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Review

Acute Myocardial Infarction and Periodontitis: Importance of Awareness and Prevention in Latin America

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Abstract: By 2030, non-communicable diseases will have accounted for more than three-quarters of deaths worldwide. Cardiovascular diseases (CVDs) have been the leading cause of death worldwide for several years. Acute myocardial infarction (AMI) is a CVD characterized by necrosis of the heart at the myocardial level due to prolonged ischemia caused by the reduction or sudden absence of coronary blood supply. The prevalence of AMI is higher in men at all ages. The incidence of AMI has decreased in industrialized nations; however, it has been on the rise in Latin America (LATAM) due to lifestyle changes. These changes have caused the combined incidence of CVDs and unresolved health concerns in LATAM, such as infections and malnutrition. It is well known that periodontitis, a highly prevalent chronic infectious inflammatory disease, has been associated with systemic diseases, such as diabetes, kidney diseases, and AMI. This review addresses proposed aspects of the correlation between periodontitis and AMI, explains the importance of preventing periodontitis and CVDs, and analyzes the preventative measures being implemented in LATAM, particularly in Mexico.

Keywords: acute myocardial infarction; periodontitis; prevention; cardiovascular risk

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1. Introduction

Cardiovascular diseases (CVDs) are among the leading causes of death worldwide [1], with ischemic heart disease (IHD) being the main cause. Ischemic refers to the lack of blood and oxygen supply, in this case, to the heart. It is also known as coronary artery disease (CAD) or coronary heart disease and defined as a disorder caused by narrowed coronary arteries that decrease the blood supply to the myocardium. Acute myocardial infarction (AMI) occurs when the heart's blood supply is disrupted [2]. Since 2000, IHD-related deaths have increased dramatically, from 2 million to 8.9 million annually [1]. The leading cause of mortality is CAD, with 7.4 million deaths annually [3]. More than 80% of deaths occur in low- and middle-income countries [4,5]. In Latin America (LATAM), particularly Mexico, IHD is the leading cause of CVD-related death [6].

Non-communicable diseases are expected to account for more than three-quarters of deaths worldwide by 2030, with CVD alone being responsible for more deaths in low-income countries than infectious diseases, maternal and perinatal conditions, and nutritional disorders combined [4].

Periodontitis is a common disorder that leads to tooth loss and reduced quality of life in advanced cases. The etiology of periodontitis is multifactorial, including local, systemic, environmental, and genetic factors [7]. To achieve a successful outcome when controlling periodontitis, dental professionals must understand the pathogenesis, including the primary etiology, risk factors, contributing factors, and treatment protocols [8]. A careful diagnosis should consider eliminating the causes and encouraging the patient to initiate changes in their habits to help reduce the modifiable risk factors. These aspects are important for patient-led prevention and can support its successful treatment [9]. Subsequently, periodontal maintenance therapy at regular intervals and long-term follow-up are essential [10]. A 99.6% prevalence of inflammatory periodontal diseases in LATAM was recently reported in Mexico, Colombia, and Costa Rica [11].

For the development of periodontitis, a patient must present with an increase in the population and activity of a specific group of periodontal pathogens, predominantly gram-negative anaerobic bacteria. These bacteria are responsible for altering the normal symbiotic relationship between the host and its resident microbiota, leading to an alteration in the immune response and provision of a proinflammatory environment [12]. The immune response triggered can be a "double-edged sword", since it is also responsible for degrading periodontal tissue [13]. Moreover, periodontitis has been associated with other systemic conditions, such as adverse pregnancy outcomes, CVDs, diabetes, respiratory disorders, chronic renal disease, lupus, cancer, neurodegenerative diseases, and metabolic syndrome [14,15]. These associations are mainly related to the systemic inflammatory burden associated with periodontitis [14,16]

This review addresses the proposed mechanisms of the correlation between periodontitis and AMI, explains the importance of curbing the development of periodontitis as well as AMI in LATAM (specifically Mexico), and highlights the importance of applying preventive measures, since both pathologies are highly prevalent.

2. Acute Myocardial Infarction

AMI is defined as cardiomyocyte necrosis in a clinical setting, consistent with acute myocardial ischemia [17], as a consequence of a prolonged reduction or sudden absence of the coronary blood supply that compromises one or more myocardial areas [18]. In most cases, this results from the rupture or erosion of a vulnerable atherosclerotic plaque [19]. The above results in an intraluminal thrombus which leads to the partial (at least 70%) or complete occlusion of one or more of the coronary arteries [17,18]. Five types of AMI have been defined (Table 1).

Table 1. Types of AMI [17,19]. ECG: 12-lead electrocardiogram.

Type		Description
1		Atherosclerotic plaque disruption with resulting intraluminal thrombus (acute atherothrombosis), leading to decreased myocardial blood flow and/or distal embolization with subsequent necrosis of the myocardium.
2		Due to an imbalance between myocardial oxygen supply and demand, results from hypo/hypertension, arrhythmias, anemia, hypoxemia, coronary artery spasm, dissection or embolism, and so on, not as a consequence of acute atherothrombosis.
3		An infarction that causes sudden death without the opportunity to obtain biomarkers and/or ECG confirmation.
4	a	AMI is related to percutaneous coronary intervention.
	b	AMI is related to thrombosis of a coronary stent.
5		AMI is related to coronary-artery bypass grafting.

IHD manifests as acute coronary syndrome (ACS) [20] with symptoms consistent with myocardial ischemia, such as recurrent or persistent chest pain and the radiation of pain to the left arm, lower jaw, or neck [21]. Other chest pain-equivalent symptoms include

dyspnea and epigastric pain [17]. Less typical presentations include nausea, vomiting, fatigue, syncope, or palpitations [21]. AMI is the most severe manifestation of CAD [22].

2.1. Epidemiology

AMI accounts for more than one-third of all deaths in developed countries [22]. Its incidence is lower in industrialized nations and tends to increase in developing countries, such as South Asia, LATAM, and Eastern Europe [23].

Premenopausal women are at a lower risk of AMI than age-matched men [24,25]. It is assumed that exposure to endogenous estrogens during the reproductive years delays the manifestation of atherosclerotic disease in women [24,26]. Moreover, estrogens play a role in several metabolic factors by regulating lipids, inflammatory markers, and coagulation [26] as well as promoting a direct vasodilator effect through alpha and beta receptor activation in the vessel wall, which stimulates angiogenesis and decreases oxidative stress [25]. The average risk of AMI is three times higher in men than in premenopausal women. However, premenopausal women tend to have an equal risk of AMI to that of men when certain cardiovascular risk factors are present, such as hypertension, smoking, and diabetes [26,27].

Certain risk factors are strongly associated with the development of AMI, such as smoking, hypertension, diabetes, dyslipidemia, psychosocial stressors, obesity, alcohol consumption, physical inactivity, and a diet low in fruits and vegetables [23,27]. According to the INTERHEART study, these risk factors account for more than 90% of an individual's overall risk [28].

2.2. Epidemiology of AMI in LATAM

Since 2000, CVDs including AMI in LATAM have shown an upward trend due to lifestyle changes, economic evolution, urbanization, industrialization, globalization, and a demographic transition from a young population toward an aging population [29]. In 2001, 31% of the overall deaths in LATAM were attributed to CVD [30]; this figure has only increased since. The population of LATAM has a high prevalence of cardiovascular risk factors, primarily overweight/obesity, smoking, physical inactivity, and alcohol consumption [31].

The INTERHEART study is an international case-control study that determined the impact of conventional and emerging cardiovascular risk factors on AMI [31,32]. Between 1999 and 2003, the INTERHEART was conducted in LATAM; to date, it is the most representative study of the risk factors for AMI in this region [28,32]. It was performed specifically in Argentina, Brazil, Colombia, Chile, Guatemala, and Mexico, where 1237 cases of AMI and 1888 controls were registered. Obesity, smoking, and dyslipidemia reportedly represent an 88% risk of AMI [32].

2.3. Epidemiology of AMI in Mexico

Of the countries that are part of the Organization for Economic Cooperation and Development (OECD), Mexico has had the highest AMI-related mortality rate in patients over 45 years of age since 2013 [33,34]. In 2019, Mexico was the only country that showed an increase in deaths due to AMI and other IHD, as the rest of the OECD countries presented decreases (Figure 1) [35].

In 2015, the National Institute of Statistics and Geography recorded 116,002 deaths due to CVD, 70% of which were AMI-related [36]. Every 4.3 min, an estimated one person dies of IHD, making it the leading cause of years of healthy life lost due to premature death and disability [37]. Mexico has a high prevalence of CVD risk factors, such as obesity, diabetes, systemic arterial hypertension, smoking, sedentary lifestyle, and a high-carbohydrate, high-fat diet, among others [38].

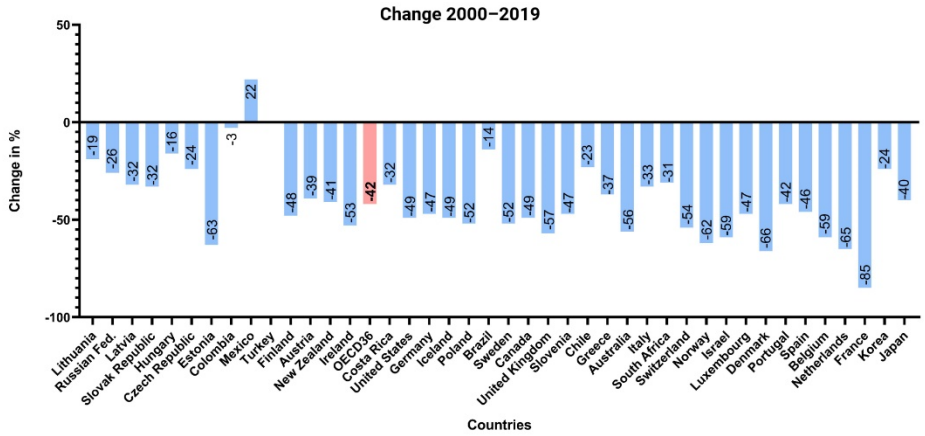

Figure 1. Acute myocardial infarction and other ischemic heart disease mortality change from 2000–2019 (Taken and modified from: Health at a Glance 2019–© OECD 2019) [35].

The RENASCA (Real-World Study in Mexico), performed at the Mexican Social Security Institute (IMSS), represents the largest study on ACS to date in Mexico [33]. In 2010, this study documented that up to 68% of the Mexican population had at least three associated risk factors for ACS [33]. The most recent RENASCA-IMSS study included 21,827 patients enrolled between 1 March 2014 and 25 December 2017. It reported that, of the enrolled patients, 73.2% suffered ACS due to AMI with ST segment elevation; for the rest, it was due to AMI with non-ST segment elevation. The predominant risk factors for the development of these conditions were high blood pressure, smoking, diabetes, dyslipidemia, and metabolic syndrome [33].

2.4. Predisposition to the Development of CVDs in LATAM

In recent years, socioeconomic status, education level, and ethnic origin have been demonstrated as the independent predictors of an increased risk of CVD-related death. Furthermore, risk factors such as smoking, age, blood pressure, sex, and cholesterol remain important predictors [39]. For example, an association between education and the development of certain diseases has been observed. In this sense, a study found that in Eastern European countries, women aged 15–44 years with a lower education level showed a 2.3 times higher risk of AMI than those with a higher education level. However, among non-European women, the risk of AMI was 33% higher in those with a higher education level. This suggests that a low education level is associated with an increased risk of AMI in Eastern Europe but not in the other three regions. Thus, factors are differentially involved in the interplay of population-specific characteristics affecting educational differences in the risk of AMI and stroke [40]. In another study, individuals in high-income countries that have large seasonal oscillations in temperature could be influenced by cold weather and develop CVDs. In these countries, winter can produce biological mechanisms, such as higher sympathetic nervous system activation, uncontrolled hypertension, and an increased incidence of respiratory diseases. Other conditions such as shorter days, reduced physical activity, depression, and higher pollution levels were involved. Moreover, in low- and middle-income regions with tropical and subtropical climates (Brazil), the numbers of heart failure and AMI hospitalizations also increase in winter. This is not related to the temperature oscillations. However, other factors, such as precarious housing conditions, lack of thermal insulation, and greater pollution might increase the seasonal effect of winter on risk [41].

Regarding ethnicity, some authors reported marked racial and ethnic disparities with respect to access to a diagnosis and adequate treatment of valvular heart disease. In addition to the scarcity of research on the causes of heart disease, some authors reported that, during patient recruitment for determining the in-depth causes of AF, most observational studies and clinical trials have included predominantly white populations with an under-

representation of minorities' racial and ethnic differences, highlighting the need for an inclusive participation in research [42].

Thus, CVDs show an increased prevalence in LATAM countries (specifically Mexico), given that LATAM probably has the greatest economic disparities that cause high poverty, malnutrition, disease, and limited opportunities [43]. Unique features have allowed the development of health problems specific to this region [40]. Regardless, health infrastructure and research are lacking.

On the other hand, additional AMI-associated factors have demonstrated an upward trend due to the particular characteristics of LATAM populations. For example, the rate of increase of obesity appears to be slowing in most high-income countries; however, it continues to rise in many low- and middle-income countries [44]. The possible causes for this vary, but some authors cited that the prevalence of excess weight and obesity has increased since the signing of the North American Free Trade Agreement in Mexico. This was caused by the new economic model that allowed rural populations to move from rural to urban centers, resulting in a food transition [45]. This transition increased food security, augmented the availability of cheap sources of vegetable oils, resulted in more meals away from home, decreased the arduous nature of working, and increased passive recreation (especially television). These pathways have transformed the dietary and physical activity patterns and consequently tipped the scales in favor of obesity [46].

3. Periodontitis

Periodontitis is a chronic and infectious inflammatory disease with a variety of related factors [47,48]. When periodontitis is detected in the initial stage, the dentist may be able to provide appropriate treatment that restores the patient's oral health [49]. However, if it is not detected and treated in time, continuous bleeding, pain while brushing, and bad breath often occur. Periodontal pockets can also form, leading to the loss of one or more teeth in severe cases [49] (Figure 2).

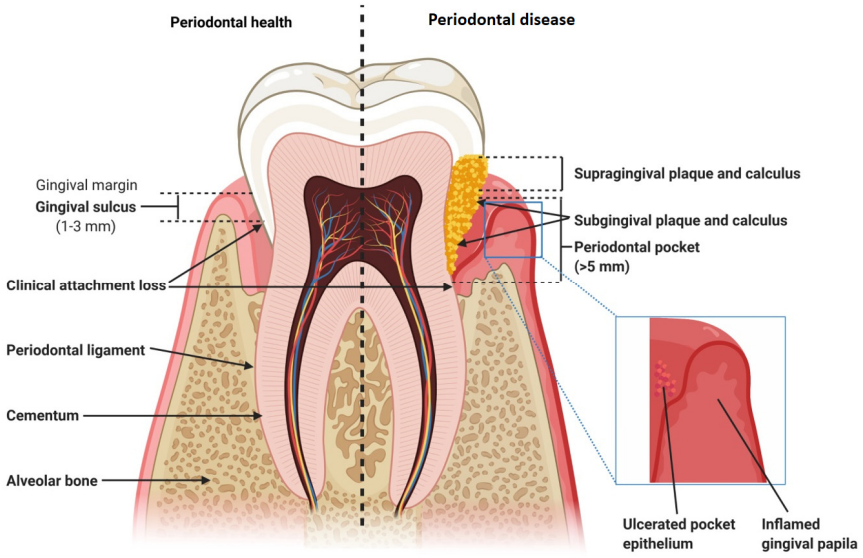

Figure 2. The progression from periodontal health to periodontitis disease. The alveolar bone and connective tissue are covered by the oral epithelium in periodontal health, and the gingival sulcus is 1–3 mm. However, periodontitis is developed when the periodontal pockets are <5 mm deep, and gingival inflammation in sites with apical migration of the epithelial attachment onto the root surfaces is associated with loss of connective tissue and alveolar bone [50].

3.1. Epidemiology of Periodontitis

Periodontitis also has a high prevalence; in 2017, it was the eleventh most prevalent condition worldwide [51]. It is estimated that periodontitis, in its various stages, affects 45–50% of the world's population. Its most severe form affects 11.2% of the world's

population [52]. In addition, severe periodontal disease has a sustained prevalence, with no data currently indicating a decrease [53]. Moreover, the prevalence of periodontal disease is expected to increase owing to the aging population [54].

3.2. Epidemiology of Periodontitis in LATAM

Developing countries generally have a higher prevalence of periodontal disease signs, which is clearly reflected in comparisons of adult populations [47]. Overall, periodontal disease affects approximately 20–50% of the world's population [47]. However, the epidemiological data on gingivitis and periodontitis in LATAM are scarce. The reported data show significant variations in the results between different LATAM countries. Generally, the data revealed that the prevalence of the periodontal disease is higher in LATAM populations than those in the United States or Europe [55]. It was recently reported that, on average, the prevalence of severe forms of periodontal disease in North and South America in adults 35–44 years is 20%, or 40% for less severe presentations [56].

3.3. Predisposition to the Development of Dental Diseases in LATAM

Regarding dental diseases, the behavior is similar to the panorama summarized in CVDs, since both are important health problems to which socioeconomic factors predispose residents of low-income regions. For example, dental health resources comprise 5–10% of health care spending costs per year in developed countries, and oral disease is the fourth most expensive disease to treat [57]. Treating dental caries in children alone often exceeds the total budget for children's health care [58]. This is aggravated by a recent unprecedented migration crisis in Venezuela and Central America that creates a complex and inhospitable scenario that complicates the management of dental diseases [59].

On the other hand, education can also have an influence, and health education is the most cost-effective method of disease prevention. It is well documented in dentistry that knowledge can empower populations, allowing them to take action to protect their health [60].

Ethnic influence has also been explored with discrepant results. One study explored whether there were ethnic differences in oral health that could be explained by differences in sociodemographic or lifestyle factors or the use of dental services in the UK and reported that, despite generally lower use of dental hygiene and preventive dental services, Black and South Asian participants were less likely to report tooth extractions and tooth loss. The above may reflect genuinely better oral health, especially as some of these differences could be explained by a lower consumption of cakes and sweets. However, the study did not provide detailed information about sugar consumption amount and frequency. The authors suggest that dietary sugar may be the main driver of overall and ethnicity-specific oral health [61].

LATAM presents its peculiarities; dental care in Mexico is generally provided in private, public, or social security services. However, the public health services offer basic care and do not include orthodontic treatment or aesthetic rehabilitation. Thus, they use private services to complete their treatment. Because these low-income populations lack access to dental care due to its high cost, notably, these inequities reflect social problems since citizens who can pay do have access [62]. In addition, it must be considered that the population presents several risk factors in dietary practices, such as a high intake of total and added sugars [63].

4. Interaction between Periodontitis and AMI

Periodontitis is associated with AMI in several populations [52]. Moreover, periodontitis and AMI share common risk factors, such as smoking and diabetes [14]. This is especially important because of the close link between diabetes and AMI, since the latter is the most frequent cause of mortality and morbidity in diabetic populations [15]. Patients with periodontitis tend to have an increased frequency of being overweight and experienc-

ing endothelial dysfunction, hypertension, platelet hyperreactivity, dyslipidemia, and a prothrombotic state [16], which are known risk factors for AMI [64].

Local/systemic inflammation caused by periodontitis also contributes to the risk of CVD [65,66]. This is supported by a large number of studies that show an increase in the circulation of inflammatory mediators in patients with periodontal diseases [66], such as C-reactive protein (CRP), interleukin-6, fibrinogen, and platelet-activating factor, among others, compared to healthy controls [66,67]. Moreover, an increased serum leptin concentration has been reported due to periodontal disease, which promotes atherosclerosis by enhancing platelet aggregation, the production of proinflammatory cytokines such as interleukin-2 and interleukin-6, and arterial wall calcification [65,68]. In addition, the translocation of periodontitis-causing microorganisms into the bloodstream and their accumulation in atheroma plaques may contribute to plaque instability and reduce the risk of AMI development [16].

Evidence has confirmed the presence of bacterial DNA in atheromatous plaques [69]. The bacterial species most commonly found were *Porphyromonas gingivalis*, *Actinobacillus actinomycetemcomitans*, *Tannerella forsythia*, *Prevotella intermedia* [70], *Fusobacterium nucleatum*, and *Campylobacter rectus* [71], suggesting the migration of these oral pathogens to distant body sites [69].

The mechanisms by which periodontitis can participate in AMI development include bacteremia and associated systemic inflammatory sequelae, including elevations in CRP and oxidative stress [52]. These mechanisms favor atherosclerotic plaque formation and instability [65,66]. Several authors have proposed that periodontitis may be a non-traditional modifiable risk factor for AMI [52].

4.1. Pathophysiology and Effect of Periodontitis on AMI

It is well known that periodontitis raises inflammatory markers such as CRP and fibrinogen. These proteins lead to the release of cytokines, such as tumor necrosis factor-α and inerleukin-6, through certain processes [72]. Moreover, bacteria in the oral cavity that induce periodontitis can cause local and systemic inflammation, causing the liver to respond and enter an acute phase [66,72].

Stein et al. showed a strong relationship between periodontitis patients and pathogens from AMI patients. They found a high association between periodontitis and heart disease and concluded that pathogens such as *P. gingivalis* could be considered risk factors for AMI [73]. Furthermore, *P. gingivalis* can reportedly evade innate immune detection by toll-like receptor 4, favoring chronic vascular inflammation [69,74]. According to Pussinen et al., the levels of immunoglobulin A against *P. gingivalis* were risk factors for AMI [75]. Likewise, Holmlund et al. reported that the levels of immunoglobulin G against *P. gingivalis* increased upon deterioration in patients with AMI [76].

The search for bacteria associated with periodontitis continues. Through immunofluorescence microscopy, pathogens such as *Tannerella forsythensis* and *P. intermedia* have been demonstrated to be associated with a greater risk of AMI [77]. Moreover, a more recent study of *P. intermedia* placed its relationship with periodontitis and AMI closer to the spotlight [78]. A meta-analysis by Bahekar et al. of five cohort studies showed that people with periodontal disease had a 1.14 times higher risk of developing CAD compared to controls independent of confounding factors [79]. Some relevant sample studies are shown in Table 2.

Other studies reported that a small dental intervention such as the removal of tartar (a form of hardened dental plaque) could increase the risk of periodontitis in patients presenting with bacteremia. This would cause pro-inflammatory mediator activation by these microorganisms within the bloodstream, increasing the inflammation of atheroma plaques and the risk of their detachment or fragmentation [87]. Figure 3 shows a diagram of the microbial components of atherogenesis.

Table 2. Pathogens involved in the development of periodontitis and CVD.

Bacteria	Pathology	Findings	Reference
Porphyromonas gingivalis (Pg).	Oral diseases Atherosclerosis	*Pg* can influence the malfunction of the endothelium, it is considered a promoter of foam cells, it stimulates the calcification of the smooth muscle cells of the vessels, it alters the regulatory and auxiliary T lymphocytes.	[80]
Aggregatibacter actinomycetemcomitans (Aa) Porphyromonas Gingivalis (Pg) Prevotella intermedia (Pi) Prevotella nigrescens (Pn) Tannerella forsythiaen (Tf).	Coronary artery disease	Periodontal bacterial DNA was found in a high percentage in atheromatous plaques.	[81]
Aggregatibacter actinomycetemcomitans (Aa) Porphyromonas gingivalis (Pg) Tannerella forsythia (Tf) Prevotella intermedia (Pi)	AMI Periodontal Disease	Correlation between periodontitis and AMI. Periodontal destruction correlated with the representation of periodontal pathogens. *Pg* as an indicator of potential risk for AMI.	[73]
Porphyromonas Gingivalis (Pg) Aggregatibacter actinomycetemcomitans (Aa) Tannerella forsythia (Tf).	AMI Cardiovascular disease	Periodontal status in patients with AMI is characterized by unsatisfactory and poor hygiene, increased indices of bleeding on probing, and periodontal pocket depth compared to patients without cardiovascular pathology.	[82]
Tannerella forsythia (Tf) Campylobacter rectus (Cr) Eikenella corrodens (Ec) Porphyromonas gingivalis (Pg) Treponema denticola (Td) Prevotella nigrescens (Pn) Aggregatibacter actinomycetemcomitans (Aa) Prevotella intermedia (Pi)	Periodontal disease Coronary artery disease	Patients with CAD present a mayor growth of periodontal bacteria in dental biofilms surface in comparison of healthy subjects.	[83]
Porphyromonas gingivalis (Pg) Aggregatibacter actinomycetemcomitans (Aa)	Coronary artery disease	Presence of red complex bacteria in samples of coronary plaques, Aa could not be identifies in these samples.	[84]
Porphyromonas gingivalis (Pg)	Atherosclerosis Periodontal disease	DNA of the Pg is commonly located in atheromatous plaques of patients with periodontal diseases.	[85]
Porphyromonas gingivalis (Pg) Aggregatibacter actinomycetemcomitans (Aa) Tannerella forsythia (Tf) Treponema denticola (Td) Prevotella intermedia (Pi)	Atherosclerosis Coronary artery disease	Bacterial presence in carotid and coronary atherosclerotic vessels is correlated with the degree of periodontal inflammation. Relationship between periodontal pathogenic bacterial and atherogenesis.	[86]
Porphyromonas gingivalis (Pg) Aggregatibacter actinomycetemcomitans (Aa)	Atherosclerosis Periodontitis	The presence of bacteria in the atheromatous plaque in the carotid artery recovered by the removal of atheromatous plaques is ratified. Presence of a possible association between periodontitis and cardiovascular diseases	[70]

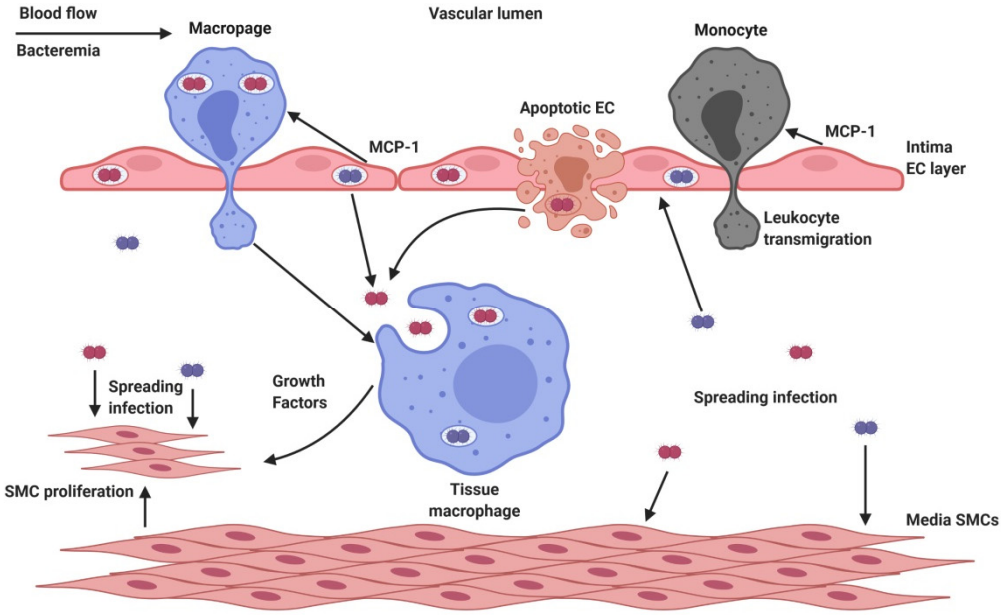

Figure 3. The microbial component of atherogenesis. The bacteria invade the endothelial cells (EC) layer causing apoptosis. The endothelium releases chemokines as monocyte chemoattractant protein 1 (MCP-1) in the lumen, inducing the activation of blood monocytes and macrophages and promoting their adhesion and diapedesis. Moreover, the transmigrating leucocytes can harbor viable bacteria, which allow systemic bacterial dissemination to distant sites. Atheroma can grow due to the proliferation of smooth muscle cells (SMC), which is mediated by macrophages-secreted growth factors [88].

4.2. Biomarkers for the Detection of Periodontitis and CVDs

For several years in dental care, clinical methods such as periodontal probing and radiographic techniques have been used to diagnose periodontal disease [89]. Recent attempts have been made to use markers associated with this and other diseases, including CVD, to identify periodontal disease [90]. These procedures are useful. The dentist can offer the patient a diagnosis specific to the patient's condition and assess whether the delivered treatment is the most appropriate [90].

Oral fluids play an important role in the diagnosis of periodontitis. Saliva and crevicular fluid have been used, as they are the two elements through which inflammatory molecules can be collected in places where there are alterations in the periodontal tissues [91]. Additionally, serum and peripheral blood have been used to search for periodontal and CVD markers [92].

The following table summarizes the main conclusions of studies on periodontitis and heart diseases in which biomarkers have been used to correlate them (Table 3). Notable reviews addressing this point were published previously [93].

Table 3. Biomarkers and their association between periodontitis and CVDs.

Biomarkers	Findings	References
Plasma cholesterol, glucose, CRP, fibrinogen, and NTproBNP	The prevalence of chronic periodontitis (CP) in patients with AMI was extremely high and associated with a history of previous levels of MI, PAD, smoking, diabetes, TC, LDL, and hsCRP.	[94]
Interleukin (IL) 6 and C-reactive Protein (CRP)	Moderate periodontal disease compared to no or mild periodontal disease was associated with an increase in IL-6 levels. The high levels of CRP found in this population warrant further investigation.	[95]

Table 3. *Cont.*

Biomarkers	Findings	References
Vascular cell adhesion molecule (VCAM-1)	The data suggest that the total amount and concentration of neopterin and VCAM-1 in GCF appear to be strongly associated with the severity of periodontal disease in patients with AMI.	[96]
Adiponectin/C-reactive Protein (CRP)	The potential that serum and/or salivary biomarkers can help assess CVD risk requires knowledge of how the individual's oral health would affect the effectiveness of these biological measures. Serum CRP levels increased in patients with AMI, regardless of their oral health, and both serum and salivary CRP were significantly elevated in patients with ST-segment elevation myocardial infarction.	[97]
Cardiac troponin I and myoglobin	The severity of periodontitis is positively associated with the size of the acute myocardial infarction as measured by the serum levels of troponin I and myoglobin.	[98]

5. Association between Periodontal Disease, AMI, and Other Health Conditions

Periodontitis, a chronic inflammatory disease, is one of the most common human diseases and associated with systemic inflammation [52]. Inflammation has been hypothesized to promote the initiation and evolution of atherosclerosis. Accordingly, systemic inflammation induced by periodontitis stimulates the development of atherosclerotic cardiovascular disease and contributes to acute atherothrombotic complications in AMI [52,99]. The immune response plays an important role in the development and clinical manifestations of atherosclerotic plaques. Moreover, some clinical studies suggested a correlation between inflammatory circulating markers such as CRP and homocysteine and a susceptibility to AMI [99].

Chronic inflammation is also related to insulin resistance and worsening glycemic control, and in patients with diabetes, the aggressive treatment of periodontitis is associated with improved glycemic control and vascular function [100,101]. An association has been found between dyslipidemia and periodontal disease in which low-density lipoproteins are reportedly smaller and denser, which promotes atherogenesis [101,102]. Obesity and periodontitis share common risk factors, such as dietary components, diabetes, and suboptimal lifestyle behaviors. Adipocytes contain activated macrophages, and as the number of adipocytes increases, these activated macrophages induce the production of cytokines such as pro-inflammatory interleukins and tumor necrosis factors [101]. Dental plaque could possibly serve as a reservoir for respiratory pathogens, causing respiratory tract infections and pneumonia [69]. Recent studies reported a relationship between periodontitis and oral, pancreatic, head, neck, and lung cancer [69,103]. Inflammation is the suggested link between periodontal disease and Alzheimer's disease, as the brain undergoes diverse inflammatory processes, such as complement activation and cytokine production, that favor its development [69]. Periodontal disease is also associated with adverse pregnancy outcomes; due to hormonal changes, pregnant women are more susceptible to gingivitis and periodontitis than non-pregnant women [104]. The mechanisms proposed are bacterial translocation from the oral cavity and across the placental barrier, thereby reaching the amniotic fluid and the entering fetal circulation, and the systemic dissemination of endotoxins and inflammatory mediators derived from oral pathogens which could affect fetal development or trigger a spontaneous abortion [69].

6. Importance of Prevention in Periodontitis and AMI

6.1. Lack of Effectiveness of Periodontitis Preventative Measures in LATAM

In analyzing why periodontitis is a larger problem in LATAM than in more economically powerful countries, we must consider certain fundamental aspects. For instance, there is insufficient knowledge among LATAM populations of risk factors, possible systemic

effects, prevention, diagnosis, and treatment. For example, several patients in LATAM do not consider the clinical signs of periodontal disease a health problem. Habits such as flossing are rarely practiced in LATAM populations [105]. Moreover, focusing on individuals is important in prevention. However, there has been little governmental intervention, such as public strategies related to oral health prevention in LATAM (91). Another aspect recently highlighted is the average income of the population, which is significantly lower than that of people in developed countries. Their lack of purchasing power means that the bulk of people in developing countries do not have access to adequate dental care [106]. Furthermore, oral care centers are often located far away, and it is difficult to find locations where people in need can be seen by experts [107]. This is caused by low investments in oral care [108]. Moreover, although public oral care centers are cheaper than private ones, they continue to present high costs because dental materials are expensive [109]. Another aspect to consider is the difficulty of performing high-quality epidemiological studies in the region [110], which leads to a lack of precise data about oral care on which ideal therapy for LATAM people may be planned [111]. Several studies to date have not followed a methodology that increases our understanding of which risk factors are related to periodontal diseases, or the information is incomplete. Since the completion of some studies, the results have been cast into doubt [110].

Considering the above information, well-conducted cross-sectional and longitudinal studies with clear objectives and sound methodologies are required [110] to enable the planning of regional interventions with adequate follow-up periods that facilitate rehabilitation [112].

6.2. Lack of Efficacy of AMI Prevention Measures in Mexico

Attempts have been made to reduce the frequency of AMI cases along with proposals to analyze the current situation in Mexico. Some authors consider that the existing problem is mainly caused by delays before, during, and after the detection of AMI. The first delay is that the patient does not know the symptoms of an AMI; therefore, they do not request timely medical attention, commonly taking up to 5 h to decide to go to the hospital. As a result, 50% of patients die in their homes. The second delay occurs when doctors who receive a patient with symptoms associated with AMI fail to diagnose it, as occurs in approximately 80% of cases due to a lack of knowledge or diagnostic studies. The ideal situation would be that no more than 10 min pass from the first contact with the doctor until the point of diagnosis. The third and last delay is the one that occurs between diagnosis and start of treatment [113].

Some risk factors for AMI development have already been mentioned, among which it is important to consider that the majority of the Mexican population is diabetic and has high blood pressure. In addition, there is a high prevalence of overweight or obese, as an estimated 80% of the population over 20 years of age is above their ideal weight [114].

Although the high prevalence of diabetes and hypertension in Mexico is almost equivalent to that in high-income countries, as in many developing countries, there are insufficient resources and infrastructure in Mexico to supply the demand for treatment of these conditions, which presents a challenge for the healthcare system [20].

6.3. Importance of Prevention to Avoid the Development of Periodontitis in Mexico

Mexico currently has an aging population whose number of elderly people is increasing. Notably, a large part of this population has lost one or more teeth due to cavities and periodontal disease. Accordingly, there is a need for dentists to educate these patients about their oral health to improve their quality of life [115]. Substantial evidence from observational studies highlights how certain oral health interventions, such as proper oral hygiene habits, increased dental visits, dental prophylaxis, and periodontal treatment, reduce the incidence of CVD-related events [52].

Notably, Mexico is a nation with very restricted oral care, and a high portion of the population has insufficient resources to cover dental expenses. Therefore, it is challenging to restore the oral health of these patients and help them to improve their quality of life [116].

Furthermore, there is little awareness of oral care in the young population. They are not aware that with good oral brushing, the development of diseases such as gingivitis can be avoided. In addition, when they go to the dentist, the advice they are given is not usually followed, meaning that they often contract diseases that could progress to periodontitis [117].

6.4. Importance of Prevention to Avoiding AMI Development

Due to the limited possibility of applying the most advanced and efficient treatments to the population with AMI, it is vitally important to reinforce primary prevention programs that focus on diseases and lifestyles that facilitate the progression of CVDs. However, the prevention of mortality must also be stressed, and once the AMI has already manifested, we must establish and promote a methodology that allows patients to access definitive treatments. Preventive measures are closely related to time, since the less time wasted, the greater the possibility of saving lives [20].

Health promotion and continuing medical education are considered preventive measures [20]. The first refers to offering campaigns to the general population to raise awareness about AMI, emphasizing lifestyle changes (not smoking, engaging in physical activity, and eating healthily, among others) [34] and the identification of symptoms suggestive of AMI so they can seek medical attention as soon as possible [20].

When first- and second-level doctors manage to treat a patient with AMI in a timely manner, the patient can remain stable until they are treated in a third-level medical unit, where they will be operated on for final treatment (coronary reperfusion), a process that decreases their risk of mortality from 20% to less than 10%. This can reduce the likelihood of or prevent heart failure due to the loss of heart muscle secondary to necrosis caused by an AMI [20].

7. Discussion

CVDs are the leading cause of global mortality and major contributors to disability [118]. Thus, it is important to understand the pathophysiology of these diseases to identify timely treatment solutions [119]. However, it is also important to determine the main associated risk factors to enable the establishment of preventive measures [120]. In this sense, different studies have associated periodontitis with a higher risk of AMI. Although the involved molecular mechanisms are not completely clear, inflammatory and bacterial factors play a part in the most studied underlying mechanism [121].

Periodontal disease is a highly prevalent disease associated with comorbidities that are quite common, such as diabetes and obesity [122,123]. Notably, these same comorbidities are intricately linked to the development of CVDs, and the alteration of inflammatory factors seems to be the common denominator. Accordingly, inflammatory factors have been considered possible biomarkers, mainly for monitoring or diagnosing CVDs in relation to periodontal disease.

Understanding the relationship between these two diseases could aid in the development of preventive strategies that benefit those populations that are highly affected by both diseases, such as the Mexican population. Thus, studies that determine the causal relationships and molecular mechanisms involved should be conducted to establish schemes for the prevention or treatment of these diseases.

8. Conclusions

Periodontitis and AMI share risk factors, and several studies have reported an association between them, even indicating that periodontal disease may be a modifiable risk factor for AMI and other CVDs. However, uncertainties remain; therefore, we must continue this research to determine the details of their causal relationship. Further interdisciplinary studies are required in LATAM to support efforts to establish preventative measures for periodontitis and AMI, since both diseases are prevalent in this population.

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