MARCJASZ, Piotr, BIOŁY, Anna, BOROŃCZYK, Agnieszka, ZAJĄC, Piotr, BULISZAK, Agnieszka, and BABCZYŃSKA, Monika. Peridontal Diseases as a Risk Factor for Severe Course and Mortality in COVID-19 – An Interdisciplinary Analysis in Light of Available Studies. Quality in Sport. 2025;40:59831. eISSN 2450-3118.
https://dx.doi.org/10.12775/QS.2025.40.59831
https://apcz.umk.pl/QS/article/view/59831

The journal has had 20 points in Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 28.03.2025. Revised: 11.04.2025. Accepted: 22.04.2025. Published: 22.04.2025.

Periodontal Diseases as a Risk Factor for Severe Course and Mortality in COVID-19 – An Interdisciplinary Analysis in Light of Available Studies

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ABSTRACT:

Introduction: COVID-19 can progress to life-threatening illness in some patients, and identifying modifiable risk factors for severe outcomes is crucial. Periodontal diseases cause systemic inflammation and share risk factors with conditions linked to worse COVID-19 outcomes [7]. Recent studies worldwide have suggested that periodontitis may independently aggravate COVID-19 severity [5]. This interdisciplinary analysis aims to examine current

evidence on whether periodontal disease is a risk factor for severe COVID-19 progression and mortality.

Materials and methods: A literature review was conducted using the databases such as Pubmed and Google Scholar.

Summary of Current Knowledge: An emerging body of global research indicates a significant association between poor periodontal health and adverse COVID-19 outcomes. Multiple studies report that COVID-19 patients with periodontitis experience higher rates of severe complications, including need for intensive care, mechanical ventilation, and death [1, 2].

Conclusion: Current evidence suggests periodontal disease is a plausible and potentially modifiable risk factor for severe COVID-19. Interdisciplinary efforts in dentistry and medicine are warranted to further clarify this relationship and to integrate oral health into risk assessment and management of systemic diseases like COVID-19.

Keywords: periodontal diseases, periodontitis, COVID-19, coronavirus, SARS-CoV-2

1. Introduction

The coronavirus disease 2019 (COVID-19) pandemic has posed unprecedented challenges to global health. While many infections are mild, a subset of patients develop severe pneumonia, acute respiratory distress syndrome (ARDS), and multi-organ failure, leading to high mortality[7]. Established risk factors for severe COVID-19 outcomes include advanced age and chronic comorbidities such as cardiovascular disease, diabetes, obesity, and immunosuppressive conditions[7]. Notably, several of these comorbidities have well-known links to chronic oral diseases like periodontitis. Periodontitis is one of the most prevalent inflammatory conditions worldwide, characterized by progressive destruction of the periodontal tissues (gum attachment and bone) due to bacterial infection and host immune responses [6]. It is also considered a chronic non-communicable disease and shares common risk factors with severe COVID-19, including older age, smoking, diabetes, and poor general health status [7]. These observations prompted investigation into a possible association between periodontal disease and the progression and outcomes of COVID-19 [6].

Periodontal disease might influence COVID-19 severity through multiple mechanisms. Firstly, periodontitis elevates systemic levels of inflammatory mediators (e.g. interleukin-6, tumor necrosis factor-α, C-reactive protein) and a prothrombotic state [1]. This systemic inflammation could exacerbate the hyperinflammatory "cytokine storm" phase of severe COVID-19 [4]. Secondly, the oral cavity – especially periodontal pockets in periodontitis – may serve as a reservoir for respiratory pathogens. Aspiration of periodontopathic bacteria has been implicated in hospital-acquired pneumonia [6], suggesting that oral infections could similarly worsen COVID-19–related lung infections. Additionally, the tissues affected by periodontitis highly express SARS-CoV-2 entry factors (ACE2 receptors, TMPRSS2 protease), potentially facilitating viral load in the mouth and subsequent spread to the lungs [8]. These hypotheses underline an interdisciplinary problem bridging dentistry, infectious disease, and immunology. If periodontitis indeed contributes to severe COVID-19, it would highlight oral health as an important – and modifiable – factor in systemic disease outcomes.

2. Aim

This paper reviews and synthesizes current knowledge on the role of periodontal diseases as a risk factor for severe COVID-19 progression and mortality. We draw on global research from the past five years, including clinical studies, meta-analyses, and mechanistic investigations, to assess the strength of the association and the biological plausibility. The goal is to provide an interdisciplinary analysis of whether improving periodontal health could impact COVID-19 severity, and to identify gaps for future research. By challenging and building upon existing findings, this review aims to inform both dental and medical professionals of the potential importance of oral health in the context of COVID-19 and other systemic illnesses.

3. Review of Current Knowledge

3.1 Epidemiological Association Between Periodontal Disease and COVID-19 Severity

A growing number of studies from around the world have examined COVID-19 outcomes in patients with and without periodontal disease. Overall, these studies consistently report that pre-existing periodontitis is associated with more severe COVID-19 progression. One of the first robust investigations was a case-control study by Marouf et al. in Qatar (2020), which analyzed health records of 568 COVID-19 patients [1]. After adjusting for age, smoking, and medical comorbidities, periodontitis was found to be significantly associated with COVID-19 complications. Patients with periodontitis had markedly higher odds of intensive care unit (ICU) admission (adjusted odds ratio [OR] ~3.54), need for mechanical ventilation (OR ~4.57),

and death (OR ~8.81) compared to periodontally healthy patients [1]. In the periodontitis group, blood levels of inflammatory and coagulatory biomarkers (white blood cell count, D-dimer, C-reactive protein) were also significantly elevated, paralleling the worse clinical outcomes [1]. This study provided early clinical evidence that oral health status might impact the course of COVID-19.

Subsequent research has reinforced these findings across diverse populations. For example, a case-control study in India (Macherla et al. 2024) compared 43 moderate-to-severe COVID-19 cases with 120 mild/asymptomatic controls and carefully documented periodontal status [2]. The presence of periodontitis was associated with a 3.7-fold increase in the odds of developing severe COVID-19 symptoms ($p = 0.002$) [2]. Patients with periodontitis also tended to have longer hospital stays and a higher incidence of certain symptoms (e.g. headaches, dizziness) [2]. Although that particular study found only a slight increase in mortality risk (OR ~1.03) with periodontitis [2], the low number of deaths in the sample may have limited statistical power. Overall, its conclusion aligned with others: there is a positive association between periodontal disease and COVID-19 severity, supporting the notion that managing periodontitis should be part of comprehensive COVID-19 patient care [2].

Large-scale data analyses and systematic reviews provide further weight to this association. A 2023 systematic review by Al-Maweri et al. aggregated evidence from 22 studies encompassing over 90,000 patients across the USA, Europe, Asia, the Middle East, and South America [3]. Most individual studies (19 out of 22) reported a significant link between poor periodontal health and worse COVID-19 outcomes [3]. In meta-analysis, periodontitis was associated with markedly higher odds of severe COVID-19 symptoms (pooled OR ~6.95) and ICU admission (OR ~3.15) [3].

The association with mortality was more modest (pooled OR ~1.92) and did not reach statistical significance in the initial overall analysis ($p = 0.21$) [3]. However, when considering disease severity, patients with severe periodontitis (extensive gum and bone loss) had significantly greater risk of COVID-19 death than those with milder periodontal disease [3, 31]. In fact, severe periodontitis appeared particularly deleterious – one analysis noted that severe periodontal disease was associated with higher ICU admissions and mortality even after accounting for other factors [3]. This gradation suggests a dose-response relationship, where worse periodontal status confers incrementally higher risk for severe COVID-19 outcomes. Not all studies used clinical periodontal exams; some leveraged existing data sets with oral health

proxies. An example is a UK Biobank analysis (Larvin et al. 2020) that used self-reported oral health measures in over 1,600 COVID-19 patients [12]. In that study, indicators of periodontal disease (such as gum bleeding or loose teeth) were associated with a significantly higher risk of COVID-19 mortality (OR ~1.71, 95% CI 1.05–2.72) despite relying on self-report [12]. Interestingly, periodontal disease indicators did not significantly increase the risk of contracting the SARS-CoV-2 infection itself [13]. This suggests that while poor oral health may not affect susceptibility to the virus, it can influence the severity of illness once infected – a pattern also observed in other studies [12, 13]. Similarly, a retrospective study of ~59,000 UK patients found that periodontal disease by itself did not raise the odds of testing positive for COVID-19, but among obese individuals, it had an additive effect on outcomes [13]. In obese patients, coexisting periodontal disease was linked to a 57% higher hazard of COVID-19 hospitalization compared to obese patients without periodontal issues [13]. This points to a possible synergy between oral inflammation and other risk factors (like obesity), compounding the risk of severe COVID-19.

Prospective clinical studies in hospitalized patients have further solidified the link. In a 2022 study of 128 hospitalized COVID-19 patients who received detailed dental exams, periodontitis was highly prevalent (≈48% of patients) and significantly correlated with worse outcomes [14]. Patients with periodontitis had increased rates of critical COVID-19 symptoms and ICU admission, and over twice the risk of death compared to those without periodontitis, even after adjusting for age and underlying comorbidities [14]. Specifically, the incidence rate ratio (IRR) for mortality in the periodontitis group was about 2.05 (95% CI 1.12–3.76) and for ICU admission was 1.44 (95% CI 1.07–1.95) in multivariate models [14]. Another clinical investigation (Gupta et al., 2022) examined 82 COVID-19 patients with direct periodontal examinations and found dramatically higher odds of adverse outcomes in those with severe periodontitis [11]. Different study showed that advanced periodontal breakdown was associated with an OR of 14.58 for mortality, OR 7.45 for needing ventilatory support, and OR 36.5 for hospital admission, compared to mild/no periodontitis [5]. These extremely high odds ratios underline the potential impact of severe gum disease, though the sample size was relatively small. The authors cautioned that while periodontitis "seems to be related to poorer COVID-19 outcomes," direct causality could not be confirmed and residual confounding might exist [5]. Nonetheless, their findings emphasize that assessing oral health – even with point-of-care tests – could help identify high-risk patients during a pandemic [5]. When pooled together, the evidence strongly suggests that periodontal disease correlates with

more severe COVID-19 illness and higher mortality. A recent comprehensive review summarized that patients with periodontitis are at higher risk for severe COVID-19 symptoms, ICU hospitalization, and death, especially if the periodontal disease is advanced [31]. In quantitative terms, meta-analyses have estimated this risk to be on the order of 3- to 7-fold for the most critical endpoints [4]. It is important to note that these associations have been observed across different countries and healthcare settings, lending a global consistency to the findings. However, as most data come from observational studies, one must consider the possibility of confounding. Researchers have tried to adjust for known factors (age, smoking, systemic conditions), but there may still be unmeasured variables (e.g., socioeconomic status or access to care) influencing both oral health and COVID-19 outcomes. Despite these limitations, the convergence of results from epidemiologic studies makes a compelling case that periodontal disease is a noteworthy risk indicator for COVID-19 severity.

3.2 Biological Plausibility and Mechanisms Linking Periodontitis to Severe COVID-19
Several biological mechanisms have been proposed to explain how periodontal disease could contribute to the progression of COVID-19. Central to these theories is the concept that periodontitis induces a chronic state of systemic inflammation that can predispose patients to the hyperinflammatory response seen in severe COVID-19 [6]. In periodontitis, pathogenic bacteria in dental plaque chronically stimulate the immune system, leading to elevated circulating levels of pro-inflammatory cytokines (such as IL-1β, IL-6, TNF-α) and acute-phase reactants (like C-reactive protein) [6]. Notably, severe COVID-19 is characterized by an exaggerated cytokine release (often termed a "cytokine storm"), with studies showing that patients with complicated COVID-19 have dramatically higher IL-6 levels (approximately 2.9-fold) than those with mild disease [6]. Periodontitis could thus prime patients by increasing baseline inflammatory cytokine levels. Indeed, COVID-19 patients with periodontitis in the Marouf et al. study had significantly higher serum CRP and white blood cell counts than those without periodontitis [7], reflecting an immune system already on "high alert." This pro-inflammatory milieu might accelerate the deterioration of COVID-19 in the lungs, tipping the balance from a controlled immune response to a harmful systemic overreaction. Local entry and spread of the virus in the oral cavity is another plausible link. The primary entry point for SARS-CoV-2 is via the ACE2 receptor on host cells, aided by proteases like TMPRSS2 and furin that activate the viral spike protein [7, 8]. Research has found that these key receptors/co-factors are abundantly expressed in oral tissues – especially in the gingival

epithelium and periodontal ligament cells – and their expression is upregulated in patients with periodontitis [8]. In essence, chronic periodontal inflammation may increase the density of cellular "doorways" for the virus in the mouth. A recent review noted that ACE2, TMPRSS2, and CD147 (another putative SARS-CoV-2 receptor) are all over-expressed in diseased periodontal tissues, potentially creating a permissive environment for the virus [8]. This raises the possibility that periodontal pockets could serve as reservoirs for SARS-CoV-2. The virus may accumulate in these deep gum spaces, infecting the adjacent pocket epithelium and then spreading via the rich vasculature of inflamed periodontal tissues. It has been hypothesized that ulcerated pocket epithelium in periodontitis can allow viruses and bacteria to directly enter the bloodstream [7]. From there, SARS-CoV-2 might disseminate to the lungs and other organs more readily in a patient with periodontal disease, potentially increasing viral load and exacerbating infection severity [7].

Additionally, aspiration of oral pathogens provides a mechanistic bridge between gum disease and respiratory illness. Patients with periodontitis harbor a dysbiotic oral microbiome laden with aggressive bacteria. These bacteria (or their products) can be aspirated into the lower airway, especially in critically ill patients or those with poor oral hygiene. Aspiration pneumonia is a known complication in patients with poor oral health; for instance, meta-analyses have shown that periodontitis significantly increases the risk of nosocomial pneumonia in ICU patients [6]. In COVID-19, a secondary bacterial infection or an immune response modulated by oral bacteria could worsen lung damage. Some investigators have suggested that enzymes and toxins from periodontal pathogens may potentiate lung inflammation or coagulation. Moreover, tissue-destructive enzymes (like matrix metalloproteinases) elevated in periodontitis could degrade the protective mucosal barriers, making it easier for both viruses and bacteria to invade respiratory tissues [5]. The net effect is that a patient with periodontitis might have lungs that are "pre-injured" or more vulnerable when COVID-19 strikes.

There are also intriguing molecular links being explored. One example is galectin-3, an inflammation-related protein that is highly expressed in periodontal disease and has a structure resembling the SARS-CoV-2 spike protein. It's speculated that galectin-3 might interact with viral components or modulate immune responses in a way that influences COVID-19 severity [7]. Another angle is the hyperactivity of neutrophils in periodontitis – including the formation of neutrophil extracellular traps (NETs) – which could synergize with the neutrophil-driven tissue damage in COVID-19 pneumonia. Both diseases show evidence of NET-mediated pathology (excess NETs have been found in diseased gum tissues and in the lungs of severe

COVID-19 patients), suggesting a common pathway of immune dysregulation. While these molecular connections are still under investigation, they add depth to the biological plausibility that poor oral health can have systemic consequences.

It is important to emphasize that periodontal disease and COVID-19 also share risk factors and bidirectional relationships with other conditions. This complicates the mechanistic picture but is part of an interdisciplinary understanding. For instance, diabetes mellitus is a major risk factor for periodontitis and is known to worsen COVID-19 outcomes. Chronic periodontitis can itself worsen glycemic control, creating a vicious cycle between oral health and diabetes [6]. A patient with poorly controlled diabetes might have severe periodontal disease and then experience severe COVID-19, with inflammation from each condition feeding into the other. Similar triangles of interaction exist with obesity, heart disease, and other chronic illnesses that cluster with periodontitis [7, 8]. In one position paper, researchers described COVID-19 and chronic diseases (including periodontal disease) as syndemic – mutually exacerbating epidemics [6]. This means that part of periodontitis's impact on COVID-19 might be indirect, via amplifying systemic conditions that in turn worsen COVID-19. Supporting this, some analyses have found the periodontitis-COVID link strongest in younger patients without other comorbidities, suggesting it's not entirely explained by shared risk factors [7]. Nonetheless, disentangling these factors is challenging. Current evidence indicates that even after adjusting for common risk factors, periodontitis remains an independent predictor of COVID-19 severity [1, 14]. This lends credibility to a direct role of the chronic oral infection in influencing systemic disease outcomes.

4. Discussion

If a causal relationship between periodontal disease and worse COVID-19 outcomes exists, the implications are far-reaching. Periodontal disease is preventable and treatable; thus, it could be targeted as part of public health strategies to improve population resilience against COVID-19 and other respiratory infections. Basic oral hygiene measures (regular toothbrushing, flossing, dental check-ups) and periodontal therapy (professional cleanings, treatment of gum inflammation) might reduce systemic inflammation and pathogen load, potentially lowering the risk of severe infections. In fact, periodontal treatments have been shown to improve systemic inflammatory marker levels in patients with comorbid conditions [7]. Translating this to COVID-19, one might hypothesize that maintaining good oral health could result in milder illness if one contracts SARS-CoV-2. Some clinicians have even called for periodontal health assessments to be included in COVID-19 patient management protocols [14]. For example,

simple screenings for gum disease signs in COVID-19 wards could identify patients who might benefit from antiseptic mouth rinses or antibiotic prophylaxis to reduce oral bacterial burden during their illness.

Moreover, the pandemic has highlighted the need for integration between dental and medical care. During the initial COVID-19 outbreaks, many dental services were suspended or limited to emergencies, which led to a decline in oral health for many individuals [31]. One study in Spain documented that a large proportion of routine periodontal treatments were not performed during the first wave of the pandemic, potentially increasing the burden of untreated gum disease in the population [15]. Such disruptions in oral healthcare could have inadvertently heightened risk factors for severe COVID-19. This underscores that oral health should not be neglected even amid a pandemic. On the contrary, ensuring access to dental care and promoting oral hygiene should be components of public health planning in health crises. Interdisciplinary collaboration – for instance, medical teams advising high-risk patients about oral care, or dentists being alert to systemic health changes – can be beneficial.

From a research perspective, the observed linkage between periodontitis and COVID-19 opens new questions. Could treating periodontitis improve outcomes in COVID-19 patients? Some ongoing trials are exploring whether interventions like intensive dental cleanings or localized oral antimicrobial treatments in COVID-positive individuals lead to reduced complications. Additionally, the periodontitis-COVID connection serves as a model for understanding connections between oral health and other respiratory diseases. It revives interest in classic topics like the oral–systemic health axis and suggests that oral infection control might form part of the arsenal against future pandemics or diseases. The fact that oral health status is potentially modifiable makes it an attractive target – unlike fixed factors such as age or genetic predispositions.

However, it is also clear that more evidence is needed before drawing firm conclusions. Most studies to date are observational; high-quality prospective cohort studies and intervention trials are necessary to establish causation. There is also a need for standardized measures – in the studies reviewed, periodontal status was assessed variously by radiographs, clinical exams, or self-report, and COVID-19 outcomes ranged from symptom scores to need for ventilation. Harmonizing these definitions in future research will allow more precise meta-analyses. Some experts have pointed out that publication bias might overstate the association (studies finding no link may be less likely to be published). Therefore, continuing research, including well-

controlled longitudinal studies, is critical to confirm or challenge the existing findings [3, 14]. If periodontitis is conclusively shown to worsen COVID-19 outcomes, it provides a strong argument for integrating oral health promotion into general preventive medicine. Even if the association is partially confounded, improving oral health has minimal downsides and numerous known benefits for systemic health.

In summary, current knowledge – drawn from epidemiology, clinical studies, and biological plausibility – supports the concept that periodontal disease can act as a risk factor for severe COVID-19. This nexus of oral and systemic health exemplifies why an interdisciplinary approach is needed in healthcare. Dentists, physicians, and scientists must work together to further elucidate this relationship and to develop collaborative strategies that improve patient outcomes. The COVID-19 pandemic, devastating as it has been, offers lessons about the interconnectedness of bodily systems; one such lesson may be that a healthy mouth contributes to a healthier immune response against respiratory viruses.

5. Summary

Periodontal diseases, especially chronic periodontitis, have emerged as a potential risk factor for severe COVID-19 progression and mortality. An analysis of global studies from the past five years indicates that patients with poor periodontal health are more likely to experience critical COVID-19 outcomes such as respiratory failure requiring ICU care and even death. This association persists across various populations after accounting for common confounders. Biological mechanisms provide credible explanations: the systemic inflammation from periodontitis may amplify COVID-19's inflammatory damage, and oral pathogens or locally enhanced viral entry could worsen infection in the lungs. While direct causation is not yet definitively proven, the consistent correlation and mechanistic plausibility suggest that maintaining good periodontal health might play a supportive role in improving COVID-19 outcomes. From a public health standpoint, these findings encourage closer integration of oral health in managing general health and highlight the importance of oral hygiene and regular dental care. In conclusion, periodontitis appears to be an important piece in the complex puzzle of COVID-19 risk factors. Strengthening periodontal care and awareness could be a valuable adjunct in our fight against not only COVID-19 but also other systemic illnesses that share inflammation as a common denominator. Ongoing research and interdisciplinary collaboration are essential to fully understand and harness this connection for better health outcomes.

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All authors have read and agreed with the published version of the manuscript.

FUNDING STATEMENT

This research received no external funding.

INSTITUTIONAL REVIEW BOARD STATEMENT

Not applicable.

INFORMED CONSENT STATEMENT

Not applicable.

DATA AVAILABILITY STATEMENT

Not applicable.

ACKNOWLEDGEMENTS

Not Applicable.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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