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Poor Oral Health and Fertility Problems: A Narrative Mini-Review

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ARTICLE INFO	ABSTRACT
<i>Article type:</i> Narrative Mini-Review	 Background & aim: Currently, it has been known that oral infections, especially periodontitis, may affect the pathogenesis of a number of systemic conditions. Evidence has also suggested a possible role of oral diseases in subfertility and infertility. Therefore, this study aimed to evaluate the association between poor oral health and fertility problems. Methods: In this narrative review, relevant English articles, or those with English abstracts with no publication date limitation, were extracted from PUBMED, Scopus, ScienceDirect and Google Scholar. Moreover, research keywords were "subfertility", "infertility", "sperm count", "erectile dysfunction", "conception", "oral hygiene", "oral infections", "periodontitis" and "periodontal disease". In total, 40 titles were found, from which letters to the editor, commentaries, as well as case reports and series were excluded, leading to the final assessment of 37 original articles. Results: In this study, a consistency was observed among studies conducted to assess the association between poor oral health and signs of fertility problems, such as improper spermatological parameters, erectile dysfunction (ED), increased time to conceive (TTC) and endometriosis. However, no significant association was observed between maternal periodontitis and male subfertility in future. Conclusion: According to the results of this study, oral hygiene could be an important component of general health and also a contributing factor for improved sexual health. Control of oral inflammation and regular dental check-ups by men and women, particularly prior to conceiving, could enhance reproductive ability.
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Introduction

Several epidemiological studies have been conducted to evaluate the relationship between poor oral health and cardiovascular diseases, inadequate glycemic control in diabetics and some other conditions (e.g., rheumatoid arthritis and osteoporosis) (1). Periodontitis is one of the most common chronic inflammatory oral diseases, probably associated with the mentioned systemic diseases and multiple adverse reproductive outcomes, such as preterm birth, low birth weight, fetal growth restriction, preeclampsia and perinatal mortality (2). In addition, several scientific studies have assessed the association between oral infections and fertility problems, including subfertility and infertility in men and women, some of which will be discussed in this paper. The term subfertility is generally used for any form of reduced fertility in couples, who have been trying to get pregnant unsuccessfully (3), whereas infertility is defined as failure to conceive after one year of unprotected intercourse (2, 3).

Fertility problems are associated with cost burdens, constituting a crisis in families. These problems may cause marital conflicts, leading to divorce and more serious issues in societies where women are primarily stereotyped as mothers (4, 5). In addition, reproductive problems can result in various psychological-emotional disorders, inclu-

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ding depression, anxiety, hopelessness, guilt and feelings of worthlessness in life, especially in women (6). According to the literature, an association has been found between oral infections and reduced fertility (7, 8). Given the fact that oral health problems, especially periodontitis, are treatable (9), improvement of oral health through periodontal and dental treatments may contribute to overcoming impediments to childbearing. With this background in mind, this study aimed to evaluate the association between oral infections and fertility problems.

Materials and Methods

This literature review focused on research question of: "Is there a relationship between poor oral health and fertility problems?" An overview of studies published in English or at least containing an English abstract without any publication date limitation was carried out in April 2016. Databases used in this research were PubMed, Scopus, ScienceDirect and Google Scholar. In addition, search keywords used in this study were "subfertility", "sperm count", "erectile dysfunction", "conception", "oral hygiene", "oral infections" and "periodontitis". In total, 40 titles met the inclusion criteria and were assessed by our researcher. However, letters to the editor, commentaries, as well as case reports and series were excluded, leading to the assessment of 37 original articles.

Results

In this research, related articles were divided into five sections to classify different aspects of the association between oral and sexual health.

I. Oral infection and spermatological parameters

In 1982, Linossier et al. demonstrated the possibility of sperm immobilization by spermatozoal immobilization factor from *Escherichia coli*, obtained from necrotic dental pulp (10). In another study, Bieniek et al. (1989) evaluated the semen specimens obtained from sperm donors for intended in-vitro fertilization. According to the results of the mentioned research, 36 male patients with bacteriospermia resistant to antibiotic therapy were recognized. Further examinations revealed oral foci of infection with a microbial spectrum similar to persistent bacteriospermia. Treatment of oral infection could resolve the relevant problems and improve fertility parameters. In this regard, Bieniek et al. identified a relationship between oral microbiota and bacteriospermia conditions and consequent subfertility (11). Moreover, Bieniek et al. (1993) demonstrated the high incidence of potential dental foci in samples obtained from the semen of subfertile men. Another spermiogram analysis was performed six months after dental treatment and two-thirds of the spermiograms proved sterile. In addition, a significant improvement was observed in the spermatological characteristics of subjects, including motility, morphology and density.

In line with the results obtained by Ensslen et al., Bienek et al. (1993) reported a relationship between microbial colonies and therapy-resistant bacteriospermia, which could be the main cause of subfertility (12, 13). On this theme, Klinger et al. (2011) evaluated the relationship between infertility and periodontal diseases. According to the results of the mentioned study, a positive association was observed between deep periodontal pockets and sub-motility. Bacteriospermia sperm and production of cytokines due to periodontal diseases can increase the possibility of male infertility through dissemination in the circulatory system (14). Nwhator et al. (2014) performed basic dental and periodontal examinations on 76 spouses requiring semen analysis as part of an infertility investigation. Obtained results of the mentioned study were indicative of a positive association between subnormal sperm count and periodontitis in only one age group. However, there was a significant association between poor oral health and subnormal sperm count among all age groups (15).

According to Abaje et al., a significant reduction was observed in semen volume of men with diabetes, which could be associated with increased sperm nuclear mtDNA damage with possible adverse effects on reproductive capability of diabetic men (16). On the other hand, it has been suggested that diabetic subjects with periodontitis have a six-fold higher risk of worsening of glycemic control over time, compared to diabetic patients without periodontal diseases (17). Therefore, it seems that periodontitis indirectly reduces fertility in this group of patients, caused by poor glycemic control.

II. Periodontitis and erectile dysfunction (ED)

In a study by Oguz et al. (2013), a significant relationship was suggested between chronic periodontitis and ED in young adults within the age range of 30-40 years. According to the results of logistic regression analysis in the mentioned study, a significant association was observed between this disability and severity of chronic periodontitis (18). On this theme, Keller et al. conducted a nationwide population-based study and found a higher risk of diagnosis of chronic periodontitis in patients with ED. In addition, this association was much stronger among the population aged <30 and >69 years (19).

Results obtained by Zadik et al. (2009) were also indicative of an association between ED and chronic periodontal diseases (CPD), which are consistent with the theories that associate these two conditions with systemic inflammation, endothelial dysfunction and atherosclerosis (20). In another study, Zuo et al. indicated that decreased expression of endothelial nitric oxide synthase (eNOS) in penile tissue (an important factor in the mechanism of erection), caused by systemic inflammatory changes in periodontitis, may be one of the important risk factors for ED (21).

Eltas et al. conducted a randomized controlled trial to evaluate the effect of periodontal treatment on improved ED at baseline and at one month and three months after intervention. According to the results of the mentioned study, periodontal treatment significantly contributed to the treatment of ED (22). Uppal et al. (2014) and Matsumoto et al. (2014) also confirmed the statistically significant correlation between chronic periodontitis and ED (23, 24). In another study, Matsumoto suggested that ED was related to the damage caused by endothelial dysfunction and the systemic inflammatory changes, which are associated with CPD (24). In a study by Eastham et al. (2015), it was marked that oral health could be one of the risk factors for sexual health. According to the results of the mentioned study, members of dental team should be aware of the association between the extent and severity of CPD and ED, sperm motility and TTC (25).

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III. Oral infection, low birth weight and future subfertility

Evidence suggests a relationship between maternal periodontitis and low birth weight (26, 27). A study evaluated the relationship between low birth weight and subsequent male subfertility in future, which could be resulted from possible prenatal growth restrictions (28). Nevertheless, the pathophysiological mechanism governing this association has remained unknown. On the contrary, Ozturk et al. identified no difference between the samples of the case and control groups, suggesting that low birth weight possibly had no impact on male fertility later in life (29). Therefore, further studies must be carried out to confirm this association.

IV. Periodontitis and TTC

In a study by Hart et al., an association was reported between periodontitis and increased TTC. In the mentioned study, it was suggested that periodontitis might be a factor affecting a woman's TTC since it can lengthen the time it takes for a woman to become pregnant by an average of an extra two months. It is noteworthy that this factor negatively affects individuals similar to obesity (30). Nwhator et al. also concluded that CPD was positively associated with increased TTC, and women in childbearing age must have regular preventive dental checkups in order to maintain good oral and periodontal health (31). Hart demonstrated in a research that while some factors (e.g., age, body mass index and smoking status) which affect female fertility were controlled, the presence of periodontal disease still had adverse effects on TTC. It is noteworthy that such diseases have been more observed in Asian pregnant women and could be due to the higher susceptibility of Asian females to inflammatory cytokines, which are disseminated through the bloodstream in the presence of periodontal diseases. After covering the endometrium, these cytokines may disrupt implantation. Another theory is that periodontitis is just a marker of inflammation, which is present throughout the whole body, including the endometrium. Asian women are more prone to this marker, leading to less chances of conception (32).

V. Periodontitis and endometriosis

In a study by Kavoussi et al., evaluation of collected data from 4,136 women (aged 18-50 years) suggested a possible association between endometriosis (a potential cause of infertility) and periodontal diseases. According to the results of the mentioned research, while multifactorial endometriosis could increase due to the immune response to infectious agents, the potential underlying relationship between periodontitis and endometriosis may be a generalized, global immune dysregulation. Each disease is characterized as a chronic, inflammatory disorder associated with an altered immune response (33).

Discussion

Over the past two decades, a significant association has been observed between systemic diseases and poor oral health. In this regard, some phrases have attracted more attention over time ("You cannot have good general health without proper oral health", "The mouth is part of the body") (34). Some oral pathogens cause chronic periodontal infections through dissemination into the bloodstream and affecting other organs (35). The 'focal infection theory' was first proposed by Miller (1891), indicating that "microorganisms" or their products enter the body parts adjacent to or remote from the oral cavity. Three different mechanisms by which oral microbiota may contribute to systemic diseases have been described, as follows:

1) Metastatic infection caused by bacterial translocation; 2) metastatic injury from the effects of microbial toxins and 3) metastatic inflammation caused by immunological injury (36).

Different hypotheses, including common susceptibility, systemic inflammation, direct bacterial invasion, immunological crossreactivity and molecular mimicry between bacterial and self-antigens, have been proposed to demonstrate the relationship between CPD and systemic problems (37). In gynecology, inflammation has a significant impact on ovaries, uterus, embryo and implantation (38). A remote, low grade oral infection may trigger inflammation of the maternal-fetal unit similar to bacterial vaginosis. Additionally, some oral bacteria can induce placental inflammation and decidual hyperplasia (39). On the other hand, inflammatory cytokines could have a negative

impact on sperm production. Inflammation is also related to the level of oxidative stress and the latter is well known to impair sperm function. Oxidative stress also damages sperm DNA, leading to sperm apoptosis (40). These general explanations, as well as those mentioned distinctly in this article, represent some probable mechanisms of association between poor oral health and infertility. However, further research is required as to clarify the causes of the synchronicity of these two events.

According to the mentioned results, women who intend to become pregnant must be ensured of their health and consider oral and dental examinations in addition to checking different factors involved in their general health. Since most oral inflammations (e.g., periodontitis) are treatable, all women should be encouraged to visit a dentist before trying to conceive (32). Given the fact that seminal parameters could be improved in men after treatment of periodontal disease, it is suggested that dental examinations be also performed on male partners (12). Recognition of such relationship between oral health and decreased fertility by gynecologists and dentists can contribute to the prevention of serious side effects of these problems.

Literature review revealed no systematic or narrative review study on the association between dental health and fertility problems. Given the limited number of studies on the impact of oral hygiene improvement and periodontal treatment on enhanced fertility, it is recommended that similar studies, especially clinical trials, be conducted in this area to confirm such association.

Conclusion

According to the results of the present study, oral hygiene is an important component of general health and also a contributing factor for improved sexual health. Control of oral inflammation and regular dental check-ups by men and women, particularly prior to conceiving, could promote to enhanced reproductive ability.

Conflicts of interest

Authors declared no conflicts of interest.

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