FEMALE SEX HORMONES AND PERIODONTAL HEALTH: ASSESSMENT OF KNOWLEDGE AND AWARENESS AMONG WOMEN OF WESTERN MAHARASHTRA

Sharaya Kulkarni, Sameer Zope, Girish Suragimath, Siddhartha Varma, Apurva Kale

ABSTRACT

Sex hormones play an important role in periodontal health and disease. For example, puberty, menses, pregnancy, menopause, and oral contraceptive use influence a woman’s periodontal health by causing a biological impact on the periodontal microbiology, by altering gingival cell function and vasculature, the local immune system and thus affecting inflammation process. Therefore, it’s crucial to assess awareness about hormonal effects on periodontal health in women and educate them about various modalities to reduce these effects. Thus current study aims to assess awareness and knowledge regarding the effect of female sex hormones on periodontal health among the female population of Western Maharashtra. This was a questionnaire-based cross-sectional study which was surveyed among the Female population in Western Maharashtra. This questionnaire consisted of 15 pre-tested validated close-ended questions assessing respondents’ awareness and knowledge regarding female sex hormones and periodontal health relationships. Following the provision of the Subject information sheet filled consent form was obtained before enrolling the subjects into the study. The filled questionnaire was collected and analyzed using SPSS 20.0 software after data collection. Results showed overall low awareness (66%) among majority of the study population followed by average awareness among the rest (34%) of the participants related to hormonal influence on periodontal health. 43% general female population had knowledge about the possible correlation between pregnancy and periodontal health. We concluded that awareness of female sex hormones and periodontal health relationships in females of Western Maharashtra lacks. Therefore, creating awareness about this relationship is necessary to prevent periodontal diseases.

Key words: Female sex hormones, Menopause, Periodontal diseases, Pregnancy, Puberty.

Introduction

Periodontal disease results from a complex interplay between host susceptibility and microflora of the oral cavity. Various systemic conditions and factors alter the severity and progression of periodontal diseases. Sex hormones play a major role in the pathogenesis of periodontal diseases, as hormonal variation affects the physiology of host-parasite interactions in the oral cavity [1]. The woman’s body undergoes continuous variation in hormonal levels throughout her life from prepuberty, puberty, and menstruating years to the postmenopausal stage.

Hormonal fluctuations influence a woman’s periodontal health by causing a biological impact on the periodontal microbiology, altering gingival cell function and vasculature, altering the local immune system, and thus affecting the process of inflammation. Estrogen act on gingival tissue proliferation, while progesterone on vasodilation and the creation of new blood vessels [2]. This may lead to gingivitis and further to periodontitis.

Evidence-based reports have indicated that increased hormonal levels during puberty affect gingival tissues and the subgingival microflora [3]. Prevotella intermedia and Capnocytophaga species are found to be exponentially elevated during puberty in women [4]. Previous literature has proved that pregnancy may influence periodontal health and periodontal diseases may alter pregnancy outcomes [5]. Alterations in periodontal health have been observed in females suffering from Polycystic Ovarian Disease (PCOD) [6].

Recent studies conducted among gynecologists and pregnant women highlight a lack of proper understanding of the role of female sex hormones in periodontal health. Therefore, the present study was conducted to assess knowledge and awareness of female sex hormones on periodontal health among the general female population of Western Maharashtra. Dynamic changes occur in various metabolic systems including hormone regulation, alterations of body fat distribution and mental and insulin sensitivity. It is also said that Pregnancy puts a great deal of stress on the thyroid gland, so women with iodine deficiency or reduced thyroid reserve may develop hypothyroidism [7].

Materials and Methods

Study design, place of study, and participants

This was a community-based cross-sectional survey.
conducted to assess knowledge and awareness about the effect of female sex hormones on periodontal health among women in Western Maharashtra.

The sample size was determined using a formula, \( n = \frac{Z^2 \cdot \alpha/2}{\text{SD}^2 / (M \times \varepsilon)^2} \). A purposive sampling technique was used in selecting study participants. This study included 538 women between 25-60 years of age in Western Maharashtra. This age group belonged to the young age group category (25-44 years) and middle age group category (45-60 years) as per the revised Age Standard system (WHO 2015).

Females below 25 years and above 60 years of age, those having communication barriers, and mentally challenged females were excluded from the study.

Ethical clearance was obtained from The Institutional Ethical committee of Krishna Institute of Medical Sciences, Deemed to be University (KIMSDU), Karad, Maharashtra, India [Ref. No: KIMSDU/IEC/2XI/2021]. The study was conducted for a period of three months, from January 2022 to March 2022. Following the provision of the Subject information sheet, informed consent was obtained before enrolling the subjects in the study.

**Data sources and collection procedure**

The structured questionnaire consisting of 15 close-ended questions was prepared to assess respondents’ awareness and knowledge regarding female sex hormones and periodontal health relationships. The questionnaire was prepared in English and translated to the regional language Marathi with responses presented as yes/no. These questions were pre-tested to confirm their validity and reliability and to avoid ambiguity.

A Google form application was used to distribute questionnaire forms through social media platforms such as WhatsApp, Facebook, Instagram, and E-mail.

The data collection tool consisted of questions on sociodemographic factors like age, marital status, and education. International Standard Classification of Education (ISCED) classifies education as Less than basic, Basic, Intermediate education, and Advanced education category. After data collection, it was identified that our study participants belonged to the Intermediate education and Advanced education category.

We also asked certain questions to determine knowledge and awareness related to certain variables like the influence of fluctuating hormonal levels on the prevalence of periodontal diseases.

**Data analysis**

Data obtained was entered into an Excel sheet and subjected to statistical analysis using Statistical Package for Social Sciences (SPSS) version 20.0. Mean and standard deviation were calculated and the Chi-square test was used to analyze the intergroup variability.

**Results and Discussion**

Five hundred and Thirty-Eight females in the age range of 25-60 years, participated in this study. Analysis of general demographic data revealed that there were more participants in the young age group as compared to the middle age group in both categories. Among the study population, 437 women were married and 101 women were unmarried (Table 1).

**Table 1. Distribution of Sociodemographic variables**

| Group I (Intermediate Education) | Group II (Advanced Education) |
|---------------------------------|-------------------------------|
| Young age N (%) (25-44 years)    | 204 (68%)                     |
| Middle age N (%) (45-60 years)  | 96 (32%)                      |
| Mean                             | 29.02                         |
| SD                               | 11.05                         |
| Married N (%)                    | 221 (73.7%)                   |
| Unmarried N (%)                  | 79 (26.3%)                    |

| SD: Standard deviation, %: Percentage |

The present study assessed the knowledge and awareness about the effect of female sex hormones on periodontal health among the general female population of Western Maharashtra. Study results were expressed in percentages as described in Table 2.

| Frequency (Percentage %) | Yes | No |
|--------------------------|-----|----|
| 1. Are you aware of gum diseases like bleeding gums, swollen gums, and red gums? | 332 (79.04%) | 90 (21.42%) |
| 2. Do you use oral hygiene maintenance aids (like toothbrush, floss, mouthwash, and interdental brush) regularly? | 249 (59.28%) | 176 (41.90%) |
| 3. Do you know hormonal changes can cause changes in your gums? | 144 (34.28%) | 278 (66.19%) |
4. Are you aware that during your puberty gums can become red or there may be an increased tendency of bleeding gums?  

| Intermediate Education category | Advanced Education category | Chi-square test value | p-value, Significance |
|--------------------------------|-----------------------------|-----------------------|-----------------------|
| 238/300 (79.3%)                | 190/238 (79.8%)             | Chi = 0.001           | p = 0.977             |

5. Have you heard about the possible correlation between oral health and pregnancy?  

| 181 (43.09%) | 241 (57.38%) |

6. Do you know that pregnancy-related hormonal changes make your gums bleed, swell, and become red?  

| 161 (38.33%) | 261 (62.14%) |

7. Have you heard that pregnancy-related hormonal changes can increase the tendency of developing a “pregnancy tumor” in the oral cavity?  

| 64 (15.23%) | 358 (85.23%) |

8. Are you aware of mild tooth mobility during pregnancy?  

| 138 (32.85%) | 284 (67.14%) |

9. Do you think that extra care for oral hygiene is needed during pregnancy?  

| 275 (65.47%) | 145 (34.53%) |

10. Do you think it is advisable to get your gum diseases treated before or during pregnancy?  

| 332 (79.04%) | 90 (21.42%) |

11. Have you observed prominent gingival bleeding and red-colored gingiva during the menstrual cycle?  

| 71 (16.90%) | 351 (83.57%) |

12. Are you aware that frequent use of oral contraceptive pills can increase the tendency of swelling and bleeding in your gums?  

| 20 (4.76%) | 400 (95.23%) |

13. Are you aware of the association of osteoporosis (bone becomes porous) with menopause?  

| 294 (70.0%) | 128 (30.0%) |

14. Do you know that there are more chances of developing gum diseases in females with PCOD (Polycystic Ovarian Disease)?  

| 112 (26.66%) | 310 (73.80%) |

15. Are you aware that Hormone replacement therapy during menopause can affect the health of your gums?  

| 94 (22.38%) | 328 (78.09%) |

% : Percentage

In the present study, 41% of study participants reported the use of other oral hygiene maintenance aids like floss, mouthwash, and interdental brush in addition to regular toothbrushing.

Only 34% of respondents were knowledgeable about the effects of hormonal changes on periodontal health which was an alarming finding of the present study. The majority of the female population had limited awareness about gingival bleeding during pubertal age and the menstrual period.

Our study reported that 57% of participants had knowledge and awareness about a possible correlation between pregnancy and oral health. But 62% of study participants had inadequate knowledge about the development of gingivitis during pregnancy. Also, they had limited knowledge about “pregnancy tumors” which is a common clinical finding during pregnancy.

However, the majority of the respondents were concerned about taking extra care of oral hygiene maintenance and almost 80% of them thought that it is advisable to get gum diseases treated before or during pregnancy.

The results of this survey showed that only 4% of study participants had awareness of the correlation between frequent use of oral contraceptives and gum diseases while 74% of the general female population was unaware of the possible bidirectional link between PCOD and gum diseases.

Satisfactory knowledge was observed in 73% study population related to the association of osteoporosis with menopause while 78% of participants were unaware of the effect of hormone replacement therapy on gum health.

As described in Table 3, no significant difference was observed in the level of knowledge and awareness among the intermediate and advanced education categories except for the finding of mild tooth mobility during pregnancy where the advanced education category had significantly better knowledge than another category (p = 0.004*).

| Table 3. Level of knowledge and awareness of subjects enrolled in the study |
|--------------------------------|-----------------------------|-----------------------|-----------------------|
| 1. Are you aware of gum diseases like bleeding gums, swollen gums, and red gums? | 238/300 (79.3%) | 190/238 (79.8%) | Chi = 0.001 | p = 0.977 |
| 2. Do you use oral hygiene maintenance aids (like toothbrush, floss, mouthwash, and interdental brush) regularly? | 172/300 (57.3%) | 146/238 (61.3%) | Chi = 0.883 | p = 0.347 |
| Question                                                                 | Yes (%)       | No (%)       | Chi          | p Value |
|-------------------------------------------------------------------------|---------------|--------------|--------------|---------|
| 3. Do you know hormonal changes can cause changes in your gums?         | 99/300 (33%)  | 83/238 (34.9%) | 0.208        | 0.648   |
| 4. Are you aware that during your puberty gums can become red or there may be an increased tendency of bleeding gums? | 95/300 (31.7%) | 85/238 (35.7%) | 0.977        | 0.323   |
| 5. Have you heard about the possible correlation between oral health and pregnancy? | 117/300 (39%) | 108/238 (45.6%) | 2.347        | 0.125   |
| 6. Do you know that pregnancy-related hormonal changes make your gums bleed, swell, and become red? | 109/300 (36.3%) | 90/238 (37.8%) | 0.125        | 0.724   |
| 7. Have you heard that pregnancy-related hormonal changes can increase the tendency of developing a “pregnancy tumor” in the oral cavity? | 47/300 (15.7%) | 31/238 (13%) | 0.747        | 0.387   |
| 8. Are you aware of mild tooth mobility during pregnancy?               | 79/300 (26.3%) | 90/238 (37.8%) | 8.121        | 0.004*  |
| 9. Do you think that extra care for oral hygiene is needed during pregnancy? | 197/300 (65.7%) | 160/237 (67.5%) | 0.202        | 0.653   |
| 10. Do you think it is advisable to get your gum diseases treated before or during pregnancy? | 234/300 (78%) | 188/237 (79.3%) | 0.138        | 0.710   |
| 11. Have you observed prominent gingival bleeding and red-colored gingiva during the menstrual cycle? | 46/300 (15.3%) | 32/238 (13.4%) | 0.382        | 0.537   |
| 12. Are you aware that frequent use of oral contraceptive pills can increase the tendency of swelling and bleeding in your gums? | 58/300 (19.3%) | 47/238 (19.7%) | 0.015        | 0.904   |
| 13. Are you aware of the association of osteoporosis (bone becomes porous) with menopause? | 206/300 (68.7%) | 165/238 (69.3%) | 0.027        | 0.869   |
| 14. Do you know that there are more chances of developing gum diseases in females with PCOD (Polycystic Ovarian Disease)? | 64/300 (21.3%) | 63/238 (26.5%) | 1.942        | 0.163   |
| 15. Are you aware that Hormone replacement therapy during menopause can affect the health of your gums? | 59/300 (19.7%) | 55/238 (23.1%) | 0.942        | 0.332   |

% : Percentage

Knowledge and awareness about the influence of female sex hormones on periodontal health had been assessed so far only in specific groups like adolescent girls, the pregnant female population, and gynecologists. This was the first study to be conducted in the general female population of Western Maharashtra with a focus on assessing knowledge and awareness regarding the effects of female sex hormones on periodontal health.

Periodontal disease has been associated with self-reported signs and symptoms like swollen gums,’ ‘sore gums,’ ‘receding gums,’ ‘loose teeth,’ ‘drifting teeth,’ ‘and bad breath.’ Our study showed that most of the study participants were knowledgeable about these findings [8] which is in accordance with a study by Nadia Alzammam, and Alaa Almalki in 2019 among Jordanian University students [9].

In the menstrual cycle of the luteal phase, there is an increase in the level of progesterone hormone. This causes a response in gingival tissue, which becomes more sensitive to the plaque on the teeth and produces inflammatory reactions [10]. A study done by Shiba et al. in 2019 showed only 4% of adolescent girls participants were aware of the possible association between gingival changes during menstruation. In our study, 34% of the general female population was aware of this possible association between gingival changes and menstruation.

During the pregnancy period, both progesterone and estrogen are elevated due to the continuous production of these hormones by the corpus luteum [11]. Susceptibility to infections increases during early gestation due to alterations in the immune system and can be explained by the hormonal changes observed during pregnancy [12], suppression of T-cell activity, decreased neutrophil chemotaxis and phagocytosis, altered lymphocyte response, and depressed antibody production [13] and even chronic maternal stress. Pregnancy gingivitis is an extremely common finding and affects 30-100% of all pregnant women [14]. The awareness of the participants of the relationship between Pregnancy and periodontal disease was 24.3% in a study by Olubunmi.
Polycystic ovary syndrome (PCOS) is a complex endocrine, reproductive and metabolic condition, characterized by hyperandrogenism and polycystic ovary [21]. It has a worldwide prevalence ranging from 5–15%. A meta-analysis by Vanessa Machado et al. in 2020 revealed that PCOS females have 28% more risk of periodontal diseases, and females with periodontitis have 46% more risk to have PCOS [22]. PCOS females with periodontal diseases had higher gum bleeding, periodontal pocket depth, and clinical attachment loss than non-PCOS females with periodontal diseases. Based on the available evidence, it is possible to assume a bidirectional link between PCOS and periodontal diseases. Also, Kellesarian et al. in 2017 suggested that women with PCOD are at increased risk of developing the periodontal disease [23]. Awareness level was reported to be 8% in our study regarding this relationship.

Oral contraceptives (OCs) enhance periodontal breakdown by reducing the resistance to dental plaque and can induce gingival enlargement in otherwise healthy females. The long-term use of OC may cause clinical attachment loss (CAL), increased gingival inflammation, and gingival enlargement [24]. Castro et al. in their meta-analysis concluded that the use of hormonal contraceptives may be associated with the severity of periodontal diseases [25]. In a study by Al-Qahtani on gynecologists of hospitals across the five areas of Riyadh in 2019, 50% of gynecologists indicated that gingival changes could be induced by the long-term use of oral contraceptives [26]. Our study stated that the majority of the study population 78% were unaware of this association.

During menopause estrogen deficiency is one of the most frequent causes of osteoporosis in women and a possible cause of bone loss. A survey by Ergin A et al. in 2017 reported 90.5% awareness of osteoporosis in postmenopausal patients. In contrast to this study, awareness about postmenopausal osteoporosis was 70% in our study.

HRT plays an important role in preventing osteoporosis by reducing postmenopausal bone mass loss [27]. Since periodontal diseases are also affected by the state of the alveolar bone, various studies have attempted to demonstrate the association between HRT and periodontal disease [28].

The analysis of menopausal women aged between 45 and 74 years old showed that the HRT group was less likely to develop periodontal diseases than the non-HRT group. However, a study by Pizzo et al. evaluated 91 Italian menopausal women and reported that there was no difference in periodontal pocket depth between the group who underwent HRT and the group who did not, but the group who did not undergo HRT had a higher plaque level [29]. Our study revealed that the majority of the respondents had limited knowledge related to the association between HRT and periodontal disease.

Conclusion

Within the limitations of the study, it can be concluded that there is a lack of knowledge and awareness among women of Western Maharashtra about the relationship between female sex hormones and periodontal health. Therefore, creating awareness about this relationship is necessary to prevent periodontal diseases and improve systemic conditions affecting the female population. This can be achieved by coordinated efforts from general dentists, periodontists, and gynecologists which will ensure good periodontal health of a woman.

Future prospective

The results obtained would serve as baseline information for identifying areas of deficiency in the women's knowledge regarding the effects of female sex hormones on periodontal health and to educate them about various modalities to reduce these effects. It would help plan oral health education programs aimed at improving the oral health of women.

Acknowledgments: None

Conflict of interest: None
Financial support: None

Ethics statement: Ethical clearance was obtained from The Institutional Ethical committee of Krishna Institute of Medical Sciences, Deemed to be University (KIMSDU), Karad, Maharashtra, India [Ref. No: KIMSDU/IEC/2XI/2021].

References

1. Patil SN, Kalburgi NB, Koregol AC, Ward SB, Patil S, Ugale MS, et al. Female sex hormones and periodontal health-awareness among gynecologists: A questionnaire survey. Saudi Dent J. 2012;24(2):99-104. doi:10.1016/j.sdentj.2011.12.001
2. Robo I, Heta S, Agrushi E, Kapaj S, Kapaj E, Ostreni V. Gingival changes by hormonal oscillations at female patients. Ital J Med. 2019;4:54-65.
3. Jahan SS, Hoque Apu E, Sultana ZZ, Islam MI, Siddika N. Oral Healthcare during Pregnancy: Its Importance and Challenges in Lower-Middle Countries (LMICs). Int J Environ Res. Public Health. 2022;19(17):10681.
4. Yokoyama M, Hinode D, Masuda K, Yoshioka M, Grenier D. Effect of female sex hormones on Campylobacter rectus and human gingival fibroblasts. Oral Microbiol Immunol. 2005;20(4):239-43. doi:10.1111/j.1399-302X.2005.00222.x
5. Komine-Aizawa S, Aizawa S, Hayakawa S. Periodontal diseases and adverse pregnancy outcomes. J Obstet Gynaecol Res. 2019;45(1):5-12. doi:10.1111/jog.13782
6. İşik Y, Telatar GY, Neselioglu S, Biçer C, Gürlek B. Evaluation of periodontal status in different phenotypes of polycystic ovary syndrome in untreated patients of early reproductive age: A case-control study. J Obstet Gynaecol Res. 2020;46(3):459-65. doi:10.1111/jog.14179
7. Hussein K. Hypothyroidism and hypothyroxinemia in pregnancy: An overview in the time of coronavirus disease. 2019. Pharmacophore. 2021;12(2):22-31.
8. Needleman I, McGrath C, Floyd P, Biddle A. Impact of oral health on the life quality of periodontal patients. J Clin Periodontol. 2004;31(6):454-7. doi:10.1111/j.1600-051X.2004.00498.x
9. Alzamam M, Almalki A. Knowledge and awareness of periodontal diseases among Jordanian University students: A cross-sectional study. J Indian Soc Periododontol. 2019;23(6):574-9. doi:10.4103/jisp.jsp.424_18
10. Setjiyanto RD, Rahayu MV, Bramantoro T, Wening GR, Rudhanton RA, Ramadhani A, et al. Gingival Inflammation in 2 Phases of Menstrual Cycle and its Relation to Oral Hygiene of Female Dentistry Students. J Int Oral Health. 2019;11(6):388-92. doi:10.4103/jioh.jioh_232_18
11. Markou E, Eleana B, Lazaros T, Antonios K. The influence of sex steroid hormones on gingiva of women. Open Dent J. 2009;3(1):114-9. doi:10.2174/187421060903010114
12. Smith L. Foodborne infections during pregnancy. J Food Protec. 1999;62(7):818-29.
13. Zachariasen D. The effect of elevated ovarian hormones on periodontal health: oral contraceptives and pregnancy. Women Health. 1993;20(2):21-30. doi:10.1300/J013v20n02_02
14. Mealey L, Moritz J. Hormonal influences on periodontium. Periodontol 2000. 2003;32(1):59-81. doi:10.1046/j.0906-6713.2002.03206.x
15. Onigbinde AO, Sorunke ME, Adenuga-Taiwo OA, Awotide AA. Awareness of the association between periodontal diseases and adverse pregnancy outcomes among the general female population in Lagos. Nig J Dent Res. 2019;4(2):106-12.
16. Tarannum F, Prasad S, Muzammil, Vivekananda L, Jayanthi D, Fazipizzuddin M, et al. Awareness of the association between periodontal diseases and pre-term births among general dentists, general medical practitioners, and gynecologists. Indian J Public Health. 2013;57(2):92-5. doi:10.4103/0019-557X.114992
17. Penmetsa GS, Meghana K, Bhavana P, Venkatalakshmi M, Bypalli V, Lakshmi B, et al. Awareness, attitude and knowledge regarding oral health among pregnant women: A comparative study. Niger Med J. 2018;59(6):70-3. doi:10.4103/nmj.NMJ_151_18
18. Sajan P, Puttanshetti J, Padmini C, Nagatham VM, Sajjanar M, Siddiqui T, et al. Oral health related awareness and practices among pregnant women in Bagalkot district, Karnataka, India. J Int Oral Health. 2015;7(2):1.
19. Ergin A, Akçay G. The Investigation of the Awareness of Osteoporosis in Postmenopausal Women. Glob J Obes Diabetes Metab Syndr. 2017;4(3):068-071. doi:10.17352/2455-8583.000028
20. Senthilraja M, Cherian KE, Jeebasingh FK, Kapoor N, Paul TV, Asha HS, et al. Osteoporosis knowledge and beliefs among postmenopausal women: A cross-sectional study from a teaching hospital in southern India. J Family Med Prim Care. 2019;8(4):1374-8. doi:10.4103/jfmpc.jfmpc_95_19
21. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril. 2004;81(1):19-25. doi:10.1016/j.fertnstert.2003.10.004
22. Machado V, Escalda C, Proença L, Mendes JJ, Botelho J. Is There a Bidirectional Association between Polycystic Ovarian Syndrome and Periodontitis? A Systematic Review and Meta-analysis. J Clin Med. 2020;9(6):1961. doi:10.3390/jcm9061961
23. Kellesarian SV, Malignaggi VR, Kellesarian TV, Al-Kheraif AA, Alwageet MM, Malmstrom H, et al. Association between periodontal disease and...
24. Prachi S, Jitender S, Rahul C, Jitendra K, Priyanka M, Disha S, et al. Impact of oral contraceptives on periodontal health. Afr Health Sci. 2019;19(1):1795-800. doi:10.4314/ahs.v19i1.56

25. Castro MM, Ferreira MK, Prazeres IE, de Oliveira Nunes PB, Magno MB, Rösing CK, et al. Is the use of contraceptives associated with periodontal diseases? A systematic review and meta-analyses. BMC Womens Health. 2021;21(1):1-22.

26. Al-Qahtani A, Altuwaijri SM, Tulbah H, Al-Fouzan A, Abu-Shaheen A. Gynecologists’ Knowledge of the Association Between Periodontal Health and Female Sex Hormones. Cureus. 2019;11(4):e4513. doi:10.7759/cureus.4513

27. Levin VA, Jiang X, Kagan R. Estrogen therapy for osteoporosis in the modern era. Osteoporos Int. 2018;29(5):1049-55. doi:10.1007/s00198-018-4414-z

28. De Villiers TJ, Gass ML, Haines CJ, Hall JE, Lobo RA, Pierroz DD, et al. Global consensus statement on menopausal hormone therapy. Climacteric. 2013;16(2):203-4. doi:10.3109/13697137.2013.771520

29. Lee Y, Kim I, Song J, Hwang KG, Choi B, Hwang SS, et al. The relationship between hormone replacement therapy and periodontal disease in postmenopausal women: a cross-sectional study the Korea National Health and Nutrition Examination Survey from 2007 to 2012. BMC Oral Health. 2019;19(1):151. doi:10.1186/s12903-019-0839-9