

Oral Health Status and Fertility Treatment Including IVF

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Abstract Oral health is extremely important for the general wellbeing of the individual. From a number of research articles, it is established that there is a definitive connection

between periodontal health and many systemic diseases, like type II diabetes, cardiovascular diseases and even preterm labor and low birth weight of babies. The significant rate of failure in the treatment of infertility and IVF (in vitro fertilization) even with multiple advancements in the last decade has made scientist take interest in newer parameters of health, an important one among them being periodontal health. From the limited number of studies available on the relationship between periodontitis and reproductive health, it can be inferred that periodontitis can act as a focus of infection leading to bacteremia which can lead to complications in conceiving naturally or through IVF in women. A limited number of studies have also reported an association between male factor infertility (MFI) and dental health status of men. Although more

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research is needed to understand and explore this connection, this article reviews the current literature available linking poor oral health to infertility and poor outcomes of IVF.

Keywords Oral health · Fertility · In vitro fertilization · Antenatal counseling

Introduction

The oral cavity is often regarded as a mirror to general health. The fact that oral health has a direct effect on overall physical health has been established by a large number of studies and researches worldwide [1]. Although the association of chronic periodontitis with type II diabetes, cardiac disease, low birth weight babies and preterm deliveries is well known, more recently it has also been linked to the reproductive health and fertility problems in men and women [2]. The fetus, from the moment of conception until birth, is constantly influenced by the stimuli the expectant mother subjects it to, and data that prove that developmental defects like cleft palate and enamel hypoplasia are caused by various febrile diseases and chronic infections that the expectant mother suffers from [3]. A significant failure rate in the various methods applied to treat infertility even today, despite the progress of knowledge and techniques being used, has recently triggered further research regarding other parameters of health including periodontal health in the achievement of pregnancy. However, it is only in the last couple of years that scientists have focused their interest on the effect of periodontal disease and the bacteremia it causes on the achievement of pregnancy either normally, or assisted by medications for infertility, or through the use of IVF (in vitro fertilization) [4]. Even though there are only a limited number of studies available on the connection between poor periodontal health and infertility, in both the sexes more extensive research is required to understand this correlation better; this article reviews the data, knowledge, and the few studies available on the said topic.

The Focal Theory

It was during the 19th and early 20th centuries that the focal theory of infections was promulgated stated that “foci” of sepsis were responsible for the initiation and progression of a variety of inflammatory diseases such as arthritis and cardiovascular disease [5]. Human periodontal environment is associated with complex interaction of microflora. Over 200 species (in apical periodontitis) and more than 500 species (in marginal periodontitis) have

been identified. The bacterial levels in humans can reach more than 10^{11} microorganisms per mg of dental plaque [6]. These bacterial populations are predominantly anaerobic, with gram-negative rods being the most common isolates. The systemic spread of bacterial products, components, and immune complexes is facilitated by the anatomic closeness of these microflora to the blood stream, which can cause systemic bacteremia. Recently, it has been identified that the maternal bacteremia caused by periodontal focus of infection can hamper not only the fetus but also the in the achievement of a pregnancy, primarily due to endotoxins and bacterial products in the blood circulation which cause bacteremia in the uterus [4].

Periodontitis and Infertility

Periodontitis is defined as an inflammatory disease of supporting tissues of teeth caused by specific microorganisms or groups of specific microorganisms, resulting in progressive destruction of the periodontal ligament and alveolar bone with periodontal pocket formation, gingival recession, or both [7]. The term “infertility” is defined by the International Committee for Monitoring Assisted Reproductive Technology and the World Health Organization (WHO) as 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 [8]. Typically, only 10–15% of women experience infertility problems, while 80–85% of women conceive normally within a year. Infertility has been correlated directly with age, and majority of the couples experiencing infertility lie within the 30–40 year age group in both sexes [4].

One of the main causes of male infertility is abnormality of endocrine function or testicular abnormalities. Correspondingly, female infertility is associated with the ovulation dysfunctions, disorders of the cervical mucus, endometriosis, endometrial adhesions, and other anatomic abnormalities of the fallopian tubes or the uterus, etc. Even though there is only limited research available forming a direct relation between poor periodontal health and fertility problems, the fact that systemic bacteremia due to sub-clinical infections can hinder the reproductive functions in both sexes is well established [9–11].

Maternal Periodontitis and Infertility

Initially, the primary treatment in cases of possible infertility is a scheduled sexual contact during a normal reproductive cycle, without any medication to begin with, and then with the administration of the appropriate medication

if required. One of the most common hormonal treatments includes the administration of clomiphene citrate due to the drug's anti-estrogenic action. Another common treatment to achieve multiple follicular development and ovulation induction is the use of gonadotropin, which is administered intramuscularly or subcutaneously in small doses. Specific receptors present on the gingival tissues attribute to their ability to bind to sexual hormones [12]. It is also well established that there are vast changes in the hormonal balance of a woman while she is pregnant or receiving hormonal therapy for infertility. These hormonal changes that occur during pregnancy are known to have a definite impact on the gingival tissues and worsen existing periodontitis. Pregnancy gingivitis and pregnancy tumor or epulis are common findings during the course of pregnancy [13]. If preexisting gingival inflammation is present, the metabolic activity of these hormones in the gingival tissues is greater than in healthy periodontal tissues [14]. This ability to bind and high metabolic activity account to significant changes in the permeability and underlying microcirculation of the gingival capillary vessels. These changes can cause increase in inflammatory response, suppression of cell-mediated immunity, and even changes in the microflora that thrive in the periodontal environment [15, 16].

Hart et al. evaluated data from 3737 pregnant women in the context of a multicenter study (Smile study) in Australia. Excluding all women who had received any form of fertility treatment ultimately, data of 3416 women were studied. Of these 29.7% (i.e., 1014) women were found to have periodontitis. The parameter used for diagnosis was the presence of pocket depth of ≥ 4 mm on at least 12 teeth. The study concluded that women who suffered from periodontitis took approximately two months longer to achieve the desired gestation (7.1 months {95% CI 5.7–8.6}) compared to those women who did not have periodontitis (5.0 months {95% CI 4.4–5.5}). Also, it was important to note that since the incidence of periodontitis in Caucasian women was found to be 23.8% and in non-Caucasians was 41.4%, that the period to achieve a pregnancy was significantly increased (12 months and longer) only in non-Caucasian (13.9 vs. 6.2%, OR 2.88 {95% CI 1.62–5.12}; $p < 0.001$) and not in Caucasian women (8.6 vs. 6.2%; OR 1.15 {95% CI 0.74–1.79}; $p = 0.534$) [9].

Thus, it can be assumed that more women who suffer from periodontitis also suffer from bacteremia in the uterus and spread of bacterial products and endotoxins such as lipopolysaccharides in the blood circulation. This maternal bacteremia is known to activate the immune system, initiating the overproduction of pro-inflammatory cytokines and prostaglandins. They are likely to take longer to conceive and hence opt for infertility treatment including both hormonal supplementations or other drugs and IVF [4, 9].

Paternal Periodontitis and Infertility

It has been estimated that more than 48.5 million couples worldwide are unable to conceive, and at least 40–50% of the cases are associated with male factor infertility [17]. Klinger et al. evaluated the fertility parameters of male subjects attending a fertility and in vitro fertilization clinic and tried to associate that with the periodontal status of the men [18]. Seventy-five men attending the clinic for sperm analysis before homologue semen insemination or IVF were included in the study. The WHO criteria were used to evaluate the quality of sperm, and all the participants also received a clinical dental examination on the same day. The number of extracted teeth, the plaque and gingival index, the number of mobile teeth, the pocket depth and loss of clinical attachment were recorded in the process of the examination. The participants were then categorized into specific groups, those who presented with gingivitis (with at least two surfaces had gingival index 1, 2, or 3, but no clinical attachment loss) (30 subjects, 40%) and those patients with periodontitis, (when at least two sites had pocket depth ≥ 4 mm and simultaneously and the presence of bleeding on probing) (36 subjects, 68%). Through this study, it was noted that although there was a correlation between poor sperm mobility and the number of sites with deep pockets, it was not statistically significant [11]. In 2014, a study conducted by Nwhator et al. [19] concluded that there was a significant association between the level of periodontal disease and low sperm count in men aged between 33 and 38 years.

Dental Infections and In Vitro Fertilization (IVF)

With an increase in the average age at which couples have kids, there have been a number of reproductive health issues that have surfaced. However, along with these changes, there has been substantial growth in the practice of assisted human conception. In vitro fertilization (IVF) is usually applied as a treatment modality only when all efforts of medication treatment in combination with scheduled sexual contact fails. The procedure being extremely sensitive has a number of specific criteria, like the age of both the partners, state of the ovaries, and quality of sperm [20, 21]. Although it is advised to get rid of any source of infection or foci of infection in the mother prior to the procedure of IVF, the relationship between maternal periodontal infection and the success of an IVF programme is a relatively new field of research [4, 22].

In 2013, Pavlatou conducted a study to investigate the possible effect of the periodontal status of women on the effectiveness of IVF. This was assessed based on a number of parameters like the ability of ovarian stimulation, the

development of multiple eggs, the choice of the most suitable embryos for implantation and ultimately, the achievement and progress of the pregnancy. Sixty women of reproductive age were selected for the study; the inclusion criteria being that none of them would have received any hormonal drugs and periodontal therapy at least for the last 6 months. The subjects were categorized into subgroups based on their preexisting periodontal condition. Thus, 20 subjects with healthy periodontium, 19 with gingivitis, and 21 with mainly mild periodontitis were evaluated. The qualitative or quantitative changes that may occur in the subgingival microbial flora during an IVF were the parameters focused during the clinical and microbiological examination of the periodontium. A tendency of correlation was found between the gingival index before the IVF and the number of oocytes obtained after ovarian stimulation ($r = -0.26$; $p = 0.04$) and that of the number of embryos suitable for implantation with the gingival index after IVF [23].

To conclude, it can be interpreted that the maternal periodontium is affected by the administration of the hormonal medication therapy before the application of IVF and this can also affect the effectiveness of this treatment [23]. As we know, periodontal diseases are generally caused by gram-negative anaerobic bacteria. These bacteria are capable of producing multiple inflammatory mediators like prostaglandins, interleukins, lipopolysaccharides, and endotoxins. These bacteria and their metabolic products can gain entry into the blood and increase the production of inflammatory mediators [13]. Once into the circulation, these products pose a risk to the wellbeing of the mother and can cross the placental barrier and cause fetal toxicity. Also, the sudden surge in inflammatory mediators like prostaglandins secondary to the host response to periodontitis can trigger preterm labor [13]. A number of studies have proven that there is an indisputable connection between maternal periodontitis and low birth weight in their babies [13, 24]. Thus periodontitis along with causing difficulty in conception, either naturally or through IVF, can affect the progression of the pregnancy and also the health of the fetus ultimately.

Inclusion of Oral Health in Antenatal Counseling

It is a less known fact that consequences of poor oral health on the pregnancy are not limited to low birth weight and other birth complications but can have a lifelong impact on the life of the baby especially throughout early childhood. It is also seen that pregnancy is considered to be a “teachable moment” as women are motivated to change their behavior to protect and improve their as well as their baby’s health [13]. Hence, the time in a woman’s life when

she is planning to have a child or receiving any form of infertility treatment is an opportune time to inculcate healthy lifestyle habits including oral health care. Even though majority of the gynecologists agreed that the oral screening should be a part of prenatal care, they also agreed that they rarely checked the oral cavity of their patients as a part of routine prenatal checkups or even referred their patients to dental care [25]. Hence, oral health checkups must be made a mandatory part of antenatal counseling and also pre-IVF. More emphasis should be paid to oral health care and its implications on the maternal and fetal health.

Conclusion

The fact that even after boundless advancement of knowledge and techniques in the treatment of infertility and assisted conception, a significant failure rate still exists proves that newer avenues of health parameters need to be explored. One such important parameter is oral health of the expectant mother and also the father. From the limited number of studies available, it can be inferred that a connection does exist between oral health, especially periodontal health and the ability to achieve pregnancy both naturally and through the use of IVF (in vitro fertilization). However, further research is needed to explore and understand this connection better.

More emphasis must be given to educating the expectant couple about the importance of their oral health and how they are required to maintain it in order to eliminate any possible focus of infection from the body. Oral health care must become an irrefutable part of antenatal counseling.

Compliance of Ethical Standards

Conflict of interest The authors declare no conflict of interest.

References

1. Diabetes and oral health. American Dental Association. http://www.ada.org/sections/scienceAndResearch/pdfs/patient_18.pdf.
2. Shanthi V, Vanka A, Bhambal A, et al. Association of pregnant women periodontal status to preterm and low-birth weight babies: a systematic and evidence-based review. *Dent Res J*. 2012;9(4):368–80.
3. Czeizel AE, Bártfai Z, Bánhidy F. Primary prevention of neural-tube defects and some other congenital abnormalities by folic acid and multivitamins: history, missed opportunity and tasks. *Ther Adv Drug Saf*. 2011;2(4):173–88.
4. Pavlatou A, Dokou P, Tsami A. Periodontal disease, infertility treatment and in vitro fertilization (IVF). *J Fertil In Vitro IVF Worldw Reprod Med Genet Stem Cell*. 2015;3(2):148–54.
5. Hart R. Periodontal disease: could this be a further factor leading to subfertility and is there a case for a pre-pregnancy dental check-up? *Women’s Health*. 2012;8(3):229–30.

6. Hajishengallis G, Lamont RJ. Beyond the red complex and into more complexity: the polymicrobial synergy and dysbiosis (PSD) model of periodontal disease etiology. *Mol Oral Microbiol.* 2012;27(6):409–19.
7. Newman MG, Takei H, Klokkevold PR, et al. Carranza's clinical periodontology. 11th ed. California: Elsevier; 2011. p. 151–2.
8. Zegers-Hochschild F, Adamson GD, de Mouzon J, et al. International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO) revised glossary of ART terminology. *Fertil Steril* 2009;92:1520–4.
9. Hart R, Doherty DA, Pennell CE, et al. Periodontal disease: a potential modifiable risk factor limiting conception. *Hum Reprod.* 2012;des034:1332–42.
10. Vilvanathan S, Kandasamy B, Jayachandran AL, et al. Bacteriospermia and its impact on basic semen parameters among infertile men. *Interdiscip Perspect Infect Dis.* 2016;6:2016.
11. Klinger A, Hain B, Yaffe H, et al. Periodontal status of males attending an in vitro fertilization clinic. *J Clin Periodontol.* 2011;38(6):542–6.
12. Mariotti A, Mawhinney M. Endocrinology of sex steroid hormones and cell dynamics in the periodontium. *Periodontology* 2000. 2013;61(1):69–88.
13. Khanna S, Dhaimade PA. Coalition of oral health care and antenatal counseling: formulation of guidelines. *Int J Obstet Gynaecol Res.* 2015;2:155–63.
14. Suri V, Suri V. Menopause and oral health. *J Mid-life Health.* 2014;5(3):115.
15. Otenio CC, Fonseca I, Martins MF, et al. Expression of IL-1 β , IL-6, TNF- α , and iNOS in pregnant women with periodontal disease. *Genet Mol Res.* 2012;11(4):4468–78.
16. Vasudevan S, Renuka JV, Sylvia DS, et al. Evaluation of gingival inflammation in patients using ovulation induction drugs before and after scaling. *J Contemp Dent Pract.* 2013;1(14):1165–8.
17. Agarwal A, Mulgund A, Hamada A, et al. A unique view on male infertility around the globe. *Reprod Biol Endocrinol.* 2015;13(1):37.
18. Klinger A, Hain B, Yaffe H, et al. Periodontal status of males attending an in vitro fertilization clinic. *J Clin Periodontol.* 2011;38(6):542–6.
19. Nwhator SO, Umezudike KA, Ayanbadejo PO, et al. Another reason for impeccable oral hygiene: oral hygiene-sperm count link. *J Contemp Dent Pract.* 2013;15(3):352–8.
20. Agarwal A, Durairajanayagam D. Are men talking their reproductive health away? *Asian J Androl.* 2015;17(3):433.
21. Ray A, Shah A, Gudi A, et al. Unexplained infertility: an update and review of practice. *Reprod Biomed Online.* 2012;24(6):591–602.
22. Lalasa G, Murthy KR, Pavankumar S, et al. Periodontal status in infertile women attending in vitro fertilization clinics. *Indian J Dent Res.* 2014;25(1):50.
23. Pavlatou A. Influence of the periodontal condition on the success of in vitro fertilization: clinical and microbiological data. Doctoral Dissertation. University of Athens; 2013.
24. Souza LM, Cruz SS, Gomes-Filho IS, Passos-Soares JS, et al. Effect of maternal periodontitis and low birth weight—a case control study. *Acta Odontol Scand.* 2016;74(1):73–80.
25. Patil S, Thakur R, Madhu K, et al. Oral health coalition: knowledge, attitude, practice behaviours among gynaecologists and dental practitioners. *J Int Oral Health.* 2013;5(1):8.