PREVALENCE, CAUSES AND MANAGEMENT OF DENTAL CARIES

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ABSTRACT

Dental caries, a chronic disease is unique among human and is one of the most common important global oral health problems in the world today. It is the destruction of dental hard acellular tissue by acidic by-products from the bacterial fermentation of dietary carbohydrates especially sucrose. It progresses slowly in most of the people which results from an ecological imbalance in the equilibrium between tooth minerals and oral biofilms which is characterized by microbial activity, resulting in fluctuations of pH due to bacterial acid production, buffering action from saliva and the surrounding tooth structure. The microbial community of caries is diverse and contains many facultative and obligate-anaerobic bacteria. *Streptococcus mutans* is the most primary associated with it. Dental caries can affect the human in various ways i.e. presence of tooth pain, infection or dysfunction of the stomatognathic system can limit the necessary ingestion of foods, affecting the growth in children and adults as well as their learning, communication skills and recreational activities. Moreover, oral and pharyngeal cancers and oral tissue lesions are also significant health concern. Due to this, treatment is needed for dental diseases which cost normally high and is not feasible for all due to limited resources such as time and money. Therefore, prevention is more affordable. Personal hygiene cares and dietary modification should be recommended.

KEYWORDS: Dental caries, Fluoride, Pathogenesis, *Streptococcus mutans*, Cavernous sinus thrombosis, Oral Biofilm, Prevention.

1. INTRODUCTION

Dental caries has been the most common non-communicable illness and a major health issue worldwide. It is the most common disease in the 2016 Global Burden of Disease Study, ranked first for permanent tooth decay and 12th for temporary tooth decay. Dental caries can be avoided by eliminating free sugars in the diet. Furthermore, dental caries is mainly avoidable by easy and low-cost population-wide and specific treatments, however treatments is expensive and frequently unavailable in low- and middle-income nations. The bulk of dental caries remains untreated in low-income nations (Bridge *et al*., 2021). Caries-affected teeth are frequently removed (taken out) if they induce distress. Serious dental caries can have a negative impact on one's life quality. Dental caries, for instance, can cause difficulty in sleeping, and in its later stages (abscesses), it can cause discomfort and persistent disease (Gomes Silva Cerqueira *et al.,* 2021).

Dental caries is also linked to abnormal development patterns. Furthermore, dental decay is a common cause of frequent absences or job. Dental caries affects about half of the worldwide people, and declared as most common of all health disorders. Middle-income nations with significant sugar intake have increased rates of dental caries. Health systems in such nations face challenges in providing preventative population-wide programmes, and basic healthcare

is frequently unavailable (James *et al*., 2021). Dental caries affects everybody, but children and teens are more vulnerable. Since dental caries is a progressive illness, the majority of cases develop in adults. Sugar intake and tooth cavities have a strong dose–response association. The illness is also linked to socioeconomic level, with higher prevalence among poor populations (Munteanu *et al.,* 2022).

Interactions between dental tissues and microbes produce the microbial biofilm on the tooth surface, and carbohydrates, salivary and genetic effects, all contribute to tooth decay. The dynamic caries procedure involves quick alternating phases of dental remineralization and demineralization, which culminates in the beginning of particular caries lesions at specific anatomical predilection spots on the tooth if net demineralization happens over a significant duration. It is critical to strike a balance between the protective and pathogenic variables that cause the onset and development of dental caries. Protective variables encourage remineralization and lesion arrest, while pathogenic factors tip the scales in favor of dental caries and disease development. Many sources believe that the regular use of fluoride toothpaste is the primary remedy for the global drop in caries over the last few decades; the potency of such toothpastes is associated with changing the balance of the oral flora against health (Tokue and Tsushima, 2021).

There is no clear relationship among the level of a caries and discomfort or pain a patient encountered. Even so, serious ailment can be incapacitating, and disease and septic shock caused by caries which expands to involve the dental pulp can or sometimes lead to more serious systemic consequences, like spreading local infectious disease and, in rare instances, treatment-related death (because of anesthesia), and also loss of teeth (Vos *et al.*, 2016). Usually, dentists do a careful visual assessment of clean teeth to identify caries. Although sharp-pointed dental probes (or explorers) are still commonly employed, they offer no additional diagnostic advantage and can cause considerable injury. In practice, dental radiographs or other supporting diagnostic procedures are also required to detect lesions that are not visible to the naked eye, particularly those located on the proximal surface of the tooth (Pitts and Zero, 2016).

Dental caries can cause teeth to appear sensitive to illness, from an evolutionary perspective standpoint, tooth are a high-valued organ system engaged in food pretension and processing, as well as defence, and phonetic articulation. The outer surface of the tooth crown is made up of enamel, the body's toughest component, with saliva, a specialized fluid, released during the day to maintain integrity. The morphology of the present dentition has evolved mostly as a result of our changing food habits over millennia. Interestingly, high-sugar foods are soft and frequently liquid; teeth are not necessary for swallowing, which may explain why teeth can be swiftly removed (Koussoulakou *et al.,* 2009).

1.1 Epidemiology

Caries epidemiological research have been conducted over many decades, and that some of the data accessible through the WHO and other organizations. However, in order to assess and plan policy, epidemiology must offer timely, reliable, and intelligible data for important age groups on the overall quantity of illness present (prevalence), the rate of disease process (incidence), and disease changes over time (Alyami, 2021). Furthermore, information on disparities in illness levels across and within nations is required, as well as estimates and trends in health inequalities (that is, discrepancies in health status between groups within populations). However no reliable, up-to-date, clinically significant information is available that satisfies these standards anywhere in the world (Wen *et al*., 2022).

Dental caries is an ignored issue, despite the WHO's recognition that it is still a serious health concern in most developed nations, affecting 60–90 percent of children and the great majority of adults. Caries is always thought to be a pediatric condition, but it now affects adults as well. There are health disparities in the incidence of dental caries both in adults and children. Dental caries is the most prevalent chronic childhood illness, and its incidence is anticipated to have recently increased in children aged 2 to 5, giving this age group a global key action area (Pitts *et al.,* 2009). In the most recent National Health and Nutrition Examination Survey (NHANES) from 2012 to 2013, roughly 25% of children aged 2–5 in the United States had dental caries in milk teeth. Furthermore, the same data indicated that around 10% of children between the ages 2–5 in the United States had undiagnosed tooth decay (Dye *et al*., 2010).

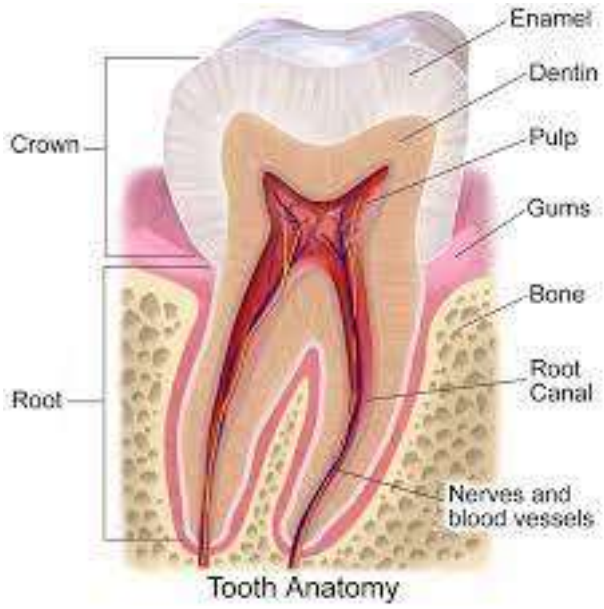

Figure 1: Tooth anatomy (Bhargavi *et al*., 2013)

1.2 Types of Dental Caries

1.2.1 Early childhood caries (ECC)

Early childhood caries is a pattern of decay found in young children with their milk teeth. The teeth most likely affected are the maxillary anterior teeth, but all teeth can be affected. This type of caries comes as a result of allowing children to fall asleep with sweetened liquids in their bottles or feeding children sweetened liquids multiple times during the day (Wang *et al*., 2019). The risk for ECC also may be determined by pre-existing developmental defects of the enamel called hypoplasia. Hypoplasia predisposes teeth to early colonization by *Streptococcus mutants* and malnutrition. ECC exhibits a characteristic pattern related to the emerging sequence of the teeth and the tongue position during feeding. The lower teeth are protected from exposure to ingested liquids by the tongue during feeding and by the pooling of saliva and so usually are not affected. The incisors are the first upper teeth to emerge and are most affected by ECC. Depending on how long the caries process is active, the upper first primary molars are often involved, followed by the upper second molars and canines, and in severe cases, the lower teeth (Mathur and Dhillon, 2018).

1.2.2 Rampant caries

Rampant caries are severe decay on multiple surfaces of many teeth. It may be seen in individuals with xerostomia, poor oral hygiene, stimulant use due to drug-induced dry mouth and or large sugar intake. If rampant caries is a result of previous radiation to the head and neck then it is called as radiation-induced caries. Problems can also be caused by the self-destruction of roots and whole tooth resorption when new teeth erupt (Adair *et al*., 2004).

Table 1: Types of dental caries

Types	**Description**
Primary caries	Decay at a location that has not experienced previous decay
Secondary caries	Appears at a location with a previous history of caries and is frequently found on the margins of fillings and other dental restorations.
Arrested caries	A lesion on a tooth that was previously demineralized but was remineralized before causing a cavitation

2. Pathogenesis of dental caries

The classic description of the cause of dental caries includes three factors: host, bacteria and diet. Dental caries occurs when a susceptible tooth surface is colonized with cariogenic bacteria and dietary source of sucrose or refined sugar is present. Bacterial pathogen produced lactic acid from fermentation of carbohydrates and this acid dissolves the hydroxyapatite crystal structure of the tooth which causes caries (Islam *et al.,* 2000).

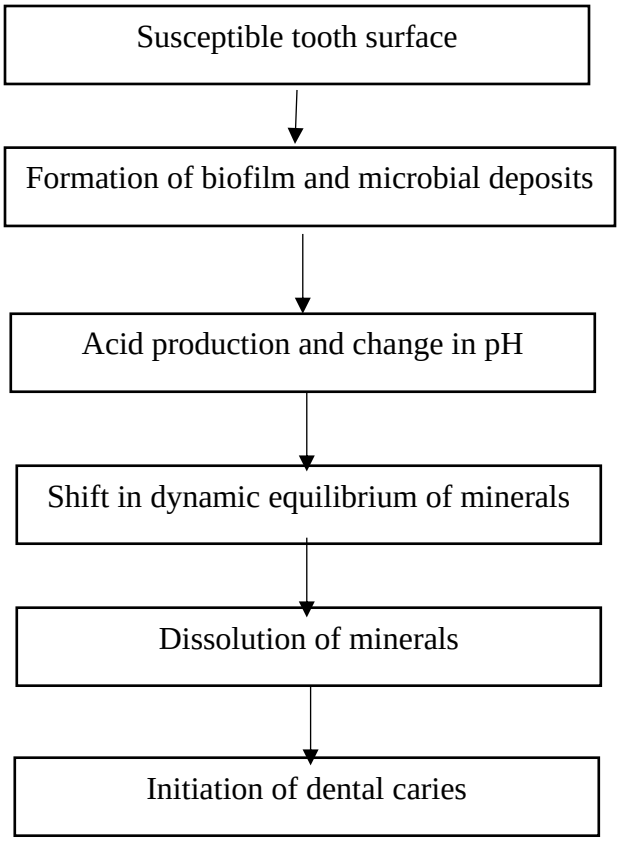

Figure 2: Pathophysiology of dental caries

2.1 Enamel

Demineralization of enamel by caries follows the direction of the enamel rods, the different triangular patterns between pit and fissure and smooth-surface caries develop in the enamel. As the enamel loses minerals, the enamel develops several distinct zones are: translucent zone, dark zones, body of the lesion, and surface zone. The translucent zone coincides with 1/2% loss of minerals. Dark zone is slight remineralization of enamel. The greatest demineralization and destruction is in the body of the lesion. The surface zone remains relatively mineralized until the loss of tooth structure results in a cavitation (Putri *et al*., 2022).

2.2 Dentine

In dentine form the deepest layer to the enamel, the distinct areas affected by caries are the advancing front, the zone of bacterial penetration, and the zone of destruction. The advancing front represents a zone of demineralized dentine due to acid and has no bacteria present. The zones of bacterial penetration and destruction are the locations of invading bacteria and ultimately the decomposition of dentin. The zone of destruction has a more mixed bacterial population where proteolytic enzymes have destroyed the organic matrix (Kidd *et al.*, 2004).

2.3 Cementum

The incidence of cemental caries increases in older adults as gingival slump occurs from either trauma or periodontal disease. It is a chronic condition that forms a large, shallow lesion and slowly invades first the root's cementum and then dentin to cause a chronic infection of the pulp (Robinson *et al*., 2000).

2.4 White spot stage

The acid produced by bacteria and yeast in dental plaque dissolve the mineral matrix of teeth. In the earliest stage, dental caries appears as a chalky white spot on the tooth. At this stage, the surface is intact, and the subsurface lesion is reversible. White spot resulting from incipient caries can be difficult to distinguish from developmental hypo calcification. Further, white spot changes to black staining stage (Burt, 2005).

2.5 Cavity stage

If mineral continues to be lost because of acid challenge, the surface is eventually broken or "cavitated" and the lesion cannot be reversed. If the lesion progresses, large areas of tooth can be lost. Active cavitated lesions are usually golden brown. Long standing lesions are darker, sometimes nearly black. Depth of the color is not a good indicator of the severity of the lesions because arrested decay is often the darkest (Yadav and Prakash, 2015).

3. Microbiology and dental biofilms

Dental plaques are the oral microbiota that grow functionally and structurally on surfaces in the form of organized population of species (Nobbs *et al.,* 2011). It is a type of biofilm that is formed in several stages. a conditioning film consisting of glycoproteins and proteins derived from saliva play role in the formation of tooth surfaces, but this surface also have some bacterial derived products or components, food, blood, gingival crevicular fluid. For adherence binding sites are provided by acquired pellicle by existing bacterial colonies on tooth surface and results in the formation of biofilm and behave as barrier that prevent the diffusion of acid (Jakubovics *et al*., 2014).

Between conditioning film and external layers of the bacterium bacteria can be held reversibly and weakly with the help of van der Waal forces. Attachment becomes more permanent and stronger if interactions occur among complementary receptors of conditioning film and molecules on the bacterium (Devine *et al.,* 2015). To the early colonizers secondary colonizing species attach which results in increasing the complexity of the biofilm. Then it undergoes antagonistic or synergistic microbial interactions and maturation. Polymers that are secreted in external environment known as bacterial exopolymers results in the formation of matrix and along with exopolymers, DNA and polysaccharides derived by metabolism of sugar also helps. On the surfaces biofilm retained by matrix that affect movement and penetration of molecules within the biofilm. Bacteria is protected by biofilm against antimicrobial agents. On different surfaces of tooth composition of biofilm vary on the basis of different environmental conditions (Wright *et al.,* 2010).

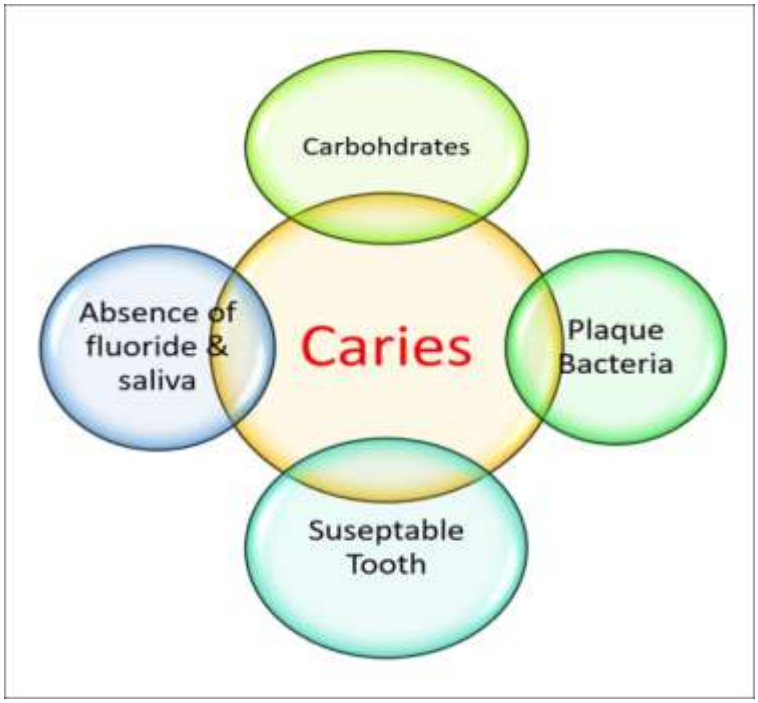

Figure 3: Etiology of dental caries (Mathur and Dhillon, 2018).

3.1 Oral microbiota in health.

Oral microbiota are the microorganisms of different types that colonize in mouth since birth like other body surfaces. Bacteria is among the most common group of microbes but Archaea, protozoa, mycoplasmas, viruses and yeasts can also be present. These microbes have mutualistic or symbiotic relationship with the host. Nutritious and warm habitat provided by human provide residential benefits to microbes that also play role in repelling harmful microbes, crosstalk with the host to down regulate excess pro-inflammatory responses and contribute in host defense (Latti *et al.,* 2018). In maintenance of beneficial microbes saliva play role by buffering oral environment at pH that is optimal for metabolism and growth of oral microbes by providing glycoproteins and proteins as nutrients (Lif Holgerson *et al*., 2015).

3.2 Microbial etiology of dental caries.

Synergistic relationship among host and resident microbiota is dynamic that can be perturbed by alterations to the biology of the mouth or changes in lifestyle and such alterations can predispose sites to disease. Reduced saliva flow and frequent consumption of fermentable dietary carbohydrates are among the risk factors of dental caries (Klein *et al*., 2015). Many longitudinal epidemiological and cross-sectional studies have suggested a change in microbiota balance at the sites with dental caries as compared to sites with the sound surfaces. From different literature studies lesions of dental caries found to have higher incidence of *Streptococcus sobrinus* and *Streptococcus mutans* in higher proportions than sound enamel Lactobacillus species that were separated from advanced lesions. Literature studies suggested that dental caries caused by limited set of microbial species that are present in dental biofilms. Lots of

epidemiological studies had been performed about dental caries and found that dental caries observed in the absence of oral microbiota (Sheiham and James, 2014).

Various other laboratory based studies suggested that within dental biofilms other types of bacterial species that are present could also lower the pH by sugars, but other also play role in the reduction of destructive impacts of lactic acid by utilizing it as a source of nutrient and convert them into weak acids, or by synthesizing alkalis by the metabolism of urea or arginine in saliva. These indications supported the nonspecific plaque hypothesis that supposed that dental caries are due to biofilm metabolic activities (Rosier *et al*., 2014). Recently, molecular approaches or classic culture approaches have found relationship between acid-tolerating bacteria, acid-producing bacteria including *Scardovia wiggsiae, Propionibacterium spp. Actinomyces spp., Bifidobacterium spp.*, and caries. On ecological principles alternative concepts have been proposed that describe the incidents associated with caries. The most plausible explanations about microbial aetiology of caries is explained these ecological plaque hypotheses (Takahashi and Nyvad, 2008).

Caries related microbes may be present on enamel in the biofilm, but activity level is clinically very low. An unfavorable shift in balance of microbiota that reside there due to alterations in dental environment results in caries. When plaques regularly exposed to fermentable dietary sugars that results in lowering the pH in biofilm and favor metabolism and growth of acid-¬tolerating bacteria by inhibiting the beneficial microbes that can grow easily at pH 7. By interfering with the factors that directly inhibit implicated bacteria or those that play role in deleterious shifts in oral communities of microbes like by using snacks that contain artificial sweeteners which cannot be metabolized by oral bacteria to acid or lowering the frequency or amount of sugar in diet can prevent the disease (Marsh, 2003).

Recently ecological plaque hypothesis has been discovered that reflect the oral microbiota ability to adapt to acid stress during condition of low pH. Main factor that select acid-tolerating or acid-generating bacterial community is by acidification of the plaque and increase in its development rise the chance of caries. It is not an infectious disease but occur due to changes in environmental conditions like by the shift of balance of beneficial microbiota or other lifestyle changes (Hong *et al.,* 2009).

4. Diagnosis, screening and prevention

Prevention, screening, risk assessment and diagnosis are all very important factors for the successful control and understanding of caries both at population and individual level. In different countries specific public health definition is screening that is different from clinical practice, but this is not a topic of discussion in this review. Main focus is to determine where are the high ratio of patients that interact daily with oral health doctors at the individual patient level around the world. To control or prevent caries, individual level and public health level interventions are required to be aligned and optimized (Fisher *et al.*, 2012). Dedicated meetings and International Dental Federation (FDI) has analyzed and discussed the risk of dental caries on the basis of available system of classification. In some countries number of assessment systems has been carried out at developing stage but there is a shortage of holistic clinical systems, evidence-informed, internationally applicable and comprehensive systems that allow consensus processes (Ismail *et al*., 2013).

For modern caries management, a number of systems for undertaking some parts of the clinical tasks are needed. A unifying framework to define the key points should be used developed by International Caries Classification and Management System (ICCMSTM) (Pitts *et al.*, 2013). The elements of caries risk assessment in ICCMSTM at intra-oral levels and patient level along with classification of caries by assessing lesion activity and staging lesion severity on the basis of ICDAS system, decision can be taken. This data can be used for producing a personalized care plan that can be applied for control and prevention of dental caries by following risk-based follow-up plan. Main elements of ICCMSTM 4D Caries Management help in formulation and comprehensive assessment of personalized caries care plan (Ismail *et al*., 2015).

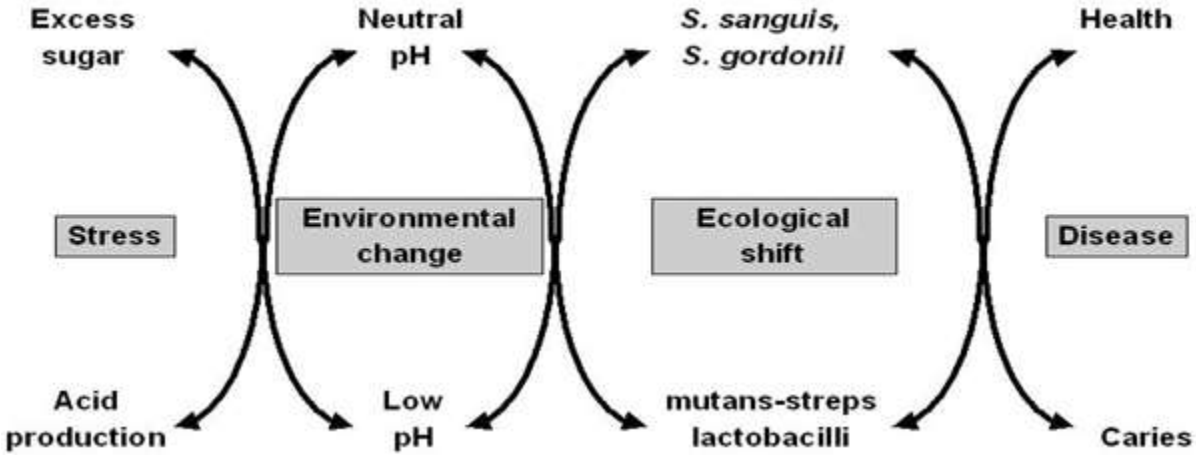

Figure 4: Factors associated with dental caries (Kutesa *et al*., 2015)

5. Prevention and Public health management

Main goal of prevention from dental caries is to promote natural healing processes by preventing demineralization of enamel and sound tooth structure (Ismail *et al*., 2013). To promote healthy behaviours interventions can be implemented at the population level with public health approaches, regulation, legislation, health policies (Watt, 2012). For assuring equity prevention programs may target higher-risk groups or entire population like sugar taxes and water fluoridation to seek and increase effectiveness of cost. There are some considerations about fluorides and prevention of caries given in table below the text. High caries prevalence, low oral health literacy, low fluoride exposure, restricted dental care access, low family income, are some risk factors of caries at population level (Jürgensen and Petersen, 2013).

The best ways to target those having higher risk of suffering from caries is under investigation. at groups with special health care or medical needs like those having antihistamines, dry mouth due to frequent use of medicines, ectodermal dysplasia, palate and cleft lip, genetic disorders like salivary dysfunction developmental or cognitive

disabilities that made oral hygiene difficult, compromised immunity or HIV patients, Sjögren syndrome due to salivary dysfunction etc can also be targeted by prevention programs. Complementary interventions can be more effective as compared to single interventions as dental caries is a multifactorial disease. According to WHO there is a need of oral health prevention program that must be combined with policies, educational and chronic disease prevention programmes having common risk factors (Pitts *et al.,* 2017).

In future social media, mobile smart devices, electronic health records may help in health awareness campaigns (Weintraub, 2011). An international public health advocacy charity known as Alliance for a Cavity-Free Future has been promoting a comprehensive agenda of resources and activities for the purpose of preventive from caries progression and initiation. Education efforts and advocacy including behavioral changes and public awareness to improve the oral health by clinical caries management, advancing research and lowering the consumption of sugar (Freeze and Lehr, 2009). Most of the water supplies have naturally occurring concentration of fluoride. The adjustment of fluoride levels at community level known as community water fluoridation may help in prevention of caries at an optimal level. It is equitable population approach and cost effective that benefits all age groups and meets public health criteria (Ran *et al.,* 2016).

Concentration of fluoride according to US Public Health Service should be 0.7mg per l to increase the chance of prevention of caries by lowering the dental fluorosis risk (Peckham and Awofeso, 2014). This strategy is found to be cost effective (Griffin *et al.,* 2001).When setting national standards a higher concentration (1.5mg per l) of fluoride in water consumed and intake from other resources must be considered according to WHO (Magtibay *et al.,* 2015). When iodized salt is combined with salt fluoridation, it will be very effective that can used frequently to prevent caries at population level. It has been using mainly in South America, Europe where concentration of fluoride in the drinking water is low. In such countries other forms of fluorides and water fluoridation are used frequently (Marthaler, 2013). In salt concentration of fluoride is 250–300 parts per million (Ppm) and least expensive strategy for prevention from caries (Yeung *et al.,* 2015).

In some countries, like United Kingdom and Hungary milk fluoridation programmes has been using (Wright *et al.,* 2015). To arrest the progression of initial non-¬cavitated carious lesions or prevent disease in healthy teeth professionally applied resin material known as dental sealants are are brushed on fissured grooves or caries-prone pit to the occlusal chewing surfaces (Burgess, 2015). This method does not require anaesthesia and can be applied with portable equipment in school-based programmes. An effective community approach is sealant programmes that are cost effective and can be applied in school going children or for middle class families (Li *et al*., 2014).

For school based interventions, many children that are enrolled in Reduced or Free Price Meal Program in US are targeted (Siegal *et al.,* 2010). As prevention approaches must result in societal cost saving and cost effective, so, prevention programmes should be followed because medical treatment programs are expensive. Impact of infection and dental pain on quality of life must be considered. Time frame, intervention effectiveness, material costs, caries prevalence are some factors on which preventive strategies depend (Weintraub *et al*., 2001).

5.1 Individual patient level

Most of the strategies and approaches that are used at population level can also be used in community clinic level or dental office level. Different Cochrane systematic reviews, clinical guidelines and evidence-based toolkits taken together with WHO guideline on consumption of glucose may give a strong proof to support the prevention of caries at the dental office. Patients suffering from diabetes or other must reduce or control the consumption of sugar at individual level if they want to be secured from dental caries. They should prefer more intensive preventive interventions, use supplements on the basis of caries risk status by fissure sealants or use those toothpaste that contain fluoride (Mariño *et al*., 2012).

6.1 Prevalence of dental caries in US

The frequency of dental caries varies significantly across the United States. Early childhood caries is a common, multifactorial, bacterially mediated illness characterized by substantial decay of the teeth of children 6 years of age; it is regarded by some to be transmissible from caregivers to their children but is completely avoidable. International statistics on Early childhood caries are sparse since most countries only record caries in children aged 6 or 7 (Luban *et al.,* 2021).

Caries prevalence has traditionally been low in underdeveloped nations, but it is higher in developed countries. This geographical scenario has gotten more complicated as a result of the rapid economic growth and changes in habits and cuisine in many nations. Although there may be gender or ethnic variances, they are modest when compared to variables like sugar consumption, lifestyle, and economic variations. This underscores the actual issues confronting comparable data from across multiple nations, which have been gathered at different time-points with extremely diverse degrees of training and calibration and, as a result, record caries at different thresholds (Friedman *et al.,* 2014).

When oral health themes were included to the ongoing Global Burden of Disease Study, it was discovered that oral disorders are extremely common, impacting nearly 3.9 billion people globally. This significant study is useful since it permits comparisons with other illnesses in terms of burden, but it is also innovative in terms of caries epidemiology because it does not employ the DMF (decay-missing-filled) Index (Abramovitz *et al.,* 2021). Untreated cavitation in permanent teeth was the most common problem studied across all medical conditions, with a global incidence of 35% for all ages combined, affecting 2.4 billion individuals. It is worth noting that some of these permanent teeth will have been present in children and teenagers. Untreated caries in children's primary teeth ranked tenth in terms of prevalence, impacting 621 million children globally (Aguirre *et al.,* 2018).

6.2 Prevalence in Pakistan

A fundamental component of wellbeing and general health is oral health. Dental caries among all various oral health is continue to affecting a huge number of people around the world, even though large of health awareness campaigns have been conducted but still it's ratio is very high (Griffin *et al.,* 2009). It is one of the most common disease of recent times. It can affect anyone irrespective of socio-economic status, gender, age and ethnicity. Risk assessment is very necessary for management of dental caries and most important thing is to find out the prevalence ratio. Dental

caries remains a big issue for every country according to world health organization. It is a multifactorial disease that is caused by different factors like acidogenic bacteria, fermentable carbohydrates and many other factors (Umer *et al*., 2016).

In plaque and saliva, bacteria ferment dietary carbohydrates which results in acid development that is the principal cause of dental caries. Normally in healthy plaque and saliva a relatively very small amount of carcinogenic bacteria are found. Due to low pH conditions, increased consumption of fermentable carbohydrates, environmental and biological disorders acid tolerant bacteria will proliferate and become a burden throughout the entire life. Disability, functional disability may results if it is untreated (Al Agili, 2013). The occurrence of dental caries among adults is very high that affects about 40% people around the world, while it is mostly preventable (Dawani *et al.,* 2012). Along with periodontal diseases dental caries is a common cause of tooth loss (Madanlou *et al*., 2010).

Dental caries has long burden on health, quality of life throughout the world. About 70-90% of the children are affected by dental caries according to WHO (Starr *et al*., 2008). For solving this problem there is a need to prepare health promotion programs, educational training by estimating it's ratio in a particular geographical location (Peron *et al.,* 2022). For designing public health policies and planning strategies the extent of disease distribution is very important. Most crucial research methods for getting accurate estimation on disease indicators. Meta-analysis method of found to be satisfactory method. Following is the table that shows the ratio of dental caries in different countries of Pakistan (Khan *et al*., 2022; Siddiqui *et al*., 2020).

Table 2: Prevalence of dental caries in Pakistan (Siddiqui *et al*., 2021).

Prevalence of dental caries (n)	Sample size	City	Age group	Year
414	982	Peshawar	11-20	2022
115	226	Bhakkar	11-12 years	2018
110	400	Peshawar	12-17	2017
262	753	Rawalpindi	4-17	2017
336	500	Karachi	5-14	2018
477	1008	Sialkot	Not reported	2016
195	384	Rawalpindi	5-6	2017
124	153	Quetta	12	2009
320	500	Multan	6-15	2018
74	568	Faisalabad	18-29	2019
111	196	Karachi	6-18	2020
358	377	Karachi	20-80	2019
391	642	Lahore	3-8	2013
7409	12,971	Lahore	2-19	2017
1114	1600	Karachi	6-12	2015

274	392	Karachi	12-15	2014
312	349	Islamabad	12	2019
388	400	Bahawalpur	11-70	2012
189	384	Islamabad	3-5 years	2020
196	395	Hyderabad	6-12	2017
90	100	Hyderabad	8-12	2015
238	518	Sargodha	3-12 years	2016
168	278	Hyderabad	Not reported	2015
94	152	Multan	5-12	2015

7. Prevention

7.1 Chemical Agents

There are different chemical agents that can affect the adherence of bacterial cells and their metabolism like triclosan, delmopinol and chlorhexidine are found as the potent inhibitors for maturation and development of biofilm (Stewart *et al.,* 2020). The destruction of the serosa permeability barrier against bacterial cells is known as the chlorhexidine bactericidal activity mechanism. Partial cytoplasmic leakage is caused by low concentration of chlorhexidine, but cytoplasmic denaturation and condensation will occur from the higher concentration of chlorhexidine. Stannous fluoride, sodium fluoride and amine fluoride are the fluorides that act as powerful agents for preventing dental caries. In sodium fluoride free fluoride ions can interfere with the metabolism of bacteria by bacterial cell membranes (Van der Mei *et al*., 2008).

A cationic antimicrobial compound is amine fluoride having unclear mechanism of action. It was found from literature that amine fluorides bind to bacterial cell surfaces and then stability of the bacterial membrane is disturbed. Inhibitory effects against the carcinogenic microbes are restricted by limited penetration of antimicrobial compounds (Naumova *et al.,* 2019). The duration of exposure and concentration of agents may affect the anti-caries efficiency. Oral flora may be unbalanced by higher concentration of chemical compounds and may have adverse impacts like tooth staining, mucosal desquamation, diarrhea and vomiting. Promising tool for prevention of dental caries is the use of natural products (Cao *et al*., 2019).

7.2 Natural Products, Plant Extracts, and Probiotics

In the treatment of dental caries, the effectiveness of several natural compounds have been proved by clinical trials including flavone, quinine, emetine and catechol. From plants phytochemical compounds can be isolated and they act as economical and effective treatment for caries 31. But some plant products like spices and herbs may be toxic for cells, so their dose controls can be estimated by cytotoxicity tests. Usha *et al* confirmed that Stevia rebaudiana leaves extract at a concentration of 0.5% can reduce the cariogenic microbes and also for those patients having chance if caries promote buffering capacity of the saliva (Usha *et al*., 2017)..

Recently, research interest has been increasing towards probiotics that can be beneficial for the buccal cavity. It has been found from literature studies that some probiotics have the ability to control cariogenic microorganisms through the production of bacteriocins, hydrogen peroxide (Goel *et al.,* 2020), and microcin. Another research compared the standard milk with milk supplemented with probiotic lactobacilli for checking its impact on patients having higher risk for caries. Results suggested that patients receiving the probiotic showed less number of lesions as compared to those receiving standard milk. So, that research study demonstrated that use of probiotic lactobacilli for caries can be effective (Rodríguez *et al*., 2016).

Table 3: Probiotics mechanism of action for dental caries and target organisms (Chen *et al*., 2020)

Action Mechanism	**Type of Biofilm Model**	**Target Bacteria**	**Probiotics**
A strong competitor of *S. mutans* for spatial and temporal niches	Rat oral cavity	*S. salivarius*	*Lactobacillus plantarum*
Integrate with bacterial communities by adherence to biofilm.	Static, Multi-species biofilm	*S. parasanguinis,*	*L. casei*
Act against oral pathogens	Static, Multi-species biofilm	*Streptococcus spp.,*	*L. paracase*
Peroxide, Organic acid	S. mutans–biofilm, static, Single specie biofilm, Lactobacillus spp.	*S. mutans*	*L. salivarius, L. reuteri*
Bacterins	plaque-disclosing solution	*S. mutans*	*Streptococcus salivarius*
Act against oral pathogens	Static, Double species	*C. albicans, S. mutans*	*L. salivarius*
Integrate with bacterial communities by adherence to biofilm.	Human oral cavity	*S. mutans lactobacilli*	*L. rhamnosus*

7.3 Plant-Derived Cariogenic Biofilm Inhibitors

Scientists are looking for plants that produce higher amount of antimicrobial compounds. The importance of medicinal plants as an efficient source of drug have realized by international dental practitioners. In the inhibition of dental caries some plants showed satisfactory results as compared to synthetic medicines with low side effects (Abdalla *et al*., 2020). About 80% of the world's population according to WHO depend on natural products for treating diseases. Mostly one botanical molecule is contained by herbal medicines. Malvania *et al.* suggested that licorice extract as compared to sodium fluoride produced higher inhibitory effect against cariogenic microbes. Dry or fluid plant extracts if added to oral caring products like, oral care functional food, mouthwash or toothpaste may increase the anti-caries properties (Malvania *et al*., 2019). While filling cavities in treating caries pain plant ingredients are also used (Rosas-Piñón *et al.,* 2012).

In plants secondary metabolites are mostly antibacterial substances that are not needed for growth of plants but can be used for physiological functions. They include organic acids, flavonoids, phenols and alkaloids (Shad *et al*., 2014). Still lot of research work is needed for determining the mechanisms of the anti-caries potential of plant based products. For many years, plants have been used as an alternative to synthetic medicines for treatment of oral health and most of them have reducing infection and antibacterial properties (Yabuta *et al.,* 2018). The inhibition of glucosyltransferase that play a very important role for synthesis of water-insoluble glucan is an anti-caries compound that prevent the formation of cariogenic biofilms (Farkash *et al*., 2020). So, it is very important to investigate the plant extracts containing different bioactive compounds. Coriander, clove and cinnamon are very effective for controlling dental caries. Phenolic acids antimicrobial activity is related to position and number of substituents on the benzene ring. Length and saturation of side chains can be affect the antimicrobial activity (Ferreira-Filho *et al.,* 2020).

The formation of hydrogen bonds between proteins in the cell membrane and hydroxyl groups in xanthorrhizol is the antibacterial mechanisms of xanthorrhizol. To the cell membrane of C. albicans hydroxyl groups bind and affect the permeability of membrane which results in cell lysis (Chen *et al.,* 2020). The suppression of the pathogen cytokinesis is one of the process of antimicrobial action of alkaloids. In pathogens cellular enzymes are inactivated by Polyphenols. About the mechanism of action of bioactive compounds involved in anti-caries require detailed research. Additionally, along with antimicrobial compounds, antioxidant compounds are also produced by plants due to the presence of flavonoids and polyphenols. For controlling dental caries plant based compounds can be an adjunct therapy. Specific or whole plant parts can be used in reducing global incidence of caries by preventing formation of dental biofilm (Choi *et al.,* 2017).

Table 4: Bioactivity of Plant extracts against cariogenic microorganisms (Devi and Ramasubramaniaraja, 2009: Chen *et al.,* 2020).

Biological Activity	**Target Organism**	**Extracts & Bioactive Compound**	**Plants**
Antimicrobial, Antifungal	*Lactobacillus casei, S. mutans, Candida albican*	quassinoids, β-carboline alkaloids, canthin-6-one alkaloids, Ethanol extract,	*Eurycoma longifolia jack*
Antimicrobial	*S. mutans*	Glycyrrhizin	*Licorice Root*
anti-biofilm, Antimicrobial	*S. mutans*	Water extract	*Cinnamomum burmannii*
Antimicrobial	*Candidaalbicans*	Cinnamaldehyde, Methanol extract	*Cinnamon bark*
Anti-cariogenic properties, Antimicrobial,	*S. mutans*	glycosides, Organic acids,	*Sterculia lychnophora Hance*
Antimicrobial	*Lactobacillus casei*	terpenoids, sterioids,alkaloids,	*Quercus infecteria*

		glycosides, cardiac, Tannins,	
anti-GTase, antimicrobial, anti-biofilm	*Candida albicans, S. mutans*	Flavonoid, Phenolic compound	*Thuja orientalis*
anti-GTase, antimicrobial, anti-biofilm	*Candida albicans, S. mutans*	Flavonoid, Phenolic compound	*Camellia japonica*
Antimicrobial	Microorganisms collected from extracted teeth	Catechins	*Tea tree*
Antimicrobial	*S. mutans*	Lipids, oeloc acid, oleic acid,	Clove
Antimicrobial	*S. mutans*	Allicin, Gingerol	*Acacia catechu*
Antimicrobial	*S. mutans*	Allicin	*Pongamia pinnata*
Anti-biofilm, Antimicrobial	*Lactobacillus fermentum, Staphylococcus epidermidisand, , Streptococcus agalactiae*	lipids, Eugenol, oleic acid	*Cymbopogon citratus*
Antimicrobial, Anti-biofilm	*C. albicans*	Methanolic extract	*Curcuma xanthrorrhiza*
anti-demineralizing, Antimicrobial	*Bifidobacterium dentium, Prevotella nigrescens, Lactobacillus casei, Fusubacterium nucleatum, Candida albicans, Streptococcus sanguinis, , Streptococcus sanguinis, S. mutans*,	Methanolic extract	*Bauhinia forficata*
Antimicrobial, Anti-biofilm	*Streptococcus spp*.	Lemon Grass Essential Oil	*Bauhinia forficata*
Anti-biofilm	biofilm-forming microbes	Ethanol extract	*Melia azedarach L.*
Antimicrobial, Anti-biofilm	biofilm-forming strains	Tincture	*Tamarix aphylla*
Antimicrobial, Anti-biofilm	biofilm-forming strains	water extract. acetone, ethanol extract	*Acacia Arabica*

CONCLUSION

The present review documents several risk factors of dental caries which had numerous interventions to prevent caries. Since extensive damage from caries can lead to major problems for the individual, affecting quality of life both functionally and esthetically. Increasing the awareness and knowledge about dental caries in general can increase their knowledge and skills in oral health care. Hence, preventing caries is an important element in public health efforts. Personal hygiene cares (proper brushing with flouride tooth paste and flossing daily) and dietary modification (minimizing snacking, chewing gum, milk and green vegetables) should be recommended. Raising public awareness about dental check-up may assist in early diagnosis.

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