BULLETIN OF STOMATOLOGY AND MAXILLOFACIAL SURGERY
Volume 21, Issue 2

DOI: 10.58240/1829006X-2025.2-130

Literature Review

EXPLORING THE INTERSECTION OF PROSTATITIS AND PERIODONTITIS

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Received: Dec 25, 2024; **Accepted**: Jan 10, 2024; **Published:** Jan 15, 2025

Abstract

Background: Periodontitis which is an immune-inflammatory condition which can either be caused by systemic disease or can cause a systemic disease. The complex association between prostatitis and periodontitis involves immunological, microbiological, and systemic health factors. Interestingly, studies have shown a positive relation between patients with poor oral hygiene and prostatitis. Therefore, it is important to get regular dental checkups to evaluate periodontal health. Here, in this review we will dive to know about link between periodontitis and prostatitis as well as their bidirectional relation.
Materials and methods: PubMed, Scopus, Web of Science, Google scholar was searched using pre-specified search strategy. Narrative and systematic reviews are included for the data synthesis.
Results: Extensive literature search was carried out using pre-defined search strategy was carried out. A total of 48 titles were screened rigorously by two independent evaluators and after duplicate exclusion, removal of irrelevant titles, 22 articles were included.
Conclusion: Periodontitis has a very strong relation with prostatitis. Most of research has found out to have a positive association between both of them. Having thorough knowledge all systemic diseases is very important for today's clinicians since these diseases negatively impact the progression of periodontitis and vice versa. Positive association can be established with further larger studies.

Keywords: Periodontitis, Prostatitis, Oral hygiene, Stress.

INTRODUCTION

Periodontitis which is the most common oral immune inflammatory condition was once thought to be caused only by inevitable consequence of aging.[1] Many factors cause periodontitis which include local factors such as poor oral hygiene, abnormal tooth position, dislodged restorations, smoking, stress etc.[2] Similarly, various systemic diseases also cause periodontitis or periodontitis can indirectly cause systemic diseases. These include diabetes, hypertension, renal diseases, liver diseases, obesity, metabolic syndrome, rheumatoid arthritis. Respiratory diseases, cognitive impairment, prostatitis etc.[3]

As the research progressed, many authors have found out that periodontitis was not caused only by aging but has various risk factors and indicators. This discovery of risk components has led to new concept of linking systemic health, conditions and diseases to periodontal health. One of the important systemic disease which has a potential link with periodontitis is prostatitis.[4] Let us discuss about prostatitis in detail and its relation with periodontitis.

Prostatitis is basically inflammation of prostate gland which accounts for about 50% of Indian men by the

age of 60. Prostatitis clinically manifests as painful penis and testicles which leads to pain during micturition, difficulty in emptying the bladder, increased urination frequency, pain in penis increases during ejaculation, with associated fever and chills.[5]

The main etiology of prostate infection has been employed to gram negative bacteria such as Escherichia coli and Klebsiella species.[6] Other mechanism which is thought to be a causative factor for prostate infection id role of immune system which is mediated by proinflammatory cytokines, such as interleukin (IL)-1b and tumor necrosis factor-α (TNF-α). This involvement of pro-inflammatory mediators in prostatic inflammation significantly contributes to increased serum Prostate-specific antigen (PSA) levels.[7]

Prostate-specific antigen (PSA), a glycoprotein is a biological or tumor marker which is produced mainly by the epithelial acinar cells of the prostate gland. This is secreted into the lumen of prostate gland, and then passes through the prostatic ducts into the semen. It mainly helps in diagnosis of benign prostatic hyperplasia, prostate cancer. In contrast to individuals with a PSA volume, those with a PSA level below 4.0 ng/ml are considered normal, and those with a level over 0.35 ng/ml/year have a comparatively increased chance of death from prostate cancer.[8]

The National Institutes of Health classified prostatitis into four clinical categories:

Table 1. Classification of clinical categories of prostatitis[7]

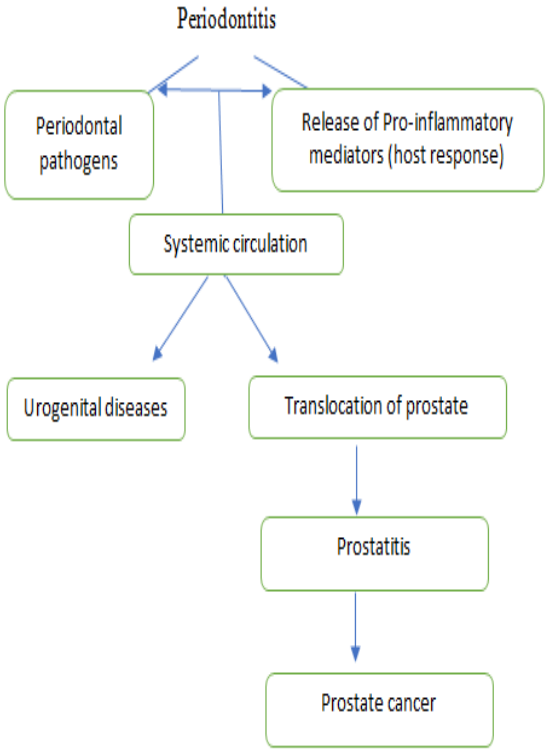
Category	*Prostatitis*
Category I	Acute bacterial prostatitis;
Category II	Chronic bacterial prostatitis;
CategoryIII a	Inflammatory chronic pelvic pain syndrome
CategoryIII b	Non- inflammatory chronic pelvic pain syndrome
Category IV	Asymptomatic inflammatory prostatitis

Unveiling the link between Prostatitis and periodontitis

Men with periodontal disease have been found to release significantly more prostate-specific antigen.[9] Periodontitis can cause immune inflammatory condition in the body leading to release of pro-inflammatory mediators in turn causing urogenital diseases and translocation of prostate. This translocation can cause prostatitis and finally may lead to prostate cancer.[10]

According to research, PSA values are greater in men with prostatitis and periodontal disease than in individuals without these conditions.

Pathophysiology of periodontitis causing prostatitis



Flow chart 1. Periodontitis and Prostatitis[10]

Other mechanisms of periodontitis causing prostatitis

According to available data, periodontal disease increases the host's inflammatory burden by elevating C-reactive protein and proinflammatory cytokines such Tumor Necrosis Factor-a, interleukin 1, 6. It has also been reported that males with prostatitis had higher serum levels of TNF-a and IL-1 than do healthy people. Thus, by boosting the inflammatory response in the prostate and disseminating cytokines that exacerbate pre-existing inflammation of the gland, periodontitis may indirectly contribute to prostate gland inflammation.[11]

These pro-inflammatory mediators can be released from periodontal tissues as well. This might result in a persistent inflammatory weakness that could trigger the emergence of systemic illnesses. A bacterial prostatitis may be explained by the potential inflammatory effect of cytokines.[12]

Another explanation is that inflammatory reactions degrade the prostate glandular epithelium, which increases PSA leakage into the blood.[13]

The third explanation is that prostate gland enlargement can lead to inflammatory reactions

which can increase the production of PSA. This increase in PSA can cause seepage into the bloodstream. Another distant, non-prostatic source of PSA, such as the periodontium, can also result in elevated blood PSA levels. Research is required to ascertain whether serum PSA levels, the impact of inflammatory mediators on the prostate gland, and the integrity of the prostate epithelium are impacted by non-prostatic PSA sources.[4]

Materials and methods: PubMed, Scopus, Web of Science, Google scholar was searched using pre-specified search strategy. Narrative and systematic reviews are included for the data synthesis.

Results: Extensive literature search was carried out using pre-defined search strategy was carried out. A total of 48 titles were screened rigorously by two independent evaluators and after duplicate exclusion, removal of irrelevant titles, 22 articles were included.

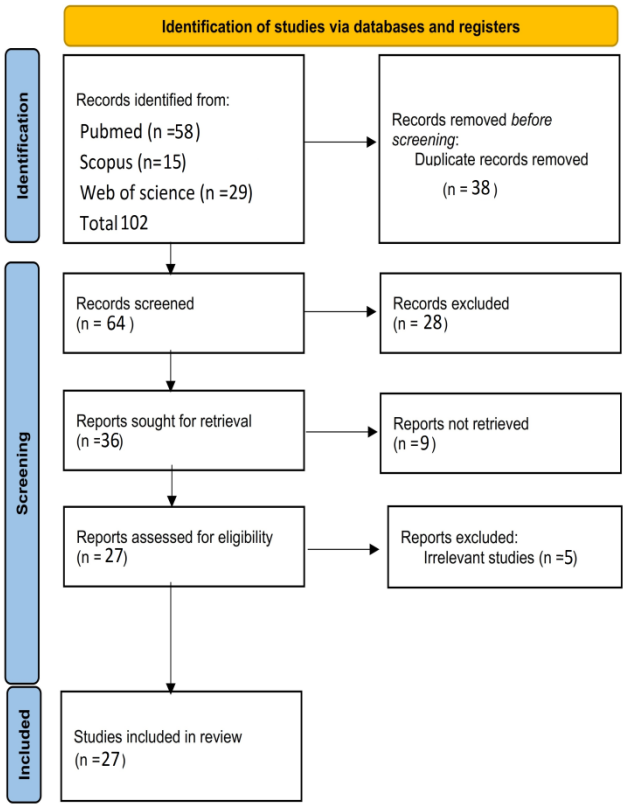


Figure 1. Prisma flow chart

Literature review

Fu et al in 2020 conducted a study on 5510 patients with chronic periodontitis and found out in this National Health Insurance Research Database cohort study that patients with periodontitis had 4.6-fold high risk of developing prostatitis than control group i.e., without periodontitis.[14]

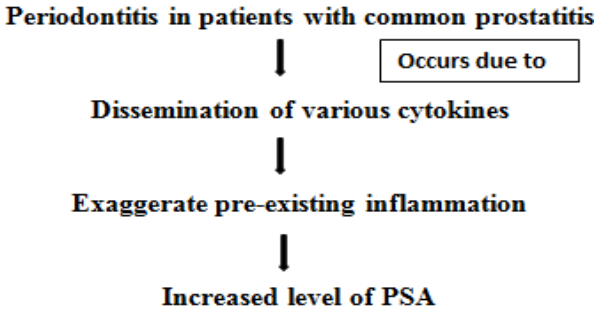
Two recent studies done by Lee et al and Corbella et al found out positive correlation between periodontitis and prostatitis and prostate cancer.[15,16]

Inflammatory burden in periodontitis and prostatitis

PSA levels in periodontitis and prostatitis patients:

Now having a better insight of etiopathogenesis of periodontitis and prostatitis, we know that there might be a connection between these two conditions, which may show up as higher blood PSA levels.

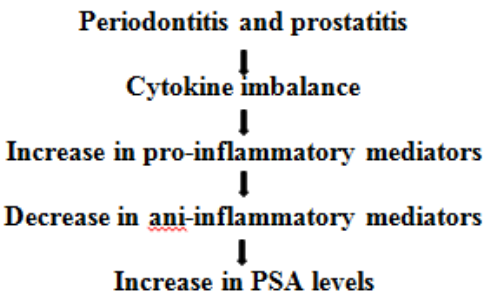
Patients with common prostatitis may have elevated PSA levels due to periodontitis, which most likely happens as a result of the spread of several cytokines that might exacerbate pre-existing inflammation. Joshi et al. in 2010 found that PSA levels were lower in little or mild periodontitis then in those with moderate to severe periodontitis which shows clear association of periodontitis and prostatitis.[4]



Flow chart 2 Periodontitis causing increase in PSA levels in prostatitis patients[4]

Hypothesis II

Gram-negative bacteria have been proposed as the causative agents of category I and II prostatitis as well as periodontitis. However, the bacterial cause of types III and IV prostatitis has not yet been determined. Both periodontitis and prostatitis have been linked to cytokine imbalance, with increased proinflammatory and reduced anti-inflammatory cytokines.[11,12]



Flow chart 3. How does PSA levels increase in both periodontitis and prostatitis?

Hypothesis III

Lastly, a different theory suggests that a localized rise in PSA levels-which may even take place in the periodontium-causes the prostate glands inflammatory reaction.

The production of PSA in the tissues of the periodontium would suggest that pro-inflammatory mediators are altered systemically, indicating a dysfunction of these mediators.[17]

Assessment of PSA levels

Important tool in interpreting increased PSA values (PSA density) is the measurement of prostatic size. Variations linked to prostate gland enlargement may be revealed by interpreting increased PSA values and density. However, only a small portion of the gland is represented by prostate needle biopsy specimens.[18]

According to Kandirali and colleagues, there is a positive link between serum PSA levels and the degree and severity of prostate inflammation in biopsy specimens.[19] This is supported by the higher PSA levels observed in individuals with moderate/severe prostatitis. This similar conclusion was also supported by Hasui et al who suggested that the elevated blood PSA was caused by a disruption in the prostate gland's epithelial integrity rather than a direct rise in PSA production.[20]

In a study to evaluate the changes in serum PSA and inflammatory cytokine levels like CRP and IL-1β following nonsurgical periodontal treatment in men with chronic periodontitis, Alwithanani et al. found that the periodontal treatment reduced PSA values and improved prostate symptom scores in men with chronic periodontitis.[21]

Ramanaryana B et al in 2019 conducted a study on 100 chronic periodontitis patients and found out a positive correlation between PSA levels and CAL, PD scores indicating mutual dependency between both.[9]

Serum PSA levels were found to be directly correlated with prostate volume by Morote et al., but not with the degree or kind of inflammatory infiltration.

Given this uncertainty, it's likely that the rise in PSA levels could be caused by a different non-prostatic source of PSA, like the periodontium, which is comparable to the PSA produced by the female breast.[22]

Recommendations for budding dentists and hygienists

Since we know oral health is gateway to many systemic diseases, dentists should include prostatitis has a regular health checkup condition to avoid complications such as prostate cancer. Dentists can conduct a regular checkups for risk of periodontitis and can educate the patients for the connecting systemic diseases.

As there is 4.6-fold higher risk pf prostatitis in periodontitis patients, these patients should be evaluated for further management.

Conclusion

Having thorough knowledge all systemic diseases is very important for today's clinicians since these diseases negatively impact the progression of periodontitis and vice versa.

This knowledge can help in all diagnostic and therapeutic procedures.

Since prostatitis prevalence is increasing, the association between prostatitis and periodontitis should be established with further studies which can characterize the importance of periodontal pathogens on bacterial prostatitis.

DECLARATIONS

Conflicts of interest and financial disclosures

None declared

Ethical approval

Not applicable

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