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Review Article

Enamel Demineralization: A Comprehensive Literature Review - Part I

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Abstract

Dental caries is a dynamic disease resulting from the interaction of cariogenic bacteria, host, and environmental factors. Enamel demineralization pathogenicity and related factors, particularly the impact of orthodontic biomaterial with detection and management modalities, have yet to be reviewed thoroughly. This article reviews incidence and prevalence, pathological process, histological presentation, and etiological factors; providing a comprehensive understanding of factors that affect the oral environment and contribute to lesion formation. Thus, better knowledge for clinicians, researchers, and future material/research improvement.

Keywords: *Dental Enamel; Dental White Spots; Tooth Demineralization; Preventive Dentistry*

Introduction

Dental caries is a complex and dynamic disease caused by a complex time-dependent interaction between the cariogenic biofilm, host, and fermentable carbohydrates when the equilibrium between the pathological or demineralization factors and the protective or remineralization factors is disturbed [1,2]. White spot lesions (WSLs) are considered the initial stage of enamel demineralization, which produced by bacterial plaque activity that is retained over enamel surfaces for a prolonged period [2].

WSLs are characterized by a dramatic mineral loss from the enamel surface, which turns the enamel surface into a rough, opaque, milky-white area that becomes apparent when dried by air and by a surface consistency softer than that of the intact enamel [2-6]. This appearance reflects the direct association between enamel translucency and its mineral content [5,7].

Fixed orthodontic appliances are strongly attributed to WSLs; appliance irregularities act as plaque stagnation areas which cause difficulty in maintaining good oral hygiene and prevent salivary and muscular cleansing activity [6]. The inevitable formation of WSLs with fixed orthodontic appliances is discouraging to a specialty that involves dentofacial esthetic improvement among its goals, thus, proper knowledge of WSLs is crucial for prevention, early detection, and intervention [8-10].

Incidence and prevalence of WSLs

Related studies showed a wide incidence and prevalence rates of WSLs among orthodontic patients [11,12]. This variation is related to the lack of standardization of WSLs definition, detection, and the sensitivity of different diagnostic methods [11,12]. However, there is an agreement on its rapid development, within one month of fixed appliances bonding that increased dramatically with the longer treatment duration [12,13].

Akin., *et al*. (2015) revealed that the incidence of WSLs in newly treated patients was 32% at the end of treatment duration [14]. Other findings found the incidence of WSLs ranges between 42 - 45% during orthodontic treatment with fixed appliances [6,15].

A detected WSL prevalence of 38 - 42% after the placement of a fixed appliance and with an extended treatment period of six months, and an even greater prevalence within a treatment period of 12 months [5,15]. A systematic review and meta-analysis showed high WSL prevalence rates of 68.4% [6].

Pathogenesis of WSLs

Oral microorganisms and organic components aggregate and colonize on dental surfaces, forming dental plaque [2,16]. Pathogenic and acidogenic species, mainly *Streptococcus mutans* (*S. mutans*) and *Lactobacilli* are capable of metabolizing fermentable carbohydrates producing acidic by-products [17,18]. WSLs occur slowly through frequent, episodic, and persistent exposure to acidic media of potential hydrogen (pH) equal to or below 5.5, initiating enamel hydroxyapatite dissolution (demineralization) [2,4]. If the causative factors and environmental conditions get changed to a more favorable status, plaque pH will be normalized to 7.0, arresting the mineral loss process (remineralization) [2,4].

During the demineralization phase, hydrogen ions begin to be transferred from the dental plaque that was initiated by cariogenic pathogens into the enamel surface, resulting in crystal dissolution and enamel porosity [19]. The dissolved minerals are released into the dental plaque against their concentration gradient, driven by the resultant energy of the hydrogen ion active transport influx [2]. Such a mineral release lowers the required pH needed to dissolve the enamel further, thus, suppressing the demineralization process to some extent [2,16]. Therefore, allowing fluoride fusion into the enamel, forming fluorohydroxyapatite, makes it more resistant to dissolution [2,16].

Initial demineralization involves two stages and can be detected in both of them. In the first stage, the outer surface of the enamel is affected, resulting in the preferential removal of the interprismatic substance, which is referred to as surface softening or the demineralization width or extent [6,20]. Second, the deeper part of the enamel is affected while some remineralization occurs on the outer layer, leaving a porous and highly mineralized outer surface that is referred to as a subsurface lesion or the demineralization depth [6,20].

The initial enamel lesion is characterized by a 10- to 100-µm thick intact surface layer with a subsurface core lesion, which is a consequence of the lower crystal density at the enamel core than at the outer layer [16,19,21]. Lesion pores contribute to surface roughness, and more light scatters from the porous areas, resulting in a loss of surface translucency and shininess as well as an alteration of the internal reflection (refractive index) that causes the enamel to appear opaque [22,23]. In these early stages, the enamel is intact even though the lesion can be easily cavitated if a pointing force is applied to it; the lesion can progress to jeopardize the esthetics more or ultimately lead to dental cavitation [16,19].

Histology of WSLs

Histologically, WSLs display four zones that reflect the dynamic mineral content fluctuation within the enamel structure.

(A) The demineralized translucent zone is characterized by the loss of the enamel structure by a 1% pore volume from the initial mineral loss [2,16]. Under a polarized microscope, a stain penetrates the microcavities between the enamel prisms, which makes the enamel appear translucent [2,16,21,22].

(B) The dark zone is characterized by a 2 - 4% pore volume filled with air, which leads to a difference in the refractory indices of the enamel and the air that causes the opaque clinical presentation [2,16]. Under polarized light, this zone appears dark, as the microcavities are too small to absorb the stain [16,21].

(C) The demineralization core zone is situated approximately 15 - 30 µm beneath the overlying intact enamel surface [2]. It is characterized by a structureless enamel, with the highest pore volume of 5 - 25% [2]. This reflects continuous mineral loss, in addition to water imbibition, which leads to a different refracting index that separates this layer from the first one [2,16].

(D) The remineralization surface zone forms the outermost intact surface overlying the lesion, with < 5% pore volume [2]. Following the enamel mineral loss, the fluoride present in the oral environment or dental plaque is incorporated into the enamel with low mineral content [2,16].

Etiological factors of WSLs

The pathogenicity of the WSLs' prolonged cycle is connected to the complexity of the oral environment and biofilm. Hence, factors that affect the oral environment and the biofilm will also influence the lesion pathogenicity cycle, occurrence, and extension.

Cariogenic bacteria

Acidogenic bacteria presence in the oral cavity is normal including *Streptococcus mitis, Streptococcus gordonii, Streptococcus sobrinus, Actinomyces species, Streptococcus oralis*, and *Streptococcus anginosus* [23]. In particular, *S. mutans* and *Lactobacilli* are capable of fermentable carbohydrates' rapid metabolization, resulting in demineralization [10,11,25].

Host-related factors

Dental anatomy

Anatomical variations that can retain dental plaque, such as deep pits and fissures, can contribute to localized demineralization [26].

Enamel characteristics

Enamel solubility is related to crystal lattice arrangement and mineral content; a well-packed crystalline structure and high mineral content provide fewer impurities and lead to a more acid-resistant enamel surface [27,28]. Enamel thickness influences its acid solubility indirectly; the thinner the enamel layer, the shallower the dentinoenamel junction which characterized by high carbonate content [28]. Carbonate ions act as a substitute for phosphate or hydroxyl content and fit poorly into the crystal lattice, disturbing its stability, making it more prone to acid diffusion, and eventually increasing crystal solubility [27,28].

An increase in the roughness and porosity of the enamel can promote plaque retention, bacterial adherence, acid transport, and demineralization while triggering the other direction toward remineralization [29-31]. Moreover, an altered crystal density due to gradient mineral content or crystallographic defects leads to a more porous, which can increase the diffused acid concentration and contribute to demineralization acceleration [19,27].

Furthermore, there is a direct relationship between the mineral volume of the enamel and its hardness, which is reflected in the differences in the surface characteristics and the inorganic content of the tooth layers [32,33]. WSLs jeopardize enamel hardness which contributes to lesion progression [34,35].

Saliva

An adequate salivary flow rate acts as a self-cleaning mechanism and as a mineral reservoir favoring remineralization [33,36]. An abnormal salivary flow rate can be seen in some health conditions or caused by some medications (Table 1) [25,37,38].

Factors decrease the salivary flow rate	
Disease/health conditions	Autoimmune disease, diabetes mellitus, salivary gland pathological blockage
Therapies/medications	Antiarrhythmics, anticholinergics, anticonvulsants, antidepressants, antiemetics, antihypertensives, antimetabolites, antiparkinsonian agents, antipsychotics, antihistamines, beta-adrenergic, chemotherapeutic agents, diuretics, large doses of vitamin-D, narcotic analgesics, sedatives, and tranquilizers)
Aging	-
Gender	Female had a lower flow rate
Factors increase the salivary flow rate	
Medications	Hormone replacement therapy, oral contraceptives, and pilocarpine
Masticatory or gustatory stimulation	-

Table 1: *Factors affecting the salivary flow.*

The saliva buffering capacity works to balance acidic pH due to its organic and inorganic composition; it is predominantly related to bicarbonate (HCO_3^-), phosphate, and protein [39]. Bicarbonate removes the increased amount of hydrogen ions (H^+) produced by bacteria, thus, shifting the environment into a more alkaline medium [22]. Most saliva proteins and phosphate make a minor contribution to buffer capacity when pH is below the physiological state [33,39]. Beyond that, bacterial enzymes break down salivary arginine-rich protein into urea and ammonia shifts toward an alkaline pH [40]. Furthermore, the protein inhibits *S. mutans'* growth through an iron-independent mechanism [25].

The salivary composition includes secretory antigens and antibodies in the saliva allowing immune detection and the neutralization of microorganisms' products [25]. Salivary enzymes such as peroxidase, lysozyme, lactoferrin, and histatins inhibit glucose metabolism by limiting microorganism growth and disturbing the bacterial outer layer [38,40]. In addition, salivary enzymes promote bacterial aggregation while preventing adherence to tooth structures, thus eliminating bacteria [25,36,39,41]. Other proteins/enzymes act as binding ions, making them media for bacterial adherence and growth [38].

Gender

Although the literature has concluded that differences between genders in the risk of developing WSLs are insignificant; males tend to have a slightly higher risk of developing WSLs than females which can be attributed to variations in their compliance with oral hygiene standards, their motivation to do so, and their meticulousness in observing such standards [42].

Genetic susceptibility

The genetic component of enamel demineralization has a complex interaction with non-genetic factors, which is reflected in its regulation of saliva composition and flow, tooth morphology, and enamel formation and characteristic [43,44].

Genetics affect the host by influencing the dental substrate development. Mutation of specific amelogenin X-linked (AMELX), ameloblastin (AMBN), enamelin (ENAM), tuftelin, and dentine sialophosphoprotein (DSPP) genes; will interfere with enamel and dentin formation and their crystallization, surface properties and integrity, acid resistance, and demineralization susceptibility [45].

A more recent concept was derived from the genetic or hereditary regulation of taste sensitivity, specifically by the bitter marker known as 6-n-propylthiouracil (PROP) controlled by taste 2 receptor member 38 (TAS2R38) gene with other genes [43,45,46]. Individuals with a greater sensitivity to tasting PROP have a lower threshold sensation to other flavors in comparison to medium tasters and non-tasters [46,47]. Furthermore, those who are more sensitive to the taste of PROP have been found to consume fewer sugary items in comparison to non-tasters, who tend to have a higher sugar intake and higher prevalence of WSLs [46,47].

Genetics influence microbial colonization through several genes that found on the short arm of chromosome 6 that control immune molecules against oral colonization and enamel demineralization susceptibility [45]. Studies showed an association between the lactotransferrin (LTF) gene and an overall lower caries susceptibility as well as higher levels of salivary flow [45,48].

The WSL phenotype has a powerful marker for gene mapping due to its contribution to the heritability of caries and similar genetic regulation [44]. Future research evaluating the epidemiological prevalence of such genetic factors in the population, and the physiological and environmental adaptation of the affected individuals will help to enhance understanding of such factors and the extent of their impact on the oral biofilm and WSLs.

Environmental-related factors

Socioeconomic status

There is no direct relation between different socioeconomic status and enamel demineralization risk; however, other findings have demonstrated that individuals of low socioeconomic status tend to have higher demineralization susceptibility due to different priority needs, education levels, and access to preventive programs [25,49].

Diet

Dietary habits influence the development of WSLs directly; higher sugar and acidic consumption considered a major contributory factor that leads to dramatic pH drops and enamel demineralization [11]. Furthermore, with increased carbohydrate intake frequency, the enamel is exposed to a repeated acidic attack with less time for repair [10,11,29].

Chewing gum that contains xylitol can help prevent enamel demineralization as it stimulates saliva secretion, inhibits bacteria attachment, and directs the environment toward remineralization [10,33]. Additionally, xylitol is a type of carbohydrate (polyol) that is not metabolized by S. mutans bacteria, thus stopping acidic substrate release [10,33,50].

Oral hygiene

Good oral hygiene maintenance will mechanically control dental plaque quantity, disturb the metabolism of fermentable carbohydrates in addition to balancing pH, and allow remineralization through fluoride-containing toothpaste [10]. Failing to maintain proper oral hygiene or the presence of obstacles, such as dental appliances or faulty restorations, favors plaque accumulation and contributes significantly to WSL initiation [10,51].

Altered oral environment

Fixed orthodontic appliance

WSLs have been linked to orthodontic fixed appliances; when a foreign body is inserted into the mouth, including any dental biomaterial, it acts as new housing for microorganism accumulation with a pathological potential [52,53]. Introducing orthodontic fixed appliances in the mouth favors oral biofilm formation and maturation with an increased level of acidogenic bacteria [13,18,54,55].

In essence, the bonding of fixed orthodontic appliances is accompanied by a lowered resting pH, while poor oral hygiene can determine the drop in pH toward the critical value [56]. Differences in oral hygiene and their resulting pH fluctuations are represented in the Stephan

curve (Figure 1) [56]. Many factors related to fixed orthodontic appliances influence WSL development, including appliance design, ligation method, type of material, and adhesive system.

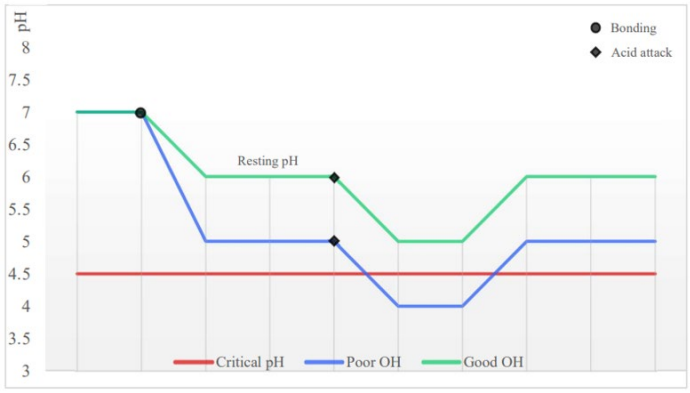

Figure 1: *Stephan curves in orthodontic patients with good/poor oral hygiene.*

Design

Different fixed appliance specifications influence the amount of plaque accumulation and demineralization occurrence. Smaller bracket designs with lower profiles, such as Begg and self-ligating brackets, have better plaque control than pre-adjusted brackets [57,58]. Even so, WSL incidence with different bracket designs has been inconsistent due to carbohydrates and oral hygiene being the determinant factor [59].

Ligation method

Current data show that steel ligation provides better plaque control than elastomeric modules. However, inconsistencies in WSL incidence are attributed to the increased demineralization risk with the use of elastomeric modules over a self-ligating system [60].

Bracket material

Although the initial affinity of *S. mutans* to metal brackets has been demonstrated to be significantly lower than to plastic or ceramic brackets due to the surface texture of metal brackets, ceramic brackets exhibit less long-term biofilm accumulation than metal brackets due to the higher surface tension of stainless steel brackets, which increases plaque retention [45,46]. However, WSL formation was higher among those with ceramic brackets than among those with metal brackets, which can be attributed to the more porous and rougher surface of ceramic brackets [20,32]. The higher WSL incidence with metallic brackets than ceramic brackets is related to higher microleakage, particularly at the bracket-adhesive interface due to higher metal dimensional changes than ceramic, enamel, or adhesive resin [12,23]. Furthermore, the longer the duration of orthodontic treatment is, the higher the risk of developing WSLs regardless of bracket material [42].

Adhesive system

In general, white lesions due to orthodontic treatment occur on the buccal surface of teeth and in areas that are difficult to clean [9]. Bonding resin is covered with plaque and mixed pathogens in all areas due to its roughness [43]. The flash-free adhesive bracket system has significantly less plaque than regular non-flash-free systems [55].

Other studies have found that the adhesive system did not influence the WSL development [43,54]. A systematic review and meta-analysis concluded that the current evidence is not sufficient to correlate WSLs to type adhesive systems [49].

Bonding process

Bonding orthodontic appliances onto dental enamel requires a surface treatment to allow appliance attachment. The mechanical properties of an etched enamel surface are affected by the degree of demineralization and the penetration of the resin tags during bracket bonding, which is important in understanding the iatrogenic damage caused by fracture during debonding and the discoloration from the retained resin tags [41]. A self-etch surface treatment causes a minimal decrease in the hardness of the enamel surface, unlike the conventional total-etch surface treatment [32,34].

Although self-etch contains acidic monomers assumed to increase the risk for WSLs; the released minerals will prevent demineralization progression [15]. WSL depth was found to be related to the etchant penetration capability, which is higher for total-etch surface treatment [33-36]. Such a contributory factor would be more important in individuals at higher risk of WSL development, particularly the one that includes enamel surface alternation as a preparation for the bonding process.

Erbium-doped yttrium aluminum garnet (Er:YAG) laser is a recent modality for enamel surface conditioning that was found to have a similar enamel demineralization rate as conventional etching [50]. However, it contributes to lower mineral loss during enamel conditioning than conventional etching [58]. Even though, further studies are required to standardize the recommended protocol for its clinical use.

Conclusion

The occurrence of WSLs is related to the interaction of multiple factors. Introducing dental biomaterials into the oral cavity, particularly, fixed orthodontic appliances would increase the complexity of such interaction. More studies on the contributions of the different orthodontic components, adhesive systems, and etchant types to WSLs will provide a better understanding of the disease and, thus, will enable better prevention of WSLs for patients seeking orthodontic treatment.

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