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| RESEARCH ARTICLE

The Interplay between Metabolic Syndrome and Oral Health – A Possible Unexpected Link with Cognitive Dysfunction

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| ABSTRACT

Metabolic syndrome (MetS) is not a single disease but a cluster of conditions that significantly increase medical risks. It is typically defined by the presence of five metabolic risk factors: atherogenic dyslipidaemia, high blood pressure, hyperglycaemia, a prothrombotic state, and a proinflammatory state. MetS is a global pandemic that involves chronic inflammation and insulin resistance, leading to higher risks of heart disease, diabetes, stroke, and other disabilities. It also includes visceral adiposity, dyslipidaemia, endothelial dysfunction, genetic susceptibility, and hypertension. The connections between MetS, cognition, and oral health are complex and multifaceted. This narrative review aims to describe the relationships between each pair of conditions and a broader interconnection among all three. MetS has a bidirectional relationship with oral health, influenced by insulin resistance and local inflammation, impacting both masticatory function and glycaemic control. Additionally, there is a significant link between oral health and cognition, involving various aspects of daily life, such as poor oral hygiene practices, nutritional deficiencies, and intricate biological mechanisms, including inflammatory and immunological responses. Nutrition plays a crucial role in influencing all three areas. Essential nutrients such as proteins, carbohydrates, fats, minerals, and vitamins are vital for maintaining and improving metabolic health, cognitive function, and oral health. The nutritional factors affecting MetS, cognition, and oral health are interrelated. Poor nutrition can lead to MetS, which can impair cognitive function and increase the risk of oral health issues. Furthermore, inflammation and oxidative stress, common in MetS, are also involved in cognitive decline and periodontal disease. Among the different nutritional factors, malnutrition, antioxidants, omega-3 fatty acids, and dietary fibers are especially crucial, as they collectively aid metabolic processes, prevent cognitive decline, and support oral health. Healthcare professionals must understand the mechanisms linking MetS, cognition, and oral health to develop effective preventive and therapeutic strategies.

| KEYWORDS

Insulin resistance, mild cognitive impairment, MMSE, malnutrition, tooth loss.

| ARTICLE INFORMATION

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1. Introduction

The term metabolic syndrome (MetS) does not refer to an individual disease but to a group of conditions that pose a high medical risk. MetS is typically characterized by the presence of five metabolic risk factors: atherogenic dyslipidemia, high blood pressure, hyperglycemia, a prothrombotic state, and a proinflammatory state (Grundy et al., 2005). These risk factors are often grouped and have been well-documented in clinical practice and prospective studies through statistical analysis (Hanley et al., 2002). MetS is a global pandemic, consisting not only of chronic inflammation and insulin resistance that lead to an increased risk of heart disease,

diabetes, stroke, and other disabilities (Saklayen, 2018) but also visceral adiposity, dyslipidemia, endothelial dysfunction, genetic susceptibility, and hypertension (Sebastian et al., 2024). MetS, cognition, and oral health are interconnected in numerous complex ways, with relationships between either two of the conditions, but ultimately being closely related altogether.

2. Literature Review

MetS has a bidirectional relationship with oral health, influenced by insulin resistance and local inflammation, affecting masticatory function and glycemic control (Nóbrega et al., 2021), but also a complex relation with cognitive function. Insulin resistance and hyperinsulinemia, key features of MetS, have been identified as significant risk factors for cognitive decline in the elderly (Lai et al., 2020). There is also an important connection between oral health and cognition, which is layered in many aspects of daily life, comprising inadequate oral hygiene techniques or nutritional deficiencies and complex biological mechanisms, both inflammatory and immunological. Ultimately, nutrition can be a pivotal factor influencing all three domains. Nutritional components, including proteins, carbohydrates, fats, minerals, and vitamins, play critical roles in maintaining and enhancing metabolic health, cognitive function, and oral health. The nutritional factors that influence MetS, cognition, and oral health are closely interconnected (Ahn & Hwang, 2022; Kouvari et al., 2022). Poor nutrition can lead to MetS (Rus et al., 2023), which in turn can impair cognitive function (Alsuwaidi et al., 2023) and increase the risk of oral health issues (Kotronia et al., 2021). Moreover, inflammation and oxidative stress, common in MetS, are also implicated in cognitive decline and periodontal disease (Naomi et al., 2023). Healthcare professionals need to understand the mechanisms involved in MetS-cognition-oral changes to develop effective preventive and therapeutic measures (Nóbrega et al., 2021).

3. Methodology

We conducted this narrative review to synthesize existing knowledge of the complex interplay between MetS, cognitive dysfunction, and oral health. We separated our literature search into four sub-themes: "Relation between MetS and oral health," "Relation between MetS and cognitive dysfunction," "Relation between cognitive dysfunction and oral health," and "Nutritional factors involved in the interplay between MetS-oral health-cognitive dysfunction" – the forth category betng one of the most important factors interconnecting the three entities. A literature search was performed on electronic databases (PubMed, Embase) from their earliest records. Database-specific search terms included the keywords ''metabolic syndrome,'' ''oral health,'' ''cognition,'' and relevant synonyms. The inclusion criteria were all type of articles. The exclusion criteria were articles in other languages than English. From the articles retrieved in the first round of search, additional references were identified by a manual search among the cited references.

4. Results and Discussion

4.1 Relation between MetS and oral health

Chronic oral disease increases the likelihood of MetS through chronic inflammation due to the immune system's response to plaque bacteria, leading to alveolar bone and gingival degeneration (Marcaccini et al., 2009). Dental caries is directly or indirectly related to metabolic conditions. They represent a long-term and irreversible process caused by poor oral hygiene and previous chronic infections and inflammations (Si et al., 2017).

MetS and periodontal disease may influence each other through dysbiosis of the oral and gut microbiome. MetS can alter the oral microbiome, causing dysbiosis. Intestinal dysbiosis has been associated with an intensification of MetS, also aggravating the severity of periodontal disease. Periodontal disease and oral dysbiosis can contribute to intestinal dysbiosis, thus influencing the severity of MetS (Pirih et al., 2021).

MetS associated with inflammation and dysbiosis of the intestinal and oral microbiome, can affect bone metabolism. Increased osteoclastic activity and decreased osteoblastic maturation disrupt bone homeostasis and promote bone resorption. Insulin receptor dysfunction and insulin resistance can cause hyperinflammatory states (De Oliveira et al., 2020). Hyperglycemia associated with MetS can lead to vascular damage and delays in angiogenesis and wound healing. These problems can cause peri-implant disease and loss of attachment around dental implants, especially in the presence of a bacterial challenge (Froum et al., 2018). Furthermore, periodontal bacteria can enter the bloodstream, contributing to systemic inflammation (Leite & Nascimento, 2021).

Studies on the impact of MetS on oral health are scarce, making the relationship between MetS and oral health controversial. The systematic review and meta-analysis by Santoso CMA et al (Santoso et al., 2021) investigated the association of oral hygiene status and care with MetS. The authors concluded that better oral hygiene status, frequent tooth brushing, and frequent interdental cleaning were associated with a lower risk of MetS and that poor oral hygiene can lead to dental infections and affect systemic health (Bui et al., 2019). This association was not consistent across studies. Studies from New Zealand (Shearer et al., 2018) and Finland (Pussinen et al., 2020) did not find an association, possibly due to the younger age of their samples compared to other studies that had a higher mean age.

Periodontal disease is a significant risk factor for MetS, which increases the risk of heart disease and diabetes. Periodontal bacteria cause local and systemic inflammation, which can lead to weight gain and insulin resistance, a characteristic of type 2 diabetes. Furthermore, insulin resistance contributes to the development of the MetS (Komazaki et al., 2017). Studies in mice have shown that infection with Porphyromonas gingivalis alters the gut microbiome, reducing insulin sensitivity and affecting skeletal muscle metabolic function (K. Watanabe et al., 2021). A study evaluated infection with Streptococcus mutans, one of the known causes of tooth decay, which induces the production of inflammatory cytokines that accumulate in blood vessel walls, increasing the risk of obesity and MetS. (T. Iwasaki et al., 2019).

Some authors state that the association between MetS and oral health can be attributed to common factors, such as poor dietary habits, without a direct correlation (Nibali et al., 2019)). A study evaluating the association between periodontitis, MetS, and associated risk factors found that demographic and socioeconomic factors, as systemic and oral health behaviors, may interfere as confounders in this association. However, by isolating these confounding variables, it was concluded that the frequency of daily tooth brushing and periodontitis were associated with MetS in both men and women (J.-S. Kim et al., 2019). Brushing teeth, a crucial self-care measure to control plaque and prevent periodontal disease is recommended twice a day (Lertpimonchai et al., 2017). Studies have shown that brushing less frequently may be ineffective in preventing diabetes (Fu et al., 2019). Daily interdental cleaning reduces periodontal bacteria and interdental inflammation. Poor oral hygiene can worsen MetS by increasing inflammation (S.-W. Kim et al., 2016). Dental treatments can help lower blood sugar in patients with MetS and diabetes, while statins used for dyslipidemia can have beneficial effects on dental health (Tahamtan et al., 2020). Moreover, daily flossing is independently associated with a lower prevalence of MetS (Moradpour et al., 2023).

Socioeconomic disparities affect oral health (Hamasha et al., 2019). Due to the high cost of dental care services, most people cannot afford regular dental checkups. In addition, the level of awareness regarding oral and dental health behaviors is not high enough (Esfanjani et al., 2023). Oral health professionals can proactively increase awareness and healthcare to prevent MetS (Moradpour et al., 2023).

4.2 Relation between MetS and cognitive dysfunction

Cognitive impairment in individuals with MetS is becoming increasingly common and represents a complex public health issue. The effects of MetS and its individual components on cognitive function range from mild cognitive impairment to dementia, including vascular dementia and Alzheimer's disease (Atti et al., 2019). Some researchers have suggested the term "metabolic-cognitive syndrome" to describe this condition, which combines MetS with cognitive impairment of either degenerative or vascular origin (Frisardi et al., 2010).

When examining the cognitive domains impacted by MetS, as well as the contributing factors, underlying mechanisms, and research findings, it becomes clear that cognitive impairment is a significant concern for these individuals. This condition can lead to deficits in memory, attention, concentration, language, executive function, and visuospatial skills, highlighting the broad consequences of MetS (Panza et al., 2010).

The field of research assessing mild cognitive impairment (MCI) remains challenging, with few longitudinal studies exploring the relationship between cognitive impairment and components of MetS (Panza et al., 2011). Understanding the factors from insulin resistance to vascular and metabolic complications, both peripheral and cerebral, is essential for developing effective prevention and intervention strategies through a comprehensive, interdisciplinary approach (Kouvari et al., 2022).

Dementia, a condition causing gradual, serious, and long-term declines in brain function, affected 46.8 million people worldwide in 2015. It is associated with poor quality of life, increased mortality, and significant socioeconomic costs (Prince et al., 2016). The prevalence of dementia is expected to nearly double every 20 years, particularly in East Asia, where the proportion of people aged 60 and older with dementia is projected to increase by 193% from 2015 to 2050 (Prince et al., 2016).

MetS appears to accelerate cognitive decline, though no association has been found in individuals aged 85 and older. Several cross-sectional and case-control studies have linked MetS with overall dementia in women and Alzheimer's disease. Prospective cohort studies have also reported positive associations between MetS and general dementia, as well as vascular dementia, and a lower risk of Alzheimer's after age 75. However, few studies have explored the relationship between MetS and MCI. One population-based cross-sectional study (Roberts et al., 2010) found no overall association between MetS and MCI, except when high levels of inflammation were also present, which was significantly associated with non-amnestic MCI.

4.3 Relation between cognitive dysfunction and oral health

Frailty is positively associated with poor oral health status, indicated by a reduced number of natural teeth and poor oral function (Hakeem et al., 2019). In Japan, the concept of oral frailty, which represents a decrease in oral functionality, was proposed in 2013.

In 2020, the Japan Dental Association has broadened it to include age-related changes and a variety of intraoral health conditions that involve the number of teeth, oral hygiene, and oral functional inability and also reduced caring toward the health of the mouth in general and reducing physical and mental resistance (Y. Watanabe et al., 2020). This increase in oral fragility can lead then to the impairment of the capacity to eat and reduce general physical and cognitive skills.

Individuals suffering from cognitive dysfunction exhibit more severe oral health issues and a higher prevalence of periodontal diseases. Research indicates that tooth loss, which can be influenced by factors such as age, smoking, economic status, diet, and oral health, is associated with an elevated likelihood of developing dementia and Alzheimer's disease. This connection may be attributed to nutritional deficiencies and inadequate oral hygiene. Yu et al. performed a cross-sectional study in which the prevalence of periodontitis increased with poorer cognitive test scores. They found a relationship between periodontal disease and cognitive impairment among elderly persons (Yu & Kuo, 2008). Zhang et al. supported this to the extent that it showed a positive relationship between poor oral hygiene and an increased risk of developing dementia. The researchers in one prospective cohort study of 425,183 individuals found those wearing dentures to have reduced cortical surface area in the inferior temporal cortex, inferior parietal cortex, and middle temporal cortex. The authors have hence highlighted that improvement of dental health care should be important for preventing dementia (Zhang et al., 2023).

The Nun Study established a correlation between tooth loss and an increased susceptibility to Alzheimer's disease, a finding that was corroborated by numerous epidemiological studies (Stein et al., 2007). In a prospective cohort study of 597 older American males, each lost tooth per decade increased the risk for a lower MMSE (Mini-Mental State Examination) score by 9–12% over 32 years (Kaye et al., 2010). Findings were in concordance with the 5-year study of Batty et al. in 11,140 type 2 diabetes patients, showing that individuals without teeth had a higher risk for dementia and cognitive decline compared to those with 1–22 teeth (Batty et al., 2013).

A UK longitudinal cohort study also found that patients with no teeth had less good memory and motor abilities compared with the teethed group, and this was more pronounced in the elderly who were aged 60–74 years (Tsakos et al., 2015). A cross-sectional study conducted on 3,063 individuals found that dementia patients had a mean of 18.7 missing teeth in comparison to 11.8 in people with MCI and 9.3 in those with normal cognition; more than 16 teeth lost was significantly associated with dementia (OR: 1.5, 95% CI: 1.12–2.18) (Luo et al., 2015). In China, Li et al. found out that over the 13-year follow-up, the MMSE score of cognitive function gradually dropped with increasing number of lost teeth at 0.01 point (J. Li et al., 2017). In a 5-year Japanese prospective cohort, a significant relationship was seen between a lower number of remaining teeth and all-cause Alzheimer disease, as well as vascular dementia (Takeuchi et al., 2017).

Kato et al. also found that, in a cross-sectional study conducted among Japanese elders, those who possessed more than 20 artificial teeth had MMSE scores that were significantly higher than those with fewer than 19 natural teeth, indicating that artificial teeth are associated with better cognitive health (Kato et al., 2019).

Sung's study established an association between severe periodontitis and low cognitive function (Sung et al., 2019). Nagatani M. discovered a strong correlation between oral frailty and the occurrence of MCI (Nagatani et al., 2023). The group of individuals who suffered from periodontitis recorded lower results in the digit symbol test as compared to those who did not suffer from periodontitis (Kamer et al., 2012). The study conducted by Iwasaki et al. reported a strong interrelation between periodontal disease and cognitive impairment based on MMSE as well as Hasegawa Dementia Scale-Revised criteria (M. Iwasaki et al., 2015). In practice, patients with periodontitis showed an increased susceptibility to acquiring dementia; this further escalated when considering the social demographic variables. Furthermore, there was a significant association between the presence of chronic periodontitis and the odds of developing Alzheimer's disease (Chen et al., 2017; S. Choi et al., 2019; Tzeng et al., 2016).

Tooth loss may result in masticatory dysfunction, associated with poor nutrition a decrease in cerebral blood supply, and often is related to memory problems. Animal studies report that tooth loss results in lower acetylcholine due to chewing problems and is linked to a reduction of hippocampal pyramidal cells and subsequent cognitive decline (Fang et al., 2018). It may also be that although there is limited evidence regarding the relation between periodontal disease and the development of frailty, the frailty status can be influenced by the presence of periodontal disease with its association with inflammatory biomarkers. Yet, the relationship between frailty and inflammation is not established. The possible relation of tooth loss as a consequence of periodontitis and its effect on food choice and, consequently, on nutritional status cannot be ruled out (Hakeem et al., 2019).

Loss of teeth significantly affects brain structure and functions, particularly memory-related and cognitive functions. Animal studies show that the prolonged absence of molars reduces the level of brain-derived neurotrophic factor (BDNF) in the hippocampus, which is important for learning and memory. Furthermore, the molarless mouse presented cognitive dysfunction and an altered expression of BDNF mRNA into the hippocampus (Takeda et al., 2016).

In humans, imaging studies revealed that, especially in the brain areas related to memory and cognition, people who have lost their teeth show significant cerebral atrophy. Tooth loss is known to be linked with the reduction in total gray matter volume of the brain, which further increases the risk of shrinkage in the brain's memory-, learning-, and cognition-related regions. This can accelerate the cognitive decline (Dintica et al., 2018; Kobayashi et al., 2018).

Poor oral hygiene and high levels of oral bacteria infiltrating the human brain can be associated with age-related cognitive decline and an elevated risk for the onset of Alzheimer's disease (Panza et al., 2018). Moreover, periodontal disease is linked to an increase in aggregation of amyloid-β in those regions of the brain that are susceptible and characteristic of Alzheimer's disease (Kamer et al., 2015). Patients with Alzheimer's disease present less diversity of microorganisms in saliva, increased levels of some bacteria (Moraxella, Leptotrichia micronomyces, Sphaerochaeta), and a reduction in Rhodotella. Certain reports are suggestive of potential changes in the oral microbiota in patients with Alzheimer's disease, including lower diversity and increased pathogenic bacteria like Lactobacillus, Streptococcus, and Bacteroides (Dominy et al., 2019; Panza et al., 2019).

It was shown that oral pathogens may influence the brain structures by circulating throughout the body with the proinflammatory cytokines or pass through the nerves directly to gain entry into the central nervous system. Oral bacteria, such as Porphyromonas gingivalis, contribute to generating toxic substances that harm the tau protein in neurons while increasing general inflammation within the body. Porphyromonas gingivalis and Treponema have been detected in brain tissue, trigeminal ganglion, and cortical samples of Alzheimer's disease patients (Poole et al., 2013).

Several studies reveal a decrease in the alpha diversity of oral microbiota in Alzheimer's disease patients, while an increased diversity was also reported in some of the studies. Hence, it implies that oral microbial communities in those suffering from cognitive impairment are characterized by complexity and variation in population structure (Wu et al., 2021).

The above findings have provided very compelling evidence to show that maintaining good dental hygiene can be a means of preventing or at least reducing Alzheimer's and cognitive decline.

Inflammation has just recently been reported to be a critical mechanism by which dentition and the onset of cognitive problems are associated. A recent study demonstrated a decrease in circulating cytokines in patients with severe periodontitis (Yang et al., 2021). Montoya and colleagues observed a notable reduction in the levels of epidermal growth factor (EGF), interleukin 8 (IL-8), interferon γ-induced protein 10 (IP-10), and monocyte chemoattractant protein-1 (MCP-1) in patients with cognitive impairment suffering from severe periodontitis. (Gil Montoya et al., 2020).

Another important mechanism is the ability to avoid the immune system, which causes the development of Alzheimer's disease (Zheng et al., 2021). Porphyromonas gingivalis inhibits the innate immune response, hence making it easier to avoid the host defense system. It also exacerbates Alzheimer's disease through inhibition of interferon-γ, inhibition of the degradation of amiloid β plaques, and potentially through impairment of EGF signaling pathways that lead to cognitive decline (Olsen et al., 2016). EGF is a central factor in the models of Alzheimer's disease for memory restoration and reduction of cognitive decline (Pyrc et al., 2013). Several cytokines have been suggested to serve as mediators between periodontitis and Alzheimer's disease. The exact role of IL-8 in cognitive impairment is still not well known and requires elucidation. IL-8 is one of the most degraded chemokines by Porphyromonas gingivalis and is downregulated in dementia and cognitive impairment, but it is mostly upregulated in Alzheimer's disease, which is a sign of neuroinflammation (Vaz et al., 2021). Porphyromonas gingivalis suppresses the expression of IP-10 by secreting gingipain R, hence fewer infiltrations of lymphocytes in the brain due to weakened T cell responses. Increased concentrations of IP-10 (CXCL10) have been linked with neuroinflammation, which drives cognitive decline in Alzheimer's disease and most dementias (Mohd Hasni et al., 2017). High levels of interleukin 1-β (IL-1β) found within the salivary concentrations indicate that periodontal diseases serve to be an element in the activation of pathways that encourage inflammation. Elevated levels of IL-1β within a brain inflicted by Alzheimer's disease lead to an increase in neurotoxicity and hold the ability to cause the progression of Alzheimer's disease to worsen (Huang & Sheng, 2010). Taken together, these findings highlight the relation between periodontal disease and its associated cognitive decline, showing that periodontal pathogens, including Porphyromonas gingivalis, mediate immune responses to promote neurodegeneration, specifically in Alzheimer's disease.

4.4 Nutritional factors involved in the interplay between MetS-oral health-cognitive dysfunction

Research has shown that there is a reciprocal relationship between nutrition and oral health, where inadequate nutrition can exacerbate oral health issues such as dental caries, periodontal diseases, and oral cancer (M. Choi, 2024). Various vitamins and minerals have been identified as essential for oral health, including calcium, phosphorus, fluorine, vitamins A, D, E, and K, as well as B-group vitamins and vitamin C (Alsuwaidi et al., 2023; Lešić et al., 2024). Vitamin D, in particular, has been highlighted for its protective effects against oral health issues such as caries and periodontitis (Gül Aydın & Özdemir, 2021). Studies have shown that

vitamin D deficiency is associated with significant changes in oral health diseases (Z. Li et al., 2023), and vitamin D supplementation has been linked to improved oral health outcomes, particularly in enhancing periodontal health (Ab Malik et al., 2023; Swapna & Abdulsalam, 2021).

The role of vitamins in oral potentially malignant disorders, oral cancer, and periodontal health has been documented, emphasizing the importance of these nutrients in preventing oral diseases (Cetrelli et al., 2022; Shah et al., 2023). Furthermore, research suggests a correlation between dietary intake of vitamins and oral health behaviors. Consuming vitamin-rich foods like green and yellow vegetables has been associated with better oral health behaviors and outcomes (Ariizumi et al., 2023). Inadequate nutrition can lead to oral diseases, highlighting the importance of a well-balanced diet for maintaining oral health (Magret Muyide & Taibat Oduneye, 2021). For instance, a diet high in sugars and refined carbohydrates has been associated with an increased risk of MetS, which can also contribute to poor oral health outcomes such as dental caries (Lešić et al., 2024). Moreover, the consumption of nutrient-rich foods like fruits, vegetables, whole grains, and lean proteins can help prevent MetS and support good oral health (Swapna & Abdulsalam, 2021). These foods provide essential vitamins and minerals that are beneficial for both metabolic health and oral health (M. Choi, 2024). Conversely, diets high in saturated fats and sugars have been linked to an increased risk of MetS and oral health issues (Lešić et al., 2024). Furthermore, the relationship between MetS and oral health can be influenced by lifestyle factors such as dining habits and nutritional intake. Poor dietary choices and eating out frequently may contribute to MetS risk factors and impact oral health. Conversely, being mindful of nutritional choices and maintaining a balanced diet can help reduce the risk of MetS and support good oral health (80).

Among the various nutritional factors, malnutrition, antioxidants, omega-3 fatty acids, and dietary fibers are the most important, as they collectively support metabolic processes, protect against cognitive decline, and maintain oral health.

Malnutrition can have profound and enduring impacts on MetS, cognitive function, and dental health. Nutritional status is probably related to changes in neural plasticity and cognitive performance, even if the exact processes behind the influence of diet on cognitive function remain unclear (Feng et al., 2022). Poor oral health, leading to malnutrition and unhealthy eating habits, is a potential contributing factor. Malnutrition can affect oral health and quality of life in older adults, while oral health can impact dietary intake and nutritional status (Lešić et al., 2024). Moreover, cognitive function has been identified as a mediating factor in the relationship between geriatric oral health and quality of life, indicating the intricate connection between oral health, cognition, and overall well-being (Chang et al., 2022). Poor oral health has also been associated with the development of dementia, highlighting the importance of maintaining good oral health for cognitive function (Daly et al., 2017). A systematic review revealed that diminished cognitive function is associated with poor mastication, with impaired chewing emerging as a significant predictor of dementia or mild memory impairment (Tada & Miura, 2017). Especially in older persons, poor dental health can have an impact on dietary choices and nutritional intake. The range of oral issues that older adults face can make it difficult for them to chew food, which might alter their diet choices and result in malnutrition (Azzolino et al., 2019). The main oral nutrition concern is the incapacity to sustain an appropriate oral food intake. As a result, there may be an endless loop whereby poor oral health has an adverse effect on nutritional status, which then causes abnormalities in the structure or maturation of teeth or defensive mechanisms, making teeth more susceptible to dental illnesses (Magret Muyide & Taibat Oduneye, 2021). Madhusudhan and Pallavi highlighted the adverse effects of malnutrition on pediatric oral health, emphasizing how malnutrition can negatively affect oral structures and lead to poor oral health, creating a cycle where poor oral health contributes to malnutrition (Siddaiah Madhusudhan & Pallavi, 2023).

Antioxidants play a vital role in addressing oxidative stress, a key factor in the pathogenesis of various chronic conditions, including MetS, cognitive decline, and oral health issues. Their beneficial effects are well-documented across these domains, offering neuroprotective benefits and enhancing periodontal health so highlighting their potential as therapeutic agents. Numerous studies have explored the influence of antioxidants in these health domains. Antioxidants help mitigate this stress by neutralizing free radicals, thereby improving metabolic profiles (Chaudhary et al., 2023). Among the antioxidants that have received the most research are resveratrol, green tea, and curcumin. These compounds have high concentrations of polyphenols, which have a variety of health benefits, including anti-inflammatory, neuroprotective, immunomodulatory effects (Malcangi et al., 2023). Studies have shown that antioxidant supplementation can enhance insulin sensitivity, reduce blood pressure, and lower lipid levels (J. Wang et al., 2022), suggesting a significant role in managing and potentially preventing MetS. Research also indicates that natural plant-based antioxidants, such as those found in berries, green tea, and nuts, can improve cognitive function and delay the progression of neurodegenerative diseases (Baroni et al., 2021). For instance, Franzoni et al. demonstrated the potential of antioxidants to substantially improve brain functions and postpone the possible emergence of neurodegenerative diseases (Franzoni et al., 2021). Oral health is closely tied to oxidative stress, which contributes to conditions like periodontal disease. Tripathi et al. highlighted the positive effects of antioxidants, particularly lycopene and green tea extract, on periodontal health. Their findings indicated a reduction in oxidative stress, improved antioxidant status, and decreased inflammatory markers in periodontal disease (Tripathi et

al., 2019). A possible influence of foods such as coffee was also noted, showing a significant negative association with MetS, indicating that daily coffee consumption may reduce the risk of MetS (T. Iwasaki et al., 2019).

Research has shown that omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), have beneficial effects on MetS by assisting in controlling type 2 diabetes mellitus, reducing obesity and related metabolic diseases (Werida et al., 2023). Studies have also indicated that omega-3 fatty acids are associated with better cognitive function, slower rates of cognitive decline, and a reduced risk of developing dementia in aging populations (Barnes et al., 2021). Furthermore, higher serum levels of DHA have been linked to slower cognitive decline in patients with Alzheimer's disease (Chu et al., 2022). Regarding oral health, omega-3 fatty acids are beneficial in promoting insulin sensitivity and improving metabolic health, which can have positive implications for oral health as well (Da-Ming & Chieh, 2023). The relative ratio of omega-6 to omega-3 fatty acids in the diet has been associated with spatial memory, learning, and overall cognitive function in older adults, suggesting the importance of maintaining an appropriate balance of these fatty acids for optimal cognitive health (Andruchow et al., 2017). One study focused on the use of omega-3 oral supplements, demonstrating a decrease in the severity of aphthous ulcers and an improvement in oral health-related quality of life (Hadian et al., 2021), and the findings suggest that omega-3 supplementation can indeed have a positive impact on oral health. Their anti-inflammatory properties, cardiovascular benefits, and neuroprotective effects make them essential components of a healthy diet that can positively influence overall health and well-being.

Dietary fibers play an essential role in improving insulin sensitivity, promoting gut health, reducing systemic inflammation, and benefiting the oral microbiome. Extensive research has explored the multifaceted impacts of dietary fibers on these health aspects. Dietary fibers are pivotal in improving metabolic health by enhancing insulin sensitivity and reducing the risk of metabolic diseases (Bulsiewicz, 2023). Moreover, Wang et al. noted the positive impact of dietary fibers on metabolic processes through the increase of microbiome-derived metabolites (Z. Wang et al., 2024). Dietary fibers significantly influence gut health by modulating the gut microbiome. In particularly, resistant starch significantly increases microbiome-derived metabolites, underscoring its positive impact on gut health and metabolic processes (Koay et al., 2019). One study highlighted the beneficial effects of xylan in alleviating dysbiosis induced by fiber deprivation, promoting the growth of beneficial bacteria such as Bifidobacterium pseudocatenulatum (Z. Wang et al., 2021). Dietary fibers' role in reducing systemic inflammation is linked to theirs effects on the gut microbiome and immune modulation (Ranganathan & Anteyi, 2022). Although not as extensively studied as its effects on gut and metabolic health, dietary fibers also benefit oral health by supporting a healthy oral microbiome. High-fiber diets can help reduce oral inflammation and promote the growth of beneficial oral bacteria, contributing to overall oral health (Sedghi et al., 2019; Swarnamali et al., 2023). Also, among the benefits of fibers for the human body is their ability to delay the onset of dental caries by increasing saliva production and decreasing the absorption of glucose (Mazurkiewicz et al., 2023).

Dietary patterns provide a thorough understanding of a diet by considering the amounts, types, and combinations of foods as well as the associations between these elements (Curtis et al., 2023). These patterns provide insights into the relationship between diet and health outcomes, capturing the complexity of human eating behaviors. A healthy dietary pattern is one that is low in added or refined sugars, animal-derived proteins, trans and saturated fats, and high in foods that promote health, such as plant-based foods, fresh fruits and vegetables, antioxidants, soy, nuts, and sources of omega-3 fatty acids (Pistollato et al., 2018). Healthy dietary patterns, such as those rich in fruits, vegetables, nuts, low-fat dairy products, and legumes, have been associated with a reduced risk of MetS (Lithander et al., 2024). Similarly, plant-based dietary patterns rich in fruits, vegetables, and whole grains have been linked to improved cognitive function (Zhu et al., 2022), and diets rich in nutrients and balanced in composition have been linked to better oral health outcomes (Andreeva et al., 2019). Moreover, unhealthy dietary practices, like the Western dietary pattern characterized by high consumption of high-fat foods, processed meat, refined grains, and sugar-based desserts, have been linked to adverse health outcomes (Lei et al., 2021). Dietary patterns that frequently involve consuming simple carbohydrates—mainly in the form of dietary sugars—have been linked to a higher risk of dental caries in terms of oral health. (Chauhan et al., 2024). Also, high-sugar snacks and drinks that are consumed between major meals are one of the dangers to dental health since they supply the substrate that the caries process needs to develop (Mazurkiewicz et al., 2023).

5. Conclusion

Research until now has found unexpected associations between MetS, cognitive dysfunction and oral health. They are interconnected in numerous complex ways, with inflammatory, immunological, and nutritional factors being the main actors involved in this interplay. In this context, also inadequate oral health behaviors play an important role, compelling evidence showing that maintaining good dental hygiene can be a means of preventing or at least reducing cognitive dysfunction.

Moreover, a diet rich in essential nutrients, including vitamins, minerals, and healthy macronutrients, plays a significant role in preventing MetS and maintaining good cognition and oral health. By making informed dietary choices and prioritizing nutrient-dense foods, individuals can support their overall health and well-being, benefiting both their metabolic and oral health. Therefore,

a holistic approach to nutrition, focusing on whole foods and balanced diets, can positively impact these three interconnected health areas.

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