some species dominant on a particular site but they were less reported on the other sites. The most common species which are mostly reported on both the oral sites are *L. gasseri, L. rhamnosus, L. reuteri, L. paracasei, L. plantarum, L. acidophillus, L. oris, L. fermentum, L. casei, L. salivarius, L. brevis,* and *L. vaginalis.* The caries-associated species are *L. gasseri, L. fermentum, L. vaginalis* and *L. casei* which are reported in all most all relevant studies. Where *L. gasseri,* previously detected in childhood and adult caries, *L. fermentum,* detected in childhood caries, *L. vaginalis,* reported in caries-active young women’s saliva and *L. casei* reported in childhood and adult both caries. Most of the species were detected by molecular methods from children and adult’s saliva, dental plaque, tongue, and carious lesion. In contrast, the *L. rhamnosus, L. acidophilus, L. plantarum,* and *L. reuteri,* which are used in probiotic infant enteric and oral anti-caries therapy, showed negative associations with caries. Moreover, most of the studies were quantitative in respect of *Lactobacillus* in the oral cavity; the review reported that lactobacillus count higher in the active caries groups while less detected in the caries free groups. So we concluded that, if the sugar consumption is increased in the diet sugar degrading bacteria also increases and produces acid from their metabolic activity, this acid cases demineralization of teeth for his result, dental caries occur.
Thus, *Lactobacillus* does not directly cause dental caries but their secondary metabolic product, *i.e.* lactic acid plays a major role in dental caries formation.

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