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Ministry Of Higher Education And Scientific Research

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A survey study on The Relationship between systemic diseases and dental caries in children

A project submitted to the council of the collage of Dentistry at the University of Misan, Department of Conservative in partial Fulfillment of the Requirement for B.D.S degree

BY

Ruqaia Abdullah Hussein

Sara qasim lsmail

Supervised by

Dr. Majeed Hussein Majeed

Certification of the Supervisor

I certify that this project entitled **" Relationship between systemic diseases and dental caries in children "** was prepared by the fifth-year students **Ruqaia Abdullah Hussein and Sara qasim lsmail** under my supervision at the College of Dentistry/University of maysan in partial fulfilment of the graduation requirements for the bachelor's degree in Dentistry.

Supervisor Signature

Dr Majeed Hussein Majeed

Dedication

To the one who brought us out of the darkness into the light... To the

first one who defended the woman and gave her rights at a time when the female was buried and she was still alive... To the one who advised us to diligently seek knowledge... To the city of knowledge... Our Nobel Prophet Muhammad (PBUH)

To all martyrs and people of my injured country Iraq with love.

To my family particularly, to my parents for their love and support throughout my life.

Acknowledgment

First of all, I thank "Allah" almighty for granting me the will and strength to accomplish this research and I pray that his blessings upon me may continue throughout my life.

I am indeed internally thankful to my supervisor Lecturer. Dr. Majeed Hussein Majeed for his continuous guidance, generous advice, and without their encouragement and wise supervision; the present project would not see the light of the day.

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List of abbreviations

RA	**Rheumatoid Arthritis**
AD	**Alzheimer disease**
S-ECC	**severe early childhood caries**
BMI	**Body mass index**
CF	**Cystic fibrosis**
CD	**Celiac disease**

Aim of the study

The aim of this study was to investigate the presence and distribution of developmental enamel defects and caries in children with systemic diseases and to evaluate and present evidence from animal and human clinical studies on associations between dental caries and systemic diseases, and to suggest potential mechanisms that might explain such associations.

INTRODUCTION:

Dental caries is one of the most prevalent conditions worldwide [1] and accounts for significant morbidity [2]. Importantly, the prevalence of untreated dental caries has increased [1, 2]. While there is a direct effect of untreated dental caries on oral health and associated quality of life, identification of indirect associations between dental caries (including untreated dental caries) and systemic health are of potential interest but have received little attention [3].

Associations have been more studied between periodontitis and systemic diseases and the contribution of oral inflammation and microbiota to diseases such as atherosclerosis, diabetes mellitus, pneumonia, chronic obstructive pulmonary disease, rheumatoid arthritis (RA) and Alzheimer disease (AD) [45,]. In addition to epidemiologic evidence, laboratory and animal studies provide biological plausibility for periodontal systemic associations [6,7].

While both dental caries and periodontitis are biofilm mediated diseases, the pathogenesis of dental caries is complex and multifactorial and differs from periodontal disease. Dental caries is a biofilm-mediated disease with multiple contributing factors that drives net localized demineralization of the teeth [8]. The plausibility of systemic consequences from untreated dental caries and mechanistic role of the associated oral microbial inflammatory process in these associations requires further inquiry through human and animal studies. The ability of oral microbiome to spread into systemic circulation from dental caries is plausible and would parallel mechanisms already studied for periodontal disease.

In dental caries, involvement of root canal space ormarginal periodontium are the most likely pathways for direct systemic extension of oral microbiota [9].

Host factors and pathogenic traits in oral microbiota can promote dental caries and increase the like lihood of oral-systemic spread. Such factors would include diseases[10]and medications[11]that result in reduced saliva production, adhesin expression in S.mutans for collagen binding [12,13], dysbiosis of the oral microbiota[14,15],genetic factors that predispose to dental caries and share common mechanistic underpinnings with systemic diseases [16].

The hypothesis of systemic spread of oral microbiota from carious lesions is reasonable but mechanisms by which systemic diseases exacerbate dental caries requires considerable future research. Metabolic diseases such as diabetes and obesity share various common environmental determinants with dental caries, including hyperglycemic state and high-carbohydrate/ sugar-rich diet [17]. Our current understanding of metabolic disease-dental caries associations and use of animal models[18,19]can serve to expand understanding of associations between dental caries and other systemic diseases .Animal models allow for study of systemic variables in dental caries due to the ability to longitudinally study disease phenotype within a reasonably short time frame.

This scoping review compiled and evaluated recent evidence from animal and clinical human studies that assessed associations between dental caries and systemic diseases and potential mechanisms for such associations. Specifically, a scoping review was undertaken to establish areas in which evidence on associations between dental caries and systemic diseases is available [20].

1 Diabetes Mellitus

Several human clinical studies and animal studies have addressed the connection between dental caries and diabetes. Outcomes other than caries were also studied, including salivary composition, microbiology and periodontal status. Hegde et al. found that caries active participants who were diabetic demonstrated significantly reduced salivary calcium and significantly increased alkaline phosphatase when compared to caries active non-diabetic participants [21].

Similarly, Al-Badr et al. demonstrated that children with type 1 diabetes had s nificantly lower salivary pH and higher counts of Lactobacilli. Reduced salivary pH and higher lactobacilli count are crucial factors for demineralization of teeth and exacerbation of dental caries [22]. Reduction in salivary pH and increase in counts of cariogenic microbiota can occur secondary to cariogenic diet and poor plaque control and was demonstrated as such by Kamran et al. [23]

Two other studies showed that lifestyle, dietary and oral care factors were significantly different between groups with controlled and uncontrolled diabetes measured by glycated Hb [24,25]. Similarly, when pediatric cohort with phenylketonuria and those with type 1 diabetes were compared, children with phenylketonuria had significantly higher caries experience [26].

Animal studies used rodent models of diabetes (primarily type 1 diabetes) and hyperglycemia to study its relationship with dental caries and other tooth-related changes [18,19]. Changes in enamel, dentin, pulp and salivary glands with alveolar bone loss were compared, both to control groups and groups with intervention

using fluoride application and insulin administration. Consistent results from animal models demonstrated that hyperglycemia in diabetic rodents was associated with increased dental caries [27,28]. In addition, these studies showed that there were histological and morphometric changes in enamel, dentin and pulp in diabetic animals. There were reduction in volume of pulpal con- nective tissue and enamel and dentin, along with excessive wear of enamel [18,29,19,30]. Salivary histological change included vacuolization in acinar cells and functionally, reduction in saliva production that resulted in xerostomia [19,30]. Carious lesions positively correlated with gingivitis and periodontitis [31,27]. Lastly, both fluoride application and insulin administration interventions resulted in reduction of dental caries, marginal gingivitis and periodontitis [32,33].

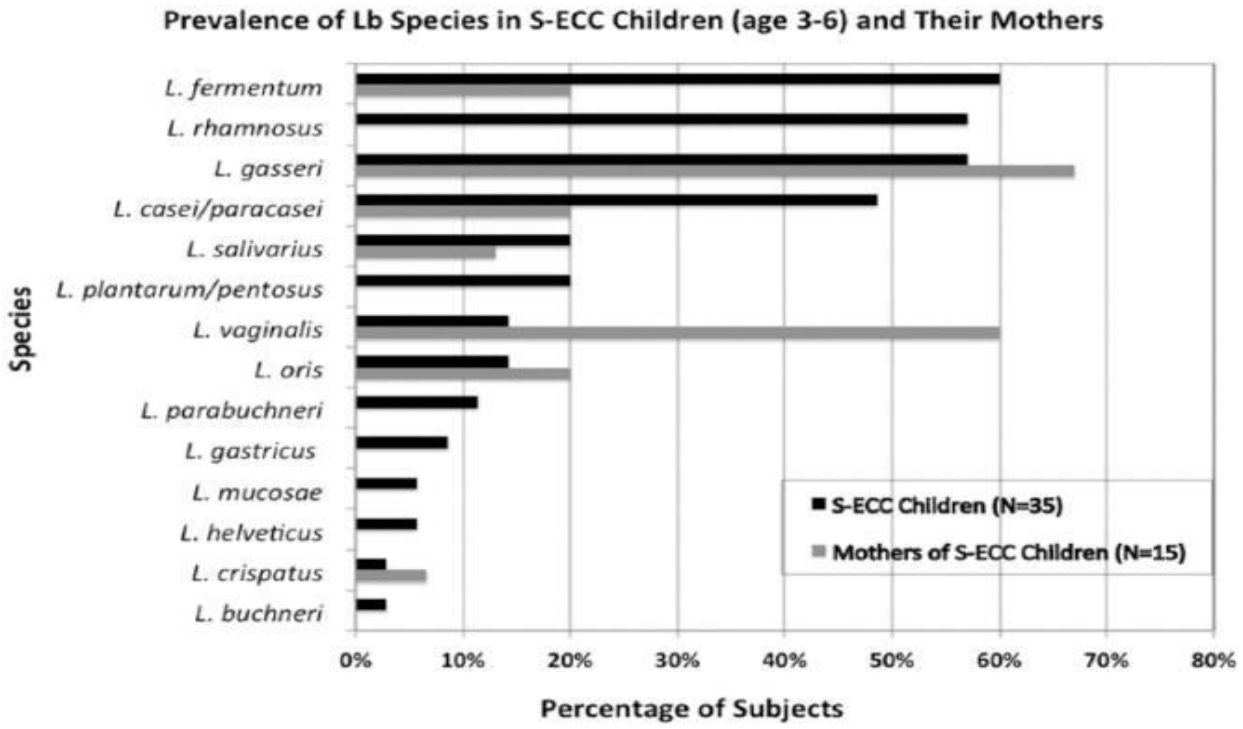

Table 1

Prevalence of the different Lactobacillus species isolated from children with severe early childhood caries (S-ECC) (n = 35) and their mothers (n = 15)

2 Obesity

Of all systemic diseases, an association between obesity and caries was more robust than noted for other systemic conditions, as documented in twenty-two human clinical studies including eight longitudinal clinical studies. Data from longitudinal studies did not consistently find an association between obesity and dental caries and

studies with larger samples sizes did not find association between dental caries and obesity [31, 32, 33, 34, 35,36, 37, 38, 39, 40, 41]. In studies where obesity and metabolic syndrome were found to be associated with caries, odds ratio ranged from 1.01 to 3.7 [31, 32, 42, 43, 41,44]. Interestingly, a relationship between low BMI and dental caries was noted and an inverse relationship between overweight status and caries was seen in some studies [45, 46, 38]. Chala et al., through statistical modeling found a U-shaped relationship between BMI and caries, which means that caries was associated with both under- weight and overweight status [45] and this U-shaped relationship between BMI and caries has been reproduced in two recent studies. Untreated dental caries can impact overall nutritional status and subsequently BMI. Further, reduction in masticatory efficiency can promote intake of softer foods and increase in dental caries burden [47, 48]. Longitudinal studies are needed to examine relation- ship between onset and progression of dental caries and their effect on BMI. A study showed significant weight gain in children when teeth with severe dental caries and pulpal involvement were extracted [49]. Mixed results on the association of BMI and dental caries are also indicative of the complex etiologic nature of dental caries. Various factors including access and attitude to dental care, socio-economic status, maternal education, oral habits, diet, biological and microbiological factors interact in caries

etiopathogenesis [50]. Additionally, variable definitions and surrogate markers used in association studies further complicate consensus and ability to synthesize reproducible conclusions [51]. An important implication of the mixed results observed for caries association with systemic conditions likely results in lack of reliable, reproducible risk prediction tools for dental caries [52]. It appears that past and current caries experience along with frequent follow ups and use of fluoride for caries prevention remain the most effective tools for caries prevention in clinical practice.

3 Cystic fibrosis

Cystic fibrosis is a complex, lethal, multi-system autosomal recessive disease resulting from mutations on chromosome 7 that cause dysfunction of an ion channel located on epithelial surfaces. Pulmonary disease is the leading cause of morbidity and mortality in CF. The specific dental manifestations of the disease may result from the condition itself or from complications of treatment.

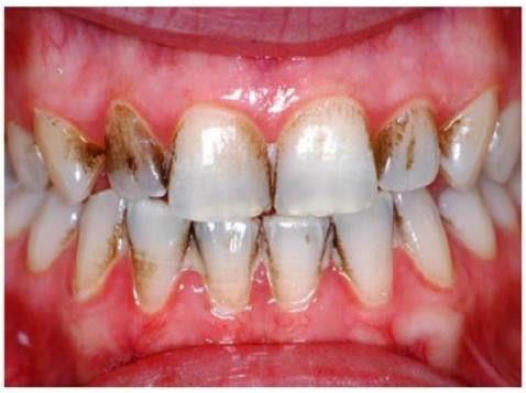

Figure 1

Black discolouration of teeth following the

utilisation of the carbapenem antibiotic meropenem [53]

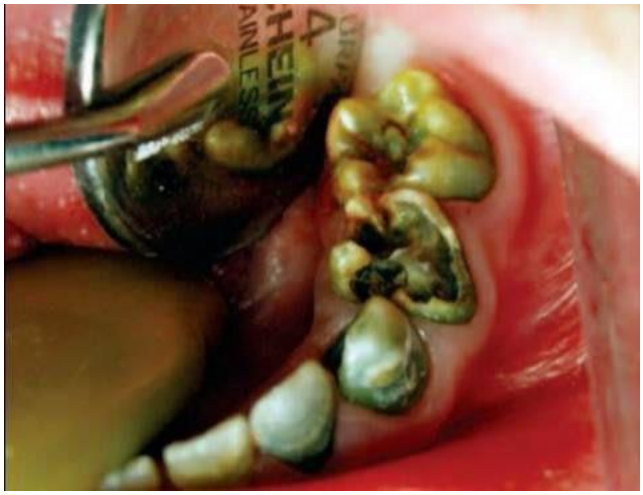

Figure 2

Clinical picture of primary maxillary left mandibular molars showing hyperbiliruminemia stain affecting enamel and dentin, caries and enamel hypoplasia [54].

3.1 •Dental caries

The etiology of the most common oral diseases (dental caries, periodontal disease) is multifactorial. Health conditions, drug therapy, salivary profile, socioeconomic factors and habits are important in the initiation and progression of these diseases [55]

3.2 Factors influencing caries initiation and progression in patients with CF

Theoretically, patients with cystic fibrosis could be considered as patients at high risk for caries [56].

Due to the thickening of mucus, nutrient absorption from food is reduced, resulting in pancreatic insufficiency [57] requiring a special diet and constant supplementation with pancreatic enzymes. The daily caloric requirements for

adequate weight maintenance in CF are 130-150% of the regular requirements of healthy adults. These requirements are met by frequent consumption of high-energy meals and snacks, such as confectionery, sweetened beverages and baked goods [58].

To reduce the risk of caries, nutritional needs can be met by offering nutrient-dense foods, such as those rich in fats and oils, instead of foods high in sugar.

This can be accomplished by adding butter to foods such as soups, adding creamy rich sauces to meals, and encouraging the child to eat cheese with crackers as a snack [59].

Frequent use of supplements containing glucose polymers that break down in the oral cavity into monosaccharides is also recommended. These supplements are typically used as powders added to dishes or as high-sugar drinks [58].

The use of aerosols with mucolytic and expectorant properties, the increased use of specific antibiotics, and the correct use of dietary supplements and pancreatic enzymes have allowed cystic fibrosis patients to survive longer. Unfortunately, the acidity of the aerosols, combined with the carrier (lactose or other sugar), may play an important role in the development of caries [60].

People with cystic fibrosis have to take different treatments several times a day, frequently taking medication in the form of syrups or sweetened suspensions for long periods of time [58]; oral antibiotics, for example, are usually dosed in sweetened suspensions to modify the taste [57].

This explains the presence of carious lesions, especially in the upper temporary teeth [58].

3.3 In addition, many other factors may put patients with cystic fibrosis at high risk for dental caries: [61] [53] [59] [62] [56] [63]

- The increase in intraoral levels of Streptococcus mutans;
- High prevalence of gastroesophageal reflux disease;
- High prevalence of enamel alterations.
- Oral breathing caused by chronic nasal and sinus obstructions;
- Irregularity of dental examinations,
- Insufficient use or even refusal of topical fluoride.
- The composition and properties of saliva are also considered; however, reports on this issue are often inconclusive

4 Celiac disease

The existence of an association between gastro- intestinal disorders and dental enamel defects has been known since the turn of the century.

Dental enamel defects, mainly characterized by pitting, grooving and sometimes by complete loss of enamel, were first reported in children with CD by Aine[64].

Bossu et al.[65] analyzed on scanning electron microscope, two samples of enamel fragments from hypoplastic teeth, both deciduous and permanent, harvested from celiac children, and demonstrated that the enamel hypoplasia of deciduous and permanent teeth in CD is highly hypomineralized with shorter prisms, more irregularly distributed and less interprismatic substance than observed in the nonceliac enamel hypoplasia.

Other enamel defects, defined as disturbances in hard tissue matrices, including enamel hypoplasia, enamel opacities, and enamel discolorations that were not symmetrical or chronological in all four sections of the dentition were considered unspecific[64].

The presence or absence of enamel disturbances is presumably dependent on the timing of enamel formation. Enamel mineralization disturbances secondary to CD do not occur before a period of gluten intake coinciding with enamel mineralization. A possible explanation for the enamel defects could be hypocalcemia or, more likely, a particular genetic condition that leads to a specific immune response to glute.[66,67,68]

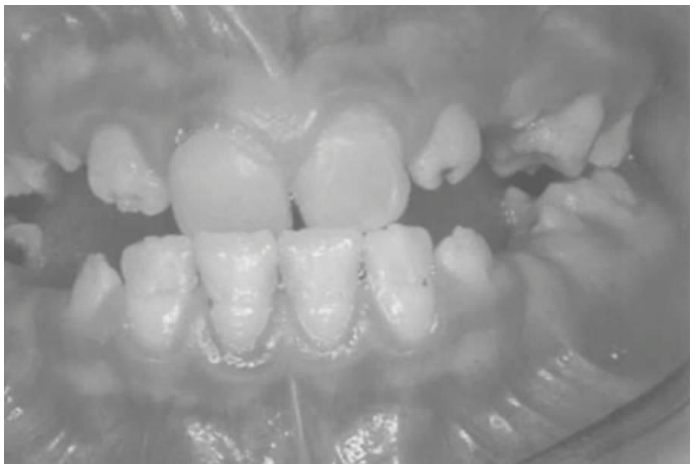

Figure 3

Systematic dental enamel defects on middle third of mandibular incisors and incisal third of maxillary lateral incisors

Location of enamel defects	CD group n=38 (%)	Control group n=20 (%)
Incisors	35 (92.1%)*	13 (65%)
Canines	15 (39.5%)**	5 (25%)
Premolars	9 (23.7%)	4 (20%)
Molars	27 (71.1%)*	9 (45%)

* $p<0.001$.
** $p<0.05$.

Table 2

Location of Enamel Defects in Different Groups of Teeth in Celiac Disease (CD) and Control Subjects

Coronal third	CD group n=38 (%)	Control group n=20 (%)
Incisal	11 (28.9%)	10 (50%)
Middle	8 (21.1%)	7 (35%)
Cervical	6 (15.8%)	3 (15%)
Incisal and middle	7 (18.4%)	0
Complete crown	6 (15.8%)	31 0

Table 3

Coronal Distribution of Enamel Defects in Patients with Celiac Disease(CD) and Controls group

Regarding the distribution of enamel defects on the coronal surface, the incisal third was the most affected surface in children with CD. Enamel defects on coronal surface other than incisal third were higher than those reported by previous investigations[66]. This again can be linked to the time course of the disease in relation to odontogenesis.

Characterized by small bowel mucosal villous atrophy, CD heals after introduction of gluten- free diet[69,70]. Strict gluten-free diet led to a normal enamel formation and reintroduction of gluten in early childhood resulted in defective enamel re-development[71]. Forty-four of the children with CD, who adhered strictly to the gluten-free diet, showed fewer enamel defects than both those who adhered almost strictly and those who did not follow the diet recommendation.

Intestinal damage leads to malabsorption in patients with CD and some authors suggested that a possible explanation for the presence of enamel defects in these children is that enamel hypoplasia is caused by hypocalcemia, although they did not explore the role of vitamin D[68]. There were no differences in mean serum calcium concentration between children with or without enamel defects in the present study, so it seems unlikely that enamel defects could depend only on calcium metabolism.

Conclusion

Limited clinical evidence was found connecting several systemic diseases and dental caries.

When adequate clinical results were available, it offered mixed evidence of such associations.

Interesting animal studies were noted that could generate clinical hypotheses and further investigations in rodent models for cardiovascular injury and hyperglycemia.

Best evidence from human and animal studies described the association between metabolic diseases and dental caries. Animal studies using rodent models demonstrated significant changes in dental tissues following hyperglycemia.

Also, an association between hyperglycemia and dental caries was consistently noted in animal studies.

Inadequate data was found to suggest any modifications to current clinical practice or prevention guidelines.

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