American Journal of Men's Health
1–9

DOI: 10.1177/1557988316655529
ajmh.sagepub.com
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Male Infertility and Dental Health Status: A Systematic Review

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Abstract

A limited number of studies have reported an association between male factor infertility (MFI) and dental health status (DHS). The aim of the present study was to assess the association between DHS and MFI through a systematic review of indexed literature. To address the focused question—"Is there a relationship between DHS and MFI?"—indexed databases were searched up to March 2016 using various key words "infertility," "periodontal disease," "periodontitis," "dental infection," "caries," and "odontogenic infection." Letters to the editor, case reports, commentaries, historic reviews, and experimental studies were excluded. In total seven studies were included in the present systematic review and processed for data extraction. All the studies reported a positive association between MFI and DHS. The number of study participants ranged between 18 and 360 individuals. Results from six studies showed a positive association between chronic periodontitis and MFI. Three studies reported a positive relationship between MFI and odontogenic infections associated to necrotic pulp, chronic apical osteitis, and radicular cysts. One study reported a relationship between caries index and MFI. From the literature reviewed, there seems to be a positive association between MFI and DHS; however, further longitudinal studies and randomized control trials assessing confounders are needed to establish real correlation. Dentists and general practitioners should be aware that oral diseases can influence the systemic health. Andrological examination should include comprehensive oral evaluation, and physicians detecting oral diseases should refer the patient to a dentist for further evaluation.

Keywords

infertility, semen quality, dental health status, chronic periodontitis, caries

Introduction

According to the International Committee for Monitoring Assisted Reproductive Technology and the World Health Organization (WHO), infertility is a disease of the reproductive system characterized by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse (Zegers-Hochschild et al., 2009). It has been estimated that more than 48.5 million couples worldwide are unable to conceive, and at least 40% to 50% of the cases are associated with male factor infertility (MFI; Agarwal, Mulgund, Hamada, & Chyatte, 2015; Kumar & Singh, 2015). MFI is defined as alterations in sperm morphology, concentration, and/or motility in one sample of at least two sperm analyses, collected between 1 and 4 weeks (Azenabor, Ekun, & Akinloye, 2015). It has been reported that approximately 31 million men worldwide are infertile. The prevalence of infertile men in Germany and Australia has been calculated in 7.5% and 9%, respectively (Agarwal et al., 2015). Louis et al. (2013) reported that the prevalence of infertility in the United States among men aged between 15 and 44 years was 12%. The etiology of MFI is considered multifactorial, and several risk factors have been associated with this condition. These include bacteriospermia, elevated reactive oxygen species levels, urogenital infections, immunological and endocrine diseases, environmental factors, and genetic disorders (Azenabor et al., 2015; Ko, Sabanegh, & Agarwal, 2014; Kovac, Khanna, & Lipshultz, 2015; Ould Hamouda et al., 2016; Vilvanathan et al., 2016). However, in half of the cases the etiology of MFI remains unexplained (Guzick et al., 2001).

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Oral diseases (OD) are a group of chronic infections originated primarily from dental caries, a bacterial demineralization of teeth hard tissues (enamel and dentin) that can progress and compromise the pulp tissue vitality; second, from chronic periodontitis (CP), a disease of the supporting structures of teeth, specifically cementum, gingiva, periodontal ligament, and alveolar bone (Bahl, Sandhu, Singh, Sahai, & Gupta, 2014; Lopez-Piriz, Aguilar, & Gimenez, 2007). According to the Global Burden of Disease 2010 study, where estimates of the burden of 291 diseases and injuries are reported, OD affected 3.9 billion people around the world, and untreated caries was the most prevalent condition among all the diseases (Marcenes et al., 2013). In the past 30 years, a bidirectional linkage between OD and several systemic conditions such as atherosclerosis (X. T. Zeng et al., 2016), myocardial infarction (Rathnayake et al., 2015), diabetes mellitus (DM; Javed & Romanos, 2009), and erectile dysfunction (Kellesarian et al., 2016) have been reported. Interestingly, a limited number of studies have identified an association between male infertility (Bieniek & Riedel, 1989, 1993; Bustos-Obregon, Linossier, & Thumann, 1983; Ensslen, Riedel, Bieniek, & Hafner, 1990; Klinger, Hain, Yaffe, & Schonberger, 2011; Nwhator, Umeizudike, et al., 2014; Zhu, Qin, Huang, Li, & Feng, 2010), and female infertility (Hart, Doherty, Pennell, Newnham, & Newnham, 2012; Nwhator, Opeodu, et al., 2014) with OD. Linossier, Thumann, and Bustos-Obregon (1982) reported that an *Escherichia coli* filtrate obtained from 200 extracted teeth with open necrotic pulp resulted in a 25% reduction in sperm motility in vitro. Klinger et al. (2011) examined the association between fertility parameters and the periodontal status of men attending a fertility and in vitro fertilization clinic. These results reported a significant association between sperm motility and periodontal parameters, such as probing depth (PD) and clinical attachment loss (CAL). In the study by Nwhator, Umeizudike, et al. (2014)., a significant association between PD and low sperm count was reported in men aged between 33 and 38 years. Similar results were reported by Zhu et al. (2010).

It is hypothesized that a direct relationship exists between dental health status and MFI. To our knowledge from indexed literature, the association between dental health status and MFI has not been systematically reviewed. The aim of the present study was to assess the association between dental health status and MFI through a systematic review of indexed literature.

Method

Focused Question

Based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, a specific question was constructed according to the Participants, Interventions, Control, and Outcomes principle. The focused question was, "Is there a relationship between dental health status and MFI?"

Literature Search Protocol and Eligibility Criteria

In order to identify studies relevant to the focused question, an electronic search without time or language restrictions was conducted using PubMed (National Library of Medicine, Washington, DC), Google-Scholar, EMBASE, MEDLINE (OVID), and Web of Knowledge databases up to March 2016 using different combinations of the following key words: (a) "infertility + periodontitis," (b) "infertility + periodontal disease," (c) "infertility + gum disease," (d) "infertility + dental infection," (e) "infertility + gingivitis," (f) "infertility + caries," (g) "infertility + odontogenic infection," (h) "infertility + dental abscess."

The eligibility criteria were as follows: (a) clinical studies, (b) prospective and retrospective studies, and (c) studies assessing the relationship between male infertility and dental health status. Letters to the editor, commentaries, historic reviews, case-control, and experimental studies were excluded. Titles and abstracts of studies identified using the above-described protocol were screened by two authors (SVK and FJ) and checked for agreement. Full texts of studies judged by title and abstract to be relevant were read and independently evaluated for the stated eligibility criteria. Reference lists of potentially relevant original and review articles were hand-searched to identify any studies that could have remained unidentified in the previous step. Once again, the articles were checked for disagreement via discussion among the authors (Figure 1).

Quality Assessment

Quality Assessment of studies was performed using the Critical Appraisal Skills Program (CASP) Cohort Study Checklist (X. Zeng et al., 2015). This was done to grade the methodological quality of each study included in the present systematic review. This tool is based on 12 criteria: (a) study issue is clearly focused, (b) cohort is recruited in an acceptable way, (c) exposure is accurately measured, (d) outcome is accurately measured, (e) confounding factors are addressed, (f) follow-up is long and complete, (g) results are clear, (h) results are precise, (i) results are credible, (j) results can be applied to the local population, (k) results fit with available evidence, and (l) there are important clinical implications. According to the CASP scale, each criterion is given a response of either "Yes," "No," or "cannot tell," and the maximum score a study could have was 12.

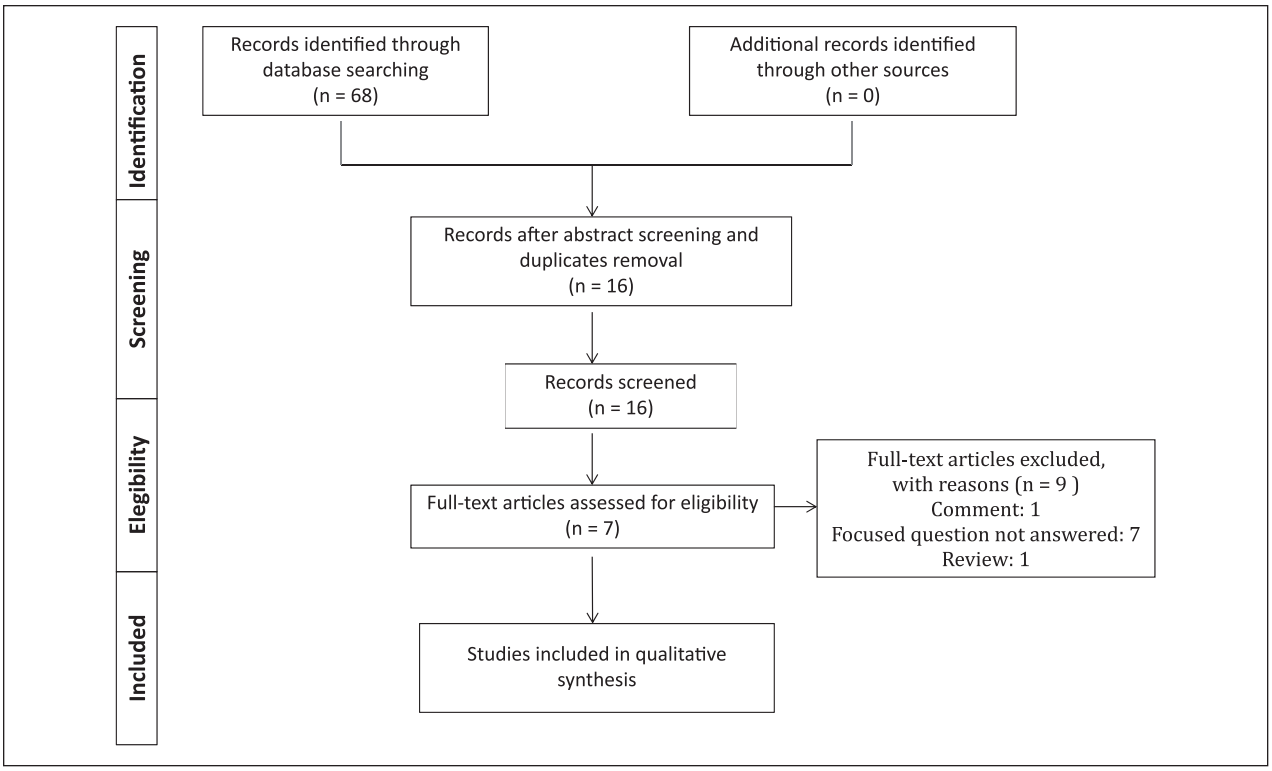

Figure 1. Article selection flow chart for the systematic review according to PRISMA guidelines.
Note. PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Results

Study Selection and Characteristics

Through the initial search, 68 titles that potentially meet the inclusion criteria were identified. After reviewing the abstracts, 52 publications were duplicates or did not answer the focused question. In the second step of evaluation, nine more articles were excluded, which were reviews, commentaries, and/or did not answer the focused question (see the appendix). In total, seven studies (Bieniek & Riedel, 1989, 1993; Bustos-Obregon et al., 1983; Ensslen et al., 1990; Klinger et al., 2011; Nwhator, Umeizudike, et al., 2014; Zhu et al., 2010) were included in the present systematic review and processed for data extraction. Four studies (Bieniek & Riedel, 1993; Bustos-Obregon et al., 1983; Klinger et al., 2011; Nwhator, Umeizudike, et al., 2014) were published in English, two studies (Bieniek & Riedel, 1989; Ensslen et al., 1990) in German, and one study (Zhu et al., 2010) in Chinese.

All studies (Bieniek & Riedel, 1989, 1993; Bustos-Obregon et al., 1983; Ensslen et al., 1990; Klinger et al., 2011; Nwhator, Umeizudike, et al., 2014; Zhu et al., 2010) had a cross-sectional design and were performed on humans and under health care or university settings. These primary studies (Bieniek & Riedel, 1989, 1993; Bustos-Obregon et al., 1983; Ensslen et al., 1990; Klinger et al., 2011; Nwhator, Umeizudike, et al., 2014; Zhu et al., 2010) were conducted in the following countries: Chile, China, Germany, Israel, and Nigeria. The number of study participants ranged between 18 and 360 individuals with age ranging between 22 years and 56 years. Bustos-Obregon et al. (1983) did not report the age of the participants, and Klinger et al. (2011) only reported the participants' mean age (32.7 years).

Dental Health Status and Infertility Diagnosis

In all studies (Bieniek & Riedel, 1989, 1993; Bustos-Obregon et al., 1983; Ensslen et al., 1990; Klinger et al., 2011; Nwhator, Umeizudike, et al., 2014; Zhu et al., 2010), the patients received a comprehensive oral examination to diagnose caries, periodontal status, and/or other possible dental infection sources. In five studies (Bieniek & Riedel, 1989, 1993; Bustos-Obregon et al., 1983; Ensslen et al., 1990; Zhu et al., 2010), radiographs (full periapical series and/or panoramic) were used to detect possible odontogenic infections. In three studies (Bieniek & Riedel, 1989, 1993; Ensslen et al., 1990), bacterial swab was conducted to identify oral microflora. Nwhator, Umeizudike, et al. (2014) used lateral immunoassay kit to detect levels of active membrane metalloproteinase-8 to diagnose CP.

Six studies (Bieniek & Riedel, 1989, 1993; Ensslen et al., 1990; Klinger et al., 2011; Nwhator, Umeizudike, et al., 2014; Zhu et al., 2010) reported the association between CP and MFI. In three studies (Bieniek & Riedel, 1989, 1993; Ensslen et al., 1990), the relationship between MFI and odontogenic infections associated to necrotic pulp, chronic apical osteitis, radicular cysts, retained roots, and impacted teeth was assessed. Bustos-Obregon et al. (1983) reported the relationship between MFI and index of caries, a tool used to establish the prevalence of dental caries in an individual, obtained by calculating the number of decayed, missing and filled teeth.

The fertility/infertility diagnosis was assessed in all studies (Bieniek & Riedel, 1989, 1993; Bustos-Obregon et al., 1983; Ensslen et al., 1990; Klinger et al., 2011; Nwhator, Umeizudike, et al., 2014; Zhu et al., 2010) using seminogram (seminal fluid analysis) to study sperm properties such as count, motility, morphology, volume, and/or survival rate.

Confounding Factors

In four studies (Bieniek & Riedel, 1989, 1993; Bustos-Obregon et al., 1983; Ensslen et al., 1990), confounding variables were not assessed. Klinger et al. (2011) adjusted the data for confounding factors including history of family infertility, smoking, and exposure to antibiotics within the preceding 12 months. Nwhator, Umeizudike, et al. (2014) adjusted the data in four age groups: 27 to 32, 33 to 38, 39 to 44, and 45 or older. Zhu et al. (2010) assessed several confounders, such as occupation, education level, alcohol, drugs and tobacco exposure, systemic diseases, reproductive history, and genitourinary infections (see Table 1).

Main Outcomes

In all studies (Bieniek & Riedel, 1989, 1993; Bustos-Obregon et al., 1983; Ensslen et al., 1990; Klinger et al., 2011; Nwhator, Umeizudike, et al., 2014; Zhu et al., 2010), a positive relationship between MFI and oral diseases associated to caries, necrotic pulp, and/or CP was reported (see Table 2). In the study by Bustos-Obregon et al. (1983), a higher caries index was reported in subfertile men compared with normozoospermic men; likewise, improvement in sperm progressive motility was reported after restorative dental treatment among subfertile men. Similar findings were reported in three studies (Bieniek & Riedel, 1989, 1993; Ensslen et al., 1990) where a significant improvement in bacteriospermia levels (66% of the samples were bacteria free), and sperm parameters (morphology, density, and motility) were reported in subfertile patients with bacteriospermia resistant to antibiotics after comprehensive dental treatment; in addition, 33% of the patient's female partners were able to conceive through in vitro fertilization after the men received dental treatment.

Nwhator, Umeizudike, et al. (2014) reported a significant association between PD and subnormal sperm count in men aged between 33 and 38 years; however, the relationship was negative for the other three age groups: 27 to 32, 39 to 45, and 45 or older. Similar findings were reported by Klinger et al. (2011) where a significant association between PD, clinical attachment loss, and sperm motility was identified; however, no relationship between periodontal parameters and sperm count was reported.

Zhu et al. (2010) reported a higher prevalence of CP in infertile men compared with normozoospermic controls (odds ratio [OR] = 2.01, 95% confidence interval [CI] = [1.31,3.10]); along with the increase of CP severity a deterioration of sperm parameters (concentration, motility, and abnormality) was reported (mild periodontitis, OR = 1.37, 95% CI [0.75, 2.50]; moderate periodontitis, OR = 2.30, 95% CI [1.28, 4.10]; and severe periodontitis, OR = 3.30, 95% CI [1.39, 7.83]).

Quality Assessment of Included Studies

Through the quality assessment we identified that all studies (Bieniek & Riedel, 1989, 1993; Bustos-Obregon et al., 1983; Ensslen et al., 1990; Klinger et al., 2011; Nwhator, Umeizudike, et al., 2014; Zhu et al., 2010) were conducted on humans and the total quality score ranged from 8 to 10. The most common shortcoming among all studies (Bieniek & Riedel, 1989, 1993; Bustos-Obregon et al., 1983; Ensslen et al., 1990; Klinger et al., 2011; Nwhator, Umeizudike, et al., 2014; Zhu et al., 2010) was the short-term, incomplete follow-up of the groups, and omission of assessment of confounding variables like genitourinary infections. Thus, on average, the quality of included studies on the relationship between dental health status and MFI was good, and limitations of short-term follow-up, and omission of confounding limit the application of these study outcomes. Quality assessment of the articles included in the systematic review is summarized in Table 3.

Discussion

Interestingly, results from all the studies (Bieniek & Riedel, 1989, 1993; Bustos-Obregon et al., 1983; Ensslen et al., 1990; Klinger et al., 2011; Nwhator, Umeizudike, et al., 2014; Zhu et al., 2010) reported a positive association between poor dental health and MFI. It has been proposed that OD contributes to the etiology of MFI by two mechanisms. First, the increased bacterial load associated to chronic infections originated from OD can result in bacteriospermia (Bustos-Obregon et al., 1983; Linossier

Table 1. General Characteristics of the Studies Included in the Present Review.

Authors (region of study)	Study design	Study groups	Age range in years (mean)	Infertility diagnosis method	Dental health status diagnostic method	Confounding variables assessed
Bieniek and Riedel (1989) (Germany)	Cross-sectional	Total: 36 18 Subfertile + BS + dental treatment 18 Subfertile + BS + without dental treatment	25-43 (NA)	Seminogram	Oral examination Radiographs (FMX and PAN) Bacterial swab	NA
Bieniek and Riedel (1993) (Germany)	Cross-sectional	Total: 36 18 Subfertile + BS + dental treatment 18 Subfertile + BS + without dental treatment	25-43 (NA)	Seminogram	Oral examination Radiographs (FMX and PAN) Bacterial swab	NA
Bustos-Obregon et al. (1983) (Chile)	Cross-sectional	Total: 18 9 Normospermic 9 Subfertile	NA	Seminogram: Sperm count, motility, morphology	Oral examination Radiographs Index of caries	NA
Ensslen et al. (1990) (Germany)	Cross-sectional	Total: 36 18 Subfertile + BS + dental treatment 18 Subfertile + BS + without dental treatment	25-43 (NA)	Seminogram	Oral examination Radiographs (FMX and PAN) Bacterial swab	NA
Klinger et al. (2011) (Israel)	Cross-sectional	Total: 75 28 Normospermic 36 Oligozoospermia 11 Azoospermic	NA (32.7)	Seminogram: Volume, sperm cell concentration, motility (overall and progressive), morphology, white cells	Oral examination: Number of missing teeth, plaque score, GI, BOP, PD, CAL	Antibiotics Family infertility Smoking
Nwhator, Umeizudike, et al. (2014) (Nigeria)	Cross-sectional	Total: 76 25 Normospermic 41 Oligospermic 10 Azoospermic	27-56 (NA)	Seminogram: Count and motility	Oral examination: OHIS, CPITN Lateral immunoassay	Age
Zhu et al. (2010) (China)	Cross-sectional	Total: 360 180 Normospermic 180 Subfertile	Normospermic: 24-39 (28.4 ± 4.4) Subfertile: 22-46 (27.5 ± 3.2)	Seminogram: Density, motility, survival rate, and deformity rate	Oral examination: PD, GI, CAL, ABL	Occupation, education, alcohol, tobacco, medications, systemic diseases, congenital malformations, genitourinary infections, nutritional deficiencies

Note. BS = bacteriospermia; FMX = full periapical radiograph; PAN = panoramic radiograph; PD = probing depth; GI = gingival index; CAL = clinical attachment loss; ABL = alveolar bone loss; BOP = bleeding on probing; OHIS = oral hygiene index score; CPITN = community periodontal index of treatment need.

et al., 1982) impairing sperm mobility. Second, pro-inflammatory cytokines associated to OD, such as TNF-alpha could lead to a chronic systemic inflammation inducing sperm apoptosis and lower sperm count (Nwhator, Umeizudike, et al., 2014). It is therefore hypothesized that individuals with OD are more likely to develop MFI as compared to individuals without OD. However, it is pertinent to mention that a variety of factors may have biased the results of the included studies, and these findings need to be interpreted with caution. First, it has been established that MFI and OD present common risk factors such as poorly controlled DM, alcohol abuse, tobacco smoking, and coronary heart disease (CHD; Eisenberg, Li, Behr, Pera, & Cullen, 2015; Eisenberg, Li, Cullen, & Baker, 2016; Javed, Bashir Ahmed, & Romanos, 2014; Javed & Romanos, 2009; Kataria et al., 2015; Kotsakis, Javed, Hinrichs, Karoussis, & Romanos, 2015; Segura-Egea, Martin-Gonzalez, & Castellanos-Cosano, 2015). It is noteworthy that nearly 72% among the included studies (Bieniek & Riedel, 1989, 1993; Bustos-Obregon et al., 1983; Ensslen et al., 1990; Nwhator, Umeizudike, et al., 2014) did not adjust the results for smoking, and approximately 86% of the studies (Bieniek & Riedel, 1989, 1993; Bustos-Obregon

Table 2. Primary Outcomes of the Studies Included.

Authors	Oral disease reported	Relationship between oral infection and infertility
Bieniek and Riedel (1989)	Chronic periodontitis, necrotic pulp, chronic apical osteitis, radicular cysts	Positive
Bieniek and Riedel (1993)	Chronic periodontitis, necrotic pulp, chronic apical osteitis, radicular cysts	Positive
Bustos-Obregon et al. (1983)	Caries	Positive
Ensslen et al. (1990)	Chronic periodontitis, necrotic pulp, chronic apical osteitis, radicular cysts	Positive
Klinger et al. (2011)	Gingivitis and chronic periodontitis	Positive
Nwhator, Umeizudike, et al. (2014)	Gingivitis and chronic periodontitis	Positive
Zhu et al. (2010)	Chronic periodontitis	Positive

Table 3. Critical Appraisal Skills Program Quality Assessment of the Reviewed Articles.

Authors	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Total quality score (0 to 12)
Bieniek and Riedel (1989)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Bieniek and Riedel (1993)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Bustos-Obregon et al. (1983)	Yes	Cannot tell	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	8
Ensslen et al. (1990)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Klinger et al. (2011)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Nwhator, Umeizudike, et al. (2014)	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	8
Zhu et al. (2010)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	10

et al., 1983; Ensslen et al., 1990; Klinger et al., 2011; Nwhator, Umeizudike, et al., 2014) remained unadjusted for DM, alcohol consumption, and CHD. It is speculated that OD are simply a risk indicator for MFI, originated from common exposures, such as chronic hyperglycemia, cardiovascular disorders, environmental factors, or elevated systemic levels of pro-inflammatory cytokines. Hence, additional prospective studies including confounder assessment are needed.

MFI diagnosis is based on the results of a seminogram. Although different classification systems have been proposed to establish a distinction between normal and abnormal sperm, the WHO-2010 criteria is the most commonly used. WHO-2010 criteria uses cutoff values to establish abnormal sperm parameters including volume (<1.5 mL, hypospermia), concentration (<15 × 10^6 spermatozoa/mL, oligozoospermia, and azoospermia when no spermatozoa are present in the ejaculate), motility (<32%, asthenozoospermia), and morphology (<4% normally formed, teratozoospermia; WHO, 2010). On a vigilant evaluation of all the studies (Bieniek & Riedel, 1989, 1993; Bustos-Obregon et al., 1983; Ensslen et al., 1990; Klinger et al., 2011; Nwhator, Umeizudike, et al., 2014; Zhu et al., 2010) included in the present systematic review, it was identified that in those studies (Bieniek & Riedel, 1989, 1993; Bustos-Obregon et al., 1983; Ensslen et al., 1990) conducted before 2009 the parameters values used to classify sperm during the seminogram and establish MFI diagnosis were not reported and/or remain unclear. In the studies (Klinger et al., 2011; Nwhator, Umeizudike, et al., 2014; Zhu et al., 2010) conducted after 2010 MFI diagnosis was based in the WHO-1999 criteria (WHO, 1999). It is noteworthy that WHO-2010 criteria (WHO, 2010) establish new reference values for human semen parameters that are notably lower than those in WHO-1999 criteria (Esteves et al., 2012). Murray et al. (2012) reported that WHO-2010 reference values compared with WHO-1999 result in infertile men being reclassified as fertile. It is possible that they might have been normozoospermic patients diagnosed with MFI and vice versa. Hence, the authors of the present systematic review suggest extremely caution interpreting

the conclusions of the studies included in the present systematic review.

Studies have reported that the severity of OD is related to several factors such as frequency and duration of smoking habit, glycemic levels in patients with DM, and oral hygiene routine (Al Amri et al., 2016; Javed, Al-Rasheed, Almas, Romanos, & Al-Hezaimi, 2012; Javed & Romanos, 2009). It is therefore feasible that the severity of OD may also be associated with the deterioration in sperm parameters. It is pertinent to mention that only Zhu et al. (2010) and Bustos-Obregon et al. (1983) reported that the progression in the deterioration of sperm parameters is associated to CP severity and caries index, respectively. Well-designed randomized control trials studying the association between sperm parameters and OD focusing on the severity of both conditions are needed. It is noteworthy that all the studies (Bieniek & Riedel, 1989, 1993; Bustos-Obregon et al., 1983; Ensslen et al., 1990; Klinger et al., 2011; Nwhator, Umeizudike, et al., 2014; Zhu et al., 2010) were short period investigations, conducted in only five countries, with a reduced number of participants, and without assessment of sociocultural factors associated to MFI, such as ethnicity, taboos, religious practices and beliefs, attitudes, and habits. Therefore, additional prospective studies are needed in this regard.

It is well known that the treatment of CP reduces the systemic burden of inflammation. Nonsurgical periodontal therapy (NSPT) has been reported as an effective tool in reducing glycemic levels in patients with DM (Al Amri et al., 2016; Ghiraldini et al., 2015; Oates, Dowell, Robinson, & McMahan, 2009). Javed, Kellesarian, et al. (2016) reported that NSPT combined with adjunct laser therapy is effective in reducing serum pro-inflammatory cytokines levels in patients with CHD. Igoumenakis et al. (2015) reported that the extraction of teeth associated to odontogenic infections resulted in decrease of axillary temperature, white blood cell count, fibrinogen, and C-reactive protein. Therefore, it is hypothesized comprehensive dental treatment of OD including NSPT, extractions of infected teeth, and root canal therapy may also contribute in the treatment of patients with MFI by reducing bacteriospermia, decreasing levels of pro-inflammatory mediators, reactive oxygen species, and oxidative stress. From the literature reviewed, four studies (Bieniek & Riedel, 1989, 1993; Bustos-Obregon et al., 1983; Ensslen et al., 1990) tested this hypothesis. Bustos-Obregon et al. (1983) reported improvement of sperm progressive motility in subfertile patients after restorative dental treatment. Similar findings were reported in three studies (Bieniek & Riedel, 1989, 1993; Ensslen et al., 1990) where patients diagnosed with MFI and bacteriospermia resistant to antibiotics received comprehensive dental treatment including dental extractions, root canal therapy, and NSPT to eliminate oral bacterial foci resulting in the improvement of sperm parameters (morphology, density, and motility) and bacteriospermia.

Conclusion

Within the limits of the current available evidence there seems to be a positive association between MFI and dental health status; however, further longitudinal studies and well-designed randomized control trials assessing confounders are needed. It is emphasized that dentists and general practitioners should be aware of the fact that OD can influence the systemic health, including men's reproductive health. Therefore, patients undergoing andrological examination and attempting to conceive should receive comprehensive oral evaluation. Physicians detecting OD should refer the patient to a dentist for further evaluation and treatment.

Appendix

1. Hart, R., Doherty, D. A., Pennell, C. E., Newnham, I. A., & Newnham, J. P. (2012). Periodontal disease: A potential modifiable risk factor limiting conception. *Human Reproduction, 27*, 1332-1342. (Focus question not answered)
2. Hart, R. (2012). Periodontal disease: Could this be a further factor leading to subfertility and is there a case for a prepregnancy dental check-up? *Women's Health, 8*, 229-230. (Commentary)
3. Kazemi, E., Moradi, M. T., Yari, K., Mousavi, S. A., & Kahrizi, D. (2015). Association between manganese superoxide dismutase (MnSOD Val-9Ala) genotypes with the risk of generalized aggressive periodontitis disease. *Cellular and Molecular Biology, 61*, 49-52. (Focused question not answered)
4. Lalasa, G., Murthy, K. R., Pavankumar, S., & Raju, G. A. (2014). Periodontal status in infertile women attending in vitro fertilization clinics. *Indian Journal of Dental Research, 25*, 50-53. (Focused question not answered)
5. Nwhator, S. O., Umeizudike, K. A., Samuel, T. A., Soroye, M. O., & Umeizudike, T. I. (2013). Periodontitis & sub-fertility: Opinions and practices of Nigerian specialists. *West African Journal of Medicine, 32*, 267-271. (Focused question not answered)
6. Nwhator, S., Opeodu, O., Ayanbadejo, P., Umeizudike, K., Olamijulo, J., Alade, G., . . . Sorsa, T. (2014). Could periodontitis affect time to conception? *Annals of Medical and Health Sciences Research, 4*, 817-822. (Focused question not answered)

7. Pavlatou, A., Tsami, A., Vlahos, N., Mantzavinos, T., & Vrotsos, I. (2013). The effect of in vitro fertilization on gingival inflammation according to women's periodontal status: Clinical data. *Journal of the International Academy of Periodontology, 15*, 36-42. (Focused question not answered)
8. Pavlatou, A., Dokou, P., & Tsami, A. (2015). Periodontal disease, infertility treatment and in vitro fertilization (IVF). *Journal of Fertilization: In Vitro, IVF-Worldwide, Reproductive Medicine, Genetics & Stem Cell Biology.* doi:10.4172/2375-4508.1000148 (Review)
9. Yang, T. H., Masumi, S., Weng, S. P., Chen, H. W., Chuang, H. C., & Chuang, K. J. (2015). Personal exposure to particulate matter and inflammation among patients with periodontal disease. *Science of the Total Environment, 1*, 585-589. (Focused question not answered)

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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